

Enhancing Emotional Insight after Traumatic Brain Injury: A Treatment for Alexithymia

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Objective: Alexithymia is a common problem after traumatic brain injury (TBI), with a prevalence ranging between 30 and 61%. Characteristic features of alexithymia are poor emotional awareness, difficulty labeling and differentiating emotions, and poor interoceptive awareness. Alexithymia is often associated with emotion dysregulation, including anxiety, depression, and anger. The purpose of this study was to explore the preliminary effectiveness of an intervention designed to improve emotional insight in people TBI.

Methods: Seventeen adults who had a moderate to severe TBI, who were a minimum of one year post-injury and had moderate to severe alexithymia, completed an intervention targeting problems with alexithymia. The study was a within subject design with three assessment times: baseline, post-test, and 2-month follow-up. Primary outcome measures were the Toronto Alexithymia Scale-20 (TAS-20) for alexithymia, and the Levels of Emotional Awareness Scale (LEAS) which is a performance-based assessment pertaining to emotional cognizance and labeling. Secondary outcome measures evaluated anxiety (Trait Anxiety Inventory, TAI), depression (PHQ-9), Anger (State Trait Anger Expression Inventory, STAXI), affect (Positive and Negative Affect Scale, PANAS,) and overall emotion dysregulation (Difficulty with Emotion Regulation Scale, DERS). The intervention consisted of eight 60-90 minute sessions (2 per week) for one month. Sessions were one-on-one between a therapist research assistant and participant, in which a web-based training program was used to deliver structured content and exercises aimed at enhancing participants' emotional vocabulary, emotional insight, and interoceptive awareness.

Results: Thirteen participants completed the intervention. Repeated measures ANOVA revealed significant improvements on the TAS-20, LEAS, TAI, STAXI, Positive Affect, and DERS, which were followed by planned comparisons. Changes on these measures were all significant between baseline and posttest. Changes between baseline and 2-month follow-up continued to show significant improvements on the TAS-20, LEAS, TAI, and Positive affect. Effect sizes were mostly medium to large. Post-treatment satisfaction scores showed strong satisfaction for the program.

Conclusions: These preliminary findings suggest that alexithymia can be reduced after TBI with treatment, and may also coincide with better emotion regulation. More research needs to be conducted using a randomized controlled trial and a larger sample.

The Influence of Alexithymia, Depression and Anxiety on Aggression After Brain Injury

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Objective: The aims of this study were twofold: 1) To determine differences in aggression severity and prevalence in people with traumatic brain injury (TBI) and healthy controls (HC), and 2) examine the influence of alexithymia (blunted emotional insight), depression, and anxiety on aggression.

Methods: Forty-six participants with moderate to severe TBI and 49 age and gender matched HCs. Participants with TBI were a minimum of 3 months post-injury. Participants completed measures of trait aggression (Buss Perry Aggression Questionnaire); depression (Patient Health Questionnaire-9); trait anxiety (State Trait Anxiety Inventory (STAI)); and alexithymia (Toronto Alexithymia Scale-20).

Results: Participants with TBI had significantly higher total aggression, physical aggression, verbal aggression, anger, and hostility than HCs. Compared to HCs, significantly more participants with TBI were classified as having higher than average total aggression (34.8% vs 14.3%), verbal aggression (41.3% vs 18.4%), anger (39.1% vs 20.4%), and hostility (45.7% vs 20.4%). Together alexithymia, depression and anxiety accounted for 34.2% of the adjusted aggression variance for participants with TBI, and 45.7% for HCs. The largest unique contributor to these models was alexithymia for participants with TBI, and depression for HCs.

Conclusion: This study provides empirical data showing that aggression is more severe and prevalent in people with TBI than HCs. Moreover, our findings suggest that alexithymia is a major contributing factor to aggression after TBI. This is concerning since alexithymia is prevalent in up to 61% of people with TBI. Because people with alexithymia have poor emotional insight, they may not have the awareness needed to properly regulate escalating feelings of anger and aggression. Clinical implications for the treatment of aggression will be discussed.

The Relationship Between Anger and Negative Attribution Bias After Brain Injury

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Objective: Negative attributions pertain to judgments of intent, hostility, and blame that one makes regarding other people's behaviors. Negative attribution bias is when someone has the tendency to perceive actions significantly more negative than the general population, especially when actions are ambiguous or benign. The aim of this study was to examine if people with traumatic brain injury (TBI) make stronger negative attributions than healthy controls (HCs), and explore the relationship of these attributions with situational anger.

Methods: Forty-six adults with moderate to severe TBI and 49 HCs who were frequency matched for age and gender, participated in the study. Participants were presented with hypothetical scenarios describing characters' behaviors that ultimately resulted in hypothetically negative outcomes for the participant. Actions described in the stories were clearly hostile, ambiguous, or benign, resulting in three story types. Participants rated characters' behaviors for intent, hostility, and blame, as well as how angry they would be in response to each scenario.

Results: Compared to healthy controls, participants with TBI had significantly stronger anger ratings in response to scenarios ($p < .05$). Additionally, participants with TBI rated characters' behaviors to be significantly more intentional, hostile, and blameworthy than healthy controls for benign, ambiguous, and hostile scenarios ($p < .05$). Negative attributions significantly predicted 72.4% of anger variance for participants with TBI, and 65.3% of variance for HCs.

Conclusion: People with TBI appear to be biased in judging others' behaviors as more intentionally hostile and blameworthy. Furthermore, it appears that these negative attribution biases are contributing to anger problems after TBI. These findings have important clinical implications, which will be discussed. Future studies investigating factors that contribute to negative attribution biases are critical to understanding and treating anger deficits in the TBI population.

The Use of an Algorithm and a Modified Agitated Behavior Scale to Evaluate the Effectiveness of Interventions and the Necessity for Constant Supervision with Brain Injured Inpatients

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Individuals who suffer severe traumatic brain injuries often exhibit agitated and aggressive behaviors early in their recovery (Rancho 4) which impact both patient and staff safety. Determining when constant supervision or every 15 minute observation is necessary can be difficult. In order to facilitate the decision making process, an algorithm was developed to assist staff in determining if a patient requires one to one supervision or another alternative safety measure. The Agitated Behavior Scale (Bogner, J, 2000) has been developed to identify and evaluate the level of agitation for a designated period of time. The scale lists 14 specific behaviors which are rated from 1 (none) to 4 (extreme). However, valuable information is lost with regard to the effectiveness of interventions including; medications, sleep patterns, the identification of specific behaviors (eg. restlessness versus agitation) and whether there are certain periods of time when agitation is more likely to occur. In order to maximize the effectiveness of the Agitated Behavior Scale as a clinical tool, a version that examines behavior over a longer period of time was developed which utilizes a 24 hour monitoring approach in which all 14 behaviors are rated on an hourly basis. One to one observation is necessary to use this version. This version has been found to be valuable with regard to assessing the response to interventions, including medications, tracking recovery from a behavioral perspective and determining when an individual can be taken off one to one supervision. The lecture will provide information on the algorithm and Agitated Behavior Scale as a clinical tool in treatment planning for brain injured individuals.

Report to Congress on the Management of Traumatic Brain Injury in Children

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Background: Children and adolescents have some of the highest rates of emergency department visits due to traumatic brain injury (TBI) and are vulnerable to a range of long term consequences following TBI. TBIs in children may be particularly damaging as they may precede or occur during critical stages in brain development. Further, neurocognitive and neurobehavioral impairment can impact academic and social outcomes in ways that reverberate throughout the lifespan. Consequently, follow-up care and monitoring beyond the acute injury phase are critical. Although most TBIs in children are considered mild, even a mild TBI can have long term impact.

The TBI Act of 2014 directed the CDC in consultation with the National Institute of Health, to conduct a review of scientific evidence related to brain injury management in children and to submit a Report to Congress (RTC) that describes the results and makes recommendations related to improving the management of TBI in children. The purpose of this presentation is to describe the key findings and recommendations of the Report to Congress on the Management of Traumatic Brain Injury in Children.

Methods: The report was developed through a collaboration between CDC scientists and researchers that specialize in the medical and educational management of TBI. A diverse group of external reviewers provided feedback on the initial outline and first draft of the report. The goal of the current RTC will identify gaps in the research and provide action-oriented recommendations for researchers, clinicians, consumers, advocates and policy makers. The report is scheduled for release in March 2017.

Results: The management of TBI in children is complex, and dependent upon multiple service delivery systems. These systems are not optimally coordinated to provide care across the child's lifespan. In particular, there is large variation in follow-up care and service delivery at the state level with respect to pediatric trauma center utilization, service delivery in the schools, early intervention services, service access, transition to adulthood, and family support. This variation and lack of understanding by caregivers, healthcare professionals, and educators, regarding the potential for TBI effects beyond the initial injury creates challenges for optimal care. Addressing identified barriers can promote children's achievement of long term milestones as adults, such as high school graduation, employment, and engagement in healthy lifestyle practices. Improving the developmental trajectory for children with TBI through consistent, state-of-the-art management approaches is a critical public health issue.

Conclusion: Improving the management of TBI in children is critical to reducing the public health burden of TBI. Report findings and recommendations will support action at the federal and state levels and will assist individual communities in ensuring optimal management of TBI in children.

Neuro-Net: An Innovative Continuum of Care Pilot for Those with Catastrophic Brain and Spinal Cord Injury

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The future of healthcare services whether through bundled payments or accountable care organizations, is challenged to meet the triple aim of healthcare by providing good outcomes, at a reasonable price and with satisfied consumers.

Neuro-Net is an innovative pilot continuum of care model designed for persons with catastrophic brain and spinal cord injury. We have long known the creation of a clinically integrated expert continuum of care for persons suffering catastrophic neurological injuries was needed. The vast majority of these patients are currently treated in separate and often fragmented systems that do not provide good clinical integration. The result can be poor outcomes resulting in higher costs and compromised health for these patients.

Four expert providers of catastrophic care joined forces through an innovation pilot to begin such a continuum: They are Santa Clara Valley Medical Center, Level 1 Trauma and Acute Inpatient Rehabilitation, Care Meridian, sub-acute care, Learning Services, a residential and day treatment facility for persons with brain injury, and Rehab Without Walls, rehabilitative treatment in the home and community. Neuro-Net is a private/ public partnership, combining health care providers with different cultures, payment systems and outcome methodologies.

The presentation will include an overview of the coordination of care model managed by a nurse case manager. Admission and clinical protocols and procedures, a shared medical records system, and the outcome measurement system will be presented. Preliminary data from the first 70 participants including treatment gains, re-hospitalization as well as consumer satisfaction and input will be presented. Outcomes will be compared to those not participating in a continuum of care model and compared with national averages. We will discuss the challenges in designing and implementing such a model and well as future directions and replication of the model.

Hope and Engagement Following Acquired Brain Injury: A Qualitative Study

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Background/Aims: It is widely recognised within rehabilitation services for people with Acquired Brain Injury, that there is wide variation in the degree of engagement with therapy, and that this has the potential to affect outcomes. While it is recognised that subjective beliefs are an important factor in engagement, little is known about how clients perceive their experience, what expectations they have in relation to recovery and rehabilitation, and how their perceptions impact on engagement with rehabilitation. While some studies have considered expectations retrospectively, none have taken a prospective approach in relation to an ABI population.

This research aimed to explore clients' perspectives and increase knowledge of clients' expectations of recovery and rehabilitation, prior to beginning community based rehabilitation; and to develop a theoretical explanation, upon which improvements in service delivery and practice can be based.

Method: The research aims were explored through a qualitative methodology, using a symbolic interactionist theoretical perspective to grounded theory, which was chosen to facilitate the process of theory generation (Glaser & Strauss 1967, Charmaz 2006). Twenty-one people, with complex problems following ABI, were interviewed prior to being seen by a specialist community rehabilitation service. The context of qualitative research is critical and taken into account when interpreting findings. People with communication and cognitive impairments were purposefully included, if they had capacity to consent to the research.

Results: The central theme that emerged was hoping-despairing, with five further main categories: Making sense of what has happened, moving forward, what can I do?, trusting/doubting others, and accepting. An explanatory framework was developed and a model was proposed, by which belief in self/others and belief in recovery/progress interact to generate hope and readiness to engage. A focus group consisting of specialist clinicians was conducted, to compare the expectations of clients and clinicians.

Conclusions: The findings suggest that expectations and beliefs at this stage in the rehabilitation pathway influence the degree of engagement with rehabilitation services, and that this has implications for clinical intervention. While the context of qualitative research is critical in interpreting findings, it is felt that there are wide implications for ABI services and other areas of health care.

The Effect of Post-Injury Erythropoietin Administration on Mortality and Glasgow Outcome Scales of Patients with Traumatic Brain Injury: A Meta-analysis

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Objectives: To determine whether post-injury treatment with erythropoietin provides lower mortality rates and improved Glasgow Outcome Scales in patients with traumatic brain injury (TBI).

Methods: Randomized controlled trials (RCTs) were searched through PUBMED, Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, and www.google.com. The reference list of a systematic review was also searched.

Results: Four RCTs comparing erythropoietin and placebo, regardless of dose, dosing regimen, and route of administration were reviewed. Data analysis showed that mortality rates for the erythropoietin group (OR 0.63, CI 0.43, 0.93) was significantly lower compared to the placebo group. However, there was no significant difference in the Glasgow Outcome Scales of TBI patients given erythropoietin compared to placebo.

Conclusion: Post-injury treatment with erythropoietin, regardless of dose, dosing regimen, and route of administration yielded lower mortality rates in patients with traumatic brain injury but had no significant effect on Glasgow Outcome Scales. It is recommended that further large scale randomized controlled trials be performed in order to fully establish the safety and support the efficacy of erythropoietin administration in patients with traumatic brain injury.

Long-Term Adaptive Strategies Addressing Cognitive and Emotional Deficits of Brain Injury for Survivors and Primary Caregivers

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Creating adaptive strategies for long-term recovery of brain injury survivors is essential for both survivors and caregivers as they transition from rehabilitation level of care to home and work. This presentation will highlight adaptive cognitive and emotional strategies aimed at dealing effectively with the deficits of brain injury including short-term memory loss, personality changes, and anger. The strategies may be applied to clinic and private practice settings.

Purpose: The purpose is to identify long-term adaptive strategies identified by brain injury survivors and primary caregivers and with this knowledge add to the development of theory related to rehabilitation. The deficits identified include short-term memory loss, anger, and personality changes. Further, suggestions for healthcare professionals are identified to more effectively treat survivors of brain injury, spouses, and the family system as they transition to home and work.

Procedure: Phenomenological qualitative research approach with seventeen respondents participating in a series of semi-structured interviews. Participants were asked the same initial questions. From their responses, additional questions arose to gain a more in-depth understanding of the coping strategies used to address the needs and deficits associated with brain injury. Significant to this study was the development of coping and adaptive strategies by the participants after their discharge from inpatient and rehabilitation treatment. Survivors were at least 3 years post-injury.

Results: Both brain injury survivors and primary caregivers identified a myriad of deficits that required adaptive strategies specific to the area of brain injury. The findings indicated that problem-focused coping and emotion-focused coping were utilized to some degree throughout the rehabilitation process. Problem-focused coping were behaviors and helps that addressed a specific need associated with a deficit. Emotion-focused coping addressed the emotional disturbances that are common to brain injury. In addition, primary caregivers identified specific adaptive strategies to address their needs as they live with their loved one affected by brain injury. Resources and practical suggestions are given to assist healthcare professionals work most effectively with brain injury survivors and primary caregivers. Presentation highlights Dr. Adams work, "Coping and adaptive strategies of traumatic brain injury survivors and primary caregivers" published in *NeuroRehabilitation: An Interdisciplinary Journal* August 2016.

Personal Story: Patti Foster, TBI Survivor, Author, Inspirational Communicator will present her story of survival and adaptive strategies learned through her recovery of a severe traumatic brain injury sustained June 18, 2002. As a former radio personality and now international speaker, Patti shares her experience of learning to live again, making a difference now (MAD Now!), and leaning into life as a TBI survivor....triumphantly and with unwavering hope.

Neuropsychological Rehabilitation in Adolescent with Brain Injury: Results of Individualized Program

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Cases of acquired brain injury can take place in patients of different psychological ages. Specific paths and strategies for neuropsychological assessment and rehabilitation should be applied in order to obtain favorable clinical results. The methods for neuropsychological rehabilitation should be developed on the basis of precise clinic assessment and diagnosis. The program should include the tasks considering not only affected brain mechanisms but also aspects of motivation and personality of psychological age of adolescence.

The goals of the study consist of presentation of the content of items for neuropsychological assessment before and after the work with the patient with program of individualized rehabilitation.

The masculine patient of 14 years old, right handed, pupil of the 3th year of Secondary Private School of the city of Puebla (Mexico) was included in the study. The patient has suffered traffic accident, which provoked severe brain injury and loss of lateral vision. The patient was hospitalized during 2 months showing absence of speech and locomotion. After hospitalization the patient assisted traditional speech therapy and rehabilitation of movements for several months. Brief Neuropsychological Assessment for Adults in Spanish was applied before and after the work with program of rehabilitation. The tasks of assessment included: copy of objects with elements of spatial orientation, free drawing, production of drawings by categorical instructions. Results of neuropsychological assessment revealed strong difficulties with regulation of control of voluntary activity and spatial integration on material, perceptual and verbal levels. Verbal level was especially affected, which was a strong obstacle for all kinds of abstract intellectual activity.

On the basis of results of this assessment, individualized program for neuropsychological rehabilitation was designed. The program of rehabilitation was carried out in 55 sessions during 4 months. The goals of rehabilitation consisted in organization of intellectual activity by training of mechanisms of control and spatial analysis. Original interactive tasks were created in order to elevate motivation of the patient. The tasks were provided on concrete, perceptive and verbal levels as ordered steps of the program. Tasks for regulation and control included table games based of external orientation provided by therapist, reflective analysis of grammar rules, analysis of sense and logic relations in texts.

After rehabilitation program positive changes were observed in intellectual and emotional sphere of the patient. The patient started to fulfill school tasks independently, obtained high marks at school and became able to read complex texts and solve mathematic problems; motivation for intellectual activity became stronger. We discuss the necessity of individualized approach instead of standard general proposals for patients with acquired brain injury. Aspect of personality and motivation should be included as fundamental aspects of creation and application of neuropsychological rehabilitation in adolescent patients.

Quality of Return-To-Work in Patients with Mild Traumatic Brain Injury: A Prospective Investigation of Associations Between Post-Concussion Symptoms, Neuropsychological Functions, Working Status and Stability

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Objective: Although ‘return to work’ (RTW) has been identified as one of the most important outcome measures for patients with mild traumatic brain injury (MTBI), methodological drawbacks still weakened its representativeness. This study thus aims to evaluate the ‘work quality’ (WQ) originated from ‘work status’ and ‘work stability’ simultaneously, and further to explore the associations between post-concussion symptoms (PCS), neuropsychological functions and WQ.

Methods: A total of 179 participants, which included 132 patients with MTBI and 47 healthy participants, were prospectively recruited. The work quality index (WQI) was developed to evaluate WQ. All patients were evaluated for their PCS, neuropsychological functions and WQ at 2 weeks post-injury (T1), while PCS and WQ were further recorded by 1 month post-injury (T2).

Results: At T1, more than half of patients were unemployed, while only 15% of patients can retain their pre-injury works stably. At T2, 26% of patients were still unemployed, while 36% has returned to work stably. In addition, WQ at T1 was significantly associated with patients’ educational levels, while WQ at T1 and physical PCS at T2 can be significantly associated with WQ at T2.

Conclusions: Simultaneously considering work status and stability to reveal quality of RTW is merited. Moreover, ameliorating physical symptoms is also necessary to get favorable WQ by 1 month after MTBI.

Evidence Based Rehabilitation for Cognitive-Communication Reading Comprehension Deficits: Identifying Evidence (I-V) and Clinical Implications

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Objectives: Reading deficits after acquired brain injury (ABI) can impact upon participation in rehabilitation, independence in the community and successful return to work or study. Cognitive-communication reading comprehension (CCRC) deficits are typically managed by speech-language pathologists (SLPs) across the rehabilitation continuum. Providing evidence-based services includes using “external” research evidence, “internal” clinical practice evidence and patient preferences. This study aimed to explore the evidence base for CCRC interventions during subacute SLP rehabilitation; and investigate and compare internal clinical practice evidence with current external evidence to provide levels I-V evidence.

Methods: Internal clinical practice evidence was collected from Australian SLPs with experience in subacute brain injury rehabilitation via an online survey, to provide “expert opinion” (Level V evidence). A systematic review (SR) of the literature for comprehension-based discourse reading interventions following ABI provided Levels I-IV evidence. Data were compared within the World Health Organization’s ICF model, to allow comparison of interventions from different theoretical frameworks in a structure that is relevant to practicing clinicians.

Results: Only results from completed surveys were used in the study (n=19); while small this number is similar to other studies investigating subacute ABI communication rehabilitation in Australian SLPs. The majority of surveyed SLPs (73%) were experienced clinicians. They provided impairment based (94.7%), activity / functional (94.7%) and reading strategy interventions (100.0%) in subacute CCRC rehabilitation. Strong similarities between SLP practice and the SR include using 1:1 service delivery and strategy-based interventions; other similarities include treatment hierarchies, and aspects of functional and impairment based interventions. SLP strategy use (100%) was higher than identified in the literature. Several interventions identified in the SR were not reported in subacute clinical practice. Assessment methods were highly different.

Conclusions: Clinical SLPs are providing evidence-based CCRC interventions. Differences between practice and the literature (e.g., strategy use, assessments) may guide future CCRC research.

“I’m Trying to Be the Safety Net”: Family Protection of Patients with TBI During the Hospital Stay

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Research has shown that during the hospital stay, family caregivers of patients with traumatic brain injury (TBI) perceive one their roles is to protect the patient; however, research on this topic is limited. The purpose of this study was to investigate family caregivers’ experience of protecting patients with moderate-to-severe TBI during the hospital stay. Grounded theory was used to conduct twenty-four interviews with 16 family caregivers of patients with moderate-to-severe TBI. Findings showed caregivers worked to protect the patient’s physical and emotional safety throughout the hospital stay. Strategies to protect the patient’s physical safety included: 1) influencing the selection of staff; 2) attempting to prevent overstimulation; 3) breaking the patient’s bad habits; and 4) anticipating how to orchestrate the home environment. Strategies to protect the patient’s emotional safety were: 1) connecting on an emotional level and 2) managing visitors. These findings have practice implications for educating interdisciplinary health care providers about the experience of family caregivers during the hospital stay to improve support provided to caregivers during this time.

Standardization of Policy and Increasing Patient Matriculation Through Customized Treatment Plans in the Treatment of Chronic Traumatic Brain Injury by Developing Standard Operating Procedures and a Patient Tracking Tool.

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Picot: Will the development of a Standard Operating Procedure (SOP) and an internal tracking system aid in standardization of practice and increased patient throughput of the Traumatic Brain Injury (TBI) treatment plan for adult Soldiers enrolled in the university at the TBI facility: A nursing practice change.

P: The team consists of Physicians, Nurse Practitioners, Registered Nurses, Social Workers, Occupational Therapist, Physical Therapist, Neuropsychologist, Neuro Optometrist Chaplain, Ombudsman, Music, Yoga and Art therapist. A multidisciplinary approach to developing policy and tracking will allow input from SMEs.

I: Implementation of a SOP guided by evidenced-based practice (EBP) for standardization of university protocols and successful tracking of Soldier progress through customized treatment plans. This phase will lend itself to practice as new policies will improve the quality of healthcare delivery standardizing practice across the healthcare continuum within the TBI facility. Having a tracking process will eliminate the query of where Soldiers are in the process providing providers with the most up-to-date information on Soldier status. A designated provider will be provided transparent instructions on use of the tracking system and serve as the super user for the clinic.

C: Currently the Soldiers enrolled in the university are provided a customized treatment plan by the multidisciplinary team based on assessment data gathered during an initial assessment. Detailed information is provided to the Soldier on the process and those who will be directly involved with the care to include family and providers. The process is designed to meet the patient and family identified goals that are centered around the five pillars of the clinic to include sleep, nutrition, physical movement, pain management and resiliency; all of which can be defined with SOP development. Once implemented each discipline will know the inclusion criteria to be enrolled, how many phases of care are offered, who will gather the data, role of the providers, how Soldier care will be tracked and how the providers can immediately access information pertaining to progression. Due to the lack of a tracking system; Soldiers progress is not being monitored until the day of the appointment which does not allow proper preparation prior to the visit.

O: Standardization of practice, improved facilitation of care and throughput of TBI patients enrolled in the university. In their study Hinds and Livingston (2016) found that the identification of the need for TBI diagnosis and treatment guidelines within the Military Health System and the consideration of military service-specific and Department of Defense policy are integrated within an evidenced-based, systematic clinical recommendation development process (Abstract section, para. 1).

T: Eight weeks: The first four weeks will be spent gathering input from stakeholders developing and refining the SOP.

A Controlled Study of The Presence of Upper Cervical Dysfunction in Concussion Vs. Whiplash Patients

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Objective: Concussions or mild traumatic brain injuries (mTBI) resulting from sports-related or whiplash injuries have become a major public health issue. The extent to which neck soft tissue injuries co-occur in concussion events is not well-known nor is the extent to which the symptoms associated with these injuries contribute to post-concussion syndrome.

Methods: 43 subjects were studied: concussion (16), whiplash (13) or controls (14). Subjects completed a pain scale (VAS), the Neck Disability Index (NDI) and the Rivermead Post-Concussion Symptoms Questionnaire (RPCSQ). Three tests for cervical joint and myofascial dysfunction were conducted: joint restriction on manual palpation; tenderness to manual palpation and the Flexion-Rotation test (F-R test). Scores on all variables were compared by ANOVA or Chi-Squared testing with significance at $p = 0.05$.

Results: 73% of concussion subjects had head impact; none occurred in the whiplash group. In both clinical groups, the pain VAS, NDI and RPCSQ scores were not statistically different. Significantly more upper cervical joint restrictions, tenderness and positive F-R tests were found in the concussion group vs. controls. Joint restriction and F-R test findings were similar between concussion and whiplash groups.

Conclusion: Our results provide preliminary support for similarity of symptoms in both concussion and whiplash patients as well as similarly high levels of cervical joint and myofascial dysfunction in concussion subjects. Soft tissue injuries to the upper cervical spine should be assessed as early as possible in post-concussion management.

Te Waka Kuaka, Rasch Analysis of a Cultural Assessment Tool in Traumatic Brain Injury in Māori

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Aim: To examine the validity of a new measure in assessing the cultural needs of Māori (indigenous new Zealanders, who make up 17% of the NZ population) with traumatic brain injury, using Rasch analysis. Māori TBI is important because of the high rates of TBI compared to non-Māori and Māori cultural values about the head and brain that impact on rehabilitation following TBI. The measure was named Te Waka Kuaka (meaning a flock of godwits) because it enables whānau and health workers to organize their priorities in order to navigate the recovery journey, much as the flock of godwits organize themselves for their migrations.

Method: This novel measure was advanced from prior conceptual and qualitative work was explored with Māori in a range of settings in the North Island of Aotearoa New Zealand. The development of the measure has been reported elsewhere. Three hundred and nineteen participants with a history of TBI, their whānau (extended family members), friends, those connected via work, or interested community members (ranging in age from 11 to 76 years of age and 63% female) completed the 46-item measure. The sample also included 8 non-Māori spouses. Rasch analysis of the data was undertaken.

Results: All four subscales; Wā (time), Wāhi (place), Tangata (people) and Wairua practices were unidimensional. Ten items were deleted from the original measure because of misfitting the model secondary to statistically significant disordered thresholds, non-uniform Differential Item Functioning (DIF) and local dependence. Five items were re-scored in the fourth subscale resulting in ordered thresholds.

Conclusions: Rasch analysis enabled a robust process including theoretical reflections in validating a new version of Te Waka Kuaka ready for use in TBI rehabilitation. This is the first time such a robust process has been used to develop and validate a Māori health measure. This process provides a blueprint for other researchers.

Keywords: traumatic brain injury, Māori, Rasch analysis, measurement

Phenylephrine Protects Cerebral Autoregulation and Reduces Hippocampal Necrosis after Traumatic Brain Injury via Block of ET-1 and ERK MAPK in Juvenile Pigs

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Traumatic brain injury (TBI) contributes to morbidity in children, and boys are disproportionately represented. Cerebral autoregulation is impaired after TBI, contributing to poor outcome. Cerebral Perfusion Pressure (CPP) is often normalized by use of vasoactive agents to increase mean arterial pressure (MAP). Maturationally, a 1-5 day old pig approximates a 1-2 yr old human child while a 4 week old juvenile pig approximates an 8-10 yr old child. In prior studies of 1-5 day old newborn piglets, we observed that phenylephrine (Phe) preferentially protected cerebral autoregulation in females but not males after fluid percussion injury (FPI). The ERK isoform of mitogen activated protein kinase (MAPK) produces hemodynamic impairment after FPI. The spasmogen endothelin-1 (ET-1) is upregulated more in males than females and contributes to elevated ERK after FPI. Phe blocked upregulation of ET-1 and ERK in females but potentiated upregulation in males after FPI. In the present studies, we investigated whether Phe protects autoregulation and limits histopathology after FPI in older juvenile (4 week old) pigs and the role of ERK and ET-1 in that outcome by sex. Results show that Phe significantly protects autoregulation and prevents reduction in cerebral blood flow (CBF) in both male and female juvenile pigs after FPI. Papaverine induced dilation was unchanged by FPI and Phe, indicating lack of an epiphenomenon. Phe blocked ERK MAPK and ET-1 upregulation in both males and females after FPI. Phe blocked loss of neurons in CA1 and CA3 hippocampus of males and females after FPI. These data indicate that Phe protects autoregulation and limits hippocampal neuronal cell necrosis via block of ERK and ET-1 after FPI in both male and female juvenile pigs. In clinical studies, impairment of autoregulation following TBI appears linked to Glasgow Coma Scale (GCS), with greater autoregulatory impairment associated with worse GCS. The present data suggest that vasoactive agent support may affect cognitive outcome differently in males and females as a function of age. These data suggest that use of Phe to improve outcome after TBI is both sex and age dependent.

Turning on the Lights in TBI: Applying Smart-Home Technology in a Residential Environment. Turning on the Lights in TBI: Applying Smart-Home Technology in a Residential Environment

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Purpose: After TBI myriad type of sequelae can have a significant impact on a person's ability to access their environment to perform simple tasks with any level of independence. There are many options for Electronic Aids of Daily Living (EADL) on the market, some targeted towards the rehabilitation market and some designed and marketed for traditional consumer use. The purpose of this case presentation is to outline the key differences in cost and capability of some currently available options, as well as describe the process and choices that go into implementing a smart-home system for someone with TBI related functional challenges. This case study will describe a patient with severe TBI and resultant limitations in environmental access due to cognitive, behavioral and physical limitations.

Methodology: The process undertaken for assessing client needs and suitability of available options will be described as well as the implementation of use including anticipatory strategies and gradual skill building to facilitate successful learning. Additional lessons learned will be shared for improving the client experience by simplifying the development process for prescribing and implementing EADL use in such patients.

Findings: A retroactive pre- and post-intervention satisfaction survey was completed specific to the areas addressed by the EADL. The client reported high levels of satisfaction with the functionality of this equipment. Despite significant cognitive deficits, the patient was able to acquire the skills necessary to operate a voice activated device and perform a series of functional tasks related to leisure and home access otherwise limited by environmental access.

Conclusions and Future Directions: Consumer level smart-home technology offers affordable, flexible EADL options that aid in increased independence with environmental control for an individual with TBI living in a supported residential environment. The authors plan to continue implementation with other residents as appropriate and continue tracking functional benefits of said interventions.

Resolution of Paroxysmal Autonomic Instability with Dystonia (PAID) Syndrome with Serial Casting

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Case Description: The patient is a 3 year old girl who was struck by a vehicle while playing. On initial evaluation, GCS was 3 and left pupil was dilated. CT of the head showed: 2 mm SDH along the falx cerebri, parenchymal hemorrhages in the right parietal lobe and left temporal lobe. SAH in the pineal cistern, Bilateral parietal fractures. Extensive right parietal and right occipital edema. An ICP monitor was placed and she was admitted to the ICU.

Hospital day 2, when sedation was held there was generalized movement of her fingers to noxious stimulation, with no eye opening and her ICPs became elevated from 9 to 19.

Hospital day 6, the patient began having intermittent storming episodes associated with posturing, tachycardia, tachypnea and hypertension with unclear precipitating factors. There was noted increased tone (MAS 3) in the left upper and worsening of dysautonomia and posturing with PROM. Given concern for contracture, serial casting was decided by the family and rehab team.

Hospital day 8, patient had cast placed to left upper extremity. Following cast placement there was marked improvement in dysautonomia and emerging awareness within one hospital day. Through serial casting occupational therapy achieved -10 degrees, from initial -70 degrees. The patient continued to progress and was discharged to acute inpatient rehab on hospital day 26.

Discussion: One proposed pathophysiology of PAID is thought to be due to dysfunction of the autonomic centers of diencephalon (thalamus or hypothalamus) or their cortical connections that mediate autonomic function. Boeve et al, expanded this concept by speculating that the mechanism likely involves activation (or disinhibition) of central sympathoexcitatory regions such as the paraventricular hypothalamic nucleus, lateral periaqueductal gray substance, lateral parabrachial nucleus, or rostral ventricular medulla. Early recognition and treatment is aimed at easing care and preventing secondary injury.

There are many proposed treatments for PAID which include baclofen, benzodiazepines, and propranolol. Many of which were trialed in our patient with only short term relief of her symptoms. In a recent case report Lee et al managed intractable PAID in brain injured patient with alcohol neurolysis and botulinum toxin injection with resolution of dysautonomia following injection. With our patient, PROM of the left upper extremity was associated with worsening symptoms, we hypothesized contracture/tone may have been triggering her dysautonomic episodes. Following serial casting there was marked improvement in her tone along with resolution of her dysautonomia and improvement in her cognitive status.

Conclusions: This case shows that perhaps contracture and tone can be an initiating event for PAID and if contracture is appropriately managed it may lead to resolution of PAID.

Working in Partnership – Health & Social Care Across the Statutory & Voluntary Sector in Northern Ireland (NI). Demonstrating Impact for ABI Service Users in a Holistic Model of Service Delivery Over the Last 5 Years

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1. Context: In the UK, the Northern Ireland regional context is unique. Statutory health & social care are fully integrated and delivered through 5 Health & Social Care Trusts. For adults with Acquired Brain Injury (ABI) statutory provision is led by an interdisciplinary team. Aligned to this the voluntary sector has established services in partnership with statutory services delivering a holistic continuum of specialist provision. For example Cedar Foundation has developed services aimed at promoting employability and inclusion for people with ABI.

2. ABI Care Pathway: The ABI care pathway was devised following the Ministerial review of Brain Injury Services in Northern Ireland (2009) (1). This facilitates a smooth transition for service-users from hospital to post-acute and community-based support. There is clear alignment between the roles of both statutory and voluntary sector ensuring consistent, coordinated high quality service delivery (2). This was further validated as a model of good practice in a subsequent RQIA review in 2015 (3).

3. Partnership Impact: The impact of partnership working within the ABI care pathway was reviewed in terms of status at discharge for service-users accessing both the statutory Community Brain Injury Service and Cedar's Employability & Inclusion voluntary services in the last 5 years.

Of 512 service-users who were inactive on entry, 83% (358 people) progressed with a positive outcome on discharge as a result of the holistic intervention from both services:

- Paid work 23%
- Education 16%
- Voluntary work 24%
- Community activity 16%
- Goals completed, but inactive 4%
- Goals completed, early leaver 17%

4. Success factors: The Northern area statutory and voluntary staff teams participated in a focus group to identify the key success factors in working together:

- Sharing skills and resources to achieve service-user goals
- Good communication between services
- Good working relationships
- Regular face-to-face meetings
- Avoidance of duplication

In the last service-user evaluation based on a 73% return rate overall satisfaction was reported as 98%. The key soft outcome impacts described by service-users were:

- Confidence
- Achieving Outcomes & Goals
- Understanding & Managing my Brain Injury

5. Conclusion: Integrated health, social and statutory/voluntary sector delivery of community-based brain injury services promotes a coordinated approach to achieving inclusion outcomes for people with ABI. Service-user feedback points to the development of well-being through building resilience to manage disability-related challenges. This will be further developed to drive improvement in service interventions and measure impact that is important to our service users.

References:

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Substance Use, Criminal Behaviour and Psychiatric Symptoms following Childhood Traumatic Brain Injury: Findings from the ALSPAC Cohort

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Background: Traumatic brain injury (TBI) is associated with a range of physical, cognitive and behavioural problems. Recent research suggests a link between TBI in youth and later risk behaviour. We explored the association between mild TBI and psychiatric symptoms, substance use and criminal behaviour using data from a longitudinal birth cohort.

Methods: Participants with TBI (n = 800), orthopaedic injuries (n = 2,305) and no injuries (n = 8,307) were identified from self and parent reports up to age 16 years. The orthopaedic injuries group was included as a negative control exposure group to strengthen causal inference. Self-report measures of substance use (alcohol, tobacco and cannabis) and criminal behaviours were gathered at age 17 years. Parent-reported psychiatric symptoms were assessed using the Strengths and Difficulties Questionnaire at age 17 years. Analyses were adjusted for pre-birth and early childhood confounders. Secondary analyses investigating the effect of age at injury were conducted by separating the cohort into those with childhood injuries (from birth to age 11 years) and those with adolescent injuries (from age 12 years to 16 years).

Results: Relative to those with no injury, participants with a TBI were at increased risk of problematic use of alcohol (adjusted odds ratio (OR) = 1.56, 95% CI 1.21 to 2.01), tobacco (adjusted OR = 1.46, 95% CI 1.06 to 2.01) and cannabis (adjusted OR = 1.39, 95% CI 1.07 to 1.80), and of committing offences (adjusted OR = 1.67, 95% CI 1.22 to 2.29), being in trouble with the police (adjusted OR = 1.44, 95% CI 1.03 to 2.01), and having more parent-reported conduct problems (adjusted OR = 1.62, 95% CI 1.08 to 2.41). Participants with an orthopaedic injury were at increased risk of committing offences (adjusted OR = 1.38, 95% CI 1.10 to 1.74), but there was no clear evidence of association with other outcomes. Secondary analyses showed that participants with a mild TBI in childhood had higher odds of conduct problems and problematic cannabis use at age 17 years. While participants who incurred a mild TBI in adolescence had higher odds of problematic alcohol, tobacco and cannabis use and also higher odds of committing offences and being in trouble with the police at age 17 years.

Conclusions: Traumatic brain injury may be a risk factor for increased substance use, criminal behaviour and disruptive behaviour in late adolescence. Additional analyses suggest that age at injury may be important for certain outcomes.

The Effects of Concussion on Rapid Word Retrieval in Children

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Each year, over 150,000 sports- and recreation-related traumatic brain injuries (TBIs), including concussions, are treated in children under 19 years old. Children and adolescents have an increased risk for TBIs, with increased severity and prolonged recovery. Anomia, difficulty naming objects or people that are perceived correctly, is the most common reported disturbance. Adults with mild traumatic brain injuries have difficulty naming objects and people, even when they are perceived correctly (Ylvisaker, 1986). Not only is the accuracy of naming objects affected (e.g., saying “dog” when viewing a picture of a dog), but also there is an increase in the time that it takes the person to come up with the name (King, Hough, Walker, Rastatter, & Holbert, 2006). Examining differences in the “processing time” required to name an object may be useful in better understanding the cognitive changes that occur during the period of spontaneous recovery directly following a brain injury. For this study, 58 participants (32 injured), matched for age and gender, viewed and named 108 illustrations from the Rossion and Portouis series, an image series standardized for the most frequent English name and speed for naming each item. While groups did not differ in rate of accuracy, differences in reaction time between injured and healthy participants were significant, and those who were more accurate also tended to be faster. Comparing the trajectory of recovery for speed of naming to the average reaction time in healthy children, it was predicted that children would return to a reaction time indistinguishable from healthy children at approximately 3.1 weeks or 22 days. An error analysis also was conducted in order to better understand the differences between the groups. This information helps us further understand how even mild injuries can result in changes to cognitive-linguistic performance, which in turn result in increased difficulty in social and academic settings.

Health-Related Quality of Life, Social Participation and Coping Strategies Two Years After Mild or Moderate/Severe Traumatic Brain Injury

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Objectives: The objectives of this study were (1) to compare people with mild and moderate/severe traumatic brain injury (TBI) on health-related quality of life, social participation, and coping strategies, evaluated two years after the injury, and (2) to explore relationships between these variables.

Methods: Participants were adults who were hospitalized following a TBI in a Level I trauma centre in Canada. They completed six assessments in the first four years after TBI. The current study includes 105 individuals who completed questionnaires at the two-year follow-up (mean age = 42.1±14.5 years; 73% men; 55.2% mild, 44.8% moderate/severe TBI). The questionnaires assessed health-related quality of life (Quality of Life after Brain Injury; QOLIBRI), social participation (Participation Assessment with Recombined Tool–Objective; PART-O) and coping strategies (Brief-COPE). For the first objective, Mann-Whitney U tests were performed to compare injury severity subgroups on the QOLIBRI and the PART-O. The 5 most commonly used coping strategies among the 14 assessed by the Brief-COPE were identified for each subgroup. For the second objective, Spearman correlations were performed between the QOLIBRI, PART-O, and Brief-COPE.

Results: There were no significant differences between the mild and moderate/severe TBI subgroups on total scores of the QOLIBRI or the PART-O. However, the groups differed significantly on one of the three subscales of the PART-O, with a greater productivity in the mild TBI subgroup. The five most frequently used coping strategies were the same in both groups: acceptance, positive reframing, active coping, planning, and distraction. The level of endorsement of coping strategies was comparable between the severity subgroups except for acceptance, rated significantly higher by people with moderate/severe TBI. Regarding relationships between the constructs in the full sample, quality of life was significantly associated with social participation ($r_s = 0.52$). Coping strategies such as active coping, planning, positive reframing, acceptance, and humour were significantly positively correlated with health-related quality of life ($0.38 \leq r_s \leq 0.57$) and social participation ($0.31 \leq r_s \leq 0.36$). Other coping strategies were significantly negatively correlated with quality of life (denial, self-blame, behavioural disengagement; $-0.53 \leq r_s \leq -0.30$) and social participation (behavioural disengagement; $r_s = -0.37$).

Conclusions: Results from this study showed that injury severity does not influence health-related quality of life, social participation or coping strategies two years after TBI. However, people who had suffered a mild TBI reported higher productivity than those with moderate/severe TBI, probably because they are more likely to have returned to work. Our findings also suggest that quality of life and social participation are strongly related. Finally, the fact that the four most commonly used coping strategies are positively correlated with quality of life and social participation suggest that people instinctively use strategies that promote positive outcome.

Acute Ischemic Stroke Following Moderate to Severe Traumatic Brain Injury: Incidence and Impact on Outcome

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Background: Traumatic brain injury (TBI) is a major public health concern, leading to nearly 300,000 hospitalizations annually in the U.S. The injury also increases the lifetime risk of acute ischemic stroke (AIS). Despite recent advances in emergent treatment for AIS, its occurrence immediately following TBI may be under recognized clinically, and has not been well characterized.

Objective: To evaluate the incidence of AIS acutely following TBI, and its impact on short-term outcome.

Methods: The study was a retrospective analysis of prospective cohort data gathered at 22 Traumatic Brain Injury Model Systems (TBIMS) centers and their referring acute care hospitals. Participants were survivors of moderate to severe TBI, admitted to inpatient rehabilitation after acute hospitalization. Outcome measures were incidence of AIS; emergence from and duration of post-traumatic amnesia (PTA); Functional Independence Measure (FIM™), and Disability Rating Scale (DRS), at time of inpatient rehabilitation discharge.

Results: Between October 1, 2007 and March 31, 2015, 6,488 patients with TBI were enrolled in the TBIMS National Database. Median age was 42 years (range 16-99), and 73% were male. One hundred and fifty nine (2.5%) had a concurrent acute ischemic stroke (AIS) diagnosed during acute care. In univariate analyses, no difference was observed in demographics or initial clinical status (Glasgow Coma Scale Motor score) between patients with AIS and those without. Individuals with AIS were more likely to have early radiographic evidence of intracranial mass effect (50%, AIS patients vs. 38%, no AIS, OR 1.628, 95% CI 1.181-2.245; p=0.003), and were more likely to have a carotid or vertebral artery dissection (9.4% AIS vs. 1.5% no AIS, OR 7.0, 95%CI 4.0-12.5, p<0.001). High-velocity events were more common as the cause of TBI with cervical dissection (71% of dissections vs. 45% no-dissections, OR 2.986, 95% CI 1.961, 4.547, P<0.001). In multivariable analyses controlling for age, sex, initial clinical status and neuroanatomic injury characteristics, AIS predicted poorer outcome by all measures assessed, accounting for a 13.3-point reduction in FIM™ total score (95% CI, -16.8, -9.7; p<0.001), a 1.9-point increase in DRS (95% CI, 1.3, 2.5; p<0.001), and an 18.3-day increase in PTA duration (95% CI, 13.1,23.4; p<0.001).

Conclusions and Relevance: Ischemic stroke is observed acutely in 2.5% of hospitalized moderate to severe TBI patients who received inpatient rehabilitation, and predicts worse functional and cognitive outcome. Half of patients with new-onset AIS following TBI were age 40 or younger, and AIS patients more often had cervical dissection. These findings may help guide initial assessment and treatment decisions when AIS is suspected after TBI, and direct subsequent rehabilitation and secondary prevention. Vigilance for AIS is warranted when associated signs or symptoms are observed acutely following TBI or polytrauma, particularly after high-velocity events, given the narrow therapeutic window.

International Disaster Risk Management: Reducing the Vulnerability of Persons with Brain Injuries Through Emergency Preparedness

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Keim (2008) reports in his study that, “Global climate change will increase the probability of extreme weather events, including heatwaves, drought, wildfire, cyclones, and heavy precipitation that could cause floods and landslides. Such events create significant public health needs that can exceed local capacity to respond, resulting in excess morbidity or mortality and in the declaration of disasters. Human vulnerability to any disaster is a complex phenomenon with social, economic, health, and cultural dimensions.” Disaster “resilience” after a brain injury can be complicated by the inability of the individual to be prepared and react quickly to an event. This creates a need for very special supports for pre and post disasters. Keim discusses two areas to focus on which include the individual’s susceptibility to a traumatic event (resilience) and the capacity to fully recover from it.

The most lethal part of an emergency is the lack of preparedness in dealing with it: people are caught off guard, becoming confused, frightened, and disoriented; and these challenges are even more pronounced for those with disabilities - particularly hidden ones such as brain injuries. This became apparent in 2004 with Hurricane Katrina, when thousands of evacuated people simply fell through the cracks. After critical analysis of what went wrong, and under new legislation mandating precise procedures, we now have more refined means of guiding people through emergency situations, the efficacy of which can be seen in more recent disasters.

This poster presentation will demonstrate how to be better prepared for future emergencies by implementing the lessons learned over the last decade through specialized universally designed programs for worldwide use. It hopes to demonstrate a clearer understanding of why we should prepare before an emergency hits and what to do when that happens. This also dramatically improves aid to all persons with disabilities, especially persons with brain injuries. Further research into programs that have been successful in the area of emergency preparedness for people who have experienced the residual effects of a brain injury will also be presented.

Keim, M. E. (2008). Building Human Resilience: The Role of Public Health Preparedness and Response As an Adaptation to Climate Change, *American Journal of Preventive Medicine* 35 (5), 508-516.

Constructing a Systematic Approach to Neurobehavioral Care: A Mixed Methods Investigation

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The challenges involved in caring for individuals with brain injuries, particularly those with complex neurobehavioral challenges, has been a topic of international concern. Survivors of brain injury encounter many barriers in accessing care, including funding for services, coexisting diagnoses, and limited self-advocacy. Persistent neurobehavioral issues further compromise individuals' capacities to engage in professional, social, and educational activities. Further, providers encounter barriers that necessitate interagency training and education regarding risk assessment, psychosocial adjustment symptoms, and biomechanical causes of psychiatric symptoms.

This presentation addresses these concerns by reporting the findings of a priority, mixed methods research initiative. In order to examine this complex problem systemically and empirically, the research team conducted a comprehensive review of the literature to formulate an integrated understanding of neurobehavioral issues, evaluated best practices within and external to the state; and employed a mixed-methods investigation that evaluated influential factors (e.g., the political landscape), attended to regulatory guidelines (e.g., funding, legal), inventoried model systems of care within the United States, surveyed care providers to assess statewide needs, and conducted interviews to expand upon survey findings.

Based on comprehensive findings from this investigation, approaches to improving access are grounded in change that emphasizes a continuum of care reliant upon interagency collaboration. To address an unmet need for community-based and intensive neurobehavioral services, it is necessary to coordinate an integrative system of care that addresses three primary areas on the continuum: (1) prevention, education, and screening/identification; (2) crisis stabilization in a 24-hour, secured unit; and (3) provision of short- and long-term residential and community-based supports. As the data suggest, each component of the system should be considered when developing or expanding services. For instance, it is unreasonable to implement a 24-hour security unit for high-need cases without also considering the role of education and prevention, transitional and supportive living, and crisis stabilization.

Supported by the Commonwealth Neurotrauma Initiative (CNI) Trust fund with oversight by the Department for Aging and Rehabilitative Services (DARS), the findings of this research will and have guided public policy in the Commonwealth of Virginia to enhance the continuum of community-based and residential-based services for individuals with neurobehavioral issues. This presentation further discusses and provides updates on the work group that is currently exploring opportunities for enhancing and expanding services through a state-funded pilot program, a Medicaid waiver, or both. This interagency effort, which culminated in a decision-brief submitted to governmental decision-makers, combines the resources of numerous state agencies, to guide our next steps to address neurobehavioral care. These findings, though specific to Virginia, provide insights for other states and nations facing similar challenges.

Variations in Concussion Injury Mechanism Across the Pediatric Age Range

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Introduction: Concussion in youth has received heightened attention due to emerging evidence that it can negatively impact academics, behavior, and neurocognitive functioning. Most studies of youth concussion focus on sports-related mechanisms; however, concussions can occur in diverse settings. To better understand the diversity of concussion injury mechanisms across the pediatric age range, this study examined the distribution of injury mechanisms among children with concussions in a large pediatric healthcare system.

Methods: All patients, age 0-17 years, who had at least one clinical encounter with an ICD-9-CM diagnosis of concussion in The Children's Hospital of Philadelphia's electronic health record system (EHR) from 7/1/2012-6/30/2014 were selected (N=8233) and their initial concussion-related visit was identified. Twenty percent of the patients (N=1625) were randomly selected for manual record review to examine mechanism of injury. Mechanism of injury (MOI) codes used in this analyses are derived from similar categories utilized in external causes of injury codes (e-codes), agreed upon by study personnel.

Results: Children in the sample were primarily white (69%), male (53%), and had private insurance (81%); 30% were seen within a day of their injury and an additional 30% were seen between 2 and 7 days of injury. The distribution of age at time of injury was as follows: 4.5% were 0-4 years, 30.9% were 5-11 years, 34.5% were 12-14 years, and 30.1% were 15-17 years. Most children were seen for their initial diagnosis in a primary care setting (53.3%) compared to a specialty care practice (27%), emergency department/urgent care setting (17%) or hospital encounter (2.8%). Overall, 65% of concussions were due to sports-related mechanisms and this proportion varied by age. Only 16% of concussions sustained by children aged 0-4 were sports-related compared to those sustained by older children (61% for age 5-11, 72% for age 12-14, and 69% for age 15-17). When the concussion was non-sports related, the primary mechanisms of injury were struck object (31%) and falls (30%).

Conclusion: Although sports-related injuries in children older than 5 years of age contributed to the majority of concussions in this cohort, it is important to note that approximately one-third of concussions are from non-sports related mechanisms. The frequency of sports-related concussions increased at ages when children are more likely to join organized sports. Given the increased participation in community and organized sports activities among children, a focus on prevention efforts in youth sports is warranted; however raising awareness that concussions occur from other mechanisms, particularly among the very young, supports efforts to promote safety in multiple settings across age groups.

Perceived Needs, Barriers, Access to Mental Health Services and Self-Management Strategies for Psychological Health Issues in the First Year After Traumatic Brain Injury: Association with Injury Severity

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Objectives: The objectives were to compare individuals with mild vs moderate/severe traumatic brain injury (TBI) regarding perceived needs, use of services, self-management strategies for mental health, and practical and attitudinal barriers for obtaining help for mental health in the first year after TBI.

Methods: The sample included 210 individuals aged 18-65 years admitted to a Level I trauma centre in Québec (Canada) after a TBI (mean age: 42±15 years; 24% women; 49% mild, 51% moderate/severe). At 4, 8, and 12 months after the injury, participants were administered questionnaires assessing perceived needs for mental health services, reported use of services, self-management strategies, and practical and attitudinal barriers for obtaining services for mental health. Mild and moderate/severe TBI subgroups were compared with chi-square analyses.

Results: Among participants with mild TBI, 19-24% (depending on assessment time) reported perceiving a need for professional help for their mental health, compared to 23-25% of participants with moderate/severe TBI (n.s.). The percentage of participants who actually received mental health consultations from professionals in the first year was 45% in the mild group and 53% in the moderate/severe group. Use of prescribed psychotropic medication was significantly more frequent in the moderate/severe group at 8 and 12 months (38% mild vs. 46% moderate/severe at 8 months, 38% vs. 48% at 12 months respectively). Regarding self-management strategies, participants with mild TBI were significantly more likely to report using alcohol to cope with mental health issues (13-15% mild vs 6-9% moderate/severe depending on assessment time). There were no significant differences between injury severity levels in terms of practical barriers for obtaining mental health services: long waitlists and lack of money were most frequently reported. Concerning attitudes towards obtaining services, there were generally no differences between the mild and moderate/severe groups: 47-50% considered they should be able to deal with MH issues on their own, 8-13% did not want to discuss psychological difficulties with their physician and 17-24% with their family, and 34-48% were unwilling to take medication. A very large proportion reported that their situation would have to be critical before they would consult for mental health, significantly more so in the moderate/severe group (51-73% moderate/severe vs. 39-61% mild).

Conclusion: Access and barriers to services seems similar after mild or moderate/severe TBI in the first year after the injury. Mild TBI survivors seem to use alcohol more frequently to alleviate mental health symptoms, a coping strategy which should be investigated further. Many individuals, especially those with moderate/severe TBI, are likely to wait until their situation is critical before consulting. These results point to needs for psychoeducation regarding mental health after TBI, including strategies for adaptive coping and appropriate self-management, especially for persons no longer receiving rehabilitation services.

L-Alanyl-Glutamine Preconditioning and Neuroprotection Against Global Brain Ischemia/Reperfusion Injury in Rats

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This study aimed to evaluate the effects of the dipeptide l-alanyl-glutamine (l-ala-gln) as a preconditioning agent to potentially promote reduction in the intensity of the lesion in rats subjected to global cerebral ischemia/reperfusion (I/R) injury. Cerebral edema, neuronal death and intracellular protein kinase signaling were studied. L-ala-gln was administered intravenously (0.75g/kg), 30 minutes before sham procedure or induction of global brain I/R injury surgical procedure. Cerebral tissue was analysed 1h and 24h after reperfusion. Brain edema, red neuron counting, hippocampus concentrations of protein kinases (ERK/MAP kinase 1/2 (Thr185/Tyr187), Akt (Ser473), STAT3 (Ser727), JNK (Thr183/Tyr185), p70 S6 kinase (Thr412), STAT5A/B (Tyr694/699), CREB (Ser133) and P38 (Thr180/Tyr182) were determined. Results expressed as Mean±SD for Normal results and Median±Percentil (25-75) for non parametric data, with p<0.05. Global I/R injury promoted increase in brain edema at 24 h after reperfusion, whereas preconditioning with l-ala-gln induced no change in edema. On the other hand, l-ala-gln preconditioning reduced red neurons counting both at 1h and 24h post reperfusion. L-ala-gln promoted significant decreased concentrations of JNK after reperfusion as compared to I/R controls at 1h and at 24h post reperfusion. L-ala-gln preconditioning induced significant elevation of brain concentrations of P70 at 1h and at 24h post reperfusion, P38 at 1h after reperfusion and CREB at 24h post reperfusion. There was a significant preconditioning effect with l-ala-gln preserving red neurons counting at early (1h) and late reperfusion (24h) in the cerebral tissue. Decreased brain concentrations of JNK and elevated concentrations of P70, P38 and CREB induced by preconditioning with l-ala-gln indicate neuroprotective effects of by this peptide. More studies are necessary to explore the present results and to investigate other intracellular pathways and other mechanisms involved in this neuroprotective event.

Global Meaning in People with Stroke: Content and Changes

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After a traumatic event like a stroke people need to find meaning and control again. This study enhances knowledge on one of the driving principles behind meaning making processes: global meaning. Global meaning refers to individuals' general orienting systems, comprising fundamental beliefs and life goals. Little is known about global meaning in people with stroke and whether global meaning changes after stroke. In this qualitative study, five aspects of global meaning were found: core values, relationships, worldview, identity and inner posture. Continuity in all aspects was reported, but worldview, identity and inner posture were also subject to change.

Global Meaning and Rehabilitation in People with Stroke, A Qualitative Study

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A stroke can have implications for all areas of a person's life. In research on adaptation to stroke, finding meaning is associated with better adaptation. This study focuses on one of the driving principles behind meaning making processes: global meaning. The aim of this study was to explore whether global meaning (i.e. fundamental beliefs and life goals concerning core values, relationships, worldview, identity and inner posture) is associated with processes and outcomes of rehabilitation, as experienced by people with stroke. In depth semi-structured interviews were conducted, and analyzed using qualitative research methods. Aspects of global meaning were associated with the following elements of process and outcome of rehabilitation: motivation, handling stress and emotions, physical functioning and acceptance. The influence was mostly positive. If rehabilitation professionals took global meaning into account, respondents tended to associate this with better or faster recovery.

Building a Person Centred Approach to Acquired Brain Injury Services

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The buzz word in health care is "person centred" care. To actually implement and utilize person centred approaches on a daily basis with those that have acquired brain injuries is a challenge for most organizations. The research in this area is expanding and will be discussed in this session. Also techniques/philosophy/support must start on the leadership level and be implemented, managed and improved at the front line staff level. Exploration of ethical issues, practical implementation issues and tips to review does your organization have the correct foundations to be person centred will be explored. How person centred care happens in different cultural contexts will also be addressed. What does activity and participation look like in person centred organizations? Leave with a tool box of resources and tools to explore your person centred practices and join the continuous improvement movement that is making person centred care a reality.

Concept: An Enhanced Case Management Approach for Neurobehavioral Issues following TBI

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Purpose: This grant-funded project investigated using enhanced case management supports for individuals following traumatic brain injury who are at-risk for maladaptive, neurobehavioral symptoms. The approach, titled CONCEPT, aimed to optimize individuals' independence and productivity in the community. In addition, this project endeavored to ascertain participants' perceived quality of life (QOL) through self-ratings and to determine how these self-ratings correlated to Mayo Portland Adaptability Inventory-4 (MPAI-4) pre-post test scores.

Methods: Collaboratively, Brain Injury Services of Northern Virginia and Crossroads to Brain Injury Recovery piloted the CONCEPT program. This case management "plus" model offered services to avert escalating, maladaptive behaviors, including:

- Behavioral supports (e.g., positive behavioral supports, life skills coaching, behavioral analytics)
- Neuropsychological evaluation and consultation
- Community supports (e.g., budgeting, organizing, cooking)
- Other (e.g., home modifications, assistive devices)

Using MPAI-4, clinicians screened 100 individuals with 53 meeting the "at-risk" criterion. Outcome measurements were pre-post MPAI-4 and the Visual Analog Scale for Quality of Life (VASQOL).

Results MPAI-4 Pre-post Findings:

Results are descriptive, conforming to the funding agency's outcomes reporting requirements.

- 83% maintained or improved on Total MPAI Score. Clients maintained or improved their level of adaptability, including assessment of abilities, adjustment, and participation.
- 92% maintained or improved on MPAI Query-28 (employment). Clients maintained or improved their participation in work, school, vocational training, or volunteer activities.
- 92% maintained or improved on MPAI Query-26 (residence). Clients maintained or improved their living situation.

Visual Analog Scale for Quality of Life (VASQOL) Findings: Using VASQOL in conjunction with subscales of the MPAI-4 yielded no statistically significant correlations between clinician and client scores. Results provide insight for VASQOL and MPAI-4 as quantitative measures on perceived quality of life. No subset of the clinician-scored MPAI-4 informed clients' self-reported VASQOL ratings.

Pearson's correlation coefficient (r) yielded no significant relationship between VASQOL and the subscales or total standard score of MPAI-4 (all findings $p > .05$). Though research has supported the reliability of MPAI-4 results across rater groups, this study sought to compare scores from one rater group (clinician) to the scores from another rater group (client) obtained from a separate test. Measuring the clinician's ability to understand their client's perceived quality of life through the MPAI-4 has not been reported in the literature.

Discussions: Pre-post MPAI scores determined that clients deemed "at-risk" did benefit from the CONCEPT approach. Comparing MPAI-4 findings with VASQOL revealed a level of discrepancy between clinicians'

perceptions of their clients quality of life and their clients' self-reported quality of life. One explanation for the absence of correlation is that as clients improve and gain insight to their situation, they self-score quality of life lower. A limitation is that findings may reflect differences in scorers or the tests themselves.

Cognitive Improvement; An Exciting Discovery Using TLS Technology

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Introduction: Cognitive impairment is a typical consequence of many neurological disorders. It is generally accepted that most improvement for an individual affected by stroke occurs within the first year following the stroke. Trans-Lingual Stimulation (TLS) Technology, generally used to rehabilitate balance, posture, and gait, has a surprising impact on the recovery of cognitive function. TLS Technology combines the use of targeted therapy and non-invasive neurostimulation—delivered directly to the tongue—to enhance natural recovery mechanisms that exist in the brain. In a case of chronic stroke, cognitive improvement was a byproduct of a routine procedure designed to rehabilitate balance and gait, without additional specific training.

Method: The Tactile Communication and Neurorehabilitation Laboratory (TCNL) completed a 13-month intervention for an 80-year-old woman, four years after her stroke. For the first six months of the intervention, this individual used TLS Technology for one hour twice a day to rehabilitate balance and gait. After six months of intervention, there was a 30-day withdrawal period, followed by an additional six months resuming the exercises and device use. Cognitive improvement was measured using the Stroke Impact Scale (SIS) and Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).

Results: The “Memory and Thinking” domain on the SIS demonstrated 20.9% improvement during the first six months of the intervention. In the last six months, after a brief withdrawal period, Memory and Thinking continued to improve an additional 21.8%. In total, TLS intervention improved Memory and Thinking 47.3% from baseline. All components of the RBANS improved as a result of the intervention. Improvement on RBANS demonstrated TLS dependence, such that all of the parameters improved in the first six months of the intervention, then deteriorated during the withdrawal period, and eventually improved again when the intervention was reinstated. Percent improvement on the RBANS during the initial six months of the intervention ranged from 10-41% from baseline across all categories.

Discussion and Conclusions: TLS balance and gait training can be used to recover and improve cognitive functioning in an individual with chronic stroke. These findings present a new non-invasive brain stimulation technique with applications in cognitive and rehabilitative neurosciences. Additional research is necessary to understand the potential mechanisms of this phenomenon and optimize the efficiency of the intervention.

Cogniphobia in Mild Traumatic Brain Injury

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Objectives: Cogniphobia refers to avoidance of mental exertion due to a fear of developing or exacerbating a headache. Headaches are very common after mild traumatic brain injury (MTBI) and often become chronic. Cogniphobia is hypothesized to contribute to poor cognitive test performance and persistent disability in some patients with MTBI.

Methods: Sixty patients with MTBI and post-traumatic headaches were recruited from specialty outpatient clinics. They completed a battery of questionnaires (including the Cogniphobia Scale, Fear Avoidance Beliefs Questionnaire, PTSD Checklist-5, British Columbia Postconcussion Symptom Inventory, and a brief pain scale) and neuropsychological tests (the National Institutes of Health Toolbox Cognition Battery and the Medical Symptom Validity Test) at 2-3 months post injury (M=11.0, SD=5.9 weeks), in a cross-sectional design. A prior study involving a chronic headache sample found that the Cogniphobia Scale items load on two factors, representing avoidance of mental exertion (Cogniphobia-Avoidance) and beliefs that mental effort is dangerous (Cogniphobia-Dangerousness).

Results: Cogniphobia-Avoidance ($r=.45$ to $.54$) and Cogniphobia-Dangerousness ($r=.25$ to $.41$) were correlated with measures of headache severity, even after excluding participants who failed performance validity testing ($n=14$). Cogniphobia-Avoidance was associated with lower performance on memory testing (but not other cognitive tests), independent of headache severity. Participants who avoided mental exertion also tended to avoid physical activity and traumatic stress triggers.

Conclusions: The findings provide preliminary support for the role of cogniphobia in persistent cognitive difficulties after MTBI, and suggest that cogniphobia may reflect a broader avoidant coping style.

Preliminary Validation of the World Health Organization Disability Assessment Schedule 2.0 in Mild Traumatic Brain Injury

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Objectives: Traditional measures of functional outcome from traumatic brain injury have limited sensitivity following mild traumatic brain injury (MTBI). The World Health Organization Disability Assessment Schedule (WHODAS) 2.0 was developed as a disease-non-specific measure of disability. It covers the domains of cognition, mobility, self-care, interpersonal functioning, life activities, and community participation. The WHODAS 2.0 has become widely used in psychiatry, neurology, and chronic disease research, but has not yet been evaluated in MTBI.

Methods: Fifty-nine adults were recruited from outpatient concussion clinics, confirmed to have sustained an MTBI by the World Health Organization Neurotrauma Task Force definition, and administered an outcome assessment by telephone 6-8 months after their injury. The assessment included the British Columbia Postconcussion Symptom Inventory (BC-PSI), WHODAS 2.0 12-item interview version, MINI Neuropsychiatric Interview, and a brief pain questionnaire. The WHODAS 2.0 “simple” scoring method was analyzed in the present study.

Results: There were minimal floor or ceiling effects, with four participants (6.8%) obtaining the lowest possible score and none obtaining the highest possible score. Cronbach’s alpha was 0.91, indicating high internal consistency. The WHODAS 2.0 was strongly related to postconcussion symptom severity (BC-PSI), $r(59) = .82, p < .001$. Participants who met the International Classification of Diseases-10 criteria for postconcussional syndrome based on at least moderate severity symptom reporting on the BC-PSI had substantially higher WHODAS 2.0 scores ($n=31$; $M=30.52, SD=8.30$) than those without the syndrome ($n=28$; $M=17.24, SD=4.76$; $t(50) = 6.62, p < .001$, Cohen’s $d = 1.96$). Compared to patients without comorbid conditions, participants with (i) a co-occurring bodily injury and current moderate to severe pain in at least one body region other than head ($n=31$; $M=29.19, SD=8.97$), (ii) a current Major Depressive Episode based on the MINI ($n=16$; $M=35.19, SD= 8.44$), or (iii) any anxiety disorder based on the MINI ($n=21$; $M=32.05, SD=8.93$) had relatively high WHODAS 2.0 scores. WHODAS 2.0 scores were higher as a function of having 0, 1, or 2+ of these comorbidities, $F(2, 56) = 24.35, p < .001$.

Conclusions: The WHODAS 2.0 12-item interview may provide a more granular assessment of functional outcome from MTBI. This scale appears sensitive to postconcussion symptoms as well as comorbid conditions following MTBI. Further validation work is warranted, including with other versions of the WHODAS 2.0 (e.g., self-report, long form).

Return to Work, Absenteeism, and Presenteeism After Mild Traumatic Brain Injury

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Objectives: To examine the completeness of return to work (RTW) in a mild traumatic brain injury (MTBI) sample recruited from an outpatient specialty clinic setting.

Methods: Consecutive referrals from four outpatient concussion clinics were screened, and 67 patients met eligibility criteria (including World Health Organization Neurotrauma Task Force definition of MTBI, aged 18-65, and employed immediately prior to the MTBI) and were enrolled at their first clinic visit. Of these, 59 (89.1%) were reached for a follow-up assessment by telephone at 6-8 months post-injury. This assessment included a structured interview of RTW status, the British Columbia Postconcussion Symptom Inventory (BC-PSI), and the Lam Employment Absence and Productivity Scale (LEAPS).

Results: Although 36 of 59 (61.0%) patients had returned to work in some capacity by the follow-up assessment (IQR = 24-35 weeks post-injury), only 28 returned to the same job, with the same responsibilities and work hours. Of those 28 cases, exactly half (n=14) met International Classification of Diseases-10 criteria for postconcussional syndrome based on at least moderate severity symptom reporting on the BC-PSI. Regarding absenteeism, 57.1% of patients (n=16) missed no work, 10.8% (n=3) missed less than one full shift, 17.9% (n=5) missed 1-2 shifts, and 14.3% (n=4) missed more than two shifts over the prior two weeks because of feeling unwell. On the LEAPS, 60.7% of patients (n=17) rated themselves as getting less work done, 46.4% (n=13) as having interpersonal difficulties at work, 39.3% (n=11) as making more mistakes, and 25% (n=7) as doing poorer quality work. The severity of residual postconcussion symptoms (BC-PSI total score) was strongly related to the severity of work impairment (LEAPS total score), $r(28) = .72$, $p < .001$. Of note, 9 of the 28 patients who achieved a full RTW had previous unsuccessful attempts to RTW since their MTBI.

Conclusions: Even in patients who returned to work after MTBI, detailed assessment of RTW status revealed underemployment and productivity loss associated with residual symptoms. RTW should be considered a stage of recovery rather than an “outcome” from MTBI. More granular functional outcome measures are needed for MTBI research. Further research is needed on absenteeism and presenteeism, as well as on the durability of RTW after MTBI.

Repetitive Transcranial Magnetic Stimulation for Cerebellar Ataxia: Case Reports

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Objective: Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive technique to stimulate the cortical areas of the brain. The cerebellum has been considered as a potential stimulation site for rTMS for enhancing recovery from ataxia. We present the findings of two subjects with ataxia following rTMS intervention

Methods: The rTMS parameters used for each subject were 1-Hz frequency at 100% resting motor potential with 30 trains of 30 pulses each and with 5 sec interval between each train, applied for 5 days. The coil was on the ipsilesional cerebellar hemisphere. Both the subjects were assessed on the 9-hole peg test and Scale for the Assessment and Rating of Ataxia (SARA).

Results: In our study, both the subjects showed some improvement on 9 hole peg test and SARA in terms of improved score. Albeit, we did not incorporate any statistical tests owing to small number of sample. There were no reported side effects of rTMS treatment

Conclusion: rTMS can be used as a possible adjunct in the management of ataxia. However, there is a need for larger randomized controlled trials to further explore the role of cerebellar rTMS to ameliorate the effects of ataxia.

Keywords: rTMS, cerebellar stimulation, ataxia

Formation and Evolution of Chronic Subdural Hematoma in Elderly Patients with Head Trauma

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Background and Purpose: The incidence of chronic subdural hematoma (CSDH) has been increasing in recent years, mainly due to ageing of population. CSDHs are considered to originate from acute subdural hematoma (ASDH) or from subdural hygroma (SH) arising from traumatic tearing of arachnoid membrane to CSF passage into the subdural space. Currently, the frequency of these 2 mechanisms has not been well known. The purpose of this study is to investigate the incidence of CSDH in elderly patients with head trauma, to clarify the significance of acute traumatic intracranial hematoma (t-ICH) in the formation and evolution of CSDH.

Clinical Materials and Methods: Consecutive 614 elderly (> 70 y.o.) patients with head trauma were examined with CT within 24 hours after trauma to divide them into 3 groups as follows: patients without t-ICH as group A (n=362), with ASDH as group B (n=172), or with t-ICH other than ASDH as group C (n=80). Follow-up CT was taken to detect CSDH formation at 1 month after trauma. All patients with CSDH at 1-month after trauma were followed up to 6 months to investigate whether the CSDH become symptomatic or not. The incidences of both CSDH formation and its symptomatic evolution were compared among 3 groups, using chi-square test with Bonferroni-correction. As subanalysis, relationships between 1-month CSDH formation and the subdural space thickness on initial CT or the patient's age were also examined in group A, using Spearman rank correlation coefficient test. Statistical differences were considered significant at $p < 0.05$.

Results: The incidence of 1-month CSDH formation was 11.7% in group A, 29.7% in group B, and 25.6% in group C, being significantly higher in groups both B and C than A ($p < 0.001$). It was not significantly different between groups B and C. The incidence of symptomatic CSDH evolution was 3.3% in group A, 5.1% in group B, and 4.1% in group C, being not significantly different among 3 groups. CSDH formation is correlated with both the degree of subdural space thickness on initial CT ($p < 0.0001$) and the patient's age ($p < 0.05$) in group A.

Conclusion: This study demonstrated the incidence of both CSDH formation and its symptomatic evolution in elderly patients with head trauma, suggesting that the acute t-ICH is a risk factor for CSDH formation but not for its symptomatic evolution. In addition, since the incidence of CSDH is not different between patients with ASDH and those with t-ICH other than ASDH, the existence of acute subdural clot itself may not cause CSDH directly. The mechanism of CSDH formation and its evolution are discussed, considering the correlations between CSDH formation and both the degree of subdural thickness and the patient's age.

Making a PACT: Group Treatment to Prepare Patients with Communication Disorders for Interactions with Healthcare Providers

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Objectives: Patients with communication disorders at increased risk for adverse events in healthcare due to poor communication with their providers. Consequences including inaccurate symptom reporting, decreased patient understanding of medical information, lack of patient participation in healthcare decision-making, and poorer health outcomes can result from diminished communication during medical interactions. One way to help mitigate miscommunications is to prepare patients with communication disorders to interact with their providers. A communication framework, PACT, has been proposed as one way for speech-language pathologists (SLPs) to provide this preparation. This project focuses on piloting this specific framework with patients with communication disorders in a group setting.

Methods: Four individuals with acquired neurologic communication disorders participated in four group sessions led by graduate SLP students at the University of Washington Clinic. Sessions focused on education and application of patient-focused strategies using the PACT framework. Session one addressed challenges with and the potential impact of poor communication. Session two included direct instruction of communication-enhancing strategies, including prewritten questions, gesturing, keyword writing, using a communication notebook, and advocating for slowed rate of conversation along with preparation of information to use during appointments. Session three integrated metacognitive strategies through having participants watch recorded interactions of poor communication and identifying communication breakdowns. Strategies to avoid or repair communication breakdowns were discussed, and role play was introduced to allow participants to practice implementing strategies. The final session included reviewing all prior material and a group discussion on advocacy of communication skills. Survey data was collected (pre- and post-group intervention, and post-physician visit) from participants to determine any changes in the number or type of strategies used, confidence in communication, and application of concepts during future medical visits.

Results: All four group participants completed pre- and post-intervention surveys with two of four also completing post-physician visit surveys. During the post-intervention survey, all four participants indicated more diversity in the strategies they would use during a medical visit. The two participants completing the post-physician visit survey also indicated implementation of reported strategies, including increased use of prewritten questions, keyword writing during the appointment, and a memory notebook. Increased confidence in communication post-intervention was reported in 3 of 4 participants using a visual-analogue scale. Pre/post measurements (in millimeters) as indicated per participant: P1 79/96, P2 29/56, P3 77/100, and P4 82/76. Additionally, after intervention, participants could independently suggest strategies they and their healthcare provider could implement for improved communication.

Conclusions: The PACT framework can be successfully adapted and implemented during group therapy to help improve communication between patients with communication disorders and their healthcare providers. All four participants reported they found the intervention helpful, indicating that watching recorded interactions and discussing potential strategies along with making a preparedness checklist were particularly useful.

Post Traumatic Intracranial Hypertension (Pseudotumor Cerebri) in Mild Traumatic Brain Injury: A Specific Post Traumatic Headache Subtype; The Importance of Recognition, Evaluation and Management

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Background: Dysregulation of the osmotic gradient between the interstitial fluid, blood vessels and the brain parenchyma results in increased fluid accumulation in the brain causing increases in intracranial pressure (ICP). Cerebral edema can be a clinical manifestation of traumatic brain injury (TBI) that peaks at 36-72 hours post-injury and patients are carefully monitored for this complication. Intracranial hypertension (IH) is characterized by increased ICP in the absence of a tumor or other diseases and can result from cerebral edema, which is common after MTBI but is not considered as a consequence of mild TBI (mTBI). Intracranial hypertension secondary to a specific condition is called pseudotumor cerebri (PTC), typically associated with normal imaging findings, although subtle abnormal findings may exist in some patients. Pseudotumor cerebri is diagnosed by a lumbar puncture (LP) with a cerebral spinal fluid (CSF) opening pressure of >25 cm/H₂O in children or >20 cm/H₂O in adults. Post traumatic headache (PTH) commonly presents immediately after injury but in a subset of patients can occur 2-3 days after injury. This “secondary peak” may reflect post-traumatic cerebral edema in a select group of patients. Here we discuss a specific IH, or post traumatic pseudotumor cerebri headache (PTPTC) phenotype, found in 5 cases of mTBI and review the clinical implications.

Case Series: We conducted a retrospective case series report of 5 patients diagnosed with PTPTC in a pediatric population (5-16 years old). Patients were assessed at 2-5 days post primary injury. Symptoms that prompted hospital or clinic visits included new or changes in headache pattern (positional, intensity, “early morning”), new or change in vision (blurry, positional, diplopia), new or change in auditory function (pulsatile tinnitus, “popping”), and worsening of balance and cognition. Significant clinical findings included increases in body temperature, neck/head pain, papilledema or cranial nerve deficit (6th), and lack of coordination. We found that neuroimaging could be normal but in one case, magnetic resonance (MR) imaging showed decreased intracranial space ratio, “empty Sella”, optic nerve sheath/head enlargement, displaced cerebellar tonsils, and reduced basilar cistern space. MR venography showed diminished size of transverse or sigmoid sinus in certain patients. In every case, elevated CSF pressure was documented by LP, documented normal CSF laboratory testing and all cases improved with treatment specific to PTPTC such as acetazolamide.

Conclusions: The importance of recognizing of this specific post traumatic headache type, PTPTC, in mTBI includes: being able to tailor specific treatment with use of LP for diagnosis and relief of symptoms and treatment with carbonic anhydrase inhibitors that lower ICP, such as topiramate or acetazolamide. It is postulated that the condition of PTPTC may predispose certain athletes to a condition called second impact syndrome.

Closing the Loop in Movement Rehabilitation: Results from Stroke Therapy That Includes EEG-Based Measures of Movement Imagery

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Each year, millions of patients with movement disorders resulting from damage to the CNS, such as stroke, undergo therapy that aims to restore movement. This therapy often involves feedback training, in which the patient imagines or (if possible) performs specific movements while receiving rewarding feedback such as tones, images, movement of an on-screen avatar, activation of a functional electrical stimulator (FES), or a therapist saying "Good job!" Several groups have explored therapy that "closes the loop" in stroke therapy by linking rewarding feedback to real-time EEG measures of motor imagery. Thus, the activity of an avatar, FES, and other components only provide rewarding feedback when the patient is actively imagining the intended movement. This approach could increase patient compliance and motivation, as well as increase functional recovery by maximizing the coincident activation of damaged CNS areas and downstream peripheral neurons that are supposed to work together to produce the desired movement. This coincident activation is a critical component of Hebbian learning. If patients are simply ignoring instructions, imagining the wrong movement, or devoting little mental effort to the task, then providing rewarding feedback is not only unhelpful but could be detrimental to the therapy process.

We will present results from several different groups that have conducted research in clinical settings with stroke patients. Results will include functional improvement (assessed through conventional means such as the 9-hole PEG test), changes in cortical activity associated with movement (such as event-related desynchronization or ERD/S), changes in system performance (such as accuracy of EEG-based movement classification), and subjective report (such as user feedback). These results validate this approach in real-world settings, with many patients attaining both high classification accuracy and impressive functional improvement. Notably, many patients exhibit functional improvement even though classification accuracy is only modest, which implies that improved adaptive classification tools are needed. We will address several other questions for future study. For example, EEG-based activity could be used to guide additional components of therapy, and this approach has mostly been limited to work with upper-limb rehabilitation. Patients with traumatic brain injury or other types of CNS damage, or even spinal cord injury, could benefit as well. Related neurotechnologies involving brain stimulation could also further improve functional recovery.

However, the broader question, as with most emerging clinical research fields, is whether this new approach provides a significant improvement over conventional approaches in large clinical trials with appropriate controls. This has not yet been demonstrated, and we will address work toward that goal. This talk/poster will include a complete system for EEG-based stroke therapy – attendees can don an electrode cap and see their EEG in real-time, and try out different components.

EEG-Based Systems for Assessment and Communication in Persons with a Disorder of Consciousness (DOC)

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Patients diagnosed with a disorder of consciousness (DOC) are presumed to have little or no remaining cognitive activity, as well as little or no voluntary motor control, and thus clinical practitioners typically do not try to communicate with them. However, research using different noninvasive neuroimaging methods (mostly EEG) has shown that a minority of DOC patients are able to produce voluntary changes in neural activity in response to task instructions, indicating that they do have some cognitive function. Many of these paradigms are essentially real-time brain-computer interfaces (BCIs), in which the goal is to discriminate two different types of mental activities based on adaptive classification tools. Furthermore, since BCIs based on the EEG can provide bedside communication based on voluntary changes in neural activity, patients who exhibit sufficient cognitive function during an assessment phase might be able to communicate. Because most patients with DOC cannot use visual stimuli, BCIs used for DOC assessment and communication usually rely on auditory and tactile modalities to deliver instructions, cues, and feedback.

We will present results from assessments conducted with over 100 DOC patients across several hospital collaborators. Consistent with prior work, a minority of patients do exhibit reliable EEG patterns consistent with left vs. right hand motor imagery and/or counting specific target (and not non-target) tones or vibrotactile stimuli. These patients are usually, but not always, patients diagnosed in the minimally conscious state or MCS. Thus, they can understand, remember, and choose to follow task instructions, detect and discriminate stimuli, and maintain attention well enough to potentially use BCIs for communication. We will show results with basic YES/NO BCI communication. Results with many patients suggest fluctuations in consciousness across multiple sessions. This result requires further study, and indicates that multiple assessment sessions are needed for each patient – although the precise numbers is not yet clear. We are conducting follow-up work to develop additional paradigms to assess cognitive function in more detail, provide more advanced BCI communication, and develop BCI-based rehabilitation paradigms specialized for these patients. Our talk/poster will include a complete EEG-based BCI system for DOC assessment and communication that attendees can use. Their EEG should indicate conscious awareness.

This approach could also benefit patients whose assessments reveal that they do not exhibit reliable cognitive function, as well as their families. This outcome could support the patient's existing clinical diagnosis and thus provide some confirmation for families, and (with future research) could lead to new methods that can help physicians provide treatment or provide more detailed assessment of even very basic cognitive function. Further in the future, with additional research and clinical validation, EEG-based assessment scales could become a useful supplement to conventional scales based on behavioral responses.

A Mixed Methods Approach to Study the Effectiveness of a Primary Care Progressive Return to Activity Protocol After Acute Mild Traumatic Brain Injury/Concussion in the Military

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The thousands of U.S. service members sustaining a concussion/mild traumatic brain injury each year emphasizes the need for effective clinical guidance for managing concussion. While emerging research supports a gradual return to pre-activity levels without exacerbating symptoms, available guidance lacks specifics for this return to activity process. To fill this gap, the Defense and Veterans Brain Injury Center, in collaboration with clinical, military, and academic subject matter experts, created a clinical recommendation (CR) for primary care providers detailing a step-wise return to unrestricted activity following acute concussion. Although developed using an evidence-based approach, the CR should be evaluated to ensure positive patient outcomes, to identify barriers to implementation by providers, and to identify ways to improve the recommendation. In this presentation, we describe a multi-level, mixed-methods approach to evaluate the effectiveness of the CR in improving acute patient outcomes and to assess adherence to recommendations by providers and their patients. Outcome and adherence to guidance was compared for patients receiving treatment as usual to those receiving care according to the CR, and outcomes from acute injury to six months post-injury were collected to illustrate recovery trajectories by group. Information from providers was collected via semi-structured interview pre- and post-educational intervention about the CR, to evaluate their knowledge of the CR and its use in practice, and their perception of patient change and compliance over time. The study was implemented within complex but ecologically-valid settings at multiple military treatment facilities and operational medical units. Special consideration was given to expected challenges such as the frequent movement of military personnel, selection of appropriate design and measures, study implementation at multiple sites, and involvement of multiple military service branches. To date, all providers (N = 35) and 75 of the targeted 200 patients have been enrolled. We briefly report findings from provider baseline data revealing recommendations consistent with best practices (e.g., physical rest) albeit with some variation (e.g., duration of rest, use of specialty clinics and referrals), and highlighting barriers (e.g., patient compliance) and facilitators (e.g., leadership' attitudes about injury) for acute concussion care in the military. Preliminary data from the treatment as usual concussed group are examined to explore the extent to which patient outcomes align with practices and variability observed in provider participants. Taken together, these initial findings are consistent with previous research demonstrating that published educational material does not translate into compliance by medical providers and needs to be supplemented by face-to-face educational interventions to benefit patient outcomes. Complete study data have the potential to guide improvements to the clinical recommendation and support service members' safe return to activity and duty.

Graded Exercise Testing for Risk Stratification of Paediatric Concussion

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Hypothesis: Concussion in children is a physiologic brain injury, the concussed patient in a hypermetabolic state characterized by altered cerebral blood flow (CBF). Normalization of altered CBF has been shown to be a useful neurophysiologic marker for recovery.

With graded exercise testing (GXT), CBF increases progressively with exercise intensity. GXT, may therefore be a convenient clinical measure for assessing concussion-related physiological dysfunction due to altered cerebral blood flow and predict patient outcome.

Purpose: To determine if a GXT, performed during the subacute phase following an acute concussion, can determine readiness to commence a return to activity protocol and predict patient outcome.

Methods: Prospective study conducted at Children's Hospital at Westmead, Children's Hospital Institute of Sports Medicine (CHISM) in Sydney Australia over a 3-year period. Participants were aged 12-16years, referred to CHISM within 5-7 days following an acute concussion- subacute phase, preceded by a short period of rest, ensuring safety to exercise. Concussion was confirmed in all cases by a concussion specialist using a standard concussion test battery to determine key clinical indicators for injury, these tracked at successive visits. In addition, all patients underwent a graded exercise test to determine readiness to commence a return to activity protocol. Time to symptom onset and symptom severity were reported.

Results: There were 140 study patients, with a mean age of 12.4 years, with the majority, being males involved on organised sport. Most referrals were from Emergency Departments, with 40% reporting loss of consciousness and 35% retrograde amnesia. Subacute assessment clearly demarcated two patient groups, exercise tolerant (54%) and exercise intolerant (46%). The main clinical drivers in both groups were headache, balance/vestibular dysfunction, with M-BESS and VOMS key clinical indicators. No adverse effects from exercise were reported in either group.

Exercise tolerant patients, had mild clinical indicators, no symptom exacerbation during 10 minutes of exercise, and were determined ready to commence a RTA protocol, with recovery occurring within 14 days of injury.

Exercise intolerant patients, had high clinical indicators, significant symptom exacerbation, during 4.2 minutes of exercise, were not ready to commence a RTA protocol, needed some medical interventions with eventual recovery by 6 weeks. In the exercise intolerant group, 12% of patients, mostly females (62%), had very high clinical indicators, significant symptom surging during 2.8 minutes of exercise, needed significant medical interventions with eventual recovery by 12 weeks.

The combination of clinical indicators and exercise testing at the subacute assessment, was 93% predictive of outcome in this study population.

Conclusion: GXT during subacute assessment, can risk stratify patients to being ready to safely commence a RTA protocol. Further, when GXT combined with key clinical indicators, it makes an effective condensed model of care for predicting outcome in paediatric concussion.

The Importance of The Minimal Clinically Important Difference (MCID)

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Background/Aims: The Minimal Clinically Important Difference (MCID) of a measure is critical to identify responders to intervention. Because each holds advantages, both distribution- and anchor-based methods are commonly used together to triangulate on the MCID. Distribution-based approaches include computation of the standard error of measurement (SEM), standard deviation (SD), and various derivatives of these, e.g., $\frac{1}{2}$ SD and the Reliable Change Index (RCI=2.77SEM). Anchored methods estimate the MCID with a reference to an external indicator, such as, change on a related measure, global ratings of clinical improvement, or response to intervention. To illustrate these principles, a multimodal method approach to identify the MCID for the MPAI-4 as well as a moderate, more robust level of change (RCID) will be described. This study combined distribution- and anchor-based procedures.

Method: Data were for individuals with acquired brain injury in rehabilitation programs throughout the U.S. in the Outcome Info Database (n=3087) with two MPAI-4 ratings. Anchored estimates were referenced to a subsample with the Supervision Rating Scale (SRS; n=2726) and response to intervention. Finally, hypothesized MCID and RCID values were evaluated through clinical provider ratings of case protocols.

Results: Rasch derived T-scores (SD=10) were used in all analyses; $\frac{1}{2}$ SD = 5 on the T-score metric (5T). Other distribution-based analyses found the SEM=4.07 (generally considered to indicate a small difference); 1.96SEM=7.98 (moderate difference); and 2.77SEM=11.27 (large difference; also equals RCI). Receiver operating characteristic (ROC) analyses anchored to the SRS suggested significant change on the MPAI-4 occurred between 7.5T and 8.5T. At this point in the analyses, we hypothesized that the MCID might be 5T and a more robust change, the RCID might be 9T. Among those who received intensive rehabilitation, 72% changed $\geq 5T$ compared to 12% in supported living programs ($\chi^2=169.74$, $p<.001$); 54% in intensive rehabilitation changed $\geq 9T$ compared to 4% in supported living ($\chi^2=97.60$, $p<.001$). Virtually all clinical raters (99%) considered a 9T change to indicate improvement; depending on time since injury, a change of 5T was considered improvement by 81-87% of raters.

Conclusions: 5T represents the MCID for the MPAI-4 and 9T, the RCID. Notably both values are less than the RCI. While the RCI may be an appropriate reference value in some research applications, it essentially replicates a test of clinical significance. The difference between RCI and MCID occurs because the RCI is based on the entire distribution of scores; whereas, the MCID restricts the focus to those who have achieved a minimal but clinically significant change compared to those who have not. With this in mind, the MCID may be more appropriate for evaluating clinical services. The RCID adds an indicator of those who have received robust benefits from the clinical intervention.

Incidence and Trajectory of Obesity in Veterans and Service Members with TBI: A VA TBI Model Systems Study

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Objective: To describe the trajectory of body mass index (BMI) and weight classification 2-years post injury in a Veteran and Service Member cohort with TBI who are enrolled in the VA TBI Model Systems. Obesity is associated with many negative health outcomes in the general population, yet few studies have examined incidence of obesity and post-TBI outcomes. To date, two studies reported an association with pre-injury obesity and greater mortality and prolonged ventilation in the ICU setting, while a third study showed no association with obesity and motor recovery. Noted limitations with the current evidence include small samples sizes with cross-sectional analyses. Further, no study has examined BMI in Veterans or Service Members with TBI, although military samples may have different incidence and risk factors for obesity given occupational standards.

Methods: This study features a convenience cross-sectional sample and prospective design. Height and weight information were collected via self-report using standard VA TBI Model System procedures implemented in 2013 from the participant or proxy. Data collected are converted to BMI and then recoded using the World Health Organization Classification for Underweight, Normal, Overweight, and Obese (Class 1-3). Data are collected at time of injury, 1-year, and 2-years post-injury.

Results: The overall sample was primarily male (N=229;95%), white (N=175;74%) with a median age of 31 years. Mechanism of injury included motor-vehicle (49%), falls (15%), violence (20%), and other (16%) modalities with median initial GCS of 8 consistent with primarily severe injury. Cross sectional analyses reveal low incidence of obesity at time of injury (N=237; 15%) with higher proportions meeting obesity criteria at 1-year (N=148; 25%) and 2-years post-injury (N=190; N=26%). To understand trajectory of individual participants, the prospective sample (N=84) evidenced slightly higher obesity at time of injury (20%) with a slight increase at 1-year post injury (24%). Cross-tab analyses reveals n=2 of 27 normal weight participants and n=9 of 37 overweight participants were designated obese class 1 at one-year post-injury. Of N=17 obese participants at the time of injury, 2 worsened by 1 class in obesity status, 7 remained the same, and 8 improved with 5 subsequently rated as normal BMI. Only one participant was rated underweight in follow-up.

Conclusion: Incidence of obesity in this military and Veteran TBI cohort reveals lower incidence of obesity compared to the primarily civilian, general population samples. However, obesity was noticeable in sizable proportions of participants across study time points highlighting a potential comorbidity with untoward

health consequences. Trajectory data suggest participants change weight classes in both directions over time post TBI. Future studies are needed to develop risk criteria for development of obesity (and underweight) classification that may inform preventive measures in the chronic management of TBI.

INESSS-ONF Clinical Practice Guidelines for the Rehabilitation of Adults Having Sustained a Moderate to Severe TBI

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Introduction: At the request of rehabilitation programs seeking to improve the efficacy and efficiency of their services, the Quebec Institut national d'excellence en santé et services sociaux (INESSS) and the Ontario Neurotrauma Foundation (ONF) strategically partnered with two research teams to develop a clinical practice guideline (CPG) aimed at supporting the rehabilitation of adults with moderate to severe TBI.

Methodology: The Guidelines Adaptation Cycle process by Graham & Harrison (2005) was used to develop the INESSS-ONF guideline. A scoping review was first performed to search for existing CPGs published in English or French within the previous 14 years (2000-2014) that addressed multidisciplinary rehabilitation for moderate-severe TBI. Eight CPGs that met the inclusion criteria and were of sufficient quality were retained for the adaptation process. Second, clinicians, coordinators and managers of 48 TBI rehab programs were consulted in order to identify the priority topics to be addressed in the CPG, the format and desired supporting tools, as well as the preferred implementation strategies. A 2-day consensus conference was held in Montreal, Canada in November 2014 with 60 TBI experts and stakeholders to assess over 450 potential recommendations and other evidence statements classified into over 14 different topics relevant to TBI. The recommendations in the synoptic matrix were kept as is, revised or reformulated on the basis of evidence or expert opinion. New recommendations based on recent research and clinical expertise were also developed by consensus. Post-conference, the material was refined and completed with the help of additional workgroups. A voting process allowed for finalization of the main corpus of the guideline and classification of the recommendations. Indicators and tools were developed to support their utilization.

Results: Available in an interactive web format, the INESSS-ONF CPG contains 266 recommendations spanning 20 different topics grouped into two main sections: "Components of the Optimal TBI Rehabilitation System" and "Assessment and Rehabilitation of TBI Sequelae". Eleven of the 266 recommendations are identified as "fundamental" for optimal rehabilitation service delivery for this patient population, while 104 recommendations are categorized as "priority" practices to be put in place to improve service quality and effectiveness. In all, 126 new recommendations were formulated by the expert panel.

Discussion: The CPG draws its strength from the use of a rigorous methodological approach that included several consensual decision-making and consultative steps. A detailed implementation strategy is being developed based on the results of a gap analysis conducted with 44 clinical settings across the two provinces to assess the differences between current practices and the recommendations put forth by the CPG, and to determine which recommendations are priorities for implementation, the degree of feasibility and the main issues to consider.

Correlation Between Flow State and the Effects of Attention Training: Randomized Controlled Trial of Patients with Traumatic Brain Injury

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Background/Objective: Flow is the holistic experience felt when an individual acts with total involvement. When in flow, the individual operates at full capacity, and training in induction of the flow experience is thought to enhance training effect. However, additional training effects related to flow have yet to be investigated. The objective of this study was to examine the possibility of correlation between effects of attention training and flow experience for patients with attention deficit after traumatic brain injury (TBI) by randomized controlled trial.

Methods: We approached patients with chronic attention deficits after TBI who had a history of hospitalization or visited Hokkaido University Hospital. Twenty patients agreed to participate in this study, and they were randomly assigned to a flow group (2 women; mean age, 44.5 ± 11.2) or control group (2 women; mean age, 38.9 ± 7.2). We created two types of video game tasks for attention training: one inducing flow (flow task) and the other not (control task). These tasks had identical content, except that the flow task was designed to induce flow, such as balancing levels of skill and challenge, and giving quick feedback about the score. Flow group patients engaged in the flow task and control group patients engaged in the control task for 4 weeks, and they were assessed with the flow state scale for occupational tasks regularly. Three well-trained occupational therapists evaluated the training effect using neuropsychological tests at baseline, after intervention, and at 4 weeks after intervention (follow-up). In addition, therapists and patients were blinded to the treatment allocation.

Results: There were no significant differences in age, sex, severity of injury, education, duration since injury, or neuropsychological test results between groups at baseline. Flow state scale scores were significantly higher in the flow group than in the control group ($p < 0.05$). We employed two-way factorial analysis of variance (ANOVA) on neuropsychological tests with time (baseline, after intervention and 4-week follow-up) and group (flow group and control group) as factors. This analysis revealed significant main effect ($p < 0.05$) of time on neuropsychological measures of attention. In addition, we observed a trend towards the group main effect on the Paced Auditory Serial Addition Test (PASAT) and Trail Making Test (TMT) ($p < 0.1$). Furthermore, there was a significant positive correlation between the increase in the composite score of attention and the flow state scale score ($r = 0.545$, $p < 0.05$).

Conclusion: We found that participants in the flow group improved significantly more than those in the control group on neuropsychological tests of attention, and there is a significant positive correlation between attention training effects and flow state score. These results suggest that attention training for the induction of flow experience may facilitate improvement of attention.

Near-infrared Spectroscopy (NIRS) - Determining Cerebral Oxygen Carrying Capacity and Vasospasm after Subarachnoid Hemorrhage

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Introduction: Near-infrared Spectroscopy (NIRS) is a non-invasive method of measuring mixed arteriovenous (AV) cerebral oxygen content in the frontal head regions (regional cerebral O₂ saturation, RSO₂). The majority of work in this field has been to monitor cerebral ischaemia during carotid endarterectomy and cardiopulmonary bypass. However, NIRS utility in the Neuro ICU has lacked clinical evidence supporting its use. We report a case where the NIRS device demonstrated important real time physiological quantitative measurements when the patient was having vasospasm as well as sickle cell crisis.

Methods/Results: Case Report. 44 year old African American male with sickle cell disease who suffered a severe aneurysmal subarachnoid hemorrhage from a ruptured right PCOM aneurysm, modified Fisher four, Hunt Hess four. The patient suffered vasospasm of the middle cerebral arteries as detected on TCD by day 5 of hospitalization. Bedside frontal NIRS monitoring was applied. The data showed significantly low bilateral numbers with asymmetry (Right side 9-20% and left side 20-55% RSO₂ values). RSO₂ values were worse on the right side due to the combination of poor oxygen delivery (DO₂ equation) and vasospasm. However, both sides were lower than normal due to patient's low DO₂ from sickle cell disease and poor CaO₂ (arterial oxygen carrying capacity). The patient received packed red blood cell transfusion (PRBC) with normal donor hemoglobin and his bilateral RSO₂ values improved to 80% bilaterally along with treatment of his vasospasm via injection of intraventricular injection of 4mg nicardipine via external ventricular drain. Right MCA mean flow velocities decreased from 221cm/second to < 150cm/s after injection. A Swan Gans catheter noted no major differences in cardiac output among the variables. PaO₂ values on ABG remained relatively similar vs FiO₂. The patient continued to improve his neurological exam and on hospital day 18 was transferred to an outside rehabilitation center.

Conclusion: NIRS provides a non-invasive method of monitoring cerebral oxygenation that allows bedside physiologic inferences about blood O₂ carrying capacity as well as reduced blood supply during vasospasm. Future trials should target specific intervention thresholds (e.g., hemoglobin level below 10g/dL, RSO₂ values < 40%) to help prevent cerebral hypoxic-ischemic injury and clinical outcomes.

Monitoring Facial Changes in the Course of Inter-Professional, Individually Targeted Rehabilitation at the Department of Rehabilitation Medicine 1st. Medical Faculty of Charles University and General University Hospital in Prague

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Assessment of the effects of therapy and rehabilitation for facial palsy is not always clear. In our pilot study, we used the modern approach of photogrammetry for the assessment of facial motor function during mimicking of facial expression before and after rehabilitation. The study includes day care patients - day care being for patients who have suffered an acquired brain injury.

There is an ongoing comprehensive rehabilitation program, compiled for the individual patient. The rehabilitation program includes doctors, physiotherapists, occupational therapists, a clinical psychologist, a speech therapist and an education specialist. Part of the therapy is also made up of non-verbal psychotherapeutic methods: music therapy, dance therapy, art therapy. We also use music therapy as speech therapy. Rehabilitation takes place over 4-6 weeks. Our study includes patients who have suffered a traumatic brain injury and patients who have suffered a stroke, with precise indication and contraindication criteria.

The research is based on 3D surface scanning of the patient's face (during the second and last week of treatment) and a control group of individuals performing five facial expressions (neutral expression, raised eyebrows and forehead, eyes closed, lips pursed, inflated cheeks, smile). The process and the interpretation of the patients' results after scanning is time consuming, but we believe that the beginning of any scientific research project and searching for standard objective interpretational methodology is always so. Further, we believe that in the case of future patients, where we will already have a tested methodology and more experience in the interpretation of the results, the time factor will be reduced.

In this communication, we present two case reports of patients. The study was based on co-operation between the Department of Rehabilitation Medicine, General University Hospital in Prague and the 1st. Medical Faculty of Charles University in Prague and the Department of Anthropology and Human Genetics, Faculty of Science, Charles University in Prague.

An Ethical Framework to Design and Test Novel Technologies for People with Acquired Brain Injury

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Acquired brain injury (ABI) may result in lifelong disabilities, including cognitive and physical impairment. Commercially available assistive technology often doesn't match the needs of individuals living with complex disabilities. Emerging technologies offer previously untapped solutions, enabling communication, independence and rehabilitation for individuals with little or no muscle control. In designing and delivering such solutions, optimal design and efficacy of service is more likely to be achieved when those individuals who will benefit from the technologies are core to the research process, centred within the design, validation and implementation. This approach is called user centred design or participatory design.

Blending the exploration of new technologies within the lived experience of people living with ABI can bring a range of ethical challenges. Vigilance, awareness and sensitivity to the unknown emergent nature of the technologies is paramount to support safeguarding and good ethical and research governance. This present paper will illustrate the journey of creating an ethical framework and building it into the research design, obtaining ethical approval and governance, and maintaining an ethical approach while designing a multimodal brain computer interface system with associated services (exoskeletons and robotic arms) for people with ABI.

An overarching ethical framework and associated protocol was developed based on reflections of national and international best practice, legislation and policy. Obtaining ethical approval and research governance was undertaken in a phased approach over time, to ensure each stage of the design cycle and the engagement of stakeholders was reflected upon, with learning informing the next stage. Experience affirmed local ethics committees to be naïve to the types of technology, leading to a more paternalistic outlook and protectionist approach. The approach to obtaining consent from individuals with a cognitive impairment or those who cannot physically speak was of particular concern to the external committees. Reassurances, including alternative methods of engagement such as voice recording consent, proxy consent from a legal guardian and process consent were required.

Robust ethical and research governance is vital to safeguard both the participant and researcher. The reality of successfully delivering this generates a distinct stream of reflection and activity. The emergent challenges fell within three categories: the technology; the end user; and obtaining ethical approval. New technology solutions can be developed through strong collaborative approaches with healthcare professionals, people living with ABI and developers. This paper presents a framework to support the ethical engagement of people living with ABI in user centred design studies to develop technology solution that they could benefit from in the future.

Sex Differences in Affective and Cognitive Empathy Following Severe TBI

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Objectives: The ability to affectively respond to someone else's feelings (i.e., affective empathy) and understand another person's perspective (i.e., cognitive empathy) is fundamental to successful social interactions. Research has shown that people with TBI show a marked impairment in both affective and cognitive empathy when compared to controls. Wood and Williams (2008) additionally reported that a significantly greater proportion of men with TBI show impaired affective empathy than women. To our knowledge, sex differences in cognitive empathy following TBI have not been explored.

Method: 192 (145 males) adults with severe TBI completed The Interpersonal Reactivity Index (IRI), a self-report questionnaire with subscales for cognitive empathy (Perspective-Taking; PT) and affective empathy (Empathic Concern; EC). Each participant also identified an informant (e.g., spouse, friend) who completed the IRI by indicating how well each statement described the participant.

Results: Males and females did not significantly differ on demographic variables. Self-reported Empathic Concern (EC) did not significantly differ between males and females, $F(1,190) = .768, p = .38$. However, when their self-report scores were compared to IRI normative scores for men and women, significantly more women (47%) were found to be impaired for EC than men (15%), $\chi^2(1) = 20.11, p < .001$. Informant ratings for men and women did not differ for EC, $F(1, 154) = .284, p = .59$. Informant ratings of empathic concern for male participants were significantly lower than when men rated themselves, $t(114) = 3.47, p = .001$. Informant ratings for EC did not significantly differ from women's own ratings, $t(39) = 3.78, p = .39$.

Self-reported PT also did not differ between males and females $F(1,190) = 3.23, p = .07$. Twenty-nine percent of men were found to be impaired for PT, compared to 58% of women. This difference was not significant, $\chi^2(1) = 2.67, p = .10$. No sex differences were found for informant ratings of PT for men and women, $F(1, 153) = .704, p = .403$. Informant ratings for PT were significantly lower than when men rated themselves, $t(116) = 6.23, p < .001$ and also when women rated themselves, $t(37) = 3.63, p = .001$.

Conclusions: It was an unexpected outcome to find that men did not have significantly lower empathy scores than women. In fact, self-reported EC for women suggested greater impairment than the men. However, the fact that the informants of the males perceived their affective empathy to be significantly lower than the participant's self-report, suggests a possible self-awareness problem for the men. Men may perceive themselves to be more empathic than they are, and this discrepancy could create interpersonal strife. Similar ratings for EC by women and their informants may reflect that they had better self-awareness regarding their empathic concern. Theories and directions for future studies will be discussed.

The Role of Maladaptive Emotion Regulation Strategies in UK Military Veterans with Co-Occurring TBI and PTSD

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Objective: Deployment to the armed conflicts in Afghanistan (Operation HERRICK/Enduring Freedom) and Iraq (Operation TELIC/Iraqi Freedom) can adversely affect the physical and mental health of those deployed. This study explored the association between traumatic brain injury (TBI), post-traumatic stress disorder (PTSD) and the mediating effect of maladaptive emotional regulation strategies (MERS: anger and alcohol use) in UK military veterans.

Methods: This study used a cross sectional survey design. Participants (n=116) were ex-service UK military veterans seeking support for mental health difficulties from the UK based charity Combat Stress. Mean age was 46.91 years (sd= 12.66), the majority were male (ratio 114 males to 2 females) and had served in the British Army (n=90, 77.6%). Analyses used multiple regression with 10,000 bootstrap samples procedure and bias-corrected 95% confidence intervals to determine whether MERS mediated the effect that TBI severity had on PTSD severity.

Results: Seventy seven participants (66.4%) reported a history of TBI, the majority occurring during military service (n=52, 69.3%). The median duration of loss of consciousness was 2 min 30 sec (25th-75th percentile: 1 min 15 sec – 27 min 30 sec). Veterans scoring above the questionnaire cut-offs were as follows: n= 88 (74.5%) for PTSD (Impact Events Scale-Revised total >33); n=62 (56.4%) for hazardous drinking (Alcohol Use Disorders Identification Test total >8); and n= 90 (69.9%) for anger problems (Dimensions of Anger Reactions-5 total>12). PTSD severity was significantly positively associated with the predictor variables of TBI severity (r= .209) and anger (r= .400). However, PTSD severity was not significantly associated with alcohol use (r= .074). Mediation analyses revealed support for the role of anger in mediating the effect that TBI severity had on PTSD severity; the partial standardised effect size was 0.051 (small). There was no support that alcohol use mediated the effect of TBI severity on PTSD severity, the partial standardised effect size was 0.002 (small).

Conclusion: Findings contribute to the understanding of how anger may underlie the relationship between TBI severity and PTSD severity, i.e., TBI severity was positively associated with PTSD scores and this effect operated due to increased TBI severity leading to higher rates of expressed anger which in turn increased PTSD symptoms. Understanding of how anger emerges and influences PTSD has treatment implications, such as pharmacological intervention for anger driven by organic factors or psychotherapy to recognise cognitive schemas and internal experiences and their impact on behaviour. Future research using larger samples is required to further understand how the complicating factors of MERS affect outcome in veterans with co-occurring TBI and PTSD.

The Profile of Thyroid Hormones in Nigerian Patients with Traumatic Brain Injury

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Purpose: Traumatic brain injury (TBI) has an annual incidence of 200/100000 in Africa. There is little or no information on neuroendocrine sequelae following TBI in the Nigerian population. In this study we evaluated the effect of TBI on the thyroid axis and related it to outcome in Nigerian patients with TBI.

Patients and Methods: The patients with head injury presenting to the emergency department during the study period were recruited. Data on Glasgow coma score, serum T3, T4 and TSH and Glasgow outcome score were obtained prospectively in the acute phase of the injury. The data acquired was analyzed using IBM's statistical package for social sciences version 22.

Results: 115 patients were recruited. There were 98 males and 17 females (Male/Female ratio 5.8:1). 81 patients (71.7%) presented within 24 hours of injury. 61 patients had mild head injury, while 18 and 36 patients had moderate and severe head injury respectively. The serum levels of T3 were high, normal and low in 52.2%, 40% and 7.8% of patients respectively; T4 levels, the figures were 4.3%, 27% and 68.7% of patients respectively, while for TSH, they were 16.5%, 77.4% and 6.1% respectively. The T3 level was high or normal in 92.2% of patients ($p = 0.945$) T4 levels were low or normal in 95.7% ($p = 0.664$) of patients and TSH was normal in 77.4% ($p = 0.214$) There was no statistical correlation between the severity of head injury and thyroid hormone levels. Comparing thyroid hormone levels with the Glasgow outcome showed a consistent decline in the T3 levels from normal outcome to death ($p = 0.427$). T4 levels showed a similar decline. 77% and 23% of those with worst outcome had low or normal T4 respectively ($p = 0.523$). Patients with persistent vegetative state and death had Low T4 that was statistically significant $p = 0.012$.

Conclusion: TBI in Nigerian patients was associated, in the acute phase, with high serum levels of T3, low serum levels of T4 and normal serum levels of TSH; The Low serum levels of T4 were associated with poor outcome

Corpus Callosum Damage in Traumatic Brain Injury: Incidence and Role in Short-term Outcome

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Background: Traumatic brain injury (TBI) is a major public health issue, leading to 2.2 million U.S. emergency department visits annually. The corpus callosum is a known frequent site of injury. Less understood are effects of corpus callosal damage on outcomes.

Objective: To evaluate magnetic resonance imaging (MRI) evidence of injury to the corpus callosum following TBI, and its impact on short-term outcome.

Methods: The study was an analysis of MRI findings for a prospective cohort of patients with moderate to severe TBI enrolled in the Traumatic Brain Injury Model Systems (TBIMS) Database at an inpatient rehabilitation hospital. Outcome measures were incidence of corpus callosum (CC) injury; duration of post-traumatic amnesia (PTA); Functional Independence Measure (FIM™), and Disability Rating Scale (DRS), at times of inpatient rehabilitation admission and discharge.

Results: Between April 2005 and March 2013, 392 patients with TBI and available MRI imaging were enrolled in the TBIMS database. Median age was 33 years (range 16-71), 76% were male, and 85% white. One hundred and thirty (33%) had corpus callosal injury. In univariate analysis, patients with CC damage more often had higher velocity TBI causes (72% higher velocity vs. 27% lower velocity, OR 2.3, 95%CI 1.475-3.665, $p < 0.001$), were less likely to follow commands on initial presentation (15% CC damage vs. 85% no CC damage; OR 4.367, 95%CI: 2.262-8.430, $p < 0.001$), were younger (median age 25 years, CC injury vs. 36 years, no CC injury, $p < 0.001$), and were more likely to have intraventricular hemorrhage (44%, CC injury vs. 22%, no CC injury, OR 2.854, 95%CI: 1.801-4.522, $p < 0.001$.) All factors associated with CC damage in univariate tests independently predicted this damage when compared in a multivariable analysis. In multivariable analyses controlling for age, sex, injury severity (GCS Motor score < 6) and injury cause velocity, corpus callosum injury independently predicted poorer outcome by most measures assessed. In these models, at the time of rehabilitation admission, CC injury accounted for 14-point reduction in FIM™ Total score (95%CI: -20 to -9, $p < 0.001$) and a 3-point increase in DRS score (95%CI: +2 to +4, $p < 0.001$). At time of rehabilitation discharge, CC injury accounted for a 10-point reduction in FIM™ Total score (95%CI: -17 to -3, $p = 0.007$), but did not predict DRS score. Presence of CC injury also predicted a 19-day increase in PTA (95%CI: +5 days to +33 days, $p = 0.008$).

Conclusions and Relevance: Corpus callosum injury is observed acutely in 33% of moderate to severe TBI patients who received inpatient rehabilitation. Risk for CC damage is associated with higher velocity TBI causes, younger patient age, lower initial GCS Motor score, and concurrent intraventricular hemorrhage. Presence of CC injury independently predicts worse functional and cognitive outcomes. Further study of CC injury in TBI and its possible treatment are warranted.

Which Clinician Competencies are Important for Running Groups in Neurorehabilitation?

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Background and Aims: Group-based programs, such as those focusing on memory, fatigue, or coping skills, can be effective and cost-efficient components of neurorehabilitation. However, little is known about the effectiveness with which programs that have been developed in research contexts are implemented in clinical practice. A crucial aspect of clinical translation is training clinicians who can deliver evidence-based interventions competently, especially given that research suggests a strong therapeutic relationship is necessary to ensure full realisation of the potential efficacy of multiple intervention types. To date, there are no published studies identifying the competencies necessary for group facilitators to run effective groups. The aim of this study was to develop a checklist of group facilitation competencies for use in research, training, and clinical settings.

Method: As no existing similar measures were available, the Delphi method for obtaining expert consensus was adopted to identify relevant competencies. Experts were identified as clinicians or clinical researchers with a high degree of clinical experience or research expertise (i.e., had multiple relevant publications) in running groups. The importance and clarity of 17 checklist items were rated on a 5-point Likert scale by 15 experts. Items were grouped into four categories: Facilitating focused group discussion, Communication skills, Interpersonal style, and Session structure. The Delphi criterion of a minimum of 80% of experts endorsing the two highest ratings was adopted to determine the appropriateness of each item. The checklist was sent for further review until expert consensus was reached for all items. Qualitative feedback was also sought for each item, and experts were encouraged to suggest additional items they deemed important.

Results: After the first round of expert review, two items were removed due to not meeting the 80% consensus criterion. The wording of 5 further items was revised based on qualitative feedback. Two new items were also added in response to suggestions from multiple experts. In the second round of review focusing on the new and revised items, all items met the criterion for expert consensus. Further adjustments to wording of two items were made. Agreement tended to be higher for items in the Facilitating focused group discussion and Communication skills categories, whereas there was a slightly wider range of opinion on the importance and clarity of items grouped under Interpersonal style and Session structure.

Conclusions: After two rounds of review, a high level of expert consensus was reached on a new 17-item group facilitation competency checklist. The next step in the checklist's development will be to establish its inter-rater reliability. The checklist can then be used to evaluate clinician competencies in group facilitation, and explore the relationship between clinician competence and group participant outcomes.

Development of A Neurorehabilitation Specific Falls Risk Screening Tool

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Objective: To develop a falls risk screening tool (FRST) sensitive to the neurorehabilitation population.

Methods: This 18-month multisite prospective cohort study was undertaken in 3 metropolitan brain injury rehabilitation units in Australia. A convenience sample of 140 patients with traumatic brain injury was recruited. Patient data were collected at 2 discrete times: on a patient's admission to rehabilitation and after their first fall. Univariate and multivariate (backward elimination, elastic net and hierarchical) logistic regression modelling techniques were used to examine each variable's association with patients who fell. Each variable's utility on admission to rehabilitation was also tested. The resulting FRST's clinical validity was examined.

Results: Of the 140 patients in the study, 41 fell (29%). All 21 independent variables were significantly associated with fallers, however, a high proportion of 2 variables (visual impairment = 54%; dizziness = 46%) were unknown on admission to rehabilitation. Through multivariate regression modeling, 11 variables were identified as significant predictors for falls. Using hierarchical regression, 5 of these were identified for inclusion in the resulting FRST: prescribed mobility aid (such as, wheelchair or frame) (OR = 9.13), a fall since admission to hospital (OR = 4.41), impulsive behaviour (OR = 3.32), impaired orientation (OR = 3.83) and bladder and/or bowel incontinence (OR = 1.93). The resulting FRST has good clinical validity (sensitivity = 90%; specificity = 64%; area under the curve = 0.87; Youden index = 0.54) and predictive power (McFadden's R² = 0.34). The tool's clinical validity was significantly better (P = .037 on DeLong test) than the Ontario Modified STRATIFY FRST.

Conclusions: The developed tool, the Sydney Falls Risk Screening Tool, should be considered for use in neurorehabilitation populations and, due to the generic nature of its items, the generalisability to other patient populations could be considered.

BrainSTEPS Child & Adolescent Brain Injury School Consulting Program- Providing Interdisciplinary Support to Students, Schools, and Families Following Acquired Brain Injury

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Ten years ago, the Pennsylvania Department of Health began the statewide BrainSTEPS Brain Injury School Re-Entry Consulting Program. BrainSTEPS is now uniquely, jointly funded by the PA Department of Health and the PA Department of Education, Bureau of Special Education. BrainSTEPS is implemented by the Brain Injury Association of Pennsylvania. Since 2007, BrainSTEPS has provided training and consultation to thousands of students in Pennsylvania. Lessons learned will be explored as well as exploration of the state program descriptive data collected.

There are 30 BrainSTEPS Teams with 300 consulting team members who cover all students in the Commonwealth who have sustained any severity of acquired brain injury. The teams are based out of the PA Department of Education's Intermediate Units. BrainSTEPS consultants who serve on the teams represent a variety of backgrounds, but each team includes educational professionals, medical and rehabilitation professionals, as well as at least one parent. Medical rehabilitation professionals from over 15 facilities across PA serve on the BrainSTEPS teams. Together, the unique interdisciplinary BrainSTEPS Teams work to ensure students who are re-entering school following a new injury or those who have sustained a prior ABI and begin to experience learning issues in school, receive appropriate ongoing educational supports until graduation. The importance of annual monitoring to track all cognitive and/or behavioral issues over time as the brain develops is an integral, key facet of BrainSTEPS. Teams consult on student IEPs, 504 Plans, conduct medical, rehabilitation, and educational record reviews.

The PA Department of Education created a vast in-depth database for the BrainSTEPS Program consultants to track student educational supports, consultation activities, and changes over time until graduation. This is currently the only educational database following students of its kind. Teams also track their adherence to BrainSTEPS Best Practices as well as to set annual team goals that are tracked over time.

During the Fall of 2016, the Colorado Department of Education joined BrainSTEPS and is replicating the processes and best practices statewide, as well as the vast database for use in Colorado. Both states represented will discuss successes and barriers encountered to date, as well as future combined efforts.

(For reviewers: The BrainSTEPS Program has a secondary model within it that grew from an internal need for a screening measure at the school building level for students with concussions. It enables schools to manage students for the initial 4-6 weeks prior to making an official BrainSTEPS referral for higher level consultation/training purposes, for those students have not recovered from their concussion. It is called the "BrainSTEPS: Return to Learn Concussion Management Team" model. It is being submitted by Brenda Eagan Brown in a different session focused on concussion. This model will not be discussed in this session.)

Concussion Return to Learn: Two National Models Utilizing an Interdisciplinary Trifecta for Concussion Student and Classroom Management

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This presentation is intended to highlight the importance of an interdisciplinary team approach to student concussion focused on return to school/return to learn, utilizing consistent communication between the medical, school, student & family to facilitate recovery. It will focus on two phases of recovery: acute and persistent, and current research guiding practice will be discussed throughout. The presenters' current programs respectively include Pennsylvania's BrainSTEPS Return to Learn Concussion Management Team (CMT) model which is the only statewide program to have trained over 1,300 concussion school-based teams in 4 years, and the REAP Model in Colorado will be reviewed. Both models are considered leading national concussion return to learn models.

This training is guided by research and promising practices in the field. The first portion of the workshop will concentrate on the return to school progression following diagnosis. It will also highlight important academic management that must occur at school early in recovery. The importance of implementing universal systemic collaboration among interdisciplinary teams to maximize recovery within the first 4 weeks of a concussion will be emphasized. The second half of the training will focus on keeping students as actively engaged at school as possible throughout recovery by utilizing academic adjustments/accommodations that are monitored over time, maintaining the delicate balance between the need for cognitive rest while focusing on new learning, and addressing the issue of what the interdisciplinary team should consider when a student does not recover in the typical trajectory.

CMTs support students returning to the demands of school while promoting recovery. Descriptions of the roles that both Academic and Symptom Monitors perform as leaders of their CMT will be discussed. Both Academic and Symptom Monitors, evaluate data from the concussion monitoring tools weekly to make decisions regarding the need to increase or decrease academic adjustments to continue to appropriately support students over time. The Academic and Symptom monitors collect data to drive all educational decision making. Concussion management tools will be discussed as well as common issues that are encountered by schools, medical professionals, and families when students do not recover typically. Attendees will be provided with strategies to manage student concussion symptoms that impact academics, while promoting recovery, attendance, symptom resolution, and new learning.

The presenters of this session are co-leading the first National Concussion Return to Learn Consensus for the National Collaborative on Children's Brain Injuries to guide professionals working with students following a concussion. The results of the consensus will help inform the presentation content.

Cognitive-communication and Psychosocial Functioning 12 Months after Severe Traumatic Brain Injury

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Background: Cognitive-communication deficits after severe Traumatic Brain Injury (TBI) may contribute to chronically poor psychosocial functioning and problems reintegrating into the community. There has been a recent shift among the speech pathology profession to consider all aspects of the individual during assessment. One such facet is the influence of the impairment on an individual's activity and participation in their everyday contexts. The possible relationship between impaired cognitive communication skills and poor employment stability, difficulty maintaining relationships and reduced quality of life remains unclear and warrants investigation to enable clinicians and researchers to make evidence-based assessment and intervention decisions.

Objective: This study aims to explore the predictive variance and correlations of a measure of cognitive-communication skills with a measure of psychosocial outcome in persons one-year post-injury.

Participants: 36 adults (83.3% male, mean age 36.6) with severe TBI were evaluated at 12 months post injury.

Design: An observational study employing a cross-sectional design.

Main Measures: Participants' cognitive communication skills were evaluated with the Functional Assessment of Verbal Reasoning and Executive Strategies (FAVRES), Sydney Psychosocial Reintegration Scale-2 (SPRS-2) Form A – Informant version assessed psychosocial functioning.

Results: Two measures of the cognitive-communication assessment (Accuracy and Rationale scores of the FAVRES) contributed significantly to the total psychosocial functioning outcome measure (SPRS-2). Linear multiple regression analyses revealed these variables accounted for 29.1% of the variance. The same two cognitive-communication variables accounted for 24.0% and 28.6% of the Work/Leisure and Relationship specific domains of the SPRS-2 respectively.

Conclusion: Cognitive-communication ability was significantly related to overall psychosocial functioning, work and leisure, and relationship outcomes at 12 months post TBI. Findings revealed a majority of individuals were no longer receiving speech pathology intervention despite performing below normal limits on the cognitive-communication measure. Therefore, findings suggest continued speech pathology involvement in the latter post-acute stages of recovery may potentially improve social, vocational and overall psychosocial functioning. This provides argument for the role of speech pathologists in community rehabilitation teams and return to work programs for individuals following TBI. The FAVRES shows promise as a cognitive-communication assessment for the identification of treatable factors contributing to psychosocial outcomes for this population. Findings demonstrate the FAVRES is able to capture the same critical communicative demands that underlie social and vocational situations in the community. In clinical practice, speech pathologists should consider use of the FAVRES as a benchmark assessment measure, and to assist in the development of rehabilitation goals.

Post Traumatic Intracranial Hypertension (Pseudotumor Cerebri) In Mild Traumatic Brain Injury: A Specific Post Traumatic Headache Subtype; The Importance of Recognition, Evaluation and Management

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Background: Dysregulation of the osmotic gradient between the interstitial fluid, blood vessels and the brain parenchyma results in increased fluid accumulation in the brain causing increases in intracranial pressure (ICP). Cerebral edema can be a clinical manifestation of traumatic brain injury (TBI) that peaks at 36-72 hours post-injury and patients are carefully monitored for this complication. Intracranial hypertension (IH) is characterized by increased ICP in the absence of a tumor or other diseases and can result from cerebral edema, which is common after MTBI but is not considered as a consequence of mild TBI (mTBI). Intracranial hypertension secondary to a specific condition is called pseudotumor cerebri (PTC), typically associated with normal imaging findings, although subtle abnormal findings may exist in some patients. Pseudotumor cerebri is diagnosed by a lumbar puncture (LP) with a cerebral spinal fluid (CSF) opening pressure of >25 cm/H₂O in children or >20 cm/H₂O in adults. Post traumatic headache (PTH) commonly presents immediately after injury but in a subset of patients can occur 2-3 days after injury. This “secondary peak” may reflect post-traumatic cerebral edema in a select group of patients. Here we discuss a specific IH, or post traumatic pseudotumor cerebri headache (PTPTC) phenotype, found in 5 cases of mTBI and review the clinical implications.

Case Series: We conducted a retrospective case series report of 5 patients diagnosed with PTPTC in a pediatric population (5-16 years old). Patients were assessed at 2-5 days post primary injury. Symptoms that prompted hospital or clinic visits included new or changes in headache pattern (positional, intensity, “early morning”), new or change in vision (blurry, positional, diplopia), new or change in auditory function (pulsatile tinnitus, “popping”), and worsening of balance and cognition. Significant clinical findings included increases in body temperature, neck/head pain, papilledema or cranial nerve deficit (6th), and lack of coordination. We found that neuroimaging could be normal but in one case, magnetic resonance (MR) imaging showed decreased intracranial space ratio, “empty Sella”, optic nerve sheath/head enlargement, displaced cerebellar tonsils, and reduced basilar cistern space. MR venography showed diminished size of transverse or sigmoid sinus in certain patients. In every case, elevated CSF pressure was documented by LP, documented normal CSF laboratory testing and all cases improved with treatment specific to PTPTC such as acetazolamide.

Conclusions: The importance of recognizing of this specific post traumatic headache type, PTPTC, in mTBI includes: being able to tailor specific treatment with use of LP for diagnosis and relief of symptoms and treatment with carbonic anhydrase inhibitors that lower ICP, such as topiramate or acetazolamide. It is postulated that the condition of PTPTC may predispose certain athletes to a condition called second impact syndrome.

Effectiveness of Specific Post-Inpatient Brain Injury Rehabilitation Programs

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Objective: To examine the effectiveness and participant characteristics of 3 intensive post-inpatient brain rehabilitation (IR) program types compared to supported living services (SL).

Design: Retrospective before/after observational study. **Setting:** Network of residential and outpatient that includes 8 facilities in 6 states.

Participants: Data from 253 individuals with acquired brain injury in IR programs and 169 individuals in SL programs.

Interventions: IR programs, with the goal of achieving significant functional gains for participants, included Neurorehabilitation (n=161), Neurobehavioral Rehabilitation (n=57), and Day Treatment (n=38). SL programs aimed to assist participants to maintain current status in the long term.

Main Outcome Measure: Mayo-Portland Adaptability Inventory (MPAI-4).

Results: Analysis of covariance (ANCOVA) controlling for admission score, age at injury, and chronicity revealed significant differences between IR and SL programs on discharge/second assessment MPAI-4 Total T-score ($F=56.97$, $p<.001$), Ability Index ($F=49.43$, $p<.001$), Adjustment Index ($F=25.20$, $p<.001$) and Participation Index ($F=53.76$, $p<.001$). IR program participants improved about 1 standard deviation on MPAI-4 metrics. Change in MPAI-4 Total T-score represented a Minimal Clinically Important Difference for 74.6% in IR programs compared to 17.8% in SL programs ($X^2=131.85$; $p<.001$). Additional ANCOVAs revealed no differences on the MPAI-4 among the 3 specific IR program types. Comparisons of participant characteristics among the 3 IR programs showed no differences in length of stay, age at injury, age on admission, chronicity, gender, injury type, or funding source. However, there was a larger proportion of Caucasians in the Neurobehavioral program (84.2%) than in the Neurorehabilitation (64.0%) or Day Treatment (68.8%) programs ($X^2=8.21$, $p=.017$). IR program types also differed on admission MPAI-4 Ability Index ($F=8.28$, $p<.001$), Adjustment Index ($F=20.10$, $p<.001$), Participation Index ($F=7.23$, $p=.001$), and Total T-score ($F=15.08$, $p<.001$). Post-hoc Least Significant Difference (LSD) comparisons indicated greater disability for the Neurobehavioral group on the Ability Index, Participation Index, and Total T-score than for the Neurorehabilitation group which, in turn, showed greater disability on these measures than the Day Treatment Group. The Neurobehavioral group showed greater disability on the Adjustment Index on admission than the other two program types. In an additional analysis to control for chronicity more rigorously than as a covariate, 29 participants in each of the IR and SL program categories were matched on chronicity, age, and gender. Covarying initial T-score, age at injury, and log chronicity, ANCOVAs revealed significant differences between IR and SL participants at discharge for MPAI-4 Ability Index ($F=29.75$, $p<.001$), Adjustment Index ($F=16.97$, $p<.001$), Participation Index ($F=25.45$, $p<.001$), and Total T-score ($F=27.70$, $p<.001$).

Conclusions: Participants appear to be selected for specific IR programs based on type and severity of functional disability. With appropriate program selection, functional gains in the 3 IR program types are substantial and differ significantly from SL programs.

Keywords: Brain Injuries, Rehabilitation, Treatment Outcome

Folic Acid Ameliorates Hyperhomocysteinemia-exacerbated Short-term Memory Reduction after Traumatic Brain Injury

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Traumatic brain injury (TBI) is the devastating public health problem worldwide. It is accompanied with inflammation, which is a complex of different biological responses of vascular tissue to harmful stimuli. One of the important problems after TBI is a memory impairment, particularly loss of short-term memory. A greater role of cellular prion protein (PrPC) in cognition than that of amyloid beta is well known. We found that PrPC expression is increased after TBI along with enhanced deposition of an inflammatory marker fibrinogen (Fg). We also found that Fg forms a complex with Fg-PrPC in extravascular space after TBI.

Elevated blood level of Homocysteine (Hcy), called hyperhomocysteinemia (HHcy) is considered to be an independent inflammatory and high risk factor for many cerebrovascular diseases. HHcy itself is associated with increased levels of Fg. Enhanced levels of Hcy were found in TBI patients. Folic acid (FA) is known to lower blood level of Hcy. Thus, we hypothesize that HHcy exacerbates the TBI-induced macromolecular protein leakage resulting in enhanced Fg-PrPC complex formation leading to the short-term memory reduction, which can be ameliorated by treatment with FA.

Permeability of pial venules in pericontusional area formed after cortical contusion injury (CCI) was studied in wild-type (WT, C57BL/6J) and genetic mouse model of HHcy, cystathionine- β -synthase heterozygote knockout (CBS+/-) mice. Venular permeability was assessed by measuring the extravascular leakage of Alexa-fluor 647-labeled bovine serum albumin (647-BSA) in sham-operated mice or in mice with CCI using an intravital fluorescence microscopy. Deposition of Fg and formation of Fg-PrPC complex in brain cryosections from experimental mice was assessed using immunohistochemistry and confocal microscopy. Short-term memory changes were evaluated by a novel object recognition and Y maze (spontaneous alternation and two trial recognition) tests.

Pial venular permeability to 647-BSA was greater in all experimental animals with CCI compared to that in respective sham-operated mice. However, in injured CBS+/- mice the protein leakage was greater (201 ± 6 , % of baseline) than that (166 ± 9 , %) in WT animals with CCI. Treatment with FA ameliorated BSA leakage (132 ± 5 , %) in injured CBS+/- mice. Enhanced Fg-PrPC complex formation was found in WT animals after CCI compared to that in sham-operated WT mice. Increased depositions of Fg and PrPC was detected in CBS+/- mice compared to those in control WT group. The cognitive deficiency was noted in all mice groups after CCI. The greatest memory reduction, defined by Y maze two trial recognition test, was detected in CBS+/- mice with CCI (discrimination index, $DI=22\pm 2$ %). Treatment with FA improved memory ($DI=41\pm 3$ %) in CBS+/- mice with CCI compared to that in non-treated animals.

Thus, our study reveals a novel, an additive effect of HHcy in TBI-induced memory impairment, which can be therapeutically targeted in future.

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Vasculo-Neuronal Uncoupling and Cognition Impairment After Traumatic Brain Injury in Mice

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Many inflammatory and cognitive disorders are accompanied by elevated blood level of fibrinogen (Fg), called hyperfibrinogenemia (HFG). It has been shown that Fg-containing plaques are associated with memory impairment in vascular dementia and Alzheimer's disease. However, the precise mechanism of Fg effects in cognition changes are not clear. We showed that at high levels, Fg crosses vascular wall mainly via caveolar protein transcytosis leading to a complex formation with cellular prion protein (PrPC). The latter is well-known to be involved in loss of memory. We tested the hypothesis whether the deposition of Fg in extravascular space affects vasculo-astrocyte coupling in pericontusional area after cortical contusion injury (CCI).

CCI was induced in C57BL/6J mice. Fourteen days after CCI, deposition of Fg and activation of astrocytes were detected by immunohistochemistry and confocal microscopy. Astrocytes were labeled with glial fibril acidic protein (GFAP). Neuronal degeneration was detected with Fluoro-Jade and NeuN staining. Short-term memory of mice was assessed with a new object recognition test (NORT) and two Y-maze tests.

More astrocytes were activated/swollen in brain samples from mice with CCI. Deposition of Fg in vasculo-astrocyte interface defined by number of spots with co-localized Fg and GFAP after deconvolution of images, was greater (20 ± 3) in mice after CCI than after sham operation (6 ± 2). Neuronal degeneration was also found to be higher in brain samples from mice with CCI than that in samples from control mice. Discrimination ratio, assessed by NORT was lower (0.6 ± 0.03) for mice with CCI than that (0.8 ± 0.06) for sham-operated mice. Both Y-maze tests also showed a reduction in memory indicators for mice with CCI compared to those for control mice.

CCI-induced HFG increases deposition of Fg in vasculo-astrocyte interface leading to detachment of astrocyte endfeet from vessels. This causes neuronal degeneration and results in reduction in short-term memory. Our data point to the mechanism of cognition changes as a result of impaired vascular properties, and therefore, address problems related to the vasculo-neuronal dysfunction after CCI.

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Knowledge Translation: Training Everyday People To Identify and Support Individuals with Executive Dysfunction Following Brain Injury

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It is well known that many individuals after having sustained a brain injury experience difficulties managing the complexities of daily life. In fact, in a recent Ontario Brain Injury Association Impact Study 91% of nearly 600 respondents indicated that they have trouble making decisions some or most of the time. Decision making and other high level cognitive skills make up the components associated with executive functioning. Over the past decade researchers have made significant advancements in the way executive functions are understood. No longer are they viewed as individual skills, but rather as an integrated entity.

Unfortunately, despite the increases in understanding, there have not been the same advancements in the assessment and treatment of executive functioning. Typically, in the province of Ontario, Canada, executive functioning continues to be predominantly assessed through pencil and paper tasks by isolating each component. Moreover, testing occurs in the confines of a quiet office environment, with the assessor providing structure and feedback. The literature identifies this approach alone is not adequate.

Likewise, when treatment is offered it tends to mirror the assessment approach. Clinicians across rehabilitation disciplines attempt to ameliorate executive functioning deficits using worksheets and programs that are neither individualized, contextualized nor meaningful.

The challenges of knowledge translation in healthcare have been well documented. In Brain Injury rehabilitation, it is well known that a supportive environment is critical to a positive outcome for the individual. Therefore, identifying methods to educate the health care providers and more importantly the individual's naturalistic support system is critical. When treatment programs incorporate the "Participate to Learn" approach this follows best practice guidelines and knowledge translation naturally occurs because the individual's supports are able to observe functioning and strategies that facilitate participation in valued life roles.

In recent years, the authors of the I CAN Community Based Assessment of Executive Functioning have developed training methods to educate people regarding these important cognitive skills and how to observe them under real life conditions. Once these unique observational skills are developed, training proceeds to address ways of providing the appropriate levels of support within a person's natural environment. Within this context, metacognitive strategy training is incorporated as a means of generalizing to activities of everyday living.

This presentation will review the unique I CAN training approach used to incorporate current knowledge of the complexity of executive functions into real world living. Participants will gain an understanding of the advantages of sharing relevant information with everyday people regarding methods of effectively supporting those living with executive dysfunction.

Service Delivery in the Healthcare and Educational Systems for Children following Traumatic Brain Injury

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Objective: To provide a review of evidence and consensus based description of healthcare and educational service delivery and related recommendations for children with traumatic brain injury.

Methods: Literature review and group discussion of best practices in management of children with TBI was performed to facilitate consensus-based recommendations from the American Congress on Rehabilitation Medicine's Pediatric and Adolescent Task Force on Brain Injury. This group represented pediatric researchers in public health, medicine, psychology, rehabilitation, and education.

Results: Care for children with TBI in healthcare and educational systems is not well coordinated or integrated, resulting in increased risk for poor outcomes. Potential solutions include identifying at-risk children following TBI, evaluating their need for rehabilitation and transitional services and improving utilization of educational services that support children across the lifespan.

Conclusion: Children with TBI are at risk for long-term consequences requiring management as well as monitoring following the injury. Current systems of care have challenges and inconsistencies leading to gaps in service delivery. Further efforts to improve knowledge of the long-term TBI effects in children, child and family needs, and identify best practices in pathways of care are essential for optimal care of children following TBI.

Medical Co-Morbidities and Functional Decline 10 Years After Traumatic Brain Injury

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There is accumulating evidence that a subset of individuals with TBI experience progressive functional decline over the years subsequent to TBI, while others show improvement or remain static (Corrigan et al., 2012; Hammond, Grattan et al., 2004; Hammond, Hart et al., 2004; Ishibe et al., 2009; Masel & DeWitt, 2010). This evidence raises the question whether TBI should be considered a chronic health condition for those at risk of decline. A recent meeting of professionals in brain injury rehabilitation (May 2012 Galveston Brain Injury Conference) termed the persistent and deteriorating phenotypes of TBI as “chronic brain injury” (CBI). Because CBI impairs the brain as well as other organ systems it must be proactively managed as a life-long condition in order to optimize a person’s health, independence and life satisfaction.

The notion that the natural course of TBI may include delayed onset or progressive deterioration is not reflected in the typical care, services and resources currently available for individuals living with TBI. To adequately care for those with TBI, there is a need to delineate the medical, including psychiatric, problems occurring years following injury and their role in functional decline. The TBI Model Systems National Database (TBIMS NDB) provides a unique opportunity to study the prevalence of such conditions and to determine their association with functional decline.

A consecutive series was compiled of 422 individuals completing 10-year follow-ups in 6 TBIMS NDB centers. To be included in analyses participants had to have at least 2 Functional Independence Measure (FIM) or Satisfaction With Life Scale (SWLS) scores administered at years 1, 2, or 5 post-injury. The supplemental interview at 10 years post-injury included the Medical and Mental Health Co-morbidities Interview (MMHCI) which yielded the extent and chronicity of physical health and mental health comorbidities present for each individual’s lifetime, and whether diagnosis occurred before or after the index TBI that resulted in TBIMS NDB enrollment.

Random-effects models were used to determine the effects of each co-morbidity on 3 outcomes (FIM Motor, FIM Cognitive and SWLS) as a function of time. Overall, regardless of covariates or co-morbidities, significant negative quadratic relationships were found for FIM scores but not SWLS, which showed no change. Demographic, injury severity, and rehabilitation discharge characteristics were used as covariates in modeling to determine the effect of individual co-morbidities occurring over one’s lifetime. Additional models were computed that only included co-morbidities that developed after the initial inpatient rehabilitation. Highest prevalence concomitant with or following TBI and strongest relationship with functional outcomes was apparent for back pain (22%), depression (21%), anxiety (20%), sleep disorders (12%), and panic attacks (11%). Results will be presented in greater detail and implications for an evidence-based approach to disease management will be discussed.

Transpalatal Penetrating Brain Injury Caused by A Toy Arrow: A Case Report

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A case of a 6-year-old girl with a transpalatal toy-arrow injury to the brain is presented who suffered a penetrating craniocerebral injury caused by a toy-arrow in her mouth under the case of falling down. At admission she was in somnolence (Glasgow Coma Scale of 13) without hemiparesis. Computerized tomography revealed fracture of the left middle cranial fossa, intracranial hemorrhage and pneumatosis, the foreign body adjacent to cavernous sinus. The foreign body was safely removed by a left frontotemporal craniotomy as a result of detailed radiological evaluation and preoperative planning. The necessity of continuous monitoring of new environmental risks as they occur, and the requirement for the prevention of recreational brain injuries in children, is stressed.

Incidence of Associated Medical Conditions and Treatment Complications, and Impact on Outcome Following Moderate to Severe Traumatic Brain Injury

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Background: Traumatic brain injury (TBI) leads to nearly 300,000 hospitalizations in the U.S. each year. Short-term outcomes have been studied extensively for associations with patient and injury characteristics. Less understood is how associated medical conditions, present concurrently or as complications of treatment, may influence recovery.

Objective: To assess incidence of acutely occurring associated medical conditions and treatment complications on outcome for survivors of TBI.

Methods: Patients with moderate to severe TBI enrolled in the TBI Model Systems (TBIMS) National Database (NDB) were evaluated. Medical conditions, identified by ICD-9 code recorded during the acute hospital phase of treatment, were selected and grouped in a total of 75 Healthcare Cost and Utilization Project (HCUP) categories, or groupings of categories. Outcome measures include FIM™ and Disability Rating Scale (DRS) at the time of inpatient rehabilitation discharge, and rehabilitation length of stay (LOS). The predictive effect of categorized conditions on outcome was assessed using general linear regression, controlling for: age, sex, injury cause (high vs. lower velocity), injury severity (Glasgow Coma Scale motor score <6), presence of intracranial mass effect, and presence of subcortical injury. A Bonferroni correction of 0.0007 was used to determine statistical significance.

Results: Between May 2007 and December 2013, 3,686 patients in the NDB with complete data were included in the analysis. Mean age was 46.1±20.6 years, 72% were male and 66% white. Forty-four percent of injuries were caused by high velocity events, 46% of patients followed commands at initial presentation, 20% had subcortical damage, and 40% intracranial mass effect. The most frequently co-occurring medical conditions were: adult respiratory failure (42%), other nervous system disorder (42%), crush injury (35%), fluid and electrolyte disturbance (32%), pneumonia (19%), dysrhythmia (16%), other bacterial infection (8%), and septicemia (6%). Predictors of worse functional outcome in multivariable models, with degree of effect on FIM™ total score, include: spinal cord injury (-10.5); paralysis (-9.5), coma (-8.9), device complications (-8.9); pneumonia (-7.5), septicemia (-7.5), other bacterial infection (-6.5), and gastrointestinal (GI) disorders (-5.0). Among these conditions, respiratory failure and pneumonia were associated with worse outcome by all measures. Conditions predicting improved outcome and effect on FIM™ total score included: headache or migraine (+9.9), attention deficit disorder (+7.2), alcohol-related disorders (+5.7), and substance-related disorders (+3.9).

Conclusions: Co-occurring medical conditions and treatment complications are common in TBI and can significantly impact outcome, independent of patient characteristics, injury severity, and neuroanatomic features. These conditions include spinal-cord injury, paralysis, and GI dysfunction. Treatment complications including pneumonia, respiratory failure, device-related factors, and septicemia, predict poorer outcomes.

The findings suggest co-occurring conditions, and hospital complications warrant incorporation in prognostic models for TBI, and attention during acute treatment for improvement of outcome in these severely injured patients.

Incidence of Post-decompressive Craniectomy Hydrocephalus after Traumatic Brain Injury: Is Duraplasty a Risk Factor?

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Introduction: Decompressive craniectomy (DC) is considered as a life-saving procedure for treatment of refractory raised intracranial pressure (ICP). Duraplasty with either autologous pericranium or artificial dura is the accepted standard after bone flap removal and/or hematoma evacuation. Incidence of hydrocephalus after DC ranges from 10%-50%. Multiple risk factors have been proposed for the development of post-DC hydrocephalus but duraplasty as a risk factor has not yet been studied.

Methods: 2 ½ year retrospective analysis. 2 groups-duraplasty(group I), no duraplasty(group II). Exclusion criteria-DC performed for non-traumatic etiologies, bifrontal procedures, patients who expired in hospital/ those without atleast 8 weeks of follow-up and mild-moderate ventriculomegaly. Demographic, clinico-radiological and preoperative details, postoperative course, incidence and treatment of hydrocephalus.

Results: After exclusion, 37 cases (groupI-13, groupII-24) were analyzed. Mean age was 39.2 years (range 17-69 years). Males predominated. Majority were of severe head injury. Acute subdural hematoma was the commonest finding. Overall incidence of hydrocephalus was 24.5% (9/37); on subgroup analysis-group I- 6/13 (46%) and group II-3/24 (12.5%). This difference was statistically significant. Other parameters such as type of hemorrhage, severity of head injury, intraventricular hemorrhage, midline shift, operative duration, blood loss, infectious sequelae and craniectomy margin from the midline were not significant for occurrence of hydrocephalus. All had a minimum of 12 weeks of follow-up.

Conclusion: Hydrocephalus is a common occurrence noted after decompressive craniectomy. Ours is the first study to document the correlation of duraplasty with hydrocephalus after DC. Stronger evidence is needed from future randomized studies to confirm these findings

Outcome of Traumatic Brain Injury in Elderly Population: An Indian Perspective

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Introduction: Traumatic brain injury (TBI) is one of most common causes of morbidity and mortality worldwide. The increasing ratio of the elderly because of improved medical facilities has contributed to the increased incidence of brain trauma in this subset of population. Authors put forward their institutional experience in dealing with TBI in this age group.

Materials and Methods: A 2½ -year retrospective analysis of 73 consecutive patients aged ≥ 65 years admitted with TBI at our university hospital was performed. The following were excluded-concussion injuries, chronic subdural hematomas, patients discharged against medical advice and declared dead soon after arrival (within 6 hours). Mode of injury, clinico-radiological features, management and outcomes were analysed. Glasgow outcome scale (GOS) was used to assess outcome.

Results: Males predominated (82%) and road accidents (54%) and trivial domestic falls (44%) were common injury modes (54%); however, constituted a significant proportion (44%). Mean age was 72.1 years (range 65-97 years) and 20 were aged ≥ 75 years. Co-morbid illnesses were present in 40 (54%) cases. There were 37 mild, 18 moderate and 18 severe head injuries (HI). On radiology, contusions (basifrontal and temporal) constituted the majority, followed by acute subdural hematoma (aSDH). Subarachnoid haemorrhage was noted in 11 cases. Fifty-five (75%) cases were managed conservatively while 18(25%) underwent surgery. There were 7 deaths (9.5%)-of these, 6 were of severe (85%) and 1 moderate (15%) HI. Forty six patients had GOS 5, 8 had GOS 4, 2 had GOS 3, 10 had GOS 2. Overall poor outcome was 26%, while it was 45% in patients aged >75 years. The poor outcome rate in severe HI for the entire elderly cohort was 83% (15/18) and was 100% (7/7) for the very elderly patients.

Conclusions: Traumatic brain injury in elderly is quite different from young patients. Domestic falls are relatively common modes of injury. Contusion and subdural hematomas are seen in majority while extradural hematoma is uncommon. Most of them respond to conservative management. Age ≥ 75 years, severe HI, presence of contusion and aSDH are poor prognostic factors. Benefit of surgery in severe HI is unlikely and surgery needs to be considered judiciously, keeping in mind the cost-effectiveness and fate of caregivers, especially in developing countries.

Steroids and Traumatic Brain Injury: Does it Necessarily Mean Poor Outcome?

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Background: Brain edema is a common finding noted after TBI that may result in increased intracranial pressure (ICP) and neurological deterioration. Based on spinal cord injury trials, there existed a controversy as to whether or not to use steroids in patients with traumatic brain injury. However, the 2004 CRASH multicentric trial concluded that steroids are contraindicated in head injury. We describe 2 cases of head injury with delayed edema managed with steroids.

Methods: Various experimental studies were analyzed to document the mechanism of brain edema formation and possible role of steroids. It has been experimentally proven that brain edema is initially cytotoxic and later vasogenic in nature. Also, multiple mediators are released after brain trauma that alter the membrane permeability. Hence, theoretically, steroids should also be able to counteract the vasogenic/inflammatory edema after TBI and reduce ICP.

Hospital records were retrieved to analyze our cases.

Results: 2 males, aged 22 and 35 years were admitted with moderate head injury after a road traffic accident. They initially improved with conservative treatment but had a delayed deterioration after 7-10 days. Imaging showed worsening of brain edema. Dexamethasone was started in tapering doses for 5-7 days. Both had excellent outcome. Till date, in all studies pertaining to steroids in TBI, steroids (either dexamethasone or methylprednisolone) were given in the acute period (mostly given within 6-8 hours) of trauma, during which the edema in fact is cytotoxic in nature. Also, the dosages used have been very high.

Conclusions: We are of the opinion that steroids may have a role in delayed brain edema after TBI. The timing of steroid usage and dose of steroids are important key aspects that might determine its efficacy in TBI.

Decomposition of Leg Motions During Over Ground Walking in Individuals with Traumatic Brain Injury

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Walking is an essential activity of daily living in humans. Successful performance of this task requires precise temporal coordination of lower extremities, composed of several joints and segments. Motions at the ipsi- and contralateral leg joints must be initiated, continued and terminated simultaneously with switching activity at certain phases of the gait cycle to allow smooth body progression in the desired direction without loss of balance. The ability to coordinate movements can be affected after a traumatic brain injury (TBI). The purpose of the present study was to investigate the effects of brain injury on inter-joint coordination of the legs during over ground walking. Ten individuals with TBI (7 males; mean age \pm SD standard deviation, SD, 45.2 \pm 12.78 years, ranging from 26-66 years of age), and 10 healthy sex- and age- matched participants (mean age \pm SD, 44.0 \pm 14.43 years, ranging from 25-66 years of age) without known neurological, orthopedic, or cognitive deficits participated in the study. Participants with TBI presented with some degree of ataxia, as well as postural and gait abnormalities, with their clinical test score ranged: a) 2–18 points (mean \pm SD: 7.9 \pm 6.1 points) on the Ataxia Test by Klockgether; b) 45–54 points (mean \pm SD: 51.0 \pm 3.6 points) on the Berg Balance Scale and c) 14–27 points (mean \pm SD: 22.8 \pm 4.3 points) on the Functional Gait Assessment Test. All participants walked a 12-m distance at self-selected speed in three experimental conditions: normal walking without any additional task; walking with the narrow base of support, and walking while holding a cup full of water. Participants' movements during walking were recorded with a 12-camera Vicon T160 Motion Capture system at 100 Hz with 39 markers, placed according to the Plug-in-Gait Full Body Model. Inter-joint leg coordination was analyzed as the percentage of gait cycle during which the leg motion was decomposed, with 0% indicating simultaneous motions at the two joints (i.e. hip-knee, knee-ankle, and hip-ankle) or 100% indicating motion of only one joint at the time. Decomposition was calculated for each pair of joints and for the left and right leg separately. Participants with TBI showed greater decomposition indices than control individuals for all joint pairs ($p < 0.01$). The inter-joint coordination was even more affected in participants with TBI, when walking was challenged by narrowing a base of support or holding a cup. Results may indicate impaired mechanisms of inter-joint coordination following TBI or presence of compensatory strategies to improve walking. These abnormalities should be taken into consideration while planning physical therapy programs for individuals after brain injury.

Management and Outcome of TBI Patients in the State University Hospital of Haiti During a 2 Years Period

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Objectives: Traumatic brain injury is one of the leading causes of death and disability worldwide. In developing countries, the mortality rate is even higher due to non-availability of material and human resources. In this study, we investigated the effects of lack of appropriate resources for the management of TBI patients on their outcome.

Methods: A cross-sectional and retrospective study was realized in a single institution: State University Hospital of Haiti. We reviewed the charts of TBI patients from the department of surgery between January 2013 and December 2014. The relationship between death rate and availability of resources for standard care was assessed.

Results: The patients were divided into two groups according to availability of appropriate resources for standard management. Group I comprises the patients who received standard care; Group II was made of patients who did not. 8 patients out of a total of 43 constituted the group I. 75% of them were discharged from the hospital, 25% died. From the 35 patients of the group II, 91 % of them died; only 9% were discharged from the hospital. The difference was highly significant according to Chi-square statistic (= 17.365 superior to the critical value of $\chi^2 = 3.8$ for $\alpha = 0.05$). The most common cause of injury was motor vehicle accident (70%). 81% were male and the majority of the patients were between 20 and 40 years old.

Conclusion: The availability of resources significantly reduced the risk of mortality in TBI patients at the State University Hospital in Haiti. A politic to reinforce the hospitals by supplying them with appropriate materials and trained personals will have a positive impact on the outcome of the patients with TBI.

The Neurotrophic Hypothesis of Depression Revisited

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Brain-derived neurotrophic factor (bdnf) is an important factor in brain plasticity as it has been shown to induce axonal sprouting and long term potentiation of synapses. Therefore it plays an important role in brain injury recovery. However, bdnf is also implicated in many psychiatric disorders such as depression. Since patients with brain injury often develop depression, it is important to better understand the role of bdnf in the etiology of depression. The neurotrophic hypothesis of depression was postulated as a working model for this. It states that stress reduces bdnf availability which consequentially causes depression due to a lack of neuronal plasticity. Serum bdnf levels are indeed consistently found to be lower in depressed patients compared to healthy controls and in short open-label antidepressant treatment trials the bdnf levels were found to be higher post-treatment than pre-treatment. However, many previous studies were relatively small, precluding the possibility to correct for potential confounding. We performed several studies to identify potential determinants of peripheral bdnf measurements (1,2) and used these variables to correct for potential confounding. In a large naturalistic cohort of patients (n=2981) with depression and/or anxiety as well as healthy controls we analyzed the cross-sectional associations between depression and bdnf (3). Next we used longitudinal data in the same sample to test the temporal assumptions of the neurotrophic hypothesis of depression (4).

Although we did find a statistically significant association between depression and lower bdnf in our cross-sectional data, our longitudinal analysis reveals that it is more likely that bdnf serum levels are lower as a result of depression than that they represent an etiological factor for the illness. Furthermore we found a decrease in bdnf after exposure to stress, but the decrease was most profound in patients with chronic depression. These findings show that the neurotrophic hypothesis of depression is more complex than previously assumed, as it is in sharp contrast to the original assumptions of the neurotrophic hypothesis. Nevertheless, they also implicate that brain recovery can be seriously impeded by a comorbid depressive disorder due to diminished neuroplasticity because of a decrease in the availability of bdnf.

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Repeated Transcranial Direct Current Stimulation of The Posterior Parietal Cortex in Patients in Minimally Conscious State: A Sham-Controlled Randomized Clinical Trial

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Background: We assessed the effect of transcranial direct current stimulation (tDCS) targeted to posterior parietal cortex in patients in minimally conscious state (MCS).

Methods: In a randomized double-blind sham-controlled crossover study, MCS patients at least 1 month after acute traumatic or nontraumatic insult received one sham and one real tDCS session (2mA during 20 minutes once a day for five days) in a randomized order separated by five days of washout over the posterior parietal cortex. Coma Recovery Scale-Revised (CRS-R) assessments were performed directly on enrollment, before the first session and after each real and sham tDCS as well as five days later. Follow-up outcome data were acquired 1, 3, 6, 12 months after inclusion using the CRS-R.

Results: 33 patients were included (interval 6±5 months; 20 traumatic). We found a treatment effect after 5 days of stimulation ($p=0.012$; effect size: 0.31). The effect did not last for 5 days after the end of the stimulation ($p=0.135$). We identified 9 (27%) tDCS-responders (i.e., showing new sign(s) of consciousness that was never observed before, lasting at least 5 days after the end of the stimulation).

Conclusion: 5 days of tDCS over the posterior parietal cortex has a small and short-lasting beneficial effect on consciousness in MCS.

Classification of Evidence: This study provides Class I evidence that 5 days of tDCS of the posterior parietal cortex has a small and short-lasting beneficial effect on consciousness in MCS.

Clinical Trial register: ClinicalTrials.gov NCT02702362

Controlled Clinical Trial of 4 Weeks of Home-Based tDCS In Patients with Chronic Minimally Conscious State

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Objectives: A recent study showed that anodal transcranial direct current stimulation (tDCS) applied to the left dorsolateral prefrontal cortex (LDLPF) transiently improves the level of consciousness in 43% of severely brain injured patients in minimally conscious state (1). Even if those first results were promising, after a few hours, patients came back to their initial states. Previous studies on pain showed that repeated stimulation increase the lasting of the effects (2). Therefore, we decided to test the potential long term effects of repeated tDCS in MCS patients. Our second aim was to evaluate the feasibility of home-based stimulations.

Methods: In this double-blind cross-over sham-controlled experimental design, patients received two sessions of repeated (5 days per week during 4 weeks) tDCS, either anodal or sham in a randomized order, with a washout period of 8 weeks in between (figure 2). Patients' relatives or caregivers were taught how to use the tDCS device. Note that the device was made for an easy use with fixed parameters and registered the number and time of stimulations delivered in order to controlled the compliance. The LDLPF cortex was stimulated during twenty minutes in 24 MCS patients (age: $40,5 \pm 15$ years old; time since injury: $7 \pm 7,2$ years; 13 TBI). Consciousness was assessed by JFK Coma Recovery Scale Revised (CRS-R) at baseline, after the first session, as well as 8 weeks later to assess the long term effects. Mann Whitney U test was performed to assess treatment effects at 4 weeks and at follow-up.

Results: A treatment effect was observed for the comparison between CRS-R at baseline and after the 4 weeks of tDCS ($p=0.026$). A trend was identified 8 weeks after the end of the stimulations ($p=0.065$). When comparing pre versus post stimulation, a significant improvement was observed after 4 weeks of stimulation ($p=0.022$) as well as at follow-up ($p=0.011$). The compliance was good ($90 \pm 15.5\%$). We did not observe any side-effect (i.e., sign of pain, sign of seizure, complication).

Conclusion: 4 weeks of home-based tDCS significantly improve responsiveness of patients in MCS. The absence of adverse events and the good compliance of the tDCS device showed that this technique is safe and can be used in rehabilitation programs or by patients' relatives at home as a daily care.

Characterization of High Speed and Biaxial Stretch as in Vitro Models of Traumatic Brain Injury on the Blood-Brain Barrier

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Traumatic brain injury (TBI) is one of the major causes of disability in the United States. It occurs when external mechanical forces induce brain damage as a result of impact, penetration, and/or rapid acceleration/deceleration that cause deformation of brain tissue. TBI is also associated with alterations of the blood-brain barrier (BBB), a structure that consists mainly of brain endothelial cells (BECs) and protects brain tissue from substances circulating in the blood. Due to the high incidence and drastic consequences of TBI, it is important to understand the critical events that accompany damage in order to develop effective treatment approaches. Using primary rat BECs as an in vitro BBB model, the effects of two different types of stretch that mimic aspects of TBI were characterized. Deformation due to biaxial stretch (BS) was achieved at 5, 10, 15, 25 and 50% by infusing pressurized gas into flexible bottom culture plates using a commercially available system. Deformation due to uniaxial high-speed stretch (HSS) at 5, 10 and 15% was achieved by moving a linear actuator, coupled to a polydimethylsiloxane chip on top of a silicone membrane at a strain rate of 100 s⁻¹. Live/dead cells, LDH release, caspase 3/7 staining and tight junctions (TJ) protein expression were evaluated 24 hours after a single stretch episode. BS induced a deformation-dependent increase in LDH release, cell death and activation of caspase 3/7, suggesting the induction of apoptosis. Interestingly a low percentage of stretch increased the expression of TJ proteins, whereas high percentage decreased the expression. Meanwhile, HSS increased LDH release only at 15% stretch and increased cell death at 10 and 15% stretch. Once again, a low percentage of stretch increased the expression of TJ proteins. In summary, some of the events that occur in the BBB after TBI were successfully replicated in vitro using BS and HSS and the severity of the TBI produced in vitro depends on the degree and orientation of cellular deformation. These data support the use of BS and HSS as valuable tools in the study of TBI in vitro, by defining stretch intensities. These methods may also be useful in evaluating potential drug treatments for this condition.

Moderate Traumatic Brain Injury Produce Blood-brain Barrier Damage Modulated by Tight Junction Proteins

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Traumatic brain injury (TBI) remains one of the major causes of death and disability. Due to the heterogeneity of its causes, the events that occur after TBI can be quite varied and are not well understood. Regardless of the cause, deformation of the brain tissue leads to neuronal, glial and endothelial cell death as well as other cellular and molecular responses, including changes in blood-brain barrier (BBB) permeability. Understanding the events that occur after TBI is important in the development of therapeutic approaches. The aim of this study is to evaluate the effects of mild and moderate TBI on the BBB in mice using the weight drop method. Mice were anesthetized using isoflurane and placed on a soft foam pad. An acrylic tube was placed directly above the head of the mouse and a 50 gram weight was dropped onto the mouse head from either 30cm (mild) or 120cm (moderate) height within the tube. 24 hours after a single TBI episode BBB permeability was evaluated using the Evans blue method and by quantifying the plasma concentrations of the glial-specific protein S100 β . The expression of the tight junction proteins zonula occludens-1 (ZO-1) and occludin was evaluated by western blot. Mild TBI did not affect the Evans blue extravasation, S100 β concentration and did not change the expression of the tight junction proteins; however, moderate TBI significantly increased the Evans blue extravasation and the plasma concentrations of S100 β , indicating an increase in BBB permeability. This effect was related to a decrease in the expression of ZO-1 and occludin. In summary, we demonstrated that moderate TBI increases BBB permeability due to a decrease in the expression of tight junction proteins using the weight drop model of TBI. Further studies are necessary in order to understand the implication of the BBB damage to the neuronal and glial cells. This model can be used as a tool to test potential treatments that can protect the BBB after TBI.

Fatigue After Traumatic Brain Injury Is Linked to Altered Striato-Thalamic-Cortical Functioning

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Mental fatigue is a common symptom in the chronic phase of traumatic brain injury. Despite its high prevalence, no treatment is available for this disabling symptom and the mechanisms underlying fatigue are poorly understood. Some studies have suggested that fatigue in traumatic brain injury and other neurological disorders might reflect dysfunction within striato-thalamic-cortical loops. In the present study, we investigated whether functional magnetic resonance imaging (fMRI) can be used to detect chronic fatigue after traumatic brain injury (TBI), with emphasis on the striato-thalamic-cortical loops. We included patients who had suffered traumatic brain injury ($n = 57$, age range 20–64 years) and experienced mental fatigue >1 year post-injury (mean = 8.79 years, SD = 7.35), and age- and sex-matched healthy controls ($n = 27$, age range 25–65 years). All participants completed self-assessment scales of fatigue and other symptoms, underwent an extensive neuropsychological test battery, and performed a fatiguing 27-minute attention task (the modified Symbol Digit Modalities Test) during fMRI. Accuracy did not differ between groups, but reaction times were slower in the traumatic brain injury group ($p < 0.001$). Patients showed a greater increase in fatigue than controls from before to after task completion ($p < 0.001$). Patients showed less fMRI blood oxygen level–dependent activity in several a priori hypothesised regions (family-wise error corrected, $p < 0.05$), including the bilateral caudate, thalamus, and anterior insula. Using the left caudate as a region of interest and testing for sensitivity and specificity, we identified 91% of patients and 81% of controls. As expected, controls showed decreased activation over time in regions of interest – the bilateral caudate and anterior thalamus ($p < 0.002$, uncorrected) – whereas patients showed no corresponding activity decrease. These results suggest that chronic fatigue after TBI is linked to altered striato-thalamic-cortical functioning. The high precision of fMRI for the detection of fatigue is of great clinical interest, given the lack of objective measures for the diagnosis of fatigue.

Efficacy and Safety of Amantadine for Behavioural Problems Due to Acquired Brain Injury: A Systematic Review

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Introduction: Acquired brain injury, especially frontal lesions, often lead to behavioural consequences with severe impact. Amantadine is used to reduce behavioural problems in acquired brain injury, with clinical experience suggesting a positive effect. However, the use of amantadine to reduce behavioural problems has not been established as evidence-based medicine.

Objective: To systematically review the literature on the effectiveness and safety of amantadine on reduction of behavioural problems (aggression/agitation, apathy, dysexecutive syndrome), increased participation and increased quality of life, in patients suffering from acquired brain injury.

Search: Systematic search in PubMed/EMBASE/CINAHL (last search 8-4-2016), keywords: brain injury, prefrontal cortex, neurobehavioral manifestations, amantadine, participation, behavioral disorders, quality of life.

Selection: Data selection and extraction was done by two independent reviewers.

Inclusion: Adults with acquired brain injury, use of quantitative outcome measurements on behavior/ participation/ quality of life. **Exclusion:** neurodegenerative diseases and disorders of consciousness. Quality of included randomized studies was assessed using CONSORT criteria or Single Case Experimental Design Scale by Tate.

Evaluation and Results: Of 571 records identified, 19 were assessed full-text. Two articles, found by hand search of the references of excluded reviews, were additionally assessed full text. Nine articles were selected (3 case-reports/series, one prospective cohort study, one retrospective study, one single case experimental design, 3 randomized controlled trials). The two high quality randomized controlled trials are conflicting about the effect of amantadine on irritability, one showing positive and one showing no effect. One randomized controlled trial measuring executive functioning and agitation without effect of amantadine was of low quality. A Single Case Experimental design of low quality showed positive results on agitation and apathy. A prospective cohort study of moderate quality showed a positive effect on executive functioning. Four non-randomized studies measuring effect of amantadine on behaviour were of poor quality (positive effect in 1 study measuring aggression/agitation, positive effect in 1 study measuring apathy, positive effect in 2 studies measuring executive functioning, no effect in 1 study on apathy and no effect in 1 study on dysexecutive syndrome). QoL and societal participation were not measured in the included studies. Amantadine was well-tolerated.

Conclusion: Results of good quality studies are inconclusive. In low quality studies weak evidence is found for a possible effect of amantadine on several behavioural domains. QoL and participation were not addressed. No unknown side effects emerged in the included studies. High quality experimental studies are

needed to learn more about the effect of amantadine on behavioural problems, but RCT's are difficult to perform in this heterogeneous patient group. Currently we are conducting a series of single case experimental designs.

Chronic Cerebrovascular Abnormalities in A Mouse Model of Repetitive Mild Traumatic Brain Injury

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Repetitive mild traumatic brain injury (r-mTBI) is a risk factor for development of Chronic Traumatic Encephalopathy (CTE), a disease characterized by Tau pathology throughout the cortices, and often co-presenting with conditions such as Alzheimer Disease (AD). It has been well documented that mild to severe TBI can result in transient reductions in Cerebral Blood Flow (CBF), with severe injuries often accompanied by presence of varying degrees of vascular pathology post-mortem. Aberrant CBF readings precede gross Amyloid pathology in AD patients, suggesting that hypo-perfusion is key in the pathogenesis of conditions such as CTE and AD, for which r-mTBI is a pre-disposing factor. We have herein expanded on our previous animal model of r-mTBI, showing robust neuroinflammation and pronounced spatial memory deficit in wild type mice as late as 18 months post-injury. We now show this pathology and concomitant behavioral phenotype to be emulated in a separate animal model of r-mTBI, described herein, and accompanied by chronic impairment of global CBF, and altered expression of cerebrovascular markers. These results are the first to demonstrate chronic cerebrovascular dysfunction in the pathogenesis and evolution of r-mTBI-induced illness, and validate this model for investigation of CTE.

Curious About Concussions: An Evaluation of an Education Session about Concussion and Mild Traumatic Brain Injuries Management

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Introduction: Education can be a powerful influence on health outcomes. Without the proper translation from knowledge sources children and adolescents recovering from a concussion or mild traumatic brain injury (mTBI) and their caregivers frequently misunderstand its management and outcomes. This results in increased apprehension about the potential persistent somatic, sleep-related, cognitive and affective symptoms associated with these injuries. Previous literature has shown that the provision of proper education and reassurance soon after an injury reduces post-concussive symptoms in adults. There is little evidence available about the effectiveness of educational strategies using a developmental approach in improving outcomes for children and adolescents. We developed a one-time education session for children who had recently sustained a concussion with their parents. Our goal was to determine if the session increased knowledge about concussion and reduced parental concerns to act as a preparatory step to a larger trial to evaluate the impact of the education program on child and parent outcomes.

Method: The study involved a non-randomized, prospective cohort study of recently injured youth and their families in order to determine the feasibility and effectiveness of a 20-minute education session for concussion and its management. Sessions were conducted in small groups at the Alberta Children's Hospital, Calgary, Alberta. The educational resources and primary outcome measure (self-assessment questionnaires) were designed by the study team, healthcare providers, patients and their families. The self-assessment Likert questionnaires were administered before and after each education session, and consisted of 5 questions assessing knowledge and concerns about concussions. Statistical analysis was done using IBM SPSS Statistics (Version 24) with Kolmogorov-Smirnov, Wilcoxon signed rank and paired t-tests.

Results: Eighty-five participants (58 adults, 27 teens) completed pre- and post-session questionnaires. The children and adolescents (12.66 ± 2.90 years, 30.5% males) were between 11.39 and 19.76 days post-injury at the time of the session. Participants expressed having difficulties coping with post-concussion symptoms (34.9%) and with daily activities (44.2%). Knowledge increased significantly from pre- to post-session about return to learn guidelines (adults: $z = 6.219$, $p < 0.001$; teens: $z = 4.149$, $p < 0.001$) and return to play guidelines (adults: $z = 6.207$, $p < 0.001$; teens: $z = 3.781$, $p < 0.001$). Overall, parents reported decreased concerns about the impact of concussion on their children ($z = 3.898$, $p < 0.001$).

Conclusion: The results show the potential of education sessions to increase knowledge about concussions and to reduce parental concern. With these observed outcomes, the next step of this project is to evaluate the designed program's influence on child and parent outcomes via a randomized trial of the intervention.

History of Abuse and Traumatic Brain Injury (TBI) In Female Offenders

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Purpose: To examine and explore the link between abuse and TBI in an adult female offender sample.

Background: Traumatic Brain Injury (TBI) is now recognised as a significant issue among offender populations. Significant gender differences have been observed between male and female offenders, with females more likely to have experienced a TBI prior to incarceration (Colantonio et al., 2014). Despite female offenders reporting a higher mean age for their first TBI than males (Colantonio et al., 2014; Fishbein et al., 2014) past research has focused primarily on childhood abuse (Brewer-Smyth & Burgess, 2008) with limited examination of domestic abuse.

Method: A cross-sectional study was conducted with 65% (n=29) of adult female offenders in Northern Ireland. TBI prevalence and severity were assessed using the Brain Injury Screening Index (BISI) while childhood abuse and domestic abuse were examined using the Childhood Trauma Questionnaire and the Abusive Behaviour Index. A demographic questionnaire gathered information on past mental health diagnoses, alcohol abuse, and substance abuse, as well as asking participants to judge if they believed they had a brain injury. Pearson's correlation explored the relationships between TBI scores and measures of abuse.

Results: The prevalence of TBI within the sample was 72%. Of those with a past TBI (n=21), 38% reported having 5 or more injuries, yet only 29% believed they had sustained a brain injury. Forty five percent of participants reported experiencing childhood physical abuse and 65% reported being assaulted by their partner, suggesting high rates of past abuse within the sample. TBI presence was correlated with domestic abuse ($p=.01$), mental illness ($p=.023$), and alcohol abuse ($p=.031$).

Conclusions: Despite the high prevalence rate, many women failed to acknowledge the presence of their brain injuries, suggesting that such injuries may go unidentified and untreated. Improved screening and early identification is needed to ensure that women with TBI can access appropriate care pathways. Additionally, this study highlights the prevalence of abuse within this sample.

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Post-Traumatic Brain Injury (TBI) Cannabinoid Receptor Expression Downregulation in Basolateral Amygdala of Alcohol-Drinking Rats

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Brain injury triggers release of the principal endogenous cannabinoids, 2-arachidonylglycerol (2-AG) and anandamide (AEA). The endocannabinoid system (ECS) modulates synaptic plasticity, particularly through retrograde signaling mediated by the cannabinoid 1 receptor (CB1R). CB1R-mediated retrograde signaling dampens pre-synaptic neurotransmitter release, suggesting its potential role in suppression of excitotoxic amino acid (i.e., glutamate) release. In addition, CB2R agonists have been shown to be effective suppressors of inflammation. Thus the ECS represents a novel therapeutic target to decrease excitotoxicity and ameliorate neuroinflammation resulting from TBI. Previous work from our laboratory has shown that post-TBI inhibition of monoacylglycerol (MAG) lipase, a major enzyme involved in 2-AG degradation, with JZL184 reduces neurobehavioral deficits (including anxiety-like behavior), suppresses neuroinflammation, and attenuates neuronal hyperexcitability in the region of injury. In addition, our studies show that the post-TBI period is associated with increased alcohol self-administration and progressive ratio responding (an index of the motivation to drink). These findings suggested that ECS dysregulation may be an underlying mechanism for neuroinflammation, neuronal hyperexcitability, and neurobehavioral dysfunction. Whether the ECS receptor expression is modulated following TBI had not been previously examined.

The aim of this study was to determine the impact of TBI on CB1R and CB2R expression in the basolateral amygdala (BLA) of alcohol-drinking animals. Briefly, adult male Wistar rats were trained via operant conditioning to self-administer alcohol so that post-TBI alcohol intake could be assessed. Following the establishment of stable alcohol preference, the rats (n=6) underwent a 5-mm left, lateral craniotomy. Mild-to-moderate TBI (25ms, 30 PSI) (n=3) or sham injury (n=3) was delivered three days later via lateral fluid percussion over the sensorimotor cortex. Brains were collected ten days post-TBI, and specific brain regions, including the site of injury, cingulate cortex, and central (CeA) and basolateral amygdala (BLA), were dissected and frozen until analyzed. CB1R and CB2R protein expression was determined by Western blot.

Our data show reduced CB1R and CB2R expression in BLA, an area enriched in CB1R and important for anxiety, fear processing, and stress reactivity in TBI animals. No changes in CB1R or CB2R expression at the site of injury, cingulate cortex, or CeA were noted. That these changes are observed ten days post-TBI suggests that TBI produces sustained alterations in endocannabinoid signaling that may mediate post-TBI behavioral changes.

Posterior Cingulate Cross-Hemispheric Functional Connectivity Predicts the Level of Consciousness in Traumatic Brain Injury

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Previous studies have demonstrated that altered states of consciousness are related to changes in resting state activity in the default-mode network (DMN). Anatomically, the DMN can be divided into anterior and posterior regions. The anterior DMN includes the perigenual anterior cingulate cortex and other medial prefrontal cortical regions, whereas the posterior DMN includes regions such as the posterior cingulate cortex (PCC) and the temporal parietal junction (TPJ). Although differential roles have been attributed to the anterior and posterior DMN regions, their exact contributions to consciousness levels remain unclear.

To investigate the specific role of the posterior DMN in consciousness levels, we investigated 20 healthy controls (7 females, mean age=33.6 years old) and 20 traumatic brain injury (TBI) patients (5 females, mean age=43 years old) whose brain lesions were mainly restricted to the bilateral frontal cortex but retained a well-preserved posterior DMN (e.g., the PCC and the TPJ) and who exhibited varying levels of consciousness. A Siemens Magnetom Verio 3.0 T MRI was used to scan the patients. All subjects' MRI scans were acquired under resting states. For each patient, consciousness assessment were performed according to the standardized Glasgow Coma Scale (GCS) and CRS-R. All MR imaging data were analysed using Analysis of Functional Neuroimage (AFNI) software. We investigated the intra- and cross-functional connectivity strengths (FCSs) between the right/left PCC and the right/left TPJ and their correlation with consciousness levels.

Significant reductions in both the intra- and cross-hemispheric FCSs were observed in patients compared with controls. However, only cross-hemispheric (rPCC-lTPJ and lPCC-rTPJ) resting state FCSs (but not intra-hemispheric resting state FCSs) predicted the level of consciousness in the TBI patient group.

Taken together, our results show that the cross-hemispheric posterior DMN is related to consciousness levels in a specific group of patients without posterior structural lesions. We therefore propose that the PCC may be central in maintaining consciousness through its cross-hemispheric FC with the TPJ.

Limbic Encephalitis Associated with Relapsing Polychondritis: A Case Report

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Rationale: Relapsing Polychondritis (RP) is a rare autoimmune disease involving systemic inflammation of cartilaginous structures. The clinical spectrum of RP varies from intermittent pain and swelling of cartilaginous structures such as the ears and nose, to multi-organ dysfunction. Central Nervous System (CNS) manifestations of RP are rare (estimated at 3%) but serious, including seizures, aseptic meningitis, limbic encephalitis (LE), and ischemic stroke. Fewer than 20 cases of LE associated with RP have been reported in the literature, most reporting initial symptoms of confusion or disorientation, headache and memory impairment.

Clinical Findings: A 66-year-old male presented to hospital with syncope. He was confused with altered mental status. He was admitted to neurology. CT head demonstrated normal intracranial structures, and pagetoid features of the skull. Initial MRI brain was unremarkable, but repeat MRI 6 weeks later showed symmetrically increased T2 signal in the bilateral medial temporal lobes, right corona radiata, periventricular white matter, left insula, frontal operculum and hypothalamus. Infectious workup and paraneoplastic/neuronal antibodies were negative. Neurological findings included severe anterograde memory impairment, decreased alertness, disorientation and behavioural dysregulation.

Interventions: Treatment with IVIG led to mild improvement, and was followed by tapering oral prednisone, starting at 80 mg daily. Five sessions of plasmapheresis led to improvement in his memory, attention and alertness.

He was admitted for intensive cognitive rehabilitation. During 6 weeks of rehabilitation, he was diagnosed with SIADH, which resolved with fluid restriction. He was irritable, emotionally labile and reported depressed mood. He was started on Escitalopram. He scored 0/12 on the Rivermead Behavioural Memory Test, 15/30 on the Montreal Cognitive Assessment (MoCA), and was apraxic. His processing speed was slowed, he was noted to confabulate, and was easily disoriented. He had impaired insight into his cognitive deficits.

Outcomes: One year post-discharge, this patient continued to report memory impairment, fatigue, and significant irritability with frequent verbal and physical outbursts leading to property damage. He scored 19/30 on the MoCA. Eighteen months post-discharge, he continued to struggle with depressed mood and irritability. He declined pharmacological management of his agitation and aggression, and declined involvement of a community rehabilitation counsellor. He experienced suicidal ideation, and briefly participated in group therapy for managing powerful emotions, but left the group as he did not find it beneficial. He has been unable to return to work or driving.

Main Lessons: LE is a rare but serious potential complication of RP. Common neuropsychiatric signs and symptoms include memory impairment, disorientation, affective symptoms and behavioural dysregulation. Case reports support evidence of improvement with pulse steroid therapy. This condition and constellation of clinical findings have the potential to lead to significant long-term functional limitations, despite treatment.

Keywords: Case Reports, Limbic encephalitis, Memory Disorders, Neurobehavioral Manifestations, Relapsing Polychondritis.

To Study the Serum Biomarkers in Patients with Mild Traumatic Brain Injury (mTBI) and Correlate with Cognitive Deficits

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Objective: To study the serum biomarkers in patients with mild traumatic brain injury (mTBI) and correlate with cognitive deficits.

Setting: Tertiary care center for Neurotrauma

Participants: Patients with mTBI (n=20) and age, gender and education status matched healthy controls (n=20)

Design: Prospective longitudinal observational study

Main Measures: Ubiquitin C Terminal Hydrolase (UCH-L1), S100B and Neuropsychological tests

Materials and Methods: This is a prospective case-control study of patients with mTBI. The operational definition of mTBI used was “an acute alteration in brain function or loss of consciousness for 30 minutes or less caused by a blunt external force and Glasgow Coma Scale (GCS) score of 14 to 15 at time of presentation”. The inclusion criteria were age between 19 - 40 years, presentation to casualty within six hours of trauma, and classified as mTBI. The following patients were excluded: patients with multiple trauma, deterioration in GCS after inclusion, and patients with pre-existing neurological disease, medications, or with history of alcohol consumption, that can interfere with neuropsychological functioning. The controls comprised of age, gender, and educational status matched healthy volunteers without neurological or psychiatric disorders.

Biochemical Analysis: Blood samples were collected at two time points (first within 6hr of injury and second 6-12hr of injury) for UCH-L1 and S100B measurement. Samples were allowed to clot in an upright position for at least 30 minutes but not longer than 1 hour and centrifuged at 2800-3000 rpm for 10-12 minutes. Serum was separated and stored at -80°C until the time of analysis. The assays were carried out in duplicates. The mean values were taken in the study.

Neuropsychological Assessment: Neuropsychological assessment was done at three months after injury using NIMHANS neuropsychological battery. These tests are standardized to Indian population with normative data.

The data was analysed using the statistical software SPSS ver 22. Mann Witney-U test was used for the groups that did not follow normal distribution. The correlation coefficients were calculated using the Spearman’s rho.

Results: There was marginally increase in the serum S100B and UCH-L1 levels in patients with mTBI. Patients with mTBI had significant cognitive deficits at three months after injury, suggestive of involvement of diffuse areas of brain, particularly premotor, prefrontal and medial inferior frontal lobes and basitemporal region. The correlation of biomarkers with cognitive deficits in mild head injury was found in following domains: working memory, verbal learning, verbal fluency, and visual memory in short term.

Conclusion: The serum biomarkers may differentiate patients with mTBI from normals, and have correlation with neuropsychological outcome.

Keywords: Ubiquitin C Terminal Hydrolase; S100B neuropsychological outcome; serum biomarkers; traumatic brain injury; mild traumatic brain injury.

Developing Immersive Dual-Tasks in the Computer Assisted Rehabilitation Environment (CAREN) for the Assessment of Service Members with Comorbid Mild Traumatic Brain Injury and Posttraumatic Stress Disorder

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Background: For service members (SMs), mission-essential tasks often require dual-tasking skills, which may be impaired by mild traumatic brain injury (mTBI) and posttraumatic stress disorder (PTSD). Conventional dual-task assessments cannot incorporate visual cognitive tasks during gait, are often time-consuming, and are not military-relevant. The Computer Assisted Rehabilitation Environment (CAREN) enables the incorporation of visual cognitive tasks by integrating multi-planar motion and locomotion with interactive virtual environments (VEs). Thus, our objective was to determine the efficacy of military-relevant dual-task assessment for SMs with comorbid mTBI-PTSD using the CAREN.

Methods: Male SMs (N=37: mTBI-PTSD = 25; uninjured = 12) completed the PTSD Checklist - Military Version (PCL-M) and three CAREN VEs: 1) Balance Balls (BB), requiring weight-shifting; 2) Balance Cubes (BC), requiring step-shifting; and 3) Dual-Tasking Rank Insignia (DTRI), requiring three single-tasks (walking, rank insignia recognition, and rank insignia discrimination) and two dual-tasks combining walking and the rank insignia tasks (i.e. DTRI-Disc and DTRI-Rec). The main outcomes were time for the BB and BC tasks, and dual-task cost (% change in gait speed) and cognitive error (CE; % change in accuracy) for the DTRI tasks.

Results: BB time was significantly correlated with BC time ($r = 0.777$; $p < 0.001$), DTRI-Rec cost ($r = 0.374$; $p = 0.025$) and both DTRI-Disc cost ($r = 0.494$; $p = 0.002$) and CE ($r = 0.574$; $p < 0.001$). DTRI-Disc and DTRI-Rec cost, but not CE, were significantly correlated ($r = 0.903$; $p < 0.001$), and DTRI-Disc cost and CE were significantly correlated ($r = 0.480$; $p = 0.003$) such that gait speed increased as accuracy decreased. When controlling for mTBI history, BC time was significantly associated with PCL-M score ($\beta = 1.053$, $p = 0.028$), such that SMs endorsing higher PCL-M scores spent more time on the BC task. BB and DTRI outcomes did not vary with PCL-M score.

Conclusions: Developing immersive, military-relevant dual-task assessments is essential for improving treatment planning and clinical outcomes. Similar to published reports, we found that accuracy was inversely correlated with gait speed when SMs completed a visual discrimination task during ambulation, supporting dual-task assessment in the CAREN. Moreover, consistent with our previous retrospective study in SMs with TBI of any severity, those endorsing greater PTSD symptoms spent more time step-shifting, providing further evidence for utilizing the BC task in identifying comorbid mTBI-PTSD. Future research will determine whether multi-tasking assessments that integrate step-shifting with the visual cognitive tasks are more sensitive to group differences.

Disclaimer: The views expressed in this work are those of the authors and do not reflect the official policy of the Department of Army/Navy/Air Force, Department of Defense, or U.S. Government.

BBB Damage, Fibrinogen Extravasation and Inflammation: A Novel Treatment Target in Traumatic Brain Injury

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Background: Despite being a devastating disease, traumatic brain injury (TBI) has no evidence-based treatment. Recent interest has focused on two potential therapeutic targets: the blood brain barrier (BBB) and inflammation. It is not known if damage to the BBB initiates pro-inflammatory processes, or if such processes are protective or injurious to axons and neurons. We hypothesized that BBB damage, and the ensuing extravasation of fibrinogen, would lead to microglial activation, and neuronal loss.

Methods: Five brain regions from 15 cases of acute TBI (survival <2 months) and 6 cases of chronic TBI (survival >1 year) were compared with 15 age- and sex-matched controls. Immunohistochemistry (IHC) was used to measure the extent of fibrinogen and immunoglobulin G (IgG) extravasation, neuronal density, and axonal injury. Microglial lysosomal activation (CD68) and microglial density (Iba1) were also measured. The presence of haemorrhage was assessed by hematoxylin and eosin (H&E) staining. Aperio ImageScope™ was used to quantify IHC staining in an unbiased fashion. Results from >1500 tissue sections were compared by ANOVA, Spearman's Rank Correlation Coefficients, and Linear Regression.

Results: 1. BBB damage in acute TBI results in significant extravasation of fibrinogen and IgG in all brain regions except the brainstem. Here, IgG but not fibrinogen is significantly raised suggesting the response to TBI differs in the anterior and posterior circulations.

2. Fibrinogen extravasation is observed even when no macro- or microvascular haemorrhage is identified by H&E staining.

3. The extent of fibrinogen extravasation - but not IgG extravasation - correlates significantly with microglial activation (CD68/Iba1) (rs 0.60, p 0.03) and neuronal density (rs -0.68, p 0.04).

4. Microglial activation correlates negatively with neuronal density (rs -0.77, p 0.006).

5. Areas high in fibrinogen overlap those areas showing greatest microglial activation and greatest neuronal loss.

6. Linear regression analysis demonstrates a significant interaction between fibrinogen, microglial activation and subsequent neuronal loss (examples: R^2 0.45, p 0.006 to R^2 0.79 p 0.001, frontal and cingulate cortices).

7. No significant extravasation of fibrinogen is seen in chronic TBI.

8. No relationship is seen between fibrinogen extravasation and axonal injury.

Discussion: Acute TBI results in global BBB injury. The resulting fibrinogen extravasation promotes microglial activation and neuronal loss. Secondary neuronal injury might be decreased by preventing the binding of fibrinogen with its microglial receptor.

Brain Tissue Strain and Balance Impairments in Adolescents Following a Concussion

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Background: Balance impairments present in at least 30% of cases of concussion, and longitudinal balance testing provides important information regarding recovery. Biomechanical reconstructions model the degree and location of brain tissue strain associated with injury. The objective was to examine the relationship between the magnitude and location of brain tissue strain and resulting balance impairment following a concussion.

Methods: Adolescents 1-month post-concussion (n=33) and non-injured adolescents (n=33) completed two balance conditions while standing on a Wii Balance Board (WBB) that recorded the movement of the center of pressure under their feet during: i) double-leg stance with eyes closed (EC), ii) dual-task (DT) combining double-leg stance while simultaneously completing a Stroop colour-word test. Participants with concussion were identified as having impaired balance for the EC condition if they showed a value of at least 2 standard deviations above the control group mean for the 95% ellipse and were identified as having impaired balance on the DT condition if they showed a value of at least 2 standard deviations above the control group mean for the medio-lateral velocity. Injury reconstructions were performed for ten of the participants with concussion according to the description of the events obtained through patient and parent interviews. A 5th percentile Hybrid III headform was used in the reconstructions to obtain linear and rotational acceleration time-curves of the head impact. These data were input in the University College Dublin Brain Trauma Model (UCDBTM) to calculate maximum principal strains (MPS) and cumulative strain damage values at 10% (CSDM-10) and 20% (CSDM-20) for different brain regions. Correlations between balance and reconstruction variables were calculated for the ten cases on which reconstructions were performed.

Results: Out of the ten reconstructed cases, six participants had impaired balance on the EC condition and seven had impaired balance on the DT condition. For MPS values, correlations with balance variables ranged from 0.00187 to 0.192 for the DT condition and from -0.181 to 0.152 for the EC condition. For CSDM-10 values, correlations with balance variables ranged from 0.0871 to 0.487 for the DT condition and from -0.103 to 0.252 for the EC condition. For CSDM-20 values, correlations with balance variables ranged from -0.108 to 0.190 for the DT condition and from -0.353 to -0.155 for the EC condition.

Conclusion: In this limited sample of adolescents, no association was established between the presence of balance impairment and magnitude and/or location of brain tissue strain. Maintaining balance is a complex process integrated into multiple subcortical regions, white matter tracts, cranial nerves and other neural tissue, which may not be represented with adequate resolution in brain models to permit determination of cause-effect.

Cognitive Behavioral Intervention Compared to Telephone Counselling Early After Mild Traumatic Brain Injury: A Randomized Trial

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Background and Aims: Many patients do not return to work (RTW) following mild Traumatic Brain Injury (mTBI) due to persistent posttraumatic complaints that are often resistant to therapy in the chronic phase. Earlier studies found that patients who report a high number of complaints in the acute phase, are most at risk for developing persistent posttraumatic complaints. Recent studies suggest that psychological interventions should be implemented early after injury to prevent patients from developing chronic complaints instead of treating them in the chronic phase. The primary goal of this study was to examine the additional effectiveness of a newly developed cognitive behavioural intervention early after injury on RTW in comparison to telephone counselling, which was already found to be effective in lowering posttraumatic complaints. Part of these patients also took part in an fMRI study that investigated functional network connectivity over time, of which the results are presented in another abstract submitted by our research group. Both studies are part of a larger prospective cohort-study on outcome following mTBI (UPFRONT-study).

Method: The study is a randomized controlled trial as part of a larger prospective cohort-study on outcome following mTBI (UPFRONT-study). In this intervention study, the effectiveness of an investigational CBT intervention (CBTi) targeting unrealistic illness perceptions was compared to telephonic counseling (TC) that provided information and reassurance in at risk mTBI patients. Patients underwent either five sessions of CBT treatment or five conversations by phone starting 4-6 weeks after trauma. The main outcome measure was the level of RTW six months and one year after trauma. Secondary measures comprised functional outcome (GOSE-E) one year after trauma and depression, anxiety and reported posttraumatic complaints at three, six and twelve months after injury.

Results: Of the 1150 patients of the cohort, 91 patients at-risk patients were randomized into one of the treatment conditions. After excluding drop outs, CBTi consisted of 39 patients and TC of 45 patients. No significant differences were found with regard to RTW, with 65% of CBTi patients and 67% of TC patients reporting a RTW at previous level. However, TC patients reported less posttraumatic complaints at three months (8 vs. 6, $p=.010$) and twelve month post-injury (9 vs. 5, $p=.006$), and significantly more patients in the TC group showed a full recovery twelve months post-injury compared to the CBTi group (62% vs. 39%).

Conclusions: The UPFRONT-intervention study is an innovative study examining the potential beneficial effects of an early and brief cognitive behavioral intervention following mTBI. The results of this study suggest that early follow-up of at risk patients can have a positive influence on the patients well-being, and that this follow-up could potentially consist out of a low-intensive, low-cost telephonic intervention.

A Longitudinal Resting-State fMRI Study on Posttraumatic Complaints and The Effects of An Early Psychological Intervention in Patients with Mild Traumatic Brain Injury

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Background and Aims: It seems likely that (pre-injury) psychological factors, such as coping style and illness beliefs, have a stronger influence whether complaints after mild traumatic brain injury (mTBI) convert into chronic complaints than the injury itself. In fact, studies have shown that psychological interventions are effective in preventing persistent posttraumatic complaints. Functional MRI (fMRI) has been used to study longitudinal changes in brain network connectivity in patients with mTBI, but fMRI studies on the effect of psychological interventions after mTBI are scarce.

In the current resting-state fMRI study, functional network connectivity was investigated over time in patients with and without posttraumatic complaints in the sub-acute phase post-injury. Patients with complaints took part in a randomized controlled trial on the effectiveness of early cognitive behavioral therapy (CBT) compared with telephone counseling (TC), of which the results are presented in another abstract submitted by our research group. Both studies are part of a larger prospective cohort-study on outcome following mTBI (UPFRONT-study).

Method: Questionnaires were used to measure posttraumatic complaints, anxiety and depression at two weeks and three months post-injury. Outcome was determined at 12 months post-injury using the Glasgow Outcome Scale Extended. Patients with complaints at two weeks post-injury were randomized for either CBT or TC, and underwent fMRI before (one month post-injury) and after (three months) treatment. Patients without complaints (PTC-absent) underwent scanning at similar time intervals. Independent component analysis was used to identify components of the default mode network (DMN), executive networks (EN) and salience network (SN). Subsequently, within- and between-component functional connectivity (FC) were analyzed. In addition, it was examined whether FC before treatment was correlated with complaints, anxiety and depression scores after treatment, and with outcome at 12 months post-injury.

Results: Thirty patients with complaints (13 CBT and 17 TC) and 19 PTC-absent patients were included in this fMRI study. Aside from changes in small frontotemporal clusters (<5 voxels) of the DMN in patients with and without complaints, no longitudinal changes in FC were found for any of the groups. Furthermore, no significant group differences in within- or between-component FC were found between the CBT, TC and PTC-absent groups. Pre-treatment FC in small clusters (1 voxel) of the DMN was related to complaints and anxiety at three months, and outcome at 12 months post-injury. More importantly, pre-treatment FC between the anterior and posterior DMN components was significantly correlated with the number of complaints after treatment ($\rho=0.56$, $p=0.003$).

Conclusions: This study showed limited effects of time or treatment on network FC after mTBI. Nevertheless, our results suggest that the DMN may serve as a biomarker for identifying patients with mTBI who are prone to develop persistent complaints and whether or not patients will respond to psychological therapy.

Increased Risk of Psychiatric Diseases in Patients with Mild Traumatic Brain Injury: A Population-Based Cohort Study

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Background: It is known that psychiatric disorders after traumatic brain injury are frequent. However, the relationship between mild traumatic brain injury and psychiatric diseases has never been established. We conducted a study of patients with mild traumatic brain injury to evaluate if they had a higher risk of psychiatric diseases compared with the general population.

Methods: We utilized a sampled National Health Insurance claims database containing one million beneficiaries. We followed all beneficiaries from January 1, 2005 to December 31, 2013 to determine if they were diagnosed with psychiatric diseases. The definitions of psychiatric diseases in our study are schizophrenia, bipolar disorders and major depression. We further identified patients with mild traumatic brain injury and compared their risk of psychiatric diseases with the general population.

Results: We identified 76,991 patients with mild traumatic brain injury and 881,511 patients without mild traumatic brain injury. After controlling for age, gender, urbanization level, socioeconomic status, liver cirrhosis, chronic obstructive pulmonary disease, diabetes, hypertension, coronary artery disease, hyperlipidemia, history of alcohol intoxication, malignancies, smoking, obesity, chronic renal insufficiency and Charlson Comorbidity Index score, the adjusted hazard ratio for psychiatric diseases was 1.46 (95% confidence interval, 1.29—1.64).

Conclusion: Mild traumatic brain injury may be associated with diagnoses of psychiatric diseases.

Increased Risk of Ischemic Stroke in Patients with Venous Thromboembolism: A Nationwide Cohort Study

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Background: Conflicting results have been obtained by studies attempting to assess the risks of ischemic stroke in patients with venous thromboembolism, while the long-term risk of stroke in survivors of venous thromboembolism remains unexplored.

Objective: We evaluated whether the risk of ischemic stroke in patients hospitalized with venous thromboembolism is higher when compared to the general population.

Methods: One million patients from National Health Insurance beneficiaries in Taiwan were sampled. There were 2,145 patients who had been hospitalized with diagnosis of venous thromboembolism and 727,607 unexposed subjects. All adult patients were followed from 1 January 2005 to 31 December 2013 to evaluate if ischemic stroke was diagnosed. Cox regression models were applied to compare the hazards adjusted for potential confounders.

Results: After controlling for age, gender, urbanization level, socioeconomic status, diabetes, hypertension, coronary artery disease, hyperlipidemia, history of alcohol intoxication, malignancies, congestive heart failure, atrial fibrillation, smoking, peripheral artery disease and Charlson Comorbidity Index, the adjusted hazard ratio of ischemic stroke was significantly increased in patients with venous thromboembolism (2.47; 95% CI, 2.16–2.83). A subgroup analysis based on patients who survived longer than 12 months in the cohort also revealed higher hazard ratio in the patients with venous thromboembolism. (1.32; 95% CI, 1.05–1.66).

Conclusion: The possible risk of ischemic stroke is significantly higher in patients hospitalized with venous thromboembolism than in the general population.

The Role of Ferroptosis in Defining Outcome after Traumatic Brain Injury

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Introduction: Traumatic brain injury (TBI) triggers multiple pathways of neuronal death, possibly including ferroptosis – a form of non-apoptotic glutathione peroxidase 4 (GPX4)-dependent death. We showed that insufficiency of GPX4 or glutathione (GSH) results in ferroptosis executed via 15 lipoxygenase 2 (LOX2) driven oxidation of arachidonic (AA) and adrenic (AdA) acid-containing phosphatidylethanolamines (PE). The role of ferroptosis in acute CNS injury has not been evaluated. We hypothesized that ferroptosis is activated after TBI, and suppression of PE oxidation (via LOX inhibition) or AA/AdA esterification into PE, via (long-chain acyl-CoA synthetase type 4) (ACSL4) inhibition confers neuroprotection.

Methods: Hippocampal neurons (HT22 cells) were exposed to pro-ferroptotic insults, including RAS-selective lethal compound3 (RSL3), BSO, erastin, or in vitro TBI (mechanical stretch). Adult C57/B6 mice underwent controlled cortical impact (CCI). GSH levels (ThioGlo assay) and GPX4, 15LOX2, ACSL4 expression (Western Blot) were measured in CCI vs naïve (4/grp). Effects of ferroptosis inhibitors on histological (fluorochrome B [FJ] staining) and cognitive (Morris water maze) outcomes were evaluated in CCI+inhibitor, CCI+vehicle, and sham groups (9-10/grp).

Results: Pro-ferroptotic insults and in vitro TBI caused neuronal death (LDH release) rescued by ferrostatin-1, liproxstatin-1 (lipid radical-trapping antioxidants), triacsin C (ACSL4 inhibitor) and baicalein (LOX inhibitor). At 4 and 24h post-CCI, 15LOX2 expression and PE-OOH levels increased, GSH levels decreased, and GPX4 expression was unchanged in ipsilateral hippocampus vs naïve. Local administration of triacsin C decreased FJ (+) cells in hippocampus vs vehicle at 24h. Administration of baicalein i.v. after CCI improved swim speed and acquisition of spatial learning vs vehicle on d10-15.

Conclusions: TBI results in thiol and lipid disruptions consistent with ferroptosis activation. Inhibition of regulatory pathways of ferroptosis such as 15LOX and ACSL4 confers neuroprotection against TBI.

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Reducing Cellular Damage in Traumatic Brain Injury Using Ubiquinol

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Background: With traumatic brain injury (TBI), there is increased oxidative stress, impaired cellular bioenergetics, and insufficient antioxidants to scavenge reactive oxygen species leading to alterations in brain function and structure. Thus, a more potent antioxidant such as ubiquinol (active/reduced form of coenzyme Q10) could be used before and after a TBI to reduce oxidative stress and maintain cellular bioenergetics.

Objective: To determine if administering ubiquinol (100 mg/kg) before and after TBI will reduce brain cellular damage.

Methods: Adult male F344 rats (250-300 grams) were randomly assigned to one of three groups (TBI untreated, ubiquinol 30 minutes before TBI, or ubiquinol 30 minutes after TBI, n = 10 each group). A craniotomy (6 mm diameter) was completed over the right sensorimotor cortex directly lateral to the bregma and centered midway between bregma and the temporal ridge. The TBI was delivered to the dural surface (3.5 m/s; 2 mm depth) using an electromagnetically controlled impact device mounted on a stereotaxic manipulator. Immediately after TBI, the animal was transferred under continuous anesthesia to a Varian 9.4 Tesla scanner for 1H-MRS in vivo. To assess brain oxidative stress we measured glutathione and ascorbate; for brain bioenergetics we measured N-acetylaspartate, lactate, serine, alanine, creatine, phosphocreatine, and glucose. After scanning was completed, the brain was removed and samples of cortex under the impact site were dissected for analysis of apoptosis using fluorescent microscopy and mitochondrial damage using transmission electron microscopy (TEM).

Results: There was $22.3\% \pm 0.71\%$ brain cortex apoptosis in the TBI group. The rats that received ubiquinol before TBI or after TBI had a significantly lower percentage of brain cortex apoptosis respectively ($1.8\% \pm 0.11\%$; $9.84\% \pm 0.44\%$). TEM images of injured cortex from the rats that received ubiquinol demonstrated substantial reduction of mitochondrial swelling, disarray of cristae structure, and fragmented outer membranes compared to untreated TBI. 1H-MRS revealed significant effects of TBI on all neurochemical markers of oxidative stress and bioenergetic impairment. Treatment with ubiquinol attenuated the injury-induced changes in ascorbate, lactate, alanine, and glucose.

Discussion/Conclusion: We have observed increased brain oxidative stress and reduced bioenergetics within 1 hour after TBI using 1H-MRS. In addition, when we administered intra-arterial ubiquinol, rats had a significant reduction in brain apoptosis and mitochondrial damage. Our in vivo 1H-MRS results support antioxidative and bioenergetic mechanisms of ubiquinol cellular protection in TBI. Ubiquinol may be a promising adjunct therapy for TBI that could be used to reduce cellular damage and preserve mitochondrial function.

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A New Tool to Assess Responsiveness in Disorders of Consciousness (DoC): A Preliminary Study on the Post-Coma Scale (PCS)

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Introduction: The most successful scales to assess coma and outcome are respectively the Glasgow Coma Scale (GCS) (Teasdale and Jennett, 1974) and Glasgow Outcome Scale (GOS) (Jennett and Bond, 1975) for their easiness and rapidity of administration.

Aim: The Post-Coma Scale (PCS) is a brief and easy diagnostic tool for individuals with disorders of consciousness (DoC), that could distinguish patients in the minimally conscious state (MCS) from those in unresponsive wakefulness syndrome (UWS) (Laureys et al, 2010), formerly defined as vegetative state (VS). The PCS consists of 7 items assessing eye tracking, command-following, spontaneous motility, decerebrated and decorticated posturing, psychomotor agitation, the ability of safe oral feeding, and the presence of recurrent infections and/or hyperthermia (yes; sometimes/partially; no).

Aim of the study was to assess the diagnostic validity of the PCS in comparison with the Coma Recovery Scale-Revised (CRS-R) (Lombardi et al., 2007), the Disability Rating Scale (DRS) (Rappaport et al, 1982), the Level of Cognitive Functioning (LCF) (Hagen et al., 1979) and the GOS.

Methods: In an Italian Multicenter Study on patients with DoC, 210 post-acute rehabilitation wards, 384 long term care centers, and 8 family associations participated to data collection. The sample consisted of 545 patients (mean age \pm SD = 56.06 \pm 17.26, years, 59% males, 70% diagnosed as UWS) and the median interval from injury to assessment time was 27 months (Interquartile Range, IQR: 42 months). Spearman correlation coefficient was used to assess correlations between variables. Odds Ratio (OR) was computed for analyzing the relationship between PSC score and diagnosis together with 95% confidence interval (IC95%). ROC curve allowed to analyze the sensitivity and specificity of PSC. Alpha-level was set for all the analysis at 0.05.

Results: Statistically significant correlations were found between PCS and the other clinical scales: $R=0.586$ ($p<0.001$) with LCF, $R=-0.566$ ($p<0.001$) with DRS, $R=0.622$ ($p<0.001$) with CRS-R. The PCS scores resulted significantly correlated with the time from acute event ($R=0.117$, $p=0.006$).

For patients with a GOS score = 2 the mean PCS was 1.84 \pm 1.19, and for GOS score = 3 it was significantly higher 3.88 \pm 1.71 ($p<0.001$). Similarly, for patients in vegetative state/ UWS the mean PSC score was 1.71 \pm 1.09, significantly ($p<0.001$) lower than that for patients with minimally conscious state (PSC=3.83 \pm 1.29).

Finally, the agreement of PCS and clinical diagnosis was of 84.4% (variance explained), with an odds ratio OR=3.781 (95%CI=3.026 – 4.725, $p<0.001$). A threshold of PSC=2.5 resulted to have a sensitivity of 87.7% and specificity of 79.4% with respect to diagnosis.

Conclusion: Since the importance of long-term follow up outcome studies on large populations of persons with DoC, the PCS could be proposed as an easy and brief tool to be administered, also by telephone interviews, to monitor the possible long-term responsivity changes.

Financial Management after Acquired Brain Injury: A Conceptual Framework Based on Qualitative Inquiry

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Financial management is a vital everyday living activity for most adults and influences participation in life areas including self-care, home, work, leisure, and transportation. Decreased independence in financial management activities can negatively impact social relationships and autonomy in other daily life areas, and financial mismanagement can have calamitous consequences for the person living with brain injury and her or his dependents. Unfortunately over 30% of people living with acquired brain injury report difficulties with financial management activities. While many rehabilitation practitioners often address limitations in this area for clients living with brain injury, there is little evidence guiding practice, resulting in variability in how it is assessed and addressed.

Objectives: To develop a conceptual framework for financial management after acquired brain injury that can guide rehabilitation practices in this area.

Methods: This grounded theory qualitative study is based on semi-structured interviews, and aims to gain perspectives of 15 to 35 adults living with brain injury and close-others who help the person with brain injury with financial management activities. Participants living with brain injury are being recruited from brain injury and stroke organizations and are included if they sustained a brain injury at age 18 or older, are at least one year post-injury, and are able to participate in a face-to-face verbal interview. Close-others are recruited via discussions with participants who have had a brain injury about people that help them with their financial management activities. Interview audio recordings are transcribed and coded, and a conceptual framework is being developed iteratively with analysis of past interviews refining the interview process for subsequent interviews and the framework until no new information is found.

Results: Preliminary results show that everyday financial management performance after brain injury is a complex interaction of financial management activity task factors (e.g., budgeting, monitoring spending), person factors (e.g., cognitive abilities; financial resources), and environmental factors (e.g., social relationships, technology available). These factors change over time, and pre-injury factors can influence post-injury performance. However, the use of financial management strategies and supports (e.g., automatic payments, simple budgeting systems, learning from knowledgeable others) can help bridge performance issues when person and environmental factors do not align with financial management task demands.

Conclusions: Understanding the experiences of people living with brain injury will help identify the key financial management issues relevant to this population, thereby guiding rehabilitation practice in this area to maximize the future financial management independence and success of people living with acquired brain injury.

The Impact of Concomitant mTBI on Pain Perception and Return to Work in Patients Suffering from an Isolated Limb Fracture

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Introduction: Orthopaedic trauma (OT), such as fractures, is the most common type of injury treated in a hospital setting each year. Return to work (RTW) is often used as an outcome measure of functional recovery after such injury. Although naturally observed after an ILF, pain is known as the main factor delaying RTW.

Interestingly, mild traumatic brain injury (mTBI) is frequent among individuals who have suffered from an ILF, an incidence rate estimated at 23%. Furthermore, mTBI is known to induce pain and can also interfere with RTW, especially when occurring in concomitance with other injuries. Considering the common symptomatology shared by both injuries, it appears important to study the impact of mTBI on the recovery of ILF when occurring concomitantly to better adapt treatment.

Methods: Subjects were selected from a sample of 252 participants with an ILF recruited at an orthopaedic clinic of a Level 1 Trauma Hospital. Among them, 58 had suffered from a concomitant mTBI (ILF+mTBI). To compare the difference in the level of pain between the groups (ILF and ILF+mTBI), 42 subjects with ILF + mTBI were matched with 42 ILF patients according to age, sex, type of injury and time elapsed since accident. As for the data on RTW, 170 subjects (41 ILF+ mTBI and 129 ILF) were contacted through phone-interview to obtain information about the number of days taken before RTW, among which 52 patients were under workers' compensation (17 ILF+ mTBI and 35 ILF).

Results: Relative to ILF patients, the ILF+mTBI group reported significantly higher levels of persistent pain ($F=28.57$; $p<0.0001$) at the time of assessment (mean=86 days post-accident; $SD=102.57$). This difference was not explained by age ($r=0.097$; $p=0.54$), sex ($r=0.069$; $p=0.66$) or secondary gains ($F=0.25$; $p=0.62$). Furthermore, the ILF+mTBI group took significantly more days (329.7 days) before RTW after the injury when compared to the ILF group (150.3 days) ($F(1,169)=11.29$; $p=0.001$), even after controlling for workers' compensation (ILF+mTBI group= 299.4 days versus ILF group= 105.2 days; ($F(1,117)= 12.89$; $p<0.0001$). Sex ($F=7.5$; $p=0.007$), but not age ($F=0.1$; $p=0.79$), significantly affected RTW delay.

Conclusion: Mild TBI significantly interferes with recovery after an ILF injury by increasing both the perception of pain and the delay taken to RTW. These results are particularly alarming considering the staggering individual and societal burden associated with work absenteeism and the high incidence of polytrauma. These findings expand our understanding of the impact of mTBI on recovery following a trauma and highlight the need to further explore the underlying mechanisms.

Circulating Myeloid-derived Suppressor Cells in Acute Ischemic Stroke

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Background: Stroke is a major cause of disability and death in adults worldwide. Recent investigations showed that cerebral ischemia not only leads to brain damage and subsequent local inflammation but also to profound immunosuppression capable of restricting inflammatory response as well as inducing infections. The mechanisms of immune alterations are largely related to activation of sympathoadrenal system and inflammatory cytokines. Much more unclear are the contributions of the immature myeloid progenitor cells that can be mobilized from bone marrow under inflammatory conditions.

Objectives: To investigate, whether myeloid-derived suppressor cells (MDSCs) would be increased in acute stroke patients and would correlate with inflammatory response and immunodeficiency.

Patients and Methods: Eighteen patients with moderate and severe ischemic stroke (NIHSS >7) were enrolled in this study. Lesion volume was measured using magnetic resonance imaging and outcome was based on the discharge Rankin scores and improvement of NIHSS. Ten age-matched healthy subjects were studied as a control. MDSCs were identified as HLA-DR-, Lin-, CD33+ cells using flow cytometry. The level of C-reactive protein (CRP) was measured as marker of systemic inflammatory response.

Results: The percentage of MDSCs was significantly higher in acute ischemic stroke patients [median 14.5% (LQ-UQ: 9–21)] relative to the controls [5% (2.7–6.0), $P=0.0007$]. Patients with moderate stroke had significantly higher levels of MDSCs than those with severe stroke (Me 15.5 versus 7.3%; $P=0.04$). The levels of HLA-DR-, Lin-, CD33+ cells in patients with CRP level of 10 - 70 mg/L [20% (16–25)] significantly exceeded amounts of these cells in patients with low (<10 mg/L) and high (>70 mg/L) levels of CRP evidencing that low and exacerbated inflammatory response fails to induce effective mobilization of MDSCs. We did not find any correlation between MDSCs number and lymphocyte count or infection rate. Nevertheless, in non-severe stroke group favorable outcome (improvement of NIHSS to 3 and more points) was associated with a trend to lower level of MDSCs ($P=0.07$).

Conclusion: The data obtained indicate that acute ischemic stroke is accompanied by mobilization of MDSCs that is most pronounced in non-severe stroke patients with “controlled” systemic inflammatory response. The increase of MDSCs apparently is not related to immunodeficiency and subsequent infection, but may negatively influence early neurological recovery.

Blueprint for Recovery from Traumatic Brain Injury; ICU to Community a Decade's Journey

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The continuum of care ICU -Home: The need for a continuum of care and its importance will be discussed as often the patient is unable to be followed from one segment of their recovery to the next.

At the Scene of the accident: Cooling helmets and cranial cooling -Super oxide dismutase and ICP.

ICU:

Pressure Monitoring Craniotomy and bone flaps.

The use of the bispectral monitor while in a coma.

Restoring circadian rhythm the endogenous circadian clock and synaptic plasticity in the hippocampus.

Cognition what is its importance while in a coma.

Use of pharmacology in a coma including the use of botox, anti seizure medication and brain stimulants.

Contracture prevention.

Waking the brain

INPATIENT REHAB:

Removal of tubes asap.

How aggressive is too aggressive when it comes to therapy.

Pharmacology Mood modulators, sleep promoters, attention deficit medications.

Restraint therapy and cortical reorganization.

Patterned Electrical Neuromuscular stimulation it's advantages -synaptic drive to motor neurons.

Vision and how to assess it.

Impulsivity and hyperactivity.

Restoring lost memory.

Canine therapy.

OUTPATIENT REHABILITATION:

Consistency in the home -schedules that make sense interactive computer programs.

Continued OT PT CT Speech.

Aquatic therapy and proprioception.

Empowering the consumer.

Hippotherapy and improved functional outcomes.

Preparing for the Transition to home.

COMMUNITY:

HCBS waivers how to apply for them and utilization of services that are available -27 states have HCBS waivers.

Transitional living specialists what do they do?

Appetite and brain injury.

Flooding after brain injury strategies to cope.

Medicaid and Medicare.

Exercise.

Neurobiofeedback and documented results for sleep, memory and reorganization of brain waves.

Summarization: TBI is a long term process with small windows allowing opportunities for recovery. Often these windows are missed and then shut. Full recovery may take 10 years or more. Health care providers and family must believe in the plasticity of the brain and the potential for recovery. There must be protocols for each level of recovery and a continuum of care must be maintained.

Thinking outside of the box is beneficial as each brain injury differs and there is a much to gain little to lose philosophy.

Let us share with you the ability of the brain to rewire and remodel as we have seen with our daughter. Memory can be regained (short and long term), critical thinking, muscle memory, vision, behavioral issues and executive function can be once again where it was no more. Let us tell you how.

Individual and Population Level Impacts of Traumatic Brain Injury, Age at Injury and Maternal Characteristics on Subsequent Offending Behaviour

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Background: Traumatic brain injury (TBI) disproportionately affects subgroups of the population, particularly prisoners, with TBI occurrence highest among adolescent men. In addition, although the significant, and often sustained, adverse outcomes of TBI including neuropsychiatric and behavioural problems such as depression, anxiety, criminal offending and substance use, have been widely reported, the effect of age at TBI on short and long-term outcomes remains unclear. Primary objective of this study is to evaluate the individual and population level impacts of combination of factors including TBI and certain maternal characteristics as well as age at TBI on subsequent criminal conviction.

Research Design: A retrospective record linkage study. A total of 30,599 individuals were included in the study.

Methods: Along with Cox proportional hazard regression models, a novel statistical method, population attributable risk percentage (PAR%) was used to assess individual and population level impacts of the risk factors.

Results: In the gender-specific analyses, evidence of TBI was significantly associated with an increased risk of subsequent criminal conviction (aHR: 1.48, 95%CI: 1.36, 1.60, $p < 0.001$ for men; aHR: 1.45, 95%CI: 1.22, 1.73, $p < 0.001$ for women). At the population level, minimum of 15% (males) and 25% (females) of the criminal convictions were attributed to TBI. Combined impacts of TBI and certain maternal factors, namely, being young, single and multi-parity, on incident of offending were estimated to be 57% and 67% for men and women respectively with non-overlapping 95%CIs. In a subgroup analysis, compared to those who had a TBI before the age of five, those who had a TBI at: 5-9, 10-15, and 16+ years of age were more likely to have a subsequent criminal records (adjusted hazard ratio (aHRs): 1.47 to 4.69 for men and aHRs: 1.84 to 10.51 for women). Along with a TBI, low socio-economic status, mental illness, and maternal characteristics were also identified as predictors of a criminal conviction.

Conclusions: This study provides evidence that majority of the criminal behaviours were associated with traumatic brain injury, poor mental health and low socio-economic status as well as certain maternal characteristics. Age at brain injury may also play a significant role in predicting criminal behaviour among. Those who had TBI during adolescence may be at higher risk for criminality. This is the first and the largest study to assess impact of brain injury on offending behaviours not just at individual level, but at a population level using a robust sample size. The identification of priorities from a public health intervention perspective requires an understanding of the impact of age at brain injury along with several risk factors of subsequent criminal behaviour.

Behavioral Disturbances Are Related to Deficits in Social Cognition After Aneurysmal Subarachnoid Hemorrhage

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Objective: Disturbances in social behavior, such as apathy and impaired self-awareness, are often found after aneurysmal subarachnoid hemorrhage (aSAH). Impaired social cognition (SC) is a possible underlying cause of these social behavioral changes. However, the presence of SC deficits and more importantly, the relationship between SC and behavioral disturbances have not been investigated after aSAH. Therefore, we aimed to investigate different aspects of SC (emotion recognition, Theory of Mind [ToM], and empathy) and associations with behavioral disturbances, specifically apathy, daily life psychosocial problems, and impaired self-awareness.

Participants and Methods: 88 aSAH patients (mean age 53.3 years) were assessed with neuropsychological tests for SC (emotion recognition, Theory of Mind, affective empathy) in the subacute phase (mean = 4.7 months) post-SA. Results were compared to age-, sex-, and education-matched healthy controls (HC). Three different categories of behavioral disturbances were investigated. Apathy and daily life psychosocial problems were examined with the Apathy Evaluation Scale (AES) and Patient Competency Rating Scale (PCRS) respectively, in a self-evaluation version and a proxy version. Self-awareness was investigated using the difference scores (AES-dif and PCRS-dif = self minus proxy) and inter-rater agreement scores (Kappa, κ). Pearson correlations were used to investigate relationships between SC and behavioral problems.

Results: All measured aspects of social cognition, i.e. emotion recognition, ToM, and empathy, were impaired in aSAH patients compared to HC. Deficits in ToM and emotion recognition were significantly correlated to proxy ratings indicating daily life psychosocial problems and apathy, however not to patient ratings. Although mean scores on the questionnaires did not differ significantly between patients and proxies ($p > 0.05$), agreement between patient and proxy ratings according to Kappa was low ($\kappa < 0.60$), which is indicative for impaired self-awareness. Moreover, significant correlations between measures of SC and indications of impaired self-awareness were found.

Conclusions: In the subacute phase after aSAH, deficits in several aspects of social cognition, i.e. emotion recognition and ToM, were related to apathy and daily life psychosocial problems as reported by proxies and to impaired self-awareness. Consequently, a combination of SC tests, self- and proxy ratings should be used in clinical practice, to improve detection and treatment of behavioral disturbances after aSAH.

Clinical Subcategorization of Minimally Conscious State According to Resting Functional Connectivity

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Introduction: Patients in a minimally conscious state (MCS) have been recently subcategorized in MCS plus and MCS minus, that is, with and without command following capacity respectively. We here aim to characterize this residual capacity in MCS plus as compared to MCS minus by means of resting functional magnetic resonance imaging (fMRI).

Method: Resting state fMRI was acquired in 292 MCS patients. A resting state seed-based fMRI analysis was conducted on a convenience sample of 19 MCS patients (10 MCS plus and 9 MCS minus) and 38 healthy controls. We investigated the left and right frontoparietal networks (FPN), the auditory network and the default mode network (DMN). We employed a ROI-to-ROI analysis to investigate the inter-hemispheric connectivity and we investigated inter-group differences in grey and white matter volume by means of voxel-based morphometry (VBM) method.

Results: We found a higher connectivity in MCS plus as compared to MCS minus in the left FPN, specifically in the left temporo-occipital fusiform cortex. Functional connectivity of auditory network, right FPN and DMN, ROI to ROI analysis and VBM of grey and white matter did not show differences between patient groups.

Discussion: Our results suggest that the clinical subcategorization of MCS is sustained by connectivity differences in left FPN, known to be a language-related network. Command following ability is seemingly not influenced by auditory capacity, perception of surroundings and internal thoughts, nor by differences in inter-hemispheric connection and morphological differences.

Effect of Phosphodiesterase-5 inhibition on Cerebrovascular Reactivity in Chronic Traumatic Brain Injury (TBI)

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Background/Objectives: Traumatic vascular injury (TVI) is an understudied endophenotype of traumatic brain injury (TBI) and can be assessed noninvasively by measuring cerebrovascular reactivity (CVR). CVR in response to hypercapnia can reliably be measured by functional MRI with excellent spatial resolution. Potentiation of CVR in response to phosphodiesterase 5 (PDE5) inhibition is a potential prognostic and pharmacodynamic biomarker for therapies that may improve vascular function. Our objectives are to: 1) investigate CVR using MRI- blood oxygen level dependent (BOLD) with hypercapnia challenge in TBI and healthy control subjects; 2) assess the correlation between CVR and neurocognitive symptoms and neuropsychological testing in chronic TBI; and 3) assess the effect of a single dose of sildenafil (a potent PDE5 inhibitor) on CVR and TVI in chronic TBI.

Methods: 55 adults were enrolled: moderate/severe TBI (n=35) and healthy controls (HC) (n=20). Subjects were 79% male, mean age 39±9 years, and mean 32 months after injury. Subjects underwent MRI-BOLD with hypercapnia challenge before and after administration of sildenafil 50 mg. A focused neuropsychological battery adapted from the TBI Common Data Elements, and neurobehavioral symptom questionnaires were administered. The individual TBI neurobehavioral data (mean symptom scores and neuropsychological test Z-scores) were correlated with the individual TBI CVR data (global, gray matter, white matter).

Results: Mean CVR measures were calculated for whole brain (WB), gray matter (GM) and white matter (WM) and were lower in TBI patients than HC. All CVR measures distinguished TBI from healthy controls (Cohen's $d=0.988$, 1.001 and 0.705 for WB, GM and WM CVR respectively; $p=0.006$, 0.006 , and 0.048 , respectively). Receiver Operator Characteristic analysis yielded Area Under Curve (AUC), as follows: WB CVR 0.744 , $p=0.007$; GM 0.748 , $p=0.007$; WM 0.682 , $p=0.043$. CVR maps in chronic TBI subjects show patchy, multifocal CVR deficits. Sildenafil increased CVR in TBI subjects (mean +10.9%) compared to HC ($p=0.0005$). Of the neuropsychological battery administered, only the Rivermead 13 and Neurobehavioral Symptom Inventory (NSI) scores showed a trend for a correlation (NSI correlation with the global CVR is 0.385 ($p=0.052$)). Mean global CVR correlated best with somatic neurobehavioral symptoms in chronic TBI subjects.

Conclusion: In chronic TBI, MRI-BOLD with hypercapnia challenge reliably distinguishes TBI from HC, with GM CVR showing the largest effect size. Single dose sildenafil improves CVR in TBI compared to HC. CVR correlates best with post-concussive symptoms. PDE5 inhibitors are a candidate therapy for TVI.

Neuropsychological Potential of Uznadze Fixed Set Method

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Introduction: In recent years increase of interest to integrative brain activity research was detected. It is not only about hemispheric interaction, related to the commissural system work, but also about intra hemispheric bounds, providing in particular the consistency in the different analyzer system work. Determination on inter-analyzer interaction (IAI) disorder should be important at the solving of diagnostic and expert tasks especially in the case when the symptomatic related to the central nervous pathology is not expressed. It is possible to judge about the process of diseased psychological functions recovery by the condition of IAI, as well as about the effectiveness of rehabilitation measures with him.

Aims: The intermodal tracts of white matter pathology in vascular disease are characterized with the expressed lateral variations that arises few questions in front of neuropsychology regarding the methods development for corresponding experiments conduction. The fixed set method can be used for similar aims, since the fact of the set irradiation presents from one modality to another is impossible without inter-analyzer intra and inter hemispheric bounds.

Methods: The process of the fixed set formation can be determined by two components: mnestic and regulatory. These set components can be considered from the neuropsychological factors (Luria) point of view and correlated with specific brain structures. It is possible to modify the fixed set method to the integrative brain activity research, because it corresponds to double stimulation principle, according to which the different information is given into two ears, eyes, hands what creates a special situation of conflict affecting to the final result.

Results: The modified experimental procedure of the fixed set method is created for IAI research with considering lateral differences. The procedure includes two experimental series: the setting and the critical. The materials consisting of the pair of different or equal size objects (volume, diameter). The setting experiments can be performed in any modality (for example, in visual). The critical experiments correspondingly are carried out in that modality that was not experienced the action in the setting serie (for example, in haptic). So that, there are two variants of experiment: in the setting serie the different in diameters spheres are given in the different semi-fields of respondent vision, wherein the image of the bigger sphere is given on the right/left semi-field. In the critical serie the same in mass and diameter spheres are inset into the respondent palms. The amount of illusions in haptic modality that are detected in the critical serie is an index of IAI features.

Conclusions: The procedures for fixed sets formation in different modalities can be combined in a single complex for intra - and inter hemispheric interactions research and can be used in further neuropsychological diagnostics of brain white matter.

Inter-analyzer Interaction (IAI) Disorder at Agenesis of the Corpus Callosum (CC) (The Analysis of a Single Case)

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Introduction: White matter is an anatomical base of brain integration realization; it provides the connection between different cortex zones inside one hemisphere as well as different hemisphere. Inter-system adjustments in sensor processes are important aspects of this problem. Many experimental works in neuropsychology are devoted to research of hemispheric interaction that cannot be said about the research of IAI. The paucity of such psychological studies can be partially explained by the lack of tools.

Aims: Analyze IAI disorder of the patient with white matter pathology with the help of fixed set (Uznadze) and compare his results with the results of another healthy respondent of the same gender, age and education level. Patient G. is a man 27 years old. Complete agenesia of the CC was detected of MRI data.

Methods: The methods of the fixed set by Uznadze was used. It was proven by his followers that the set has a none local character, but represents complete psychological condition, which possess generalization and irradiation properties. The later reveals in the possibility of the illusion set transposition from one correspondent organ to another, as well as from one modality to another. The setting and critical material was shown to the respondents. The materials consisting of the pair of different or equal size objects (volume, diameter) together with the instruction to express your estimation of the size ratio in each pair. The setting experiments were performed in a visual sphere. As a stimulating material the pictures of red spheres was used, in this case, the diameters of spheres were the different. The pictures were shown at the laptop screen to the different semi-fields of vision of the participants. Critical experiments were done in haptic sphere. The objects given to the respondents for the comparison were wooden spheres of the same color, mass and volumes. Participants embracing with their fingers the spheres surfaces with closed eyes were comparing their sizes. The amount of haptic illusions were estimated, which was acting as an index of the IAI preservation extend.

Results: The set formed in visual sphere transposed in the haptic sphere. Fourteen haptic illusions were the signature of the fixed set inter model irradiation of the healthy participant. The patient showed fast reduction of the set, which manifested in one haptic illusion.

Conclusions: The research in the field of IAI can complement neuropsychological syndromology, and suggested method acts as an instrument for inter-analyzer bounds preservation extend estimation at the diagnosis of white matter pathology.

Paroxysmal Sympathetic Hyperactivity in Severe Traumatic Brain Injury

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Object: To study the clinical features and outcome of a subset of patients who develop paroxysmal sympathetic hyperactivity (PSH) following severe traumatic brain injury (TBI).

Methods: This is a prospective observational study of patients admitted in the neurosurgery intensive care unit between September 2013 and November 2015 for treatment of severe TBI. PSH was defined as presence of four out of six symptoms (temperature of $>38.5^{\circ}\text{C}$; hypertension with systolic blood pressure $>130\text{ mmHg}$; tachycardia with pulse rate of >100 beats per minute, tachypnoea with respiratory rate of >30 breaths per minute; increased muscle tone, rigidity, dystonia, or decorticate/decerebrate posturing; and profuse sweating) simultaneously for a duration of atleast one cycle per day for atleast three days. The clinical characteristics and outcome of patients with PSH was compared with data from another study that included patients without PSH during the same period from same ICU. At the time of discharge patients were assessed with Disability Rating Scale (DRS), and at six months follow up with Glasgow Outcome Score Extended (GOSE). The correlation coefficients were calculated using the Spearman's rho.

Results: The incidence of PSH was 8% (29/343). Tachycardia, hypertension and sweating was seen in all the patients. Tachypnoea was seen in 24 (82.8%) patients and hyperthermia was seen in 28 (96.6%) patients. Posturing and dystonia was seen in only 13 (44.8%) patients. Thirteen (44.8%) patients had all six symptoms of PSH. There was significant difference between minimum and maximum heart rate, systolic blood pressure, respiratory rate, and temperature of each patient due to episodes of PSH. The mean number of days during episodes of PSH were seen was 10.72 ± 8 per patient. The mean number of episodes per patient per day was 2.27 ± 0.88 . Follow up data was available for 23 (79.3%) patients. At the end of six months 14 (60.9%) patients died, seven (30.4%) were severely disabled, and two (8.7%) moderately disabled. None of the patients with PSH had good recovery. There was significant correlation of GOSE with number of symptoms of PSH (Spearman's rho = 0.502, $p=0.015$). The patients with PSH had significantly higher DRS scores at discharge 25.3 (3.6) vs 19.9 (4.7), $p<0.001$; higher mortality at six months 60.9% vs 30.4%, $p<0.001$; and higher proportions with unfavorable outcome.

Conclusion: Presence of PSH in patients with severe TBI was associated with prolonged duration of hospital stay, poorer DRS at discharge, more deaths and unfavourable outcome. The number of symptoms of PSH had a significant an effect on outcome at six months.

Neurobehavioral Rehabilitation Outcomes in a Mixed Brain Injury Sample with Comorbid Serious Mental Illness

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Comorbid mental health symptoms pose a significant barrier to effective brain injury rehabilitation. Rates of psychiatric symptoms occur in up to 50% of individuals with brain injury, and premorbid mental health concerns further complicate rehabilitation and treatment (Masel & DeWitt, 2014). There is a lack of understanding and resources specific for treating this complex population, resulting in extended institutionalization, poorer outcomes, and higher utilization of financial and community resources (Wei, et al., 2005).

This specialized, highly structured rehabilitation program utilizing a transdisciplinary approach to treatment of brain injury and mental illness has been highly successful in reducing mental health symptom burden, improving cognitive functioning, and improving overall functionality and quality of life. The program includes daily skills groups for goal setting, coping, emotion regulation, social skills, yoga/mindfulness based interventions, as well as intensive individual psychotherapy and traditional rehabilitation. The average length of stay is nearly 6 months, and residents each receive an average of 2100 minutes of therapy per month, including physical, occupational, speech, recreational, and psychological therapies.

Over two years, the program has successfully discharged 14 patients to a lower level of care, 12 of whom were able to engage in pre and post treatment evaluation. Brain injury etiologies were variable, and included stroke, anoxic brain injury secondary to overdose, or traumatic brain injury secondary to a motor vehicle accident, fall, assault, or self-inflicted gunshot wound. Psychiatric diagnoses included Schizoaffective Disorder, Bipolar Disorder, Major Depressive Disorder with and without Psychosis or Catatonia, Generalized Anxiety Disorder, and Psychosis NOS.

Patients demonstrated significant functional improvement on the Mayo-Portland Adaptability Inventory - 4th Edition, with change scores ranging from 5 to 14 points. Further, patients demonstrated clinically significant reduction in depression and anxiety on the Beck Depression Inventory-II (13 point decrease) and Beck Anxiety Inventory (7 point decrease), respectively. Significant improvements were also observed on the Satisfaction with Life Scale, Patient Competency Rating Scale, and Awareness Questionnaire, suggesting improvements in overall life satisfaction, wellbeing, awareness, and ability to competently complete tasks required for everyday living. Cognitive scores also demonstrated a significant increase, on average 10 scaled score points on the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) from admission to discharge. Individual domains showed variable but overall significant increases in scaled scores (Immediate Memory = 13; Delayed Memory = 10; Visuospatial/Constructional = 10; Attention = 8; Language = 6). Such changes across all domains further translate into improved daily functioning and reduced burden on caregivers and community resources.

Recommendations for continued program development that incorporates recognition and treatment of mental health symptoms into the traditional brain injury rehabilitation model will be offered, including utilization of mental health professionals to improve overall functional outcomes in patients who have suffered a brain injury.

Ten Years Follow-Up of Patients in A Double-Blinded Randomized Study on Prostacyclin Treatment in Severe Traumatic Brain Injury

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Introduction: No prospective study has described the 10-years outcome in patients with severe traumatic brain injury (sTBI) treated according to an ICP oriented therapy based on the Lund concept. During January 2002 to December 2005 we conducted a randomized, double-blinded prospective study on the effect of prostacyclin as ad-on treatment in the Lund concept. The 10-years results are now reported.

Objective: To study if prostacyclin affected the clinical outcome 10 years after sTBI and to relate the clinical outcome to other monitored variables.

Methods and Materials: 48 sTBI patients, mean age 35.5 yrs, GCS ≤ 8 were included in the initial study. Two of the outcome parameters, GOSE and Barthel index, were administered by independent research staff. Data were prospectively collected.

Results: Initial median GCS was 6 (3-8), ISS 29 (9-50) and APACHE II 20.5 (12-32). At 6 months the mortality rate was 17% and ten years after trauma 27%. Only two patients died during the initial ICU period. Median time to death was 8 months (0.1-137). The mean \pm sd time to follow up in the alive group was 10.3 \pm 1.0 years. There was a weak correlation between the initial GCS and GOSE at ten years ($r=0.3422$, $p=0.023$ Spearman's rho). Median GOSE in those still alive and responding to the follow-up at 10 years was 7 (3-8) ($n=31$) compared to 6 (3-8) at 6 months ($p<0.001$, Wilcoxon Signed Rank). In 24 (77.4%) of these patients the median Barthel index was 100 (20-100) and corresponding GOSE 7 (4-8). There was a significant correlation between Barthel index and GOSE ($p=0.596$, $p=0.0021$, Spearman's rho). In one case there was an unproportional difference between GOSE (7) and Barthel index (20). This patient had a high suspicion of depression (MADRS score of 29). When excluding this patient from the correlation analysis between Barthel index and GOSE the figures were $p=0.677$, $p=0.0004$. Prostacyclin did not affect the mortality, GOSE or Barthel index at 10-years follow-up.

Conclusion: Our results show that even 10-years after sTBI the clinical outcome is favourable in patients treated according to the Lund concept. In some instances there is a discrepancy between outcome variables probably due to the mental condition of the patient. We were unable to demonstrate a statistical significant effect of prostacyclin on the clinical outcome.

Traumatic Brain Injury (TBI) During Deployment to a Combat Zone Results in Long Term Chronic Headache

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Introduction: Headache (HA) following TBI may produce significant morbidity. The current report deals with a controlled cohort study of headache in veterans of the Afghanistan and Iraq wars at 2 to 11 years after a Deployment-Related TBI (DTBI).

Methods: All subjects were recruited from Operation New Dawn (OND), a VA program for veterans deployed to Afghanistan or Iraq. For OND, the Veteran is screened for occurrence of a deployment-related DTBI, and, if positive, is referred to the TBI Clinic. To develop an unbiased recruitment pool, the first 500 Veterans found to have a DTBI (TBIS) were matched to controls without DTBI (CS) by age, sex, race, and time of deployment. From this pool of 500 pairs, 85 were randomly recruited. All subjects were contacted by telephone and all 170 subjects were administered 4 questionnaires (QS) including: TBI QS, Headache QS, PTSD civ, and Beck Depression Inventory 2. Data on HA included frequency, duration and intensity. HA frequency was expressed as: (a) Chronic Daily Headache (CDH – HA occurring ≥ 15 days/month); (b) Frequent Headache (FH – HA occurring 10-14 days/month); (c) Infrequent Headache (IFH - HA occurring 2-9 days/month); and (d) Very Infrequent Headache (VIFH – HA occurring ≤ 1 day/month). Comparisons of TBIS and CS were carried out with Fishers Exact Test.

Results: The 85 pairs of TBIS-CS recruited were 2 to 11 years post-TBI for TBIS, or post- deployment for CS. The TBIS and CS were pooled into two separate groups for comparison. For all TBIS, the data on headache frequency is as follows: CDH – 40 (45.5%), FH- 25 (28.4%), IFH – 20 (22.7%), VIFH – 3 (3.4%). For all CS, the data shows: CDH – 6 (7.0%), FH – 8 (9.3%), IFH – 26 (30.2%), VIFH – 46 (53.5%), ($P < .0001$ for comparison of TBIS vs CS). At 2-7 years after TBI, HA frequency data on 45 pairs shows the following - for TBIS: CDH – 20 (44.4%), FH – 14 (31.1%), IFH – 11 (24.4%), and VIFH – none; while for CS: CDH – 4 (8.9%), FH - 5 (11.1%), IFH – 12 (26.7%), and VIFH – 24 (53.3%) ($p < .0001$). At 8-11 years after TBI, HA frequencies for 40 pairs were calculated and for TBIS: CDH – 19 (47.5%), FH – 11 (27.5%), IFH – 7 (17.5%), VIFH – 3 (7.5%); while for CS: CDH – 2 (5.0%), FH – 3 (7.5%), IFH 14 (35.0%), and VIFH -21 (52.5%) ($P > .0001$). Comparing TBIS data at 2-7 vs 8-11 years after TBI found no difference.

Conclusion: DTBI results in HA occurring ≥ 10 days/month in 74% of TBIS compared to 16% of CS. HA frequency does not improve over time up to 11 years after TBI.

Proposal of A Systemic Description of The Clinical Phases in Neurocritical Illness

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While numerous treatment strategies for acute brain injury have been presented during the last decades, only few authors have addressed the huge variability in clinical course within the different categories of brain injury.

Whether the patient suffers from traumatic brain injury, intracranial bleeding or an ischemic insult there is a typical clinical course beginning with the insult and continuing until rehabilitation. The clinical course is influenced by several factors - patient comorbidity, timing and quality of the treatment applied and obviously the severity of the insult.

To improve the understanding of the pathophysiological dynamics and time course of the neurocritical illness, a description of four typical clinical phases is proposed. These phases are representative of acute brain injury and related to an arbitrary timeline. The acute phase is characterized by the immediate consequences of the insult. In the acute phase therapeutic measures are added in order to control the consequences of the insult. When the patient is stabilized, no further treatment modalities needs to be added. Then the patient enters the stabilization phase. The duration of the stabilization phase is typically longer than the acute phase. Depending on the severity of the insult, treatment is kept at the same or slightly lower level for several hours or few days. When the patients intracranial conditions are considered stable with no need for further escalation in basic or optional therapy, the patient enters the awakening phase. In the awakening phase, treatment modalities are withdrawn starting with optional therapy. If weaning of optional therapy is uncomplicated, weaning of sedation can be commenced. The patient is then gradually weaned from sedation until awake or unседated. Then the patient enters the rehabilitation phase. While unседated and still vulnerable to new insults and possibly in need of some kind of neurocritical care, the patient in the rehabilitation phase is gradually awakening and able to participate in rehabilitation therapy. The rehabilitation phase indicates that the patient is in the last stage of his illness. As mentioned above, the time line for the course is arbitrary and the different phases can last for a shorter or longer period of time.

Recognition of the different clinical phases of neuropathology allows the clinician to offer the right treatment at the right time, assessment in the right context, identification of normal or pathologic reaction to different treatment strategies. Applying the same treatment modalities on patients in different phases might potentially lead to different results or conclusions. Likewise lack of understanding of the clinical phases might potentially lead to false conclusions and mistimed interventions. Finally, the four phases concept helps the clinician to communicate the status of the patient correctly in a broader context.

Aspects of Striatal Engagement in TBI Depression

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Compared to rates of depression reported in the general population (6.7%), the occurrence of depression after traumatic brain injury (TBI) is substantially higher, with studies reporting between 50% to 77% of individuals with TBI being diagnosed with clinical depression. Feedback processing deficits have been shown to be associated with depression in non-TBI individuals. Since both feedback and depressive constructs rely on the fronto-striatal network, we first examined overall depressive symptomology and striatal activation during positive (monetary wins) and negative (monetary losses) feedback in individuals with TBI who had higher levels of depression compared to healthy controls (HCs). We further went on to examine the influence of depression on neural mechanisms of individuals with TBI who reported high and low depression. Specifically, we examined how the level of depression modulates brain activity during a task that presents TBI participants with positive and negative feedback, since the fronto-striatal activation associated with feedback processing has been shown to be impaired in depressed individuals without TBI. Based on prior findings in individuals with depression, we expected hypoactivation in the ventromedial prefrontal cortex (VMPFC) and the striatum in individuals with TBI showing higher rates of depressive symptomology.

Participants (TBI and HCs) underwent MRI of the head while performing a gambling task where they could either win \$1 for correctly guessing a value on the card or lose \$0.50 for incorrectly guessing a value on the card. Using a volumetric analysis after segmentation of sub-cortical structures, a significant difference was found between groups in the ventral striatum (VS) volume, bilaterally (right: $p=0.003$; left: $p=0.009$). Using a whole brain analysis, a significant difference during positive feedback presentation was found in the VS ($p=0.05$), but after accounting for the VS volumetric differences, there was no longer a difference in activation between groups. Depressive symptomology was assessed with the Chicago Multiscale Depression Inventory (CMDI), where significant between-group differences were observed on each subscale of the CMDI (Mood: $p=0.039$; Evaluative: $p=0.038$; Vegetative: $p=0.005$). The TBI group was then split between high and low scores on the CMDI-Mood subscale, using a score of 23 as a cut-off. TBI CMDI-Mood scores ranged from 9 to 40 and when divided into two groups. Contrary to our expectations, individuals with TBI who scored higher on the CMDI exhibited increased fronto-striatal network activation. Previous investigations showed similar findings in association with anxiety.

The current study provides evidence on the importance of controlling for volumetric differences in functional neuroimaging studies, specifically when there are differences in activation between HCs and TBI. The findings further describe how the neural mechanisms associated with feedback presentation are modulated by depressive symptomology in individuals with TBI and highlight the importance of examining depressive symptomology and associated comorbidities such as anxiety.

Stuck in a State of Inattention? Alterations of the Dynamic Network Connectivity in Adolescents with Concussion

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Introduction: Sports related concussions are a growing concern particularly in youth. Traumatic injury to the brain is often associated with physical symptoms (i.e. headaches, fatigue and visuomotor problems) and changes in cognition affecting attention, memory and executive function. How these symptoms and cognitive changes are related to changes in brain function is not well understood. Over the past decade, evaluation of resting state functional connectivity (rsFC) in the brain has emerged as a powerful tool to map the functional organization of the brain in both healthy and disease/injury states. We have previously reported significant differences in functional networks in the frontal regions of the brain in adolescents with sports related concussion (Borich et al, 2015). This and other studies of rsFC assume that the brain's intrinsic activity is stationary. Recently, this notion of stationary connectivity has been challenged. New approaches show that the intrinsic network architecture of the resting state is much more flexible and dynamic than previously thought. This new approach may be of great value in understanding alterations in brain function following concussion.

Aim: To evaluate the temporal dynamics of FC from our previous fMRI data of concussed (n=12) and healthy (n=8) adolescent athletes.

Methods: We were able to analyze the dynamics of the intrinsic connectivity networks (ICN) of 7 concussed and 6 healthy athletes. We computed the static spatial ICA and extracted 42 components of which 25 were identified as biological meaningful ICNs. A sliding window approach was used to compute the underlying dynamic network constellations of 25 ICNs identified by the previous ICA.

Results: The sliding windows analysis revealed two brain-states, common to both groups. Brain-state 1 was characterized by a high within-constellation correlation of 4 different attention-networks, a high within-constellation correlation of 5 visual-networks and by a high between-constellation correlation of the attention networks with the visual-networks. Brain-state 2 was characterized by a high correlation between the DMN and other networks representing higher cognitive functions, again by a high within-constellation correlation of the attention networks and a high within-constellation correlation of the visual-networks. The attention-networks constellation and the visual-networks constellation formed two separate and uncorrelated entities. The concussed group spent almost 2 times longer in brain-state 2 with a clear segregation of the attention and visual networks compared with the controls.

Conclusions: Our preliminary results suggest that concussed adolescents show alterations in dynamic network connectivity that is characterized by an internally directed focus of attention as well as a lack of flexibility in shifting from different sub-network brain states related to the attention and visual networks. This lack of dynamic flexibility in the concussed group may be reflected in the observed symptoms of cognitive fatigue and impairments in visual-motor function.

Detecting Effects of Subconcussive Impact on Brain Functioning Using Advanced Perfusion MRI

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Objective: While impacts to the head in contact sports are unavoidable and can cause serious consequence such as concussion, subconcussive impacts happen much more often and are implicated as a source for the deterioration of cerebral structure and function later in life. Emerging evidence suggests that effects of repetitive blows to the head are cumulative and that repeated exposure to subconcussive blows is connected to pathologically altered neurophysiology. Despite their high incidence, the pathophysiology of brain injury due to repetitive subconcussive impacts remains elusive. This study was aimed to characterize dynamic change of brain function using the advanced arterial spin labeling (ASL) MRI in non-concussed football players during the course of a single football season.

Methods: Eleven high school and collegiate football players underwent comprehensive clinical evaluations and MRI scans. The same clinical and imaging exam was repeated four times: three times during a game season (separated by one week each) and another after the season. In addition, baseline clinical evaluation was also performed before the season. The ASL MRI was conducted using an advanced 3D pseudo-continuous ASL (pCASL) sequence with multiple post-labeling delay.

Results: Paired t-tests on clinical data showed no decrements in cognitive performance and no increases in concussive symptoms from baseline to later evaluations. In contrast, ASL MRI showed significantly decreased cerebral blood flow (CBF) at the third (relative to the first) within-season time point. At the fourth time point (1~3 weeks) after the season, CBF showed only partial recovery.

Conclusions: These preliminary results indicate brain function and CBF changes in football players without concussion during a single season. Our findings also suggest that advanced MRI including ASL has the potential to enhance the capacity to detect sports-related subconcussive injury, monitor recovery of subconcussive neurologic effects, and track response to treatment interventions in the future.

Development of Silicon Nanowire Technology for Biomarker Testing

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Introduction: Technologies for the detection and measurement of biomarkers are being developed that allow for significant miniaturization, detection without labels and measurement directly in a specimen matrix. Silicon nanowires offer significant advantages compared to more traditional approaches, offering femtomolar sensitivity (in the range of 1000 of molecules), small sample volume (mL range), fast measurement time (seconds) and tolerance to matrix effects.

Background: Silicon nanowires are being developed for the detection of biomarkers of mild traumatic brain injury (mTBI). The measurement is based on a well-established antigen-antibody interaction. The binding of antigen to antibodies located on the surface of the nanowire results in the change of electric field in a narrow layer surrounding the nanowire, which affects conductivity of the nanowire and can be reliably measured using electronic means. This integration of biological reaction and electronics into the Tbit™ immuno-resistive™ sensor allows for the sensitive measurement in complex biological matrices, such as blood or plasma, without extensive sample preparation. Application of this technology to mTBI diagnosis promises fast delivery of actionable information about a patient's state.

Objective: This report describes the development, analytical characterization and clinical performance of the Tbit™ immuno-resistive sensor. The purpose of this study is to evaluate the ability of the Tbit™ system to predict results of computer tomography (CT) tests thus reducing effects of radiation exposure and cost.

Results: The Tbit™ sensor was developed using semiconductor manufacturing processes, resulting in a multiplex sensor that allows for measurement of concentration of S100 β and glial fibrillary acidic protein (GFAP). Single-crystal silicon nanowires were synthesized using metal nanoparticle-catalyzed chemical vapor deposition. Automated nanowire deposition onto the silicon wafer, followed by conventional photolithography, resulted in a multiplex, individually addressable immuno-resistive sensor device. Antibodies were attached to the activated surface through conventional aldehyde-primary amine chemistry, the sensors were treated with blocking reagents and dried.

Analytical characterization of the devices demonstrates that the response is proportional to the number of molecules bound to the nanowires and the response has good correlation with predicted nanowire behavior.

Analysis of clinical samples was performed using plasma samples collected 3 to 24 hours post traumatic brain injury event. We evaluated the ability of the Tbit™ immuno-resistive sensor to predict positive findings on computer tomography. The 31 clinical samples were collected at multiple clinical sites. The classification of samples was based on positive findings in CT (CT+ and CT-), and classification using Tbit™ sensor responses that combine responses in S100 β and GFAP channels. Twelve samples were CT- and Tbit- (True Negative), 9 samples CT+ and Tbit+ (True Positive), 10 samples CT – and Tbit+ (False Positive), and 0 samples CT+ and Tbit- (False Negative), resulting in sensitivity of 100% (95% CI 70-100%) and specificity of 55% (35-73%).

Validation of a Score to Determine Time to Post-Concussive Recovery

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Background: A reliable, developmentally appropriate and standardized method for assessing post-concussion symptoms (PCS) is essential to accurately determine recovery post-concussion and to effectively manage return to normal activities. The aim of this study was to develop an evidence-based, psychometrically-validated approach to determining clinically useful cut-off scores using a commonly administered PCS measure.

Method: The present study was a prospective, longitudinal observational study conducted between July 2013 and November of 2015 at a state-wide tertiary pediatric hospital. Participants were 120 children (5-18 years of age) presenting to the Emergency Department with a concussion within 48-hours of injury. PCS were assessed using the Post-Concussion Symptom Inventory (PCSI), acutely, 1-4 days post-injury and 2-weeks post-injury. Using comprehensive clinical assessment as the gold standard, we assessed the clinical cut-off discrimination ability of PCSI at 2-weeks post-injury using published approaches, and then varying each approach in an attempt to optimise their discrimination ability.

Results: Existing and potential clinical cut-off scores were explored in predicting delayed recovery. ROC curve results returned acceptable discrimination and sensitivity when PCSI items increased by severity from pre-injury by 1 or more. Compared to a published cut-off score being 3 or more items with increased severity, the present study suggests a more stringent cut-off requirement of 2 or more is better able to accurately classify symptomatic children.

Conclusion: This study provides the first validated index (2+ items, 1+ severity) of concussion recovery for children and youth. Further studies in more varied samples are needed to establish the effectiveness of this method.

Managing Challenging Behavior Following Early Childhood Traumatic Brain Injury: The Feasibility and Consumer Satisfaction of Delivering a Parenting Program with Clinician Support Via Videoconferencing

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Objectives: Traumatic Brain Injury (TBI) in early childhood conveys an increased risk for a range of poor long-term outcomes, including behavioral difficulties. Early intervention has the benefit of reducing difficult behaviors as rapidly as possible post-injury. The 'Signposts Program for Building Better Behaviour' ('Signposts') is a manualized face-to-face parenting program that was originally developed to assist parents of children with an intellectual disability in managing their child's behavior. A recent adaptation includes a TBI module, to assist parents' understanding and management of post-injury behavior. However, geographical and financial barriers remain, preventing parents from accessing the program. Clinician support via videoconferencing may eliminate many of these barriers, thus offering many benefits over traditional delivery. Videoconferencing also facilitates use of nonverbal communication, and the possibility to share program materials in real time. This study reports preliminary program feasibility and parent satisfaction when delivered with clinician support via videoconferencing.

Methods: The sample for this feasibility study was recruited from The Royal Children's Hospital, Melbourne. Parents were approached to participate if their child sustained a TBI between the ages of 2.0 and 6.11, within the previous two years. Once consent was obtained, parents met with the 'Signposts' clinician, and the program structure was explained and program materials were provided. Parents read the modules and completed homework exercises in their own time, and participated in videoconference meetings approximately once a fortnight with a clinician (5 sessions in total), using the program "GoToMeeting" on iPads. The aim of these sessions was to discuss homework responses, troubleshoot any difficulties the parent was experiencing, and to provide positive reinforcement for the parent's efforts.

Results: Preliminary feasibility and consumer satisfaction data from three mothers who successfully completed the program were analyzed. Overall, there was a good level of adherence with the program and its requirements. On average, the program took 17 weeks to complete. Videoconference sessions lasted 25 minutes. Parents reported that the videoconference technology was easy to use, and that this mode of delivery made the program easier to access than the traditional format. They reported feeling more confident in their parenting skills, and found the materials helpful. All parents reported that they received adequate clinical assistance.

Conclusions: This is the first study to investigate the feasibility of delivering a post-child TBI behavioral intervention with iPad videoconferencing as the medium of clinician support, and contributes to the burgeoning area of research utilising technology to improve post-injury outcomes. Overall, results suggest that parents are satisfied with the program when delivered with clinician support via videoconferencing.

Caregiver Outcome: Impact of Caregiver Personality and Patient Personality Change

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Objective: This abstract describes two different studies investigating caregiver outcomes after severe brain injury. Study 1 assessed whether personality traits of caregivers of individuals with severe brain injury predicted trajectories of caregivers' own health-related quality of life (HRQoL) and symptoms of anxiety and depression.

Study 2 investigated whether patient personality change was associated with caregiver outcomes: HRQoL and symptoms of anxiety and depression.

Methods: In both studies, caregiver outcomes were measured by the anxiety and depression subscales of the Symptom Checklist-90-Revised and the 4 mental subscales of the Short-Form 36 assessing HRQoL. Study 1 collected data from 52 caregivers (78.8% females, mean age=49.4 (SD12.8) years) of patients (71.2% males, mean age=41.0 (SD19.4) years) with severe brain injury at five time points during the first year after injury using linear growth models. Caregiver outcome was assessed at Neuro Intensive Care Unit, rehab admission and discharge, 3 mths. after discharge, 1 year after injury. Caregivers completed the full version of the NEO-PI-R 3 mths. after patient discharge.

Study 2 investigated a sample of 22 pairs of patients (63.6% males, mean age=43.6 (SD22.4) years) with severe brain injury and their caregivers (68.2% females, mean age=49.7(SD12.8) years). The caregiver rated the patient's premorbid personality at rehab discharge and postmorbid personality 1 year after injury using the observer version of the NEO-FFI. Measures of caregiver outcome was completed one year after injury.

Results: Study 1 found that all mental HRQoL, anxiety, and depression variables improved significantly over time. Caregivers, who were less neurotic and less conscientious, had higher vitality, social functioning, and mental health over time, while caregivers who were more agreeable had higher social functioning over time. Caregivers with lower neuroticism had lower anxiety, and depression over time, as well as a more accelerated decrease in anxiety and depression.

Study 2 found that 59.1% of patients were rated as having a personality change after their brain injury by caregivers. Generally, personality changes in patients were not associated with more distress and lower HRQoL in caregivers; however, changes in patient agreeableness were associated with lower HRQoL on the role limitations-emotional scale.

Conclusions: Caregivers' personality traits were strongly associated over time with mental HRQoL, anxiety, and depression, with neuroticism being especially important for trajectories of anxiety and depression. Patient personality changes were generally not associated with caregiver outcomes. This suggests that caregiver outcomes are highly associated with personality traits, and to a lesser extent associated with personality change in the patient. Over the course of rehabilitation, personality assessments of caregivers could help identify those most at risk for poor mental health and enable the tailoring of specific family interventions.

Chronic Bilateral Subdural Hematoma in a Young Male, a Rare Complication of Ventriculo-Peritoneal Shunt - Reporting a Case

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Hydrocephalus is a common clinical problem seen in neurosurgical practise and Ventriculo-Peritoneal shunt is a commonest surgical procedure done for its treatment. This procedure has various acute and delayed complications like intra-cerebral hematoma, infection, shunt malfunction and intra abdominal complications etc. Here we report a case of bilateral chronic subdural hematoma secondary to postoperative VP shunt done on right side for non traumatic hydrocephalus in a 21 years old male. The shunt was removed and right sided hematoma was evacuated and reinsertion of the shunt was done on the opposite side with no complications. Although rare, this complication must be kept in mind in cases of VP shunt who presents with deteriorating conscious level.

Keywords: VP shunt, Sub acute subdural hematoma.

Employment Outcome Ten Years After Moderate to Severe Traumatic Brain Injury: A Prospective Cohort Study

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Objectives: The objective of this prospective cohort study was to evaluate the probability of employment and predictors of employment in patients with moderate to severe Traumatic Brain Injury (TBI) over 10 years follow-up. 113 patients (18-67 years) were included with follow-up measurements 3, 6, 12, 18, 24, 36 months and ten years after TBI. **Main Outcome Measures:** Main outcome measure was employment probability over 10-years, and its predictors. Potential predictors of employment probability included patient characteristics, injury severity factors, functional outcome measured at discharge from the hospital with the Glasgow Outcome Scale (GOS), Barthel Index (BI), Functional Independence Measure (FIM), and the Functional Assessment Measure (FAM).

Results: Forty-eight patients (42%) completed the 10-year follow-up. Three months after TBI, 12% was employed, which gradually, but significantly increased to 57% after 2-years follow-up ($p < .001$), followed by a significant decrease to 43% ($p = .041$) after ten years. Ten years after TBI, we found that employed persons had less severe TBI, shorter length of hospital stay (LOS), and higher scores on the GOS, BI, FIM, and FAM at hospital discharge than unemployed persons. No significant differences in age, sex, educational level, living with partner/family or not, pre-injury employment, professional category, psychiatric symptoms, or discharge destination were found. Longitudinal multivariable analysis showed that time, pre-injury employment, FAM, and LOS were independent predictors of employment probability.

Conclusions: We concluded that employment probability ten years post moderate or severe TBI is related to injury severity and pre-injury employment. Future studies on vocational rehabilitation should focus on modifiable factors and take into consideration the effects of national legislation and national labor market forces.

Keywords: Traumatic Brain Injuries, Prospective studies, Outcome Measures, Rehabilitation

Disorders of Consciousness: Rehabilitation Programing

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This presentation will focus on the challenges surrounding the care of persons with disorders of consciousness. Discussion will include challenges with diagnosis and management of secondary complications. Emphasis will be given to the need for shared decision making with families during recovery as well as early mobility to prevent secondary complications. Education will be provided to introduce the Coma Recovery Scale as a outcome to track emergence in DOC patients. A case study will be presented to demonstrate use of outcome as well as treatment strategies to promote recovery.

Objectives:

- * Describe the state of disordered consciousness.
- * Identify management strategies for the prevention of secondary complications of DOC
- * Identify strategies for creating an environment of shared decision making and maintaining effective communication with family members of persons with DOC
- * Introduce the Coma Recovery Scale as an outcome measure used to track progress with DOC patients.
- * Provide a case example of a DOC patient. Identifying use of treatment strategies to promote emergence as well as demonstrate effective use of the Coma Recovery Scale to track improvement in Inpatient Rehab.

Upper Extremity Serial Casting: Applications in Chronic Brain Injury – A Case Study

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Rationale: To highlight serial casting as a treatment option for improving range of motion, decreasing spasticity and dystonia in a patient with chronic traumatic brain injury (TBI).

Background: Serial inhibitory casting is a treatment used to manage contractures and/or reduce abnormal tone after TBI. Serial casting involves applying and removing corrective casts in succession to increase extensibility of the soft tissues around and across joints along with neurovascular structures. Inhibitory casting is utilized to reduce abnormal tone by inhibitory cast components. Multiple studies have supported the efficacy of serial casting for improving range of motion when combined with botulinum toxin injections. Studies have demonstrated that unless the extremity function or weight bearing has improved that short term casting range of motion gains are not sustained.

Methods: The client was a middle aged male, 14 years after TBI with hypertonicity and dystonia in his left extremities, as well as significant left inattention. Over the course of 1 year, he demonstrated decreased active and passive range of motion in his left hand due to a maladaptive resting position of a composite fist hand and spastic wrist flexion with elbow hyperextension. Skin integrity and hand hygiene became a primary concern. He did not tolerate the use of a hand splint due to agitation and the ability to doff the splint independently. Consent was obtained for forearm botulinum toxin injections and serial casting. One week post-injection, we applied one long arm cast with elbow included to break up his synergy pattern. Three serial casts were applied. Standardized testing of 9 hole peg test, ROM, grip and pinch strength, and MAS were performed annually over 2 years.

Results: Observations of immediate changes in functional and biomechanical status after completion of the casting protocol will be presented. Left upper extremity MAS, grip and pinch strength measurements, ROM and 9 hole peg test data for the year prior to casting and the 2 years since the casting completion will be presented. Our data show that use of a multimodal serial casting approach with appropriately administered neurotoxin can have beneficial functional impact even years post-insult.

Conclusion: Serial inhibitory casting in conjunction with botulinum toxin was effective in treating decreased range of motion in the hand and wrist of a patient 14 years after TBI. Immediate changes were observed in tone patterns, which have been sustained over 2 years. These changes have been reinforced through the use of NMES, Neuromuscular re-education, Modified CIMT, and therapeutic Exercise modalities as a part of the clients existing neuromuscular treatment plan.

2 Years Outcome of Patients in Unresponsive Wakefulness Syndrome/vegetative State and Minimally Conscious State

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Background: Following severe acute brain damage, patients typically evolve from coma to an unresponsive wakefulness syndrome/vegetative state (UWS/VS; wakefulness without awareness) to a minimally conscious state (MCS; inconsistent but reproducible non-reflex behaviors). Reliable and consistent interactive communication and/or functional use of objects indicate the next boundary in the course of recovery – emergence from MCS (EMCS). There is to date no reliable predictive model of recovery from the UWS/VS and the MCS. A better understanding of patients' outcome would help in decisions regarding patients' care and rehabilitation, as well as end-of-life choices.

Methods: We collected demographic information, injury acute care history and longitudinal follow-up of 849 patients in UWS/VS and MCS admitted to 15 expert centers in Belgium (via the Belgian Federal Public Service Health). These patients were evaluated at 1, 3, 6, 12 and 24 months post-injury with the Coma Recovery Scale-Revised. The diagnosis was based on internationally accepted criteria of UWS/VS, MCS or EMCS. 24 months follow-up was available for 476 patients including 261 UWS/VS (88 traumatic, 173 non-traumatic) and 215 MCS (80 traumatic, 135 non-traumatic). Results were considered significant at $p < 0.001$.

Results: Patients who were in MCS one month after the insult were more likely to recover functional communication or object use after 24 months than patients in UWS/VS. Moreover, functional recovery occurred more often in MCS+ (79%) as compared to MCS- (29%) as well as mortality rate was more important in MCS- patients (68%) as compared to MCS+ (21%). Comparisons conducted within the UWS/VS and MCS groups based on etiology showed that traumatic patients had a better outcome at 24 months than non-traumatic patients. Among the traumatic brain injured patients, 49% of the MCS patients recovered communication or object use versus 23% of the UWS/VS patients. For patients who suffered from non-traumatic brain damage, 33% of the MCS recovered functional functions versus 3% of the UWS/VS patients. Among the non-traumatic patients, no difference was found between anoxic patients and patients with other etiologies regarding functional recovery.

Conclusion: These results confirm that patients with traumatic etiology have better prognosis than patients with non-traumatic causes. Our study also highlights that the outcome is significantly better for patients who are MCS one month post-injury as compared to patients who remain UWS/VS at that time. Concerning MCS patients, the outcome is significantly better for patients who are MCS+ one month post-injury as compared to patients who are MCS- at that time.

Fatigue Following Mild Traumatic Brain Injury: A Six-Month Prospective Cohort Study

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Objective: Fatigue is a frequent and profoundly disabling symptom following mild traumatic brain injury (mTBI), that may even persist for years. Approximately 85-90% of the patients with TBI sustain a mild TBI, and among these patients, about 68% experience complaints of fatigue in the acute phase following injury. To date, there is little published data on the specific course of fatigue following mTBI. The main objective of the current study was to examine prevalence and severity of fatigue following mTBI over 6 months. In addition, we examined correlates of fatigue, including anxiety, depression and coping styles, and we investigated early predictors of fatigue at 6 months.

Method: We included 433 mTBI patients, who all completed questionnaires at 2 weeks, 3 months and 6 months. Fatigue was assessed with the Checklist Individual Strength, comprising four subscales: Fatigue severity, Concentration problems, Reduced motivation and Reduced activity. Furthermore, we examined anxiety and depression (Hospital Anxiety and Depression Scale) and coping styles (Utrecht Coping List).

Results: The preliminary results show that severe fatigue was experienced by 37%, 22% and 20% of the mTBI patients at 2 weeks, 3 months and 6 months post-injury, respectively. There was a statistically significant effect of time on all fatigue subscales. Post-hoc comparisons indicated a significant decrease in fatigue scores between 2 weeks and 3 months, but not between 3 months and 6 months, except for the Reduced activity scale. Fatigue at two weeks contributed to 42% of the variance in fatigue at 3 months ($r=.64$, $p < .001$) and 37% of the variance in fatigue at 6 months ($r=.60$, $p < .001$), and fatigue at 3 months contributed to 67% of the variance in fatigue at 6 months ($r=.83$, $p < .001$). Furthermore, fatigue was significantly correlated with anxiety, depression, active coping and passive coping at all time intervals. Significant predictors of post-mTBI fatigue at 6 months were depression, anxiety and the presence of severe fatigue at 2 weeks.

Conclusions: Fatigue is a frequent and persistent complaint after mTBI that decreases over the first 3 months after injury but then remains relatively the same. Experienced fatigue in the early phase post-injury and levels of anxiety and depression, appear to be significant predictors for fatigue at 6 months. These findings, together with strong relations found between fatigue and coping styles, may contribute to the development of new treatments for early intervention following mTBI.

Keywords: Fatigue; mild traumatic brain injury; longitudinal study; correlates

Pediatric Concussion Evaluation in Europe: Military Medical Providers Leading the Way

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Background: This presentation outlines a performance improvement project highlighting the results of a pediatric working group to educate medical providers, coaches, parents and teachers regarding sports concussion and return to school/return to play activities for children who sustain a concussion.

Mild traumatic brain injury (mTBI) or concussion remains significantly underreported and underdiagnosed. This is of particular concern in the pediatric population as evidence is beginning to highlight how children playing impact sports may not only be at increased risk of concussion but how cumulative concussive events may degrade executive function and prolong recovery in this population. The military treatment facilities and Department of Defense Education Agency schools have collaborated in training education efforts to target pediatric concussion evaluation management using established Return to School/ Return to Play guidelines.

Methods: A retrospective case analysis of emergency room and primary care encounters on 40 pediatric patients demonstrated how pediatric concussion evaluation and screening was impacted by a substantive training effort to educate medical staff on return to play and return to school graded concussion evaluation recommendations for pediatric patients. Preliminary process results indicate that the training can be effective in engendering a cultural change towards accurate identification of concussion and identifying potential barriers that impact compliance. The retrospective case analysis consisted of (n= 41) pediatric patients diagnosed with concussion over a twelve month timeframe. Case records were paired with provider training records to correlate pediatric outcomes to provider training. Questions asked were: a) whether the providers received training and how many exposures to education and training they had in the past year, b) whether they found it beneficial to their identification and assessment of pediatric concussion and, c) whether the pediatric concussion training was beneficial to them in helping to manage return to school and return to play.

Results: Record reviews indicate a slightly higher than national average incidence of concussion and a mean age of 15.3 years. Males were twice as likely as females to experience concussion. Mechanisms of injury were varied. Results were matched in a Chi-square analysis to correlate training effectiveness to pediatric patient outcome. The statistical significance level was set at $P < 0.05$. The record review revealed that most children (and their parents) seen in the ED had been exposed to pediatric concussion education at least twice over the past 12 months.

Conclusion: Pediatric concussion is a significant health concern that is often underreported and underdiagnosed. Pediatric concussion-specific training can help not only to improve standardized medical management, but also to increase awareness and early care-seeking behaviors among school staff, sports personnel, families and student athletes. Through early recognition, prompt identification, and standardized medical evaluation, children who are concussed will likely have a faster course of recovery.

Pathological Fatigue in Young Survivors of Acquired Brain Injury

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Objectives: Fatigue is commonly described as one of the persisting sequelae after acquired brain injury (ABI), and it is reported after both traumatic (TBI) and non-traumatic brain injury. Only scant research has specifically addressed fatigue in young brain injury survivors, and no investigations have addressed to what extent young ABI individuals experience fatigue. Consequently, this study aimed at investigating prevalence and severity of fatigue in young survivors of acquired brain injury (ABI) compared to a healthy control (HC) group.

Methods: Young individuals with ABI between the ages 15-30 were seen for an interdisciplinary assessment at a regional outpatient clinic. As a part of the assessment, they completed the Multidimensional Fatigue Inventory (MFI-20) consisting of five subscales: General Fatigue (GF), Physical Fatigue (PF), Mental Fatigue (MF), Reduced Activity (RA), and Reduced Motivation (RM). Pathological fatigue was defined as a score ≥ 12 on the GF-scale. Additionally, a group of HCs completed the MFI-20 via an online-survey. Adjusted mean differences between the two groups were calculated using a MANCOVA. Lastly, logistic regression analysis was used to investigate the prevalence of pathological fatigue adjusted also adjusting for gender, age and level of education.

Results: The majority of the patient group (n=83) were females (51.8%) with a mean age of 23.8 (SD3.8) years. Most had acquired a TBI (43.4%), a tumour cerebri (18.1%) or a stroke (16.9%), and 69.1% had acquired their ABI during the last year. The majority of the HC group (n=167) was female (59.3%) and had a mean age of 26.2 (SD2.8) years.

The patient group had significantly higher scores on each of the subscales of the MFI-20 and adjusted mean differences on the subscales were as follows: GF: M=5.2, 95% CI [4.1,6.3]; PF: M=4.3, 95% CI [3.0,5.9]; MF: M=5.4, 95% CI [4.2,6.8]; RA: M=1.6, 95% CI [0.7,2.5]; RM: M=2.5, 95% CI [1.6,3.5].

In the patient group, 79.7% scored above the defined cut-off for pathological fatigue, whereas the responding in the HC group was 28.7%, and this difference was significant ($\chi^2=54.0$, df=1, $p<0.001$). A logistic regression model including gender, age and level of education found that young patients with ABI had 11.5 times (OR=11.5; 95% CI [5.1, 25.6]) higher probability of experiencing pathological fatigue than the HC group.

Conclusion: Young survivors of ABI experience significant higher levels of fatigue compared to HCs and had a much higher probability of pathological fatigue. Fatigue can potentially become a prolonged and distressing problem after ABI with considerable effect on the social life and wellbeing.

Echocardiographic Patterns of the Neurogenically Stunned Myocardium Following Traumatic Brain Injury in Adults

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Aim: To outline the echocardiographic patterns of neurogenically stunned myocardium (NSM) following traumatic brain injury (TBI). Only trauma patients with isolated severe [Glasgow Coma Scale (GCS) < 8] TBI were included.

Methods: Fourteen patients were admitted to our intensive care unit (ICU) with severe isolated TBI as their primary diagnosis. All were sedated, mechanically ventilated, and followed by the neurosurgery team. Patients received a daily echocardiography that focused on possible left ventricular (LV) abnormalities. The study was approved by our Institutional Ethics and Research Committee.

Results: Fourteen patients (38.1± 9 years old, 4 females) with an APACHE II score of 20.5 ± 0.6 participated in the study. Fourteen percent of patients presented with pulmonary edema and 85.5% exhibited ECG abnormalities. All patients were admitted to the intensive care unit (ICU) due to severe TBI (Glasgow coma scale <8, while Marshall scale on brain CT scan ranged from 3 to 4). Twenty four to 48 hours following admission, all patients exhibited clinical and radiological features of acute pulmonary edema as well as hemodynamic instability. Laboratory data showed elevation of lactate (lactate 2-4 mmol/L) and a slight elevation of troponin-I (1,2 - 2,1 µg/L). Transthoracic (TTE) and transesophageal echocardiography (TEE) revealed severe systolic dysfunction (Left ventricular ejection fraction 25-35%) while the following echocardiographic patterns were observed: a) global LV hypokinesia (14.2%), b) features of takotsubo cardiomyopathy (14.2%) and c) features of reverse takotsubo cardiomyopathy (71.4%). Follow-up echocardiographic examinations revealed that 4 patients who progressed to brain death all presented with features of reverse takotsubo cardiomyopathy which did not resolve. Cardiac function was normalized in 8 out of 10 patients who survived during a 60 days follow-up period.

Discussion: In this small cohort, we observed an echocardiographic pattern resembling reverse takotsubo cardiomyopathy in 71.4% of cases. Four patients out of fourteen progressed towards brain death; thus this might be associated with poor prognosis. Larger prospective studies are required to explore this more thoroughly.

Conclusion: Following TBI, the presence of a reverse takotsubo cardiomyopathy might be associated with poor prognosis.

Response to Neurostimulant Trials in a Clinical Sample of Children with Acquired Brain Injury and Disorder of Consciousness

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Objective: Neuropharmacologic intervention for responsiveness in pediatric brain injury patients with disorders of consciousness (DOC) is largely extrapolated from the adult literature. In several small studies (each with less than or equal to 10 participants), some pediatric brain injury patients appear to show response to dopaminergic agents (primarily amantadine and pramipexole). Our aim was to assess response to neurostimulants in a pediatric brain injury population on an inpatient rehabilitation unit with a dedicated responsiveness team.

Methods: A retrospective chart review was performed on pediatric inpatients from November 2009 to June 2016 with DOC after acquired brain injury (ABI), whose care included a trial of at least one medication to improve arousal and responsiveness. As part of clinical care, children were serially assessed using standardized measures of responsiveness (Coma Recovery Scale-Revised and/or Rappaport Coma/Near-Coma Scale). During weekly responsiveness team meetings, data from these measures were combined with input from the treating therapists to yield a consensus determination of whether or not any clear response was observed during a medication trial.

Results: Data from 29 patients was reviewed (mean age 11 years, range 1-20 years). Fifteen patients sustained a traumatic injury and 14 patients had other forms of ABI (anoxic, infectious, and oncologic were most common). Seven patients were trialed on amantadine; one (14%) had increased alertness, and 1 (14%) had adverse effects leading to medication discontinuation. Five patients were trialed on bromocriptine; one (20%) had increased alertness and none had adverse reactions. Carbidopa-levodopa was trialed in 18 patients; six (33%) had increased alertness, and the medication was stopped in 6 (33%) due to adverse effects. Methylphenidate was started in eight patients; four (50%) were observed to have increased responsiveness, and the medication was stopped in 2 (25%) due to side effects. Zolpidem was briefly trialed in 4 patients, none of who were observed to have increased arousal. In total, 12 children (41%) were felt to have a positive response to at least one medication, and 10 (34%) had adverse reactions which led to discontinuing medications. Another 5 children showed improvements but due to timing and other medical changes (weaning of sedating medications), it was not clear that gains were directly tied to the addition of neurostimulants.

Conclusion: In this small clinical sample, carbidopa-levodopa and methylphenidate, which have been less studied for responsiveness in DOC, showed promise for improving arousal but were also associated with side effects in some patients. Given the low rate of response to zolpidem identified in the adult literature, its potential for beneficial effect for a subset of children is not yet clear. Overall, future work is needed to identify a strategy for identifying which children may respond to which medications at which times post-injury.

Factor Analysis of the Everyday Memory Questionnaire in Persons with Traumatic Brain Injury

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Objectives: To investigate the factor structure of the Everyday Memory Questionnaire (EMQ) in persons with traumatic brain injury (TBI).

Method: This was a secondary analysis based on baseline data from two clinical trials targeting memory impairment after TBI. Participants were 169 persons with complicated mild, moderate, or severe TBI who were an average of 41 months post-injury. They completed the EMQ via clinical interview. Factor analysis was conducted using a three-factor maximum likelihood model with a polychoric matrix and oblique rotation.

Results: The three factors accounted for 49.2% of the variance, with moderate correlations observed between the factors. The three factors appeared to represent general everyday memory (prospective and episodic), conversational memory, and spatial or action memory.

Conclusions: The three factors of the EMQ are consistent with the heterogeneity of memory impairment observed after TBI. The factor scores may be used to target treatments for impaired memory and to evaluate their effectiveness.

Concurrent Validity of the Rey Tangled Line Test in Traumatic Brain Injury

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Introduction: Batteries of neuropsychological assessment have been compiled to assess cognitive impairments across a range of cognitive domains. With many measures, it is well established which domains are assessed, while with other tests, there is still debate as to which domains are being tested¹. The Rey Tangled Line Test (RTLTL) is a neuropsychological test which is less frequently used and less well understood.

The primary goal of the current study is to determine concurrent validity of RTLTL latency time compared to scores on other standardized neuropsychological tests representing measures of a variety of cognitive domains. A further goal of this study is to determine if RTLTL performance is robust enough to be effected by impairments in different cognitive domains or is a test of a specific domain. If the RTLTL test is a more robust measure it may show utility as a rapid screening measure of cognitive impairment.

Methods: Participants - 100 participants were selected from a NIH IRB approved natural history study of non-penetrating TBI. The subjects first assessment point was used, which, due to the nature of recruitment, was anywhere from 30 days to five years post injury. All subjects were able to accurately complete a reading screening; all patients with impaired vision were excluded.

Analysis: Pearson's correlations (r) were calculated between RTLTL latency (time to complete) and other standardized neuropsychological measures. Subjects were divided by injury severity for further examination of correlations. Correlations were also calculated for all subjects at 180 days since injury, to ensure correlations were not driven by time point. A MANOVA was run to examine the effects of injury severity, time since injury, and the interaction of the two on psychometric test scores

Results: There were significant correlations between completion time on the RTLTL and at least one test in each cognitive domain with the exception of construction for mild and moderate TBI subjects. There were no significant correlations between RTLTL and any other neuropsychological measure for those with severe TBI. The following tests were significantly correlated with the RTLTL for both mild and moderate TBI: Trails A & B, symbol search and digit span.

Discussion: These results demonstrate high concurrent validity with multiple neuropsychological measures. This finding is important in that the RTLTL does not appear to assess a single cognitive function but rather is a more general measure of the intactness of cognitive functioning. This finding may indicate that the RTLTL might serve as a useful screening measure for presence of mild to moderate TBI.

The Effect of Post-Traumatic Stress Disorder Related Symptoms on Longitudinal Neuropsychological Performance and Brain Volume

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Introduction: Post-traumatic stress disorder (PTSD) is a common comorbidity of mild traumatic brain injury (mTBI). While symptoms associated with mTBI are expected to subside, 15-20% of cases report persistent complaints and it has been shown that brain volume and neuropsychological performance differ in patients with mTBI and PTSD versus mTBI (Lopez et al., 2016). The purpose of the present study is to longitudinally examine brain volume and neuropsychological performance differences between those with mTBI and those with mTBI who endorse PTSD-related symptoms. A secondary goal is to assess whether the aforementioned findings were attributable to PTSD uniquely; thus, a lower PTSD Checklist (PCL) cut-off is utilized to include those who exhibit symptoms of disorders related to PTSD, including those with elevated levels of anxiety and depression.

Methods: T1-weighted images were collected on a Siemens Biograph MR 3T scanner. Image segmentation was conducted using the FreeSurfer software package (version 5.3) longitudinal pipeline. Bilateral amygdala, hippocampus, entorhinal cortex, middle temporal cortex, and parahippocampal cortex were selected for analysis.

Neuropsychological tests selected to measure learning, memory, and processing speed were the California Verbal Learning Test-II (CVLT-II) Total score and Long Delay Free Recall, Wechsler Adult Intelligence Scale- IV (WAIS-IV) Processing Speed Index (PSI) and Working Memory Index (WMI), and Trail Making Test A and B.

Subjects were divided into two groups based on their highest PCL score. A score of 36 and above was used to identify individuals who exhibited PTSD-related symptoms. Those below 36 were classified as mTBI-only.

A repeated measure MANCOVA using PCL classification as a between-group factor, controlling for intracranial volume and age, was conducted to analyze volumetric differences between 180-day and 1-year time points for PTSD and mTBI groups. A repeated measure MANOVA with PCL as a between-groups factor was conducted to assess neuropsychological differences.

Results: 26 patients (mean age: 47.7) with mild and complicated mild TBI (8 PTSD+TBI and 18 mTBI) were evaluated at 180-day and 1-year post-injury.

Analyses did not yield any significant differences between patients with PTSD-related symptoms and mTBI-only groups in brain volume or neuropsychological performance.

Discussion: This study did not find differences in any of the selected ROIs or neuropsychological tests. It is important to note that in selecting a PCL cut off of 36 instead of 44, subjects with psychopathology other than PTSD were captured. Subsequently, the absence of differences suggests that simply exhibiting symptoms related to PTSD is not enough to manifest alterations in brain volume and cognition; rather, the amalgam of symptoms that constitute PTSD may be underlying such changes. Our findings support the conclusions of Lopez, et. al. (2016), that change in brain volume and cognition associated specifically with PTSD as a disorder is distinct from other forms of psychopathology.

Screening for Hormonal Deficiencies in Serum from U.S. Marines with Blast-Related Mild Traumatic Brain Injury: Preliminary Findings

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Background: The estimated prevalence of traumatic brain injury (TBI) within the 2.3 million American troops deployed to Iraq and Afghanistan between 2001 and 2011 is 20%. A positive relationship between hypopituitarism and mild TBI (mTBI) has been found in the veteran and active duty military populations. It is not currently standard procedure to screen blast-related mTBI patients for pituitary hormone deficiencies. We sought to identify if serum hormone deficiencies characteristic of hypogonadism (HG) and growth hormone deficiency (GHD) occurred significantly more often among U.S. Marines who sustained a blast-related mTBI while deployed during Operation Enduring Freedom or Operation Iraqi Freedom than among similarly deployed Marines not blast exposed.

Methods: The Expeditionary Medical Encounter Database, which contains unique point-of-injury medical data, was used to identify male Marines meeting the study criteria: 75 with blast-related mTBI and 50 who were not blast exposed (NBE). The Department of Defense Serum Repository provided predeployment and postdeployment samples that were then measured for luteinizing hormone (LH), testosterone, and insulin-like growth factor-1 (IGF-1). Hormone deficiencies were identified based on generally accepted percentile cutoffs of a reference sample's normal distribution. HG was defined as a deficiency in testosterone levels and low or moderate LH levels (testosterone levels below the predeployment 5th percentile and LH levels above the predeployment 95th percentile, respectively). GHD was defined as IGF-1 levels below the predeployment 10th percentile. Preliminary analysis focused on individuals who were determined to be hormone deficient postdeployment and who were not hormone deficient predeployment. Fisher's exact test was used to measure significance because of the extremely small sample size.

Results: Based on the postdeployment serum sample, 7% (9/125) were classified as hormone deficient (6.7% [5/75] mTBI, 8% [4/50] NBE). Of those, 44% (4/9) were classified as HG (2 mTBI, 2 NBE) and 56% (5/9) were GHD (3 mTBI, 2 NBE). Fisher's exact tests for the relationship between each condition and mTBI were not statistically significant ($p = 0.64$ and $p = 0.64$, respectively).

Conclusions: No statistically significant relationship was found between the two hormone deficiencies and mTBI status in this sample of male enlisted Marines. This contrasts with the significant effects of mTBI on hormone abnormalities found in recent studies of veterans. Two factors may contribute to this discrepancy. First, the veteran population was significantly older, had a lower fitness level, and was receiving outpatient medical treatment. Second, hormone deficiencies in the Marines may be underestimated. Hormonal screening generally involves measuring a larger number of hormones and using provocative testing to identify deficiencies more accurately; however, the serum volume available for the current study was limited. Further investigation is warranted to determine the prevalence of posttraumatic hypopituitarism in active duty service members.

White Matter Integrity and Visual-Spatial Cognitive Performance in TBI using The Rey Complex Figure Test

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Introduction: The association between visual perception and construction in traumatic brain injury (TBI) and the early onset of Parkinson's (PD) has been studied using the Rey Complex Figure Test (RCFT).

Investigators have successfully utilized Diffusor Tensor Imaging (DTI) in PD to explore tracts involved in performance on the RCFT. The present study aims to examine the relationship between DTI measures and RCFT in TBI patients.

Methods: Participants were selected from a larger longitudinal study. Those who were seen one year post injury were included.

Measures: Twenty tracts (including left/right counterparts) were preselected based on their implication in visual-spatial construction. DTI measures of fractional anisotropy (FA), radial diffusivity (RD), and axial diffusivity (AD) were computed from diffusion-weighted images using the SINAPS [1] software package that includes motion and distortion correction, as well as white matter tract segmentation (Bennett, et al. 2013). Construction was measured using the RCFT copy trial using RCFT Total Raw Score and RCFT Time in seconds.

Analysis: An independent samples t-test was used to determine DTI tract mean differences. Pearson's r partial correlations were calculated between DTI tracts, RCFT Score, and RCFT Time controlling for age.

Results: A total of 36 TBI patients (Mage: 50.54 ± 18.33) were grouped based on MRI findings: MRI positive (N=23) and MRI negative (N=13). There were significant DTI differences between groups on 3 FA, 16 RD, and 18 AD measures.

Significant correlations between DTI measures and RCFT included tracts such as the corpus callosum and inferior fronto-occipital fasciculus (right). Correlation ranges for FA included $r = .410$ to $.518$ (Score) and $r = -.481$ to $-.482$ (Time).

The MRI positive group had significant correlations between RCFT Score and 3 FA measures including the corpus callosum. The MRI positive group's RCFT Time significantly correlated with the FA measure of corpus callosum (front) and RD measure of inferior fronto-occipital fasciculus (left). The MRI negative group's RCFT Score significantly correlated with the RD measure of cingulum (left). There were no significant correlations for the MRI negative group's RCFT Time and DTI measures.

Discussion: Our hypotheses that DTI measure are significantly correlated with the performance on the RCFT were supported. Specifically our finding that there were significant differences in MRI positive and negative groups indicate that there is less likely to be axonal damage in those without other MRI findings. Thus, the MRI positive group is of interest. DTI measures that correlate with both RCFT Score and Time (regardless of group) may be showing areas that are generally used in construction tasks, such as the corpus callosum (front and posterior), cingulum (left and right), and inferior fronto-occipital fasciculus (left). This finding lends additional support to the literature regarding the neural pathways associated with construction and spatial orientation.

Executive Function in Relation to Subjective and Objective Outcomes after TBI

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Introduction: Strength in Executive Function (EF) can serve as a protective and adaptive factor for outcomes in Traumatic Brain Injury (TBI). Outcomes are measured in various ways, including subjective experience and objective health-related functional outcomes and symptoms. The goal of this study is to investigate if specific aspects of Executive Functioning are most closely related to different types of outcome measures. We hypothesize that more problem solving and cognitive flexibility (applied) measures of executive functioning will correlate more strongly with objective outcome measures; while more abstract reasoning (abstract) measures of executive functioning will correlate more strongly with measures of subjective experience.

Methods: Participants - Participants included 61 adults selected from a larger natural history study of TBI one year post-injury. Participants had sustained mild, moderate and severe TBI.

Measures: Abstract EF included Wechsler Adult Intelligence Scale-IV (WAIS-IV) Similarities (SI) and Matrix Reasoning (MR) subtests. Applied EF included Booklet Category Test (BCT) and Trail Making Test-B (TMT-B). Health-related outcome measures were: subjective, Satisfaction with Life Scale (SWLS) and the 36-Item Short Form Health Survey (SF-36)-Mental and Physical Component Summary; while objective measures included the Extended Glasgow Outcome Scale (GOS-E), Headache Frequency, and Neurobehavioral Symptom Inventory (NSI).

Analysis: Pearman-Brown Correlation was used to explore the relationships between EF measures and outcome measures.

Results: Subjects mean age was 47.99 (SD = 17.68) and mean education was 15.62 years (SD = 2.67). As hypothesized, one applied EF measure was highly correlated with objective outcome measures. However, abstract EF measures were also correlated with one objective outcome and were not correlated with subjective outcomes. Correlations were: BCT—GOS-E (.321), BCT—NSI (-.290); WAIS-IV-SI—GOS-E (.305), WAIS-IV-MR-GOS (.390).

Discussion; The results support a strong correlation between objective outcomes and applied EF. Results also reveal a strong relationship between one objective outcome and abstract EF. Notably, while no subjective outcome measures were correlated with any EF measures, both were significantly correlated with two objective outcome measures. GOS-E was the only outcome measure (whether objective or subjective) to reflect both abstract and applied EF.

Self-assessment of subjective experience after TBI does not appear to be influenced by either problem-solving/cognitive flexibility or abstract reasoning. Additionally, objective assessments based solely on symptom-reporting are limited in their ability to reflect Applied EF. GOS-E, which allows health professionals to assign an objective outcome categorization based on a patient interview targeting a variety of functional domains, was the outcome measure most correlated with both abstract and applied Executive Function. Individuals' ability to meaningfully contribute to the GOS-E process alone however, does not appear to

translate into their ability to independently measure and report functional outcomes, regardless of their strength in executive function.

Trajectory of Anxiety, Depression and Neurobehavioral Symptoms in the First Three Years Following Traumatic Brain Injury

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Introduction: Anxiety and depression are common psychiatric comorbidities after traumatic brain injury (TBI), with prevalence rates ranging between 13-70% and 18.5-61%, respectively. Increased depression and anxiety have been linked to a prolonged recovery including longer lasting neurobehavioral symptoms. However, there is disagreement as to how these symptoms evolve over time. The present study aims to examine how anxiety and depression symptomatology change over the first three years post-injury as well as how they correlate with scores on the Neurobehavioral Symptom Inventory (NSI) at each measured time point. We hypothesized that anxiety and depression symptoms would decrease significantly over the three year period and that they would correlate positively with changes in NSI scores at each time point.

Methods: Participants were involved in a natural history study of TBI. Individuals who completed initial visits within 30 to 180 days after a TBI and follow-up visits at the one year and three year time points were included.

Measures: Participants completed the Brief Symptom Inventory 18 (BSI-18) and the NSI at all time points.

Analysis: Repeated measures ANOVAs were used to determine longitudinal changes in NSI scores and the anxiety and depression portions of the BSI-18. Pearson correlations were used to correlate the total NSI scores and the anxiety and depression portions of the BSI-18. The affective portion of the NSI was not included in the total NSI score to prevent artificial inflation of the correlations.

Results: Twenty-four individuals (14 male), aged 44.8 ± 17.7 years with 16.0 ± 2.4 years of education, participated. Repeated measures ANOVAs revealed a significant decrease in anxiety from the initial visit to the three year time point ($p=.038$), as well as a significant decrease in the total NSI score over the same time frame ($p=.009$). There were no significant changes in depression scores over time. Pearson correlations revealed significant positive correlations between the NSI and the BSI-18 anxiety score at all three time points (initial $p=.0003$; year one $p<.0001$; year three $p=.0009$). However, only the year one and year three depression scores were significantly correlated with total NSI scores (year one $p=.001$; year three $p<.0001$).

Discussion: In agreement with our hypotheses, anxiety and neurobehavioral symptoms appear to correlate positively with each other as well as decline over time. Depressive symptoms, however, appear to remain unchanged over time and correlate with neurobehavioral symptoms to a lesser extent than anxiety. These findings corroborate previous research findings indicating that TBI patients with higher levels of anxiety have more enduring neurobehavioral symptoms. Additionally, these findings suggest that anxiety symptoms may be more likely to emerge in soon after injury which is important when evaluating and providing care for TBI patients in the first months after their injury.

Cognitive Complaints Two Years after Traumatic Brain Injury in Adults: Preliminary Data from a Longitudinal Cohort Study

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Objectives: The objectives of this study were to describe the severity and nature of self-reported cognitive problems two years after traumatic brain injury (TBI), according to injury severity, and to explore correlates of significant cognitive complaints.

Methods: This project is derived from a larger longitudinal cohort study on mental health after TBI. Participants were aged 18-65 years, had sustained a TBI, and were admitted to a Level I trauma centre in Québec or Montréal, QC, Canada. The sample included 132 participants who completed the two-year post-TBI assessment (mean age = 42.3±14.3 years; 31.1% women; 58.5% mild, 20.8% moderate, 20.8% severe TBI). The main outcome measure was the Medical Outcomes Study Cognitive Functioning Scale (MOS-COG), a self-reported questionnaire including six items documenting the frequency of difficulties with reasoning, concentration, confusion, forgetfulness, sustained attention, and reacting slowly. Individual items and the total score are transformed into a 0-100 scale, higher scores suggesting better cognitive functioning. Significant cognitive complaints were defined as reporting cognitive difficulties most or all of the time (MOS-COG total score < 40). Potential correlates of significant cognitive complaints were injury severity, age, sex, education, work status, and a diagnosis of major depression, anxiety disorder, and substance use disorder (assessed with the Structured Clinical Interview for DSM-IV disorders).

Results: There was no significant difference between injury severity subgroups on the MOS-COG total score, although participants with severe TBI reported poorer cognitive functioning (M=54.0) compared to those with mild (64.3) or moderate (68.2) TBI (p=.094). These mean scores are 0.9 to 1.7 standard deviation below normative data from the MOS sample (Stewart et al., 1992; M=82.4±16.5). Forgetfulness was the most frequent cognitive problem in all three subgroups, while the least frequent problem was reasoning for participants with mild and severe TBI, and sustained attention for those with moderate TBI (conversely, this was the second most frequent problem in the severe TBI subgroup). Individuals with severe TBI were more likely to present significant cognitive difficulties (MOS-COG < 40) compared to other injury severity subgroups (mild, 10.5%; moderate, 11.1%; severe, 29.6%; p=.046). Results of a logistic regression revealed that the model accounted for 37% of the variance, and two variables were significantly associated with the presence of significant cognitive complaints: the presence of an anxiety disorder (p=.003) and work status (i.e., not working).

Conclusions: These data suggest that two years after their injury, adults with TBI report poorer cognitive functioning compared to the general population, even for those who sustained a mild TBI. Research efforts should be directed towards long-term, post-rehabilitation initiatives, such as objective measurement of cognition, documentation of functional limitations associated with cognitive problems, and development of accessible and adapted cognitive rehabilitation strategies.

Training Workplace Social Skills after Traumatic Brain Injury Using Work Related Communication Training for Employment Readiness (WoRCTER), a Computerized Role-play Program

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Objectives: People with traumatic brain injury (TBI) have difficulty modifying spoken word choices across social contexts. Politeness Markers (PMs) are word choices (e.g. would/could, possibly, and maybe) that soften the force of speech and are important to professional communication by indicating a cooperative tone. [1] People with TBI under-use PMs in discourse and this may affect work outcomes. [2,3] We examined the efficacy of a new web-based social/professional communication training program (WoRCTER) that targets PM use in individuals with severe TBI.

Participants: Eight participants with severe TBI completed training. Mean time post-onset (years)= 16.6(10.0). Mean age (years)= 37.5(10.6). Mean education (years)= 14.1(1.2); 4 males; 3 Caucasians, 3 African Americans, 2 Hispanics.

Procedure: WoRCTER is based on sociolinguistic theory of workplace talk. [1,4] It has four computerized training modules, each lasting 1.5-2 hours, administered on four consecutive days. Each module trains PM use for professional communication in one of four communication conditions (informing, requesting, advising, clarifying). WoRCTER software training includes verbal behavior modeling, audio/visual feedback, and new skill rehearsal in work related role-play scenarios. Participant performance during novel role-plays was recorded three times at baseline and three times post-treatment. WoRCTER software automatically transcribed the role-play audio. The number of trained and untrained PMs served as the dependent variables.

Analysis: We visually analyzed graphic displays and assessed the magnitude of change between pre-treatment and post-treatment by calculating a modified d statistic individually and averaged across participants for group statistics. [5]

Results: Six/eight participants increased total PM use (average modified d= 4.45). Five/eight participants increased trained PM use (average modified d= 5.38). Six/eight participants increased untrained PM use (average modified d= 1.13).

Conclusion: Computerized role-play training increased PM use in workplace role-plays in participants with severe TBI. Generalization to untrained PM use was observed in six participants.

Discussion: Role-play audio recordings together with graphic displays of the data will be presented for each participant with discussion of responders versus non-responders. Feasibility and importance of targeting PM training in individuals with TBI to improve workplace communication skills will be discussed and future research and clinical directions will be addressed.

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Evaluating Outcomes of Skills Retraining During Posttraumatic Amnesia Using Goal Attainment Scaling

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Background: Posttraumatic amnesia (PTA) is a phase of recovery from traumatic brain injury characterised by confusion, agitation and anterograde amnesia. The extent to which patients can benefit from active non-physical therapy during PTA has not been established. In a randomised controlled trial we evaluated the efficacy of activities of daily living (ADL) retraining during PTA.

Objective: This paper will examine attainment of specific ADL goals using Goal Attainment Scaling (GAS) by patients receiving ADL retraining during PTA.

Method: The treatment group included 39 patients with PTA >7 days. ADL retraining during PTA was guided by a therapy manual following errorless learning principles and targeted personal care (bathing, grooming, dressing, self-feeding) and basic meal preparation. After completing functional assessments, Occupational Therapists developed individualised goals using the GAS framework with a 5-point outcome scale (from -2 to +2). Goals were scored at PTA emergence as below expectation (-2, -1), at expectation (0), or above expectation (+1, +2).

Results: Thirty-four participants had GAS completed, with 5 participants (12.82%) deemed independent in all functional domains within the retraining program following assessment. Eighty-nine goals were set for the 34 participants with an average of 2.62 goals per participant. Of the 89 goals, GAS outcomes scored at PTA emergence were 6 below expectation (6.74%), 14 at expectation (15.73%), and 69 above expectation (77.53%). GAS outcomes were relatively consistent across the various domains of intervention. Sixty-eight personal care goals were developed with outcomes of 6 below (8.82%), 8 at (11.76%) and 54 above (79.41%) expectation. Within personal care, 23 participants had bathing goals; 3 performed below (13.04%), 1 at (4.35%) and 19 above (82.61%) expectation. Eight participants had grooming goals; 2 performed at (25.00%) and 6 above (75.00%) expectation. Twenty-eight dressing goals were set in total, with outcomes of 2 below (7.14%), 3 at (10.71%) and 23 above (82.14%) expectation. Within dressing, ten participants had upper body dressing goals; 1 performed below (10.00%), 1 at (10.00%) and 8 above (80.00%) expectation. Twelve participants had lower body dressing goals; 1 performed below (8.33%), 1 at (8.33%) and 10 above (83.33%) expectation. Six participants had full-dressing goals (combined upper and lower body); 1 performed at (16.67%) and 5 above (83.33%) expectation. Six participants had self-feeding goals; 1 performed below (11.11%), 2 at (22.22%) and 6 above (66.67%) expectation. Beyond personal care, 17 participants had basic meal preparation goals; 4 performed at (23.53%), and 13 above (76.47%) expectation. Finally, 4 participants had goals extending beyond an achieved goal where further independence could be reached. Of these, 2 performed at expectation and 2 above.

Conclusion: Results demonstrate that individuals in PTA have potential to make substantial gains in response to ADL retraining across domains of personal care and basic meal preparation.

Efficacy of Activities of Daily Living Retraining During Posttraumatic Amnesia

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Background: Posttraumatic amnesia (PTA) is a transient state after traumatic brain injury (TBI) characterised by disorientation and anterograde amnesia. In many settings patients in PTA do not receive active non-physical therapy due to risk of agitation and uncertain effectiveness due to amnesia. This approach, however, lacks evidence and ignores that amnesic patients may still benefit from some therapies (e.g., via implicit learning). To date there has been limited evaluation of the effectiveness of therapies, such as retraining of activities of daily living (ADLs), during PTA.

Objective: To assess the efficacy of ADL retraining during PTA, as compared with ADL retraining commencing after emergence from PTA.

Method: A randomised controlled design was used. Participants with severe TBI, admitted to rehabilitation and remaining in PTA for > 7 days, able to follow commands, medically stable, and independent in personal ADL pre-morbidly, were randomised to receive either ADL retraining with treatment as usual (TAU) or TAU alone (daily physiotherapy, speech therapy for swallowing and communication) during PTA. An independent assessor completed Functional Independence Measure (FIM) assessments at admission to inpatient rehabilitation, PTA emergence, discharge, and 2-month follow-up. Secondary outcome measures included PTA duration, length of rehabilitation inpatient stay, Agitated Behaviour Scale scores, and Community Integration Questionnaire (CIQ) scores at 2-month follow-up. The 92 participants recruited to TAU or treatment (Tr) groups did not differ significantly in age (TAU M=39.82, Tr M=45.63), years education (TAU M=11.20, Tr M=11.64), GCS (TAU M=8.17, Tr M=8.12), days post injury to admission (TAU M=16.73, Tr M=16.84), sex (TAU 77.55% male, Tr 76.74% male) or injury cause.

The therapy manual was developed to guide treatment based on errorless and procedural learning principles. Occupational Therapists completed initial functional assessments to develop individualised therapy goals. Treatment patients received up to one-hour daily of ADL retraining. TAU participants did not receive ADL retraining while in PTA. Both groups received Occupational Therapy as usual following PTA emergence.

Results: On the primary outcome measure, FIM total, random effects regressions revealed a significant interaction of group and time ($p < 0.01$). The treatment group had greater improvement than TAU in FIM total change scores from baseline to PTA emergence, which was maintained at hospital discharge, although not at two-month follow-up. Agitation did not differ between the groups during PTA. PTA duration and length of inpatient stay were not significantly different between groups although the TAU group showed a trend toward longer length of stay (M=78.59, SD=93.39) than treatment condition (M=63.12, SD=42.20), and longer PTA (M=53.14, SD=77.18) than the treatment group (M=44.23, SD=32.52). Groups did not differ on CIQ scores at follow-up.

Conclusion: Results suggest individuals in PTA can benefit from skill retraining during PTA despite significant cognitive and behavioural difficulties.

Self-Reported Anger and Depression in Middle-Aged Men: Implications for Diagnosing Chronic Traumatic Encephalopathy

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Introduction: Some former athletes and veterans with past exposure to repetitive neurotrauma are believed to be at risk for chronic traumatic encephalopathy (CTE). Recently, it has been proposed that problems with anger control and depression are defining clinical features of CTE. The purpose of this study was to examine self-reported anger problems and depression in middle-aged men from the general population and to relate those findings to the proposed criteria for CTE.

Methods: Participants were extracted from the normative sample database for the National Institutes of Health Toolbox, a battery of tests measuring cognitive, emotional, motor, and sensory functioning. A sample of 166 community-dwelling men between the ages of 40 and 60 were included in this study. All participants denied a history of head injury or traumatic brain injury. Participants completed scales assessing anger (Anger–Affect Short Form, SF), hostility (Anger–Hostility SF, Perceived Hostility SF), aggression (Anger–Physical Aggression Short Form), anxiety (Fear–Affect SF), and depression (PROMIS Depression 8b SF).

Results: For the item “I felt angry,” 21.1% of men reported sometimes and 4.8% reported often. When asked “If I am provoked enough I may hit another person,” 11.5% endorsed that item as true. There was a strong correlation between then Depression and Anxiety scales ($r=0.76$). There were moderate correlations between Depression and Affective Anger ($r=0.55$), Hostility ($r=0.52$), and Perceived Hostility ($r=0.34$). Furthermore, there was a strong correlation between Anger and Anxiety ($r = 0.61$). In response to the question “I feel depressed” in the last seven days, participants were dichotomized into a “depression group” (responses: Sometimes, Often, or Always; $n=49$) and a “control group” (responses: Never or Rarely; $n=117$). There was a significant difference between the control group and the depression group in Anxiety ($t=9.05$, $p<.001$, $d=1.51$), Anger ($t=5.40$, $p<.001$, $d=0.97$), and Hostility ($t=5.41$, $p<.001$, $d=0.97$).

Discussion: Some degree of anger and aggression are reported by a sizable minority of middle-aged men in the general population. Anger and hostility are correlated with depression and anxiety, meaning that all tend to co-occur. The comorbidity of affective dysregulation in men in the general population is important to consider when conceptualizing CTE.

Acquired Brain Injury and the Bonny Method of Guided Imagery and Music: A Case Study

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Objective: To test the Bonny Method of Guided Imagery and Music (GIM) with the spouse of a person living with profound acquired brain injury. Recognizing that it can be difficult for a spouse to process issues, it is hypothesized that GIM will allow the management of emotion and life changes, specifically anxiety and grief.

Methods: Helen Bonny created a therapeutic method of processing issues through imagery and music. Working in LSD experiments of the 1960's she surmised that images could be created using relaxation and music without the drug. GIM employs a dyad approach, with the Guide and client using specially programmed music. There are several components of a session, beginning with a relaxation, moving to the music and imagery, and then processing with color and form using a Jungian Mandala. The client is urged to keep a journal of insights between sessions. This Case Study concentrates on a 59-year-old woman whose husband suffered a stroke during hip replacement surgery. She was now the primary caregiver. The husbands' symptoms were extensive with his mental state being psychotic and paranoid, his short-term memory non-existent and some of his long-term memory gone.

Results: Before using this method to address her issues, she was swimming in uncharted waters with few navigational tools. Her imagery had many Jungian archetypes including a warrior woman who presented her with a sword and shield, tools to help her stay strong in the battle. She imaged a tree growing on a rocky bluff, with her process of this image as being able to weather a storm; that it took strong roots to keep the tree from toppling, that their marriage had been built on strong roots. Over the course of 10 sessions she had many images of being stuck in a dark place with no visible means of escape, only to find that by thinking outside the box in the world of the imagery she could indeed find her way, whether it be to squeeze through a keyhole or create an escape route in the images. In one of her final sessions the warrior woman reappeared and the client gave her back the sword and shield, realizing that she had found her inner strength and no longer required these items. This Method allowed the client to process her grief in real time without changing her husbands' perception of his life. He had become very intuitive to her mood and related it to his own life, causing increased anxiety and paranoia. She needed tools to remain neutral while caring for him.

Conclusion: The Bonny Method of Guided Imagery and Music can be a successful tool for a trained therapist. This Method provides alternatives to traditional talk therapy and medication.

Cerebrospinal Fluid (CSF) and Vibration of Skull in Acoustical Analysis of the Human Head to Monitor Brain ICP

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Non-invasive measurement of the Intracranial Pressure (ICP) is still a challenging issue in health monitoring and TBI. An accurate device to monitor the ICP non-invasively is a necessity particularly for patients in any clinical and transient situations. One novel non-invasive method can be based on transcranial acoustics signal processing in which the signals from intracranial and extracranial signals of different frequencies can be captured to be correlated to the ICP. For this reason acoustics and vibration characteristics of intracranial contents such as CSF, skull, etc. should be obtained and calibrated. Additionally the fluid structure interaction impedance is a necessity in acoustics analysis. In this study the effects of CSF pressure variation on the vibration of the skull at low and high-frequency modes have been examined. The human skull is approximately modeled as a hemispherical shell with mechanical characteristics of skull bone. CSF is considered as an inviscid and incompressible fluid since the range of in vivo CSF pressure variation is less than 80 mmHg (brain death). We study the influence CSF by pressure wave acoustic equation which is based on the fluid parameters such as density and sound speed. This unsymmetrical eigenvalue problem is solved by a finite element scheme to obtain the first 100 natural frequencies. In addition, the symmetrical and unsymmetrical mode shapes are obtained to show the skull vibration sensitivity due to CSF static pressure. The primary results show that the increase in CSF pressure causes small decrease in the unsymmetrical and symmetrical vibration frequency modes. Moreover, the modes of skull vibration sensitivity with respect to the CSF pressure variation are calculated. The sensitivity diagram demonstrates that the skull vibration in higher frequencies modes is more sensitive to CSF pressure variation than lower vibration modes.

Keywords: Non-invasive Intracranial Pressure Monitoring – Vibration Analysis – Finite Element – Acoustics – Fluid Structure Analysis.

Modifying the Acute Hospital Environment to Reduce Length of Post-Traumatic Amnesia After Brain Injury: A Pilot Randomised Controlled Trial

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Introduction: Post-traumatic amnesia (PTA) is a common sequela after traumatic brain injury (TBI). PTA disrupts engagement in occupation and relationship. Reorientation programs that aim to encourage appropriate interactions, improve environmental orientation, and increase awareness of time are an important component of neurotrauma treatment. Length of PTA has been strongly linked to eventual outcome following brain injury, and therefore understanding whether a comprehensive orientation program increases the likelihood of emergence remains an area of great interest. However, to date, few studies have investigated the effectiveness of reorientation.

Objective: The objective of this randomized controlled trial was to determine the effectiveness of an environmental reorientation program on time to emergence from PTA after TBI in an acute care hospital setting.

Method: This study used a pilot, randomized controlled trial design with concealed allocation and intention-to-treat analysis with n=40 adults with TBI in PTA. Participants were recruited on admission to a large, metropolitan trauma hospital in Melbourne (Australia), and use of a waiver of consent ensuring timely commencement on the study. The control group received usual care (inconsistent verbal orientation) and the intervention group received a standardised environmental reorientation program aimed at improving orientation to person (signage, photographs and familiar items), place (signage and cueing) and time (calendar clock and cueing to environment). The intervention was designed to include the elements of previously published orientation programs, such as North Star project. Outcome of time to emergence from PTA was measured on the Westmead PTA scale which was administered daily by an occupational therapist who covered all environmental cues prior to testing.

Results: Groups were equivalent at baseline (mean age of sample was 36 years, 80% of the sample were male) and there were no adverse responses to the environmental orientation program recorded during the study. While differences between groups in time to emerge from PTA were not statistically significant, the average time to emergence was shorter for those who received the standardised environmental reorientation program. This positive trend in favour of the experimental group suggest that our study was underpowered.

Conclusion: While this pilot study was underpowered, it provides promising feasibility data for a future, larger randomized controlled trial. In addition, both staff and family members indicated that the program was clinically valuable. Findings, however, must be interpreted with caution. While it seems common sense that environmental orientation aides, such as calendars and clocks, would hasten emergence from PTA, rigorous testing has not yet occurred.

Transcranial Direct Current Stimulation and Neural Reorganization after Aphasia Treatment

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Introduction: Recent studies have shown that transcranial Direct Current Stimulation (tDCS) may enhance the effect of aphasia treatment in people with post-stroke aphasia. tDCS is a noninvasive brain stimulation technique that modulates cortical excitability through a weak electric current delivered via electrodes on the scalp. It is assumed that anodal tDCS over language-related brain regions in the left hemisphere (LH) enhances aphasia recovery by facilitating recruitment of perilesional LH structures. This study aims to investigate the effect of LH anodal tDCS on the neural reorganization of language in the context of aphasia treatment.

Methods: We performed a neuroimaging study nested within a randomized controlled trial investigating the effect of tDCS on language functioning in aphasic patients in the subacute stage of stroke. Participants in the main study (n = 58) received two separate weeks of daily sessions of word-finding therapy, combined with either anodal tDCS (1 mA for 20 minutes) or sham tDCS over Broca's area, a LH area crucially related to language recovery. All participants' language abilities were assessed before and after the intervention. Those who were eligible and consented to MRI examinations, were also scanned directly before and after the intervention period.

- Structural MRI data were obtained during the pretreatment scanning session. These data will be used to determine lesion location and volume, and to check whether the tDCS target Broca's area was anatomically intact.
- Functional MRI (fMRI) data were obtained pre- and posttreatment sessions using an auditory comprehension task and a naming task (post treatment only). These task-related activation data will be used to identify the contribution of the left perilesional and right contralesional cortices during auditory comprehension, pre and post intervention, and naming function, post treatment. Lateralization indices (LI) will be calculated and used to relate fMRI changes to functional language outcome measures (word-finding / Boston Naming Test; functional verbal communication / Amsterdam-Nijmegen Everyday Language Test; spontaneous speech / Aphasia Severity Rating Scale). Lis will be compared for patients receiving anodal tDCS versus patients receiving sham, both pre and post treatment, to establish whether anodal tDCS enhances recruitment of perilesional LH structures.

Results: Thirteen participants took part in our neuroimaging study, with 6 and 7 participants per tDCS treatment group. The analysis is ongoing and is still blinded. Results will be available in March 2017.

Discussion: The results of this study will improve our understanding of the roles of the left and right hemisphere language reorganization in the early stage post stroke and will contribute to the ongoing investigation of tDCS as adjunct to rehabilitation facilitating brain plasticity.

Glycomic and Neuroproteomic Alterations in Experimental TBI: Comparative Analysis of Aspirin and Clopidogrel Treatment

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The number of patients sustaining traumatic brain injury (TBI) and concomitantly receiving pre-injury antiplatelet therapy such as Aspirin (ASA) and Clopidogrel (CLOP) is on the rise as the population ages. These drugs have been linked with unfavorable clinical outcomes following TBI, where the exact mechanism involved are still unknown. In this novel work, we aim to identify and compare the altered proteome profile imposed by ASA and CLOP when administered alone or in combination, prior to experimental TBI. Furthermore, we assessed differential glycosylation post-translational modification (PTM) patterns following experimental controlled cortical impact (CCI) model of TBI, ASA, CLOP and ASA+CLOP. Ipsilateral cortical brain tissues were harvested 48 hours post injury and were analyzed using an advanced neuroproteomics Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) platform to assess proteomic and glycoproteins alterations. Of interest, differential proteins pertaining to each group (22 in TBI, 41 in TBI+ASA, 44 in TBI+CLOP, and 34 in TBI+ASA+CLOP) were revealed. Advanced bioinformatics, systems biology and clustering analyses were performed to evaluate biological networks and protein interaction maps illustrating molecular pathways involved in the experimental conditions. Results have indicated that proteins involved in neuroprotective cellular pathways were upregulated in the ASA and CLOP groups when given separately. However, ASA+CLOP administration revealed enrichment in biological pathways relevant to inflammation and pro-injury mechanisms. Moreover, results showed differential upregulation of glycoproteins levels in the sialylated N-glycans PTMs which can be implicated in pathological changes. Omics data obtained have provided molecular insights of the underlying mechanisms that can be translated into the clinical bedside setting.

Evaluation of Vestibular Dysfunction Using the Virtual Reality and Eye Tracking Technologies

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Objective: The objective of this study was to develop the method of assessing the vestibular dysfunctions using the virtual reality and eye tracking technologies. The method would be very useful to identify and assess evidence on rehabilitation in patients with traumatic brain injury.

Study Design: To achieve this goal the vestibular dysfunctions were initiated in healthy participants during the perception of visually induced self-motion illusion (called “vection”). The vection illusion was evoked by the virtual environment rotation in the CAVE virtual reality system. To evaluate the vestibular dysfunctions eye movements were recorded during the self-motion perception.

Patients and Methods: To test the method forty four healthy participants took part in the experiment. Two groups were formed: the control group (23 participants) that had significant experience in resisting the vection illusion, and the experimental group (21 participants) with reduced ability to resist the illusion. A circular vection illusion was formed arising under the global rotation of optic flow in virtual environment. The quantitative evaluation of vestibular dysfunction was based on eye movement characteristics which were registered during the vection illusion perception. Simulator Sickness Questionnaire (SSQ) was used as a standard subjective measure of vection strength and negative symptoms (nausea, vomiting) level.

Results: Results showed that there were significant differences in eye movement characteristics and SSQ scores for participants of control and experimental groups. Participants of the control group showed the most active eye movements –higher blink and fixation frequencies and lower fixation durations and saccade amplitudes. They also showed the lowest SSQ scores. Other participants showed significantly lower blink and fixation frequencies and higher fixation durations and saccade amplitudes. However their SSQ scores were higher compared to the control group’s results. The positive correlation between SSQ scores and eye movement characteristics was revealed. Thus eye movement data were consistent with subjective measure of the vection illusion strength.

Conclusions: Testing vestibular function can be effectively performed using virtual reality systems, which enable to initiate different types of vestibular disturbances and to evaluate their strength in real-time mode. Our method based on eye movement characteristics revealed the ability to motion sickness resistance during vection illusion perception. So it may be successfully applied in diagnostics of vestibular disturbances during rehabilitation for patients with traumatic brain injury.

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Characterization of Concussion in Youth Ages 5-18 from 2014 National Electronic Injury Surveillance System Data

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Background: Sport-related concussion in school aged youth is a growing public health concern. 400,000 concussions occurred in High School athletics during the 2008-2009 school year and between 2006-2012 emergency department visits for sport-related traumatic brain injury increased by 140% in males ages 10-14 (Bakhos, Lockhart & Meyers, 2010; Coronado et al, 2015). Legislation and educational initiatives are increasingly targeting youth sports.

Objective: Characterize the nature of concussion occurring in youth aged 5-18 according to age, gender, nature, location and season of injury.

Method: Retrospective analysis of 2014 National Electronic Injury Surveillance System (NEISS) data. Categorical ages related to grade levels were utilized (ages 5-8 = early elementary, 9-11 = late elementary, 12-14 = middle school and 15-18 = high school).

Results: The sample of 5,235 children ages 5-18 was predominantly male (65.8%) with a mean age of 12.5. Pearson Chi-Square results were significant for differences between categorical age groups and gender, nature, location, and season of injury ($p=.000$ for all four comparisons). Distribution of concussion between age group and nature of injury showed sport related injuries to be most common in late elementary (ages 9-11), middle school (ages 12-14) and high school (15-18). Most common season of injury related to concussion was fall for all age groups except early elementary (ages 5-8). Distribution of age and gender revealed a higher number of male concussion in the late elementary age group (72.5%) with the highest number of female concussion occurring in the high school age group (39.1%).

Conclusion: Results indicate a considerable occurrence of sport-related concussion in late elementary, middle school and high school aged youth. Results warrant increased attention to the study of concussion in younger age groups, specifically late elementary and middle school. Fall may be a key season to target educational interventions around prevention and management of sport-related concussion.

Keywords: Concussion, Youth, Sports, Mild Traumatic Brain Injury, Pediatric

Employment Stability in Veterans with TBI: A VA TBIMS Study

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Objectives: Traumatic brain injury (TBI) is linked with chronic health conditions and disability in civilian and military populations. Individuals who sustain a TBI may face a multitude of challenges such as including physical, cognitive, and psychosocial limitations and functional deficits. These limitations typically result in dynamic consequences that negatively affect one's ability to reintegrate into their communities. [1-3] Vocational return is a viable means to enhancing cognitive, behavioral, and physical recovery after TBI. Employment instability after return to work (RTW) is common across TBI populations and occurs at higher rates among Veterans and Service members (V/SM). The objective of this study is to examine incidence and predictors of employment stability following RTW in V/SM with TBI.

Design: Prospective observational cohort study.

Setting: Four Department of Veterans Affairs (VA) Polytrauma Rehabilitation Centers (PRCs).

Participants: Enrolled in the VA PRC Traumatic Brain Injury Model Systems database within 2 years of injury who were discharged between January 2009 and June 2015. Individuals were > 18 and < 61 years of age. Eligible individuals completed post-injury follow-up data collected at one and/or two years post-injury with known injury severity and reported competitive employment at time of injury.

Main Outcome Measures: Employment stability (competitive employment at follow-up).

Results: The final sample included (n= 110) male (94%) V/SM with mild (26%), moderate (22%) and severe (52%) TBI. Over half (n=61, 55%) were stably employed at the time the first competitive employment date was recorded. Stably employed individuals were single (49%), Caucasian (79%), and had slightly better scores on the FIM (cognitive and motor) at discharge. Based on univariate analysis, more severe injuries and higher FIM motor scores at discharge were found to be significantly associated with employment stability. Comparison of follow-up data between the groups (stably and not stably employed) indicate V/SM who are stably employed have better scores on FIM motor, FIM cognitive, PCL-C severity, NSI, GAD-7 and PHQ-9.

Conclusions: Members of the Armed Forces serving in Operation Iraqi and Operation Enduring Freedom sustain TBIs and report symptoms within the initial years following injury. A number of unique factors affect employment stability in V/SM with TBI. Study findings identify V/SM who are stably employed and predictors of employment stability.

Neurological Outcomes in Australian-Rules Footballers with A History of Sports-Related Concussion

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Sports-related concussion is a common form of mild traumatic brain injury, and often occurs in collision sports. There is some evidence that persisting, cumulative and/or long-term neurological consequences can result from sports-related concussion. However, few studies have investigated these potential effects in Australian-rules football (AFL) – one of Australia’s most popular collision sports. The aim of this study was to examine cognitive, psychological, ocular motor and MRI outcomes in AFL players with a history of self-reported sports-related concussion. Participants were 15 active male amateur AFL players (average age = 24.3; average years of education = 15.07) with a history of sports-related concussion (average previous concussions = 2.2), and 14 sex-, age- and education-matched athlete controls (average age = 23.36; average years of education = 15.21) who had no history of neurotrauma or participation in collision sports. All participants completed a clinical interview, as well as psychological, cognitive, and ocular motor testing. MRI investigation involving structural, functional, and diffusion sequences was also completed. A significant group difference was found on the ocular motor switch task, a measure of cognitive flexibility, with AFL players scoring significantly worse than the athlete control group. However, the AFL players ability on this task was still within a clinically normal range, and there was no correlation between the number of previous concussions and performance. In the Hayling test, a measure of executive function, the AFL players performed significantly better than the controls, with both groups performing within a clinically normal range. There were no other significant group differences or clinically significant abnormalities on any of the other measures. The results from this preliminary study suggest that young-adult AFL players with a history of sports-related concussion had no clinically significant deficits on MRI, neuropsychological, and ocular motor measures, and did not differ from sex-, age- and education-matched athlete controls with no history of neurotrauma or participation in collision sports on all but two of the measures.

Neurosurgical Recovery Treatment Step-By-Step in Children with Severe TBI

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The main aim of treatment severe TBI is to preserve the injured brain within the primary level, in turn, supposes a maximally possible recovery of brain. On the other hand, functional restoration involves certain conditions.

From 2011 till 2015 in the Clinical and Research Institute of Urgent Pediatric Surgery and Trauma 96 patients with sTBI (GCS 4-8 scores) had a course of acute and early rehabilitation. In the majority of cases early rehabilitation started on 2nd week after the trauma, the time when most of patients regain their consciousness after coma. 44% of patients had rehabilitative surgeries because of extensive defects of the calvaria. The average time for the defect closure was 58 ± 12 days. 12% of patients were operated on for posttraumatic hydrocephaly.

Early rehabilitation principles included: support of vital functions, prevention of infectious and inflammatory processes, recovery and support the nutritional care, recovery of anatomical relations.

34% of patients had an early surgical rehabilitation due to defects of the skull (after DC). The average time to close the defect was 58 ± 12 days. 12% of patients were operated on for post-traumatic hydrocephalus. One month after the injury GOS was 1-2 - 24,5%; 3- 33,5%; 4-5 - 42%. After 6 months post-treatment increased the number of good results. Among survivors GOS was 2 - 4%, 3% 27, 4.5 - 69%.

Conclusion: The work of a multidisciplinary team at the beginning of the recovery period is similar to the work of the rescue team, as errors can lead to irreversible degradation, decay and death. The correct sequence of treatment is very important.

The most important thing is to find out the leading syndrome, which prevents further rehabilitation. From this point of view trephined syndrome it is one of the important reasons for the limited future rehabilitation. Restoration of the integrity of the skull leads to increase of the cerebrospinal fluid pressure, increase in the cerebral arterial pulsation, improvement in the cerebral blood flow, improvement of the cerebral metabolism and improvement the functions.

Brainstem Auditory Evoked Potentials (BAEP) as Diagnostic and Prognostic Neurophysiological Markers in Patients with Brain Concussion

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Introduction: Traumatic brain injuries (TBI) are public health problem of great importance. About 80% of them are mild TBI (MTBI). The standard approach in patients with concussion includes neurological /neurosurgical examination and imaging (CT/MRI). Despite normal results from these examinations, complaints of the patients persist and disturb their efficiency and quality of life for different long period of time - in 34% among patients it is established temporary disability up to 3 months and in nearly 9% of patients - up to 1 year after the trauma. The aim of this study is to investigate changes of BAEP in patients with brain concussion as diagnostic and prognostic neurophysiological markers and to estimate their role in monitoring and tracking the dynamics of pathological process and the effect of the applied treatment.

Method: Thirty four patients age range 18-50, with brain concussion (road, work accidents, domestic and sports injuries) were included in the study. Control group includes 35 subjects. In all 34 patients CT/MRI was conducted to exclude more severe TBI. All patients were conducted BAEP in the first month after injury. In 13 patients a BAEP follow-up was carried out on the 3rd, 6th month after the trauma, one patient -1 year, one patient -2 years after the injury.

Results: The abnormal rate of BAEP in the brainstem pathway for patients with concussion was 82,35%, indicating dysfunction of the brainstem in those patients. There was a statistically significant difference between the abnormal rate of patients and that of healthy persons.

In the first month after the trauma 28 patients (82,35 %) had abnormalities: delayed peak latencies, abnormal prolongation of I-III, III-V, I-V interpeak intervals, interaural differences, low amplitude or absence of main BAEP waves. 17 of them had more than one type of abnormalities. Six patients (17,65 %) had normal BAEP. In control BAEP in 12 patients the abnormalities persist.

Conclusions:

1. BAEP can be applied as a diagnostic method in patients with concussion for objectifying some functional disturbances in patients with normal CT/MRI.
2. Conducting control BAEP (3, 6 months) has an important role in monitoring the dynamics of pathological process.
3. Persistent abnormalities in BAEP can be used as diagnostic and prognostic neurophysiological markers for establishment of incomplete recovery – for temporary disabilities and legal claims for compensation (road, work accidents and sports injuries).
4. In patients with MTBI with normal CT/MRI it is recommended expansion of the diagnostic algorithm with BAEP as objective, sensitive, reproducible and highly informative indicator of brainstem disturbances.

The Psychiatric Implications of Traumatic Brain Injuries: A Seminar Series to Improve Graduate Education

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The psychiatric implications of traumatic brain injury (TBI) are a significant, yet understudied, field in the areas of psychiatry and neuroscience. The public and many health care professionals are unaware that the risk for psychiatric disorders can double following a TBI. Most universities, including medical schools, do not have programs to educate students on this important subject. This highlights a large gap in learning for graduate students involved in clinical practice or research in the field.

To address this disparity, a team including a psychiatrist, psychiatry resident, and a neuroscientist presented a seminar series on the psychiatric implications following TBI at the University of Toronto. The course consisted of six two-hour sessions. The sessions examined the six most prevalent psychiatric issues associated with TBI: depression, anxiety, addiction, agitation, aggression, and associated stigma. Each session explored diagnoses, associated neuroscience and biopsychosocial management through didactic, interactive, multimedia elements and group activities. Learners were provided with relevant articles before each lecture and were expected to discuss this material at each session. Multiple expert guest lecturers were invited to present non-pharmacological approaches to treatment, such as Cognitive Behavioral Therapy, Mindfulness, motivational interviewing, to increase student engagement and to facilitate a focus group discussion. Additionally, the sessions were centered on a patient case study to enhance the students' learning and conceptual understanding of the sequelae of TBI.

The course heavily relied on continuous student feedback and evaluation to improve future presentations of this seminar series. After each session, the students evaluated the presenters, the course materials, and the guest speaker. A test was administered before and after the seminar to measure the students' learning. Our data suggests this course was helpful in enriching the students' understanding and interest in the field. Students reported that the course improved their understanding of psychiatry, neuroscience, and TBI clinical case studies. Students were encouraged to be critical of the content and how the information was presented to promote growth of the seminar by identifying gaps in knowledge and meeting the needs of the varied audience. The students also provided their recommendations on topics and materials they suggested be added to the course curriculum. Based on the feedback, future directions for the next series include simplified descriptions of medical concepts and more in-depth neurological mechanisms.

This seminar series introduces information not widely presented in graduate education for clinicians and non-clinicians alike. It serves as a catalyst for future research in public education and awareness in this field and increases enthusiasm and vigor to an under-served medical and psychiatric condition.

Virtual Reality Efficacy During Zero Gravity Arm Training in Post Stroke Patients

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Successful upper limb rehabilitation after stroke occurs only in 20% of cases. It is known post stroke paresis leads to physiological movement pattern become impossible or poor energy-efficient, resulting in formation of abnormal muscle synergies. The successful recovery of movements requires task oriented training provided in close to real environment, active patient's participation, interactive feedback, allowing the patient to control the correct execution of motor tasks and adapt their own efforts to correct pathological synergies in hand.

Materials and Methods: 24 patients met the inclusion criteria (12 males and 12 females) were included. The median age was 52 years (38; 61), with a median of 9.5 months ago stroke (3; 23). Patients were randomized into 2 groups: main group (n=17), the control group (n=7). The groups were comparable in terms of age, time elapsed after stroke, and the degree of neurological deficit (Fugl-Meyer scale, MRCW scale, Modified Ashworth scale, ARAT scores).

Patients from the main group were trained using exoskeleton system with arm weight unloading (Armeo Spring) and 3D virtual reality feedback. Unloading weight was set according to the weight of the patient's arm, so the arm were in relaxed position with 45 degrees of flexion in the shoulder joint and forearm in a horizontal position. All trainings were conducted with all degrees of freedom in upper limb. This condition is necessary for learning patient to actively prevent the pathological synergistic pattern during task oriented training.

Control group received course of conventional kinesiotherapy reaching and grasping trainings with use of weight unloading technology and visual movement control.

Both groups received 10 sessions of 45 minute training.

Results: Were found significant changes ($p < 0,05$) in the Fugl-Meyer scale assessments: an increase of active movements in the arm, in the wrist and hand, the range of passive movements, the deep sensitivity improvement, total arm functionality score. Significant ARAT scale improvement: cylindrical grip, pinch grip, the total score. Also main group showed significant improvement in movements out of synergy, measured using Fugl-Meyer scale. In the control group, statistically significant improvement was observed only in passive movement increasing (Fugl-Meyer scale).

Discussion: The use of combined virtual reality and weight support method for arm motor training it is more effective way to restore the impaired motor function in patients after cerebrovascular accident than conventional therapy. This approach contributes to the reorganization of the motor pattern through biomechanical and visual feedback, projected into the virtual space. The use of such techniques can significantly intensify the rehabilitation process and improve movement pattern by decreasing pathological synergies.

A Systematic Review and Best Evidence Synthesis of Brain Biomarkers in Children and Youth with Mild Traumatic Brain Injury (mTBI)

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Background: Concussion is a major public health concern, particularly in children and youth who have a vulnerable, developing brain. Yet, biomarkers that could index brain injury and recovery after mild traumatic brain injury (mTBI) in this population remain largely unexplored. The objective of this study was to investigate candidate biomarkers of brain recovery in children/youth with mTBI, considering measures of symptoms, time since injury, and age at injury.

Methods: Literature search of English language studies was conducted using MEDLINE Ovid, EMBASE Ovid, CINAHL EBSCO, and PsycINFO up to 6 July 2016. Studies were independently screened by two authors and were included in the review if they met the following predetermined eligibility criteria: (1) children/youth (aged 5 to 18 years old); (2) diagnosis of mTBI, as defined by each study's criteria; (3) assessments at any time period post-mTBI; (4) any non-pharmacological intervention or no intervention delivered. Two authors independently appraised study quality. A best evidence synthesis was used to summarise the data.

Results: 1421 studies were identified by the search strategy, with 717 studies remaining after duplicates were removed. 28 studies met the eligibility criteria involving 559 participants with an mTBI, average age of 12 years. Time post-injury ranged from 1 day to 10 years. Eight studies included only brain imaging data with no associated measures of cognitive function. Nine different imaging methods were identified, including diffusion tensor imaging (32%), functional magnetic resonance imaging (25%), electroencephalogram (18%), magnetic resonance imaging (21%), and susceptibility weighted imaging (11%). Seventy-five tests/subtests of function or symptomology were used (e.g., cognitive tests, symptom reporting). Best evidence synthesis did not identify any specific biomarker that had strong evidence.

Discussion: Collectively, the studies had large heterogeneity of study type, imaging method, age of participants, time since injury, and symptoms collected. Across the modalities included in the review, there were no biomarkers identified that were appropriate to employ in clinical practice at this stage. Findings from this review suggest that future research should use common data elements across imaging methodologies and measures of function and symptomology in order to unify the literature and facilitate gains in understanding of the relationships between brain biomarkers and recovery from mTBI.

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Hyponatremia in Patients with Moderate and Severe Traumatic Brain Injury: Risk Factors, Prevalence, and Short-term Consequences

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Objectives: Hyponatremia, a common electrolyte disorder associated with traumatic brain injuries (TBIs), has been associated with high morbidity and mortality rates. In addition, hyponatremia is one of the main causes of disability in TBI patients. Mild symptoms of hyponatremia include irritability, headaches, nausea, and poor balance with severe symptoms that include confusion, seizures, coma, and even death. The pathophysiology of hyponatremia in TBI is not completely understood, but in large part is explained by the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) and cerebral salt wasting (CSW). Despite the importance of sodium disorders in TBI the incidence has been little studied. The aim of this study is to identify the incidence of and risk factors for hyponatremia in adult persons with moderate to severe TBI.

Methods: Patients who were admitted to our level one trauma center with moderate or severe TBI between May of 2011 and May of 2016 were retrospectively reviewed. Patients admitted with spinal cord injury and TBI were excluded as spinal cord injury could confound the cause of hyponatremia. The relationship between the occurrence of hyponatremia and age, sex, type of injury, Glasgow Coma Scale (GCS) score, Glasgow Outcome Scale score at discharge, whether the patient underwent surgery, the presence of cerebral edema, skull fracture, and intracranial injury were analyzed statistically using a χ^2 test and multivariate logistic regression analysis.

Results: Out of the 3460 subjects retrospectively reviewed for the study (2145 males and 1315 females; age of 45 ± 13 years), 1214 (35%) suffered from hyponatremia which was defined as a serum sodium level <135 mmol/L. Hyponatremia was associated with longer hospital stay ($P < .001$) and bad outcome which was defined as a Glasgow Outcome Scale score of severe disability or higher on discharge ($P < .05$). Multivariate analysis indicated that hyponatremia following TBI was not related to age ($P > 0.05$), sex ($P > 0.05$), or surgical history ($P > 0.05$) but that it was related to the intracranial hemorrhage (odds ratio = 3.11, $P < 0.05$), a GCS score ≤ 8 (odds ratio = 4.25, $P < 0.001$), penetrating head trauma (odds ratio = 5.83, $P < 0.001$), the presence of cerebral edema (odds ratio = 6.85, $P < 0.001$), and skull fracture (odds ratio = 5.91, $P < 0.001$).

Conclusions: To increase the understanding of hyponatremia in persons with TBI the present study investigated the prevalence and etiology of hyponatremia in the setting of TBI. The prevalence of hyponatremia following TBI was not associated with age, sex, or whether the patient underwent surgery. TBI patients with intracranial hemorrhage, GCS score ≤ 8 , presence of cerebral edema, penetrating head trauma, and skull fracture are particularly prone to developing hyponatremia. These patients require close monitoring of sodium and prompt treatment of hyponatremia to normalize serum sodium levels to prevent deterioration of their condition.

Competitive Employment Outcomes in Veterans with TBI: A VA TBIMS Study

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Objectives: Return to work (RTW) is an important outcome for individuals with traumatic brain injury (TBI).[1-8] Productive activity is recognized as an important need,[9-13] and the negative health effects of unemployment following TBI are well documented.[4,7,14-16] Research has identified multiple demographic and injury-related variables that are associated with RTW following TBI, including age, injury severity, level of education, pre-morbid employment status, substance abuse, cognitive and behavioral impairments, minority status, and social/community support. [2,4,5,7,9,10,17-27] Many Veterans and service members (V/SM) are diagnosed with TBI, [28] yet most studies on RTW have been conducted within civilian samples. [2,7,29] The objective of this study is to examine the length of time RTW among V/SM with TBI and to identify variables predictive of RTW.

Setting: Department of Veterans Affairs Polytrauma Rehabilitation Centers (VA PRC).

Participants: V/SM enrolled in the VA PRC Traumatic Brain Injury Model Systems database who were of 18 to 60 years of age and admitted with the diagnosis of TBI.

Design: Prospective observational cohort study.

Main Outcome Measures: Employment status at 1 year follow-up; time to return to work (in days) as documented during 1 year post-injury follow-up.

Results: The final sample (n=293) included male (96%) V/SM with severe TBI (67%). Approximately 21% of the sample participants were employed at one year post-injury. Younger individuals who self-identified as non-minority returned to work sooner. Significant associations were observed for time to employment for cause of injury and injury severity.

Conclusions: Few V/SM with moderate to severe TBI returned to work at 1-year post injury. Predictors such as younger age at time of injury, minority status, and severity of TBI affected time to and probability of RTW. Findings from this study have important implications for rehabilitation planning and service delivery across the continuum of recovery.

Intensive Semantic Memory Training: A Comparison to Traditional Episodic Memory Therapy

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Episodic memory deficits are long-lasting sequelae of traumatic brain injury (TBI). Traditional episodic memory therapy approaches involve practicing the recall of events, using compensatory strategies, or both; however, these approaches have not shown consistent results therapeutically. Although a great deal of research has examined the relationship between semantic and episodic memory during encoding and retrieval, semantic training has not been systematically examined as an intervention for episodic memory impairment. In a preliminary study of intensive semantic memory training, nine TBI patients with documented episodic memory deficits showed significant improvement from pre- to post-training in episodic memory as well as word fluency, self-assessment of memory, and attention. These improvements were quite promising, and provided impetus for further study of intensive semantic training using a larger sample of 35 TBI patients, minimum one year post injury with documented episodic memory (10 measures) deficits. Standardized pre- and post-testing for episodic memory and related cognitive domains was completed. To determine the effectiveness of the approaches, subjects were randomly assigned to eight sessions of either intensive semantic memory training or traditional episodic memory therapy, or to a wait-list control group. The two treatment groups showed positive change on all of the episodic memory outcome measures, whereas the control group demonstrated positive change on five and negative change on five of these measures. Sampling issues, testing issues, and heterogeneity of the TBI population influenced the outcomes; however, overall both therapy approaches showed promise in episodic memory treatment. Future work will focus on the use of intensive semantic memory training in combination with traditional TBI episodic memory rehabilitation.

A Case Study of Frontal Lobe Syndrome

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Method: Clinical information and data from investigations in single case was collated and reviewed.

The frontal lobe syndrome is a permanent personality change disorder with characteristic clinical pictures, which followed by frontal lobes damage. Frontal cortex is responsible for planning of behaviors, controlling of the emotions, goal-oriented classification of mental activities, forecasting the consequences, ability to solve the complex abstract problems and controlling the functions according to the social rules. Frontal lobe symptoms, such as apathy, abulia, akinesia or on the contrary impulsiveness and aggressive behavior, change the way people feel or express emotions, are widely described in literature. An individual with brain injury can have several types of emotional problems, such as mood swings and emotional lability, anxiety, depression, temper outbursts, sudden episodes of crying or laughing without feeling sad or happy. This case report is a patient 27 years old, single man who was subjected to forensic observation and was charged with appropriation of money to the detriment of the office he worked for by Municipality. History data indicate that he was employed in the said office over the period of 8 years as an accountant and until the disclosure of the crime he had had the company's full confidence. He had a fine reputation at the place of her residence as well. more than 14 months before undertaking criminal actions he had sustained a head injury (temporal fracture) as a result of a car accident. Before he had not been penalized administratively or legally. After brain injury he had suffered from head injuries with a loss of consciousness less than 24 hours. After 4 months he was asymptomatic. During forensic and psychiatric observation, psychiatric, psychological, neurological and electroencephalographic examinations were carried out, skull films was taken and computerized tomography of head was conducted. Clinically it was diagnosed as a frontal organic brain damage syndrome complicated by mood swings and depression. Experts' examinations were steered by psychopathological image, especially axial symptoms of defective function of the frontal lobe. lack of initiative and spontaneity, deficiency of higher emotions, decline of criticism and lowering of psychomotor drive. Although psychological examination showed that the results of 'organic tests' were within normal range, qualitative analysis of the structure of mental functions disclosed impairment of abstract thinking, especially using associative processes. Essential data were gathered from computerized tomography of head which demonstrated cortical atrophy of frontal and temporal lobes and precentral gyri. However, neurological and electroencephalographic examinations did not bring any significant information.

Feasibility Study of Graded Exercise Testing and Aerobic Exercise Intervention for Adults with Residual Concussion Symptoms

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Objective: The empirical basis for treatment of persistent post-concussion symptoms (PPCS) is largely derived from extrapolated evidence on treatment of related conditions. In athletes, standardized exercise testing as a means to delineate specific PPCS subtypes, followed by a program of controlled and monitored aerobic exercise is used to treat one proposed cause of refractory symptoms; i.e., physiologic dysfunction which “may include altered autonomic function and impaired autoregulation and distribution of cerebral blood flow” (pg. 241 Leddy et al., 2013). The goal of this study was to evaluate the feasibility and effectiveness of graded exercise testing and aerobic exercise treatment in 18-55 year old adults, 2 months to 24 months post-concussion with residual symptoms.

Design: Case series using a pretest-posttest design with description of feasibility and adherence findings.

Setting: Outpatient rehabilitation brain injury clinic (BIC).

Participants: Adults 18-55 years, 2 months to 2 years post-concussion seen in outpatient BIC.

Interventions: Subjects used a sports-type heart rate (HR) monitor (Garmin Vivofit HR) and exercised at a predetermined HR, below symptom threshold established by treadmill (TT), for 20 minutes, 5-7 days per week for 12 weeks. Patient response and adherence were monitored weekly and HR prescription increased 5-10 beats when tolerated to 85-90% of age-predicted or estimated HR maximum. To evaluate feasibility, all subjects were allowed to participate even if TT was not symptom limited.

Main Outcome Measures: Study completion and adherence to exercise prescription (workouts per week and limiting factors limiting), as well as symptom self-report on Neurobehavioral Symptom Inventory (NSI). Secondary measures included self-report (Beck Depression, Beck Anxiety Inventory, Patient-specific Functional Scale (PSFS)), physical performance (Revised High Level Mobility Assessment Tool and estimated VO₂ maximum), and neurocognitive performance (Rey Auditory Verbal Learning Test, Comprehensive Trails Making Test, Verbal Fluency, NAB Digits forward/Digits Backward Test, Symbol Digit Modalities Test, Wide Range Achievement Test).

Results: 15 subjects (3 male), average age 41.1 years (range 23-55 years) enrolled with 13 of 15 participants completing the study. Compared to subjects who completed the study, the two who withdrew were symptom limited on submaximal TT by headache, had high levels of baseline anxiety and NSI scores and reports of organizational difficulties on PSFS. For the subjects who completed the study, exercise logs and HR monitors showed varying adherence for mixed reasons. Availability of gym equipment appeared to factor in subject ability to achieve higher HR. Overall, symptom reduction occurred, as did an improvement in fitness as measured by estimated VO₂ max for those with highest adherence. Minimal changes were found in neurocognitive performance.

Conclusions: Graded exercise testing and a progressive, 12 week, subsymptom threshold aerobic exercise program in adults with PPCS appears to be feasible, with complex factors likely explaining differences in tolerance and adherence.

Evaluating Social Competency in Pediatric Traumatic Brain Injury Using PEERS: A Computerized Assessment of Social Skills

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Background: Social skills are a fundamental aspect of all human interactions. Mature social skills are necessary for developing and sustaining rewarding relationships and are therefore vital to quality of life across the lifespan. Social skills deficits are hallmark outcomes after pediatric traumatic brain injury (TBI). However, there are currently no comprehensive, ecologically valid assessment tools of pediatric social competency, limiting the ability to provide tailored remediation for specific social weaknesses. The Pediatric Evaluation of Emotions relationships and Socialization (PEERS) is a new assessment tool designed to address these gaps in pediatric social skills assessment. This study aimed to firstly evaluate the feasibility of administering PEERS to children and adolescents with a TBI, and secondly to assess the sensitivity of PEERS to social skills deficits typically experienced by young people with a TBI.

Methods: 6 children aged 4-18 years with a TBI completed a selection of PEERS subtests along with an age appropriate assessment of IQ between June-December 2016. Parent report of medical and developmental history, and social behavior was also collected. Age based z scores were derived using data collected from typically developing controls (TDC) in a large-scale standardization study.

Results: Both assessors and participants provided positive user feedback regarding the administration and completion of PEERS. Comments from assessors suggest that PEERS is easy to administer, light-weight and portable, and engaging for the children/adolescents. Participants report being engaged during the assessment and enjoying the “game” element of tool. Compared to TDC, the TBI group displayed relatively weaknesses in emotion recognition/perception and social information processing.

Conclusions: Preliminary results support the feasibility and sensitivity of PEERS in children and adolescents who have experienced a TBI. Standardization of PEERS with a larger TBI sample as well as other clinical groups where social skills are a core symptom will strengthen the support for the adjunctive use of PEERS in clinical evaluations. PEERS provides a promising method of detailing the social skill profile after pediatric TBI, which will assist with tailoring individualized social skills interventions.

Barriers and Facilitators to Rehabilitation after Traumatic Brain Injury Using Interdisciplinary eHealth Strategies: A Systematic Review

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Introduction: Individuals with severe traumatic brain injury (TBI) require lengthy involvement with medical, nursing and allied health to address their complex needs. These needs are best met through a multidimensional and interdisciplinary approach, usually provided in face-to-face rehabilitation settings. However, ready access to Internet and communication technologies (ICT) that is eHealth, has the potential to supplement or replace the need for practitioners and the individual to always be physically co-located.

Aim: To identify and describe the existing evidence of eHealth technology used by interdisciplinary teams in the provision of care for people living with TBI.

Method: A systematic review was conducted with searches of CINAHL, Embase, Medline, PsychINFO, Scopus and Web of Science to identify studies which a) described the feasibility and effectiveness of interdisciplinary eHealth interactions for the care of people with a TBI and b) the barriers and facilitators of eHealth implementation and adoption.

Results: The search resulted in 1092 papers of which six papers reported on interdisciplinary eHealth interventions for people with TBI, delivered by two or more health professionals. The most commonly used intervention was videoconferencing. Barriers to interdisciplinary eHealth interactions included environmental factors such as technology issues and clinicians' assumptions. Organisation and clinical leadership was identified as a key enabler for influencing change.

Conclusions: Despite the widespread adoption of ICT, its use for eHealth interventions has been limited for those with a TBI and their families. Ongoing education along with support from clinical leaders is thought to be essential for the management of change.

Predicting Level of Functioning One Year after Moderate to Severe Traumatic Brain Injury: A Systematic Review

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Background: Prognostic studies on outcome after moderate to severe traumatic brain injury (TBI) usually focus on survival 6 months to one year post TBI. In clinical decision making and planning of allocation of limited resources a more detailed prediction of the expected level of functioning is of paramount importance. The aim of this study was to identify prognostic factors for level of functioning one year post TBI.

Objective: To systematically review the literature for cohort studies that investigated prognostic factors for the level of functioning as measured with the Barthel index (BI), Functional Independence Measure (FIM) or Glasgow Outcome Scale Extended (GOSE) one year after moderate to severe traumatic brain injury (TBI).

Data Sources: Pubmed, Embase, Psycinfo and Web of Science were searched up to march 2016.

Review Methods: Articles were selected if the study assessed potential predictors for level of functioning measured with BI, FIM or GOSE in adults at least one year after TBI.

Inclusion criteria were: persons with moderate or severe TBI based on Glasgow Coma Scale (GCS) less than 13, posttraumatic amnesia duration longer than 24 hours, unconsciousness longer than 30 minutes and/or visible traumatic brain injury on CT/MRI. Intervention trials, case reports and articles focusing on diagnosis were excluded, as well as articles not written in English or Dutch. Two reviewers independently included articles, extracted data, and assessed methodological quality. Discrepancies were solved by consensus. Levels of evidence (strong, moderate, limited, inconclusive) were assigned based on quality and number of studies with consistent findings.

Results: 50 articles involving a total of 22557 patients were included (mean age 36 years, 76% men). The independence scales used were: GOSE in 30 studies, FIM in 23 studies, Barthel in 2 studies. Significant predictors for a higher level of functioning after TBI were: normal pupil reactions (3 studies; strong), lower intracranial pressure (2 studies; moderate), lower Traumatic Coma Data Bank classification (2 studies; moderate), absence of diffuse axonal injury on FLAIR scan (2 studies; moderate).

Not predictive for level of functioning were: gender (10 studies, strong), substance abuse (5 studies, strong) and TAI lesions in T2 GRE scan (3 studies, strong). Due to differences in definitions of outcomes and methods of analysis, most evidence was heterogeneous and inconclusive.

Conclusion: Available research varies greatly in outcome definition, methodology, and predictors of interest, which causes differences in results and scattering of evidence. Evidence is lacking regarding the prognostic value of cognitive tests, CT parameters, and EEG for the prediction of level of functioning one year post TBI.

Clinical Outcomes Following Traumatic Brain Injury in A Combined Multidisciplinary Neurotrauma Clinic: Experiences from A Tertiary Centre

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Objectives: The Walton Centre NHS Foundation Trust is part of the major trauma centre collaborative for the North West of England, UK. Of the 2.4 million patients under the remit of this collaborative, the Walton Centre as a specialist neuroscience institution provides surgical intervention and rehabilitation services for those admitted following traumatic brain injury (TBI). TBI specifically accounts for 3.4% of emergency department admissions in the UK.

A broad spectrum of physical, cognitive and psychological sequelae occurring in patients with TBI has been identified as late as 2 years post-injury. These symptoms have been found in patients regardless of the severity of their original brain injury. Indeed, those with mild injury may often fare worse due to oversights in management early on, as early rehabilitation has been shown to be associated with better outcomes.

To aid in the management of such patients, a combined, multidisciplinary neurotrauma clinic led by a neurosurgeon and specialist in neurorehabilitation has been initiated at The Walton Centre. The clinic provides specialist management for the wide range of problems that follow TBI.

The primary objective of this study is to describe outcomes of patients following TBI who attended a multidisciplinary neurotrauma clinic at a tertiary centre.

Methods: All patients who had attended the clinic since its inception were eligible. The following data was collected for each patient: basic demographics, mechanism and severity of injury, initial CT findings, information on hospital stay and discharge, symptomatology in clinic, and outcomes (including further investigations, referral to other specialties or services and return to employment).

Results: 305 patients (98.1%) had clinic notes available and were included in the study. Mean age was 47.5 and the majority of patients were male (72.1%). The commonest mechanism of injury was falls (53.1%). 17.4% of injuries were classed as mild, 68.2% as moderate, and 14.1% as severe. Frontal (21.6%) and temporal (16.1%) injuries were the commonest locations with contusions (37.4%) and subdural haematomas (27.9%) the commonest type of injury found on initial CT scan. In clinic the most frequent physical complaints were headache (47.9%), memory problems (42.0%) and loss of driver's license (28.5%). 41.6% were referred to further services or other specialties, the commonest being psychology (19.3%) and neuropsychiatry (18.4%). Of 184 patients known to be in employment before their injury, only 48.4% of these had returned to work before their last appointment. Further analysis of the data is ongoing.

Conclusions: The information gathered in this study about the characteristics of the TBI population and their outcomes should allow for better targeting of suitable patients for referral to a multidisciplinary clinic. This kind of data is essential for planning of health care provision, and improving efficiency and ultimately patient outcome.

Neuropsychological Interventions for Treating Neuropsychiatric Consequences of Acquired Brain Injury: A Systematic Review

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Objective: Within the most occurring neuropsychiatric symptoms after acquired brain injury (ABI) are apathy, anxiety, aggression/agitation and disinhibition. These symptoms can lead to functional impairment and reduced social integration. This systematic literature review aimed to provide an overview of neuropsychological interventions for treating these neuropsychiatric consequences of ABI with a critical classification of level of evidence.

Methods: Pubmed, EMBASE, PsycINFO, CINAHL and the Cochrane Library were searched. Hand searches were conducted after checking reference lists of included studies and reviews on the topic. Inclusion criteria for relevant studies were: publication between January 2000 and June 2016; a population of patients with ABI without premorbid psychiatric diagnoses, aged 18 to 65; apathy, anxiety, aggression/agitation or disinhibition were specifically addressed by the examined neuropsychological intervention; and effectiveness was examined quantitatively. Methodological quality of studies was classified according to methods of Cicerone et al. (Arch Phys Med Rehab, 2011) and single case experimental designs according to the description of Tate et al. (2016) and Oxford Centre for Evidence-Based Medicine (Oxford, UK, 2011).

Results: Systematic searches led to a total of 5207 studies, of which 45 met the inclusion criteria. This included two studies for apathy, 23 for anxiety, 18 for aggression and six for disinhibition. Two studies addressed two domains of interest and one study three domains of interest. Three Class I studies (randomized controlled trials) showed significant decreases in anxiety after cognitive behavioural therapy (CBT). 'Third wave' CBT (mindfulness based; acceptance and commitment therapy; compassion focused therapy), showed promising results but lack replication of effects. Ten studies (of which six Class III) consistently showed significant decreases in aggression/agitation after behavioural management techniques. Anger management sessions showed significant decreases as well, replicated in five studies (of which three Class III). Eight studies in total addressed apathy or disinhibition (of which seven Class I/II) with, for each symptom, substantial variability in types of examined interventions. Slight progression was seen towards the use of higher level designs in the last five years compared to the preceding 10 years.

Discussion: Considerable evidence exists for the use of CBT, anger management sessions and behavioural management techniques. This particularly accounts for anxiety and aggression/agitation. Evidence-based neuropsychological interventions addressing apathy and disinhibition after ABI show to be very limited. Overall, replication and comparison of studies is complicated due to poorly described methods and heterogeneity in intervention content. This also affected the objectivity of our inclusion process. Firm conclusions and recommendations for the clinical practice are considered too premature for these reasons. High class designs have increased in use but are still required, as well as better description of and consistency in intervention content. Future research might aim for 'third wave' CBT and implementing behavioural management techniques in community settings.

Expression of Novel Markers of Senescence After Traumatic Brain Injury in A Mouse Controlled Cortical Impact Model

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Cellular senescence refers to irreversible growth arrest that occurs when cells experience stress and damage from exogenous and endogenous sources. Senescent cells secrete various factors that can contribute to tissue dysfunction. We hypothesized that senescent cells appear in the brain as a response to traumatic brain injury (TBI). We performed histochemical and immunohistochemical analyses in the brain for senescence-associated β -galactosidase (SA- β gal) and p16, markers of senescent cells, at 1, 4, 7 and 14 days after TBI in a controlled cortical impact (CCI) mouse model. On comparing the data from control and TBI animal groups, we found that SA- β gal and p16 were preferentially expressed in the cortex ipsilateral to the site of the injury on 4, 7, and 14 days after TBI. Double immunohistochemical analyses showed that astrocytes expressed p16 at the site of cortical contusion. These findings suggest that senescent cells are associated with TBI. Because senescent cells are deleterious to brain tissue, the appearance of senescent cells may contribute to the progression of post-TBI brain damage.

From Miserable Minority to the Fortunate Few: The Other End of the Mild Traumatic Brain Injury Spectrum

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Background and Aim: Traditionally, almost all research endeavors on mild traumatic brain injury (mTBI) have been focused on the patients with residual complaints or those with a suboptimal recovery. This so-called “miserable minority” is studied extensively to find factors potentially leading to an unsuccessful recovery. However, no study so far has zoomed in on the remarkable patients that report zero complaints early after injury, a group that we named the “fortunate few”. With this study, we aimed to describe the demographics, clinical and premorbid characteristics of this patient group, and to examine whether they would remain asymptomatic throughout the first year after injury.

Method: This study was part of the prospective UPFRONT-study, a multicenter cohort study conducted in the Netherlands between 2013-2015, during which 1151 patients were included. Patients received questionnaires at several time intervals after injury, covering posttraumatic complaints (HISC), anxiety and depression (HADS), outcome (GOS-E) and quality of life (WHOQOL-BREF). For the current study, we included only those patients who reported zero complaints two weeks after injury.

Results: Our sample consisted of 70 mTBI patients (Glasgow Coma Scale [GCS] score 13-15). There was considerable heterogeneity in recovery in this group, as more than half of patients (57%) developed complaints at a later stage ($M=2$, $p<.001$). These secondary complaints were related to higher levels of anxiety ($M=3.2$, $p=.004$) and depression ($M=1.4$, $p=.002$), as well as to less favorable outcome ($p=.014$) and a lower quality of life ($p=.006$) one year after injury.

Conclusion: We demonstrated that even a part of the fortunate few group, who seem fully recovered early after injury, may develop secondary complaints leading to unfavorable outcome and lower quality of life. Therefore, the truly fortunate are in even fewer numbers than expected. We plead that more future mTBI research should be focused on early signs of psychological distress. This may be a better criterion to discern patients with optimal and non-optimal recovery than the presence of posttraumatic complaints, which holds important implications for clinical practice.

Paediatric Intentional Head Injuries in the Emergency Department: A Multicentre Prospective Cohort Study

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Background: While the majority of head injuries in children are non intentional, there is limited information on intentional injuries outside abusive head trauma.

Objective: To investigate intentional head injuries in terms of demographics, epidemiology, and severity.

Methods: Planned secondary analysis of prospective multicentre cohort study of children aged <18 years across 10 centres in Australia and New Zealand. Victorian state epidemiology codes (intent, activity, place, mechanism) were used to prospectively code the injuries. Data were descriptively analysed.

Results: Intentional injuries were found in 441 of 20,137 (2.2%) head injured children. Injuries were caused by peers (166, 37.6%), by caregiver (103, 23.4%), by sibling (47, 10.7%), due to attack by stranger (35, 7.9%), attack by person with unknown relation to patient (19, 4.3%), intentional self-harm (7, 1.6%), other cause or undetermined (64, 28.2%). Children were <2 years old in 75.7% injuries caused by caregivers and 8.3% in other causes. Overall, 71.0% of victims were male. Admission rates varied from 77.7% for assault by caregiver, 37.1% attack by stranger, 22.3% by peer and 8.5% by sibling. Peer assaults were related to sports in 69 cases (41.6%), with highest frequency in contact sports, rugby (40.6) and Australian football (26.1%).

Conclusion: Intentional head injuries are infrequent in children. The most frequent cause is peer assault, often during sports, and injuries caused by caregivers.

Paediatric Abusive Head Trauma in the Emergency Department: A Multicentre Prospective Cohort Study

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Background: Abusive head trauma (AHT) is associated with high morbidity and mortality. It may be difficult to detect in the emergency department (ED).

Objective: To determine how cases of suspected AHT differ from non abusive head injuries in the ED setting.

Methods: Planned secondary analysis of prospective multicentre cohort study of children aged <18 years across 10 centres in Australia and New Zealand with head injuries. We identified cases of suspected AHT when ED clinicians identified such suspicion on a clinical report form or based on research assistant assigned epidemiology codes. We compared suspected AHT cases and non AHT cases using risk ratios with 95% CIs. We assessed the rate of clinically important traumatic brain injuries (ciTBI: death; neurosurgery; intubation >1 day, admission >2 days with abnormal CT scan).

Results: AHT was suspected in 103 of 20,137 (0.5%) head injured children. Mean age was 2.4 years (SD 4.0). GCS was <12 in 9 (8.7%). 12 (11.7%) presented with seizures. 71 (68.9%) underwent CT head, of which 49 (69.0%) were abnormal. 80 (77.7%) children were admitted. Neurosurgery was performed in 3 and 2 children died. 23 (22.3%) had ciTBI.

RR (95% CI) for AHT vs. non AHT were: LOC 1.4 (0.7-2.7), vomiting 1.6 (1.2-2.2), scalp haematoma 2.3 (2.0-2.6), GCS <12 8.5 (4.5-16.0), abnormal neuroimaging 16.4 (13.2-20.4), neurosurgery 7.4 (2.4-22.9), mortality 29.9 (6.8-130.9), ciTBI 17.4 (6.8-25.5).

Conclusion: In the ED clinical presentation in children with suspected AHT differ from non AHT cases. Suspected cases of AHT are at increased risk of abnormal CT scans, ciTBI and death.

The Effect Evaluation of Combined Cognitive and Vocational Interventions After Mild-To- Moderate Traumatic Brain Injury: A Randomized Controlled Trial and Qualitative Process Evaluation - Presentation of A Study Protocol

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Mild-to-moderate traumatic brain injury (TBI) can result in long-lasting somatic, cognitive, and emotional symptoms which may affect return to work (RTW) rates. Maintaining employment over time is also a major challenge, due to these symptoms. The persons own perceptions regarding RTW, and the impact of the workplace environment are also associated with RTW after sickness absence. At a service delivery level, the collaboration between the health related rehabilitation services, the Labor and Welfare Administrations (NAV), and the work-place is typically weak after TBI. There are barely any well-controlled intervention studies regarding RTW in patients with mild-to-moderate TBI, and vocational rehabilitation interventions are rarely included. Rehabilitation and vocational science perspectives will be applied in the current project which will start data piloting in January 2017.

Through a mixed methods approach comprising a randomized controlled intervention trial and a qualitative process evaluation, this project will:

- a) explore the effect of combining a group-based manualized cognitive rehabilitation program (Cog SMART) 1 and supported employment in real-life competitive work settings 2 for patients who have not returned to work 8 weeks post-injury compared to a control group receiving treatment as usual provided by a multidisciplinary rehabilitation team;
- b) explore roles, time commitment, and methods in the supported employment process. Semi-structured interviews will provide an empirical base for increased knowledge on job content and skills requirements, work environment, employers roles, work organization and needed support.

Cost-effectiveness of the intervention will be established. In this multicenter study, research groups from the medical rehabilitation sector and vocational sciences (The Work Research Institute and the NAV Department of Vocational Rehabilitation) will collaborate. This will enable the project to obtain new knowledge about RTW as a multi-disciplinary and multi-sectorial process that can be applicable to other patient groups.

1 Twamley, E.W., Jak, A.J., Delis, D.C., Bondi, M.W. & Lohr, J.B. (2014). Cognitive Symptom Management and Rehabilitation Therapy (CogSMART) for veterans with traumatic brain injury: pilot randomized controlled trial. *J Rehabil Res*, 51(1), 59-70.

2 Drake, R.E., Bond, G.R., Becker, D.R. (2012). *Individual Placement and Support: An Evidence-Based Approach to Supported Employment*. New York: Oxford University Press.

They Survived but Never Came Back - Family Life in the Face of Persistent Disorders of Consciousness After Brain Injury

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Introduction: A minority of patients with acquired brain injury remain in a state of prolonged disorders of consciousness (DoC), i.e. in a Vegetative (VS) or a Minimally Conscious (MCS) state. Family members experience abrupt and dramatic changes associated with the injury, and longstanding requirements to adapt to persistent and severe changes both in the loved one and in the family as a whole. Despite increased research on DoC, little systematic knowledge has been obtained regarding family experiences.

Methods: As part of a larger qualitative research project regarding family life after severe physical injury, a focus group interview was conducted with five family members of three patients with persistent low level MCS. Time since their traumatic brain injuries was four, four and ten years. None showed functional communication, and all lived in institutional care facilities. The informants were three mothers, one father and one sibling. The interview lasted two hours, and was led by authors M.L. and A.G.

The main aim was to explore how family members of patients with DoC subjectively described the processes they have lived through. There was particular emphasis on the mental and practical strategies they had applied in moving forward. The construction of hope in the face of such severe injury was explored, as was the families' experiences with the health care system.

Results: The informants noted the importance of time. It took time before they realized the chronicity of the injury severity, it took time before the patients came into a stable living situation, and it took time to trust that professional careers would provide good enough care. Despite the pressure they had been under, the informants had made active choices along the way regarding how to act and deal with the circumstances. They uniformly described that their close and extended families had suffered tremendously. They did not find it easy to see positive family aspects, but described a great deal of normalization of everyday life. Over time, the face of hope was described to shift from hope of major medical progress, to smaller changes in e.g. communication and motor skills that could provide enhanced autonomy and quality of life. Communication with the welfare and health services was highlighted as challenging. Economic and practical issues was demanding for families to deal with, as is dealing with what they saw as pessimistic diagnostic and prognostic evaluations from rehabilitation experts.

Conclusions: Families deal actively with their demanding situation. Over time they realize the severity of the situation. Family life finds a new normality, and hope becomes focused on small functional improvements. Families of patients with DoC need health professionals that are sensitive to their experiences, and whom are willing to share a common referential ground.

Development of a Prediction Model for Post-Concussive Symptoms following Mild Traumatic Brain Injury: A TRACK-TBI Pilot Study

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Background: Post-concussive syndrome (PCS), including cognitive, somatic and emotional complaints, occurs frequently after mild traumatic brain injury (mTBI). Predicting patients at greatest risk of incomplete recovery is of high clinical importance. Nevertheless, according to a recent systematic review (Silverberg et al. 2015) previous predictive studies in the field of mTBI suffer from methodological shortcomings. In addition, previous efforts have relied on surveying the entire constellation of PCS symptoms, while it has been suggested that complaints in the cognitive and somatic/emotional PCS domain are predicted by different demographics and clinical variables. The objective of this study was to develop a prediction model for both cognitive and combined somatic/emotional PCS based on patient demographics and clinical variables available at baseline.

Methods: mTBI patients, as defined by an emergency department admission Glasgow Coma Scale (GCS) score of 13-15, were prospectively enrolled from three Level I trauma centers in the United States from 2010-2012 in the Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) Pilot study. PCS was assessed using the Rivermead Post-Concussion Symptoms Questionnaire (RPQ) at 6-months post-injury, utilizing the cognitive and somatic/emotional subscales. Twelve candidate predictors were selected based on systematic literature search, and the predictive value was determined using univariable and multivariable linear regression analyses. The final prediction models were developed using Lasso shrinkage.

Results: We included 277 mTBI patients (70% male, median age 42y), of whom 147 (53%) reported more than three post-concussive symptoms after six months. Scores on the cognitive and combined somatic/emotional RPQ scale were predicted by different variables; e.g. the cognitive RPQ scale was predicted by age, years of education, female gender, pre-injury psychiatric disorder, prior TBI and loss of consciousness, while the somatic/emotional RPQ scale was predicted by the same variables plus pre-injury migraine/headache, computed tomography abnormalities and posttraumatic amnesia. Predictors explained 17% and 22% of the variance for the cognitive and somatic/emotional subscales, respectively. A scoring algorithm was developed in order to predict RPQ scores at six months post-injury based on the predictor variables.

Conclusion: Demographic and clinical variables available at baseline are predictive of 6-month PCS following mTBI, but explain only a small part of the total variance in outcome. Cognitive and combined somatic/emotional PCS symptoms are predicted by different demographic and clinical variables. Validation and further improvement of the model are needed before clinical implementation.

Predicting Post-Concussive Symptoms following Mild Traumatic Brain Injury: External Validation and Updating of an Existing Model

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Introduction: Around 10-30% of the mild traumatic brain injury (mTBI) patients develop persisting post-concussive syndrome (PCS). Early identification, and possibly treatment, of these patients is of paramount importance. Prediction models can be used to identify patients at risk, but despite an abundant number of prognostic studies in mTBI, the large majority used small sample sizes and was of poor methodological quality. In addition, none of the developed models was externally validated in an independent patient sample, while this is a crucial step before implementation in clinical practice. The objective of this study was to externally validate and update existing prognostic models for 6-month PCS following mTBI.

Methods: For validation, mTBI patients (Glasgow Coma Scale 13-15) were prospectively enrolled from three emergency departments in the Netherlands between 2013-2014 in the UPFRONT study. PCS after six months was measured with the Head Injury Symptom Checklist (HISC). Patients were classified as having PCS if they reported at least 3 out of 8 symptoms according to the International Classification of Diseases (ICD)-10 diagnosis of PCS. Prognostic models were identified through literature search and included in the current study if they were: (1) developed in a clinical cohort; (2) assessed 6-month PCS; (3) included predictors of which $\geq 80\%$ was measured in the UPFRONT study; and (4) met at least one of our quality criteria. Only one model met our inclusion criteria (Stulemeijer et al., 2007). In this model 6-month PCS was predicted by pre-injury comorbid physical problems, early PCS and early posttraumatic stress disorder (PTSD) symptoms. Performance (discrimination and calibration) was determined and the model was updated by adding nine relevant predictors in a backwards selection procedure ($p < 0.157$). The updated model was internally validated using bootstrapping with 100 samples.

Results: We included 591 patients (median age 51, 41% female), among whom 241 (41%) met the ICD-10 diagnosis of PCS after six months. The Stulemeijer model obtained poor discrimination in our data (Area under the curve (AUC): 0.60, 95% CI 0.56-0.64). In addition, observed outcomes did not agree well with predicted outcomes (Calibration intercept: 1.29; Calibration slope: 0.48). Updating the model resulted in weaker effects for all predictors. Female gender was added to the updated model since we found a significant association with PCS (OR = 1.52; 95%CI 1.04 – 2.22). The AUC for the updated model after internal validation was 0.75.

Conclusion: A previously proposed prediction model for 6-month PCS after mTBI performed poorly in an independent sample. After updating the effect estimates and the addition of gender, the predictive performance improved. External validation and further improvement is needed before the current model could be implemented in clinical practice.

Impaired Physical Fitness and Unfavorable Physical Behavior in the First Year after Aneurysmal Subarachnoid Hemorrhage

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Background: Aneurysmal subarachnoid hemorrhage (a-SAH) is caused by a bleeding of a ruptured aneurysm into the subarachnoid space. Even among those who are classified as having a 'good outcome', the incidence of clinical deficits is significant. Fatigue is reported as being one of the most distressing symptoms. Fatigue may be triggered by impaired physical fitness caused by physical deconditioning, physical inactivity and sedentary behavior.

Aim: To longitudinally investigate physical fitness and physical behavior in the first year after a-SAH, and explore their relationships with patients' characteristics and fatigue.

Methods: Measures of physical fitness and physical behavior were obtained at six and twelve months post a-SAH, and compared to age- and sex-matched healthy controls. Patients' characteristics were collected and body anthropometrics measured from which BMI, waist circumference, and percentage body fat were calculated. Cardiorespiratory responses to a progressive cardiopulmonary-exercise-test (CPET) were obtained from which peak oxygen consumption ($\dot{V}O_{2peak}$) was determined. Maximal isokinetic knee muscle strength was assessed with a dynamometer at 60°/s and 180°/s, from which we established peak torque (newton-meter). Physical behavior, with separate attention for physical activity (PA) and sedentary behavior (SB), was objectively measured with an accelerometer-based activity monitor. Fatigue was assessed using the Fatigue-severity-scale. Independent t-tests were used to test for differences between patients and healthy controls, and mixed model analysis were applied to test for changes in physical fitness and physical behavior, and their relationships with patients' characteristics and fatigue, over time.

Results: Thirty-three patients and thirty-three controls participated. Six months post a-SAH, patients had a higher BMI ($p=0.02$), waist circumference ($p<0.01$) and percentage body fat ($p=0.03$). Furthermore, cardiorespiratory fitness and knee muscle strength were lower in patients than in controls; 64-69% of controls ($p<0.05$) and 64-78% of controls ($p<0.01$), respectively. Patients participated 35 min/24h less in PA than controls ($p<0.01$), and particularly less in cycling ($p<0.01$) and running activities ($p=0.02$). The total time spent in SB did not differ between groups ($p=0.396$). Mixed model analysis revealed that cardiorespiratory fitness ($\dot{V}O_{2peak}$: +1.13 ml/kg/min; $p=0.08$; PO: +8.2 Watt, $p=0.07$), knee muscle strength (extension 60°/s: +5.24Nm, $p=0.07$; extension 180°/s: +3.84Nm, $p=0.09$; flexion 60°/s: +1.67Nm, $p=0.37$; flexion 180°/s: +0.05Nm, $p=0.97$), and physical behavior (PA: +0.2%, $p=0.23$, SB: -0.1%, $p=0.54$) did not improve over time. Significant relationships were found between fatigue and cardiorespiratory fitness ($p=0.02$) and knee muscle strength ($p<0.01$), and between treatment procedure (clipping/coiling) and cardiorespiratory fitness ($p=0.02$).

Conclusions: Cardiorespiratory fitness and knee muscle strength were considerably lower in patients with a-SAH than in healthy controls, and patients were less physically active. Measures of physical fitness or physical behavior did not improve over time. Furthermore, measures of physical fitness were related to fatigue. Present findings have implications for treatment.

Temporal Evolution of Poststroke Cognitive Impairment Using the Montreal Cognitive Assessment

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Background and Purpose: The Montreal Cognitive Assessment (MoCA) is nowadays recommended for the screening of poststroke cognitive impairment. However, little is known about the temporal evolution of MoCA-assessed cognition after stroke. The objective of this study was to examine the temporal pattern of overall and domain-specific cognition at 2 and 6 months after stroke using the MoCA, and to identify patient groups at risk for cognitive impairment at 6 months after stroke.

Methods: Prospective cohort study in which 324 patients were administered the MoCA at 2 and 6 months post stroke. Cognitive impairment was defined as MoCA<26. Differences in cognitive impairment rates between 2 and 6 months post stroke were analyzed in different subgroups. Patients with MoCA-score<26 at 2 months, who improved by ≥ 2 points by 6 months were defined as reverters. Logistic regression analyses were used to identify determinants of 1) cognitive impairment at 6 months post stroke, and 2) reverter status.

Results: Between 2 and 6 months post stroke, mean MoCA-score improved from 23.7[3.9] to 24.7[3.5], $p<0.001$. Prevalence of cognitive impairment at 2 months was 66.4%, compared to 51.9% at 6 months ($p<0.001$). More comorbidity and presence of cognitive impairment at 2 months were significant independent predictors of cognitive impairment 6 months post stroke. No significant determinants of reverter status were identified.

Conclusions: Although cognitive improvement is seen up to 6 months post stroke, long-term cognitive deficits are prevalent. Identifying patients at risk of cognitive impairment is therefore important as well as targeting interventions to this group.

Psychiatric Disorders and Cognitive Consequences in Neurological Patients

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Introduction: Apart from a multitude of physical complaints, neurological disorders can also lead to various kinds of psychiatric and cognitive disorders like mental and cognitive changes or reduced Quality of Life (QoL). The most important neuropsychiatric consequences include HOPS, PTSD, Depression, Neurocognitive deficits, Quality of Life (QoL) deficits and Quality of Sleep (SQ) deficits, which are targeted in neurological and neurosurgical rehabilitation.

In such cases, mental health, mood, attention, vigilance and/or memory may be affected as well as the actual mental and/or cognitive processes themselves. Important factors in this can be the severity of the disorder on one hand, and the duration of prior therapy on other hand.

Methods: The study was carried out involving two groups of randomly selected persons, neurology patients and healthy participants. All patients were selected according to their clinical diagnosis (ICD-10).

Instruments applied by us are:

1. Gathering of general datas (e.g. demographic, anthropomorphic, clinical datas)
-> Patient Questionnaire (Büttner 2001)
2. Gathering of neuropsychiatric datas (e.g. Depression)
-> Beck's Depression Inventory (BDI) (Beck et al. 1961; 1987)
3. Determination of neurocognitive functions (e.g. Vigilance)
-> Vigilance Test „Carda“ (Randerath et al. 1997)
4. Determination of Quality of Life:
-> Münchner Lebensqualitäts-Dimensionen-Liste (MLDL) = Munich Quality of Life Questionnaire (Bullinger 1991, Rupprecht 1992, Westhoff 1993)

So far, data have been gathered more than 50 healthy persons (42 male; 9 female) and around 150 neurological patients (101 male; 47 female) (with various neurological clinical pictures) using different tests to research the psychiatric/mental and cognitive status as well as the QoL.

Findings: Testing of psychiatric, cognitive and QoL achievements revealed highly significant differences between healthy persons and neurological patients (all parameters: $p < .001$).

Testing of neuropsychiatric diseases / difficulties and traumatism revealed a highly significant difference between untreated neurological patients and patients, who had undergone therapy (after 3 weeks of neurological rehabilitation) between $p < 0.001$ and $p < 0.05$.

Analysis of the degree of severity showed for neurology patients no significant differences between mild and severe status ($p > .050$).

Discussion: The study revealed that patients with neurological diseases (strokes, cerebrovascular diseases, brain traumas, brain tumors etc.) show problems, deficits and disorders concerning in different areas of psychiatric/mental and cognitive achievements as well as in multidimensional QoL. In contrast, the degree of severity of the disorders (neurology patients) was not relevant.

Cognitive Impairments and Subjective Cognitive Complaints During the First Year after Surviving a Cardiac Arrest

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Background and Objective: Cognitive impairments are common in cardiac arrest survivors but large prospective cohort studies are lacking. Whether subjective cognitive complaints are of predictive value on cognitive impairment is also unknown. The present study aimed to investigate the prevalence of cognitive impairments and subjective cognitive complaints at two weeks (T1), three months (T2) and 12 months (T3) after cardiac arrest. Second we investigated whether cognitive impairments are related to subjective cognitive complaints.

Patients and Methods: Cardiac arrest survivors were recruited from seven coronary care/intensive care units in the Netherlands between 2007-2010. Cognitive impairments were assessed at T1, T2 and T3 by a cognitive screening battery, including validated tests for memory, information processing speed and executive skills. Cognitive complaints were rated using the Cognitive Failure Questionnaire.

Results: 141 participants were included. Cognitive impairments varied from 16-29% at T1 to 10-22% at T3. Results showed statistically significant differences on scores between T1 and T3, indicating a considerable amount of recovery, especially in the first months after cardiac arrest ($p=0.000-0.010$). Speed of information processing and cognitive flexibility remained impaired in 20% of the patients. 79-96% of cardiac arrest survivors with cognitive impairments did not complain about their impairments.

Conclusions: Cognitive impairments following cardiac arrest are common and mostly recover during the first three months post injury. However, most survivors with cognitive impairments do not recognize their impairments. Specific neuropsychological assessment is essential for determination of cognitive impairment, since cognitive complaints alone are not representative for actual impairments and should be part of standard care. Adequate referral for cognitive rehabilitation should follow accordingly.

The Effect of Goal Setting Interventions for Patients with Acquired Brain Injury: A Case Series

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Background: Each patient with acquired brain injury (ABI) has unique needs for rehabilitation at different stages of recovery. Patient-centred goal-setting interventions were found to improve self-efficacy and long-term psychological outcome for patients after their brain injury.

Objectives: To describe perception and satisfaction of patients with ABI with the goal-setting intervention (Goal Management Training, GMT), and to discuss its clinical implications as a mean for early promotion of self-efficacy and goal attainment for patients with ABI in a sub-acute hospital setting.

Methods: Three participants with ABI received GMT during their in-patient stay for 4 weeks, working towards their own identified goals. Measurement of self-efficacy and quality of life were obtained before and after the intervention. Semi-structured interview for qualitative data collection was conducted after the intervention to record experiences of participants towards the goal-setting intervention.

Results: Participants showed progress towards their goals after the 4-week intervention. Increasing trends were noted for their self-efficacy and self-perceived physical conditions, however, different directions of changes were found for their self-perceived psychological conditions. Participants appreciated the goal-setting intervention, which provided them a patient-centred and active-participated rehabilitation process. Rehabilitation needs beyond goal achievement was also raised for the psychological outcome.

Conclusion: Goal-setting intervention provides patients with ABI a satisfactory rehabilitation experience, and the findings also address the importance of psychological coping in a comprehensive neuro-rehabilitation for promoting long-term well-being of patients with ABI.

Emergency Treatment for Pediatric Traumatic Brain Injury

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Despite prevention efforts, pediatric head trauma remains the most common cause of serious injury and death in children. Obviously, Emergency Treatment for Pediatric Traumatic Brain Injury is different with adults, and particularly important. Summarizing cases of children under 10 years old suffering from traumatic brain injury between January 2000 - June 2016 in department of neurosurgery emergency treatment, we obtain the following experience: First, pre-hospital treatment: focus on the maintenance of blood pressure and oxygen saturation; Second, NICU treatment:

1. ICP monitoring is appropriate if $GCS \leq 8$, and treatment for intracranial hypertension should begin at an $ICP \geq 20$ mm;
2. Cerebral perfusion pressure has to be maintained above 40mmHg, and a CPP between 40 and 65 mmHg probably represents an age-related continuum for optimal treatment threshold;
3. Strict control of the surgical and decompressive craniectomy indications and restore the bone flap as far as possible. Pediatric traumatic brain injury prognosis is better than adults'. Thus, satisfactory results from timely and effective emergency treatment for pediatric traumatic brain injury is quite possible.

The Influence of Traumatic Axonal Injury on Level of Consciousness: A Clinical MRI Study

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Objective: To explore how traumatic axonal injury (TAI) lesions in brain stem and “TAI-like” lesions in thalamus and basal ganglia detected in clinical MRI is associated with the level of consciousness in patients with moderate and severe traumatic brain injury (TBI).

Methods: Consecutive patients with moderate or severe TBI were prospectively included in a database and Glasgow Coma Scale (GCS) scores were registered either before intubation or at admission. 158 patients (7-70 years) with MRI and with no mass lesions were included. Early MRI (1.5T) was performed at median 7 days (range 0-35), and analyses were done blinded for clinical information. TAI lesions were depicted in T2* weighted gradient echo (GRE), fluid attenuated inversion recovery (FLAIR) and diffusion weighted imaging (DWI) sequences. TAI lesions were classified as unilateral or bilateral TAI and according to their location (white matter in hemispheres, corpus callosum and brain stem), as were “TAI-like” lesions in thalamus and basal ganglia.

Results: Out of all patients 82% had TAI. 20% had TAI lesions in thalamus (7% bilateral), 18% in basal ganglia (2% bilateral) and 29% in brain stem (9% bilateral). The finding that best predicted low GCS scores was bilateral TAI lesions in thalamus (odds ratio [OR] 35.8, [CI: 10.5-121.8], $p < 0.001$), followed by bilateral TAI lesions in basal ganglia (OR 13.1 [CI: 2.0-88.2], $p = 0.008$) and brain stem (OR 11.4 [CI: 4.0-32.2], $p < 0.001$).

Conclusion: This study demonstrates that patients with bilateral TAI lesions in thalamus, basal ganglia or brain stem had particularly low consciousness at admission. Bilateral TAI lesions in thalamus had the highest impact on consciousness. Early clinical MRI can visualize such important injuries and explain the low consciousness in some of the patients without mass lesions.

Neuroimaging Findings in High School Football Players in Japan

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Objective: The goal in this research was to reveal the result of clinical neuroimaging abnormality performed in High school football players in Japan.

Methods: The authors conducted a retrospective review of medical records and neuroimaging findings for all players referred to a Medical clearance program between 2011 and 2015.

Inclusion criteria were as follows: 1) age \leq 19 years; and 2) physician-diagnosed No-SRC. All players underwent evaluation and follow-up by the same neurosurgeon.

The 2 outcomes examined in this review were the frequency of neuroimaging studies performed in this population and the findings of those studies.

Results: A total of 28 players (mean age 17 years, 0% female) were included this study. Overall, 27 patients (96.4%) underwent neuroimaging studies, the results of which were normal in 81.5% of cases.

Abnormal CT findings included the following: arachnoid cyst (1 player), cavum vergae (4 players).

Conclusions: Results of clinical neuroimaging studies are normal in the majority of high school players with No-SRC in Japan. However, in selected cases neuroimaging can provide information that impacts decision making about return to play and retirement from the sport.

Two Promising Evidence-Based Interventions for Suicide Prevention among Veterans with Moderate to Severe TBI

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Research Objectives: US Veterans with traumatic brain injury (TBI) have higher suicide rates than members of the general Veteran population. A partnership was established between the Liverpool Brain Injury Rehabilitation Unit and the Rocky Mountain Mental Illness Research, Education, and Clinical Center to adapt and evaluate two cognitive behavioral group therapies (CBT) for Veterans with moderate to severe TBI and current hopelessness. The first intervention, Window to Hope (WtoH), was culturally adapted from the original developed in Australia. The second was a novel intervention employing Problem Solving Therapy and Safety Planning for suicide prevention (PST-SP).

Design: Two open, non-randomized acceptability and feasibility studies and one Randomized Controlled Trial (RCT) with a waitlist cross-over design.

Setting: Urban VA medical center.

Participants: Veterans with hopelessness and moderate to severe TBI.

Interventions: WtoH and PST-SP, outpatient groups, 20 hours over 10-sessions.

Main Outcome Measures: Client Satisfaction Questionnaire-8 (CSQ-8), Narrative Evaluation of Intervention Interview; Beck Hopelessness Scale.

Results: Feasibility of both interventions was supported by high attendance and low attrition. Quantitative data supported the acceptability of both interventions [WtoH RCT (n=33): mean CSQ-8 = 27.8, SD=4.3; PST-SP (n=13): mean CSQ-8 = 27.8, SD=4.78]. Qualitative results also supported the acceptability and feasibility of both interventions. RCT participants in the WtoH condition reported clinically and statistically significant decreases in hopelessness compared to those in the waitlist condition, after adjusting for baseline differences.

Conclusions: Findings support the acceptability and feasibility of delivering WtoH and PST-SP to Veterans with moderate to severe TBI. Data from the WtoH RCT supported its efficacy for reducing hopelessness, a significant risk factor for suicide. Limitations included small sample size and variability in reported symptoms.

Neuropsychological Outcomes from a Phase II, Randomized, Sham-Controlled Trial Hyperbaric Oxygen for Post-Concussion Syndrome

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Anecdotes and small case series have suggested symptomatic improvement from hyperbaric oxygen (HBO2) for military members suffering from persistent post-concussion symptoms. Dose, duration, and attribution of the improvement to the HBO2 were relatively unknown due to the lack of randomized trials. As such, a Phase II trial was conducted which evaluated HBO2 as an adjunct to standard traumatic brain injury (TBI) care in a military population still symptomatic from deployment-related concussion at least four months after their most recent injury. The trial was conducted at four military hospitals located near major troop centers. Seventy-two active duty service members were randomized into one of three arms: routine TBI care, TBI care plus sham daily, or TBI care plus HBO2 daily. The dose of HBO2 selected was 100% O₂ at 1.5 atmospheres absolute (ATA) administered for 60 minutes per session, given for 40 sessions within a 10 week period. The sham received room air at 1.2 ATA while in the chamber. Primary outcome measures were self-reported post-concussive symptom scores at baseline, after 20 sessions, and at the end of the intervention.

Neuropsychometric testing and questionnaires assessing post traumatic stress disorder symptoms, sleep, health-related quality of life, and satisfaction with life were also administered at these time points. Initial findings, which have been widely reported, suggested no difference between the HBO2 group and the sham group on the primary measure of post concussive symptoms ($P = .70$). Full neuropsychological results, both standard and computerized, have yet to be reported. Analyses are being conducted and data will be presented at this meeting.

Exploring Accelerometry Versus Questionnaire Assessment of Sleep in Youth with Concussion

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Primary Objective: To examine the relationships between accelerometer-based and self-report assessment of sleep disturbance among youth with post-concussive injury.

Research Design: From a larger prospective cohort of youth 5-18 years of age with post-concussive injury, preliminary analysis of 12 participants with self-reported sleep disturbance were evaluated using accelerometers.

Methods: Participants completed the Pittsburgh Sleep Quality Index (PSQI) every 48 hours and also had sleep measured via accelerometry. Measurements included counts per hour of time in bed, efficiency, average awake time and number of awakenings per hour of sleep. Correlations were conducted matching PSQI scores to consecutive nights of accelerometry assessment.

Results: Accelerometer-measured median (range) sleep efficiency was 80.7% (67.3-87.2%), with normal sleep defined as >85%. The median PSQI score was 11 (2-16) out of 21, with a recommended cut-off of >5 indicating subjective insomnia. PSQI scores were poorly correlated with actigraph sleep recordings and only average number of awakenings was significant ($r = -0.3$; $p = 0.035$).

Conclusions: Preliminary results from this ongoing data analysis suggest the PSQI and accelerometry may be measuring different attributes of sleep. Both may be needed as actual sleep is important but so is perception of good sleep. These findings call for further validity testing of objective sleep assessment measures like accelerometry, as well as commonly used self-report tools.

Portable Neuromodulation Stimulation (PoNS™) Therapy Efficacy for the Treatment of Traumatic Brain Injury Compared to Standard of Care

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Traumatic Brain Injury (TBI) is prevalent in society with over 5 million Americans living with the sequelae and every year a further 2 million suffer TBI. No definitive cures exist for balance and gait disorders resulting from TBI. Currently, the standard of care (SOC) for patients suffering from TBI is physical therapy. Although improvement is seen in patients with TBI undergoing physical therapy regimen, these improvements are not statistically significant and are negated upon discontinuing treatment.

Prior studies at the University of Wisconsin Tactile Communication and Neurorehabilitation Laboratory (TCNL) treating subjects with TBI induced balance disorders were reviewed by a third-party (Optum Healthcare Solutions). The purpose of this retrospective analysis was to examine the effect of neuromodulation inducing neuroplasticity in patients with resistant neurological conditions (>6 months without symptomatic improvement) secondary to disease or trauma and how PoNS(TM) Therapy, combining per-oral non-invasive cranial nerve neuromodulation in conjunction with a proprietary course of therapy (balance, gait and breathing and awareness training), may improve patient outcomes when compared to the SOC.

Four studies were completed, totaling 98 subjects (56 females and 42 males), with an average age of 52.1 and no subjects lost to follow up. Subjects were consolidated into a population of individuals who (1) had been diagnosed as resistant to SOC; (2) had a diagnosis fitting criteria for TBI and (3) participated in PoNS(TM) Therapy. The tests recorded and used in this analysis are widely accepted, objective metrics such as the Dynamic Gait Index and Sensory Organization Test.

All studies and tests presented in this analysis have met the criteria for being statistically significant ($p < 0.05$). When results of studies using PoNS(TM) Therapy are compared to SOC, not only are the results statistically significant, but denigration of benefit gained was reduced when subjects continued PoNS(TM) Therapy at home. In conclusion, PoNS(TM) Therapy leads to a significantly better outcome and quality of life in patients with TBI compared to physical therapy alone (i.e. SOC). PoNS(TM) Therapy is now being evaluated in a prospective, multi-center, double blind sham controlled trial to address balance issues in subjects as a direct and proximate result of TBI.

The concept of neuroplasticity was posited by Drs. Marian Diamond and Paul Bach-y-Rita among others and our data suggest PoNS(TM) Therapy induces a neuroplastic response reflecting recovery from distressing symptoms of TBI. Completion of the study referenced above and the parallel study from TCNL will go a long way towards defining the role of PoNS(TM) Therapy in TBI.

Acknowledgement: We wish to thank Dr. Yuri Danilov, Mitch Tyler, Kurt Kaczmarek and Kim Skinner at TCNL for their tireless pursuit of therapeutic options for those afflicted by neurologic disease and trauma.

Brain SPECT Abnormalities and Spontaneous Intracranial Hypotension After Consecutive Concussions

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Case of a 49 y/o woman (subject) that has no prior medical or psychiatric history who was involved in two motor vehicle accidents (MVAs), on 1/9/16 and on 5/20/16. She developed tinnitus, neck pain, and headaches that progressively worsened. She was also diagnosed with benign paroxysmal vertigo. She had a neuropsychological evaluation on 5/11/16 that showed the subject was suffering from cognitive impairment, including impaired memory recall. She also demonstrated interference of her affective problems with attention and concentration. She had a brain MRI on 8/10/16 that showed she had multiple subdural hygromas and cerebellar tonsils 1 mm through the foramen magnum on the left. These findings are consistent with spontaneous intracranial hypotension. A brain SPECT was done on 8/29/16 that showed focal areas of abnormal cortical hypoperfusion in the frontal, temporal, parietal, and occipital lobes. In addition, focal areas of abnormal subcortical hypoperfusion were noted in the basal ganglia areas. The finding of increased thalamic activity coupled with orbito-frontal hypoperfusion has been associated by several authors with various mood disorders. The finding of increased activity in the basal ganglia has been associated by several authors with various anxiety disorders. A DSM-5 Neuropsychiatric Diagnostic screen was administered to the subject on 8/23/2016. Accordingly, she met the following diagnostic criteria: Major Depressive Episode and Social Anxiety Disorder.

Do Profiles on Objective Measures of Emotions Vary by Severity of Traumatic Brain Injury (TBI): An Exploration of Recent Research

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Objective: The Center for Disease Control and Prevention (CDC) estimates that Traumatic Brain Injury (TBI) affects annually 1.7 million people in the USA leading to lifelong disability. Studies estimate that the prevalence of emotional disturbances reported (e.g. depression, anxiety) following a TBI ranges from 11 to 77%. Other studies have shown that emotional disturbances may still be present after cognitive complaints dissipate in mild to moderate TBI. Objective of this study was to systematically review the differences between the TBI severities and their reported emotional disturbances in objective measures in order to delineate how emotional factors may impact course and treatment.

Method: Studies containing information related to TBI and emotional disturbances were identified using a defined search strategy. Results were limited to peer reviewed and full text articles. Databases used were Cobimet, Psych Info, ProQuest, PubMed and Academic One File. Inclusion criteria were studies examining the different severities of TBI and disorders of emotional disturbances, and outcome measures of emotional state. Exclusion criteria were studies that exclusively addressed cognitive deficiency, organic etiology of TBI, litigation process, and inclusion of psychotic disorders. This search rendered 14 studies.

Results: In the 14 studies reviewed, participants had a mean age of 36.21(SD= 12.04) and an education mean of 12.45 (SD=2.46). Seven studies demonstrated clinical elevations with mild to moderate TBI (e.g. MMPI-2, NSI, and CES-D). Studies that used the MMPI-2 demonstrated elevations on the scales of hypochondriasis, depression, and hysteria including elevations on one of the subscales (i.e. Hy3 Lassitude-Malaise). On the CES-D, a score of ≥ 16 or higher was highly correlated with a depressive diagnosis. Five studies showed clinical significant scores on moderate to severe TBI, and severe TBI (e.g. PAI and DASS-21). The PAI identified clinical elevations two standard deviations away from the mean on somatic complaints, depression, borderline features, paranoia, and schizophrenia scales. The DASS-21 identified depressive symptoms as its most elevated scale followed by an increase of reported stress. One study that used the BDI-II reported minimal elevations in mTBI, while moderate-severe TBI reported mild depressive symptoms. The remaining studies identified emotional disturbances; however, these elevations were not correlated to a specific TBI.

Conclusions: Results demonstrated that there are differences between the reported levels of emotional disturbances in objective measures and different TBI severities with mild to moderate TBI reporting more emotional disturbances than moderate to severe TBI across different objective measures. These differences may be secondary to individuals with milder presentations experiencing greater deficit awareness or being more susceptible to adjustment difficulties. These findings indicate a need to incorporate psychiatric treatment to other treatment modalities in this population.

Effects of Traumatic Brain Injury on Neuropsychological Tests and MRI Scans in the Framingham Study

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Background: The long-term effects of traumatic brain injury (TBI) on cognition and brain morphology are documented in high TBI risk populations. There is, however, a lack of research in community-based samples. The purpose of this study was to determine the relationship between TBI and brain aging.

Methods: Between 2009-2013, 2,517 Generation 3 and Omni Generation 2 participants from the Framingham Heart Study (mean age = 48.31 ± 8.96 ; 46.9% men) were administered a brain MRI scan and a neuropsychological test battery; 100 of whom self-reported previous history of TBI, a subset of which were corroborated by medical records. Using chi-squared tests, the percentage of neuropsychological scores in the lowest tertile was compared between the participants with and without TBI. For Trails A and B, percentages of participants in the top tertile were used for comparison. Total and lobar volumetric MRI measures in the lowest tertile were also compared between those with and without probable TBI.

Results: There was significant difference in the percentage of TBI participants scoring in the top tertile for Trails A compared to those without TBI ($p = 0.0283$). Further, there were significantly more participants with TBI that had total hippocampal volumes in the lowest tertile ($p=0.0090$).

Conclusions: In a young to middle age community-based sample, those with a self-reported history of TBI performed worse on a test of simple attention and had smaller hippocampal volume when compared to those without TBI. These results suggest that chronic effects of TBI may be related to greater risk for accelerated brain aging.

Cross-validation and Extension of the Concussion Prediction Index (CPI) in an Auto Injury Population

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A recent study described the development and initial validation of the Concussion Prediction Index™ (CPI) on a sample of 666 post-auto accident patients, producing high ROC (AUC=.947, $p<.0001$), sensitivity (91.5%), and specificity (89.5%) for presumptive concussion diagnosis using ImPACT test scores as the primary outcome.

This study replicates the previous design using a sample of new outpatient accident patients to determine the reproducibility of those findings, the effect of using a lower CPI cutoff score, and the overall prevalence of concussions arising from automobile accidents.

We divided 679 consecutive eligible patients, presenting for treatment approximately 10 days after auto accidents, into two groups based on their CPI scores, which reflected their self-report of accident characteristics and symptom severity.

Patients with CPI scores 0-9 (n=336) were placed into a No Concussion group and received no further head injury evaluation. Patients with CPI scores of 10-63 (n=343) were placed in a Possible Concussion Group and neuropsychologically evaluated using the ImPACT computerized concussion test at approximately 5 days into treatment. As in the earlier study, the ImPACT percentile ranked scores for verbal memory, visual memory, visual motor speed, and reaction time served as outcome criteria. In this study, we used a lower cutting score of 10 to reduce false negative cases.

Demographics of this group were similar to the previous study: 61% vs. 60% female, mean age 33.7 vs. 35.7, and racially equivalent. Overall average CPI scores were 17.09 vs. 17.92. With the lower CPI cutoff, 50.5% vs. 48.2% were assigned to the Possible Concussion group.

We obtained an equivalent area under the ROC curve (AUC) of 0.944 ($p<.0001$). vs. .947, At a cutting score of 9, CPI showed a sensitivity of 99.66 and a specificity of 86.60. Using the previous CPI cutting score of 13, sensitivity was .90 (vs. 91.54) and specificity was .89 (vs. 89.51). The lower CPI cutting score produced a concussion prevalence of 42.9% vs. the original sample's prevalence of 41.3%.

Results of this cross-validation demonstrate a stable demographic background for accident outpatients, with more women than men and average age in the mid-30's. In both samples, the prevalence of presumed concussion based on cognitive impairment falls above 40%. This exceeds the rate reported in previously published research (24%), by the CDC (11%), or by our patients' reported concussion diagnosis prior to entrance into our treatment (13%). As such, we believe that accident concussions are much more common than previously thought, with many diagnoses being missed by traditional estimates.

This study also demonstrated the high predictive value of the CPI for early detection of concussed auto accident victims, with AUC's $>.90$ when using a brief, structured self-report questionnaire.

Improving Identification of Auto Accident Concussions Using the Concussion Prediction Index (CPI)

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Concussions or mild TBI have been extensively studied in sports, but not as much in automobile accidents. Because concussions are rarely observed directly in auto trauma, they are often underdiagnosed in emergency settings and outpatient rehabilitation programs. While diagnosis is straightforward in patients who struck their heads and lost consciousness, many without direct head trauma or with no observed loss of consciousness will develop symptoms of Postconcussional Syndrome (PCS). PCS often reflects an important neurological injury that impairs cognition, mood, and function. Better assessment would document injury, avoid potential second impacts from premature return to sports, and guide accommodations for school and jobs.

We studied 666 consecutive eligible patients who presented approximately 10 days after auto trauma at a large outpatient medical rehabilitation practice. At initial evaluation, each patient completed a one-page self-administered questionnaire listing 6 common accident characteristics and rated the severity of 10 cognitive, emotional, and sensory symptoms commonly found after concussions. The accident characteristics were given a priori weightings and combined with the sum of the symptom severities to produce a Concussion Prediction Index™ (CPI), ranging from 0-63 points.

Patients with CPI scores 0-14 were placed into a No Concussion group and received no further head injury evaluation. Patients with CPI scores of 15-63 and between ages 10-60, were placed in a Possible Concussion Group and neuropsychologically evaluated using the ImPACT computerized concussion test at approximately one week (mean= 6.3 days) into treatment. The ImPACT produces percentile ranked scores in four key cognitive areas (verbal memory, visual memory, visual motor speed, and reaction time). ImPACT possesses a large normative base and extensive scientific publication history. It is used currently by NASCAR and is FDA-approved as a Computerized Cognitive Assessment Aid for Concussion.

Of 666 patients (345 No Concussion and 321 Possible Concussion) 60% were female, mean age 35.7 ±12.8, with 37% Caucasians, 38% Hispanics, 20% Black, 5% other.

Results from each of four ImPACT components were automatically scored by the program. A conclusion of cognitive impairment due to concussion resulted if two components scored at ≤16th percentile rank or one was ≤8th percentile.

On ROC analysis, CPI scores produced an area under the ROC curve (AUC) of 0.947, (p<.0001). Using optimal cutting scores, CPI showed a sensitivity of 91.54 and a specificity of 89.51 with a concussion prevalence of 41.3%.

This prevalence rate is much larger than previously reported in a Canadian ER study (24%) or by the CDC (11%) and suggests that concussions are very common in auto accidents, possibly exceeding the rate in sports. Furthermore, a brief, self-administered questionnaire identifies more of those patients who deserve additional study and management, and shows high sensitivity and specificity for predicting impaired cognition.

An In-depth Evaluation of a Non-Pharmacological Intervention for People with Prolonged Disorders of Consciousness in Long-Term Residential Care Settings

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Introduction: Disorders of consciousness are an increasing phenomenon and people are living longer with these conditions. The care needs begin with acute medicine and ICU care and frequently end up with life-long nursing care (Royal College of Physicians, 2013). This group of patients will require care for many years following injury (Fins, 2013). This can place strain on budget limited healthcare systems. Interventions should be aimed at minimising caregiver burden and developing individualised programmes (Wheatley-Smith et al., 2012). Local, individualised, timely and integrated services which are flexible and responsive to personal need are the goal for future neuro-rehabilitation services (Health Service Executive, 2011). This study developed and implemented such local individualised programmes for people with prolonged disorders of consciousness (PDoC).

Method: Five in-depth case studies were conducted in 4 long-term residential care settings. An individualised therapeutic programme was developed and implemented for each participant. Each intervention was 3-6 months in duration. This study was evaluated from three perspectives: the participant with PDoC, their family and the professional staff caring for them. The behavioural changes for participants were measured using three standardised assessments, the Wessex Head Injury Matrix (WHIM), the Sensory Modality Assessment and Rehabilitation Technique (SMART) and the JFK Coma Recovery Scale Revised (CRS-R). Quantitative measures were also used to record changes in family members and professional care staff's knowledge, anxiety, caregiver strain and attitudes towards people with PDoC.

Results: Significant positive statistical and clinical changes were recorded for participants, family members and care staff. Staff attitudes towards care were shown to have significantly changed ($p < .05$) following the study. Family strain and anxiety were also reduced. A positive impact on reducing misdiagnosis and increasing behavioural repertoire was shown for participants. The cost effectiveness of the programme was also evaluated.

Conclusion: In depth case study methodology contributes rich and valuable data to the study of treatment for PDoC. This study highlights the value and importance of such non-pharmacological interventions for PDoC and their practical implementation in long-term settings.

Variation in Blood Transfusion and Coagulation Management Policies Across 70 European Neurotrauma Centers

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Introduction: In patients with severe traumatic brain injury (TBI), optimizing the blood- and coagulation status is essential. However, no conclusive evidence exists on optimal hemoglobin thresholds for blood transfusion or on coagulation management, likely leading to variation in treatment policies. Our aim was to quantify such variation in treatment between European intensive care units (ICUs).

Methods: We conducted a provider profiling survey to assess current local practices as part of the 'Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury' (CENTER-TBI) study. Questionnaires were completed by 71 centers from 20 countries across Europe and Israel. For this study, we used the ICU questionnaire focused on: 1) hemoglobin target levels (Hb-TL) and 2) coagulation policies, i.e. correction of coagulopathy with bleeding diathesis versus deep venous thrombosis (DVT) prophylaxis and its timing.

Results: Seventy centers completed the ICU questionnaire (response rate= 99%). The questions were mostly completed by intensivists (N= 31; 44%), neurosurgeons (N= 19; 27%) or neurologists (N= 5; 7%). Half of the centers (N=36; 53%) had a Hb-TL in their general ICU protocol. Specifically for TBI patients, 28 (15%) centers indicated they would use a Hb-TL between 70 and 90 g/l, and 39 centers (40%) between 90 g/l and 110 g/l. To treat hemostatic abnormalities use of fresh frozen plasma (N= 51; 72%) or platelets (N= 36; 49%) was most often reported, followed by the supplementation of vitamin K (N= 27; 38%), Fibrinogen (N= 20; 28%), Prothrombin Complex Concentrate (N= 18; 26%), Tranexamic acid (N= 9; 13%) or Novo VII (N= 3; 4%). Most centers reported to use DVT prophylaxis frequently (N= 20; 29%) or always (N= 45; 65%). In the absence of hemorrhagic brain lesions 15 centers (22%) indicated to wait 72 hours (after the trauma incident) with DVT prophylaxis. However, in the presence of hemorrhagic brain lesions 31 centers (47%) indicated to wait 72 hours. Low molecular weight heparin was reported as the prophylactic drug of choice (N= 57; 84%).

Discussion: This study shows a lack of consensus in European ICUs on the optimal hemoglobin target levels, coagulopathy management, and DVT prophylaxis in severe TBI patients. The large between-center variation provides research opportunities on the effectiveness of different approaches in comparative effectiveness research.

The Dutch Neurotraumatology Quality Registry (Net-QuRe); Study Design and Pilot Phase

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Objectives: This study focuses at the chain of care for patients with moderate to severe traumatic brain injury (TBI) from acute care to specialized rehabilitation and hereafter. Variability in process and structure of care in different regions in the Netherlands will be assessed aiming to answer questions such as; what is the effectiveness of a direct operative evacuation compared to an (initial) expectant strategy in acute subdural hematoma?; which factors determine discharge destination and what factors predict long-term outcome at several ICF domains? The ultimate aim of the study is to develop a high quality database covering the total chain of care for patients with moderate to severe TBI.

Methods: Net-QuRe is a prospective observational multi-institutional cohort study. Approximately 1500 patients age >15 years old with moderate to severe TBI will be recruited from several Dutch level-1 trauma centers and will be followed for two years. Assessments are scheduled in the hospital phase and 6, 12, and 24 months post-injury. Two to three extra assessments are added in case of rehabilitation in a participating center (including outpatient care). Outcome measures include quality of life, participation, awareness, cognitive functioning, depression and anxiety, language, neuropsychiatry, fatigue, functional independence, functional outcome, walking ability, employment and healthcare use.

Current status: In the first phase of the study outcome measures were defined by rehabilitation professionals from the participating rehabilitation centers using Delphi rounds. In the meantime we started with the development of the database in GemsTracker. To test and improve the data collection procedures, a pilot phase was started in four trauma- and two rehabilitation centers, which together resulted in two closed chains of care. The Net-QuRe study design, including details of the data registration and results of the pilot phase will be presented.

Findings from Subacute Visual Oculomotor Assessments in MTBI Patients Differ from Age Matched Trauma and Healthy Controls

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Background: Many patients with MTBI return to previous activities within a few weeks of injury but up to 40% of patients report persistent symptoms. Disruptions in visual functioning after MTBI have recently been described, and these may play a role in sustaining or aggravating chronic symptoms.

The diagnosis of MTBI is mostly based on self-reported symptoms. Objectively signs for diagnosis and monitoring of MTBI are still lacking. Reported rates of vision-related symptoms in MTBI vary from 1-75%.

Objectives: Aim of the study was to investigate whether objectively measurable visual disturbances are observed more often in MTBI patients than in two groups of age matched controls: individuals with minor trauma without head injury, and healthy controls. In addition, we evaluated whether self-reported vision related symptoms after MTBI correlated with objectively detectable changes in visuomotor performance.

Methods: This prospective observational study included 15 consecutive MTBI patients (age 18-40) with GCS 14-15 at presentation to the emergency department, and required acute CT scan, and two age matched control groups: 15 patients with minor orthopaedic trauma without head injury and 15 age matched healthy controls.

All study participants completed questionnaires and were examined by an optometrist 7-10 days and 3-6 month after the injury. The following outcome measures were assessed: Rivermead Postconcussional Symptoms Questionnaire (RPQ), Hospital Anxiety and Depression Scale (HADS), Revised Convergence Insufficiency Survey (CISS, assesses near vision related symptoms). Visual examination included assessment of visual acuity, accommodation, and eye alignment. Oculomotor measures of saccades, fixation, and reading performance were recorded with eye tracking.

Results: Patients with MTBI reported statistically significantly more near vision related symptoms in CISS compared to each of the control groups, while no difference was observed between both control groups. In MTBI group CISS median value (24) at the baseline was above the cut-off score (21), reflecting abnormal symptom levels. Median values of CISS score were reduced in MTBI group at the follow up. The CISS score in control groups were below cut-off level at both time points.

A significantly worsened near point of convergence was found in MTBI patients compared to control groups at baseline, but not at follow up.

A correlation was found between increased near vision symptom score (CISS) and reduced positive fusional vergence at near ($r = -0.6$; $p = 0.02$).

MTBI patients reported significantly more symptoms in RPQ than controls at the baseline. No difference in RPQ symptom load was found between groups at follow up. RPQ symptom load decreased significantly in MTBI group between the baseline and follow up.

Conclusion: Preliminary results suggest that during the subacute period there are transient measurable visual changes in MTBI patients.

Ceftriaxone Attenuates Alcohol-Drinking and Anxiety-like Behavior Following Mild Traumatic Brain Injury in Rats

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Traumatic brain injury (TBI) affects an estimated 1.7 million individuals annually, notably young, otherwise healthy individuals (e.g., contact-sport athletes, motorists, and military personal). The high incidence of TBI is troublesome due to the lack of an effective therapeutic treatment and the negative behavioral changes that follow TBI, including increased anxiety. Reports from clinical studies also show an increased odds ratio for risky alcohol consumption following TBI. Our pre-clinical studies using a rodent model of TBI have demonstrated that exposure to alcohol from either alcohol vapor or self-administration procedures exacerbates neuroinflammation and prevents neurobehavioral functional recovery post-TBI. A likely mechanism for these pathological sequelae is the downregulation of astrocytic glutamate transporter protein expression (GLT-1 in rodents) responsible for maintenance of glutamate homeostasis at the synapse. We propose that neuroinflammatory-induced excitotoxicity likely triggers apoptosis and neuronal loss, which may represent underlying mechanisms of post-TBI neuropathology including increased anxiety-like behavior and escalation of alcohol consumption. Ceftriaxone, a β -lactam antibiotic, upregulates GLT-1 expression in rodent models of alcohol self-administration. We tested the hypothesis that upregulation of GLT-1 via ceftriaxone would improve negative behavioral outcomes post-TBI, specifically anxiety-like behavior and escalation of alcohol drinking. Adult male Wistar rats (n=15) were trained to consume alcohol via operant conditioning procedures. Individual levels of alcohol and water consumption were measured. Baseline values for alcohol consumption, neurological function (neurological severity scores [NSS]), and neurobehavioral function (neurobehavioral scores [NBS]) were established prior to TBI, which was produced by the lateral fluid percussion procedure. Briefly, 5 mm-diameter craniotomies were performed on all animals, and following a two-day recovery period, the rats received a sham injury (n=5) or a mild to moderate TBI (~2 ATM (~30 PSI); ~20ms impulse) over the left sensorimotor cortex. Thirty minutes post-TBI, TBI animals were assigned to receive either intraperitoneal ceftriaxone (TBI/CFT; 200mg/kg; n=5) or vehicle (TBI/VEH) such that each group had equivalent alcohol-drinking baseline values. Determinations of daily alcohol consumption, NBS, and NSS were obtained at selected timepoints post-TBI. Open field, Y-maze, and novel object recognition paradigms were used to assess anxiety-like behavior and working memory. All animals were sacrificed 10 days post-TBI and brains were extracted, dissected, and frozen for future analysis. TBI/CFT animals exhibited a trend for decreased alcohol consumption relative to sham and TBI/VEH groups. Moreover, TBI/CFT animals displayed reduced anxiety-like behavior, as well as improved motor and sensorimotor function, relative to TBI/VEH animals. In summary, our results indicate that ceftriaxone may effectively treat negative behavioral changes post-TBI and warrant further studies to elucidate the neurobiological processes that underlie these observations.

Mild Traumatic Brain Injury Exacerbates Alzheimer's Disease Brain Pathology. Neuroprotective Effects of Nanowired Mesenchymal Cells and Cerebrolysin

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Traumatic brain injury (TBI) either concussive or piercing in military personnel resulting in life long disabilities that often precipitates in development of Alzheimer's disease (AD). TBI induced AD brain pathology is quite complicated and so far no suitable therapeutic strategies have been worked out. We have undertaken a series of investigation to expand our knowledge on AD pathology induced by TBI in laboratory animal models to explore novel treatment strategies including nanomedicine. In this investigation we examined effects of concussive head injury (CHI) on amyloid beta peptide (A β P) infusion induced simulation of AD brain pathology. In addition, role of mesenchymal stem cells (MSCs) and the multimodal drug cerebrolysin either alone or in combination was investigated using their nanodelivery in CHI induced AD brain pathology.

CHI was induced in Equithesin anesthetized rats by dropping a weight of 114.6 g over the right parietal skull from a distance of 20 cm through a guide tube resulting in 0.224 N impact over the skull surface without fracture. These animals were allowed to recover 24 h. In these animals as well as in control group of rats without CHI A β P was infused (A β P1-40, 250 ng/10 μ l) into the right lateral cerebroventricle once daily for 4 weeks. This dose of A β P results in AD like symptoms as seen on behavioural and neuropathological disturbances in the brain. Thus, after 4 weeks deposits of A β P was seen in several brain regions as well as significant elevation of Tau protein, decrease in neprilysin and increase in α -synuclein both in the CSF and in the brain. In this AD model, breakdown of the blood-brain barrier (BBB), leakage of albumin, formation of brain edema and neuronal, glial and myelin damages are prominent. Interestingly, when A β P was infused in CHI rats these physiopathological symptoms were further exacerbated by 3 to 7 folds in the brain and in CSF. This suggests that CHI aggravate AD brain pathology. In these rats when either TiO₂-nanowired MSCs (1 million) or cerebrolysin (a suitable composition of several neurotrophic factors and active peptide fragments, 2.5 to 4 ml/kg, i.v.) given daily after 1 week of A β P infusion and continued for 2 weeks resulted in mild to moderate neuroprotection in CHI rats with AD. However, co-administration of TiO₂-nanowired MSC and cerebrolysin significantly attenuated BBB disturbances, brain edema formation and brain pathology in AD rats in CHI group. In these animals reduction in Tau and α -synuclein as well moderate increase in neprilysin was also observed. This indicates that co-administration of nanowired MSCs and cerebrolysin has the most superior effects on neuroprotection in AD cases after CHI, not reported earlier. These results raises hope for effective treatment in soldiers with TBI for better rehabilitation in future strategies.

Subarachnoid Haemorrhage Secondary to Traumatic Intracranial Aneurysm of the PICA – Case Report

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Introduction: Delayed traumatic intracranial aneurysms (TICA) of the posterior circulation caused by nonpenetrating head injury are rare. The subarachnoid haemorrhage secondary to post-traumatic aneurysm is a potentially treatable cause of neurological mortality and morbidity. The true incidence and natural history of these aneurysms are not fully known.

Results: We report a case of an 18-year-old man who primarily suffered from a multiorgan injury caused by a car accident. On initial head CT there was no sign of SAH. Because of multiorgan injury he was treated in ICU. He was sedated for 1 day. After cessation of sedation he was alert and in good neurologic condition. After a few days he deteriorated. The control computed tomography of the head demonstrated a subarachnoid haemorrhage of the posterior fossa. The patient underwent an MRA which demonstrated abnormal appearances of the left posterior inferior cerebellar artery (PICA), suspicious for a TICA. Digital subtraction angiography (DSA) demonstrated a saccular aneurysm of the proximal left PICA. The patient was treated successfully by microsurgical clipping.

Objective: The goal of this presentation is to present and discuss our own experience with diagnosis and treatment of this rare condition.

Treatment Program for Lower Limb Central Paresis Based on Constrained Induced Movement Therapy

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Our department of rehabilitation medicine is concerned with acquired brain injury patients for a long time. We run day treatment program for them. Three years ago we established program using CIMT (Constraint induced movement therapy) for people with central hemiparesis. The upper limb was treated during this program. Last year we introduced also program on the basis of CIMT for lower limb. CIMT was first described by Taub and Millner and is based on two basic principles – forced used of the paretic arm by restraining the unaffected arm and massed practice of the affected arm through repetitive training. It is not possible to restrain the unaffected lower limb but the other principle to use the paretic lower limb more actively doing repetitive training in restrictive time intervals is very suitable.

Method: 10 patients with central hemiparesis due to acquired brain injury age 18 and older were involved. All of them were able to walk independently without technical aid or using a cane. They come to our department from Monday to Friday for day program for four weeks. The program was for 6 hours a day, three hours and a half were oriented to group or individual activities concerning on affected lower limb. More time had to be spent with the training at home. The activities were repetitive movements of lower limb, functional electric stimulation and group activities oriented on intensive training of affected lower limbs. The evaluation of the effect was done by TUG (The Timed Up and Go test), 10MWT (Ten Minutes Walk test), 2MWT (Two Minutes Walk test) using at the beginning and at the end of the program. The patient was also videotaped at the beginning as well as at the end of the program to see the difference in gait cycle and the spasticity scales MAS (Modified Ashworth scale) and TS (Tardieu scale) were measured. The patients were also controlled one and six months after finishing the intensive program.

Results: All 10 patients finished the program. 8 of them were better in all mentioned tests, the rest two patients were better only in some of controlled parameters. All patients felt more safe and walked longer distances than before the program.

We plan to use this type of intensive day treatment program for more patients but we must be more careful in defining inclusion criteria for them. One of the most important is motivation of the patient himself and the level of his cognitive function.

Predictors and Indicators of Disability and Quality-of-life 4 Years after Severe Traumatic Brain Injury: A Structural Equation Modelling Approach

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Objective: The objective of the present study was to compare the predictors and indicators of disability and quality-of-life 4 years after severe traumatic brain injury (TBI), using structural equation modelling (SEM).

Methods: This study is a part of the Paris-TBI study, a longitudinal multi-centre inception cohort study of 504 patients with severe TBI. Among 245 survivors, 147 patients were evaluated upon 4-year follow-up, and 85 completed the full assessment. Two outcome measures were analysed separately using SEM: the Glasgow Outcome Scale-extended (GOS-E), to measure disability, and the QOLIBRI, to assess quality-of-life. Four groups of variables were entered in the model: demographics; injury severity; mood and cognitive impairments; somatic impairments.

Results: Disability was directly significantly related to injury severity, to impairments of mood and cognition, and to somatic disorders. Age and education only had an indirect effect, mediated by mood/cognition or somatic deficiencies. In contrast, the only direct predictor of quality of life was mood and cognition. Age and somatic impairments had an indirect influence on the quality of life.

Conclusion: These results suggest that disability and quality-of-life were directly related to different factors. While disability appeared to result from an interaction of a wide range of factors, including cognition, mood, somatic deficiencies and overall injury severity, quality-of-life was solely directly related to psycho-cognitive factors.

Illness and Treatment Representation as Factors of Commitment to Rehabilitation in Post Stroke Patients with Arm Paresis

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Introduction: Psychological reactions to stroke including illness and treatment representation are important factors of rehabilitation efficacy that frequently demands regularity, persistency and sensitivity to small progress. We suggest that better representation leads to clearer personal rehabilitation goals, better self-efficacy and persistency that prevent treatment-related health anxiety and helplessness leading to more effective rehabilitation and better well-being.

The aim was to reveal the role of illness and treatment representation in commitment to rehabilitation and well-being of post stroke patients.

Methods: Research design includes neurological observation and appraisal of rehabilitation efficacy and psychological interview. Patients are interviewed about illness representation (Moss-Morris et al., 2002) and rehabilitation goals, appraise importance, difficulty and self-efficacy regarding them and satisfaction with rehabilitation. To assess treatment-related health anxiety, helplessness and self-efficacy we created nine items (Cronbach's alphas .92, .86 and .91 respectively) based on Health Anxiety Questionnaire, Beck Depression Inventory - II and Health-Specific Self-Efficacy Scales. Then patients replied six items measuring rehabilitation-related intrinsic, extrinsic and impersonal locus of control (.98, .97, .90), Satisfaction with Life Scale and Scale of Positive and Negative Experience. Below are pilot data of nine post stroke patients with arm paresis undergoing rehabilitation in The Department of Neurorehabilitation and Physiotherapy in the Research Center of Neurology.

Results: Patients who had clearer current rehabilitation goals, appraised them as more important and their possibility to achieve them as high were more satisfied with rehabilitation ($r=.41-.57$) and reported less health anxiety and helplessness ($r=-.81 - -.41$). Moreover, helpless patients were less satisfied with their rehabilitation outcomes ($r=-.54$). The more patients considered their illness as long-term conditions having strong impact on their lives the more anxious and helpless ($r=.53-.87$) and less confident in their rehabilitation goals ($r=-.87 - -.53$) they were. Emotional reactions to illness were related to higher helplessness ($r=.48-.79$), lower rehabilitation-related self-efficacy and treatment satisfaction and lower subjective importance of rehabilitation goals ($r=-.79 - -.48$).

Patients with extrinsic and impersonal locus of control reported higher health anxiety and helplessness ($r=.56-.71$), lower subjective importance and self-efficacy regarding rehabilitation goals ($r=-.68-.62$). Both treatment-related helplessness and health anxiety negatively correlated with satisfaction with life ($r=-.65 - -.53$) while helplessness and low self-efficacy in rehabilitation are also related to more negative ($r=.45-.67$) and less positive emotions ($r=-.59 - -.52$).

Conclusions: Based on pilot data we suggest that optimistic view of length of condition and its impact on personal life, decrease of emotional reactions to illness, clearer and personally important rehabilitation goals could be targets for psychotherapy promoting well-being and preventing health anxiety and helplessness of post stroke patients.

Keywords: stroke, neurorehabilitation, illness representation, treatment representation, well-being.

Neuropsychological Predictors of BCI-enhanced Mental Practice Efficacy in Post Stroke Patients

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Introduction: According to the Guidelines for adult stroke rehabilitation and recovery (American Heart Association/American Stroke Association, 2016), mental practice is reasonable to consider as an adjunct to upper extremity rehabilitation services (A level of evidence) (Winstein et al., 2016). Since motor imagery (MI) is an integrative and complex cognitive process there is high demand to assess preserved cognitive functions and allocate sufficient cognitive capacity for effective mental training. It has been already shown that existing MI scales do not correlate with ability to control brain-computer-interface (BCI) based on MI paradigm. The aim of this study is to find reliable tools from neuropsychological approach, which can be prognostic for individual rehabilitation program development.

Materials and Methods: 10 hemiplegic patients after first-time stroke (mean age 51, time from onset range 2-13 month) were examined using Luria neuropsychological examination and assessment, including assessment of functions of spatial analysis and synthesis particularly with the use of Rey-Osterrieth Complex Figure Test in Taylor's modification (Taylor figure); Clock Drawing Test (CDT, predrawn modification), table and cube drawing test, 5 Shapes Test. The Motor imagery questionnaire-revised (MIQ-R) and The Kinesthetic and Visual Imagery Questionnaire (KVIQ) scales were used to measure subjective vividness of MI. After assessment patients were trained to imagine kinesthetically a movement under control of a BCI with the feedback presented via an exoskeleton. Patients underwent 10 training sessions lasting up to 40 min. BCI classifier recognition rate was analyzed as an indirect indicator of motor imagery quality. Offline EEG data processing was started. fMRI with the same task paradigm was performed before and after mental practice course followed by functional connectivity analysis.

Results: Significant correlation (0,785, $p < 0,05$) was revealed between general score of both copy and recall trials of Taylor figure test and the percentage of reliable training sessions from all sessions performed according to online classification accuracy rate. The subscale of fragmentation strategy in copy and recall trials (amount of mistakes) negatively correlated with the percentage of reliable sessions (-0,826; $p < 0,05$) and the percentage of sessions with high online accuracy rate (-0,657; $p < 0,05$). There is a moderate negative correlation between presence of qualitative errors of perseveration type in Clock drawing test, table and cube drawing test and the percentage of reliable sessions (-0,64 and -0,64 respectively, $p < 0,05$). Metrical mistakes in 5 Shapes Test are strongly correlated with the percentage of reliable training sessions and the percentage of sessions with high online accuracy rate (-0,905, $p < 0,01$).

Conclusions: It seems to be promising that neuropsychological approach can shed light into process of mental imagery and the detailed neuropsychological examination and assessment might be used as a screening before mental practice admission.

Keywords: stroke, rehabilitation, neuropsychology, brain-computer interface

Extracorporeal Shock Wave Therapy as a Novel Treatment Intervention for Neurogenic Heterotopic Ossification: A Clinical Case Series

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Background and Aims(s): Neurogenic heterotopic ossification (NHO) is one of the three major types of heterotopic ossification occurring as a complication of a neurological insult, in particular, as a complication of traumatic brain injury (TBI) and traumatic spinal cord injury (TSCI). Late clinical diagnosis does not allow for prophylactic drug therapy and the surgical option carries with it many additional health risks. Mature NHO results in a variety of complications limiting activities of daily living. No “gold standard” exists as regards treatment protocols and many ambiguous findings concerning the clinical outcomes of NHO treatment still remain unchallenged. A new, non-invasive treatment in the form of extracorporeal shock wave therapy (ESWT) has shown promising results (Ref.1).

Method: A clinical case series using ESWT on chronic NHO at the hip or knee of 11 TBI patients more than 12 months post-injury, was undertaken at a specialised rehabilitation hospital. The study was based on protocol of an earlier case study (Ref 2).

Result(s): The results obtained from this larger study supported those of the initial single case study. Using TAU-U statistical analysis results demonstrated that the participants showed an overall reduction in pain and an improvement in range of motion and function.

Conclusion(s): Only limited research into the use of ESWT on NHO exists (Ref 1). This study will add to the body of knowledge concerning the development of NHO and present a novel treatment intervention for chronic NHO in the specified patient group.

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Comparison of Field Side and Office Based Brief Cognitive Assessment in Child Athletes

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Objective: The aim of the study is to determine if a difference exists in ImPACT Pediatric baseline concussion testing scores in different environments when in the areas of (memory and/or other domain). This study was undertaken to investigate whether a brief (10 minute) iPad-based test could be administered outside of an office setting.

Methods: A sample of child football and cheerleader athletes completed a baseline pediatric concussion test (ImPACT Pediatric ImPACT) in different environments. 167 subjects (61% male and 29% females) were tested by a trained examiner field side during practice and an age and gender matched sample were tested in an office environment (derived from the ImPACT Pediatric Manual). The sample was composed of primarily African American children (98%). All subjects completed the Word Memory, Design Rotation, Memory Touch and Picture Match, and Stop and Go test modules of ImPACT Pediatric, an FDA approved cognitive assessment tool for children age 5 through 11. Test scores were compared to established for each age group from 5 through 11.

Results and Analysis: The field-side group performed similarly on almost all of the test modules compared to the group tested in an office environment. The only exception was on the Delayed Recall trial of the Word Memory Test, in which the field side group performed significantly more poorly. However, the field-side group performed almost identically of the word recognition task. This finding may be secondary to the inherent distractions of the environment (noise), or to other factors.

Discussion: Although preliminary, these results suggest that under certain circumstances, it may be possible to complete baseline testing in non-traditional, non-office based setting.

Video and Clinical Screening National Rugby League Players Suspected of Sustaining Concussion

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Background: In 2014, the National Rugby League (NRL) introduced a new ‘concussion interchange rule’ (CIR) allowing for a player to be removed from play and assessed by the club’s medical staff for his suitability to return to play in the same game. As part of that policy, it was mandated that the Sports Concussion Assessment Tool – Third Edition (SCAT3) be included in the assessment process. This study reviewed the available sideline SCAT3 performance of players using the CIR, the available video footage of these incidences, and associated decisions pertaining to return to play.

Method: Video footage and sideline SCAT3 data was available for 38 players. All uses of the CIR were independently reviewed by two raters who determined whether any of five signs (i.e., unresponsiveness or loss of consciousness, clutching or shaking of the head, vacant stare, gait ataxia, or seizures) were present, absent, or indeterminable based on the available footage of the incident for every case.

Results: A total of 21 (55.2%) rugby players were observed to demonstrate signs of unresponsiveness, gait ataxia, or vacant stare. Those with video evidence of unresponsiveness performed more poorly on the modified Balance Error Scoring System (M-BESS; $p=.04$; Cohen’s $d=.69$) and reported greater symptoms ($p=.03$; $d=.51$) on the SCAT3. Similarly, players with a vacant stare reported greater symptoms ($p=.05$; $d=.78$). Those who demonstrated all three signs (unresponsiveness, vacant stare, and gait ataxia) performed more poorly on the M-BESS ($p=.03$; $d=1.4$) and reported greater symptoms ($p=.03$; $d=1.4$) than those with no observable signs. Of the players who obtained unusually low scores (i.e., ≤ 24) on the Standardized Assessment of Concussion (SAC), only one player was returned to play during the same game (i.e., 1/10; 10%).

Conclusions: The results of this study support the notion that the SCAT3 is sensitive to the acute effects of concussion in professional athletes; however, a minority of injured athletes might go undetected by this test. This study also provides initial support for the use of video review as an adjunct to the current acute clinical assessment of concussion in rugby.

A Predictive Model of Resilience Among Family Caregivers Supporting Relatives with Traumatic Brain Injury (TBI) in Australia: A Structural Equation Modelling Approach

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Objectives: Developing a comprehensive understanding of resilience in family caregivers supporting relatives with TBI is important for mental health promotion, yet resilience has been vastly understudied compared to deficits and vulnerability based research. In response a paradigm shift into family research is underway in the field of rehabilitation, with a new emphasis on investigating positive adaption rather than psychological vulnerability among family caregivers of people with TBI. In the current study, a model based on previous empirical research and resilience theory was devised to examine the predictive and mediating relationships among caregiver resilience, personality, coping, self-efficacy, hope, social support and the outcome variables of caregiver burden and psychological adjustment among family members caring for relatives with TBI.

Method: This study used an observational cross-sectional design of family members (n = 131) of relatives with severe TBI (duration of posttraumatic amnesia > 1 day), recruited from 6 specialist rehabilitation services in New South Wales and Queensland, Australia. The study battery comprised the Connor-Davidson Resilience Scale, Eysenck Personality Questionnaire, Ways of Coping Questionnaire, General Self-Efficacy Scale, Herth Hope Scale, Medical Outcome Study Social Support Survey; and four measures of psychological adjustment including: Caregiver Burden Scale, Mental Health sub-Scale-SF36, General Health Questionnaire, and Positive and Negative Affect Scale. Structural Equation Modelling (SEM) was used to test the hypothesised model.

Main Results: The results showed the usefulness of adopting SEM to study resilience in family caregivers supporting relatives with TBI. The model as a whole fitted the data very well, as indicated by the goodness-of-fit indices ($\chi^2 = 58.521$; $p = 0.166$; NFI = 0.934, IFI = 0.989, CFI = 0.998 and RMSEA = 0.39). A substantial amount of variance (63%) in resilience was accounted for in the model by the joint influence of self-efficacy, coping strategies (problem-focused coping), and personality traits (neuroticism, extraversion) respectively. In terms of family caregiver outcomes, resilience had a direct effect on positive affect in caregivers. Resilience also played the role of a protective factor in relation to two variables associated with caregiver vulnerability. It had an indirect association with caregiver burden mediated through social support. In addition, resilience, in combination with self-efficacy, had a direct effect on hope, which, in turn, was associated with positive mental health among caregivers.

Conclusions: This is the first study to test a model of resilience in family caregivers of relatives with TBI. The research identifies resilience as a key factor importantly involved in psychological adjustment of family caregivers. The clinical significance of these findings include the possibilities that a focus on building resilience could contribute to improved hopefulness and other positive caregiver outcomes.

A Mixed Methods Approach to Evaluate Participants' and Service Providers' Perceptions of An Outpatient Rehabilitation Program for Persons with Acquired Brain Injury

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A holistic, intensive and multidisciplinary rehabilitation out-patient program was developed for persons with ABI at the Pitié-Salpêtrière Hospital, France (5 days/week for 7 weeks). The program's effectiveness was recently demonstrated (Poncet et al. 2016), however the perception of the quality of the program (as rated by its participants and service providers) has not yet been studied.

Objectives: Report the perception of program participants (adults with ABI) with regard to service quality, (2) Report the strengths, weaknesses, opportunities, and threats of the program as perceived by the service providers, and, (3) Triangulate findings to draw conclusions about the program's quality and to provide recommendations for quality improvement.

Methods: A mixed-methods design using a validated questionnaire: Perception of Quality of Rehabilitation Services (PQRS-Montreal) and interviews (structured around a SWOT analysis) was employed involving 33 program participants (mean age: 43.6 years; 50% with a TBI) and 12 service providers (average years of clinical experience: 15.9 ±12.3 years).

Results: (1) Perception of program by participants. Highest mean scores (3.5/5) were observed for the following dimensions of the PQRS: Ecological approach, Client-centered approach while lowest scores were for items pertaining to Service availability (2.5/5). (2) Perception of by service providers. Their verbatim generated 166 comments pertaining to the program's strengths (e.g. human resource management), 77 related to the weakness (e.g. small budget allocated to the program), 83 related to opportunities (e.g. maintain competencies of service providers) and 53 referred to potential threats (e.g. social and governmental policies) (3) Triangulation. In general, there was a convergence of opinion among subjects about the high quality of the program, particularly regarding the clinical team's competence and its participant-focused approach. Specific aspects of the program viewed more negatively by both groups were the lack of focus on sexuality, family involvement and return to work /volunteering /school.

Conclusion: Participants' and service providers' perceptions of the rehabilitation program under study were generally positive. A reliable and valid questionnaire and interviews helped identify aspects of the program that work well, and those that could be targeted for future quality improvement efforts.

The Impact of Thickened Fluids on Hydration Status in TBI Patients with Dysphagia: A Retrospective Study Preceding Hydration Protocol Design

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Objective: Neurogenic dysphagia, a common complication post-traumatic brain injury (TBI), is an impairment in swallowing function due to neural damage. Dysphagia often leads to dehydration, and modifying fluids or textures allows for improved intake. Despite these modifications, dehydration persists. Current research on dehydration and modified diets involves stroke patients in long-term care facilities. The goal of this study was to determine the impact of thickened liquids on hydration status in TBI patients with dysphagia in an acute care setting.

Methods: A retrospective study was conducted with participants selected from 614 patients admitted to a TBI unit of a Level I trauma center between January 2014 and March 2015. In total, 575 charts were screened, and those diagnosed with dysphagia and prescribed a modified texture or thickened fluid diet were included. Exclusion criteria included: chronic kidney disease (CKD); acute renal failure (ARF); dialysis; congestive heart failure (CHF); fluid restrictions; and nutrition support. Participants were assigned a dysphagia severity score using the “dysphagia outcome and severity scale”. Biochemical values were obtained via OACIS electronic medical records. Descriptive statistical analysis was conducted using SPSS version 23.

Results: A total of 70 patients (12.2% of screened patients) were diagnosed with dysphagia and prescribed a modified diet. However, 22 patients had exclusion criteria, and 14 had missing data, resulting in n=34, 70.6 % being male. Upon initial assessment: 23.6% had minimal to mild dysphagia; 47% had mild-moderate dysphagia; and 29.3% had moderate to severe dysphagia. Upon final assessment: 67.6% had normal to mild dysphagia; whereas 32.3% had mild-moderate to severe dysphagia. There were 53.3% participants on a modified texture or thickened fluid, whereas 47.1% had both a modified texture and thickened fluid. The average number of days on a thickened fluid was 8.7 (+/- 5.8), whereas modified texture was 5.8(+/- 5.7) days. When available, sodium and potassium were within normal limits, and creatinine levels were below normal.

Conclusion: Patients on thickened liquids often have insufficient fluid intake causing dehydration. The dangers of dehydration are well known, and the relationship between dehydration and modified textures has been established in other populations. Diagnosing dehydration in this study was not possible due to the absence of key biochemical indices. However, this study led to the creation of an interdisciplinary hydration protocol for patients prescribed thickened fluids to prevent dehydration. This research also proposes the design of a prospective study where the correlation between dehydration and modified textures may be determined.

Concussive Head Injury Exacerbates Sleep Deprivation Induced Brain Pathology. Co-Administration of Nanowired Antioxidant H-290/51 and Serotonin 5-HT₆ Receptor Antagonist SB-399885

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Military personnel are often subjected to sleep deprivation (SD) during combat or peacekeeping operations. Long-term SD leads to alterations in neurochemicals with particular references to biogenic amines leading to mental confusion, stress, depression and even brain pathologies. Additional traumatic brain injuries (TBI) in SD cases will thus further exacerbate brain dysfunction and cell injuries. Thus, the need of the hour is to explore suitable therapeutic strategies to reduce brain dysfunction in SD cases after TBI. Previous reports from our laboratory showed that SD alone induces severe oxidative stress that is further compounded by additional TBI. This suggests that antioxidants could be useful for therapeutic strategies in TBI cases in SD. Since serotonin levels are altered in both plasma and in brain following SD and in TBI, it appears that blockade of serotonin receptors together with antioxidant treatment may synergistically induce superior neuroprotective effects in SD followed by TBI.

In present investigations SD was induced in rats using an inverted flowerpot model for 24 and 48 h. In these SD animals concussive head injury (CHI) was inflicted on right parietal skull under anesthesia by dropping a weight of 114.6 g from a 20 cm height through a guide tube (impact 0.224 N) and the animals are allowed to survive 24 or 48 h after the primary insult. In these animals blood-brain barrier (BBB) permeability to Evans blue albumin (EBA) and radioiodine ([¹³¹I]-Iodine), brain edema formation and neuronal, glial and myelin injury was examined using standard protocol. Our results showed that CHI inflicted in SD rats resulted in 4 to 6 fold higher BBB breakdown to EBA and radioiodine tracers in several brain regions. These brain areas exhibited 2- to 3-% higher brain edema formation as compared to SD rats alone after CHI. Neuronal, glial and axonal damages were also 2- to 4-fold higher in rats that received CHI after SD was seen as compared to SD or CHI alone. These observations suggest that CHI in SD rats exacerbated brain pathologies. This effect was time dependent. Thus, CHI inflicted in SD of 24 h showed much more damage in the brain at 24 h as compared to identical CHI given in 12 h SD and examined after 12 h of primary brain insult.

Treatment with serotonin 5-HT₆ receptor antagonist SB-399885 (3 mg/kg, i.v.) together with H-290/51 (a powerful chain breaking antioxidant, 50 mg/kg, i.v.) given 12 h after SD or 12 h after CHI induced marked neuroprotection following SD and CHI alone. However, nanowired SB-399885 with H-290/51 is needed to induce neuroprotection in SD rats after CHI at 24 h insult, not reported earlier.

Investigating Impaired Facial Affect Recognition in Persons with Traumatic Brain Injury Through Eye-Tracking and Gaze Analysis

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Objective: To examine visual scanning differences during a facial affect recognition task in individuals following moderate to severe traumatic brain injury (TBI) and healthy controls (HC). It is widely acknowledged that patients experience significant deficits in emotion recognition and difficulties with interpersonal relationships following TBI. However, the etiology of these deficits are poorly understood. We hypothesize that one of the underlying mechanisms behind facial affect recognition deficits after TBI is suboptimal visual processing of facial expressions. Identifying factors that contribute to these deficits is critical for treating these impairments and improving interpersonal relationships after TBI.

Method: Subjects included 9 adult participants with TBI who had impaired facial affect recognition and 9 HCs. Facial affect recognition was assessed via the Diagnostic Analysis of Nonverbal Accuracy (DANVA); impairment was defined as performance >1 SD below the norm. The DANVA stimuli consisted of 24 images of individuals portraying different facial expressions (i.e. happy, sad, angry, and fearful). Images included the head, neck, and shoulders of an individual against a background and were presented for 2.25 seconds on a computer monitor with integrated eye tracking hardware (Tobii Pro TX300) that recorded their eye movements. Eye tracking was analyzed with Tobii Studio software, which was also used to generate customized areas of interest (AOIs) for each face. The seven AOIs included the 1) whole face, 2) eyes and eyebrows, 3) eyebrows and bridge of the nose, 4) bridge of the nose alone, 5) lower nose and nostrils, 6) mouth, and 7) emotion choices.

Results: Participants with TBI looked at the face significantly fewer times than HC ($p=0.041$). There was a significant negative correlation between DANVA errors and the number of fixations ($p=0.044$) and the time spent fixating in the face ($p=0.025$). There was a significant positive correlation between DANVA errors and the percent of fixations ($p=0.039$) and percent of time fixated on the lower nose and nostrils ($p=0.036$).

Conclusion: Participants with TBI spent significantly less time focusing on faces than HCs, which may indicate some attention deficit to the core stimulus, possibly due to being distracted by elements outside of the face. That subjects with TBI also spent more time fixated on the lower portion of the nose suggests they attributed greater salience to a feature that is minimally relevant for emotion detection, compared to their uninjured counterparts. These findings warrant further investigation of visual processing strategies as a potential mechanism driving facial affect recognition impairments after TBI. Understanding these visual processing deficits may lead to improved clinical outcomes in higher-level rehabilitation for patients with moderate to severe TBI.

Impaired Cerebral Vasoreactivity Persists Beyond Symptom Resolution Following Concussion in Collegiate Athletes

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Objectives: Despite the occurrence of approximately 3.8 million concussions annually in the United States alone, the pathophysiology behind the injury is poorly understood. Reduced cerebral blood flow (CBF) is linked to functional disturbances in concussion. Cerebral vasoreactivity (CVR), an important mechanism in CBF regulation, is the ability of cerebral blood vessels to alter blood flow in the brain during dynamic changes in arterial carbon-dioxide (CO₂). In active professional boxers, CVR is chronically impaired compared to age matched controls. The purpose of this study was to examine CVR in an ongoing prospective cohort of collegiate athletes during acute (day-3) and sub-acute (day-21) phases following concussion and compare them with non-injured athletes.

Materials and Methods: Sixteen male and female collegiate athletes (21±1 years) with a physician diagnosed sports-related concussion were enrolled in the study. Sixteen sports matched non-injured controls (21±1 years) were also enrolled. For the injured athletes, data was collected during the acute (day-3) and sub-acute (day-21) phase following concussion and for the controls data was collected at one time point. Components from the Sports Concussion Assessment Tool-3rd Edition were used to evaluate symptom severity and cognition (orientation, immediate memory, and concentration). Continuous middle cerebral artery blood flow velocity (MCAV) was obtained with a 2MHz transcranial Doppler ultrasonography (TCD) while subjects were seated in an upright position. End-tidal CO₂ was measured with an infrared CO₂ analyzer attached to a nasal cannula. Beat-to-beat MCAV was evaluated in response to changes in end-tidal CO₂ (PetCO₂) for 2-minutes each during normal breathing (normocapnia), inspiring a gas mixture containing 8% CO₂, 21% oxygen with balance nitrogen (hypercapnia) and, hyperventilating (hypocapnia). Cerebral vasoreactivity was analyzed as the slope of the linear relationship between end-tidal CO₂ and MCAV, which was expressed as the change in CBF velocity per mmHg change in end-tidal CO₂. Independent and paired t-tests were used to compare symptom severity, cognition and CVR between acute and sub-acute phase following concussion with the controls.

Results: As anticipated, concussed athletes exhibited higher symptom severity (26.3±0.5 versus 5±7 P=0.0007) and lower cognition (26.5±1.6 versus 28.3±2.4 P=0.03) during acute phase compared to the controls. Symptoms and cognition were resolved by day 21. Cerebral vasoreactivity was attenuated in the acute phase compared to the non-injured control (1.7±0.5U versus 2.3±0.3U, P=0.0006) and it continued to be blunted in the sub-acute phase, 21 days following concussion (1.9±0.5U P=0.04).

Conclusions: Despite symptom and cognitive improvement, cerebral vasoreactivity appears to be impaired in the sub-acute phase following concussion. Cerebral vasoreactivity utilizing non-invasive TCD may be a useful vascular biomarker for physiological recovery and aid in accurate return-to play decision-making reducing the risk of secondary injury from premature return to play.

Tying the String: Contributions of Neuropsychological and Demographic Variables to a Computerized Measure of Prospective Metamemory after TBI

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Objectives: For individuals with traumatic brain injury (TBI), prospective memory, or remembering to perform tasks in the future, is challenging. Metamemory monitoring, or how likely a person thinks they can successfully remember, is critical for people to self-cue to use strategies, like external memory devices. Tying the String, an online assessment of prospective memory, is designed to assess prospective memory and metamemory in an online virtual context. Previous work showed that adults with TBI were overly confident that they would remember prospective tasks to be performed. Objectives of this study were to determine the extent to which prospective memory and metamemory as measured by the assessment tool relate to neuropsychological and demographic variables in a sample of adults with and without TBI.

Methods: Eighteen adults with chronic moderate to severe TBI and 20 matched healthy controls played Tying the String. Participants studied prospective memory tasks and made two judgments of learning predicting the likelihood of recalling the CUE ("On your way to work...") versus recalling the TASK ("...drop a package at the post office"). Participants used a slider bar to indicate the likelihood of recall, from 0% to 100%. Participants also completed a standard battery of assessments examining immediate and delayed memory, attention, working memory, executive function, prospective memory, and metamemory beliefs. Neuropsychological measures and demographic variables were entered into multiple regression models for the dependent variables of CUE and TASK judgments and CUE and TASK performance.

Results: Results showed that differing models explained predictions and performance across the two groups. For adults with TBI, both CUE and TASK judgments were explained by certain executive functions and attention (respectively, $R^2 = 79.6\%$, $p < .001$; $R^2 = 84.1\%$, $p < .001$). For healthy adults, age and self-reported metamemory beliefs were significant predictors of CUE judgments ($R^2 = 51.5\%$, $p = .001$), and metamemory beliefs, age, prospective memory, and delayed memory for TASK judgments ($R^2 = 74.2\%$, $p < .001$). For recall performance, 66.4% of the variance in CUE recognition by the adults with TBI was explained by measures of executive function and attention ($p < .001$), while executive functions and immediate memory contributed significantly to TASK recall ($R^2 = 70.3\%$, $p < .001$). For healthy adults, both CUE recognition and TASK recall were explained by standardized scores of prospective memory (respectively, $R^2 = 30.8\%$, $p = .01$; $R^2 = 39.4\%$, $p = .009$).

Conclusions: Adults with TBI draw upon differing resources to consider their memory and perform tasks of prospective memory. Self-reported metamemory beliefs predicted judgments of healthy adults, but not adults with TBI. Similarly, prospective memory performance of only healthy adults was predicted by standardized measures of prospective memory, suggesting added value of Tying the String in describing prospective beliefs and abilities after TBI. Future work should address the disconnect between beliefs and ongoing metamemory monitoring in adults with TBI.

Severe Dysfunction of Mobility and Activity of Daily Living Performance Due to Post-Hypoxic Action Myoclonus Responsive to Kinesio Taping: A Case Report

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Case Diagnosis: Post-Hypoxic Action Myoclonus

Case Description: We present the interesting case of a 51 year old male with persistent severe disability due to decreased mobility and performance of activities of daily living due to myoclonic jerks involving his trunk and extremities following cardiac arrest due to a complication of anesthesia, leading to hypoxic-ischemic encephalopathy and post-hypoxic action myoclonus (PHAM). Over the three years prior to presentation, he had trialed multiple pharmacologic interventions, achieving partial improvement of his PHAM with a combination of intrathecal baclofen, clonazepam, levetiracetam, and lacosamide. He had trialed valproic acid, but worsening tremor and excessive sedation necessitated its discontinuation. He completed traditional neurorehabilitative therapy, achieving the ability to perform a squat-pivot transfer with moderate assistance, and bathing using a shower chair with minimal assistance for stability. He was observed to demonstrate improved performance with his transfers when his physical therapist provided specific tactile cues to his trunk. This finding, and published literature that suggest cortical dysregulation as a potential cause of PHAM, prompted the hypothesis that provision of a specific proprioceptive stimulus to the trunk would provide improved trunk stability and decreased truncal jerks with functional activities. Kinesio Taping was pursued to address truncal myoclonus with facilitation taping of the rectus abdominus and iliocostalis lumborum. After completion of taping, the truncal myoclonic jerks decreased significantly in amplitude and frequency, allowing the patient to perform a squat pivot transfer with minimal assistance. The effects were preserved by one week later, when he and his fiancée reported that he continued to only require minimal assistance for transfers, and could perform all of his bathing tasks seated in a shower chair without hands-on assistance.

Discussion: This abstract presents an effective nonpharmacologic intervention that significantly decreases post-hypoxic action myoclonic jerks in the trunk, allowing for meaningful functional improvement in mobility and performance of activities of daily living. Many cases of PHAM require polypharmacy and it is expected in most cases that these medication combinations will only be partially effective. There is evidence from published literature that proprioceptive stimuli can modulate the severity of myoclonus and other movement disorders, such as dystonia. Treatment of PHAM with multiple medications is often limited by side effects that adversely impact cognitive performance, overall function, and quality of life. We propose the use of Kinesio Taping as a safe and effective adjunctive nonpharmacologic intervention to improve functional mobility and performance of activities of daily living in PHAM.

Conclusion: A trial of Kinesio Taping should be considered as a safe and effective adjunctive treatment for patients with post-hypoxic action myoclonus.

Effects of mTBI and PTSD on ANAM Performance in OEF/OIF Active Duty Soldiers

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Background: Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) Soldiers are returning from the wars in Afghanistan and Iraq with high rates of traumatic brain injury (TBI). Although cognitive impairments and post-concussive symptoms typically resolve within days to weeks of the injury event, some individuals continue to report persistent physical, cognitive, and emotional symptoms three months post-injury. These non-specific symptoms likely overlap with psychiatric and physical health conditions (e.g., post-traumatic stress disorder [PTSD], depression, pain, insomnia), and evidence posits that these factors likely play a role in the maintenance of these persisting symptoms. Whereas mixed findings exist regarding long-term cognitive impairment following mild TBI (mTBI), there is emerging research supporting the negative impact of mTBI and PTSD on neuropsychological functioning.

Objective: The objective of this study is to examine neuropsychological performance of OEF and OIF Soldiers with and without histories of mTBI and self-reported PTSD symptoms.

Hypothesis: Soldiers with a history of mTBI and current PTSD symptoms will demonstrate worse post-deployment ANAM performance than Soldiers with a history of mTBI only or PTSD only, or neither condition.

Method: Institutional review approval was obtained at military and Veteran Affairs affiliated sites prior to study enrollment. A random sample of 25,000 Soldiers returning to two military bases from deployment in Afghanistan or Iraq between 2009 and 2014 were invited to participate in a study of deployment-related TBI. Participants were assessed for history of lifetime TBI and current symptoms of PTSD. Participants also completed the outcome measure, the Automated Neuropsychological Assessment Metrics (ANAM), a computerized system for cognitive screening. Throughput, a composite of accuracy and reaction time, was the ANAM score investigated.

Results: ANCOVA revealed that Soldiers who screened positive for mTBI and PTSD performed significantly worse ($p < 0.05$) on five of seven ANAM tests than those who screened negative for both conditions while controlling for number of lifetime TBIs, number of non-cephalic pain sites, and race. Those who screened positive for mTBI only scored significantly worse on three ANAM tests relative to those with neither condition while those who screened positive for PTSD only scored significantly worse on one ANAM test. On average, Soldiers with positive mTBI and PTSD screens performed 5.8% to 16.9% worse on ANAM than Soldiers with negative screens for both conditions. These decrements were larger than those from Soldiers with mTBI or PTSD only.

Discussion: These findings support the hypothesis, such that Soldiers whom report a history of mTBI and current PTSD symptoms perform worse on computerized neuropsychological assessments as compared to

Soldiers without a history of mTBI and PTSD symptoms. Findings provide additional support regarding the cumulative impact of these co-occurring conditions.

Neuropsychological Outcome of Anti-NMDA Receptor Encephalitis: Case Series of 9 Pediatric Cases

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Background: Anti-NMDA receptor (NMDAR) encephalitis is an auto-immune condition that commonly presents with severe neuropsychiatric symptoms, behavioural changes, seizures, abnormal movements, and cognitive dysfunction/instability. Better identification of the condition in recent years has led to improved treatment and recovery, yet beyond the acute phase, very little is known about the long-term neurocognitive consequences. Thus far, the literature only contains case studies describing adolescent and adult outcome. For example, in 3 adolescent females, neuropsychological recovery was observed over the first 6 to 24 months post-diagnosis, but lingering deficits remained which varied in severity and kind across patients. In addition, long-term anxiety concerns and neuropsychological impairments were found across tests assessing memory, executive functioning, processing speed, and social cognition in 7 patients with a history of anti-NMDAR encephalitis ranging from 16-37 years old (McKeon et al., 2016). To date, there have been no comprehensive studies describing the long-term outcome in pediatric patients.

Objective: To describe neuropsychological outcomes of children with anti-NMDAR encephalitis.

Methods: This is a cross-sectional analysis of the neuropsychological performance of children and adolescents who were followed prospectively at a tertiary care center after a diagnosis of anti-NMDAR encephalitis. Consecutive patients (2012-2016) who presented with acute neurological and psychiatric symptoms and were CSF positive for anti-NMDAR antibodies were included. Those unable to participate in neuropsychological evaluation were excluded from analysis. Impairment was defined as a standardized score of <1.5 SD below the mean.

Results: Nine patients (6 females) aged 6.08-16.08 years 0.83-5.92 years post initial diagnosis of anti-NMDAR encephalitis (initial age at diagnosis, 2.17 to 14.17 years) were included. 8/9 patients exhibited deficits in the following domains: verbal (2), visual-spatial/perceptual (3), verbal learning (1), memory (3), processing speed (1), visual-motor integration (1), math fluency (1), working memory (5), and attention (3). New-onset cognitive/behavioural concerns included learning needs (3), anxiety and/or depression (5) and language impairment (2). Time since injury was significantly associated with working memory ($r=-0.684$, $p=0.042$), false positive responses on a verbal memory test ($r=0.747$, $p=0.021$) and dual-task attention performance ($r=0.895$, $p=0.040$). Age at test and age at diagnosis were not significantly associated with any outcome variable. Two patients presented with 4 or more neuropsychological needs and learning/mental health concerns.

Conclusions: The most common neuropsychological impairments following anti-NMDAR encephalitis were within executive functioning. New-onset anxiety/depression was particularly high in this sample. It is notable that there was marked variance in our sample, with some patients presenting with more severe dysfunction than others. Although our findings are based on a small number of patients, it is the first step in understanding the long-term effects of anti-NMDAR encephalitis on the developing brain.

Toward a Postmodern Pragmatic Discourse Semioethics for Brain Injury Care. Empirically Driven Group Inquiry as a Dialogical Practice in Pursuit of the Peircean Aesthetic Ideal of 'Reasonableness'.

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A postmodern framework is proposed for conceptualizing the impact of brain injury on the subjective being of the injured person. Semiosis, the 'action of signs', is argued as necessary both as a basis for a postmodern relational understanding of cognitive function in an intersubjective context, as well as for a recovery of subjectivity that escapes the mechanistic materialism, reductionism and the Cartesian mind-matter dualism of conventional modern bioscience, and, in the process, restores personhood to the injured subject. Ethical dilemmas in brain injury care are best approached through an empirical 'semioethics' implemented as a dialogical practice among a group of selected stakeholders seeking a logical solution that best addresses the criterion of maximizing concrete reasonableness as a tempering of rationality with relational concerns in the face of the constraints imposed by the injury.

Impact of Aerobic Exercise on Attention and Visual Memory in An Aging Mild Traumatic Brain Injury Population

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Introduction: Mild traumatic brain injuries' (mTBI) effects are most evident with aging and have been associated with a higher risk of experiencing mild cognitive impairment. A recent study has even suggested an increased risk of developing dementia after sustaining a single mTBI later in life. Beyond the issue of neurodegenerative diseases, aging individuals may present a decline in cognitive function that exceeds what is expected in an otherwise healthy individual. Unfortunately, very few interventions exist to treat this population and prevent this accelerated decline of cognitive functioning. However, recent studies have shown beneficial effects of moderate levels of physical activity on cognitive functioning in neurotypical populations of different ages as well as in individuals at risk of developing neurodegenerative diseases. Therefore, this study aims to evaluate the effectiveness of this type of intervention in an aging mTBI population by assessing the impact of an aerobic exercise program on cognition.

Methods: Twenty participants, aged between 55 and 70, all sedentary and presenting with a history of mTBI sustained two to seven years earlier, were recruited to participate in a twelve-week physical exercise program. They were divided into two equal groups who were subjected to two different types of training: aerobic training on cycle ergometers (intervention group) and stretching exercise (control group). Participants were matched based on age and gender and were equivalent in regards to level of education and time elapsed since the injury. The participants' cognitive function and physical condition were evaluated before and after the training. Cognitive functioning was assessed using neuropsychological tests, whereas physical condition was assessed using cycling tests.

Results: The present study shows that participants from the aerobic exercise group significantly improved their peak exercise capacity (VO₂ max) and neuropsychological tests performance on measures of attention (Conners' Continuous Performance Test II) and episodic visual memory (Brief Visuospatial Memory Test Revised) when compared to participants from the control group. Furthermore, correlations drawn between these measures showed that the participants who most improved their physical capacities were also those who showed the biggest improvements on neuropsychological measures.

Conclusions: These results demonstrate the importance of considering aerobic exercise as a relevant intervention to improve cognitive functioning of mTBI patients. Indeed, the observed improvements involve functions known to be particularly affected following a mTBI.

High Brain Compliance after TBI May Cause Subdural Hygroma

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Background: Paradoxical herniation (PH) caused by subgaleal drainage for subdural hygroma (SH) following decompressive craniectomy has been documented, an emergency cranioplasty was recommended. But, it did not work in one case complicated by paroxysmal sympathetic hyperactivity (PSH) presented below. PSH has a high incidence following severe traumatic brain injury (TBI), causing sympathetic symptoms like tachycardia, tachypnea, systolic hypertension, hyper/hypothermia, excessive sweating, decerebration and increased muscle tone, et al. Hypocapnia caused by tachypnea can induce dramatic arterial constriction and decrease of cerebral Blood Flow (CBF). Excessive sweating, together with incorrect treatments, like percutaneous drainage and excessive hypertonic therapy, can reduce cerebrospinal fluid (CSF) in the intracranial vault, weaken the effect of CSF compensation. Skull defect, arterial constriction and loss of CSF compensation, all of them can increase brain compliance, which can cause brain shrinkage, decrease intracranial pressure and brain pulsatility, causing CSF dynamics disturbance including subdural SH and hydrocephalus.

Case Description: We present a rare case of coexistence of PH, PSH, and huge SH ipsilateral to the decompressive craniectomy after TBI. Repeated percutaneous drainages were done in local hospital and the patient developed sunken skin flap syndrome and PH. Intravenous infusion and cranioplasty were given as reported after being transferred to our hospital. Major of the SH disappeared but recurred gradually even more than before, the patient suffered severe neurological deterioration 21 days after cranioplasty. Emergency borehole drainage was performed due to severe midline-shift, a subdural drainage tube was placed, drawing of CSF for 5 ml by syringe was followed by CSF suck-back from drainage tube. Pulsatility index (PI) was acquired from transcranial color-coded duplex sonography (TCCS), both suck-back phenomenon and high PI suggested high brain compliance. We suppose the reason might be consistently low PaCO₂ caused by PSH-induced tachypnoea, so the patient was sent to neurosurgical ICU, given deep sedation and mechanical ventilation, meanwhile, high dose intravenous infusion was given with saline, nitroglycerin was given for mildly increased blood pressure. 83 days post decompression, when PaCO₂ came back to normal, on the same day, brain CT scan showed sudden disappearance of SH and recovery of brain structure, PI also decreased. 6-month follow-up showed significant improvement of neurological function, no recurrence of SH.

Conclusion: The present case highlights the possibility that SH is resulted from brain shrinkage caused by high brain compliance. CSF depletion can be useless even dangerous. In the current 4th BTF guideline for severe TBI, recommendations concerning continuous draining and larger bone flap, seem controversial with clinical facts and need further investigations.

Traumatic Brain Injury and Risk of Depression

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Background: Increased risk of depression has been associated with traumatic brain injury (TBI). This study sought to determine if a history of self-reported TBI was related to higher self-reported depressive symptoms in a community-based sample.

Methods: Recruited in 2002, 4095 Generation 3 and Omni Generation 2 participants from the Framingham Heart Study were administered the Center for Epidemiologic Studies –Depression Scale (CES-D) as part of an initial health exam. At a subsequent exam, 682 participants reported that they had previously sustained a TBI, with a subset corroborated using medical records in accordance with the American Congress of Rehabilitation Medicine TBI diagnostic criteria. We compared CES-D scores in the TBI group to the 2330 participants who reported no history of TBI and whose medical records indicated no history of TBI. All CES-D scores analyzed were post-TBI.

Results: The CES-D scores of the TBI group were significantly higher than the no TBI group (16.5 vs. 15.3, $p < 0.05$), where a score of >16 is often defined as depression.

Conclusions: Within a community-based population, self-reported TBI was related to an increase in post-injury CES-D score. These findings suggest that a history of TBI may increase an individual's risk for depression later in life.

Predictive Ability of the SCAT3/ChildSCAT3 for Paediatric Concussion in an ED Setting

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Background: Concussions are common among children and adolescents and constitute a significant public health issue. Indeed, concussions represent the vast majority of traumatic brain injury presentations to paediatric Emergency Departments (ED), accounting for up to 95% of all cases in developed countries. Currently, there are no acute concussion measures tailored for the ED that can assist clinicians with assessment and diagnosis. In contrast, the Sports Concussion Assessment Tool, 3rd edition (SCAT3) and the paediatric version (ChildSCAT3) have been specifically designed for acute concussion assessment in a sporting context. The present study aims to examine whether performance on the SCAT3/ChildSCAT3 predicts delayed symptom recovery at 2-weeks post-injury, in an acute ED setting.

Method: The present study is part of larger paediatric concussion project, the Take CARE (Concussion Assessment and Recovery Research) study. Take CARE is a prospective, longitudinal study based at the Royal Children's Hospital and the Murdoch Childrens Research Institute in Melbourne, Australia. Recruitment takes place in the ED of Royal Children's Hospital and participants are assessed using the SCAT3/ChildSCAT3. At follow up appointments, in a dedicated concussion clinic at Murdoch Childrens Research Institute, participants are assessed using the Post Concussion Symptom Inventory (PCSI) and the SCAT3/ChildSCAT3, at 1-4 days and 2-weeks post-injury. The PCSI is a developmentally appropriate, well-validated, and widely used measure to assess symptoms post-concussion. For the purposes of this study, we will focus on three components of the SCAT3 and ChildSCAT3: the symptom report, Balance Error Scoring System (BESS/mBESS), and the Standardized Assessment of Cognition (SAC/SAC-C).

Results: Using previously validated methods (Hearps et al, In Press), we will split the sample into "symptomatic" and "recovered" based on PCSI scores at the 2-week time point. We will use binary logistic regression to examine how the SCAT measures assessed in the ED predict group membership (symptomatic versus recovered) at 2-weeks post-injury.

Discussion: The SCAT3 and ChildSCAT3 are widely used instruments for the acute assessment of concussion; however, to date, the predictive abilities of the SCAT3/ChildSCAT3, in an acute ED setting, have not been examined. These results may have significant clinical implications for the clinical management of children and adolescents who sustain a concussion, particularly considering the widespread use of the SCAT3 and ChildSCAT3.

Triage of Mild/Moderate Traumatic Head Injured Patients Using a Brain Electrical Activity Marker: A Multisite Prospective Validation Trial of Clinical Efficacy

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Introduction: Traumatic Brain Injury (TBI) represents a rapidly growing proportion of Emergency Department (ED) visits, rising 29.1% while overall visits rose only 3.6% between 2006-2010, and are continuing to increase. TBI treatment is time-sensitive and early identification has been demonstrated to be associated with reduced morbidity and improved outcomes. A brain electrical activity biomarker for identifying Traumatic Brain Injury (TBI) in ED patients presenting with mild/moderate symptoms after sustaining a closed head injury has shown promise for rapid, objective, triage at the point of care. The object of this study was to prospectively validate the efficacy of an independent automated classification algorithm to predict the likelihood of being CT positive (CT+) in high functioning TBI patients (GCS 13-15).

Method: This multisite, observational validation study was conducted at 11 US Emergency Departments. Male and female patients who presented to the ED within 72 hours of closed head injury, between the ages of 18-85 years, with a GCS of 12-15 at the time of the evaluation, were candidates for study. All patients enrolled received standard clinical evaluations and acquisition of 5-10 minutes of EEG data from frontal and frontotemporal locations. Using an independently derived quantitative classification algorithm, the likelihood of each subject being CT+ was determined, and performance metrics were computed relative to blinded unanimous adjudicated CT findings. The classification algorithm used was derived from the EEG and clinical features of a large population (n=>2400) of TBI patients and controls using advance signal processing methods and machine learning, and was completely independent of the validation population.

Results: 720 TBI subjects were enrolled, 156 of which were CT+. Glasgow Coma Scale was 15 in 97%, with a mean of 14.9. Sensitivity of the binary classifier was 92.31% (87.84%, 95.50%) for detection of any brain injury visible on CT (CT+), with specificity of 51.60% (48.05%, 55.13%) and negative predictive value of 96.04% (93.18%, 97.94%). Taking into consideration those subjects close to the binary threshold using ternary classification, (CT+, Equivocal, CT-), sensitivity was 97.44% (93.57%, 99.30%), specificity of 38.65% (34.61%, 42.81%) and negative predictive value of 98.2% (95.45%, 99.51%) when Equivocal is considered positive. Sensitivity to traumatic hematomas (≥ 1 cc of blood) was 93.15 (84.74%, 97.74%) for binary and 98.64% (92.60%, 99.97%) with ternary classification.

Conclusion: Using an EEG based biomarker in head injured patients, high accuracy in prediction of the likelihood of being CT+ was obtained, with high NPV and sensitivity to any bleeding and to hematomas. Specificity was significantly higher than standard CT decision rules. The use of an EEG based classifier algorithm as an adjunct to clinical evaluation of TBI at the point of care has great potential to impact acute clinical management of head injured patients.

Socio-Demographic Analysis of the Prevalence of Traumatic Brain Injury at The Framingham Study

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Objective: While the effects of traumatic brain injury (TBI) on neurocognitive health are well documented, there is a paucity of community-based studies that have documented TBI prevalence and the relationship between TBI and major socio-demographic variables.

Participants and Methods: A retrospective review of 3,968 Generation 3 participants at the Framingham Heart Study for history of head injury was conducted. 695 (17.52%) participants self-reported head injury and were classified as TBI as defined by the American College of Rehabilitation Medicine diagnostic criteria. Of the 695 participants, 65.69% of cases had a single TBI, and 34.31% cases had 2 or more TBIs. For analysis, annual family income was categorized as low income (<\$50,000), medium income (\$50,000 to \$100,000) and high income (\$100,000). Occupation was categorized as unemployed, non-office workers and office workers. Education level was categorized as high school diploma or lower, some college education to a full degree, and those with graduate education.

Results: We found that men have a higher probability of suffering TBI than women ($p < 0.0001$). We also found that individuals with low family income (26.1% of participants) had a higher chance of reporting one or more TBIs ($p = 0.0157$). When stratified by sex, annual family income remained significantly different between the two groups for men ($p = 0.0057$) but not for women ($p = 0.0837$). There were no significant differences regarding occupation and education level.

Conclusion: Men, particularly those with a low family income, are the most likely to have one or more TBIs in their lifetime. More research must be done to determine what are the underlying factors that account for these socio-demographic differences.

Evaluation of Concussion in Athletes Using an Electrophysiological Brain Function Index

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Introduction: An estimated 300,000 sport-related traumatic brain injuries, predominantly concussions, occur in the US annually, with prevalence increasing. The likelihood of a contact sport athlete experiencing a concussion is estimated to be >19% per season. There is no “gold standard” for diagnosis of a concussion, which is currently a clinical diagnosis based largely on subjective symptom report. The need for a quantitative indicator of concussive injury is of utmost importance to reduce immediate and long term risks of this growing epidemic. Concussive injury causes changes in brain electrical activity which can be quantified and expressed as a metric relative to normal brain function, a Brain Function Index (BFI). This study evaluated the efficacy of the BFI for assessment of injury and recovery in sports related concussion.

Method: Male contact sport athletes were prospectively recruited for study from multiple locations over six seasons of play. Three hundred and fifty four (354) athletes between the ages of 14-23 years (mean 18.3, sd +/-2.1) were enrolled in the study (110 concussed athletes and 244 age matched controls). Concussion was declared by sideline criteria, following AAN guidelines. 5-10 minutes of eyes closed resting EEG was acquired on a hand-held device, from frontal and frontotemporal locations.

The artifact-free EEG data were subjected to quantitative off-line analyses to derive an extensive set of univariate and multivariate features (both linear and nonlinear) using advanced signal processing methods and age regression (z-scores). The EEG BFI was computed as a weighted linear combination of QEEG feature z-scores selected based on their association with concussive injury in the scientific literature such as those features that reflect changes in brain region connectivity, EEG signal complexity and shifts in the frequency spectra. Group comparisons were performed to test the significance of the difference in the BFI score at several time points including: preseason baseline, time of injury and 45 days following injury.

Results: There was no significant difference in BFI between concussed athletes at baseline (i.e., prior to a concussive injury) and controls at baseline ($p = 0.4634$). Concussed athletes, tested within 72 hours of injury, exhibited significant differences from controls ($p = 0.0036$). These significant differences between concussed athletes and controls were no longer observed at 45 days following injury ($p = 0.19$).

Conclusion: Controls and concussed athletes showed no differences in an EEG based metric of brain function pre-season, showed highly significant differences at time of injury, and showed no differences 45 days following injury. This data suggests that the BFI may provide a rapid quantitative assessment of the athlete’s brain function state at the time of concussive injury and can be used to assess normalization of brain function over the trajectory of recovery.

Unconventional Dosing of Amantadine in a Patient with Traumatic Brain Injury: A Case Report

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A 23-year-old female sustained severe traumatic brain injury (TBI) as an unrestrained driver in a high-speed motor vehicle collision (Glasgow Coma Scale = 3). The patient was admitted to the Disorders of Consciousness Program in an acute rehabilitation hospital in a suspected minimally conscious state (MCS), approximately 2 months post-injury. On physical exam, she was alert, awake, non-verbal, with spontaneous visual tracking in the left visual field. There was no evidence of spontaneous communication or reproducible command following. She was started on amantadine 100mg twice daily to promote functional neurobehavioral recovery. The patient emerged from a MCS and began to functionally communicate, however responsiveness was variable, with reduced verbal output at times. Her Orientation Log (O-Log) score was 8 out of 30. On two occasions, her amantadine was held due to loss of GI access. Both times, after stopping amantadine, she demonstrated paradoxical improvement, demonstrated by her mental status examination scores, verbalizations, and behavior (expectorating saliva). However, on both occasions, after a few days off amantadine, her mental status worsened again. Given this pattern, she was transitioned to an alternate-day dosing amantadine regimen, and ultimately discharged on amantadine 100 mg every other day.

Amantadine Use and Imaging Predictors of Response in Patients with Traumatic Brain Injury

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Background: Traumatic brain injury (TBI) is a major cause of disability worldwide, particularly to young adults. The subsequent development of post-concussion syndrome can result in a wide range of symptoms including headaches, cognitive dysfunction, and irritability. Amantadine, an N-methyl-D-aspartate antagonist and indirect dopamine agonist, may have a beneficial effect on patients with traumatic brain injury. In small studies, amantadine has been used to treat headaches and certain aspects of frontal lobe disorders presumably by taking advantage of the inhibition on the glutamate receptor.

Methods: To evaluate the response of TBI symptoms to amantadine, we performed a retrospective medical record review of patients evaluated following traumatic brain injury in the Neurology outpatient clinics. Data were collected on the effect of amantadine on various symptoms, with particular attention to any change in headaches. Furthermore, these effects were placed in the context of any imaging findings. Approximately 40 patients (60% male), average age 35 (range 11-78), were prescribed amantadine following traumatic brain injury. On initial evaluation, all of our patients reported post-concussive symptoms, most commonly headache (90%). Amantadine was prescribed years following the initial event in 50% of patients. Dosing and duration of use was variable with only 30% of patients using Amantadine 100mg twice per day for at least two months.

Results: More than 70% of patients that completed a full trial reported improvement in symptoms. We observed that the patients that reported an improvement (17 of 38 patients) were more likely to have been prescribed amantadine within twelve months of the trauma. Headaches were most improved, whereas other symptoms, including irritability, inattention, subjective dizziness, and poor memory, did not improve as readily. Approximately 25% of patients experienced side effects and stopped the medication early. There were no imaging predictors of response to amantadine.

Conclusions: Our experience suggests that amantadine may be a reasonable medication to prescribe for post-concussion syndrome to enhance the recovery time, particularly if started within twelve months of the initial trauma.

Electrophysiological Changes in Retired Australian Rugby Players with A History of Repeated Sports Concussion. A Study Using Transcranial Magnetic Stimulation

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There is a growing public interest in Australia in understanding the link between brain injuries (concussions) sustained in sporting activities and the development of subsequent health issues later in life. Following the publication of our first study showing electrophysiology of the brain in Australian Rules football players (Pearce et al 2014), the aim of this study was to investigate electrophysiology (corticomotor excitability and inhibition), cognitive functioning, and fine motor dexterity in retired Australian professional rugby players with a history of repeated concussions during their playing careers. Seventeen male rugby players (mean 48.3 ± 7.6 years) who had played in the National Rugby League (NRL), and had reported an average of $6.4 (\pm 5.2)$ concussions with their last concussion reported 18.3 years previously, were compared to 25 healthy age-matched male controls (49.3 ± 7.3 years) with no history of concussions. All participants completed assessments of fine dexterity, visuomotor reaction time, spatial working memory (SWM), intra-extra dimensional shift (IED) and paired associative learning (PAL). Transcranial magnetic stimulation (TMS) was used to measure corticomotor conduction time (latency), corticomotor excitability (via motor evoked potential [MEP] at 125% of active motor threshold [aMT]); and intracortical inhibition (cortical silent period [cSP], short-interval intracortical inhibition [SICI], and long-interval intracortical inhibition [LICI]). Control participants performed better than retired players in motor tasks (fine dexterity $t=2.99$, $p=0.004$; reaction time $t=5.06$, $p<0.001$; movement time $t=2.51$, $p=0.01$) and cognitive tests (PAL $t=6.33$, $p<0.001$; SWM $t=3.84$, $p=0.003$; IED $t=9.52$, $p<0.001$). TMS data revealed lower MEP amplitude in the retired players ($t=2.96$, $p=0.004$) as well as differences in intracortical inhibition (cSP $t=3.99$, $p<0.001$; LICI $t=4.50$, $p<0.001$). No differences were observed in corticomotor conduction time, stimulus threshold (aMT), or SICI. No associations were found with regards to the number of concussions and TMS alterations in the retired players group. Regression analyses, however, revealed a significant contribution to differences in motor and cognitive outcomes with the measures of corticomotor excitability and intracortical inhibition. This is the first study to demonstrate differences in motor control and electrophysiology in retired rugby players who had sustained concussions during their playing career nearly two decades previously.

Please Don't Sweep Us Under the Rug...We Care and We Can Help: A Spousal Caregiver's Concurrent Journey to Her Husband's Recovery from a "Mild" Traumatic Brain Injury Sustained in a Cycling Accident

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"This is a message for Mrs. Fast - this is the General Hospital Emergency Room calling. Your husband has been in a car, oh, I mean bike accident, please call us." Her husband had been injured would this injury affect Mrs. Fast? The definitive answer was and is "Yes".

There is much research surrounding the impact an injury has on the injured person and to a degree how it affects the people around them. Often caregivers are forced to attend to their injured family member with little time for themselves. Their feelings and observations are minimized and "swept under the rug".

This presentation focuses on the presenter's concurrent journey to her husband's recovery. A journey that has taken many a turn to a recent acknowledgment of the stress and hurt that occurred from a cycling accident almost 20 years ago.

Upon completion of this session, participants will be able to:

1. Recognize the importance of keeping the caregiver in the line of communication
2. Identify / Determine emotions that a caregiver may experience
3. Identify ways that the caregiver can assure s/he (caregiver) is being cared for / supported in his/her journey

By sharing her story, the presenter wants:

To emphasize to the professional the importance of being passionate in one's field. It is important to create an atmosphere of connecting with the uninjured spouse helping them on their journey so s/he can be the best "lifesaver" for their loved one.

To show the need for anecdotal evidence based research to give hope and to empower spousal caregivers to "hold their heads high during a tumultuous time which in turn will open the door to much-needed healing and retrospection.

In conclusion, this presentation may be new and enlightening as you return to your practice and / or "hit hard" as you grapple with your own feelings and emotions. Whoever you may be, know Rosalyn is in the thick of it. She is continuing to acknowledge her feelings and emotions 20 years after her husband's accident.

The Contribution of Resilience and Personality to The Psychological Adjustment of Family Members Caring for Relatives with Severe Traumatic Brain Injury

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Background: There is ongoing debate about whether resilience is a modifiable versus an inherent personality-based trait. Previous evidence suggests that there exists a connection between resilience and personality traits however more recent evidence suggests that resilience is a learned skill. Different theoretical models of personality traits exist, such as the three dimensional model which defines personality in terms of extraversion, neuroticism and psychoticism.

Aim: This study aimed to determine whether resilience makes an independent contribution to the psychological adjustment of family members caring for relatives with severe traumatic brain injury (TBI) beyond that which is accounted for by different personality dimensions.

Methods: Family members were recruited from six inpatient and community brain injury centres across New South Wales and Queensland, Australia. Family members (n=131) completed the Connor-Davidson Resilience Scale, the Eysenck Personality Questionnaire (revised) and 5 measures of psychological adjustment. Demographic and injury related data were collected on the family member and relative with TBI. Descriptive statistics, correlations and sequential regression analyses were conducted in SPSS.

Results: Family members were predominantly female (106/131, 81%) and parents or spouses (117/131, 89%) of the relative with TBI. On average, the relatives had severe TBIs, as measured by length of posttraumatic amnesia (days, mean 71.7±64.3, range 1-183). Five regression models were conducted with two personality dimensions (neuroticism and extraversion) entered in the first block followed by resilience scores in the second block. The 5 outcomes tested in the models were general health, caregiver burden, mental wellbeing, positive affect and negative affect. Psychoticism did not significantly correlate with any of the measures and was not included in the analyses. All models were significant predictors of scores on the five psychological adjustment measures (p=.000) and accounted for a range of 25.5 to 39.8% of the outcome variances. In the model testing positive affect (R² = .353, F (3,127) = 24.691, p =.000), resilience ($\beta=0.314$) was a significant contributor after accounting for the variance explained by neuroticism ($\beta = -.331$) and extraversion ($\beta=.195$). Resilience did not significant contribute to any of the remaining outcome measures. The modelling showed that higher levels of neuroticism were most strongly associated with having higher levels of psychological distress, negative affect, caregiver burden, and with poorer levels of mental health.

Conclusion: For family members caring for relatives with severe TBI, resilience levels and individual personality dimensions vary in the degree of their influence on different aspects of psychological adjustment. In particular, we found that resilience made an independent contribution to family members' positive affect, while the personality dimension neuroticism contributed strongly to negative psychological adjustment. This study is one of the first to investigate the contribution of personality to the psychological adjustment of family members caring for relatives with severe TBI.

Effect of Age on the Functional Outcomes in Southeast Asian Patients with Traumatic Brain Injury

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Introduction and Objectives: Age has been recognised as a predictor for poor prognosis in patients with traumatic brain injury (TBI) in some studies. The purpose of this study was to determine if age is a predictor of functional outcomes in patients with TBI.

Materials and Methods: A retrospective analysis of all 55 patients with TBI admitted to a single rehabilitation unit over a 1 year period was performed. Baseline characteristics such as age, gender, co-morbidities, polytrauma, mechanism of injury, length of post traumatic amnesia (PTA), admission Glasgow Coma Scale (GCS), rehabilitation length of stay and discharge destination were analysed. Long term outcomes were determined using the discharge Glasgow Outcome Scale (GOS) and Functional Independence Measure (FIM).

Results: There were 55 patients in our study population (age range 18-96 years). Within this population, 27 (49.1%) were geriatric patients (defined as ≥ 65 years). Falls was the predominant mechanism TBI in 20 of these patients (74.1%).

Geriatric patients had a lower mean (\pm SD) FIM score (72.5 ± 30.3 vs 89.8 ± 27.4 , $p=0.015$) and a lower mean (\pm SD) FIM gain (21.0 ± 19.4 vs 30.4 ± 24.4 , $p=0.059$) upon discharge compared to younger patients. Although a greater proportion of geriatric patients had a lower GOS score on discharge compared to the younger age group (77.8% vs 57.1%), this was not statistically significant ($p=0.062$). Geriatric patients had a lower mean (\pm SD) FIM efficiency (0.87 ± 1.07 vs 1.41 ± 2.80 , $p=0.17$) compared to younger patients, but this was not statistically significant.

There was no significant difference in rehabilitation length of stay in the geriatric population compared to the younger population (42.9 days vs 30.1 days, $p=0.083$). A majority of the geriatric patients (74.1%) were discharged home, comparable to that of the younger population (85.7%).

Conclusions: Geriatric patients with TBI had poorer functional outcomes compared to the younger patient population in terms of lower mean FIM score and FIM gain upon discharge. However, the rehabilitation length of stay and discharge destination to home were similar between geriatric and younger patient populations.

Neuro Plastic Cities: Looking Beyond Hospitals & Medical Schools for Neuro Therapy

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The presentation has two parts:

Part 1: The Brain Injury Recovery Team Model -- An Interdisciplinary Approach to Neurotrauma Rehabilitation

Part 2: Neuro Plastic Cities -- Looking Beyond Hospitals & Medical Schools for Neuro Therapy

Part 1: When TBI patients report feeling “awful” and “terrible,” an attending physician too often relies on the most extreme measures of pharmaceutical medications first before exploring root causes. Connecting patients to the right medical and therapy professionals can be blinkered and random, or it might not happen at all.

Seen as a whole person, a TBI patient’s condition and course of treatment must account for the interdisciplinary nature of a brain injury. Therapeutic interventions have as much to do with recovery as medical ones.

The Brain Injury Recovery Team Model provides a roadmap for recovery, systematizing options that attending physicians often leave unexplored. The model ensures efficiency and efficacy in building a recovery team specific to the patient.

Attending physicians can use the model to make key referral decisions deliberately. Medical and therapy professionals can use this model to work with patients and their caregivers to prevent undiagnosed and misdiagnosed brain injuries, particularly mild TBIs when the patient might “look great!”

The Model comprises specific medical and therapy specialists. Participants will be able to describe the role of these medical specialists: Endocrinologist, Neuropsychiatrist, Neuropsychologist, Neuro Optometrist, Psychopharmacologist, and Vestibular and Sleep Study Specialists. They will also learn the role of these therapy specialists: Occupational & Physical Therapist, Social Worker, Speech-Language Pathologist, and Vocation Rehabilitation Counselors.

Survivors can and should look to these specialists for: Emotional Support, Informed Guidance, and Tactical Support.

Part 2: After 2 1/2 or 3 years, rehabilitation hospitals often begin denying survivors access to their recovery team, leaving them on their own to figure out how to live the rest of their lives overcoming their cognitive deficiencies. There is a reason why we are losing 22 veterans a day to suicide: They might “look great” but they have no strategies for living inside their brain injuries.

The key point to this part of the presentation -- Neuro Plastic Cities -- is that just as a brain injury is as specific as a fingerprint, so should the course of treatments be.

Survivors of brain injury owe it to themselves to try as many therapies and treatments as they can afford, and arrive at an intricate combination that works best for them. Therapies that work for some survivors are less effective for others, hence the need for guided experimentation.

In addition to fundamental brain-healthy nutrition and exercise, I overview such treatments as Hyperbaric Oxygen Chambers, Cranial Sacral, Reiki, Acupuncture, Music, Medical Marijuana, Tai Chi, Qi Gong, Reflexology, Yoga, Faith Healing, Cognitive Behavioral Therapy.

Can the Deficits in Working Memory of Paediatric Brain Tumours Survivors Be Explained by Hippocampus Dysfunction?

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Objectives: The survival rate of paediatric brain tumour patients has increased dramatically during the last decades. At the same time, studies show that childhood brain tumour survivors exhibit substantial deficits in their working memory capacity, negatively influencing their endeavours toward academic success. Research has shown that working memory is a complex activity recruiting a numbers of neural networks. The purpose of this study is to investigate the working memory performance in a group of paediatric brain tumour survivors, considering if some effects can be attributed to tumour location, the occurrence of high intracranial pressure at diagnosis, the use of radiation as a treatment modality, and hippocampal integrity.

Method: 40 paediatric brain tumour survivors, earlier evaluated about four years after diagnosis from the perspective of their hippocampus function, were examined with five measures of working memory: simple digit span, complex digit span, and working memory index from the age-relevant Wechsler Intelligence Scale, and simple word span and complex word span from the Rey Auditory Verbal Learning Test.

Results: Childhood brain tumour survivors performed significantly lower than healthy children on the five variables investigated in this study. No effect of tumour location (supratentorial vs. posterior fossa) was found. High intracranial pressure at diagnosis was associated with lower performance on the complex digit span task and the tasks underlying the working memory index, but not simple span tasks and the complex word span task. Children who had undergone radiation therapy performed significantly lower on the complex digit span, the complex word span tasks and the working memory index but not on the simple span tasks, compared to children who did not. No significant linear relationship was found between simple digit span and any of the three measures of hippocampal integrity, whereas a significant correlation was found between complex digit span and one measure of hippocampal integrity, and a significant correlation between simple word span, complex word span and working memory index and two measures of hippocampal integrity. A significant linear relationship was found between performance in the complex digit span and the complex word span and the variable perceptual reasoning but not between performance on the simple digit span or the simple word span.

Conclusions: The results support the hypothesis of the need to distinguish simple span tasks representing short-term memory and complex span tasks representing working memory. Even if both simple and complex span tasks are impaired in childhood brain tumour survivors, the effects of increased intracranial pressure, radiation therapy and decreased hippocampal capacity significantly impact specifically complex span tasks activity meaning that working memory is dependent on hippocampus integrity and is related to fluid intelligence capacity. The implications of these findings for rehabilitation are discussed.

A Novel Bedside Neurological Monitor for Disorder of Consciousness Patients

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Objective: The diagnostic assessment of patients with disorder of consciousness (DOC) was based until recently on bedside clinical evaluation and subject to a high rate of misdiagnosis of the degree of conscious awareness. To our knowledge, there is currently no suitable bedside monitor for brain activity which can be used for assessment, monitoring, and management of DOC patients. Unfortunately, current scanners, like fMRI or PET are not suitable as bedside monitors. Potential smaller monitors such as EEG or fNIRS have not been shown to produce sufficient information that warrants their usage on a continuous basis. Furthermore, full head sensors are cumbersome, and require a technician. We present a novel functional three-electrode brain activity sensor (fBAS) which is based on a functional brain activity separation algorithm. It processes the EEG data (in real-time) and produces a large number of brain activity features (BAF), which are correlated with different functional neural network. It appears to be a promising tool for assessment, treatment and monitoring of DOC patients. The functional separation algorithm is based on Harmonic Analysis decomposition inspired by (Coifman & Wickerhauser, 1992, IEEE Trans. Info Theo.; Neretti & Intrator, 2002, IEEE NNSP).

Methods: 3 patients with minimal consciousness due to TBI (2 patients) and anoxic brain damage (1 patient) were monitored during a period of one month. During this time, recording of at least 5 hours per week were obtained. The recordings were performed during sleep, during alertness state without additional stimulation ("rest"), and during multimodal sensory stimulation (passive movements and auditory, smell, gustatory and visual stimuli). Patients were also asked to perform guided imagery tasks.

Results: Changes in brain activity were observed as different senses were stimulated. It was possible to quantify which senses respond more strongly and to what type of stimuli. For example, it was possible to determine to what taste there was a stronger response, or whether there was a stronger response to auditory or visual stimuli. In some cases, response to stimulus on the right side was radically different than response to stimulus on the left side. In one case there was no response to visual stimuli but strong response to auditory stimuli. Clear response to guided imagery was observed in 2 patients.

Conclusions: A three-electrode EEG sensor with advanced signal processing is able to provide indication of brain activity in response to various stimuli. It can also provide response indication to guided imagery, which indicates preserved higher order cognitive functioning. This may become a promising method for assessment and continuous monitoring of DOC patients

Chronic Bilateral Subdural Hematoma in a Young Male, a Rare Complication of Ventriculo-Peritoneal Shunt -Reporting a Case

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Hydrocephalus is a common clinical problem seen in neurosurgical practise and Ventriculo-Peritoneal shunt is a commonest procedure done for its treatment.

This procedure has various acute and delayed complications like intra-cerebral hematoma, infection, shunt malfunction and intra abdominal complications etc. Here we report a case of bilateral chronic subdural hematoma secondary to postoperative VP shunt done on right side for non traumatic hydrocephalus in a 21 years old male. The shunt was removed and right sided hematoma was evacuated and reinsertion of the shunt was done on the opposite side with no complications. Although rare, this complication must be kept in mind in cases of VP shunt who presents with deteriorating conscious level.

Keywords: VP shunt, Sub acute subdural hematoma.

The Clinical Diagnostic Utility of Electrophysiological Techniques in Assessment of Patients with Disorders of Consciousness Following Acquired Brain Injury –A Systematic Review

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Objectives: Advances in neuroscientific methods have led to optimism regarding potential clinical utility in diagnostic and prognostic considerations in patients with Disorders of Consciousness (DoC) after severe acquired brain injury. This is in part due to several studies indicating that residual cognition can be detected with imaging techniques despite absence of behavioral signs of consciousness. We present a systematic literature review focusing the diagnostic utility of electrophysiological recordings during active cognitive tasks in detecting residual cognitive capacities in patients with DoC.

Methods: Methods of analysis and inclusion criteria followed established recommendations for conducting systematic reviews, including the PRISMA guidelines. Systematic review of empirical research published between January 2012 and March 2016 was performed in Medline, Embase, PsycINFO, and Cochrane. Data extracted included sample size, electrophysiological technique, task design, rate of cognitive responders, rate of persons with definite voluntary behavioral responses, but no clear signs of cognitive effort in electrophysiological assessments (false negatives), rate of patients demonstrating signs of command-following in electrophysiological recordings, despite not doing so behaviorally (false positives), and number of subjects excluded from analysis. The Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) was used for quality appraisal.

Results: Twenty-four studies examining electrophysiological indices of command-following in patients with DoC were identified. Sensitivity rates in healthy controls demonstrated variable accuracy across studies, ranging from 71% to 100%. There was also a wide variety in sensitivity rates in the patient group, ranging from 0% to 100%, indicating on average that as many as one third of patients responding to command behaviorally, were not classified as responders based on their electrophysiological activity (false negatives). Specificity rates also varied markedly, ranging from 0% to 100%, implying that some patients show signs of command-following in electrophysiological recordings, in the absence of behavioral responses (false positives). The two largest studies (N=158 and 167), demonstrated false positive rates of 17% and 33%, in line with numbers obtained in fMRI studies using active tasks. Unfortunately, not all studies reported rates of excluded subjects, while others reported relatively high exclusion numbers due to artifacts, even in healthy subjects.

Conclusion: We are still far from establishing precise recommendations for standardized electrophysiological diagnostic procedures in assessment of patients with DoC, and high levels of artifacts remain an issue of concern. In summary, one needs to cautiously balance the risk of false positive versus false negative diagnostic errors in individual assessments, as it is evident that a patient with discernible signs of behavioral command-following can appear as a false negative electrophysiologically. However, in cases where factors such as severe motor deficits leave diagnostic uncertainty, electrophysiological methods may add valuable supplemental diagnostic information of covert cognition in of patients with DoC.

Combination of Protein Blood Biomarkers to Differentiate Ct-Scan Results in Mild Traumatic Brain Injury

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Objectives: Patients who suffered a mild traumatic brain injury (mTBI) might have a brain lesion. CT-scans are performed to identify these patients; however, the majority will be CT-negative. Blood biomarkers have been investigated for their capacity to reduce the number of CT-negative scans. The most studied protein is S100B with 25% specificity and 95% sensitivity. Different brain injury studies have revealed several other proteins; H-FABP, SAA, VCAM, MMP-1 and GSTP. Here we investigated if these proteins individually or in a panel could perform better than S100B alone to reduce the number of unnecessary CT-scans.

Methods: The blood levels of S100B, H-FABP, SAA, VCAM, MMP-1 and GSTP were measured using commercial immunoassays. A total of 244 mTBI patients were recruited from three different sites (Geneva, Sevilla and Barcelona), within 6h after trauma, with a GCS of 15 and one clinical symptom. The patients were dichotomized into CT-positive (n=40) and CT-negative (n=204) groups for statistical analyses using Mann-Whitney U test, ROC curves and Panelomix.

Results: The blood levels of the proteins H-FABP, S100B and VCAM were significantly increased in CT-positive patients ($p < 0.05$). The best individual performance was obtained by H-FABP (SE: 100% and SP 29%) followed by both S100B and VCAM (SE: 100% and SP 6%). All proteins and age were also evaluated in different combinations. The best performance was obtained using H-FABP, S100B and age reaching over 50% SP and 100% SE.

Conclusions: The best individual performance to reduce the number of CT-scans was obtained by H-FABP. However, a combination of H-FABP, S100B and age over-performed any single parameter. A further prospective multicentric study is warranted.

Executive Function Training in Veterans with PTSD and mild TBI

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Objective: Difficulties in executive control functions, including selection, maintenance, and execution of goal-relevant information and activities are common sequelae of both TBI and PTSD. Goal-Oriented Attentional Self-Regulation (GOALS) training was designed to target these deficits with attention regulation training applied to participant-defined goals. In previous studies both Veteran and civilian participants with chronic TBI significantly improved post GOALS, but not control training, on measures of attention/executive function, functional task performance, and self-report measures of emotional regulation (Novakovic-Agopian et al 2011, Novakovic-Agopian et al 2015), and on goal-directed control over neural processing on fMRI (Chen, et al 2011). The objective of this ongoing study is to assess effectiveness of GOALS training in Veterans with comorbid PTSD and mTBI.

Participants and Methods: 30 Veterans diagnosis of PTSD, history of chronic mTBI and mild–moderate executive dysfunction on daily living tasks, were randomized to start with either 5 week of GOALS or matched control psychoeducation (EDU) training. Assessments at baseline and post training included neuropsychological, functional task performance, and self-report measures.

Results: At week 5, post GOALS, but not EDU training, participants significantly improved from baseline on: 1) overall neuropsychological attention/executive function domain score, and following subdomain scores: sustained attention and inhibition; 2) overall complex functional task performance score, and following subdomains: maintenance of attention, task execution, switching and memory; and 3) on emotional regulation self-report measures including: significant symptom decrease on Profile of Mood States (POMS), Beck Depression Inventory II (BDI-II), and Post-traumatic Checklist Military (PCL-M). Majority of participants reported incorporating some of trained strategies into their daily life.

Conclusions: GOALS training may be promising in Veterans with concurrent PTSD and chronic mTBI. Training self-regulatory cognitive and emotional control strategies applied to actual situations in participant lives and personally relevant goals may provide meaningful improvements in cognitive, emotional, and occupational functioning. The challenges and importance of: a) assessing change in functioning at different levels, and b) using participant-defined goals applied to relevant training, will be discussed.

Sport Concussion Assessment Tool 3: Interpreting Day of Injury Scores in Professional Ice Hockey Players

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Objectives: The Sport Concussion Assessment Tool–3rd Edition (SCAT3) is widely used to evaluate the acute effects of concussion. This study examined which SCAT3 component has the most utility in day of injury concussion recognition, and whether pre-injury individual SCAT3 baseline scores are more useful than normative reference values in the sideline recognition of acute concussion.

Methods: SCAT3 baseline testing has been mandatory in the Finnish Ice Hockey league since 2013. The league recommends day of injury testing for all players with suspected concussion. Of the reported day of injury SCAT3s, between seasons 2013-2016, a total of 29 concussions were confirmed by the teams' medical staff. The measures included in the study were: (i) the individual baselines (n=29), (ii) the day of concussion scores of the injured players (n=29), (iii) the league's normative reference values [based on 2013-2014 preseason baselines (n=304)], and (iv) the limits of normal variation on the SCAT3 [based on league's preseason baselines 2013-2014 and 2014-2015 (n=179)]. The post-injury performance was ruled as abnormal if: (i) the player scored within the worst 10th percentile of the normative reference values, or (ii) the score differed from the player's own baseline more than the cut offs for 90% normal variation.

Results: The mean age of the concussed players (n=29) was 27 years (SD=4, range=19-35). Most of the players (83%) were Finnish, and all were Caucasian. SCAT3-based possible signs of concussion (loss of consciousness, balance or motor incoordination, disorientation or confusion, loss of memory, or blank or vacant look) were observed in 11 (37.9%) out of the 29 concussion cases. The area under the receiver operating characteristic curves for the ability of each SCAT3 component to discriminate between the day of concussion and the normative reference values were as follows: (i) Symptom Score=0.98, (ii) Symptom Severity=0.99, (iii) Standardized Assessment of Concussion (SAC)=0.62, (iv) Modified Balance Error Scoring System (M-BESS) =0.71, and (v) Tandem Gait=0.53. Only two concussed athletes failed the post-concussion Coordination Test. The percentages of the players who performed abnormally on post-concussion testing (individual baseline comparison vs. normative reference values) were as follows: Symptom Score: 96% vs. 100%, Symptom Severity: 96% vs. 100%, SAC: 31% vs. 22%, M-BESS: 50% vs. 50%, Tandem gait: 18% vs. 29%, and Coordination: 7% vs. 7%.

Conclusions: The SCAT3 is sensitive to the effects of acute concussion in professional ice hockey players assessed on the day of injury. The Symptom Scale was the most sensitive component of the test. Post-concussion testing conducted with individual baseline seems to be as sensitive as assessment compared to normative reference values in acute concussion recognition.

Study on the Cognitive Function Post Traumatic Brain Injury in China

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Background: The incidence of traumatic brain injury (TBI) is rising especially in developing countries such like China, as are its neuropsychiatric complications. This study aims to determine the cognitive impairment in later life the patients who were associated with exposure to TBI.

Methods: Cross-sectional study of 43 Chinese patients with above 12 months TBI history. Study participants were assessed for improvement in cognitive function, quality of life and sleep, current depressive symptoms. We defined cognitive impairment by a mini mental state examination score <24 diagnosis of dementia.

Hamilton Depression Scale to assess current clinically significant symptoms of depression, defined. While Scales for Outcomes in Parkinson's disease –sleep scale to assess sleep dysfunction, and Activity of Daily Living Scale was used to observe the participants quality of life.

Results: Forty-four patients had history of treatment for TBI as patients in our hospital (mild, moderate and severe). Cognitive dementia was defined by a mini mental state examination score according to the educational duration, and among the participants 14 patients were diagnosed dementia (31.8%). Non-dementia ones were compared with health controls (10 participants) by the tests of Montreal Cognitive Assessment-Basic (MoCA-B) Chinese Version ($P=0.0143<0.05$), copying time for Rey–Osterrieth complex figure ($P=0.0327<0.05$), copying scores for Rey–Osterrieth complex figure ($P=0.1623>0.05$), Boston scores ($P=0.0183<0.05$), recall for Rey–Osterrieth complex figure ($P=0.0073<0.05$), auditory verbal learning test (AVLT)-4 ($P=0.2077>0.05$), auditory verbal learning test (AVLT)-5 ($P=0.1950>0.05$), auditory verbal learning test (AVLT)-6 ($P=0.0145<0.05$), Tail-A ($P=0.0436<0.05$), Tail-B ($P=0.0302<0.05$), Hamilton Depression Scale (HAMD) ($P=0.0231<0.05$) and HAMD scores of TBI patients were 11.49 ± 8.59 , Scopa-sleep scales ($P=0.5327$, $P=0.1470$, $P=0.5225>0.05$), Activities daily-living scale ($P=0.5932>0.05$)

Conclusions: History of TBI is common in older men, and is associated with increased risk of depression and cognitive impairment. If this association is truly causal, then the effective reduction of events leading to TBI (e.g., motor vehicle accidents and falls) may also decrease the prevalence of depression and cognitive impairment in later life, especially in memory, executive function, and attention. This result may demonstrate that TBI cause cognitive dysfunction in many cognitive domains but not only in special one. Besides, depressive mood and sleep disorders would come together.

Usefulness of Cerebrolysin in Terms of Cognitive Recovery in Moderate to Severe Traumatic Brain Injuries

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Background: Traumatic brain injury is one of the major cause of injury-related death globally. Cerebrolysin, a neuropeptide synthetic preparation produced by enzymatic breakdown of lipid having neurotropic and neuroprotective role, being successfully used in the treatment of Alzheimer's disease, in acute cerebrovascular strokes with proven efficacy. Though it has been used successfully in traumatic brain injuries only limited studies are reported.

Objectives: We evaluated the efficacy and safety and usefulness of cerebrolysin in the treatment of traumatic brain injury in terms of cognitive recovery.

Methods: Present study was conducted at Surgical Unit of Medical College Hospital to evaluate the effect of cerebrolysin on functional and cognitive outcome in patients with moderate and severe TBI .500 patients were divided into two groups. Group I 250 patients received cerebrolysin for 14 to 20 days and Group II 250 patients received only conventional therapy as a control group. Both groups were subjected to GCS and CT Brain on admission and was compared with the degree of improvement on 14, 20 days and subsequently from the day of admission.

Results: Cerebrolysin treated group was compared to the conventional therapy (controlled) group. There was a statistically significant (p value=0.001) seen in improvement of GCS, and in terms of cognitive and functional outcome in patients treated with cerebrolysin therapy as compared with the conventional therapy control group.

Conclusions: Patients with cerebrolysin treatment showed a significant improvement and outcome in GCS as compared with conventional therapy. Our results suggest that patients with traumatic brain injuries when treated with cerebrolysin are benefitted in terms of functional and cognitive outcome.

Keywords: Cerebrolysin, Traumatic brain Injury, TBI

Dichotic Listening in Clinical Research of Local Brain Damage

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Background: Dichotic listening is one of the best noninvasive methods used for defining the hemispheric asymmetry during speech processing. Moreover, the method allows to evaluate cognitive dysfunction after different types of brain damage. There are a lot of audio-verbal dichotic listening tests that differ in stimuli (words, digits, syllables, etc.), presentation peculiarities (quantity and structure) and side factors that influence test results (order of stimuli presentation, working memory, individual's strategy, attentional biases). We expect that various dichotic listening tests are characterized by different levels of sensitivity and accuracy for estimation of brain injury localization and lateralization.

Aim: To compare the results of consonant-vowel syllable test (CV test) and word test performance by patients with local brain damage.

Method: 40 subjects participated in pilot study (20 normal controls, 20 patients with brain damage, age range 19-62 years). All the participants were right-handed. Out of 9 left-brain injured patients 8 had brain tumor (including meningioma and cavernoma), 1 patient suffered a stroke. Out of 11 right-brain injured patients 9 had brain tumors, 1 patient had arachnoid cyst and 1 patient suffered a stroke.

The CV test and the word dichotic listening test were presented to the participants.

Results: According to the results of CV dichotic listening test the right-brain injured patients showed statistically significant increase in the right ear-accuracy scores and decrease in the left ear-accuracy scores as well as the increase in laterality index at the level of statistical tendency in comparison with normal controls. Statistical difference wasn't observed in both normal controls and left-brain injured group. However, the qualitative analysis of the results showed the accuracy decrease in the ear contralateral to cerebral lesion and the accuracy increase in the ear ipsilateral to brain damage in the left-brain injured patients.

The same results were received during the word test, but the difference between both normal controls and the patients with brain injury was statistically insignificant.

Moreover, the results of the CV test showed the difference at the level of statistical tendency between both right-brain injured patients and left-brain injured patients in the right - and left – ear accuracy scores as well as in laterality index. However, the same statistical difference wasn't observed during the word test.

Conclusions: The consonant-vowel syllable test is more sensitive for "lesion" effect evaluation in comparison with the word dichotic listening. The CV test allows to define the difference not only between normal controls and patients, but also between patients with different brain damage. Apparently, word dichotic listening can show "lesion" effect at statistically significant level in case of increasing the number of patients with brain injury.

Evaluating the Use of Cognitive, Behavioural and Emotional Strategies after an Acquired Brain Injury: Development and Validation of The Strategy Use Measure (SUM)

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Background: After severe acquired brain injury (ABI), individuals experience changes to their cognition, behaviour and emotions. Strategies are key psychological and/or environmental tools employed to compensate for and minimise the impact of these changes.

Aim: The aim of this study was to develop and validate a measure which assesses strategy use after ABI across these three domains.

Methods: Item content of the SUM was developed using four methodological components including consultation with an expert committee, consumer focus groups, a file review and a consensus meeting. A total of 86 participants with an ABI completed an initial pool of 17 items and a demographic questionnaire. A smaller subset (n = 38) completed validation measures to test convergent and divergent validity (Memory Compensation Questionnaire, Memory Functioning Questionnaire, General Self Efficacy Scale, Patient Competency Rating Scale) and another subset (n=29) repeated the measure for test-retest reliability on average 8.8 days later.

Results: Exploratory Factor Analysis (Principal Axis Factoring with Varimax rotation) indicated a four factor structure accounting for 58% of the variance. The fourth factor had only two items and was excluded, as was one other item that did not meet the 0.4 threshold. The eventual three factor solution comprised 14 items, which were scored on a five-point Likert scale (range 0-4). The three sub-scales were Memory and Planning (MP, 5 items), Emotion/ Mood (EM, 5 items) and Cognitive Load (CL, 4 items). Good reliability was found for each subscale (Cronbach's alpha .82-.83).

Good convergent validity was observed between memory subscales and the MP and CL subscales (Pearson's correlation coefficients ranging from .50 to .85) and the measure also demonstrated sound test-retest reliability (ICCs=.77-.82).

Conclusion: The SUM has potential to be an invaluable tool in planning and evaluating treatment post ABI. Initial validation of the SUM is promising for the cognitive subscales with further validation recommended for the EM subscale with measures of distress.

The Effect of Pentadecapeptide BPC 157 on Cerebral Ischemic/Reperfusion Injuries in Rats

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Ischemic/reperfusion injuries are elementary pathophysiological findings in stroke, making it the third most common cause of death and the first cause of long-term disability. Pentadecapeptide BPC 157 has already been proven to counteract brain trauma; it has a beneficial effect on vessel integrity and protection; it interacts with the NO system and has healing properties in different tissues. Altogether making it a promising agent when it comes to cerebral ischemic/reperfusion injuries.

In this experiment, ischemic/reperfusion injuries are induced using bilateral carotid artery occlusion (BCAO). The effect of BPC 157 on ischemic/reperfusion injuries was investigated in male Wistar rats. After an occlusion of 20 min, the rats were randomly divided into groups. The treated group received BPC 157 (10µg/kg, I.P.) right after surgery, while the control group received saline (5ml/kg, I.P.) immediately after surgery. To test the relation with the nitric oxide (NO) system, we created three new groups: L-NAME (5 mg/kg, I.P.) alone, in combination with L- arginine (100mg/kg, I.P.) or BPC 157 (10µg/kg, I.P.) respectively. After a reperfusion period of 24 hours, the neurological assessment was performed and samples were taken. Neurological assessment was conducted using the Morrison water maze test (MWMT) and beam walk test (BWT). In the MWMT the control animals had far greater memory loss and spatial orientation loss, while the BPC 157 treated group had almost no loss in the MWMT. In the beam walk test, we also observed substantial differences between the control and treated group, where the control group walked far worse than the BPC 157 treated group. The animals treated with L-NAME scored worst, of all groups, in the MWMT as well as in the BWT. When L-NAME was administered along with L-arginine, it showed slight improvement, while the combination of L- NAME and BPC 157 abolished all the negative effects of L-NAME. The pathology findings concurred with the results obtained in the neurological assessment, showing a significant difference in neuronal death in favor of the BPC 157 treated group. On top of this we conducted a Real Time qPCR study, where we evaluated the differences in RNA expression between the two groups, with 20 genes involved in various aspects of angiogenesis and injury healing.

Pentadecapeptide BPC 157 showed that it counteracts ischemic/reperfusion injuries, saving the rats from memory and orientation loss, as well as maintaining their motor capabilities. Along with that it can successfully counteract the negative effects of NO system inhibition, even more so than L-arginine, and thereby confirming its close relation to the NO system. The results we present here are promising and prove that BPC 157 has potential as a neuroprotective agent in cerebral injuries, although further investigations should be conducted to confirm the full effects.

Towards A Characterization of Social Cognitive Profiles After Acquired Brain Injury: Evidence for Distinct Emotion Processing Subgroups

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Background and Aims: Deficits in social cognition are now well documented in a subset of individuals with acquired brain injury (ABI). Social cognitive skills, which include the ability to accurately recognise, understand and respond to emotional states, have been proposed to relate to important outcomes including social and community functioning. However, there is significant heterogeneity in the nature and severity of these deficits, and a typology of social cognitive profiles after ABI is yet to be well characterised. The aim of this study was to identify whether distinct profiles exist in the ability to perceive, understand and regulate emotions among individuals with ABI, and to evaluate clinical, cognitive and functional correlates of these subgroups.

Method: 81 adult participants with moderate to severe ABI were recruited from two specialist brain injury rehabilitation centres in Melbourne. Average time since ABI was 17 months (range: 2 months – 7 years), and all participants were living in the community at the time of assessment. Participants completed the Mayer-Salovey-Caruso Emotional Intelligence Test V2.0, Community Integration Questionnaire, Hospital Anxiety and Depression Scale, and cognitive tests consisting of Wechsler Adult Intelligence Scale subtests (Coding and Digit Span), the Wechsler Abbreviated Scale of Intelligence and the Controlled Oral Word Association Test. Socio-demographic information was collected via participant interview. Injury-related and clinical variables were collated from medical records, including clinician documentation of social or emotional deficits during inpatient rehabilitation.

Results: A hierarchical cluster analysis was conducted using Ward's method with squared Euclidean distances. Three subgroups emerged, characterised by distinct emotion processing profiles: (1) intact emotional skills; (2) global impairment in emotional skills; (3) focal deficit in strategic emotional skills (understanding and regulating emotions) with preserved emotion perception. The group with intact emotional skills tended to experience better outcomes, including high community integration. Despite poorer overall cognitive function in the global impairment group, social integration was lowest for those in the subgroup characterised by focal deficits in strategic emotional skills. Individuals in the strategic skills deficit group were also most likely to have exhibited social communication difficulties as documented by rehabilitation clinicians during their inpatient admission.

Conclusions: We found evidence for distinct social cognitive subtypes in ABI, characterised by different profiles of strengths and weaknesses in emotion processing skills. These subgroups were associated with specific clinical and cognitive features, and appear to be important for understanding differences in social and community functioning after ABI. Given preliminary evidence of the effectiveness of training programs for remediation of social cognitive skills, understanding how profiles of emotional skills deficits relate to functional outcomes after ABI may be particularly useful for targeting future intervention efforts.

The Influence of Cultural Factors on Outcome Following Traumatic Brain Injury

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Background and Aims: Most traumatic brain injury (TBI) outcome studies focus on white, English speaking patients who identify with the dominant health care system. Little is known of the experience of TBI individuals from Culturally and Linguistically Diverse (CALD) backgrounds. The present study compared outcomes following TBI in individuals from English-Speaking Backgrounds (ESB) with those from CALD backgrounds.

Method: 104 ESB and 99 CALD participants with TBI were assessed an average 22.3 months post-injury on the Brief Acculturation Scale, Craig Handicap Assessment and Reporting Technique (CHART), Activities of Daily Living scale, Coping Scale for Adults, and Hospital Anxiety and Depression Scale.

Results: Results showed no significant group differences in most demographic and injury-related variables, although CALD participants showed lower pre-injury employment. There was no significant difference between groups in therapy costs. At post-injury follow-up, CALD participants were significantly less independent than the ESB group in light domestic duties, shopping and financial management, and reported lower cognitive independence, mobility and participation in occupational and social activities on the CHART after controlling for pre-injury employment. CALD participants reported heightened awareness of post-injury deficits relative to ESB participants, and held different beliefs regarding injury consequences and factors that would aid their recovery. The CALD group also reported greater anxiety symptoms and less problem-focused coping than the ESB group. There was, however, significant variability in responses to injury across different geocultural regions. Hierarchical regression analyses showed that higher CHART total scores were associated with having a value system that is Australian, being younger in age, having more education, and spending less time as an inpatient.

Conclusions: Poorer outcomes in CALD individuals with TBI are not simply reflective of socio-demographic factors. TBI clinicians need to consider their differing beliefs about injury and recovery in order to maximize outcomes in CALD individuals.

Post-Traumatic Amnesia – How Can It Best Be Measured and Used to Predict Outcome?

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Following emergence from coma, patients with traumatic brain injury (TBI) commonly experience a phase of post-traumatic amnesia, or PTA. PTA is state of generalised cognitive disturbance, otherwise termed a delirium, characterized by confusion, disorientation, retrograde amnesia, inability to store new memories and sometimes agitation, delusions and sleep disturbance. Anterograde amnesia, or the inability to form new memories, is a hallmark feature of PTA, with recognition memory improving before free recall. The relative preservation of procedural or implicit memory, as opposed to declarative memory, has been demonstrated in individuals in PTA. In many patients there is a graduated process of resolution of orientation: to person, place, then time. However, the evidence for order of memory recovery has been inconsistent.

In a cohort of 66 patients with severe TBI monitored prospectively using the Westmead PTA Scale we have demonstrated that recovery of memories is related to their depth of consolidation, with memories such as date of birth returning first and memory for recently acquired information last.

Limited research has been conducted comparing methods for determining the duration of post-traumatic amnesia (PTA). Prospective measures include the Galveston Orientation and Amnesia Test, Westmead PTA Scale, O-Log and Confusion Assessment Protocol, but retrospective questioning is commonly used. In a cross-sectional study involving 59 individuals with severe TBI we compared prospective measurement of PTA using the Westmead PTA Scale with a retrospective interview conducted 6 months -6 years post-injury. Mean Retrospective-PTA (R-PTA) was significantly longer than mean Prospective-PTA(P-PTA) and estimates did not generally correspond. The difference between P-PTA and R-PTA was not associated with age, GCS, overall PTA duration or time post-injury of the retrospective interview. This finding calls into question the reliability of retrospective PTA estimates.

Recent Studies have shown that PTA has enhanced predictive ability over Glasgow Coma Scale scores when estimating psychosocial, cognitive and functional outcome. However there remains a lack of consistency in methods of classifying injury severity using PTA. We conducted a cohort study of 1041 individuals with TBI treated at a rehabilitation centre, emerging from PTA prior to discharge, and engaged in productive activities prior to injury. Eight models that classify duration of PTA were evaluated using area under the receiver operating characteristic curve (AUC) and model-based Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) statistics. All categorisation models showed longer PTA to be associated with poorer productivity one year post-TBI. Classification systems with a greater number of categories performed better than two-category systems. The dimensional (continuous) form of PTA resulted in the greatest AUC, and lowest AIC as well as BIC, of the classification systems examined. This finding indicates that the greatest accuracy in prognosis is likely to be achieved using PTA as a continuous variable.

Professional Education in Holistic Neuropsychological Rehabilitation after Brain Injury: Development of an Effective Model

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Introduction: Holistic rehabilitation that relies on biopsychosocial model requires special qualification of professionals. In Russia, only minority of the professional community is familiar with holistic approach. We are organizing an educatory program aimed to develop specialists in holistic neuropsychological rehabilitation.

Objectives and Aim: To review the specifics of interdisciplinary neuropsychological care in an educational setting.

Methods: The program is targeted to psychologists with at least bachelor degree. It includes lecture courses in neuropsychology and psychotherapy along with intensive practice. Each psychologist in training (PIT) is engaged in long-term (>3 month) rehabilitation of at least 2 patients with brain injury, while each patient has a PIT-case coordinator and 1-2 PIT working on specific tasks. The rehabilitation is free of charge for the patients. First, they are interviewed by the clinic coordinator (neurologist) to evaluate potential and possible directions for rehabilitation. Then, a PIT perform a neuropsychological assessment. The results of the assessment undergo supervision by an expert neuropsychologist on a weekly 3-hour group meeting. If necessary, additional neuropsychological tests, interview of family members and "in the field" observations are performed after the supervision. After the completion of the assessments, rehabilitations goals according to SMART criteria are proposed on the weekly meetings and then are discussed and confirmed with the patient by PIT-case coordinator. The rehabilitation program is developed individually in accordance with the goals. It usually includes educational sessions, neuropsychological sessions aimed towards development of appropriate compensatory strategies, psychotherapeutic sessions with patient and family members and, most of the time, specific work on the goals. The results and further rehabilitation directions are discussed on weekly meetings and all the time in a group whats-up chat. A cloud documentation is used, including assessment results, interdisciplinary goals and individual tasks, sessions reports.

Results: Eight students and 11 patients are included into a pilot program. After 3 month of ongoing program, significant results are observed. Patients included at the beginning of the program have reached first goals. One of them, a 27 y.o. male with right-side TBI, cognitive impairment, behavioral difficulties and lack of social support (he is an orphan) got paid employment after he was struggling with this goal on his own for 6 month.

Conclusions: Specially developed educational programs may be effective for professional development in holistic neuropsychological rehabilitation.

Decreased Symptoms and Increased Function in Post Concussion Syndrome Patients after Coordinated Eye-Head Movement Therapy

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Context: Sports concussions have been associated with decreases in the performance of balance, simple and choice reaction times, static and dynamic visual acuity and processing speed.

Objective: To determine if Eye-Head movement training (EHMT) might result in changes in quantitative testing of compromised psychomotor speed, reaction time, visual attention, balance and executive function as well as a decrease in symptoms in patients with post concussion syndrome.

Design: Pre-post treatment intervention.

Setting and participants: 70 subjects with disabling post concussion syndrome treated at a tertiary specialist neurology center for 5 days of therapy.

Interventions: Subjects were tested with the C3 Logix seven diagnostic modules before and after treatment with EHMT. Testing included trails making test (TMT), Computerized Dynamic Posturography, Balance Error Scoring System (BESS), Processing Speed Task (PST), Reaction Time Tests (simple and choice) and a graded symptom checklist following the recommendation of the Zurich Consensus on Concussion. Subjects were instructed in coordinated EHMT using gaze stabilization and vestibular activation by complex head movement with combinations of slow and fast eye movements in phase and counter phase of head movements.

Main outcome measures: Symptom severity scores and C3 Logix diagnostic inventories.

Results: There was strong statistical and substantive significant improvement in all outcome measures for post concussion syndrome patients undergoing EHMT. There were no reported or observed iatrogenic consequences or worsening of symptoms.

Conclusion: The addition of EHMT to a post concussion treatment paradigm has demonstrated statistically significant changes in outcome measures and is a low cost, safe, and effective complement to standard treatment.

Polymeric Nanofibers as Scaffolds for Stem Cell Transplantation in Brain Injuries

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Acute brain injuries are usually highly disabling, with a high social cost. Unfortunately, few therapeutic options are currently available. Transplanting exogenous stem cells to the central nervous system (CNS) is a promise alternative. However, cell-based therapy pre-clinical trials showed problems such as low local cell engraftment and survival. Using tissue engineering and synthetic scaffolds offers a potential alternative to optimize stem cell transplantation at brain injury sites. In this study the properties of polymeric nanofiber scaffolds (PNF) were evaluated for their ability to support mesenchymal stem cells (MSC) and neural stem cells (NSC) adhesion and survival for transplantation in a thermocoagulation brain injury model in mice. PNF were made of polylactic acid (PLA) by a jet-rotatory spinning technique and its morphology was characterized by scanning electron microscopy. MSC and NSC were obtained respectively from bone marrow and subventricular zone of adult C57/Bl6 mice. After a period of 7 days in culture, cell adhesion and morphology were evaluated by cytochemistry. BrdU was added to cells during 48 hours to evaluate cell proliferation. Viability and apoptosis were evaluated by MTT and TUNEL assays. MSC and NSC grown alone or together on PNF were transplanted on the brain of adult C57/Bl6 mice that underwent a thermocoagulation injury model. MSC were able to adhere, proliferate and spread over the scaffolds. Viability and apoptosis of MSC cultured on PNF were no different from 2D control (cells cultured on cover glass). For NSC, scaffolds have to be first coated with laminin to allow good adhesion and viability. Transplantation of MSC caused a significant reduction of the lesion area. We found evidences of local immunomodulation on mice that received PNF containing MSC, showed by decreased expression of IL4, IL6, IL10 and TNF α , when compared to mice with untreated injury. We found no evidence that the synthetic scaffold presence could increase inflammation or worse functional outcome. Disappointingly, we failed to observe new neurons originated from exogenous neural stem cells in the injured area, and consequently no brain lesion reduction was observed when only NSC were transplanted. We conclude that our PNF are biocompatible and offer a new strategy to improve cell-based therapies to acute brain injuries.

This project was approved by local ethic committee (CEUA 83682210136).

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Sleep Architecture in Acquired Brain Injury Rehabilitation Patients with Mild, Moderate and Severe Sleep Apnea

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Objective and Background: To describe sleep architecture in acquired brain injury (ABI) patients admitted for rehabilitation and diagnosed with sleep apnea (SA). Sleep architecture refers to the pattern of sleep as it shifts between its various stages (rapid eye movement [REM] and 3 non-REM stages). Healthy adults spend 20-25% of sleep in REM, 12.5-20% in N3, 50% in N2, and the remainder in N1. Sleep architecture, sleep timing, and sleep duration are critically important for healthy functioning, with 7 hours per night recommended. While precise mechanisms and functions of sleep are not fully understood, it is accepted that sleep serves critical restorative functions; likewise, disturbed sleep negatively influences health. Sleep architecture is often disturbed in SA patients. However, there is limited research characterizing sleep architecture stages in ABI rehabilitation patients during acute/post-acute recovery with comorbid SA.

Methods: Study design was a retrospective analysis. The sample included patients admitted to a VA hospital's neuro-rehabilitation center from 2009-2016 and who were referred for polysomnography (PSG). Of 197 patients, 138 received PSG, and 93 had valid results with at least 240 minutes of recorded sleep. Of these, 51 met case definition of SA (total AHI \geq 5; 30 mild and 21 moderate-to-severe). Most were male (93.5%) and White (70.3%) with traumatic brain injury (66.7%), stroke (23.7%), or other acquired brain conditions (9.7%). PSG parameters examined were: total sleep time (TST); minutes and % time in N1, N2, N3, and REM; and Arousal Index (AI; refers to arousals-per-hour). Using one-way ANOVAs, the following SA groups were compared: none/minimal (AHI $<$ 5), mild (AHI=5-14.9), and moderate-to-severe (AHI \geq 15).

Results: There were statistically significant group differences on TST (none/minimal M=362.3 \pm 54.2; mild M=352.2 \pm 54.8; moderate-severe M=325.4 \pm 54.9, p $<$.045) and AI (none/minimal M=5.2 \pm 4.1; mild M=9.0 \pm 4.8; moderate-severe M=16.2 \pm 15.8, p $<$.002). Those with moderate-severe SA had the shortest TST and greatest AI. Groups did not differ statistically in %N1, %N2, %N3, or %REM, but study may have been underpowered. Although nonsignificant, compared to those without SA, patients with SA had reduced %N3 (19.4 \pm 13.9) and %REM (13.0 \pm 7.3), and increased %N1 (10.0 \pm 9.2). Similar results were found comparing those with moderate-severe vs. mild SA (nonsignificant).

Discussion: PSG-based sleep architecture was disrupted in SA patients with ABI as it is in general SA patients. Most striking were greater number of arousals and reduced sleep time in SA patients which worsened with increased SA severity. While no statistically significant differences in sleep stages were found between subgroups, proportions of time spent in sleep stages deviated from healthy adults based on prior literature. Medication effects and derangement in brain functioning following acute injury may also have influenced sleep architecture. Regardless of cause, sleep disturbances including apneic events altered sleep architecture should be addressed to prevent obstacles in the neuro-restorative functions of sleep.

Density Change in The Commissural and Projection Fibers of The Brainstem Following Mild Traumatic Brain Injury: A Longitudinal Study

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Background: Microstructural white matter brain changes in mild traumatic brain injury (mTBI) have been documented based on changes seen in MRI parameters like fractional anisotropy (FA) reduction or changes in the fiber density of major tracts in the cerebral hemisphere. Despite often being associated with temporary alteration of consciousness (AoC), little is known about the changes of the brainstem tracts. Damage to these tracts may contribute to long term neurocognitive sequel including post-concussion syndrome. This study analyzed the fiber density of projection and commissural fibers in the brainstem immediately and six months after mTBI.

Methods: Twenty three patients with mTBI were recruited on admission. Diffusion tensor imaging (DTI) sequence was acquired within 6 hours of presentation, and a second similar sequence was acquired 6 months post trauma. In DTI, 32 directions were used with $b=700s/mm^2$. DTI tensor estimation and tractography followed tensorline approach, implemented in Diffusion Toolkit and Trackvis software. Resulting virtual fibers of the brainstem were dissected to differentiate the projection and commissural fibers from the background. Paired longitudinal registration was done using SPM12 to map velocities divergence at six-month. Finally, voxel-wise comparisons were performed between the 2 groups.

Results: Six months following the injury, fiber density reduction ($p<0.05$) were mainly seen along the dorsal tracts ($T=3.63$) and only sporadically at the transverse pontine tracts ($T=4.16$) of the brainstem. The absence of AoC was associated with higher density at the dorsal transverse pontine fibers six month after injury ($p<0.05$, $T=15.03$).

Conclusions: Mild traumatic injury may be detrimental to the structure of the fibers in the brainstem, especially the dorsal projection fibers (ascending tracts). Damage to the dorsal tracts, as evidenced by the reduced fibre density at 6 months, may have a contributing role to the alteration in consciousness experienced by the patient during initial trauma. More focused assessment of these fibres via NODDI or other tractography methods may provide a clearer picture.

Association Between Lifetime Concussion History and Depression in Adolescent Student Athletes

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Objectives: There are multiple risk factors for depression in adolescents, including genetics, demographic factors, familial/personal mental health history, and comorbid health conditions. Concussions may also increase the risk of depression, though this relationship is poorly understood. We examined the presence of preseason depression in a cohort of adolescent athletes, and evaluated the relationship between depression and concussion history. We hypothesized that a history of multiple concussions would be associated with higher rates of depression, after controlling for important confounding or moderating variables.

Method: A sample of 34,318 adolescent student athletes ages of 13-18 (M=15.5 years; SD=1.3; 53.6% boys) without concussions in the past 6 months completed ImPACT® during preseason testing. ImPACT® includes a health history questionnaire, and athletes also rate their current symptoms on the Post-Concussion Scale (PCS). Current medications were entered as free-text and coded by physician review. Athletes were classified as depressed if they either: (1) endorsed five or more symptoms of depression on the PCS (sadness, irritability, sleep disturbance, fatigue, feeling slowed down, difficulty concentrating) as “moderate” or greater in severity, one of which was feeling depressed or irritable, or (2) endorsed five or more symptoms as “mild” or greater in severity, one of which was feeling depressed or irritable, plus current antidepressant use or previous mental health treatment. Logistic regression was used to identify predictors of depression.

Results: Only 1.9% screened positive for depression (2.6% girls, 1.2% boys). Of those who reported a history of 0, 1, 2, and 3 or more prior concussions, rates of depression were 1.6%, 2.8%, 4.3%, and 6.7%, respectively. The logistic regression, including demographic factors and health/concussion history, explained 13.1% of the variance (Nagelkerke R²). Predictors of depression, in decreasing order of magnitude, were previous substance abuse treatment (OR=5.15, 95% CI=3.12-8.54), attention-deficit hyperactivity disorder (OR=5.04, 95% CI=4.10-6.21), female sex (OR=2.98, 95% CI=2.50-3.55), previous headache treatment (OR=2.90, 95% CI=2.29-3.70), three or more prior concussions (vs. none; OR=2.24, 95% CI=1.53-3.42), two concussions (vs. none; OR=2.02, 95% CI=1.44-2.86), learning disability (OR=1.95, 95% CI=1.45-2.63), one concussion (vs. none; OR=1.49, 95% CI=1.19-1.86), previous migraine treatment (OR=1.47, 95% CI=1.12-1.92), and special education (OR=1.36, 95% CI=1.01-1.83).

Discussion: Rates of depression were low in high school athletes. Girls had higher rates than boys. There was a dose-response relationship between concussion history and depression, such that the risk for depression increased as the number of previous concussions increased. Several factors were more predicative of depression than concussion history, such as prior substance abuse treatment, ADHD, female sex, and previous headache treatment. Future research is needed to replicate these findings using a more robust definition of depression caseness and a methodological design that captures the temporal association between concussions and depression onset.

The Effect of Depression on Cognition in an Adult Mild Traumatic Brain Injury Clinic Sample

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Objectives: The effect of depression on neurocognitive test performance has been mixed in prior studies, varying by cognitive domain, specific test, and patient population. The current study examined the effect of depression on cognition, using the newly developed NIH Toolbox Cognition Battery (NIHTB-CB), in a sample of adults seeking treatment for a concussion. We hypothesized that those with depression would perform worse on tasks of fluid cognition compared to those without depression, after controlling for potential confounds.

Methods: From an initial sample of 87 individuals seeking treatment at a specialty concussion clinic, 21 were excluded due to performance validity test failure (24.1%), and another 3 because of incomplete data. The remaining 63 cases were an average of 40.0 years old (SD=11.5; range=21-64), 48% were women, and they were evaluated at 10.8 weeks post injury (SD=6.0 range 2-25). Patients completed a brief cognitive test battery (NIHTB-CB) and a depression screening questionnaire (Patient Health Questionnaire; PHQ-9). Cognitive scores were adjusted for age, education, gender, and race/ethnicity. Depression was operationalized in two ways: (1) five or more symptoms of depression on the PHQ-9, including either depressed mood or anhedonia (i.e., DSM-5 based definition), and (2) total PHQ-9 score of ≥ 10 , the optimal cut-off from prior research.

Results: 23 patients (36.5%) met DSM-5-based criteria for depression, while 36 patients (57.1%) met criteria based on the PHQ-9 total score cutoff. After covarying for the number of weeks since injury and crystallized intelligence, having depression based on the PHQ-9 total score cutoff was associated with lower fluid intelligence composite scores ($F=5.76$, $p=.02$, Cohen's $d=0.45$). The effect size was marginally smaller when using the DSM-5 based definition of depression ($F=3.31$, $p=.07$, $d=0.33$). Examining specific NIHTB-CB fluid subtests, the largest group differences were seen on the Pattern Comparison ($d=0.47-0.53$) and Dimensional Change Card Sort (DCCS; $d=0.31-0.46$) task. In contrast, there were small effect size differences on the List Sort and Picture Sequence Memory tasks ($d=-0.28-0.38$), and no association between depression and the Flanker task ($d < 0.1$).

Conclusions: Depression is a common comorbidity and an important factor to consider when interpreting neurocognitive test performance in adults with concussion in a clinical setting. The newly developed NIHTB-CB appears to be sensitive to psychometrically-identified depression in this sample, both globally and specifically with regard to slower processing speed and worse executive functioning.

Agitation During Post Traumatic Amnesia: Characteristics, Predictors, and Impact on Therapy

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Background: Agitation is considered a common feature of post traumatic amnesia (PTA) after TBI, however, reported frequencies vary widely across studies and assumptions that agitation interferes with rehabilitation participation have rarely been investigated. Also relatively little is known about the best predictors of agitation and in particular the relationship between agitation and cognitive impairments during PTA.

Objectives: The aims of this study were to: 1) examine the frequency and nature of agitation during PTA using prospective measurement; 2) examine the impact of agitation on participation in therapy during PTA; and 3) examine the relationship between agitation levels and the cognitive impairments (orientation and memory) during PTA.

Method: Prospective assessment of agitation (Agitated Behavior Scale, ABS), therapy participation (time in ADL retraining) and orientation/memory (Westmead PTA Scale) were conducted in consecutive patients who were admitted for inpatient rehabilitation during the PTA phase after severe TBI.

Results: Preliminary results based on 100 admissions show that agitation was observed in approximately 50% of participants (ABS score >21) while they were in PTA, with disinhibited behaviours (i.e. distractibility and impulsivity) most common. Regression analyses found that agitation levels were not significantly associated with participation in ADL retraining during PTA with participants showing good tolerance for the ADL retraining even in those with clinically significant agitation. Regression analyses also revealed that ABS scores were associated with performance on the Westmead PTA Scale such that greater levels of disorientation and memory impairment predicted greater levels of agitation.

Conclusions: Agitated behaviour was common during PTA but it did not prevent participants from participating in ADL skills retraining. Furthermore participating in therapy during PTA did not increase agitation and suggests that patients in PTA may be able to engage in more active therapy than currently seen in some settings. The observed association between agitation and concurrent orientation and memory impairment suggests that PTA management strategies that maximise orientation and memory may also help to minimise agitation.

Value of Group Activity and Holidays for Brain-Injured Clients

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I am a brain-injury case manager and I volunteer as a coordinator of a brain-injury charity and have researched, organised, and filmed a number of group trips. I have arranged several ski trips for either adults or children, safaris in Africa, surfing in the UK, and camping in Europe. We have captured on film the feedback from clients, which shows just how much benefit they and their families are obtaining from these experiences.

These responses show clearly how valuable it is for brain-injured clients of all ages to spend time in different environments and to face new challenges, and it has boosted their confidence and self-esteem. They enjoy the 'group experience', and I show on film clients discussing how they gained an insight into their own conditions from the experience. Responses such as, 'It was the first time I felt normal' and, 'I realised that I could function in a group and enjoy myself' are on film and are part of the story of how they progressed during these trips.

We saw physiotherapy benefits from surfing in the UK and in Africa. We have a brain-injured client on a ventilator skiing in France, showing that there are no physical boundaries. We have film suitable for the conference to show feedback from just adults or from children and adults. The children's trips show the value of activities with siblings and of having the opportunity to interact equally with the family and all their activities. For example, a child going down an advanced run in contrast to the rest of the family, who are on basic runs! Similarly, the brain injured-clients can often do more than their careers when they go skiing. I consider that film is an ideal medium because it shows feedback across a number of groups that such activities benefit not just the client but also the family and careers who support them.

It is not always necessary to go overseas because for some clients similar benefits can be obtained from a surfing holiday in Devon. The trip to Africa was a very positive experience. It started in Durban, where they went snorkeling and shark cage diving, and the more physically dependent clients in electric wheelchairs went surfing. We then went into the bush and saw animals from an accessible open-top vehicle and went on to an adapted boat with the hippos. They visited a special-needs orphanage and brought the children gifts, and the next day the children joined the group for lunch. There was a great deal of bonding and friendship among the group and it became difficult to tell who were clients, guides, support workers, or family.

Report of the International Brain Injury Association, Disorders of Consciousness Special Interest Group

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Background: Current difficulties for clinical diagnosis and prognosis of patients with disorders of consciousness (DoC) have been largely discussed between clinicians and researchers, but to date no international guidelines or recommendations about diagnostic and prognostic process are available. As a consequence diagnostic and prognostic procedures for DoC could be extremely heterogeneous in different countries and, most often, across several clinical settings both in acute and in chronic phase. In this context, DoC Special Interest Group (DoC-SIG) on Disorders of consciousness will launch an international multicenter survey to identify diagnostic and prognostic procedures across countries and clinical settings.

Objectives: 1. to explore which specific diagnostic protocols or prognostic indices are adopted in the care pathway for persons with DoC in different countries and if national guidelines provide specific recommendations; 2. to propose international guidelines and recommendations as best practice and gold standard.

Methods: IBIA DoC-SIG members will receive by mail an invitation to answer to a questionnaire focused on diagnostic and prognostic procedures adopted in the routine management of DoC patients. The draft of the questionnaire has been elaborated by Drs. Rita Formisano and Anna Estraneo and discussed among DoC-SIG members during several call meetings.

The questionnaire has been organized in two distinct sections. The first section includes 8 questions investigating clinical and instrumental (e.g. neurophysiological evaluation and neuroimaging exams) tools and involvement of family-caregivers in the diagnostic procedures. The second part is constituted by 9 questions on clinical, anamnestic, instrumental markers and possible interfering factors for recovery of consciousness (e.g. previous comorbidities, medical or neurosurgical complications) routinely used by clinicians to provide prognostic information.

Conclusion: The draft of the questionnaire has been posted in the LISTSERV platform (<http://groupspaces.com/IBIADOCSIG/>), for discussing it with DoC-SIG members. The final version of the questionnaire (in which comments and suggestions from the LISTSERV forum will be taken into account) will be ready in the Survey Monkey format, in order to launch the survey in December 2016.

Transfer to a Tertiary Care Hospital Vs. Presenting Directly to a Tertiary Care Facility is Associated with Increased Mortality Among Patients with TBI In India: Results from the TITCO Database

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Introduction: Access to a tertiary care hospital that can provide rapid access to imaging and surgical specialists, has been associated with improved outcomes for individuals with traumatic brain injury (TBI) in a variety of settings. We sought to examine whether direct presentation to a tertiary care facility vs. inter-hospital transfer to the same facilities offered a survival advantage for working-age males with moderate/severe TBI in three urban areas.

Methods: Data collected at four large public tertiary care hospitals in India as a part of the "Towards improving trauma care outcomes" (TITCO) trauma registry project were examined. Males aged 18-45 with isolated serious/severe/critical TBI, identified as Abbreviated Injury Scale (AIS) scores ≥ 3 for the head/neck region and no injury with AIS >2 in any other body region were identified and differences in injury mechanism, type and severity, as well as demographic factors and total time to the tertiary care facility were compared between individual presenting directly vs. those transferred to the tertiary care hospital. In-hospital mortality during the index visit was the primary outcome of interest.

Results: A total of 3,526 males met inclusion criteria, 23.6% of whom presented directly to a tertiary care hospital. Mean age (30.1 vs. 30.4) and the proportion of patients with AIS 4 or 5 head injuries (22.1% vs. 21.0%) did not differ between direct and transfer patients, respectively; further, median time from injury to the tertiary care admission was 4.7 hours in the direct group vs. 17.1 hours for transfers (all $p>0.05$). Proportional mortality was 21.2% among patients presenting directly to a tertiary care facility vs. 26.9% among transferred patients. After controlling for patient age, injury type (blunt vs. penetrating), and severity, patients transferred to definitive demonstrated 52% greater odds of in-hospital mortality vs. those who presented directly to definitive care (aOR 1.52, 95% CI 1.25-1.84).

Conclusion: Males between 18 and 45 who experienced a moderate/severe isolated TBI and underwent interhospital transferred to a large tertiary care facility demonstrated more than 1.5 times greater odds of mortality than otherwise similar patients who presented directly to a large tertiary hospital for TBI treatment.

Pain Perception and the Interruption of Artificial Nutrition and Hydration (ANH) in Unresponsive Wakefulness patients: Neuroethics in Action

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In this presentation, we will review the recent literature indicating that some patients with Disorders of Consciousness reveal a form of residual awareness and that they are capable of perceiving painful stimuli and exhibiting consistent responses to them. Empirical evidence suggests that, when tested with the appropriate tools, these patients can exhibit consistent reactions to emotionally salient stimuli. Based on these findings, we propose that the voluntary withdrawal of ANH should be carefully reconsidered on medical and ethical grounding. For patients with severe pathologies (e.g., terminally ill), the hydration and starvation may have benefits (patients could be intolerant of enteral feeding because of abdominal distension, vomiting, diarrhea, or fluid overload) and to refuse food and fluids and to have relief of distress through provision of medicine may be a right. However, most patients in VS/UWS are unlikely to be intolerant of nutrition and hydration that are considered basic compassionate care because they promote physical and emotional well-being. Withdrawal of ANH has biologic consequences including distress and pain. Neurophysiological and neuroimage studies are finding ways to assess awareness in VS/UWS patients. The identification of the “pain matrix” along with the design of experimental tools capable of detecting consistent patterns of brain activation in response to noxious stimuli allowed us to integrate the original definitions of pain, which rested largely upon subjective experiences with objective measurements.

Comparison of Treatment for Disorders of Consciousness (DOC) Across Countries – Results of an International Survey

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Introduction: Care pathways for people with disorders of consciousness (DOC) involve several transfers between healthcare institutions from acute to long-term care. There exists no internationally accepted criteria for an optimal treatment pathway for people with DOC (Godbolt et al., 2013) and as such treatment is influenced by societal, geographical, financial and political factors. This can lead to huge variation in the length and type of treatment this patient population receives. While there has been an increased effort to improve the diagnosis of DOC, less is known about the implementation and effect of treatment for these patients in spite of recently described guidelines (Giacino et al., 2014) and some emerging promising interventions such as pharmacological agents (e.g. amantadine) or non-invasive brain stimulation (e.g. tDCS). The aim of this project is to determine the main commonalities and differences across countries for the treatment of patients with DOC. This study explores, for the first time, the health care systems and treatments available, from acute to long-term care, across countries.

Method: A subgroup of clinicians and researchers of the IBIA-DOC-Special Interest Group (SIG) conducted an international survey with the goal of identifying the structures, financial framework and the actual clinical practices for patients with DOC. The survey was developed by the lead authors with the support of members of the DOC-SIG. The first part of the survey related to the institutions, the structure of the health care system and the services available in the region/country of the respondent, separated for adults and children. The second part of the survey dealt with the specifics of type and intensity of treatments applied. Both parts of the survey were sent out to all DOC-SIG-members. The results were analyzed, using descriptive statistics.

Results: The results were not available yet at the time of the submission of the abstract.

Conclusion: The results will shed light on the actual clinical practice of treating patients with DOC across a number of countries. The implementation of international guidelines for treatment of these patients will be discussed as well as the scope for integrating new research findings on promising treatments in clinical practice.

Voice and Articulation Changes Over Time Due to Stroke and TBI

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Research and observations over the last several years have noted articulatory changes in post stroke and traumatic brain injury victims. However, little research has documented the effects of these brain injuries on the voice, voice productions and the subjective and objective changes over time associated with brain injuries. This study examined recordings of ten individuals post injury, analyzing the voice and speech with objective metrics (e.g. speech fundamental frequency, speech rate, articulation rate) and subjective metrics (e.g. rate, general aesthetics, non-lexical utterances, and pauses). These metrics were tracked over time from incident of the injury. Recordings were extracted from publicly available videos of stroke and TBI victims. Analysis was conducted on those recordings where there was an individual who was recorded at similar times post injury. Results indicated that changes in both the objective and subjective ratings of fundamental frequency as well as in roughness, breathiness, and strain occurred post brain injuries. Specific rates of change post injury will be presented.

Traumatic Brain Injury in Diabetic and Hypertensive Rats Exacerbates Brain Pathology and Functional Outcome. Role of Neurotrophic Factors and Nanomedicine

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Piercing traumatic brain injury (pTBI) cut neuronal connections by direct physical tissue damage, microhemorrhages and lacerations. Damage to the brain centers controlling movements; speech, cognitive functions as well as sensory motor disturbances lead to irreparable functional disturbances. However, if pTBI occurs in victims having hypertension, diabetes or a combination the magnitude and intensity of brain damage intensifies. In such cases axonal regenerations, bridging tissue loss and making new connections by enhancing neuroplasticity is the need of the hour. There are reasons to believe that select combination of neurotrophins could help in pTBI cases complicated with additional co-morbidity factors. In addition, use of nanotechnology to deliver neurotrophic drugs in these pTBI cases may further enhance their therapeutic efficacy in neurorepair.

Our laboratory has initiated a series of investigations on TBI associated with co-morbidity factors and showed that TBI inflicted in either hypertensive or diabetes rats caused greater damages on functional and pathological outcome as compared to TBI alone in healthy animals. However, the effects of TBI in hypertensive and diabetic animals are not well evaluated. In this investigation we examined the effects of pTBI in diabetic and hypertensive (DBHY) rats on brain pathology and functional outcome after 24 and 38 h of the basic insult. We also evaluated a combination of neurotrophic drugs with active peptide fragments e.g., cerebrolysin treatment with or without nanodelivery to achieve better neuroprotection and functional recovery.

pTBI was inflicted in rats under anesthesia by opening of the right parietal cortex (4 mm²) and a longitudinal cortical incision was made (3 mm deep and 5 mm long) using stereotaxic guidance with a sterile scalpel blade. pTBI was also inflicted in separate group of rats made hypertensive by 2 kidneys 1 clip (2K1C) method. 2K1C was also applied in a group of rats that were made diabetic by streptozotocine (60 mg/kg, i.p. for 3 days). These DBHY rats were subjected to identical pTBI and allowed to survive for 24 h after the insult. Our observations showed that pTBI in DBHY rats resulted in breakdown of the blood-brain barrier (BBB) to proteins, edema formation and cell injuries that were 4- to 6 times higher than the identical pTBI in healthy rats. In these rats cerebrolysin (2.5 or 5 ml/kg, i.v.) was able to reduce some of the pathological changes without having a significant effect on functional parameters such as Rota rod performance and grid wakening. However when TiO₂ nanodelivery of cerebrolysin was done (5 ml/kg, i.v.) significant improvement on function parameters and pathological outcome was seen in pTBI in DBHY animals. These observations suggest that pTBI associated with co-morbidity factors require nanodelivery of cerebrolysin to achieve good neuroprotection, not reported earlier.

Cerebral Cortex Morphometry in Mild Traumatic Brain Injury

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Background: Despite being considered self-limiting, mild traumatic brain injury (mTBI) leaves a significant neurocognitive deficit in a large cohort of these patients. This has been seen in numerous cognitive studies and has been backed up by microstructural changes of the white matter (WM) as seen in diffusion tensor imaging MRI studies. However, these studies have not looked in depth into the changes involving grey matter cortices. Questions remain about the possibility of significant changes in the grey matter in tandem with white matter changes and their possible relationship with neurocognitive deficits. We study the changes in the cortical grey matter (GM) volume between mTBI patients and age matched controls using voxel-based cortical morphometry at both the acute stage and six months follow up.

Methods: Patients with mild TBI presented at the emergency department (ED) of the University of Malaya Medical Centre (Kuala Lumpur), between April 1, 2013 and March 1, 2014, were recruited on voluntary basis. Controls are age-matched. All subjects underwent high resolution MRI T1-weighted imaging, at admission and six months after. The cortex volumetric image were obtained using SPM12 Segmentation tool. For the purpose of longitudinal comparison in patients with follow up scans, the two acquisitions (baseline and follow up) were registered in pairwise manner using SPM12 pairwise longitudinal registration tool. Between and within group comparisons were done with 10,000 permutation, and statistical significance was obtained using threshold-free cluster enhancement (TFCE) method. Two-sample t-test was done to compare the controls and the patients, whereas paired-t test was to examine the patient group change in cortical volume over six month period. Statistical correction for multiple comparison was performed using family-wise (FWE) correction, with a threshold of $p < 0.05$.

Results: Cortical volume was found to be statistically unchanged between the controls and patients at the baseline. However, on comparison of baseline and follow up scans in mTBI patients, cortical volume showed a significant increase, especially over the cerebellum, occipital and parietal lobes ($p < 0.05$, FWE-corrected).

Conclusion: Our findings reveal that patients with mTBI experience cortical volumetric changes over time, involving mainly the cerebellar, occipital, and superior part of the parietal cortices. This may be an effect of the postulated cerebral edema that occurs immediately after a brain injury, which would have subsided during the follow up imaging. Whether these gray matter changes have a significant effect on the neurocognitive outcome is an important question that needs to be answered.

Psychological Distress Affects Cognitive Functioning in Family Caregivers of Patients with Disorders of Consciousness: Preliminary Data

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Introduction: Patients affected by Disorders of Consciousness (DOC) need intensive and continuous assistance for their extremely severe motor and functional disabilities (1). In this respect, the crucial role played by family caregivers (2) may be associated with high levels of psychophysiological distress (3). Literature on caregivers of patients affected by neurodegenerative disorders has shown that analogous levels of psychological distress could be associated with reduced cognitive efficiency, mainly affecting executive functions, working memory and attention (4).

Our study aimed to analyze the possible presence of reduced cognitive efficiency in association with psychological distress in caregivers of patients with chronic DOC.

Methods: We assessed 27 caregivers (18 females; mean age= 49,84±10,9 years) of 25 patients affected by prolonged DOC (18 females; mean age= 51.9±22.2 years); Vegetative State= 13, Minimally Conscious State= 12; anoxic etiology n= 8, vascular n= 12, traumatic n= 5; mean time from onset= 9.4 months, range 5-24 months) admitted to the Severe Brain Injury Units of Maugeri Scientific and Clinical Institutes (Institutes of Telese Terme and Sciacca).

We assessed several aspects of psychological distress, such as anxiety (State Trait Anxiety Inventory, Form Y, STAI-Y), depression (Beck Depression Inventory-II, BDI-II), psychophysiological symptoms (Cognitive Behavioral Assessment – Psychophysiological Questionnaire, CBA-PF), prolonged grief disorder (PGD-12), psychological burden (Family Strain Questionnaire) and quality of life (Whoqol-Bref). Moreover, we evaluated cognitive functions by means of standardized neuropsychological tests assessing short- and long-term memory, executive functions and attention. Scores on neuropsychological tests were compared with those achieved by a group of 15 age- education- and gender-matched healthy subjects.

Results: A high proportion of caregivers (19/27; 70.3%) showed clinically relevant depressive symptoms (BDI-II score > cut-off 13), and high level of anxiety (15/27; 55.5%; STAI-Y score >40). Moreover, 13 of 21 caregivers whose relative had duration of DOC >6 months were affected by PGD syndrome (61.9%). Family caregivers had scores significantly lower than matched controls (p<.001) on tests for divided attention (Trail Making Test), verbal fluency (FAS) and long-term spatial memory (supra-span learning Corsi Test).

Discussion: Family caregivers of patients affected by prolonged disorders of consciousness display high levels of psychophysiological distress, with high rates of clinically relevant depression, anxiety and a complex syndrome called PGD. Caregiver's burden is associated with a significant reduction in efficiency of the frontal executive functions and long-term memory abilities. These preliminary data are of paramount importance in consideration of the delicate role of caregivers directly involved in clinical decision making and in care of their relatives with DOC [4], confirming the need to support family caregivers with appropriate psychological and cognitive therapies.

Plasma Exosomal Biomarkers for Mild TBIs and Post Concussive Syndrome

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Identifying biomarkers in the peripheral blood that relate injury processes following traumatic brain injury (TBI) may provide insights into pathophysiology, and provide diagnostic information to guide clinical management. We studied a cohort of military personnel to determine if mild-TBIs (mTBIs) and post-concussive syndrome (PCS) could be predicted using exosomal concentrations of tau, and amyloid beta (A β)₄₀ and A β ₄₂. Peripheral blood samples from military personnel with a mTBI (n=40) were compared to controls with no TBIs. A subgroup analysis further divided those within the mTBI group to compare military personnel with a mTBI and PCS, to those with only a mTBI and non-TBI controls. Concentrations of neuronal-derived, exosomal markers including: quantification of cluster of differentiation (CD) 81, tumor susceptibility gene (TSG)101 and apoptosis-linked interacting protein X (ALIX), as well as protein levels of tau, A β ₄₀ and A β ₄₂ were measured. The two groups significantly differed in concentrations of tau (F_{1, 59} =10.50, p<0.05), and A β ₄₂ (F_{1, 59} =5.31, p<0.01), such that the mTBI group had significant elevations compared to the non-TBI group, and these differences remained significant after controlling for symptoms of depression and post-traumatic stress disorder. The concentration of TSG101 was significantly lower in the mTBI group compared to controls as well (F_{2, 65} =7.73, p=0.07). Area under the curve (AUC) indicates that tau (AUC=0.79, p<0.05) and A β ₄₂ (AUC=0.73, p<0.05), and TSG101 (AUC=0.75, p<0.05) were sensitive in distinguishing mTBIs from controls. Comparing the mTBI/PCS group to the mTBI group without PCS shows significant elevations of exosomal tau and A β ₄₂, and lower concentrations of TSG101 in the mTBI/PCS group (p's<0.05). Our findings indicate that chronic symptoms related to mTBI may reflect development of tau and A β pathology and that exosomes may serve as peripherally available, diagnostic biomarkers of identifying mTBI patients at risk for developing PCS.

Towards Developing a Cognition Endpoint: Evaluating Cognition Battery Summary Scores for Traumatic Brain Injury Research

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Background: There is a need to develop and evaluate a global cognition endpoint that can be used in traumatic brain injury (TBI) clinical trials. This study compares the distributional characteristics and effect sizes of four cognition battery summary scores in a sample of patients with perceived cognitive deficits following TBI and orthopedic trauma controls.

Method: The total sample included 154 individuals with a diagnosed TBI (i.e., 62.3% uncomplicated mild TBI; 24.7% complicated mild TBI; and 13% moderate-severe TBI) and 83 orthopedic trauma controls. We selected two subgroups for comparison, TBI with subjectively-experienced cognitive deficits (n=79) and trauma controls with no perceived cognitive deficits (n= 64) based on self-report of moderate or greater (3+) symptoms on one or more of cognitive items on the British Columbia Postconcussion Symptom Inventory (BC-PSI). All participants were tested with the Neuropsychological Assessment Battery (NAB) approximately 6 weeks after injury. Four cognition battery summary scores [i.e., overall test battery mean (OTBM); global deficit score (GDS); number scores below the 16th percentile; and neuropsychological deficit score (NDS)] were derived from the 24 primary demographically adjusted T scores from the NAB. Receiver operating characteristic (ROC) curves and effect sizes (Cohen's ds) were calculated as measures of group discrimination.

Results: Participants with TBI and perceived cognitive complaints performed significantly worse than controls on all composite scores [$p < .05$]. Small to medium group mean differences were observed for all four composite scores (Cohen's $d = .34-.41$). The area under the curve (AUC) for each composite score was as follows: OTBM, AUC=.60; number of scores below the 16th percentile, AUC=.60; GDS, AUC=.62; and NDS, AUC=.61. There were no significant differences between these AUC values ($p > .05$). All were in the "poor" classification range (AUC=.60-.70).

Conclusions: Patients with subjectively-experienced cognitive deficits after TBI performed modestly worse on neuropsychological testing than trauma controls, but there was considerable overlap between the two group distributions. The four candidate cognition composite scores had very similar discriminatory power. The present study did not provide evidence to favor one composite score over another for sensitivity to TBI.

Impact of Clinical Complications on Long-Term Outcome in Prolonged Disorders of Consciousness

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Objectives: Patients with prolonged disorder of consciousness (DOC) might develop several and severe clinical complications (CC) [1,2]. The present prospective longitudinal study aimed at: 1) investigating the occurrence of CC in patients with prolonged DOC within 6 months after traumatic, vascular or anoxic brain injury; 2) evaluating the impact of CC on long-term clinical-functional outcome [3].

Methods: Subjects: 156 inpatients (95 males, mean age: 57.1 ± 17.8), with prolonged (≥1 months post-onset) DOC (118 were in vegetative state, VS and 38 in minimally conscious state, MCS), following traumatic (n=33), vascular (n=64) or anoxic (n=56) brain injury.

Procedure: We recorded CC arising in the 6 months post-injury from medical reports and family information during the acute phase and from direct observation during rehabilitation stay. CC were grouped in 10 categories with respect to the organ system involved (e.g. respiratory system) or presence of clinical manifestations (e.g. seizures), and classified them in 3 levels of severity (mild, moderate and severe). Patients' demographic data, medical history and clinical conditions at study entry (level of responsiveness assessed by CRS-R, level of disability assessed by DRS) were also gathered. All enrolled DOC patients were clinically followed-up until 30 months post-onset.

Results: We found at least 1 CC in 155/156 patients and more than 3 CC in 70% of them. Respiratory and osteo-muscular CC were the most frequent (≥70%) and severe CC (30% and 27%, respectively). The majority of patients (76.2%) developed at least 1 severe CC. Occurrence and severity of CC did not differ as a function of patients' age, clinical diagnosis and etiology. Paroxysmal sympathetic hyperactivity occurred more frequently in younger (p<.001) and anoxic (p=.001) patients whereas metabolic, cardiovascular and respiratory CC occurred more frequently in older patients (p<.05). Presence of metabolic and respiratory CC significantly impact patients' mortality at 12 or 30 months post-brain injury (p<.001 and p=.001, respectively). Presence of CC did not influence recovery of consciousness and disability level at 12 and 30 months post-onset.

Conclusions: High number of prolonged DOC patients developed at least 1 severe CC, regardless of clinical diagnosis, etiology and age. Presence of some CC significantly impacted on patients' mortality, but not on recovery of consciousness or disability at long-time post-injury. Occurrence and severity of CC in patients with DOC calls for appropriate levels of care.

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Functional MRI Imaging Signatures in Young Men with Prenatal Exposure to Dioxin-Like Chemicals

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Introduction: In 1979 an episode of food intoxication by rice oil contaminated with dioxin-like chemicals occurred in Taiwan, called Yucheng (oil-syndrome in Chinese). The children born to exposed women suffered from skin manifestations, tooth problems, reduced neurocognitive capability, etc. We aim to determine whether children born to Yucheng mothers had changes in functional MRI imaging signatures.

Methods: The fMRI study was performed using a 3T MRI scanner. Gradient-echo echo planar imaging (EPI) was used to acquire BOLD signal. Two different paradigm for fMRI, N-back task and picture rotation task, were used to simulate coding and object assembly subtest. All data were processed using SPM8 (www.fil.ion.ucl.ac.uk/spm) implemented on MATLAB.

Results: We recruited 10 men born to Yucheng mothers and 11 community controls, with mean age of 29 years. The Yucheng and control groups were similar in age, percentage of smoking and alcohol drinking, and years of education. The accuracy and response time of the N-back test and the picture rotation task between these two groups were similar. In the paradigm of the N-back test, the Yucheng men had increased BOLD signal in bilateral cingulate gyrus, dorsal medial prefrontal gyrus, and inferior occipital gyrus. For the picture rotation task, bilateral parietal cortex, occipital cortex, and dorsolateral prefrontal cortex were activated in the picture rotation task, while the medial frontal cortex, bilateral subcortical nuclei, and right temporal lobe were deactivated. Yucheng men showed reduced activation over the anterior cingulate gyrus, right inferior frontal gyrus, and medial temporal lobe in the picture rotation task. In the two-back task, Yucheng men had stronger activations over the dorsal medial prefrontal cortex and cingulate gyrus. Furthermore, these areas showed significant deactivations during the execution of the tasks. These results implied different image signatures between the two groups, less deactivations in the Yucheng subjects during the task. Similarly, the activation difference between the Yucheng men and their controls in picture rotation task could be attributed to stronger deactivations in the Yucheng descendants in the anterior cingulate gyrus, right medial temporal lobe and inferior frontal gyrus. Default mode network (DMN) on resting fMRI was obtained using the posterior cingulate cortex (PCC) as a seed, the PCC in the Yucheng group had increased connectivity with bilateral caudate nuclei, the right thalamus, and left parahippocampal gyrus but decreased connectivity with the precuneus, right medial temporal gyrus and left superior temporal gyrus.

Conclusion: Yucheng men prenatally exposed to dioxin-like chemicals had reduced deactivate of DMN nodes, as well as alterations in task-induced deactivations, implying that different brain networks were used for the Yucheng group to achieve similar levels of neurocognitive functions. Further follow-up of neurocognitive functioning is warranted due to potential of mental decline found to associate with the current fMRI findings.

Improvement Rate of Patients with Severe Brain Injury During Rehabilitation

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Introduction: Patients with severe acquired brain injury (SABI) may evolve towards prolonged disorders of consciousness (DoC) or consciousness recovery.

Thus, early predicting clinical factors have a crucial role in decision-making and information to the caregivers.

Aim: The primary aim was to evaluate the clinical evolution of a large population of patients with SABI admitted to a Post-Coma Unit from 2001 to 2016, diagnosed with severe brain injury (GCS \leq 8) in the acute phase and a coma duration of at least 24 hours.

The secondary aim was to evaluate the possible changes between the admission time to a post-acute rehabilitation Hospital and the discharge time, measured by means of Glasgow Outcome Scale (GOS) (Jennett and Bond, 1975), Level of Cognitive Functioning (LCF) (Hagen et al., 1979) and Disability Rating Scale (DRS) (Rappaport et al, 1982).

The final aim of the study was to correlate the improvement rate with some sociodemographic and clinical features of the individuals enrolled.

Methods: All patients with SABI were admitted to Rehabilitation directly from Intensive Care Units or Neurosurgical wards, as first rehabilitation admission.

Statistical Analysis: Two regression analyses identified the dichotomized independent variables influencing an outcome improvement of GOS-score and DRS-score, and reporting results in terms of odds ratio (OR), 95% confidence interval (CI95%) and p-values significant if <0.05 .

Results: Data of 890 patients were analysed (age= 39.82 ± 16.79 years, 67% males, 54% TBI, length of stay= 162 ± 186 days, GCS= 7.46 ± 1.28).

Time from the acute event (OR=0.246, CI95%=0.181-0.333), scores at admission of LCF (OR=2.243, CI95%=1.492-3.73), GOS (OR=0.138, CI95%=0.071-0.266), DRS (OR=0.457, CI95%=0.330-0.632), etiology (OR=2.273, CI95%=1.676-3.084) played a significant role ($p < 0.001$, explained variance 69.9%) for improving GOS-score.

Time from the event (OR=0.300, CI95%=0.179-0.501, $p < 0.001$), length of stay (OR=2.808, CI95%=1.694-4.653, $p < 0.001$), etiology (OR=1.769, CI95%=1.095-2.857, $p = 0.020$) led to an improvement in DRS (explained variance 91%), whereas age ($p = 0.283$), coma duration ($p = 0.810$), sex ($p = 0.450$), and scores at admission of LCF ($p = 0.168$), GOS ($p = 0.252$), DRS ($p = 0.475$) did not.

Conclusion: The most significant predictive factors for the outcome of patients with SABI, either with or without persistent disorder of consciousness, were etiology, length of stay in the rehabilitation hospital and time interval from acute event to admission in a rehabilitation hospital.

The influence of time interval from acute phase to Rehabilitation may be due to the efficacy of early rehabilitation or delay in the transfer to rehabilitation wards, because of the medical, neurological or neurosurgical complications in the acute phase (Formisano et al., 2016). Longer stays in post-intensive rehabilitation wards, may be of benefit for persons with SABI.

Preliminary Feasibility of Smartphone Technology to Assess Participation Following Traumatic Brain Injury

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Background: Participation is an important outcome in health, disability, and rehabilitation research and practice. However, the breadth of available measures, and scope of participation domains assessed makes choosing an appropriate measure difficult. Current measures of participation have been criticized for their discrepancies in operationalization, the measurement of multiple constructs, variability of domains assessed, and the static measurement of a dynamic construct. Moreover, the reliance on retrospective recall and self-reporting is a concern for disability populations, such as traumatic brain injury (TBI), for whom accurate and reliable recall may be impaired. Ecological momentary assessment (EMA) methodologies allow for the dynamic assessment of participation in the environment in which the individual lives, functions, and participates. Recent advances in smartphone application technology provide new opportunities for the efficient and effective ecologically valid assessment of a variety of outcomes. While EMA paired with smartphone application technology is a promising, novel approach to assess participation, examining the feasibility of EMA methodologies in individuals with TBI is a necessary first step in determining the utility of this approach.

Methods: The present study assessed the feasibility of using smartphone application technology to assess participation following TBI. A prospective, repeated measures design was used to examine compliance, usability, and acceptability with EMA of participation via a smartphone application over four-weeks, four times per day. The primary outcome measure, the Mobile Participation Assessment Tool (mPAT), was developed to assess participation utilizing EMA methodologies. The mPAT consists of five items to assess frequency and importance of participation, and satisfaction with participation. Feasibility was assessed in working age adults, living in the community following TBI (n =10).

Results: Participants completed 82.9% of all scheduled assessments. Compliance rates varied by week (80.4-90.6%), and time of day (79.4-84.61%). Despite observed variability, rates remained indicative of good compliance. On a scale of 1 to 5, participants reported that the mPAT (M = 4.5, SD = 0.53) and smartphone application (M= 4.5, SD = 0.71) were easy to use. Participants agreed that the mPAT was an acceptable way to measure their participation (M = 4.30, SD = 1.06), and reported being satisfied with the mPAT as a measure of their participation (M= 4.2, SD = 1.03). Additionally, participants reported feeling comfortable answering questions using the application (M = 4.60, SD = 0.52), and that it was an acceptable way to answer questions (M = 4.60, SD = 0.52).

Conclusion: Participants demonstrated good compliance, and supported the usability and acceptability of the mPAT and smartphone application. Findings provide preliminary support of the feasibility of using smartphone application technology and EMA to assess participation following TBI. The mPAT paired with smartphone application technology is a promising, novel approach to assessing the important rehabilitation outcome of participation.

Effect of Circadian Rhythm Optimization on Behavioural and Event Related Potential Responses in Prolonged Disorders of Consciousness

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Background: Patients with prolonged disorders of consciousness (PDOC) show none or minimal signs of awareness of themselves and their environment but appear to have sleep-wake cycles. However, these patients have abnormal sleep patterns and sleep structures as shown by the polysomnographic studies (PSG). This suggests that circadian rhythm of patients with PDOC is impaired. It was also shown that the more structured sleep was highly correlated with clinical scores and was associated with positive clinical outcomes.

Furthermore, several research studies have shown that it is possible to detect the presence of higher level cerebral functions in such patients, by utilizing electrophysiological methods such as event related potential (ERP) studies in cases where clinical assessments are unable to detect any behavioural sign of awareness.

Objective: The objective of this study was to examine the effect of circadian rhythm and sleep optimization on behavioural and electrophysiological responses in PDOC patients.

Methods: 10 people with PDOC, 2 to 8 years after brain injury were included in the study (5 female, age 30-71). CRS-R, 24-hour PSG and 4-hourly saliva melatonin measurements, mismatch negativity (MMN) and subject's own name (SON) experiments were performed twice at baseline and following intervention. Intervention was consisting of melatonin treatment at night and blue light and caffeine treatment in the morning for five weeks.

The PSG data were collected using an ambulatory EEG system and sleep staging was done. Melatonin results were analysed with cosinor analysis. For the MMN studies, the presented stimuli were 1000 pure tones of 1000Hz (80% standard) and 1200Hz (20% deviant), with an intensity of 70 dB and duration of 60ms (rise time 10ms), delivered binaurally through headphones. Inter-stimulus interval was 500ms. In the SON study, three different types of stimuli- subject's own name (deviant), four other people's names and four time reversed names (standards) were used. Inter-stimulus interval was 1200ms. The stimuli were delivered binaurally via headphones.

Results: Baseline sleep architecture was abnormal in all patients. With intervention, improvement of sleep stages and/or sleep-wake patterns were detected in 8/10 patients. Cosinor analysis of saliva melatonin results revealed that averaged baseline % rhythmicity was low. (Mean: 31%, Range: 13% - 66.4%, SD: 18.4). Increase in %Melatonin Rhythm following intervention was statistically significant ($p=0.012$).

7 patients had improvement of CRS-R scores with intervention. Paired samples T-test revealed statistically significant improvement of CRS-R scores ($p=0.034$). All the patients who had improvement of clinical scores also had statistically significant improvement of neurophysiological responses on MMN and SON experiments ($p=0.001$).

Conclusions: Sleep and circadian rhythms are severely deranged in PDOC. Optimization of circadian rhythms and sleep with melatonin, caffeine and blue light treatment led to improvement of all physiological parameters measured- and most importantly of CRS-R scores and event-related potentials.

Family Members Experience with In-Hospital Health Care after Severe Traumatic Brain Injury

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Family members' experience with in-hospital health care after severe traumatic brain injury

Background: Family members' experiences and satisfaction with health care services is an important indicator of the quality of care provided. There is a lack of longitudinal studies investigating relatives' experiences during the different phases of severe TBI patients' in-hospital treatment and rehabilitation.

Objectives: To describe family member experiences of the health care provided in acute care and in-patient rehabilitation settings to patients with severe traumatic brain injury (TBI) and assess predictors of a poor care experience.

Methods: Prospective national multicenter study of family members of patients with severe TBI covering all regions of Norway. Self-report data from 122 family members were collected 12 months post injury. To assess the family member's experience of health care, the recently validated instrument Family Experience of Care Questionnaire in severe Traumatic Brain Injury (FECQ-TBI) was applied. FECQ-TBI consists of 6 subscales: Organization and information acute, organization rehabilitation, information rehabilitation, discharge, hospital facilities family member and hospital facilities patient. Data on the patients' demographic variables, functional independence and rehabilitation pathway were assessed in a parallel national multicenter study.

Results: The highest scores representing good experiences were reported in the FECQ-TBI scales representing organization and information during the acute phase (mean 4.1), whereas the lowest scores were related to discharge from in-patient rehabilitation (mean 3.1). A significantly higher FECQ-TBI total score was reported in the acute phase compared with the rehabilitation phase ($p < 0.05$). Poorer experiences in some scales ($p < 0.05$) were found in family members of patients with moderate disability and patients discharged to non-specialized rehabilitation pathway. Lowest score (mean 2.3) of all FECQ-TBI items was found regarding "economical needs" (77 % poor experience) followed by an item on "the long-term consequences of TBI" with a mean of 3.0 (60 % poor experience).

Conclusions: Better care experiences were reported in the acute phase compared with the rehabilitation phase. The poorest care experience was seen in the discharge phase. Patient's dependency level and transferral to non-specialized rehabilitation pathway were predictors of a poor care experience. By understanding family members' experiences of health care, particularly within the rehabilitation field, this study may direct health care providers to improve future health care delivery provided to family members and individuals with severe TBI.

Neurocognitive and Neuroaffective Profiles of Young Adult Offenders with Self-Reported Traumatic Brain Injury

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Background and Rationale: High prevalence of TBI has been reported in those involved with the criminal justice system, which has been associated with higher rates of recidivism, increased violence in offending, earlier age of first offending and greater numbers of infractions. A causal association of TBI has been suggested, and this may be attributable in part to consequences of injury. We investigated the neuroaffective and neurocognitive profiles of young offenders with a 'substantial dosage' of self-reported TBI to examine whether there is evidence to support this, with a primary focus on facial affect recognition.

The findings from two studies will be presented, one conducted in a sample of adolescents with offending behaviour in a rural community setting (n = 35) and one conducted with young adults with offending behaviour in an urban community setting (n = 89).

Methodology: Both studies used a semi-structured questionnaire to derive self-reported histories of injury and post-concussion symptomology and investigated performance on a novel facial affect recognition task. Criminal histories were recorded, and a neuropsychology assessment was completed. The second study included a more comprehensive assessment battery, using Cantab Research Suite assessment, mental health and substance use screens and measures of aggression, personality traits and early life trauma.

Results: High prevalence of lifetime head injury was reported in both samples (relative to estimated general population prevalence), with a substantial proportion of injuries involving a loss of consciousness (LoC) and injuries classified as 'severe' (with a reported LoC elapsing 60 minutes) in the adolescent sample. Self-reported post-concussion symptomology was higher among those with substantial injury relative to those with no or minor injury, for both offender samples. There was no evidence for impairment in neurocognitive measures or differences in criminal profiles for those with injury in the adolescent sample or the young adult sample, with the exception of one attentional demand measure. Interestingly, an impairment in affect recognition was observed in the young offender sample, with no evidence of this association in the young adult offender sample. There were, however, differences observed in self-report measures for psychopathy and alexithymia.

Conclusion: High levels of self-reported TBI have been identified in both adolescent and young adult community offending samples, associated with increased TBI sequela. Our data do not suggest differential neurocognitive profiles in those with substantial injury versus those without, with the exception of affect recognition impairment in the adolescent sample. However, there are indications of differences in affective self-report measures, which may tap into more complex constructs than the neuropsychology tests used. We discuss reasons why the differences observed in affect recognition may have arisen including participant age, environment and task parameters.

Late Recovery of Responsivity after Intra-thecal Baclofen Pump Implantation: The Case of Alexandru

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Introduction: Patients with severe brain injury and prolonged disorder of consciousness (DoC) may present with severe spasticity and diffuse pain, which might impair any motor output, thus impeding any possible behavioral responsivity.

For these persons the definition of functional locked-in has been proposed (Bruno et al., 2001, Formisano et al., 2011; 2013).

Case Report: A 26 year old young man was affected by fronto-parietal hemorrhage due to the rupture of an arteriovenous malformation, neurosurgical interventions consisted of hematoma evacuation and decompressive craniectomy on April 13th 2015; coma persisted for 1 month and cranioplasty and ventriculo-peritoneal shunting (Hakim at 170 mm H₂O rate) because of secondary hydrocephalus was performed on August 7th 2015.

The diagnosis at admission to our post-acute rehabilitation (September 2015) was of vegetative state/unresponsive wakefulness syndrome (VS/UWS) according to Coma Recovery Scale Revised (CRS-R=6) (Giacino et al., 2004).

CT scan at admission (cerebral MRI was incompatible with the muscular spasms and crying episodes and the presence of ventriculo-peritoneal shunting) showed the sequelae of cranioplasty and ventriculo-peritoneal shunting; left fronto-parieto-temporo-ventricular bilateral frontal and right cerebral peduncle hypodensities, associated with moderate cortical and subcortical atrophy.

The patient was admitted to our Post-Coma Rehabilitation Unit around 5 months after the acute event and presented with severe spastic quadriplegia and sub-continuous crying, likely because of diffuse and intensive pain. This latter symptomatology and the presence of the ventriculo-peritoneal shunting did not lead the diagnostic support of neuroimaging and neurophysiological advanced techniques.

At the same time the pharmacological therapy with oral anti-spastic drugs, pain killers, Gaba-ergic drugs and benzodiazepines was of no efficacy, as well as the rehabilitation treatment. The implantation of intra-thecal baclofen pump 14 months after the acute event, even at low rate dosage (60 µg/daily) dramatically improved the behavioral responsivity of the patient (CRS=12), with intentional motor responses at the upper and lower left limbs and functional communication recovery by means of the eyelids closure and limbs movements, together with a significant reduction of the crying episodes. Video recordings before and after baclofen pump implantation are available.

Discussion: The high misdiagnosis rate up to 40% of the prolonged DoC (Schnakers et al., 2009) may be caused by several factors, such as severe motor impairment, often associated with intractable spasticity, not responsive to common pharmacological treatment. Before a definitive diagnosis of chronic VS/UWS interfering factors should be taken into account.

International Academy of Hope: A Proposed Model for the Education and Rehabilitation of Children with Acquired Brain Injury

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Severe brain injuries, especially those acquired early in life, produce challenges that face the individual, family, friends, and the larger community. These challenges are multifaceted and require the involvement of a team of caregivers who are committed to understanding the complexities of the child¹. However, the literature is replete with discussions about the paucity of services and interventions for children with severe disabilities due to brain injury².

This presentation is designed to describe an innovative program that provides integrated educational and rehabilitative services to children with acquired brain injury: The International Academy of Hope. This private school model provides rehabilitative and medical services that extend beyond those provided in traditional public, private, or charter schools. Occupational therapy, physical therapy, and speech and language therapy, are a part of every child's school day, always in one hour blocks of time to accommodate the children's need for greater response time, recovery time, proper positioning, and transfers. Often therapy is provided 5 days/week; this level of intensity is similar to an acute rehabilitation setting. In addition to these services, vision services are provided to those who require it. The school also provides one-to-one teaching with the classroom teacher, conductive education (based on the Hungarian model developed by Andras Peto), hearing education, nursing care, and one-to-one paraprofessionals assigned to each student. The school runs on an extended day which allows children to get all the services that they require each school day. It also eliminates the need for parents to find after school care which decreases the stress and expense that parents may experience trying to find adequate care.

This presentation will include a description of our interdisciplinary model of service delivery as well as our evaluation process. We will discuss program development and the evolution of our school from six to 51 children in three years. We will address the deficiencies in the current system in the United States and discuss how our program bridges the gap in services and how we have attempted to respond to the recommendations made by the children's special interest group meetings of the International Brain Injury Association that have been summarized in the recent article by McKinlay et al. (2016)².

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Family as a Resource for Improved Patient and Family Functioning After Traumatic Brain Injury. A Randomized Controlled Trial of a Family Intervention – Protocol and Pilot Study

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Objectives: To test and describe a family centered rehabilitation intervention in families with traumatic brain injuries (TBI) developed to improve family functioning and dynamics and to help family members and the family as a whole to overcome the challenges they are facing in daily life.

Methods: A pilot study comprising two families, six people, related to an RCT to be performed at Oslo University Hospital (OUH), Norway. The pilot study is conducted from October- December 2016 in close collaboration with the municipal health care service.

The registration in Clinicaltrials.gov is in process, and the registration number will be provided. Inclusion criteria: Home dwelling individuals with TBI, with a Mini-Mental State Examination >23 points who have been at home for 6-18 months after primary rehabilitation, and their family members. 66 patients between 18 and 65 years and family members between 16-65 years will be included. In arm 1 which is tested in the pilot study, the participants will receive a multi-professional theoretically based family centered rehabilitation program, Traumatic Brain Injury Family System Intervention (TBIFSI). This intervention consists of 8 weekly 90 minutes session. Participants in arm 2 will receive treatment as usual defined as an individually tailored multidisciplinary approach. Family members will attend one ongoing psychoeducational session of 2.5 hours provided at OUH. The injury-related data of the patient will be collected from the medical records whereas different self-report questionnaires will be applied for all participants at baseline, after 8 weeks and 6 months after completion of the intervention. The primary outcome measures are the SF-36 Mental Component Summary and perceived caregiver burden using the Caregiver Burden Scale (CBS). Secondary measures are Quality of Life after Brain Injury (QOLIBRI) and family dynamics using FACES IV. Other measures are Resilience Scale for Adults (RSA), The TBI-Self Efficacy Scale, Patients Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7).

Results: Results from the pilot study testing the intervention on two families will be presented regarding the process of intervention and change in family functioning from baseline and after the 8 weeks intervention. The feasibility of the intervention will be discussed.

Conclusion: The conclusion will pertain to the observed changes in family functioning and the feasibility of the intervention.

Multi-Centric Longitudinal Study on Behavioral and Electrophysiological Diagnostic and Prognostic Markers in Prolonged Disorder of Consciousness “Report of the International Brain Injury Association, Disorders of Consciousness Special Interest Group”

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Background: Management and care of patients with prolonged disorders of consciousness (DOC) has clinical, economic and ethical implications. A better understanding of DOC patients' outcome and the identification of reliable prognostic markers would allow clinicians and patients' relatives to make appropriate decisions concerning treatment and care. To date, the majority of prognostic markers for DOC patients are collected in relation to outcome within one year. Reliable prognostic markers for patients who will experience a late recovery have not been identified yet. In addition, prognostic information for minimally conscious state (MCS) patients is lacking. The IBIA DOC-SIG diagnosis/prognosis subgroup therefore proposed an international multicentric project on a large group of prolonged DOC patients.

Material and Methods: Subjects: patients in a Vegetative State/Unresponsive Wakefulness Syndrome (VS/UWS) and in a MCS will be recruited in the post-acute phase, consecutively admitted to ICU and neurorehabilitation units within 3 months post injury. Etiologies such as traumatic, vascular or anoxic brain injuries will be included.

Procedure: We will collect information from: 1) medical history (such as aetiology, in- or out-of-hospital resuscitation setting), 2) patients' clinical condition at study entry [level of consciousness measured by the Coma Recovery Scale – Revised (CRS-R), and level of disability assessed by the Disability Rating Scale (DRS)], 3) neurophysiological findings [standard EEG resting state and EEG reactivity, and various evoked potentials such as somatosensory, mismatch negativity, or P3] and 4) neuroimaging exams (e.g. MRI or PET-scan).

All enrolled DOC patients will be clinically followed for short-term outcome (until discharge and 6 months post onset) as well as for long-term outcome (12 and 24 months post injury).

A detailed version of the project, already approved by ethical committee, has been posted to the LISTSERV platform of the DOC SIG (<http://groupspaces.com/IBIADOC/SIG/>), in order to discuss the methodology of the study and to promote further consensus among DOC-SIG members before enrollment begins on December 1st 2016.

The Hull-Ellis Concussion and Research Rapid Access Clinic: Preliminary Analysis of Balance Recovery Using Symptom, Observational and Posturographic Measures

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Introduction: Although much sport-related concussion research exists, there is a lack of research relevant to individuals with acute concussion among the general public. In response, the Hull-Ellis Concussion and Research Rapid Access Clinic at the Toronto Rehabilitation Institute was developed to prospectively understand and characterize the trajectory of recovery related to concussion among the general population, while simultaneously providing routine medical care, monitoring and follow-up. Balance impairments post-concussion are common and clinical practice guidelines recommend screening for balance dysfunction¹. The purpose of the present study was to characterize balance impairments and recovery across symptom-based, observational and posturographic measures among the general population with concussion.

Methods: Patients were referred to the Clinic within 72 hours of Emergency Room visit and admitted within one week. Each patient received physician care and was additionally approached to participate in a prospective research study, collecting data specific to balance, cognition, psychosocial variables and symptoms, outwards to 16 weeks post-concussion. Participants with complete balance-related data at Weeks 1, 2, 4 and 8 were included. Symptom Evaluation Severity (SCAT3 – balance; /6), BESS (Balance Error Scoring System) total score (/60), and centre-of-pressure root mean square and velocity (anteroposterior and mediolateral) during 45 seconds of quiet standing with eyes open and closed on force plates characterized self-perceived, observer, and posturographic measures of balance, respectively. Mean (SD) or median (range; SCAT3-balance) were used to describe central tendencies. The proportion of participants at each time point exceeding the 95% confidence limit of age-matched healthy reference values^{2,3,4} for each outcome were determined.

Results: Fifteen participants were included in the analysis (10 female). Mean age was 34.6(13.8) years. Across time points, median SCAT3-balance severity was 1(0-3), 0(0-4), 0(0-5) and 0(0-5); proportionately, 53%, 47%, 23% and 13% of participants reported balance problems. At Weeks 1, 2, 4 and 8, mean BESS scores were 19.6(9.2), 19.0(10.0), 18.6(9.4) and 16.3(8.4). In parallel, the proportions of participants with BESS scores exceeding reference values were 80%, 73%, 67% and 53%. Across all posturographic measures, 20-53%, 13-60%, 13-47% and 13-67% of individuals, at Weeks 1, 2, 4 and 8, respectively, fell outside of reference values.

Discussion: The Clinic model enabled collection of balance related-data in the general population over the first 8 weeks of recovery post-concussion. The number of individuals self-reporting balance problems reduced over time; whereas, BESS and posturographic data identified the persistence of balance

impairment 8 weeks post-injury. These preliminary results differ from existing knowledge related to balance impairment and recovery after sport-related concussion. Data collection and analyses are ongoing.

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Improving Paediatric Concussion Care through Knowledge Translation and Confidence Building in Paediatric Emergency Room Nurses

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Background: Paediatric concussion is a growing international health concern. By 10 years of age, one in five children have had at least 1 head injury requiring medical attention. An estimated 750 000 children are seen in the emergency department (ED) annually in the United States. Teaching and resources in the ED are imperative. Despite the vast amount of concussion research and literature available, a lack of consistency in concussion teaching and resources leaves patients and families questioning what advice to follow and where to go for accurate information. A knowledge translation gap exists in frontline healthcare staff, specifically, paediatric emergency room nurses. Nurses are key providers in assessing symptoms and providing education about mild traumatic brain injury in children, however they may experience a lack of knowledge about and confidence in this area.

The goal of this project is to assess knowledge gaps and equip paediatric emergency room nurses with consistent, up-to-date concussion teaching and resources, thereby ensuring all families at the Alberta Children's Hospital emergency department receive consistent, accurate post-concussion teaching.

Methods: All emergency room nurses at the Alberta Children's Hospital were surveyed prior to a teaching session on ED concussion education. Nurses complete bi-annual education days and this presentation was a component of their mandatory education. 10 questions assessed nurses' confidence in recognizing, treating, and educating patients and families experiencing concussion. Resources were handed out to emphasize what all families should receive during their emergency visit.

Results: 117 nurses completed the pre-survey prior to the teaching session. Over the next few weeks the one month post teaching session survey is being sent to all nurses. This survey assesses confidence level one month later, how often resources are being handed out, and how valid the nurses felt the session was. Following survey retrieval, post survey data will be analyzed, comparing pre and post survey results and assessing the impact the teaching presentation had on nursing practice. Problems encountered and proffered solutions will be summarized. Qualitative analyses will focus on subjective themes the nurses identified as gaps and look at implementing suggestions for the department.

Conclusion: The project is in progress. Feedback from an emergency nursing perspective shows an overwhelming positivity on relevance and length of teaching session.

Effect of Peroneal Nerve Functional Electrical Stimulation on Gait in Post-Stroke Patients: Community-Based Vs. Outpatient Approach

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Background: Peroneal nerve functional electrical stimulation (FES) can be used in stroke patients with drop foot syndrome as an alternative to ankle-foot orthoses. Its main advantage is facilitation of active dorsal flexion of the foot during the swing phase of gait. Evidence supports its “orthotic” effects, which include increased gait speed, gait symmetry, stability and reduced energy cost. Further “therapeutic” effects of intense FES are expected, even when the stimulator is off – namely restoration of lost motor function and walking ability improvement resulting from neuroplastic changes. Majority of the studies suggests daily, community-based stimulation, which is not always feasible, as cost and lack of insurance coverage can be prohibitive. In current practice, FES mostly takes place at specialized outpatient medical facilities. Therefore the purpose of this study is to examine, whether both approaches can be comparatively effective.

Aims: To test whether the effect of peroneal nerve functional electrical stimulation on gait is not unacceptably less efficacious when used within intense outpatient therapeutic sessions at specialized medical facility than on daylong community-based ambulation basis.

Methods: A parallel group randomised non-inferiority trial. Individuals at least 6 months poststroke were randomised to group A (n=13; daylong community-based ambulation with FES) or group B (n=17; daily outpatient intense and dose-matched gait training sessions with FES at specialized medical facility). Outcomes including functional gait measurements (Emory Functional Ambulation Profile, 2MWT) and Gracies examination of spastic paresis were assessed in both groups after 4 weeks of intervention.

Results: 27 patients (nA=13; nB=14) finished the study. The results are processed statistically for non-inferiority of group B approach and will be available at the time of poster presentation.

The study was supported by the Charles University in Prague, project GA UK No 940214.

Selegiline in Patients with Minimally Conscious State: Preliminary Data of an Open Monocentric Pilot Study

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Introduction: Dopaminergic drugs (i.e. amantadine) seem to promote clinical recovery in patients with disorder of consciousness (DOC) [1,2], but might show severe side effects (e.g. seizure and QT enlargement). Selegiline, a selective monoamine oxidase type B inhibitor used to activate dopaminergic system in early Parkinson's disease [3], is usually well tolerated. Selegiline can also improve cognitive performance in patients with traumatic brain injury [4,5]. We aimed at evaluating effectiveness of selegiline administration in patients in stabilized and prolonged clinical condition of Minimally Conscious State (MCS).

Materials and Methods: Subjects. Four patients in a MCS (2 females; mean age: 41±23.6 years; 3 with vascular and 1 with post-anoxic etiology; mean time post-onset: 11±2.4 months); 2 patients were in MCS Plus(MCS+) and two in MCS Minus (MCS-) status.

Procedure: Treatment protocol: selegiline 5 mg/day for 1 week, followed by selegiline 10 mg/day for 8 weeks. Clinical evaluation (by Coma Recovery Scale Revised, CRS-R and Disability Rating Scale, DRS) was performed at baseline, once a week during the treatment, and once a week for one month after end of treatment.

Results: No side effects were observed. We found relevant clinical improvements in 3/4 patients after 19,25 ±19,3 days of 10 mg Selegiline administration. The two vascular MCS- patients (case 1, CRS-R= 9, DRS= 18 and case 2, CRS-R= 9, DRS= 18) improved to MCS+ (CRS-R= 15; DRS= 13 and CRS-R= 15; DRS= 15 respectively). Case 3 (vascular MCS+, CRS-R= 9; DRS= 20) recovered functional communication, meeting criteria for emergence from MCS (CRS-R= 17; DRS= 12). The clinical improvement persisted during entire period of Selegiline administration and in the one-month follow-up.

Conclusions: Despite the very small sample, these preliminary results suggest that Selegiline might promote clinical recovery in brain injured patients in prolonged stabilized non-traumatic MCS. Controlled trials are necessary to confirm the positive effect of Selegiline in improving state of consciousness and reducing the level of disability.

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Community-Based Rehabilitation System for People with Acquired Brain Injury in The Czech Republic (From the Point of View of Occupational Therapist)

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Objectives: Institutional care in the Czech Republic has still very strong position. There is lack of systemic and organizational solutions of community rehabilitation for people with acquired brain injury (ABI). Facilitators are reimbursed from four sources: 1) Health insurance companies, 2) Long term social support and services, 3) Long term support in school system for students with special needs, 4) Prevocational and vocational rehabilitation, support for employees with disabilities. Community rehabilitation obtains outpatient department, daily center for patients with ABI and visiting services at home (occupational therapists (OT), physiotherapists (PT), speech therapists etc.). Outpatient services are sufficient. There is lack of visiting home service and only one daily center at the Department of Rehabilitation Medicine in Prague Charles University, The First Faculty of Medicine.

Process and Methods: We are establishing the system based on interprofessional cooperation, especially physician, OT, PT and social worker. There is a key role of OT in linking social and health components, because of ADL and evaluation of the flat/house and indication of facilitators. We have created project, "Coordinated rehabilitation for people with acquired brain injury", granted by the Grant Agency of University of South Bohemia in Ceske Budejovice (abbr. GAJU, Grant No. 138/2016/S). It contains 30 case studies of people with ABI, providing 3-months community interprofessional intervention. Objective methods of respondents functional evaluation are International Classification of Functioning, Disability and Health (ICF, WHO, 2001) and Functional Independence Measure (FIM system[®] Version 5.2, Uniform Data System for Medical Rehabilitation). Respondent subjective status is assessed by using World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0).

Expected Main Results: Methodical handbook of home/flat evaluation, methodical manual of community based occupational therapy for people with ABI, educational material for people with ABI for better orientation in systems of health and social services and facilitators (especially compensatory aids). The aim of the project is to determine the quality of life of people with ABI and to describe interprofessional collaborative practice in coordinated community-based rehabilitation.

Conclusions: Collected data of the project should be the basis for implementation coordinated community-based rehabilitation for people with ABI, including definition of OT, PT and social worker roles (enhanced by results of the project in the form of methodical manuals for these professionals). Identifying facilitators (according ICF), analysis of environmental factors and providing social community based rehabilitation can help people to improve their independent way of life in community.

The Role of Neurotrophic Factors in the Ultrastructural Preservation of Neuron-Glial Network Under the Influence of Stress-Factors

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The search for a new neuroprotective substances is one of the most topical issues in neuroscience. Neurotrophins are important regulatory proteins which are playing a key role in the functioning of central nervous system and can be used for the development of new therapeutic strategies for brain cells protection to hypoxic damage. However, the questions concerning the neuroprotective mechanisms of neurotrophins remain unclear. The aim of the investigation was to study the antihypoxic and neuroprotective properties of BDNF and GDNF at the ultrastructural level under hypoxic condition in vitro.

The ultrastructural characteristics of intercellular contacts in the neuronal network of embryonic hippocampal dissociated culture (E18) were performed on day 14 in vitro. Hypoxia model was carried out according to the previously developed protocol by replacing the normoxic cultural medium with a medium containing low oxygen for 10 min. Ultrastructural analysis was conducted 24 hours after reoxygenation.

Hypoxia causes a decrease in the number of mature synaptic contacts and dendritic spines as well as negation of mixed contacts typical for this stage of culture development. We observed a significant decrease in the number of symmetric synapses compared to the control group. Mitochondrias in the most cases had normal morphology in the medium-sized dendrites and axons. However, in large dendrites and cells bodies mass destructive damages were found. There were various forms of swelling, violation in cristae spatial organization, enlightenment of matrix, a large number of watered mitochondria and myelin-likes structures. Preventive application of GDNF (1 ng/ml) almost completely preserved the structure of synapses, glial contacts and dendritic spines, but did not protect from ultrastructure changes in mitochondrias. On the other hand, the morphological structure of mitochondrias in neural processes in cultures with BDNF injection was comparable to the control group. In the cell bodies the changes in the spatial organization of cristae were observed. The number of synaptic contacts were significantly ($p < 0.05$) lower than in cultures with GDNF application, but higher than in "Hypoxia" group.

Thus, antihypoxic and neuroprotective properties of GDNF and BDNF at the ultrastructural level were confirmed. We identified the differences in BDNF and GDNF effects on the ultrastructure of neurons, glial cells and intracellular contacts.

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Intensive Interdisciplinary Rehabilitation in a Post-Acute Brain Injury School Produces Positive Functional Outcomes

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The effectiveness of interdisciplinary rehabilitation has been shown to improve functional outcomes in adults with Acquired Brain Injury¹. Late onset rehabilitation has shown improved gains in functional mobility for both adults and children². No study has examined the effects of increased interdisciplinary therapeutic intensity in a school setting for children with brain injury. We hypothesized that interdisciplinary and intense rehabilitation in an academic setting can improve mobility, communication, cognitive functioning, and health-based outcomes for students with severe disability as a result of acquired brain injury.

This poster will present the results of a retrospective review of students with chronic brain injury (greater than 3 years post insult). Outcome measures include Cortical Visual Impairment Range (CVI Range), Preschool Language Scale-5 (PLS), Brigance Inventory of Early Development III (IED III), Pediatric Evaluation of Disability Inventory (PEDI), attendance records, health records, and parent satisfaction.

Preliminary results support our hypothesis. There was a statistically significant improvement in CVI Range as well as the Social Functioning domain of the PEDI. Improvement in overall communication performance as indicated by the PLS and IED III. Intensive interdisciplinary rehabilitation in the school setting facilitates positive functional change in children with severe disabilities due to brain injury. These results will be updated with the latest data. Research comparing traditional post-acute care to an interdisciplinary intensive educational environment is needed.

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Cognitive Recovery Trajectories Over the First 5 Years Following Moderate to Severe Traumatic Brain Injury

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Objective: The existence of persistent cognitive impairments after moderate to severe traumatic brain injury (TBI) is well known. Most research has focused on cognitive recovery in the first year following TBI but the long-term recovery is less well documented. This study aimed to examine trajectories and predictors of cognitive recovery over the first 5 years following moderate to severe TBI. A hierarchical linear model (HLM) examined cognitive domains over 3 months, 1, and 5 years post-TBI using time, age, gender, education, employment pre-injury, severity of injury (GCS scores), post-traumatic amnesia (PTA), Abbreviated Injury Scale (AIShead), and Glasgow Outcome Scale-Extended (GOSE) to predict cognitive recovery trajectories.

Methods: A longitudinal prospective study to follow up 77 patients (23% female) with moderate (39%) or severe (61%) TBI. Patients were admitted to the Norway's largest trauma referral center, Oslo University Hospital, and enrolled in the initial study from May 2005 to May 2007. Socio-demographic and injury characteristics were assessed at the acute hospitalization. Thirteen neuropsychological tests within memory, processing speed, verbal fluency, and reasoning were administered at 3 months, 1 and 5 years post-injury.

Results: Three cognitive domains were derived by factor analysis: Verbal Memory/Speed; Fluency/Reasoning; and Visual Memory/Planning. A summary T-score was calculated for each domain and entered as the dependent variable into the HLM. Results showed significant cognitive recovery over time for all three domains ($p < .001$). The greatest cognitive recovery occurred between 3 months and 1 year, with recovery stabilizing at 1 year. The Verbal Memory/Speed domain was most affected. Predictors significantly associated with poorer cognitive recovery included: lower education, unemployment at injury, female gender, greater length of PTA, and lower functional levels (GOSE) at 3 months. Those with lower education had poorer recovery over time in the Fluency/Reasoning domain ($p < .001$). Those who were unemployed pre-injury had poorer recovery in the Verbal Memory/Speed ($p < .01$) and Visual Memory/Planning ($p < .05$) domains. Females had lower scores within the Visual Memory/Planning domain ($p < .01$). Those with greater length of PTA had worse recovery on both Memory domains ($ps < .01$). Those with lower functional outcomes had poorer recovery on Verbal Memory/Speed and Fluency/Reasoning domains ($ps < .05$). Neither age, injury severity group (moderate vs. severe TBI), nor the AIShead were associated with cognitive recovery trajectories.

Conclusions: Cognitive recovery was greatest during the first year and remained stable between 1 and 5 years post-TBI. Recovery appeared to be similar for both the TBI groups. Preexisting and injury-related factors played different roles in the longitudinal cognitive recovery over the first 5 years. Employment pre-injury and PTA were associated with domains of memory, and education with verbal and reasoning abilities. Those being unemployed pre-injury and having longer duration of PTA might require greater length of stay in specialized brain injury rehabilitation units.

Transcranial Direct Current Stimulation in Prolonged Disorders of Consciousness: A Randomized Controlled Pilot Study

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Objective: In last years, transcranial direct current stimulation (tDCS) has been proposed as a novel non-invasive therapeutic approach modulating activity of cortical networks in patients with disorder of consciousness [1,2], but no study reported a systematic follow-up of patients' conditions over the weeks after stimulation. This randomized sham-controlled double-blind crossover, single-centre pilot study aimed at: 1) evaluating the effects of a series of five tDCS stimulation sessions (run on consecutive days) on clinical status and EEG background activity in patients with prolonged DOC; 2) ascertaining whether specific patients' characteristics, clinical conditions and EEG features at baseline are associated with positive response to the tDCS stimulation.

Methods: Seven patients in vegetative state (VS) and 6 in minimally conscious state (MCS), at ≥ 3 months after brain injury, were randomized into two groups: group 1 received one week of active tDCS and 1 week of sham stimulation, separated by 1 resting week; in group 2 the order of active and sham stimulation was reversed. We performed clinical and EEG evaluations before and after the first stimulation session, two hours after the last weekly stimulation, twice during the resting week, and during a 3-month follow-up.

Results: We observed small changes of patients' conditions after the first tDCS session and immediately after the 5 active stimulations. Substantial clinical and EEG changes were observed in 5/13 patients (3 in MCS and 2 in VS) starting 2-4 weeks after active tDCS and further progressing during the next months. No baseline features distinguished "responders" from "non-responders" significantly.

Conclusions. tDCS might exert a long-term positive effect on clinical recovery in brain-injured patients with prolonged MCS and VS, and could represent a useful adjuvant strategy in neurorehabilitation.

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Implications of Key Differences in Military and Civilian TBI Cohorts Admitted for Inpatient Rehabilitation: A VA and NIDILRR TBI Model System Study

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Objective: The Traumatic Brain Injury Model Systems (TBIMS) was established in 1987 among civilian hospitals, with a parallel database established in 2008 within Veterans Affairs (VA). The civilian and VA TBIMS databases may offer a comprehensive perspective of TBI in the U.S. across private and federal health care systems. Greater understanding of the comparability between these databases is needed to inform if unique TBI sequelae exist for military and Veteran cohorts. This study compared the characteristics of civilian and VA TBIMS participants.

Methods: The sample included 550 VA and 5,270 civilian TBIMS participants enrolled between 8/1/2009 and 7/31/2015. The two groups were compared on pre-injury demographics, socioeconomic factors, military history variables, pre-injury mental health treatment and substance use, injury characteristics, and rehabilitation treatment variables. Comparisons across these variables were also made within injury etiology sub-groups.

Results: Compared to civilians, the VA sample was younger ($p < 0.001$), had a greater majority of male participants ($p < 0.001$), had fewer Black/African American participants ($p < 0.001$), obtained higher education levels ($p < 0.001$), and had a greater proportion of participants employed/in school ($p < 0.001$). Violent injury mechanism was more common in the VA cohort, while falls were more common for civilians. Prior to injury, more VA participants had utilized mental health services ($p < 0.001$), but more civilians used illicit or non-prescription drugs ($p < 0.001$). VA participants were more severely injured, as evidenced by lower GCS ($p < 0.001$), more abnormal neuroimaging ($p < 0.001$), and longer time spent in posttraumatic amnesia ($p = 0.008$). VA participants took longer to get to inpatient rehabilitation ($p < 0.001$), had longer acute ($p < 0.001$) and rehabilitation ($p < 0.001$) lengths of stay, and were admitted and discharged with higher motor and cognitive FIM scores ($p < 0.001$) and lower DRS scores ($p < 0.001$). A slightly larger proportion of VA participants died during hospitalization ($p = 0.007$). Notably, 13% of civilian participants had served in the military.

Comparisons by TBI etiology subgroup revealed that VA participants were younger than civilians in the Falls ($p < 0.001$) and Violence ($p < 0.001$) groups. Regardless of injury etiology, the VA cohort consistently showed longer time to rehabilitation admission, longer rehabilitation length of stay, and higher admission and discharge functional scores. Within the MVA and Falls groups, VA participants had lower GCS ($p < 0.05$, $p < 0.05$ respectively), and longer duration of posttraumatic amnesia ($p < 0.001$); however, in the Violence subgroup there were no differences between VA and civilian participants regarding GCS but VA participants had shorter PTA duration.

Conclusions: The VA and civilian TBIMS participants are considerably different, making direct comparison of the cohorts difficult. Differences in injury characteristics and rehabilitation variables likely reflect unique aspects of military injury and pathways to care. Implications for health services research of VA participants across civilian and military/VA settings will be described.

Outcomes, Supports and Barriers Related to Intensive Exercise Participation for Adults with Chronic Moderate to Severe Acquired Brain Injury

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Background and Purpose: Effects of high-intensity group exercise on the endurance, advanced mobility, and gait speed of adults with chronic severe acquired brain injury (ABI) living in brain injury group homes were investigated. In a subsequent qualitative study, supports and barriers related to participation in exercise from the perspectives of participants, residential staff and family members were investigated.

Participants: Fourteen adults with chronic severe ABI in supported independent living who could stand with minimal or no assist and walk with or without ambulation device were studied. Initially, eight presented with low ambulatory status, six with high ambulatory status. Interviews were conducted with all 14 intervention subjects, one person who dropped out, four family members and four residential staff.

Methods: Participants received a 6-week high-intensity exercise group intervention for 60-90 minutes, 3 days per week assisted by personal trainers under physical therapist supervision. Measures (6 Minute Walk Test, High-level Mobility Assessment Tool, and 10 Meter Walk Test) were collected at baseline, post-intervention, and 6 weeks later. Analysis included repeated measures T test and the Wilcoxon Signed Ranks Test. The qualitative study involved a brief survey and semi-structured interviews, conducted 2-6 months after the intervention, audio recorded and transcribed verbatim. Analysis used pre-existing and emerging codes (concepts), and data were double coded using qualitative data analysis software (atlas.ti).

Results: Significant post-intervention group improvements were achieved on all three outcome measures (6 MWT, HiMAT, and 10MWT) and greater than the minimal detectable change (MDC) for this population. 10MWT outcomes indicate that three participants transitioned from low to high ambulatory status and maintained the change six weeks later. Qualitative findings identified environmental and personal barriers and supports. Environmental barriers to participation included transportation (inconsistent, delayed), group format (not always person-centered), and negative family attitudes towards programming developed in-house. Personal barriers to participation were physical (vision, balance, incontinence), cognitive (memory, executive function, lack of self-awareness), behavioral (anxiety), and tendency toward a sedentary lifestyle (watching television). Environmental barriers to being physically active between exercise sessions included: staff fear for participant safety, broken equipment, and lack of access to supportive affordable fitness opportunities for this population. Environmental and personal supports for participation included enthusiasm of trainers, group format (encouraged mutual support), investments in transportation, pre-injury participation in sports, and motivation to do something meaningful that involved interacting with others.

Discussion and Conclusion: People living with chronic ABI can improve endurance, demonstrate ability to do advanced gait, and improve ambulatory status with six weeks of intensive exercise. Challenges to sustainability of exercise programs for people with chronic severe ABI include costs and transportation.

Efforts to support better lifestyle choices (improved nutritional choices, increased physical activity between sessions) are needed to enhance functional benefits of the intervention.

mTBI Telehealth in Europe: Meeting the Geographic Challenges with Innovative Technology and Treatment

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Background: This presentation outlines a performance improvement project highlighting the results of a multidisciplinary outcomes project in which innovative telehealth technology facilitated improved identification, evaluation and assessment of mTBI for a geographically dispersed patient community. Concussion or mild traumatic brain injury (mTBI), is a pernicious problem in both the civilian and military sectors of society affecting an estimated 823.7 per 100,000 annually in the U.S. civilian population 1 and over 352,000 in the U.S. Armed Forces between 2000 and 2015, with mild traumatic brain injury (mTBI) affecting over 82% of those military members injured.² Concussion is a highly prevalent and under-recognized condition.³ The estimated economic cost of TBI in 2010, including direct and indirect medical cost, is estimated to be approximately \$76.5 billion.⁴ While most symptom sequelae from mTBI resolves quickly, the condition in the military remains significantly under reported, unrecognized and untreated. Landstuhl Regional Medical Center serves geographically dispersed active duty personnel, their families, dependents, retirees, civilian support personnel as well as contractors. Therefore, developing a technological interface where patients can self-direct their care through telehealth builds responsive, innovative medical care across Europe.

Methods: An analysis of telehealth encounters for mTBI patients demonstrated an effective and innovative way to capture assessment metrics and facilitate treatment as well as rehabilitation outcomes for patients participating in multi-disciplinary mTBI care needs. While mTBI specialty care providers are located throughout Europe, focus is on a revolutionary change to both the technology platform and the policies that support medical readiness. A subjective review of provider feedback demonstrated not only ease of use, but the ability to minimize time away from military duties and facilitate return to duty.

Results: Record reviews indicate improved medical readiness and improved cost savings to telehealth implementation. Results were matched in a Chi-square analysis to correlate patient perceived benefit to provider perceived effectiveness. The statistical significance level was set at $P < 0.05$. The record review revealed that patients valued the efficiency and personalization of the telehealth platform and found the encounters comparable to an in-clinic visit noting that the responsiveness of the provider to their needs. Providers found the platform easy to deploy and efficient.

Conclusion: Technology offers a creative and responsive way to address this complex problem. By using this tele-health capability, medical providers can facilitate a more patient-centric and responsive medical treatment plan that potentially screens for and evaluates the possible impact of a concussive event in a very dynamic way. Use of tele-health for evaluation, assessment and treatment may also increase patient compliance in medical treatment as well as significantly personalize treatment for the patient in their own environment; given the facility with which tele-health can be deployed to meet patient care needs.

Training with Adaptive Body-Controlled Virtual Reality Following Acquired Brain Injury for Improving Executive Functions

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Background: Deficits in executive functions (EF) are common following traumatic brain injury (TBI). Computerized software for cognitive training is becoming more popular as a rehabilitation tool for TBI, however there is limited evidence that transfer of the improvements to real-life performance occurs. Cognitive training using motion-interaction software offers a training environment that is more realistic and natural, therefore may facilitate transfer to everyday-life performance. Cognitive software that adapts in real-time to the patient's behavior may potentially enhance usability by these individuals.

Objectives: The goal of this study was to assess the experience and safety of the training with dynamically-adaptive motion-interaction cognitive training software, and its potential benefits for improving EF following TBI.

Methods: Fourteen participants with moderate-severe TBI and EF deficits were recruited from an inpatient facility. Participants were randomly assigned to Intervention (n=8) or Control (n=6) group. Intervention included 10 computerized training sessions over 4-5 weeks using motion-based adaptive video games designed to train behavioral control, initiation, response inhibition, working memory, shifting, and attention. Control group played commercial iPad games for the same duration. Pre and post standardized assessments were conducted by a clinician blinded to the study arm, and included the Dysexecutive Questionnaire (DEX), Computerized Neuropsychological EF assessments (WebNeuro), functional EF assessments (EFPT), Functional Independence Measure (FIM), Trail Making Task (TMT), and a measure of dual task (Walking While Talking). Participants filled in a satisfaction questionnaire once they completed the intervention. Performance within the games was recorded throughout the training sessions.

Results: Preliminary results show that participants who performed the experimental intervention were gradually able to perform games involving higher EF challenge; also reflected by significantly higher performance levels in the last session than in the first session. Participants did not show adverse effects and reported enjoyment from the training. Preliminary analysis of the executive assessments shows a trend for larger improvement in EF in the intervention group than in the active control group following training.

Conclusions: The findings demonstrate the potential of using motion-based adaptive cognitive training with individuals with TBI. We are currently recruiting and training additional participants to assess the effectiveness of this training for improving EF in individuals TBI and the transfer of training into daily-life functioning.

Sensitivity and Responsiveness of Multi-Dimensional Outcome Measures After Mild TBI

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To improve research and clinical care in the field of traumatic brain injury (TBI) international observational and multi-center clinical trials are mandatory which aim at the inclusion of multidimensional outcomes with high psychometric quality. However, only few instruments have been translated and linguistically validated by accepted and comparable procedures. Center-TBI (www.center-tbi.eu) is the first study to simultaneously translate and linguistically validate open access CDE-recommended Patient-Rated Outcome (PRO) and Performance-Based Outcomes (PERBOS) into 18 European languages (English, Dutch, French, Danish, Finnish, German, Hungarian, Italian, Lithuanian, Norwegian, Romanian, Serbian, Slovakian, Spanish, Swedish, Russian, Hebrew, Arabic).

The Center TBI study aims to include 5000 patients with TBI. A selection of data on sensitivity and responsiveness from outcome assessments at 3 and 6 months after mild, moderate and severe TBI will be presented for the following PROs and constructs: amnesia (GOAT), post-concussion symptoms (RPQ), depression (PHQ), anxiety (GADS), posttraumatic stress disorder (PCL), functional recovery (GOSE), and TBI specific Quality of life after Brain Injury (QOLIBRI). Psychometric characteristics, sensitivity and responsiveness will also be reported for the following PERBOS assessing verbal memory (Rey Auditory Verbal Learning Test - RAVLT), and executive functions (Trail Making test - TMT).

The ability of the here presented tests and their translations to detect differences in outcome, e.g. concerning different grades of TBI severity and change over time, will be determined. This represents the first step in the development of a comprehensive yet short multidimensional outcome measurement system after TBI which will be internationally applicable to research, acute clinical and rehabilitation settings.

The Health System Benefit of Traumatic Brain Injury Care in Europe

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Background: Over the past decade, the U.S. Army has spent significant time and resources to better understand, identify, treat, and track Traumatic Brain Injury in Service Members and their beneficiaries. Recent efforts were initiated in 2007 after a TBI Task Force recommended that clinical capabilities be stood up across Army Medicine. The Army Medical Command implemented a strategy to promote education and training to increase early identification and treatment for those who have sustained a TBI. Across Europe, three clinics with specialty care capability were resourced with primary care, specialty, and rehabilitation providers, and an additional ten sites were identified as facilities where mild TBI could be managed on an outpatient basis. In this overview, we highlight the contributions of TBI funded providers at three Army specialty care clinic sites in Europe.

Methods: Education and training data was compiled by the Regional Nurse Educator. Workload and encounter data for fiscal years 2013 – 2016 were pulled for Army TBI-funded providers by name using Department of Defense systems (M2 database). Estimated costs for purchased care were provided by the Tricare Management System. Planned and executed TBI budgets were compared across specialty and by number of encounters.

Results: During fiscal year 2016, there were over 4000 individuals trained through face to face education and training from (November, 2015 – October 2016). Of these, 1854 service members were trained, 2559 continuing education hours were offered to TriService healthcare providers, 256 veterans, and 951 school beneficiaries were educated. In addition to face to face education, over 64,000 individuals were reached through media outlets and family groups.

A total of \$11.36M was budgeted for TBI specialty care in fiscal years 2013 – 2014 (\$7.05M at Landstuhl Regional Medical Center (LRMC), \$2.84M at Vilseck Army Health Clinic, and \$1.46M at Vicenza Army Health Clinic). During the same timeframe, the TBI specialty care providers saw a total of 43,637 encounters (21,995 of them with TBI diagnostic codes). A total of \$8.55M was obligated for TBI specialty care in fiscal years 2015 – 2016 (\$5.19M at LRMC, \$2.22M at Vilseck, \$1.14M at Vicenza). For the past two fiscal years, TBI specialty care providers saw a total of 38,840 encounters (19,460 of them with TBI diagnostic codes). Overall, providers earned a total of 119,922 relative value units during this time period. Interestingly, the costs from FY15 – 16 are 25% lower than those budgeted for FY13 - 14, while the number of encounters only decreased by 11%, perhaps indicating an increase in clinic efficiency across the three sites.

Conclusion: Providers and educators supported with specific Army Medicine TBI funds have provided significant contributions to the military health system in Europe.

Do Concussion Dosage, Gender or Reported Symptoms Affect Long-Term Cognitive Performance and Stop-Signal Reaction Times Following Sports-Related Concussion/MTBI In University Rugby Players?

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Objective: The longer-term cognitive effects of mild traumatic brain injury (MTBI) and sport-related concussion (SRC) are not always clear. Higher-level cognitive difficulties can indicate enduring neurological damage, as part of a post-concussion syndrome (PCS). This UK-based study aimed to investigate whether cognitive performance and self-reported PCS symptoms of athletes (university-level rugby players) relate to SRC, and whether gender moderates these effects.

Method: Eighty-six participants completed a questionnaire detailing SRC history (frequency and severity) and self-rated any enduring symptoms using the Sport Concussion Assessment Tool 3 (SCAT3) symptom evaluation scales, before completing the CogState Brief Battery and a stop-signal response inhibition task, "STOP-IT".

Results: No significant relationships were identified between historical SRC dosage (frequency or severity), self-reported PCS symptoms, and cognitive test performance. A greater proportion of males reported SRC compared to females, but no effect of gender was found on any of the cognitive outcome measures or self-reported PCS symptoms.

Conclusions: The results present evidence that SRC has no observable longer-term effects on cognitive test performance or PCS symptom self-reports in young adults. However, the analysis may have lacked power to detect small effects. Analysis of individual performance over time against baseline scores may be more relevant for accurate diagnosis than relying on normative test scores.

Mild TBI, Processing Speed and Age Considerations

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Mild TBI (mTBI) is often referred to as a young person's affliction, however many people in the older age ranges also experience TBI for various reasons (falls, MVA and other accidents). Research on the occurrence of TBI in older people have pointed out the resilience of older people in recovering from TBI. Some studies have indicated that although older people with TBI are resilient they seem to be hospitalized longer and recover over a longer period of time. This investigation examined 407 mTBI survivors and compared them to 209 non-injured controls on measures of processing speed, attention span, reasoning and reaction time. This investigation further divided both groups into age groups by decade beginning at adolescence to 70+ years-old. Statistical analyses indicated, as expected the mTBI group were significantly worse than normal controls on all measures 1 year following the injury. Analysis of the age factor indicated aging effects seem to be present for processing speed beginning in the 4th decade (40's). These effects became much more prominent in the 6th decade to a greater extent for mTBI survivors than normal controls. While reaction time differences were significant overall no age differences were found in either the mTBI group or the normal controls. Older mTBI survivors seemed to be resilient on reasoning measures and while their overall performance was worse than normal controls early in the recovery process there were no aging effects and there were no differences in performance between groups one year following the injury. This investigation indicates that age and mTBI should be a factor in reporting neuropsychological findings. Individuals over the age of 40 appear to experience greater impairment in processing speed which appears to worsen in the sixth decade. This age variable does not seem to be an issue on reaction time and reasoning testing until the age of 70 or greater.

Accelerated Changes in Cortical Thickness in Military Service Members with Traumatic Brain Injury

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Objectives: One challenge in the care of Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn (OEF/OIF/OND) Veterans is to find quantitative markers of traumatic brain injury (TBI) using non-invasive techniques. Even with advancing imaging studies, machine learning algorithms derived from these studies have only modest discriminative value and yield prediction accuracies below 70%. An alternative approach is to see if patterns of structural brain metrics can predict demographics, such as age. Recent work has revealed a significant discrepancy between the predicted and chronological ages of civilian TBI subjects compared to controls. In this work, we sought to examine a similar pathology in military TBI and determine for the first time which cortices are driving the altered prediction of age in TBI.

Methods: 762 healthy control subject data (36.32 ± 12.54 years-old; 373 males) were used to train our models in order to predict age from cortical thickness measures. The TBI test set consisted of 92 participants (29.67 ± 7.02 years [range: 22-57]; 88 males) with TBI (89 mild, 3 severe by VA/DoD criteria). We used Advanced Normalization Tools (ANTs) to derive the cortical thicknesses in sixty-two areas for all subjects. Using the healthy control data, we built four regression models to predict age from cortical thickness, gender and total intracranial volume: linear regression (LR), support vector regression (SVR), Gaussian process regression (GPR), and random forest regression (RFR). All four models were trained on the full healthy control training data. The models were then used to predict age for participants with TBI and for participants without TBI. We then computed the predicted age difference (PAD) by subtracting the predicted age from the patient's actual age and compared between groups.

Results: The fully trained models were then used to predict age in the military population. The predicted age difference (PAD) was significantly ($p < 0.05$, two-sample, two-sided t-tests) greater for participants with TBI compared to those without for three of the models (LR, SVR, and GPR) (Fig 6). The LR, SVR, and GPR models had mean PAD at close to zero for participants without TBI, and mean PAD scores greater than zero for participants with TBI (range of 3-5 years, $p < 0.05$). In the LR model, significant ($p < 0.05$) beta weights that drive the regression with negative correlation were the left caudal middle frontal, left isthmus cingulate, left precentral, left rostral anterior cingulate, left transverse temporal, right pars orbitalis, and right precuneus cortices and 3 regions had cortical thickness that correlated positively with age (left medial orbitofrontal, right inferior temporal, right superior parietal).

Conclusions: TBI in military personnel is associated with accelerated changes in cortical thickness over time. Accelerated thinning include several frontal cortical structures.

Using Virtual Health to Increase Access and Ease for Patients in Europe

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Background: Telehealth has been used to successfully facilitate care for a geographically dispersed patient community. Traumatic brain injury (mTBI) has been diagnosed in over 352,000 in the U.S. Armed Forces between 2000 and 2015, with mild traumatic brain injury (mTBI) affecting over 82% of those military members injured. (1) While most patients recover completely within weeks, a small percentage may have ongoing symptoms. In addition, there is a significant percentage of patients with postconcussive symptoms who also have concurrent pain and behavioral health diagnoses. Landstuhl Regional Medical Center (LRMC) is the only military medical center in Europe, serving geographically dispersed active duty personnel, their families, dependents, retirees, civilian support personnel as well as contractors. It is cost- and time-effective for LRMC specialty providers to evaluate and treat patients in outlying areas who may not be able to travel to LRMC for operational or logistical reasons. These patients are then followed by the specialists via telehealth.

Methods: Providers from LRMC coordinated with the TBI Program at Vilseck Army Health Center to provide specialty pain and physical medicine and rehabilitation services onsite. Patients generally had a diagnosis of mTBI with a chronic pain or musculoskeletal comorbidity. Two specialty providers travelled to Viseck from LRMC (4.5 hours each way) six times from January – October, 2016.

Results: Two PM&R providers travelled from LRMC to Vilseck Army Health Clinic every six-eight weeks, resulting in six two-day visits from January 27 – October 19, 2016. A total of 82 patients were seen face to face during these visits, and a total of 31 medical procedures were completed. The estimated travel cost for these six visits was \$3000. The savings in patient time, travel, and lost training/operational time was estimated at \$34,010. Patients were followed after their face to face visits with the provider via telehealth encounters.

Conclusion: By using this hybrid approach, providers were able to engage in face to face evaluation and treatment of patients over geographically disperse areas, and follow-up using telehealth capability. In this way medical providers can facilitate a more patient-centric and responsive medical treatment plan that is also cost-effective. The next step is to conduct an analysis of telehealth encounters for these patients in order to review patient and provider feedback and the positive impact on military readiness and decreased time away from military duties.

References: 1 Defense Veterans Brain Injury Center (2016). DOD TBI Worldwide Totals 2000-2016. Retrieved from http://dvbic.dcoe.mil/files/tbi-numbers/DoD-TBI-Worldwide-Totals_2000-2016_Q1-Q2_Aug-12-2016_v1.0_2016-09-20.pdf

'Brain Glue' for the Acute Treatment of Severe Traumatic Brain Injuries

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Severe Traumatic Brain Injuries (TBIs) lead to devastating disabilities and poor prognosis for the affected individuals. Although this form of TBI accounts for only 15-20% of all TBIs, they contribute to >90% of the clinical costs incurred. There are currently no effective treatments to counter the significant brain tissue loss and functional impairments caused by TBI. In order to address these deficits, we have engineered a novel Chondroitin Sulfate Glycosaminoglycan (CS-GAG) matrix that can enhance the efficacy of both transplanted and host Neural Stem Cells (NSCs) to promote endogenous repair of damaged brain tissue post-TBI. We hypothesize that engineered CS-GAG matrices administered acutely after TBI will help maintain the undifferentiated state of transplanted and host NSCs and attract neuroprotective factors necessary to prevent widespread brain tissue loss, and promote brain repair and functional recovery chronically post-TBI. We tested this hypothesis in a preclinical rat severe TBI defect. We induced a severe TBI to the rat motor cortex using a pneumatically actuated Controlled Cortical Impactor (CCI) after inducing a 5 mm diameter craniotomy. The depth of the impact was restricted to 2 mm in a repeatable manner, using an impact velocity of 2.25m/s, and a dwell time of 250 milliseconds. Two days post-TBI, animals were injected intraparenchymally with 20 μ l CS-GAG matrix preloaded with allogeneic PKH26GL labeled NSCs (n=7), trophic factors (100 ng each of FGF-2 and BDNF) (n=7), or a combination of both NSCs and trophic factors (n=7). Non-Invasive MRI and histological analysis of brain tissue 4 and 20 weeks post-injury shows a significant reduction ($p<0.001$) in lesion volume of brain tissue from CS-GAG matrix treated animals when compared to TBI only controls. Phase Gradient Mapping (PGM) studies indicate a significant ($p<0.001$) increase in regional Cerebral Blood Flow (rCBF) in CS-GAG matrix treated animals when compared to controls 20 weeks post-TBI. Quantification of NSC presence 4 & 20 weeks post-injury shows a significant increase in PKH26GL+ NSCs when delivered via CS-GAG matrices when compared to cells transplanted without matrix encapsulation ($p<0.05$). A majority of the transplanted NSCs remain self-renewing, and a significantly ($p<0.001$) greater number of host NSCs were found to infiltrate into the CS-GAG matrix implant when compared to surrounding brain tissue. Functional recovery of animals as determined by the beam-walk, and rotarod tests demonstrate the significantly enhanced ($p<0.05$) motor function recovery in CS-GAG matrix treated animals when compared to controls. In summary, our results indicate that CS-GAG matrices function as a neuroprotective 'glue' to prevent chronic brain tissue loss, and promote functional repair and regeneration of damaged brain tissue chronically after a severe TBI. Ongoing studies in large animal pig TBI deficits will determine the potential for future clinical translation of this technology.

Psychological Outcomes At 6 Years Following Traumatic Brain Injury in Occupationally-Injured Workers in Taiwan

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Introduction: Psychological and psychiatric conditions have been reported as results of traumatic injuries. More severe psychological effects have been reported after traumatic brain injuries (TBI). The purpose of this study was to determine whether occupational TBIs resulted in more severe psychological conditions than other types of occupational injuries (OIs).

Methods: Our study candidates were injured workers who were hospitalized for longer than three days in Taiwan. TBI were defined as having such diagnoses by the Authority of Workers' Compensation. Questionnaires were sent to these workers at 3 months, 12 months, and 6 years after injury. The questionnaire contained demographic characteristics, description of the OI, post-traumatic stress symptoms as assessed by post-traumatic symptom checklist (PTSC), and psychological symptoms assessed by the Brief Symptom Rating Scale (BSRS-5). Logistic regression was used to determine whether the severity score by BSRS-5 and by PTSC were different between those with TBI or non-TBI, adjusting for gender, age, education, length of hospital stay, and physical deformity due to injury.

Results: A total of 570 workers completed the 6-year questionnaires, and either 3-month or 12-month questionnaire. Among the workers completed the follow-up, 54 (9.5%) sustained TBI and 516 (90.5%) non-TBI. Severe BSRS-5 scores and for PTSC were found in 40.0% and 17.5% of participants, respectively. When compared to non-TBI group, workers sustaining TBI had higher risk (odds ratio=2.0, 95% confidence interval 1.1-3.6) of having severe BSRS-5, and higher risk of severe PTSC (odds ratio=2.0, 95% confidence interval 1.0-3.8) at 6 years after injury, after adjusting for covariates.

Conclusions: The TBI patients tended to experience more severe general psychological symptoms, and post-traumatic stress after OI at 6 years after injury. Development of preventive measures especially for those sustaining TBI is warranted.

Differences in Concussion Rates across National Collegiate Athletic Association Soccer Divisions

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Objectives: The National Collegiate Athletic Association (NCAA) has 3 divisions or competitive levels in men's and women's soccer. Each division has varying rules, scholarships, and other resources. These differences may lead to variations in the frequency and rate of concussion. To date, little is known about the differences in concussion rates by division in NCAA men's and women's soccer. The purpose of this study was to compare concussion rates by division in NCAA men's and women's soccer.

Methods: Concussion data from the NCAA Injury Surveillance Program (ISP) during the 2009/2010 to 2013/14 academic years were used for this descriptive epidemiology study. We examined concussion incidence rates by soccer division (i.e., Division I [DI], Division II [DII], Division III [DIII]). Concussions and athlete-exposures (AEs) were reported by athletic trainers (ATs). In lieu of local guidance or legislation, ATs were encouraged to follow the definition of concussion provided by the Consensus Statement on Concussion in Sport. Rate Ratios (RRs) and 95% Confidence Intervals (CIs) compared rates across divisions, for both men's and women's soccer.

Results: Overall, 38 men's soccer teams (86 team seasons) contributed data with 55 reported concussions in 159,724AEs (Rate=3.44/10,000AEs, [95% Confidence Interval (CI):2.53, 4.35]). Broken down by division, there were 25 concussions in DI, 5 in DII, and 25 in DIII. Concussion rates were highest in DI (4.10/10,000AEs [95%CI:2.49, 5.70], and lowest in DII (1.70/10,000AEs [95%CI:0.21, 3.19]) with the DIII concussion rate falling in the middle (3.61/10,000AEs [95%CI:2.19, 5.02]). However, none of the rate ratios comparing divisions were statistically significant (DI vs DII RR=2.41 [95%CI:0.92, 6.28]; DI vs DIII RR=1.14 [95%CI:0.65, 1.98]; DII vs DIII RR=0.47 [95%CI:0.18, 1.23]). Fifty-six women's teams (137 team-seasons) contributed data with 136 reported concussions in 215,489AEs (6.31/10,000AEs, [95%CI:5.25, 7.37]). Broken down by division, there were 51 concussions in DI, 21 in DII, and 64 in DIII. The concussion rate was highest in DIII (7.59/10,000AEs [95%CI:5.73, 9.45]) and lowest in DII (4.99/10,000AEs [95%CI:2.86, 7.13]), with the DI concussion rate falling in the middle (5.72/10,000AEs [95%CI:4.15, 7.29]). Again, none of the rate ratios comparing divisions were statistically significant (DI vs DII RR=1.15 [95%CI:0.69, 1.91]; DI vs DIII: RR=0.75 [95%CI:0.52, 1.09]; DII vs DIII RR=0.66 [95%CI:0.40, 1.08]).

Conclusions: There are no statistically significant differences by division in men's and women's NCAA soccer, but this may be due to a low number of concussions reported within some divisions (e.g. only 5 concussions in men's DII). Further research is needed to determine whether the concussion rate in DII men's soccer is truly lower or a result of underreporting by the athletes and/or ATs. Similarly, rates appeared higher in DIII women's soccer. If these differences truly exist, further research is needed to identify mechanisms to reduce the instances of concussions.

Defective Methionine Metabolism in the Brain after Repeated Blast Exposures Might Contribute to Increased Oxidative Stress

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Blast-induced traumatic brain injury (bTBI) is one of the major disabilities in Service Members returning from recent military operations. The neurobiological underpinnings of bTBI, which are associated with acute and chronic neuropathological and neurobehavioral deficits, are uncertain. Increased oxidative stress in the brain is reported to play a significant role promoting neuronal damage associated with both brain injury and neurodegenerative disorders. In this study, brain regions of rats exposed to repeated blasts in a shock tube underwent untargeted profiling of primary metabolism by automatic linear exchange/cold injection GC-TOF mass spectrometry and revealed acute and chronic disruptions in the metabolism of amino acids and antioxidants. Closely coupled repeated blast exposures (19 psi peak total pressure, 8 msec duration) affected the metabolism of the essential amino acids tryptophan, phenylalanine and methionine. Tryptophan levels decreased on day 1 whereas phenylalanine showed a significant increase in the brain at 28 day after blast exposure. Methionine sulfoxide, the oxidized metabolite of methionine, showed a sustained increase in the brain after blast exposure which was associated with a significant decrease in cysteine, the amino acid derived from methionine. Glutathione, the antioxidant synthesized from cysteine, similarly decreased as also did the antioxidant ascorbic acid. Reductions in ascorbic acid were accompanied by increased levels of its oxidized metabolite, dehydroascorbic acid and other metabolites such as threonic acid, isothreonic acid, glycolic acid and oxalic acid. In view of the fundamental importance of glutathione in the brain as an antioxidant, including its role in the reduction of dehydroascorbic acid to ascorbic acid, the disruptions in methionine metabolism elicited by blast might prominently contribute to neuronal injury by promoting increased and sustained oxidative stress. Increasing the levels of cysteine in the brain by dietary supplementation of cysteine or administration of N-acetyl cysteine could be a potential therapeutic strategy against bTBI.

Neurometabolites Alteration in the Very Early Phase of Mild Traumatic Brain Injury (mTBI)- an In-Vivo Proton Magnetic Resonance Spectroscopy (1H-MRS) Study

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Introduction: Magnetic resonance spectroscopy (MRS) using 1H(proton), allows quantification of neurometabolite changes associated with brain injury in-vivo. We hope to identify specific neurometabolite biomarkers that will allow us to quantitatively grade early alteration occurring in mild traumatic brain injury in a more objective manner.

Objective: To evaluate the very early alteration of neurometabolites in complicated (cmTBI) and uncomplicated (umTBI) mild traumatic brain injury (mTBI) patients in comparison to control subjects using proton magnetic resonance spectroscopy (1H MRS).

Methods: Fifty subjects (28 cmTBI patients, 7umTBI patients and 15 controls) underwent MRI scan with additional single voxel spectroscopy (SVS) sequence where a single voxel was placed close to the contusion site of cmTBI or at the frontal deep white matter of the umTBI patients and control subjects. The MRI scans for patients was done at an average of 10 hours (SD 4.26) post injury. The brain spectra were processed using LCModel to obtain the absolute and relative neurometabolite concentrations. One-way ANOVA was performed to compare the neurometabolites concentrations of the three groups (cmTBI, umTBI and control) and a correlation study was done between the neurometabolites concentration and the Glasgow Coma Scale (GCS).

Results: On assessment of the neurometabolites between the groups, significant results were obtained for the relative concentration of N-acetylaspartate (NAA). The ratio of total NAA to total creatine (tNAA/tCr) was found to be lowest in cmTBI, followed by umTBI and highest in the control group ($F(2, 43) = 3.815$, $p=0.03$). However, only cmTBI and control groups showed significant difference ($p=0.035$). The tNAA/tCr had a significant but mild correlation with the injury complexity ($\rho=0.377$, $p=0.01$) and GCS scores ($\rho=0.439$, $p=0.002$).

Conclusion: Neurometabolite alterations were already apparent at the early phase or onset of a brain injury. The tNAA/tCr ratio may be a potential biomarker that reflects injury severity, both in terms of complexity and admission GCS, in a more quantifiable and objective manner in patients with traumatic brain injury.

Predicting Pediatric Post-Concussive Symptoms with Brain-Related Salivary MicroRNA

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Purpose: Three million traumatic brain injuries occur in the U.S. each year. The vast majority are mild traumatic brain injuries (mTBIs) occurring in children. Yet, the bulk of research and clinical guidelines are based on adult data, limiting the ability of pediatricians to predict clinical outcomes for children with mTBI. Some children with mTBI have only transient headache, while others have months of physical, cognitive, and emotional changes. This study investigated the utility of salivary micro ribonucleic acids (miRNAs) for predicting the duration of pediatric mTBI symptoms. MiRNAs are non-coding, single-stranded nucleotides that post-transcriptionally regulate gene expression in response to environmental influences (such as mTBI). They are resistant to RNase degradation, have the ability to cross the blood brain barrier, and are easily measured in peripheral biofluids such as saliva. We hypothesized that: 1) levels of individual salivary miRNAs would change following pediatric mTBI, 2) these levels would reflect changes in cerebrospinal fluid (CSF) following pediatric severe traumatic brain injury (sTBI), and 3) salivary miRNA profiles would have prognostic accuracy for duration of mTBI symptoms.

Methods: High-throughput RNA sequencing was used to quantify salivary miRNA in 14 children (ages 11-20 years) presenting with clinical mTBI symptoms within 10 days of injury. Symptoms were assessed with the Sports Concussion Assessment Tool (SCAT-3) at enrollment and four weeks post-injury. Salivary miRNA profiles were compared with 14 healthy age- and sex-matched controls using Mann Whitney testing with Benjamini Hochberg False Detection Rate (FDR) correction. The miRNAs “altered” in saliva were interrogated in cerebrospinal fluid (CSF) longitudinally collected from seven pediatric patients with sTBI using quantitative real-time PCR. A partial least squares discriminant analysis (PLSDA) and logistic regression analysis using salivary miRNA profiles were employed to model mTBI-status and symptom duration.

Results: There were 16 miRNAs with differential expression ($p < 0.05$, $FDR < 0.1$) between mTBI and control groups. Two of the miRNAs (miR-92a and miR-30d) were among those altered in adult TBI studies of human serum. A partial least squares discriminant analysis of salivary miRNA profiles accurately modeled mTBI status in two-dimensions. Logistic regression analysis involving miR-30d showed predictive accuracy ($AUC = 0.822$) for differentiating children with mTBI symptoms beyond four weeks. Levels of miR-30d were also correlated with a child’s number of previous concussions ($R = 0.96$; $p = 1.0E-7$, $FDR = 1.6E-6$). Both miR-30d and miR-92a were present in the CSF following sTBI and demonstrated a trend of decreasing levels following injury.

Conclusions: Individual salivary miRNAs are altered in pediatric mTBI, show utility for predicting symptom duration, and reflect CSF miRNA profiles following sTBI. MiR-30d may also play an important role in the pathophysiology of repeat head-injury.

The Influence of Traumatic Brain Injury Severity on Health-Related Quality of Life in Caregivers of a Service Member or Veteran with Traumatic Brain Injury

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Background: Little is known about the effect of TBI severity on the family member providing care to a service member or veteran (SMV) following a TBI. The purpose of this study was to examine the impact of TBI severity on the family caregiver's health-related quality of life (HRQOL) for those providing care to a SMV following a TBI.

Methods: Participants were 31 caregivers (90.3% female; 71% spouse; Age: M=39.8 years, SD=10.6) of SMVs who had sustained an equivocal (n=9), mild (n=11), moderate (n=3), severe (n=3), or penetrating (n=5) TBI during a combat or non-combat incident. Caregivers were recruited through community outreach initiatives and multiple DoD Medical Treatment Facilities nationwide. Caregiver's participated in one of six focus groups (approx. 90 mins) designed to elicit information regarding HRQOL and access to services. Caregivers were classified into three groups based on the SMV's TBI severity: (a) equivocal, (b) mild, and (c) mod-severe/penetrating TBI. Thematic analysis using a constant comparative approach was conducted with qualitative analysis software to identify common themes across the three severity groups.

Results: The most commonly endorsed themes for all caregivers were poor physical health (80.7%), having no time for themselves (71.0%), and increased stress/anxiety (64.5%). When stratified by TBI severity group, a greater proportion of the mod-severe/penetrating TBI group reported having no time for themselves (100%) and increased stress/anxiety (100%), compared to the equivocal TBI (55.6% for both themes) and mild TBI groups (54.6% and 36.4% respectively). Similarly, a greater proportion of the mod-severe/penetrating TBI group reported being depressed (45.5%), exhausted (45.5%), having poor sleep (81.8%), and negative impacts on family life (63.6%), compared to the equivocal TBI (22.2%, 11.1%, 11.1%, and 22.2% respectively) and mild TBI groups (27.3%, 18.2%, 18.2%, and 9.1% respectively). Approximately one quarter (25.8%) of all caregivers reported a lack of access to services (e.g., health care/support groups). However, a lack of access to services was predominantly reported by the equivocal TBI group (66.7%) when compared to the mild TBI (18.2%) and mod-severe/penetrating groups (0%).

Conclusions: These results suggest that reduced HRQOL (e.g., depression, stress, exhaustion, poor sleep, and negative effects on family life) is commonly reported among family caregivers providing care to SMVs following a TBI. Although worse overall HRQOL was associated with caring for a SMV who had sustained a TBI in the higher end of the severity spectrum, some caregivers of SMVs with less severe injuries are also at risk of poor HRQOL. While the importance of providing care for an injured SMV is routinely acknowledged, it is also critical that similar care is provided to family members who adopt the caregiver role. These preliminary results demonstrate a need to increase health care provision for family members who care for injured SMVs.

Inhibition of Mammalian Target of Rapamycin (mTOR) Improves Neurobehavioral Deficit and Modulates Inflammatory Response after Traumatic Brain Injury

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Traumatic brain injury (TBI) induce primary and secondary damage on endothelium and brain parenchyma, leading neurons die rapidly by necrosis. The mammalian target of rapamycin signalling pathway (mTOR) mediates many aspects of cell growth and regeneration and is up-regulated after moderate to severe traumatic brain injury (TBI). The significance of this increased signalling event for recovery of brain function is presently unclear, here we used two different selective inhibitors of mTOR activity to explore the functional role of autophagy in a validated model of TBI, the controlled cortical impact injury (CCI).

We treated animals with KU0063794, a dual mTORC1 and mTORC2 inhibitor, and with Rapamycin a well-known inhibitor of mTOR, 1 and 4 hours after TBI.

Our results demonstrated that mTOR inhibitors, especially KU0063794, significantly improve motor and cognitive recovery after controlled cortical impact, as well as reduce lesion volumes. Moreover we observed that mTOR inhibitors treatment ameliorate the neuroinflammation associated to TBI and showed that this acute treatment significantly diminished the extent of neuronal death, astrogliosis and apoptotic process after trauma.

Our findings suggest that the neuronal mTORC1/2 activity after TBI is deleterious to brain function, and that acute intervention with mTORC1/2 inhibitor after trauma may represent an effective therapeutic strategy to improve recovery after brain trauma.

Influence of Brain Derived Neurotrophic Factor Polymorphism on White Matter Microstructural Recovery in Mild Traumatic Brain Injury – A Radiogenomic Study

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Introduction: Cognitive outcome following mild traumatic brain injury (mTBI) is very heterogeneous despite the similarity in injury mechanisms. Polymorphism of neural repair and plasticity genes are postulated as one of the reasons for this outcome. We analyzed the role of brain derived neurotrophic factor (BDNF) genetic polymorphism (Val66Met) on cerebral white matter integrity as seen with diffusion tensor imaging (DTI) and examine its effect on the cognitive outcomes of patients with mTBI over a 6 month period.

Methods: Sixty-one patients with mTBI (mean age = 27.08; standard deviation (SD), 8.55) underwent MR imaging at an average of 10h (SD, 4.26) post-trauma along with assessment of neuropsychological performance at an average of 4.35h (SD, 7.08) upon full Glasgow Coma Scale recovery. Results were then compared to 19 healthy control subjects (mean age = 29.05; SD, 5.84), both in the acute stage and 6 months post-trauma

Results: The independent t-tests results of the acute performance reveal significant changes of domain specific neurocognitive functions (attention, language, memory, visuospatial, executive function and overall) in patients with mTBI against the healthy control subjects. The Met carriers had significantly poorer performance in comparison to healthy controls in all domains except the visuospatial function ($t(52) = 0.780$, $p = 0.49$). Individuals with the Val/Val genotype had significantly lower performance in the attention domain ($t(52) = 4.197$, $p = 0.000$) only. Intragroup analysis between Met carriers and Val/Val group revealed significant difference in the language domain ($t(52) = 2.173$, $p = 0.04$) with the Met carriers performing poorly compared to Val/Val acutely. Temporal analysis of the DTI parameters against genetic allele status revealed lower FA values at 6 months post trauma in Met carriers in comparison to the control group. Similarly, the mTBI patients with the Val/Val genotype were also noted to be significantly different from the Met carriers, but to a lesser degree. In the Val/Val group, the temporal Δ (delta) within the attention, memory and executive function domain standard scores (SS) were strongly associated with the Δ in various DTI parameters of the WM. Alternatively in the Met carriers group, the Δ of attention and memory SS strongly associated with mostly the Δ of MD and RD values.

Conclusion: We show that Met substitution of BDNF gene (rs6265) results in detrimental influence on the white matter integrity and neurocognitive performance, specifically in the domains of memory and executive function both acutely and over time. This effect is due to a down regulation of BDNF expression in Met carriers, thus causing a negative effect on neuronal survival and repair. The combination of DTI metrics and BDNF (Val66Met) polymorphism provides a clearer prognostic picture for patients with mTBI.

The Relationship Between PTSD Symptoms and Tau and Amyloid Levels in U.S. Military Service Members With and Without Mild-Moderate Traumatic Brain Injury

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Background: The purpose of this study was to examine the relationship between levels of tau and amyloid-beta 42 with self-reported symptoms of Posttraumatic Stress Disorder (PTSD) in participants with and without mild-moderate traumatic brain injury (TBI).

Methods: Participants included 55 U.S. military service members with and without mild-moderate traumatic brain injury (TBI) prospectively enrolled in a longitudinal study at Walter Reed National Military Medical Center. Participants with PTSD at baseline (n=12) were matched on TBI severity and time since injury with participants without PTSD (n=36). All participants completed a baseline assessment with the PTSD Checklist (PCL) and blood draw an average of 5.4 months post-injury (SD=3.8; median=4.0). An ultra-sensitive immune-assay was used to measure levels of tau and amyloid-beta 42. Thirty-six participants were similarly evaluated at 1-year follow-up (12 PTSD-Present, 24 PTSD-Absent). Participants were excluded if their responses on the MMPI-2-RF were considered invalid. Thirty-two participants had complete and valid data at both baseline and follow-up.

Results: ANOVA revealed that PTSD was not significantly related to tau or amyloid-beta 42 at baseline ($p > .05$), but there was a medium effect size of PTSD status on tau ($d = .42$), with higher levels in the PTSD-Present group. Linear regression showed that tau and amyloid-beta 42 were not significant predictors of PCL total score, nor to scores on the re-experiencing, avoidance, and hyperarousal subscales at baseline ($p > .05$). At follow-up, PTSD status was not significantly related to amyloid-beta 42 ($p > .05$), but was related to higher total tau ($p = .047$). There was a large effect size of PTSD status on tau ($d = .75$), with levels higher in the PTSD-Present group at follow-up. There was also a medium effect size of PTSD status on amyloid ($d = .55$); however, amyloid-beta 42 level was higher in the PTSD-Absent group. Tau was significantly related to PCL total score ($F(1,34) = 7.73$, $p = .009$) and all three PCL subscales (all $p < .022$). Amyloid-beta 42 was not significantly related to PCL total score or subscales. However, a preliminary longitudinal examination of tau and amyloid-beta 42 levels from baseline to follow-up showed that change in PTSD symptoms over time was not consistently associated with changes in tau or amyloid levels.

Conclusion: These results suggest that one-year post-injury, patients with PTSD may have higher peripheral levels of tau. To a lesser extent, there was some evidence suggesting that some patients with PTSD may have lower levels of amyloid one-year post injury and higher levels of tau 4-5 months post-injury.

Contribution of Wave Propagation and Head Acceleration to the Development of Brain's Tissue Responses under Blast

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Blast-induced traumatic injury (bTBI), defined as the dysfunctionality of brain as a result of exposure to blast shockwaves, have risen many concerns during the past decade due to the increase of explosive devices, particularly among military members. Development of preventive strategies for bTBI requires in-depth understanding of the injury mechanisms. Several mechanisms such as rapid acceleration of head, propagation of shockwaves inside the cranium, and skull deformation have been suggested as possible deteriorating causes of bTBI. While it's certain that the ultimate injury occurs as a combination of all the mentioned mechanisms, understanding the individual contribution of each could be beneficial for developing effective protection tools such as helmets. To this end, a finite element (FE) study was performed using the North Dakota State University FE head model (NDSUFEHM). Three different models were developed to examine the individual contribution of wave propagation and head acceleration to the tissue responses of the brain. In the first model, both mechanisms were included (Inclusive model). For the second case, combined effects of wave propagation and linear head accelerations were considered (Linear-acceleration model), and finally for the third model, skull was considered rigid to consider only the acceleration effects (Rigid-skull model). LS-DYNA transient and nonlinear FE solver was used to perform all the simulations. All the head components were considered to be linear elastic, except for the brain tissue which was modeled as a hyper-viscoelastic material to account for the viscoelastic and nonlinear behavior of biological tissues under large deformations. The blast was modeled using a coupled multi-material Arbitrary Lagrangian Eulerian (ALE) method along with the penalty-based algorithm. A blast overpressure of 520 kPa was generated in front of the head by exploding 70 grams of TNT at a distance of 60 cm from the head. Our primary results suggested that the Inclusive model predicted higher tissue responses in terms of both intracranial pressure (ICP) and shear stress. While Rigid-skull model predicted an ICP level (152 kPa) less than half of that predicted by Inclusive model (334 kPa), Linear-acceleration model's ICP (264 kPa) was about 80% of the Inclusive model's. Both Linear-acceleration and Rigid-skull models predicted similar shear stresses (2.97 kPa and 3.15 kPa, respectively) and the Inclusive model's shear stress was 4.5 kPa. Based on the case study analyzed here, we concluded that both wave propagation and head accelerations had significant effects on the tissue responses of the head with wave propagation having a little more contribution. However, it was shown that the pressure response was more influenced by the exclusion of the wave propagation. Further analyses such as those conducted at different blast intensities and directions, as well as longer blast durations can help better understand the contribution of different mechanisms.

Spasticity Investigation by Electromyography in Patients with Disorders of Consciousness

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Context: Spasticity assessment and care for patients with disorders of consciousness is still poorly studied while this motor trouble may lead to severe pain, loss in range of motion and ability to express sign of consciousness which could lead to misdiagnosis.

Aim: Our aim is to compare the severity of using the Modified Ashworth Scale (MAS) with neurophysiological measures using the Hmax/Mmax ratio and to MRI data.

Methods: A cross-sectional study was performed on severely brain injured adult patients with unresponsive wakefulness syndrome (UWS), minimally conscious state (MCS) or emergent from the MCS (EMCS). Upper and lower limbs spasticity for each joint was assessed using the MAS and the Hmax/Mmax ratio with 14 patients (mean age=43±8 years; 8 men; 7 traumatic etiologies). The results were then compared to clinical and neuroimaging data.

Results: Electromyographic measures showed that patients with disorders of consciousness had hypertonicity (70%) rather than spasticity (28.5%), such as described in the upper motor neuron syndrome. We did not identify any significant correlation between the MAS score and the increase in Hmax/Max ratio. 11 patients had lesions involving the pyramidal tract but it doesn't always correlate with the MAS neither.

Conclusion: This study demonstrates that patients with disorders of consciousness are more hypertonic than spastic. In addition, MAS and Hmax/Mman do not seem to be the more suitable tools for assessing spasticity in these patients.

Keywords: altered consciousness state, modified Ashworth scale, spasticity, Hmax/Mmax ratio

Cortical Morphometry of the Language Areas in Patients with Mild Traumatic Brain Injury - An Acute Radiological Assessment

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Background: Mild traumatic brain injury has been shown to adversely affect language performance in patients, both acutely and over time. However, not much has been explored about the physical structural changes in the language related cortical areas of the cerebral hemispheres.

Methods: Twenty one patients with mTBI were recruited on admission. MRI brain with 3 Tesla using T1-, T2, and diffusion tensor imaging (DTI) were acquired within 6 hours of presentation, and a second similar sequence was acquired 6 months post trauma. Cortical reconstruction was done to allow for extraction of the thickness, area, and volume of the language-related cortices (opercular and triangular part of the inferior frontal gyrus (IFG), and the planum temporale of the superior temporal gyrus (STG)).

Results: The mean age of mTBI patients was 27.08 ± 8.55 years. Pairwise statistical test (Wilcoxon's signed rank) showed an increase of cortical thickness (0.034mm) and volume (107mm³) over time in the opercular part of the IFG ($p < 0.05$). No statistically significant differences were identified on the triangular part of the IFG and on the STG.

Conclusion: The cortex of the opercular segment of the IFG or commonly known as the Broca's area, experienced volumetric expansion over time after mTBI in our cohort of patients. This was contrary to our expectation in the literature that generally reveals a contraction of volume across the cerebral hemispheres. One postulation for this increase in thickness and volume might be due to reactive astrogliosis, which occurs as a repair mechanism in patients with mTBI related microstructural damage. Further study, including DTI imaging and a correlation with language function may help to improve the prognostic accuracy in this group of patients.

Sphingosine 1-phosphate Receptor Subtype 1 (S1PR1) as a New Therapeutic Target for Brain Trauma

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Traumatic brain injury (TBI) provokes secondary pathological mechanisms, including dynamic interchange between ischemic, cytotoxic and inflammatory processes. The advance in sphingosine 1-phosphate (S1P) receptor modulators such as the S1PR1 functional antagonist FTY720 (Gilenya®) which was FDA approved for the treatment of multiple sclerosis in 2010, has opened the door for a novel and effective mechanism of reducing central nervous system (CNS) inflammatory lesion activity. Moreover, it has been shown that S1PR1 is expressed in the CNS playing an important role in neural development, regulation of neural stem cells, protection against apoptosis and modulation of proinflammatory processes (shift in the balance between proinflammatory cytokines such as IL1 β towards the potent anti-inflammatory and neuroprotective cytokine, IL10). Thus, the aim of this study was to characterize the immunomodulatory effect the functional S1PR1 antagonist siponimod in Phase III clinical trials for autoimmune disorders and of the competitive S1PR1 antagonist TASP0277308 in preclinical development in an in vivo model of TBI in mice. We used the well-characterized model of TBI caused by controlled cortical impact (CCI). Mice were injected intraperitoneally with siponimod or TASP0277308 (1mg/Kg) at 1h and 4h after trauma. Our results demonstrated that these agents exerted significant beneficial effects on TBI pre-clinical scores in term of anti-inflammatory and immunomodulatory effects in particular attenuation of astrocytes activation and rescue of the reduction of adhesion molecules (i.e. occludin and ZO-1). Moreover these were able to decrease T-cell activation visible by reduction of CD4 and CD8, reduction in lesion area (measured by TTC staining) and preservation of tissue architecture. Altogether, our results showed that blocking the S1PR1 axis is an effective therapeutic strategy to mitigate neuropathological effects engaged in the CNS by TBI.

Not All That Bleeds is Abuse

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This workshop will illustrate traumatic, medical, and congenital diagnoses that may be mistaken for abusive head trauma in the clinical setting. Through the review of unique case examples and with elicited audience participation, various organic and mechanical processes that create signs and symptoms similar to those seen in inflicted neurotrauma will be explored. Emphasis will be placed on the key points of history, physical and diagnostic testing that can help clinicians differentiate from AHT and its mimics.

Objectives:

1. Consider the pathophysiology of the common clinical findings in children suffering from abusive head trauma
2. Examine alternative mechanical and medical causes of the central nervous system findings typically seen in abusive head trauma victims
3. Develop a broad differential diagnosis for findings commonly seen in victims of abusive head trauma

Local Diffusion Imaging Connectometry in United States Service Members with Mild TBI and PTSD

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Connectomics refers to methods where imaging data is used to map structural or functional connections between distinct regions of the brain. Individual connectometry, a new way of examining structural connectivity, examines the degree of connectivity between adjacent voxels using the density of diffusion spins. This tracks the local connectivity patterns along the length of fiber tracts and avoids the potential signal reliability issues of dMRI near gray matter targets often used in other end-to-end connectivity methods. Currently, there are no studies using this method in patient cohorts with mild TBI or post-traumatic stress disorder (PTSD). Thus, the purpose of this study is to use this potentially more reliable method to examine a cohort of US Service Members with mild TBI and PTSD.

A sample of 33 mild TBI, 20 PTSD only (no head injury), and 50 orthopedic injured (OI) only (no head injury, no PTSD) US Service Members were included in this study. Participants were between the ages of 18 and 60, recently (3 to 24 months) returned from combat deployment, and were not on scheduled narcotics for pain. Each participant was assessed using the same SIEMENS Verio scanner with a standardized 64 direction (TE=85ms, and TR=1270ms, b-value=1000s/mm²) diffusion scheme. The dMRI data were then reconstructed in the MNI space using q-space diffeomorphic reconstruction to obtain the spin distribution function. The spherical diffusion function (sdf) values were used in the connectometry analysis to study the effect of diagnosis. A multiple regression model was used to consider diagnosis accounting for age, sex, and education. The local significant connectomes were determined using permutation statistics that allow for estimation and correction Type-1 error inflation due to multiple comparisons.

Connectometry analyses demonstrated significant results for several regions of interest (i.e., frontal, cerebellum, more right hemisphere than left) where PTSD had decreased connectivity compared to either the OI only or mTBI groups. The mTBI group also demonstrated significant decreased connectivity in the frontal and cerebellar regions when compared to the PTSD only or OI only groups though the number of tracts generated was significantly reduced compared to the other findings.

Results from this preliminary study show that both mTBI and PTSD have measurable dMRI signal abnormalities along the length of various white matter tracts that are detectable using this localized connectometry method. Importantly, PTSD appears to have a more consistent coherent signal (more right hemisphere than left) and is an important comorbidity requiring consideration when examining Service members with mTBI. This finding appears to confirm other studies by our lab that use different methods of dMRI analyses. Future studies are required and special consideration of additional common comorbidities (pain) and clinical variables (sleep, loss of consciousness, time since injury) should be considered.

Evaluation of Patient Engagement and Acceptability, Goals and Outcomes in A Newly Developed Low Intensity Community Based Group Neuropsychological Rehabilitation Programme

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Introduction: This paper presents a pilot study of a newly developed group based low-intensity community neuropsychological rehabilitation programme. It outlines the development of this programme and presents a preliminary analysis of data collected from two completed programmes.

Intervention: A twelve-week community based neuropsychological rehabilitation programme was developed to meet the identified needs of ABI post-acute patients in NHS Grampian, one of Scotland's 14 health boards. The group ran for five hours per day, meeting weekly over twelve weeks, with a follow up session three months later. Family were also invited to attend one session. The group covered the following topics: Understanding Brain Injury, cognitive rehabilitation including Memory, Attention, planning and organisation and managing emotions. Time was also allowed for social interaction between peers.

Participants: Two groups were completed including 20 participants (10 per group), 15 males and 5 females. Reasons for brain injury included TBI, Stroke and other medical conditions

Outcome Measures: Up to three goals were identified by each patient and measured, using a specifically designed goal action plan, at four time points (start, mid, end of group and follow-up).

Standardised outcome measures were completed by participants at three time points: start, end and follow-up. Proxy measures were completed at the same time points.

Patient acceptability and engagement was assessed with likert scales, patient attendance records and qualitative feedback.

Results: 87% of goals improved with a mean 4.6 point improvement (on a ten point scale) across patients.

Patient engagement and acceptability for the programme was very high. The programme had a 0% drop out rate and a 93% overall session attendance rate. 100% of patients said they would recommend the group to others, and 95% said the group increased their confidence, on likert scale ratings. Patients reported that they found the programme very helpful and that they had experienced positive changes in their lives. Our conference presentation includes a video with qualitative patient feedback.

Standardised measures showed significant improvement in psychological aspects of Quality of Life (WHOQOL-BREF) and significant reduction in anxiety symptoms (DASS21) after completion of the group. Significant improvements in depression, impulsivity and core symptoms of Brain Injury were shown on the EBIQ. Proxy measures showed significant improvements in participants' social relationships (SPRS).

Conclusion: The initial analysis of this newly developed group showed high patient acceptability and engagement, positive moves towards goals and a number of significant changes on standardised measures. The next steps are to carry out a waiting list controlled trial. If this shows similar significant improvements

we plan to run an RCT using the group materials, which will also look at the economic impact of the group, and develop the materials for publication to make these more widely available.

Health-related Quality of Life Following Severe and Penetrating Traumatic Brain Injury in U.S. Military Service Members

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Objective: Traumatic brain injury (TBI) can lead to lifelong challenges that may affect a person's health-related quality of life. Although health-related quality of life following TBI is extremely important to understand, few studies have examined this construct. The purpose of this study was to examine self-reported health-related quality of life in service members in the chronic stage of recovery following severe and penetrating TBI.

Methods: Participants were 117 U.S. military service members (Mean Age=35.3, SD=8.9; 90.6% male) prospectively enrolled from the Walter Reed National Military Medical Center who passed symptom validity testing. Participants completed the TBI Quality of Life (TBI-QOL) at least 12 months post-injury (Mean=61.9 months, SD=43.9, range=12-159). Participants were classified into three groups: 18 severe TBI, 18 penetrating TBI, 81 trauma controls (TC).

Results: The three groups did not significantly differ in terms of age, time since injury, gender, or ethnicity (all $p > .05$). Compared to the TC group, the severe TBI group had worse scores on 12 of the 14 TBI-QOL scales ($d = .38-1.1$). In contrast, compared to the TC group, the penetrating TBI group had worse scores on TBI-QOL scales of Grief/Loss ($d = .84$), Positive Affect and Well-Being ($d = .42$), Cognitive Complaints ($d = .50-.74$), and Self-Evaluation ($d = .50$). Compared to the penetrating TBI group, the severe TBI group reported more symptoms on scales of Anger ($d = .45$), Anxiety ($d = .66$), Depression ($d = .59$), and Pain ($d = .57$). When considering all 14 scales simultaneously, the severe TBI group had a higher number of TBI-QOL scales that reflected 'poor outcome' (i.e., scores $>1SD$ from the normative mean) compared to the TC group and the penetrating TBI group (e.g., percent with 3 or more scales $>1SD$: Severe=66.7%, Penetrating=44.4%, TC=34.6%).

Discussion: In the chronic stage of recovery, service members and veterans with a history of severe TBI reported worse outcomes in many areas compared to TCs. Those with a history of penetrating TBI reported more cognitive complaints and grief/loss, and lower self-esteem and positive affect than TCs. Compared to penetrating TBI patients, severe TBI patients reported more anxiety, depression, pain, and anger. These results suggest that there are long-term consequences following severe and penetrating TBI, with particularly worse global outcome following severe TBI. It is possible these findings reflect the neurological underpinnings of these different types of TBI, as severe TBI tends to be the result of diffuse damage whereas penetrating TBI is often the result of focal damage. Continued research on severe and penetrating military TBI is necessary to elucidate factors that contribute to and moderate outcomes.

Mild Neurocognitive Disorder and Diffusion Tensor Imaging in Military Service Members following Mild Traumatic Brain Injury

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Background: Brain white matter integrity has been shown to be negatively affected by traumatic brain injury (TBI), yet less is known about the relationship between white matter integrity and neurocognitive performance. The purpose of this study was to examine the relationship between white matter integrity of the brain, as measured by diffusion tensor imaging (DTI), and Mild Neurocognitive Disorder (MNCD) following mild traumatic brain injury (TBI).

Methods: Participants were 84 U.S. military service members (Age: M=31.9, SD=8.9; 89.3% male) who sustained a complicated (n=26) or uncomplicated (n=58) mild TBI, prospectively enrolled from Walter Reed National Military Medical Center, Bethesda, MD. Participants completed a 5-6 hour neuropsychological test battery and Diffusion Tensor Imaging (DTI) of the whole brain, on average, 28.1 months post-injury (SD=31.5). From a larger neuropsychological test battery, 24 measures were selected to create six cognitive domain summary scores: (1) attention, (2) processing speed, (3) immediate memory, (4) delayed memory, (5) executive functioning, and (6) visuospatial functioning. Participants were divided into two groups based on DSM-5 symptom criteria for MNCD: (a) MNCD-Present (n=53) and (b) MNCD-Absent (n=31). Participants were classified in the MNCD-Present group if at least two out of four performances in a single neurocognitive domain were ≥ 1 SD below the mean from a control sample (n=10). For DTI, fractional anisotropy, mean diffusivity, radial diffusivity, and axial diffusivity were calculated across 18 regions of interest (ROIs). The 18 ROIs included the (a) Corpus Callosum – forceps major, (b) Corpus Callosum – forceps minor, and (c) two unilateral symmetrical ROIs (left/right) each for the Anterior thalamic radiation, Cingulum–angular (infracallosal) bundle, Cingulum–cingulate gyrus (supracallosal) bundle, Corticospinal tract, Inferior longitudinal fasciculus, Superior longitudinal fasciculus – parietal bundle, Superior longitudinal fasciculus – temporal bundle, and Uncinate fasciculus.

Results: When examining the 18 regions of interest (ROIs) individually, axial diffusivity and fractional anisotropy values were significantly lower in the left and right corticospinal tract of participants in the MNCD-Present group compared to participants in the MNCD-Absent group (Cohen's $d=.50-.87$). Additionally, measures of axial diffusivity in the right superior longitudinal fasciculus parietal bundle and fractional anisotropy in the left anterior thalamic radiation were both lower in the MNCD-Present group compared to the MNCD-Absent group ($d=.47-.50$). Mean diffusivity was significantly higher in the right uncinate fasciculus in the MNCD-Present group ($d=.44$). There were no significant differences in measures of radial diffusivity in all 18 ROIs.

Conclusions: These results suggest that overall there is little relationship between MNCD and white matter integrity. There were, however, multiple signs of reduced white matter integrity of corticospinal tract in patients with MNCD compared to patients without MNCD, suggesting that, the integrity of the corticospinal tract may be related to cognitive performance. However, replication of these results is necessary.

Subdural Hematoma Associated with an Arachnoid Cyst in a Juvenile Rugby players: Two Case Reports

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Aim: Arachnoid cyst (AC) is a cyst covered by the dura mater. AC is almost asymptomatic, and followed up conservatively. Previous reports showed that AC is ruptured due to head injury.

We present 2 cases that Subdural Hematoma Associated with an Arachnoid Cyst.

Case 1: 16 year-old male, rugby player.

It was pointed that he has AC in right middle cranial fossa and posterior cranial fossa by previous CT scan. He hit parietal in rugby match, and felt headache. This symptom continued 3 days, and he visited Toho university Ohashi medical center. His brain CT showed that AC was volume loss, and high density. subdural space of middle fossa and inter-hemispheric fissure was larger. MRI showed that AC was communicate with subdural space. We diagnosed that Subdural Hematoma Associated with an Arachnoid Cyst. AC is ruptured by head injury. We followed up conservatively, his symptom was improved and imaging findings was no change. He discharged day4.

Case 2: 15 year-old male, rugby player.

He felt headache in two weeks ago. This symptom continued, and he visited hospital. His brain CT showed that right subdual space was larger, and edge of bone with AC become thinning. MRI showed that intensity of subdural space is hematoma's signal (T1 high intensity, T2 high intensity), and SWI showed cyst's coat. We diagnosed that AC were present before head injury, and Subdural Hematoma Associated with an Arachnoid Cyst. We follow him conservatively in hospital visiting.

Conclusion: There is few reports that acute subdual hematoma associated with AC. Association is not clear of contact sports and ruptures of AC. These two cases suggest that it is necessary to prepare guidelines for contact sports players with arachnoid cysts.

Validation of the Pediatric Family Needs Questionnaire - A Partnership Approach Across Five Countries

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Background & Objective: The need for family support after paediatric acquired brain injury (ABI) is well documented. However, there is currently no standardized way to assess the extent to which family needs are met after a child sustains an ABI. Identifying families' priorities is critical given evidence of the strong relationship between unmet family needs and increased family burden. Research further identifies a bidirectional relationship between child and family outcomes after ABI. We adapted the well-validated adult Family Needs Questionnaire to create a pediatric version (Family Needs Questionnaire [FNQ-P]). Validation of the FNQ-P is underway with pediatric rehabilitation partners in Sweden, Australia, UK, and Lithuania. Here, we report initial results from the Canadian site.

Methods: A convenience sample of 21 caregivers of children with ABI (ages 2-19 years, mild to severe injury) were recruited at the Canadian site for test-retest evaluation of the FNQ-P (1 week retest interval; target ICC > 0.80). Associations between FNQ-P score and age, injury severity and time post-injury were evaluated to assess ability to predict family needs post-ABI. Construct validity was assessed using Family Burden of Injury Inventory (FBII; short form) and Strengths and Difficulties Questionnaire (SDQ) (target $r > 0.60$ with the full study sample).

Results: Analysis of Canadian data ($n=21$, mean age 12.1 years [$SD=5.8$] and mean time since injury = 3.5 years [$SD=4.5$]) revealed mean total FNQ-P scores of 68.2% ($SD=14.4$) and 65.4% ($SD=14.9$) on test and retest respectively (higher scores indicate greater needs met), and excellent test-retest reliability (ICC 0.86, 95%CI 0.68 – 0.94). There was suggestion of a weak positive association between injury severity and FNQ-P score ($r=0.22$, $P=0.32$), but no evidence of association between time since injury or age and FNQ-P score ($r < |0.10|$, $P=0.66$).

Conclusions: Preliminary single centre FNQ-P results indicated a wide range of needs, with the average 'needs' score in the FNQ-P's mid-range. The FNQ-P demonstrated excellent test-retest reliability. Lack of relationship between FNQ-P scores and injury severity suggests assumptions should not be made about needs met based on severity. Presence of no more than a weak inverse association between time since injury and needs met may reflect shifting family needs over time as one set of priorities is met and a new set emerges. More definitive association conclusions will be possible once data collection at all sites is finalized (final total sample size goal = 75). This larger 'n' will also support reporting results of the FBII and SDQ construct validity evaluation. Assuming psychometric adequacy, we anticipate that the FNQ-P will be valuable in partnerships with families as a roadmap of family needs over the course of a child's development.

Patients' Ways of Knowing: Narrative Truth in The Accounts of Families of Vegetative and Minimally Conscious Patients After Serious Brain Injury

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Objectives: We conducted qualitative interviews with family members of patients in a vegetative, minimally conscious, or locked-in state as part of a larger research study. Our objectives were to gain insight into families' knowledge of the patient's medical condition, including their beliefs about the patient's preserved cognitive function and prognosis. This presentation will focus on family members' ways of knowing and how these at times conflicted with the logic of the current medical model as well as impacted interactions with clinical staff.

Methods: Using a constructive grounded theory design, we interviewed the surrogate decision-makers of patients in a vegetative, minimally conscious, or locked-in state at two time points, before and after receiving test results from functional MRI, or electroencephalography (EEG) or both. A semi-structured interview guide was designed to capture experiences of the original precipitating event, experiences of care delivery, understanding of the family member's consciousness, and reasons for participating in the study.

Results: We interviewed 11 family members, at two time points, for a total of 22 in-depth interviews. Each interview lasted one hour or longer and were mostly conducted by telephone. Families often described poignantly how they maintained a sense of relationship with the patient despite their medical state. They described the myriad ways in which they believed their family member communicated with them, frequently attributing some degree of consciousness to them. At the same time, families perceived that healthcare workers often treated patients with brain injuries as non-persons. In sociology, epistemic privilege refers to a certain type of knowledge that can only be gained through direct experience of a phenomenon. We apply this concept in order to theorize the differences in perspective between caregivers and clinicians that remain respectful of family's ways of knowing.

Conclusions: Our team has identified points of tension between clinician and family member's understanding of the patient's condition and specifically the different meanings of consciousness they assign. Families often believe they have specialized knowledge of the patient and express this as a form of communication that may sometimes be more symbolic than literal. While families' claims are not legitimized in the hierarchy of medical knowledge, they provide important insight into the social meaning of consciousness and the role this plays in families' decision-making.

A Novel EEG-based Biomarker for Mild Traumatic Brain Injury (mTBI) in Adolescents

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Objective: There is a growing interest in examining mild traumatic brain injury (mTBI) and seeking diagnostic biomarkers in adolescents. This population is relatively underexplored compared to adults, is more susceptible to the effects of mTBI due to the immaturity of the developing brain and is characterized by large variability of physiological, psychological and behavioral measures. Electroencephalography (EEG) has been proposed as a diagnostic tool due to its objectivity and cost-effectiveness. However, no sensitive and specific application of EEG has been determined for this age group. To address this, we utilized a large age- and gender-specific healthy control database to generate an age-specific biomarker for adolescents. This novel biomarker, based on a frontal, late-latency sensory evoked potential component in healthy adolescents and described in a recent case study by Kiefer et al., showed increased negativity in a post-mTBI 15-year-old hockey player relative to the healthy population. The current study is aimed to investigate changes in this negative component in a large group of healthy and concussed adolescent athletes to see if this effect is reproducible and consistent within this population.

Methods: EEG activity was recorded in 107 healthy participants and 36 mTBI patients, while they performed an auditory oddball task. The EEG was processed using the Brain Network Analysis (BNA) algorithm reported in Stern et al. BNA features of all participants were extracted and included in repeated-measures analyses of variance (ANOVA) with EEG session gain (2nd vs. 1st, 3rd vs. 2nd), interval between sessions (< 2 months, > 2 months) and group (healthy, mTBI) as factors.

Results: During the baseline EEG recording sessions of both experimental groups (concussed and healthy controls), a large negative evoked potential component in frontal-central regions was observed at ~200-500 milliseconds following the standard stimulus. While the average negative amplitude decreased in the healthy control group's 2nd EEG recording session, it remained steady in the concussed group's 2nd (post-mTBI) session, and was significantly different than healthy controls (Group by Session ANOVA, interaction p-value = 0.01). The pre- to post-mTBI gain in amplitude was correlated with the time interval between recording sessions ($r=-0.47$, $p\text{-value}<0.05$).

Conclusions: These current results indicate that the negative component's amplitude gains are associated with mTBI exposure in adolescent athletes. Specifically, this component, possibly indicative of a neural plasticity process prevalent in the adolescent brain, is sensitive to potential disruption of such processes by mTBI, thus making it a potential biomarker for mTBI diagnosis and monitoring in adolescents.

Kiefer AW, et al. Brain network activation as a novel biomarker for the return-to-play pathway following sport-related brain injury. *Front. Neurol.* 2015; 6: 243

Stern Y, et al. Using of Spatiotemporal Features in the Brain Network Activation Analysis for Improved Data Classification. *Front Comput. Neurosci.* (In press).

Feasibility of a Locomotor Training Protocol in an Inpatient Acquired Brain Injury Program

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Introduction: The Parkwood Program for Rehabilitation Innovations in Movement Enhancement (PRIME) system is a clinical decision support system for the integration, and optimal use of available therapeutic modalities customized to individuals. The creation of this program was in response to the problem that modalities for locomotor training are often studied in isolation, whereas practice typically involves a unique combination of practices guided by patient goals, therapist experience and preferences, and resource availability/feasibility. Acquired brain injury (ABI) adds further complication to the feasibility of such therapies at the patient level. This challenge could relate to a patient's cognition level or behavioural concerns. We have explored the feasibility of such a program focused on locomotor training within an inpatient ABI program, evaluating the appropriateness of 20 consecutive patients.

Methods: 20 consecutive patients were assessed for their appropriateness of the PRIME training program, determined by present functional status, cognition level, behavioural concerns and comorbidities that could act as contraindications for therapies such as robotic or therapist-assisted overground or treadmill training. This included use of the Canadian Standing and Walking Assessment Tool as a staging tool to categorize patients by function – an approach previously employed in persons with spinal cord injury. Also collected was their length of stay, admission and discharge FIM scores, and the presence of pain, as well as pain intensity and impact on activities.

Results: Of all 20 patients, 10 were deemed appropriate for the PRIME program (included group) and 10 were deemed not appropriate (excluded group). For those who were not appropriate, 5 were excluded due to co-morbidities, 4 were excluded due to various cognitive difficulties, and 1 patient was excluded due to behavioural concerns. Length of stay between the 2 groups was not significantly different ($p=0.12$). The FIM admission and discharge scores for the included group were significantly higher than that of the excluded group ($p=0.04$ and $p=0.03$ respectively). The change in score for FIM admission and discharge was slightly higher for the included group, although was not significant ($p=0.2$). At admission, pain was present in more patients from the excluded group (8 of 10) than the included group (6 of 10), although the intensity and impact of pain did not differ. Moreover, pain was no longer an issue by discharge for 3 of the 6 patients originally reporting pain in the included group.

Conclusion: Overall, the PRIME program is feasible in the inpatient ABI context, but the appropriateness for patient inclusion needs to be evaluated on a case by case basis. Next steps include examining this in a larger group of patients and also evaluating the effectiveness of various approaches to locomotor training within in a case series of patients.

Psychological Mechanisms Underlying Post-Concussion Syndrome Following Mild Traumatic Brain Injury

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Background: Mild traumatic brain injury (mTBI) is the most frequent type of traumatic head injury. Most people who sustain mTBI return to their previous level of functioning within three months. However, a significant percentage of patients continue to report cognitive and emotional symptoms long after the injury (also known as Post Concussion Syndrome - PCS), despite the objective severity level of the injury. The aim of the present study was to explore the underlying psychological mechanism of PCS, by testing the relationship between several personality characteristics and different clinical symptoms reported by the patient, while the patient's subjective perception of his injury served as a mediating variable.

Method: 30 patients between the ages 21-57, all being at least three months past the diagnosis of mild head injury. Participants underwent a psychiatric clinical interview in which anxiety, depression, Post Traumatic Stress Disorder (PTSD), and quality of life were assessed. Additionally, subjects completed questionnaires assessing 'self-efficacy'; 'coping style'; personality traits-'big five'; 'perfectionism' and 'Acceptance of Disability' to evaluate their perception of injury.

Results: Analysis of the linear regression showed full mediation of the variable 'acceptance of disability' in the correlations found between the psychological aspects: 'self-efficacy', personality trait 'agreeableness' and perfectionism characteristic 'concern over mistakes' and each of the predicted clinical outcome (depression, anxiety, PTSD and quality of life), separately.

Conclusions: These findings identify psychological traits affecting 'self- acceptance' post injury and that the patient's subjective perception of this injury accounts more for rehabilitation outcome than the objective disability per se.

Brain Injury and Serious Mental Illness: An Overview of the Complexities and Treatment Considerations for Improving Outcomes

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Individuals with a history of psychiatric illness have been found to be nearly twice as likely to suffer a brain injury (Fann, et al., 2002; Liao, et al., 2012). In addition, nearly half of individuals who sustain a moderate to severe brain injury experience psychiatric symptoms following injury (Fann, et al., 2004). Olver et al. (1996) found that there was a higher incidence of emotional, cognitive, and behavioral changes at five years post injury, suggesting treatment of psychiatric symptoms is a lengthy process. Thus, clinicians are often faced with the challenge of treating psychiatric and neurobehavioral symptoms than can significantly impede engagement in necessary therapies, resulting in poorer overall outcomes.

In addition to the heterogeneity of the physical and cognitive deficits following an acquired brain injury, the complexities of psychiatric symptoms add another variable, arguably primary, to the rehabilitation process. Barriers to treatment can include poor engagement, decreased motivation, sabotaging behaviors, difficult family dynamics, frustration intolerance, cognitive side effects of medication, and lack of trust in providers. Psychiatric symptoms contributing to barriers in treatment can include depression, apathy, paranoia, psychosis, anxiety, identity diffusion, personality pathology, and suicidality. These barriers can result in rehabilitation facilities feeling ill equipped to treat this population, inappropriate institutionalization, caregiver burnout and poor community reintegration. Moreover, psychiatric comorbidities have been found to increase the overall expenditures in this population (Wei, et al., 2005).

Unfortunately, there is a dearth of literature for clinicians to rely upon in conceptualizing and treating these individuals. In the absence of yet-established empirically supported methods for intervention, this presentation aims to increase knowledge and provide clinicians with general guidelines for providing best-practice care for individuals with comorbid brain injury and mental illness, particularly in inpatient or residential settings.

Best practice guidelines to consider include understanding the function of behavior as primary to development of appropriate and effective behavioral interventions. Further, we will discuss the ways in which mental health professionals have a unique role on the treatment team, with further delineation of the ways in which all team members can enhance therapeutic benefit with every patient interaction. Moreover, the importance of both person-centered care and maintaining a therapeutic milieu are discussed using a trauma-informed perspective. We will also review the distinctions between lack of psychiatric symptoms and overall mental and psychosocial well-being, particularly as it relates to intervention and outcomes.

Specific case studies, behavioral interventions, behavior tracking methods, and non-violent crisis intervention strategies will be reviewed. Example case studies include treatment of severe apathy with structured behavior planning and relevant reinforcers, as well as utilizing patients' psychological needs and developing intrinsic motivation as a mechanism of change. Will also include case studies addressing treatment of impulsivity, mania, and psychosis.

The Accumulation of Subconcussive Impacts Across a Single Season of Division I Football

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The cumulative effect of multiple high intensity hits on brain structure and function is still largely unknown. Collision sports, particularly football, have been previously shown to accumulate thousands of impacts across a single season. However, unlike concussion, these cumulative impacts, or subconcussive impacts, do not get diagnosed and the long-term cognitive, motor, and psychiatric deficits are poorly understood. Therefore, we investigated the effects of the accumulation of subconcussive impacts across a single season of Division I football using advanced biomechanical technology on various cognitive processes (via virtual reality), blood biomarkers, and structural and functional integrity (via magnetic resonance imaging (MRI)). Data from 24 Penn State football players were collected before preseason, during the season, and after the season on various modalities. Before the season, data was collected on virtual reality (VR; balance, reaction time, spatial navigation), blood biomarkers (GFAP, UCH-L1, S100-B) and MRI (functional MRI (fMRI), arterial spin labeling (ASL), diffusion tensor imaging (DTI), and susceptibility weighted imaging (SWI)). During the course of the season, subjects wore helmet accelerometers (BodiTrak System) for 53 total practices. Accelerometer data was collected during each practice; if the subject met specific thresholds of 1 hit $\geq 80G$ or ≥ 28 hits of $\geq 25G$, additional VR testing was done. After the season, the VR, MRI, and blood biomarker protocols were repeated. Results revealed that there were a total of 129 hits at 80G and 3557 hits at 25G. However, during preseason (12 practices), 78.3% of the 80G hits were obtained, and during the season (43 practices) 67.4% of the 25G hits were obtained. Additionally, when broken down by position, the offensive and defensive lines had the majority of both 80G and 25G impacts. Virtual reality results revealed that before season versus post-season score significantly decreased post-season for spatial navigation ($p < 0.05$) while balance significantly increased post-season ($p < 0.05$). MRI analysis revealed there were no significant differences before and post-season on DTI metrics or cortical volumes. SWI analysis revealed that 8 of 18 subjects exhibited significant abnormalities in focal regions ($p < 0.05$). ASL data showed a significant overall increase of cerebral blood flow (CBF) at cortical regions over the season ($p < 0.05$). Additionally, functional connections to the right ICC (isthmus of cingulate cortex), left ICC, and left hippocampus seed regions were significantly changed over the season ($p < 0.05$). Blood biomarker data is currently in the process of being analyzed. These cumulative results show that there are spatial memory and multimodal imaging abnormalities after one season of football. So, even in the absence of clinical symptoms and a concussion diagnosis, these subconcussive impacts can cause physiological and cognitive changes in collegiate football players.

Efficacy of an Intervention to Promote Resilience and Adjustment after Traumatic Brain Injury

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Objective: Brain injury researchers have recently turned their attention to resilience, an individual characteristic that allows persons who experience trauma to successfully adjust, adapt, and, in many cases, thrive despite adversity. Resilience is not viewed as a trait, but rather as a set of skills which can be developed and enhanced. A number of studies involving children, adolescents, and adults with anxiety disorders, depression, PTSD, and learning disabilities have demonstrated the efficacy of resilience-based interventions. Clinical researchers have suggested that adults experiencing the lingering consequences of brain injury may also benefit from resilience-based intervention approaches. The primary purpose of the present investigation was to evaluate the efficacy of a structured, curriculum-based intervention to promote postinjury resilience and adjustment following traumatic brain injury (TBI).

Methods: The Resilience and Adjustment Intervention was designed to address post-TBI needs, concerns and challenges, emphasizing education, skill building, and psychological support. 160 outpatients with mild to severe TBI were assigned to either a treatment or wait list control group. The manualized treatment focused on highly relevant topics (e.g., common injury effects, coping with loss and change, one's role in recovery, problem solving, communication, and stress management) and was delivered in seven one-hour sessions with outcome measurement pre- and post-treatment. Outcome measures included the Connor-Davidson Resilience Scale (CD-RISC), Mayo Portland Adaptability Inventory-4 (MPAI-4), and the Brief Symptom Inventory-18 (BSI-18).

Results: Treatment group participants showed a significant improvement in CD-RISC scores, whereas controls did not. The group's pre-treatment score climbed from a mean of 21.14 (SD=8.1) to 28.44 (SD=6.9) following intervention, while the control group mean was 23.35 (SD=9.0) at first baseline and 23.74 (SD=8.1) at second baseline. In addition, the treatment group showed improvements on the MPAI-4 Ability scale as well as BSI-18 Somatic, Depression and Anxiety scales, while the control group did not. The treatment group's pre-treatment MPAI Ability score dropped (improved) from a mean of 55.01 (SD=9.7) to 50.99 (SD=8.3) following intervention, while the control group score went from 53.55 (SD=10.8) at first baseline to 54.23 (SD=9.5) at second baseline. BSI-18 results were similar with greatest changes observed for the Depression subscale; a treatment group pre-treatment mean of 63.48 (SD=12.4) and post-treatment mean of 56.83 (SD=10.7), and control group means 62.06 (SD=11.9) and 61.11 (SD=11.3), respectively. No differences were observed for the MPAI-4 Adjustment and Participation scales.

Conclusions: Investigation provided evidence that a curriculum-based education, skill-building, and support intervention can benefit individuals with TBI. Additional research is needed to ascertain the longer-term benefits of intervention and the efficacy of alternative delivery methods (e.g., via telephone and the Internet).

Comparison of Symptomology, Symptom Resolution Time, and Return to Play Time Between Concussions Sustained in the Same Academic Year

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Objectives: Heightened awareness regarding sport related concussions has garnered increasing concerns around multiple concussions sustained by one athlete. Previous research shows that, among those with a history of previous concussions, outcomes for a recurrent concussion are worse. Furthermore, the latter of two concussions that occur within two weeks of each other results in worse outcomes. Although there is an abundance of research on multiple concussions, there has been little investigation into concussions that occur in the same academic year. The purpose of this study is to examine symptomology, symptom resolution time, and return to play (RTP) time between concussions sustained in the same academic year.

Methods: Concussion data from the National Collegiate Athletic Association (NCAA) Injury Surveillance Program (ISP) during the 2009/10-2013/14 academic years and the National Athletic Treatment Injury and Outcomes Network (NATION) during the 2011/12-2013/14 academic years were examined. Concussions were reported by athletic trainers (ATs) and were included if the student-athlete sustained multiple concussions in the same academic year. In lieu of local legislation or guidance, ATs were encouraged to use the definition provided by the Consensus Statement on Concussion in Sport to diagnose concussions. Proportions and means of symptoms, symptom resolution time, and RTP time were calculated, and Chi square tests and Wilcoxon rank sum tests were used to compare these between the first and second concussions.

Results: Overall, 128 student-athletes (70 intercollegiate and 58 secondary school) sustained 256 concussions across 14 different sports. Of these, 131 (51.1%) occurred in football. The mean number of symptoms experienced was similar between the first and second concussion (5.15 vs. 4.89, respectively; $p=0.42$). No differences were observed in the types of symptoms experienced between first and second injuries. The RTP time associated with the second concussion was greater: 30.8% of second and 11.5% of first concussions resulted in participation restriction of 30 or more days ($p=0.01$). Symptom resolution time did not differ from the first to the second concussion (8.6% of first and 11.9% of second concussions took >28 days to resolve; $p=0.40$). Additionally, ATs reported a symptom resolution time within one day in 21.4% of first concussions and 14.7% of second concussions ($p=0.19$).

Conclusions: Although the RTP time was greater in second concussions compared to first, symptom resolution time did not differ. This suggests that there may be a difference in AT management of second concussions, with a more conservative, extended RTP progression. This is consistent with the management of recurrent injuries of different types and body parts. This is also consistent with previous research examining concussions in the same athletic season among secondary school athletes. Further research is needed to examine second concussions in student-athletes in which the first concussion took less than one day to resolve.

Neuroinflammation Following Traumatic Brain Injury: A Positron Emission Tomography Study

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Objective: To study microglial activation as a biomarker for neuroinflammation in patients with traumatic brain injury (TBI) compared to healthy controls, using positron emission tomography (PET).

Methods: In this study, 20 patients with TBI (age 44±15) and 8 healthy controls (age 50±8) underwent dynamic PET scan with translocator protein ligand [11C]-PK11195. For TBI patients the PET imaging was performed using GE Advance PET scanner (General Electric Medical Systems, Milwaukee, WI, USA) 507 days post-injury on average and High-Resolution Research Tomograph (HRRT) PET scanner was used for the healthy controls. Correspondingly the brain MR imaging was performed using 3T Achieva (Philips Medical Systems, The Netherlands) for TBI patients and with Philips Gyroscan Intera 1.5 T Nova Dual scanner (Philips, Best, the Netherlands) for healthy controls. Regions of interest were extracted using Freesurfer (v5.3.0). Image analysis was then done using MATLAB (R2011a) and PMOD (version 3.4, 2013 PMOD Technologies Ltd, Zurich, Switzerland) software. From the PET images, distribution volume ratio (DVR) and binding potential (BPnd) of [11C]-PK11195 ligand were calculated for evaluation of microglial activation by using supervised clustering method to find a reference region with no specific binding. DVR was estimated using Logan's method within time interval 20 to 60 minutes and BPnd was estimated with simplified reference tissue model (SRTM). Statistical analysis was performed using SPSS (version 23, SPSS IBM, New York, NY) and 95% confidence interval was considered as statistically significant for the results.

Results: We observed that patients with TBI had statistically significantly higher TSPO binding than controls in almost all regions of the brain studied. Patients showed higher binding potentials in the amygdala ($p=0.002$), brain stem ($p<0.0001$), caudate ($p<0.001$), cerebellum ($p<0.0001$), hippocampus ($p=0.001$), left cerebral white matter ($p=0.008$), lateral temporal cortex ($p<0.001$), medial temporal lobe ($p<0.0001$), occipital cortex ($p=0.003$), pallidum ($p=0.001$), posterior cingulate cortex ($p=0.021$), putamen ($p=0.026$), thalamus ($p<0.0001$), and diencephalon ($p<0.001$).

We also observed that in most patients the thalamus and brain stem had the highest binding potentials.

Conclusions: Our results indicate that patients with TBI have higher level of microglial activation compared to healthy controls in most of the brain regions studied. Thalamus and brain stem showed the highest binding potential in most subjects. This suggests that patients with TBI may have chronic neuroinflammation.

A Clue to Consciousness? Significance of Circadian Rhythms in Severe Brain Injury

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Background: Physiological and psychological functions extending from cellular processes to higher cognitive functions have been shown to vary rhythmically with a period length of about 24 hours (i.e. a circadian rhythm). In healthy individuals, also consciousness varies with a circadian pattern paralleling the sleep-wake cycle. From a clinical perspective, misalignment of circadian rhythms, that is when the sleep-wake schedule is at odds with the light-dark cycle can cause considerable stress, impair cognitive abilities such as attention and learning and have detrimental effects on the immune system. Moreover, the temporal disorganisation of circadian rhythms, that is the uncoupling of different rhythms, has been attributed pathological significance in critically ill patients and may even hinder recovery.

Methods: Here, we investigated the integrity of circadian temperature rhythms in n = 18 patients suffering from disorders of consciousness (i.e. vegetative state/unresponsive wakefulness syndrome [VS/UWS], minimally conscious state [MCS] or minimally conscious state plus [MCS+]) following severe traumatic or non-traumatic brain injury. Variations in body temperature were analysed using Lomb-Scargle periodograms. The association between the circadian rhythms and results obtained from neuropsychological assessment using the Coma Recovery Scale-Revised (CRS-R) was evaluated with correlation analyses. Beyond this, we piloted in a subsample of n = 8 patients whether bright light stimulation has a beneficial effect on circadian rhythms.

Results: Interestingly, analyses revealed that all patients still had a significant circadian temperature rhythm (range 23.5-26.3h). Furthermore, we found that especially scores on the arousal subscale of the CRS-R were closely linked to the integrity of circadian variations in body temperature. Finally, we found positive evidence for bright light stimulation being able to support circadian rhythmicity in two out of eight patients.

Conclusions: In conclusion, this study provides first evidence for an association between circadian body temperature rhythms and patients' arousal levels. Intriguingly, sufficient arousal levels are a precondition for consciousness suggesting that the integrity of circadian rhythmicity may be crucial for the emergence of consciousness in severely brain-injured patients. Thereby, our findings also make a case for circadian rhythms as a target for treatment as well as the application of diagnostic and therapeutic means at times when cognitive performance is expected to peak.

Violence-Related TBI in Justice-Involved Women

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Background: Research has shown elevated rates of TBI among justice-involved individuals, including higher rates of violence-related TBI (Shiroma, Ferguson, & Pickelsimer, 2010; Wall, Gorgens, Yeo, & Alexander, 2016). Additionally, several studies have demonstrated poorer outcomes for those with violence-related TBIs (Gerhardt, Mellick, & Weintraub, 2003; Schopp et al., 2006; Bushnik, Hanks, Kreutzner, and Rosenthal, 2003). To date, few studies have examined violence-related TBIs among justice-involved women in particular (O'Rourke, Linden, Lohan, & Bates-Gatson, 2016). A better understanding of the prevalence of these injuries and the associated vulnerabilities will help providers tailor and deliver services to mitigate the personal and societal impact of these injuries.

Method: This study used archival data from the TBI Implementation Grant database, DU IRB Protocol #674894-2. 409 individuals, 135 females and 274 males were included. Prevalence and incidence of violence-related TBI, violence-related multiple TBIs, and all multiple TBIs were compared for men and women using Pearson Chi-Square tests. Men and women were compared on total number of TBIs and youngest age of TBI using a Kruskal-Wallis one-way ANOVA. Women were grouped by presence or absence of violence-related TBI and compared on multiple potential vulnerabilities such as physical health problems, mental illness, and length of incarceration. Women were then re-grouped into violence-related multiple TBI, violence-related single TBI, and non-violence-related TBI and compared on the same variables.

Results: 1190 total TBIs were reported, 781 by men, 409 by women. 66.7% of women reported violence-related TBI, compared to 62.8% of men. 38.4% of TBIs reported by women and 36.6% reported by men were violence-related. These differences were not significant.

Gender was significantly associated with multiple TBIs (10.330, $df = 1$, $p = .001$, odds ratio = 2.2, $N = 348$), and multiple violence-related TBIs (7.074, $df = 1$, $p = .008$, odds ratio = 7.7, $N = 49$). History of violence-related TBI was significantly associated with physical health problems (7.902, $df = 1$, $p = .005$, odds ratio = 4, $N = 106$) and length of incarceration ($p = .022$, $N = 97$). There were significant differences between the multiple violence-related TBIs, a single violence-related TBI, and non-violence related TBI groups on length of incarceration ($p = .001$, $N = 100$).

Discussion: These results demonstrate elevated rates of violence-related TBI among women compared to the general population, as well as an increased prevalence of multiple TBIs and violence-related multiple TBIs among justice-involved women compared to justice-involved men. These violence-related injuries are associated with more physical health diagnoses and longer incarceration times. This study supports the importance of screening for violence-related injuries among women. Clinicians can use this information to tailor services for women with the goal of improving personal outcomes and reducing care and cost burdens to justice systems.

The Scandinavian Guidelines for Initial Management of Minimal, Mild, and Moderate Traumatic Brain Injury in Adults: A Prospective Validation Study

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Objectives: The Scandinavian Guidelines for Initial Management of Minimal, Mild, and Moderate Traumatic Brain Injury in Adults (Scandinavian guidelines) were published in 2013. The guidelines are evidence and consensus-based and for the first time incorporate serum S100B measurement as part of emergency department (ED) triage of head injury (HI) patients. These guidelines intend to reduce unnecessary head trauma computed tomography (CT) scanning. This study evaluated the Scandinavian guidelines.

Methods: The Scandinavian guidelines were implemented into clinical practice in the ED of the Tampere University Hospital, Tampere, Finland (November 2015–November 2016). The Tampere University Hospital is the sole neurosurgical referral hospital in the hospital district. All consecutive adult HI patients (N=2,612; mean age=56.4 years, SD=23.2; men=54%) that were treated at the ED were eligible for inclusion. An injury-ED admission delay of over 24 hours was considered an exclusion criterion. This validation study enrolled 297 patients (mean age=60.8 years, SD=22.6; men=50.5%). Head CTs were performed according to the on call physician's evaluation. The Scandinavian guidelines recommend S100B only with mild-low risk HI patients within 6 hours of injury. However, for this study venous blood for S100B sampling was drawn from all HI patients. For the clinical validation part of the study, only the samples collected within 6 hours after injury were used. One week following injury, a phone call and medical record review was conducted to identify possible HI-related complications (e.g., hospital/ED re-admission, repeat head CT, or death).

Results: The enrolled HI patients (n=297) were distributed to the Scandinavian guidelines' severity groups as follows: minimal=28.7% (n=86), mild-low risk=29.7% (n=88), mild-medium risk=13.2% (n=39), mild-high risk=26.7% (n=79), and moderate=1.7% (n=5). Compliance to the guidelines on head CT scanning was 71.3% (n=211); overall 66.3% (n=197) of the cases were scanned. Acute traumatic lesions were detected on 9.5% (n=19) of the scans, and three of these findings resulted in neurosurgery. One of the CT-positive patients (n=19) was scanned without a guideline-based indication. Nonetheless, this lesion did not demand any specific treatment or repeated imaging. Of the mild-low risk patients, the S100B level was under 0.1 microgram/liter (<6h post-HI) in 25.3% (n=19). Although the S100B result was negative (<0.1 microgram/liter), 10 patients (52.6%) underwent head CT. None of these scans showed a traumatic lesion. Four mild-low risk patients (9.3%) with a positive S100B results (≥0.1 microgram/liter) had a traumatic lesion on CT. Of the entire sample, 15 patients (5.1%) were re-admitted to the ED and 2 patients (0.7%) died one

week after the primary HI. None of these adverse events were directly caused by a primarily undiagnosed intracranial injury, which could have been prevented by initial CT scanning.

Conclusions: The Scandinavian guidelines have potential to reduce unnecessary head CT scanning. Additional large-scale validation studies are warranted.

Violence-related Traumatic Brain Injury

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Objectives: A substantial number of traumatic brain injuries (TBI) are caused by violence-related incidents. The purpose of this study was to determine the unique characteristics of violence-related TBIs with an emphasis on possible preventable risk factors.

Methods: All consecutive patients who underwent head CT due to an acute head injury (N=3,023) at the Emergency Department (ED) of Tampere University Hospital (Aug 2010-Jul 2012) were included. Data collection consisted of socio-demographics, injury-related data, and clinical information from the ED. In the ED, a non-contrast head CT scan was performed for all patients with a 64-row scanner. Patients with a violence-related TBI were identified (n=222, 7.3%). A detailed retrospective data collection was performed on these patients.

Results: Violence-related TBI patients (n=222) were compared to patients who sustained a TBI by other mechanisms (n=2,801). Statistically significant differences between the groups were found on the following factors: (i) age (violence: mean=35.4, median=34.1, SD=12.9; versus other: mean=56.5, median=59.1, SD=23.9, $p<0.0001$), (ii) gender (males: 78.4%; versus 54.7%, $p<0.0001$, OR=3.0), (iii) prior circulatory system disease (8.1% versus 41.9%, $p<0.0001$, OR=0.1), (iv) prior mental or behavioral disorders (43.7% versus 24.4%, $p<0.0001$, OR=2.4), (v) chronic detrimental alcohol usage (34.2% versus 17.2%, $p<0.0001$, OR=2.5), (vi) regular substance abuse (18.5% versus 2.4%, $p<0.0001$, OR=9.2), (vii) regular medication (31.1% versus 54.0%, $p<0.0001$, OR=0.4), (viii) alcohol-intoxicated while injured (59.5% versus 21.7%, $p<0.0001$, OR=5.3), (ix) narcotics-intoxicated while injured (2.7% versus 0.7%, $p=0.001$, OR=4.1), and (x) acute traumatic lesion on head CT (13.1% versus 19.6%, $p=0.017$, OR=0.6). The groups did not differ on clinical TBI signs (GCS, loss of consciousness, amnesia, or disorientation), TBI severity (mild, moderate-severe) or on the need for neurosurgery. In adjusted logistic regression, lower age ($p<0.001$, OR=0.96, 95%CI=0.95-0.97), male gender ($p=0.002$, OR=1.68, 95%CI=1.24-2.50), alcohol intoxication ($p<0.001$, OR=3.55, 95%CI=2.61-4.83), and mental or behavioral disorders ($p<0.001$, OR=1.79, 95%CI=1.31-2.43) were all independent risk factors for violence-related TBI. Among the violence-related TBI patients, hitting with a fist or kicking were the most common (61.7%) ways of assault and in most of the incidents (72.9%) the assaulter was unknown. Nearby municipalities and suburban areas were the most common (63.6%) places for injury. These injuries happened more often on the streets (30.6%) than in homes (15.8%) or restaurants/bars (12.6%). Over half (53%) of all the violence-related TBIs occurred between 10pm and 4am.

Conclusions: Young adult males with premorbid mental health history (including chronic alcohol abuse) are most prone to sustain a TBI due to a violence-related incident. These incidents are often related to alcohol intoxication, and occur on nighttime streets. However, violence was not associated with more severe TBIs than other mechanisms of injury. Preventive measures should be focused on alcohol consumption.

Predictors for Return to Work and Post-Concussion Symptoms in Subjects with Mild Traumatic Brain Injury

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Objectives: A substantial group of patients are reporting symptoms and disability after a mild traumatic brain injury (MTBI). Several authors underline the need for a greater focus on the management of persistent post-concussion symptoms (PCS) to improve return to work (RTW). However, the majority of patients who RTW still present symptoms, and recently published re-views found different predictors for functional recovery in general as compared to RTW. Identifying predictors for delayed RTW and PCS, may help to identify those who may benefit from a follow-up rehabilitation program.

The aim of this study was to identify if there are different clinical characteristics that predict RTW and PCS at 12 months for patients with persistent PCS six to eight weeks post-MTBI.

Methods: A prospective cohort study of 151 patients, 15-55 years with MTBI who either were sick-listed or at risk to be sick-listed with persistent PCS symptoms at six to eight weeks post-MTBI admitted consecutively to out-patient clinics at two University Hospitals in Norway, from January 2009 to January 2012. MTBI was defined as Glasgow Coma scale 13-15, unconsciousness less than 30 minutes and post-traumatic amnesia less than 24 hours. Exclusion criteria were other significant diseases or conditions that impact their working skills.

Preinjury-, injury-, and postinjury-related clinical variables presented at six to eight weeks post-MTBI together with some relevant clinical data from the emergency stay at hospital were used to find any significant associations with RTW and PCS 12 months post-MTBI. Rivermead Post Concussion Symptoms Questionnaire measured PCS. Sick leave data from one year before to one year post-MTBI were obtained from The Norwegian Labour and Welfare Service. Self-report questionnaires were used to obtain demographic and symptom profiles. We used a logistic regression model to assess the predictors for RTW where we stepwise reduced the dimension. To determine predictors for PCS we conducted a linear regression analysis.

Results: PCS six to eight weeks post-MTBI (OR 1.72 (1.2, 2.3)), expectation of a favourable outcome (OR -5.80 (-11.0, -0.7)) and having been sick-listed within the last year before injury (OR 4.31 (0.1, 8.5)) were predictive for PCS at 12 months. There was a significant negative association between RTW at 12 months and psychological distress (HAD), (OR 1.14 (1.1, 1.2)), severe and moderate disability at two-months post-MTBI (GOSE), being sick-listed at two months post-MTBI (OR 6.84 (2.3, 19.9)) and having been sick-listed within the last year before injury (OR 7.29 (2.6, 20.3)). None of the injury-related variables such as CT findings and different measures of pain were significantly associated with RTW or PCS.

Conclusions: We found different predictors for RTW and PCS after a MTBI, which may have clinical implications when considering vocational outcome in future rehabilitation models.

Assessing Traumatic Brain Injury Via Cortical Metrics

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Mild traumatic brain injuries are difficult to diagnose or assess and are particularly difficult to assess in circumstances where triage decisions are necessary. The majority of methods currently proposed to solve this problem are either costly, non-portable, extremely slow, often invasive, and/or in many cases fail to definitively (and quantitatively) diagnose the condition or have the resolution to assess treatment efficacy. Direct measures of brain health are difficult to achieve because of both the cytoarchitectural complexity of the brain and the resolution necessary to detect subtle changes in function. This problem provided the motivation for the development of a new system for assessing brain health that employs a portable computer peripheral to enable high resolution tests of within-brain connectivity. The system delivers tactile (skin) stimulation to the fingertips, and leverages the neuroanatomical complexity that exists between the adjacent cortical areas that are activated by fingertip stimulation. The observed sensory percepts are highly influenced by interactions between adjacent brain areas and effectively provide a potentially very high resolution metric of functional connectivity. The protocols that were both designed and validated from in vivo studies of cerebral cortical dynamics in non-human primates target a number of information processing mechanisms are called cortical metrics. These have been demonstrated in multiple independent studies to be sensitive to alterations in brain health. Viability of the method as an effective tool for tracking recovery from traumatic insult has been established in sports concussion studies (99% confidence level ($p < .01$) for differentiating individuals with and without concussion). Studies in military populations have been initiated. There are several major components of the current effort, three of which will be described, including the practical implementation of the method in the field, and delivery of easily interpretable results to end users. The second major effort involves implementation of an animal model that evaluates parallel responses evoked in the cerebral cortex. The third major effort is a physiologically realistic neuro-computational model that bridges results from the first two efforts. A series of case studies, as well as formal research findings from the human subjects effort, and interpretations extrapolated from the computational and animal experimental work, will be presented.

Detonations of Small Spherical Explosive Charges Disrupt Synaptic Integrity and NMDA Receptor-Cofilin Signaling in the Absence of Neurodegeneration in Hippocampal Slices

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Primary explosive blast waves cause common types of military-related traumatic injuries. A novel procedure was developed that generates distinct blast waves from 1,3,5-Trinitroperhydro-1,3,5-triazine (RDX), explosive (Zander et al. 2015 *J Neurosci Res* 93:1353; Smith et al. 2016 *Exp Neurol* 286:107). To study direct effects of detonated RDX spherical charges on brain tissue, rat hippocampal slice cultures were sealed in serum-free medium, lowered into a water-filled tank, and RDX assemblies detonated outside the tank. Compared to mock-treated slice cultures, the RDX blasts caused a dose-dependent reduction in pre- and postsynaptic markers. GluR1 was reduced by 25-40% after two consecutive blasts 4 min apart, and further reduced by 60-70% after three RDX blasts. The degree of synaptic marker loss correlated with increased levels of HDAC2, a histone deacetylase implicated in stress-induced reductions in glutamatergic transmission and recognition memory (Wei et al. 2016 *J Neurosci* 36:2119). The blast-induced loss of GluR1, NCAM180, and synaptophysin was rapid, with 40-50% declines evident 24 h after multiple detonations, followed by further decline at 45 h post-blast, and no indication of recovery at 72 h. Interestingly, while protein accumulation events (e.g. tau, TDP-43) are often common features of TBIs (Blennow et al. 2012:*Neuron*; Goldstein et al. 2012:*Sci Transl Med*; Smith et al. 2013: *Nature Rev Neurol*; Zhang et al. 2015:*J Cereb Blood Flow Metab*), the synaptic decline temporal profiles induced by the small 1.7-g RDX explosives aligned much closer to synaptic decline profiles from excitotoxic hippocampal slices than to the declines in protein accumulation stress studies. However, the RDX blast-induced disturbances in synaptic integrity were observed in the absence of calpain-mediated cytoskeletal damage and neuronal death, events tightly associated with synaptic marker loss after hippocampal excitotoxicity (Bahr et al. 2002, *Exp Neurol* 174:37). Also, Fluoro-Jade B staining found no indication of degenerating neurons in slices exposed to three RDX blasts, suggesting that certain levels of military explosives produce a unique type of pathology comprised of altered synaptic integrity before cellular deterioration. The results suggest that, in addition to serious brain damage from large explosions, primary blast impacts can cause synaptic compromise without producing overt neurodegeneration, perhaps explaining the cognitive and behavioral changes in blast-induced TBI sufferers with no detectable neuropathology. The monitoring of individuals' cumulative blast exposures is a critical issue in light of this study. Also, this work will help understand how military blasts might increase the risk of Alzheimer's disease. Support: This material is based upon work primarily supported by the U.S. Army Research Laboratory and the U.S. Army Research Office under grant number W911NF-14-2-0087 (BAB), and by DOD grant W911NF-15-1-0432 (BAB), NIH RISE grant 5R25GM077634-04 (UNCP), and postdoctoral and technical assistance for the collaborative study and sample analyses.

The Role of Physics in Irreversible Psychological Phenomena: Quantum Neurology and Psychology

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In the physical universe as we know it, we are only in contact with what we are allowed to see or observe within a much broader spectrum. We are not addressing the world as such, because the physical reality we perceive from the outside world does connect us with the final reality, but with symbolic transformations of what we perceive through human consciousness, transcending physical possibilities. Mental work and activity is what gives us the capacity to transcend. Indeed, to reach deeper to the finer-scale of quantum physics. The psychology and neurology of today should be approached as quantified physics and neurology. The theory of quantum physics posits that the mind and consciousness derive from neuronal activity in the brain on a subatomic or quantum scale. One specific moment which produces objective reduction to a quantum state is carried out fundamentally by microtubules inside neurons. A quantum of energy is the lowest amount of energy that can be transmitted on any wavelength in the world, in the universe. The application of quantum physics to psychology and neurology will change our view and our place in the world. Currently, a number of scholarly texts are focusing on brain plasticity and synaptic regulation via microtubules. Research is being done on improved psychoactive drugs, including antidepressants and anxiolytics, or on the anesthetic effects of neuronal microtubules. Similarly, cognition studies have reported that different memory processes are carried out via microtubules which use synaptic messengers for phosphorylation. In short, the mental and physical quantum moment is no more than the quantum state maintained during a certain period of time: what is mental is physical.

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Depression, Cognition, and Dopamine Genetics: Piecing Together the Complicated Puzzle of Behavior Following Traumatic Brain Injury

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Outcomes following moderate/severe traumatic brain injury (TBI) vary widely and often include cognitive, emotional, and behavioral sequelae. Cognitive complaints have long been associated with injury, and emotional and behavioral dysfunction is increasingly recognized as important following injury. We aim to understand the interplay of these multiple phenotypes and their relationship to the ANKK1 Taq1a polymorphism, a genetic marker in the dopamine system pathway. We measured cognition with a battery of 8 normed neuropsychological tests, creating a global cognitive composite t-score using methods we have previously published. We defined cognitive dysfunction as 1 standard deviation or more below the mean (t-score of 40 or below). We measured behavioral dysfunction using the Functional Systems Behavioral Scale (FrSBe), where a score 2 standard deviations above the mean was considered significant behavioral impairment (t-score of 70 or higher). Finally, we evaluated depression status based on the Patient Health Questionnaire-9, following established criteria. These outcome data were collected at 6 and 12 months post-injury. Our study included 68 participants with complete data who were recruited from a larger study examining long-term outcomes following TBI at the University of Pittsburgh. We conducted descriptive analysis, based on a theoretical model of behavioral outcomes after TBI that we have developed and which has been published. In these descriptive analysis, we show that for those with no depression or cognitive dysfunction, only 21% had behavioral dysfunction compared to 33% of those who did not have depression but did have cognitive dysfunction. Among those with depression but with no cognitive dysfunction, 47% had behavioral dysfunction. Finally, for those with both depression and cognitive dysfunction, 64% had behavioral dysfunction. When examining ANKK1 Taq1a genotype frequency among those with PTD, there was a significant difference ($p = 0.016$) in A2/A2 homozygote frequency by cognitive status. 86% of those who were in the poor cognition group were A2/A2 carriers compared to only 45% of those without cognitive dysfunction. No significant differences were noted in the no-PTD group, with A2/A2 frequency being 47% in the group with no cognitive dysfunction and 61% in the group with cognitive dysfunction. Overall, there appears to be a pattern suggesting additive effects of cognitive dysfunction and depression on behavioral dysfunction. Personal genetic risk may also play a role, as among those with depression and cognitive dysfunction, the frequency of the A2/A2 homozygotes is significantly greater than those without cognitive dysfunction. These preliminary findings further support the complex interactions among cognition, emotion, behavior, and personal genetics after TBI.

Effect of P2X4R Ablation after Acute and Chronic Ischemia/Reperfusion Injury in Middle Cerebral Artery Model of Stroke in Mice

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Backgrounds: P2X4 receptor (P2X4R), an ATP-activated ion channel receptor, is an important neurotransmitter receptor in the brain. Despite the known fact that excessive release of ATP occurs from dying cells during stroke, the role of P2X4R in its pathophysiology is not well understood. P2X4R mediated excessive influx of calcium leads to inflammasome activation and excitotoxic cell death in the neurons of the affected brain region. Extracellular ATP-binding to the microglial P2X4R receptor activation may initially cause brain repair but can also increase microglial proliferation and secretion of pro-inflammatory cytokines such as IL-1 β , TNF- α . On the other hand, these receptors also mediate BDNF release from microglia, which is an essential neurotrophin in maintaining synaptic plasticity, cognition, and post-stroke behavioral recovery. Therefore, we hypothesize that acute blockade of the P2X4 receptor is beneficial while chronic antagonism delays post-stroke rehabilitation.

Methods: Global P2X4R knockout mice and wild-type littermates of both sexes (~20-25g; C57BL/6), were randomized and subjected to right middle cerebral artery occlusion (MCAO-60min) followed by 3-day (acute time point cohort, used for infarct analysis) and 30-day (chronic time point cohort, used for behavioral recovery) reperfusion. Tissue infarct was quantified from 30 μ m thick cresyl violet stained sections obtained from perfused mice brain. The behavioral and functional endpoints in the chronic cohort include sensorimotor, memory, and cognitive functions starting two days after surgery then weekly for Rotarod, Corner test, OFT, ND score, and biweekly for the Y-maze test or terminal analysis (NORT and TST). Data are expressed as mean \pm S.E.M. ANOVA was performed, and a P < .05 was set for statistical significance.

Results: Mice with global P2X4Rs KO showed acute neuroprotective effects in both male and female mice. P2X4R KO mice showed approx. 50% and 26% decrease in hemispheric infarct volume in male (54.9 \pm 4.93 vs. 24.7 \pm 17.4 mm³) and female mice (50.14 \pm 3.92 vs. 37.87 \pm 3.18mm³) respectively. Parallel trends of protections were found in neurological deficit score. We found early recovery in anxiety-like behavior in female KO mice. Male P2X4R KO mice showed a progressive recovery in motor-balance coordination test using rotarod. We found a surprising but remarkable post-stroke depressive behavior phenotype in both male and female global P2X4R KO mice.

Conclusion: These findings suggest that P2X4R deletion leads to a differential effect of acute (anti-inflammatory) and chronic (depressive) time points of post-stroke recovery. A precise and time sensitive approach should be considered when targeting P2X4 receptors after stroke.

Effect of Fitting on the Protection Capacity of Ice Hockey Helmets: Analyses of Headform Kinematics and Brain Tissue Responses in the Study of mild TBI

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Falls, checking, and puck impacts are major causes of traumatic brain injury (TBI) among ice-hockey players. Accordingly, the major focus of researchers is on the development of effective protective tools to reduce the risk of TBI. A prevailing design consideration in this respect is providing a perfect fit between the helmet and the player's head for maximum protection. The effectiveness of the fit can be evaluated by monitoring the kinematic responses of the head in terms of linear and angular accelerations. Current researches on mild TBI (mTBI) mainly employ Hybrid III 50th percentile or other dummy head models conforming to the EN 960:2006 standards. While this is beneficial for standardizing laboratory procedures, the one-size-fits-all mentality results in an absence of an objective helmet fit guideline, accommodations for different head shapes in the helmet design, and inaccuracies of the embedded sensor's readings. To address these issues, for the very first time this study proposes a quantitative framework for developing fit parameters that minimize linear accelerations associated with mTBI. Three different controlled impact scenarios at a velocity of 4.5 m/s were performed using a custom monorail drop tower, a Bauer Re-AKT helmet, and three custom head forms. The first head form was fabricated to follow the exact contours of the test helmet, while the remaining head forms were systematically fabricated to vary along one axis in order to test fit scenarios where a slack was present in lateral and longitudinal axes. Furthermore, in an attempt to better understand the effect of helmet fitting on the brain injury risk, computational finite element (FE) simulations were conducted using North Dakota State University's (NDSU) validated finite element head model. FE analyses can help determine kinematic implications of varying the lateral and longitudinal gaps between the head model and a fixed helmet contour while significantly remove the needs for burdensome experimental tests. Our preliminary results show that a tight, more form fitting helmet results in incrementally higher accelerations but has a lower standard deviation in test results translating into more consistent protection performance. Our simulation results provide insights into the effect of helmet fit on the brain's dynamic responses such as intracranial pressure (ICP), shear stress and strain. We believe that our results might help to establish a framework for better comparing data from helmets designed to fit the standard EN 960 specified headform with those that are custom made for different head shapes.

Impact of Gender and Mood on Relationship between Post-Concussive Symptoms and Functional Impairment

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Objective: Previous studies have shown gender differences in symptom reporting following mild traumatic brain injury (mTBI). Further, recent findings have suggested mood may mediate the relationship between post-concussive symptoms and recovery from mTBI. The purpose of this study was to examine the impact of gender and mood on self-reported functional impairment following mTBI in a large youth sample.

Participants: 79 males and 104 females aged 10-20 who consecutively presented 0-21 days after mTBI to one of four outpatient concussion or sports medicine clinics participating in the North Texas Concussion Network Prospective Registry (Con-Tex).

Measures: Participants completed the General Anxiety Disorder-7 Item Scale (GAD-7), Patient Health Questionnaire-9 Items for Depression (PHQ-9), Pittsburgh Sleep Quality Index (PSQI), and a Concussion Symptom Log at their initial clinic visit. Self-report ratings of a) school/work, b) home, and c) social functioning on a scale of 1-10 at 3-month follow-up. A composite functional impairment score was calculated using a sum of ratings within these three domains.

Methods: Separate multivariate stepwise regressions were performed for males and females to determine if age, total concussion symptom score, GAD-7 score, PHQ-9 score, and the overall sleep quality item from the PSQI at initial clinic visit predicted self-reported functional impairment at 3-month follow-up.

Results: For females, concussion symptom score was a significant predictor of functional impairment ratings; however, once mood and sleep quality were entered into the model, the total GAD-7 score was the only significant predictor for functional impairment ($b=.44$, $p=.01$), explaining 18.2% of the variance in females at 3-month follow-up. For males, the PHQ-9 was the only significant predictor for functional impairment ($b=.59$, $p=.013$), explaining 7.8% of the variance in males' reported functional impairment at 3-month follow up.

Conclusions: For females, severity of overall post-concussion symptoms following mTBI did not predict self-reported functional impairment 3 to 4-months post-injury when the other factors were taken into account. However, anxiety symptoms did predict functional impairment. For males, only depression-related symptoms significantly predicted self-reported functional impairment several months post-injury. Although larger samples with more detailed follow-up are needed, these preliminary findings suggest gender differences in early post-mTBI symptoms that may relate to clinical outcome. Thus, screening for anxiety- and depression-related symptoms at time of clinical evaluation following mTBI in adolescents may aid treatment and recovery prediction following mTBI.

Dizziness and Balance Problems after Traumatic Brain Injury (TBI): Evaluation of an 8-week Vestibular Rehabilitation (VR) Program

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Background and Objective: Dizziness and balance problems have an incidence of 30-80 % in the TBI population. Studies show that dizziness and imbalance has the potential to restrict several aspects of personal and social life. Vestibular rehabilitation (VR) is an accepted and frequently used treatment for dizziness and imbalance. However, there is lack of evidence about its effect on patients with TBI.

The objective of the study was to evaluate the effect of a VR program on patients with dizziness and balance problems after traumatic brain injury.

Methods: A single blind randomized controlled trial study (RCT).

Participants: Sixty-five patients admitted to Oslo University Hospital with TBI (median GCS score: 15 range 7-15) and symptoms of dizziness and imbalance were included 3 months after the injury. Thirty-nine (70.8 %) were women. Mean age was 39.2 (SD: 12.9) years. The patients were randomized to the intervention group (IT) (n=34), or control group (CT) (n=31).

Intervention: Both groups received multidisciplinary assessment and evaluation at Oslo University Hospital. The intervention group in addition received an individually adapted group based VR program twice a week for eight weeks led by physiotherapists at Oslo University College, and a home exercise program.

Measurements: Functioning was tested as self-report and clinical tests at baseline and after the intervention period (8 weeks) and at 6 months after the injury. The primary outcome measurement was the Dizziness Handicap Inventory (DHI). Secondary outcome measures were Glasgow Outcome Scale-Extended (GOSE), Rivermead Post-Concussion Symptoms Questionnaire (RPQ), Vertigo Symptom Scale-sf (VSS-sf), Hospital Anxiety and Depression Scale (HADS), Balance Error Scoring System (BESS) and the High Level Mobility Assessment Tool (HiMAT). Injury-related data were collected from the medical records.

Statistical Analyzes: A linear regression model comprising 63 patients using the baseline measure of the primary outcome as covariate and type of intervention group as factor was used to assess the treatment effect on the DHI at 8 weeks as outcome. In addition, change from baseline to after the intervention period (8 weeks) was assessed.

Results: Preliminary results show that the group-based VR program had significant benefits ($p < 0.05$) in terms of dizziness related disability measured by the DHI in favor of the intervention group. Patients in the intervention group had a mean change in DHI scores of 14.75 (15.85) whereas the control group had a mean change in DHI scores of 5.09 (16.82) at 8 weeks after baseline. All participants improved their scores on the secondary outcome-measures. Further and more advanced analyses will be presented at the congress.

Conclusion: The results indicate that a group-based VR program is beneficial for decreasing dizziness-related disability after TBI.

Trial registration: (Clinical Trials # NCT01695577).

Novel Approaches for the Identification and Support of Justice Involved Individuals with Brain Injury

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A disproportionate number of youth and adults with Acquired Brain Injury (ABI) are involved in the criminal justice system. Without appropriate screening, treatment and community interventions, these individuals often end up re-offending and their level of involvement in the criminal justice system escalates. Historically, criminal Justice reform has focused on efforts to influence an individual's thinking and attitudes - to help them understand the consequences of their behavior, to make restitution, to learn pro-social behaviors. However, such approaches generally fail to appreciate that individual may have differences in their capacity to benefit from standardized interventions - especially if they have had an acquired brain injury. This symposium will highlight the progressive efforts in two states - Colorado and Pennsylvania - to make traditional interventions more effective using identification, neuropsychological screening, specialty interventions and community involvement. Epidemiology and outcome data from two statewide models will be presented.

Family Caregiver Proxy Report of the Impact of Deployment and Traumatic Brain Injury on the Health and Behavior of Children of U.S. Military Service Members

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Background: When a Service Member (SM) returns from deployment following a traumatic brain injury (TBI), it can place additional demands on the SMs children already strained from deployment. The purpose of this study was to examine the impact of a SMs deployment and injury on a child's overall health and behavior as reported by the caregivers of the SMs who sustained the TBI.

Methods: Participants were 112 caregivers (female=96.1%) of U.S military SMs who had sustained a mild, moderate, severe, or penetrating TBI. Caregivers were recruited from multiple DoD Medical Treatment Facilities nationwide, and via caregiver events and social media. Participants completed the Children's Health and Behavior Questionnaire (CHBQ), a measure designed specifically for this study. Using the CHBQ, caregivers were required to rate their children's school grades, behavior, medical health, emotional health, and participation in social activities at four time periods: (i) prior to the SMs first combat deployment, (ii) in the month prior to the SMs TBI, (iii) within 2 years after the SMs TBI, and (iv) 2-or-more years after the SMs TBI. Ratings were obtained for 248 children; i.e., 1 child (n=33 caregivers), 2 children (n=40), 3 children (n=28), 4 children (n=7), 5 children (n=2), 6 children (n=2).

Results: Overall, caregivers reported that a substantial number of the SM's children had experienced a decline in emotional health (79.1%), behavior (70.9%), school grades (59.7%), social activities (56.5%) and medical health (41.7%) following the SMs TBI. Of those children that had a decline, (a) 68.8% to 75.5% declined within the first 2 years post-injury, followed by improvement or stabilization, (b) 6.7% to 15.6% declined only after 2-or-more years post-injury, and (c) 15.6% to 25.0% declined within the first 2 years post-injury and then again 2-or-more years post-injury. In addition, of those children that experienced declines in these five areas, 16.9% to 26.5% had initially experienced a decline as a result of deployment, followed by an additional decline after the SMs TBI.

Conclusion: In this sample, both deployment and TBI had a negative effect on a child's school grades, behavior, mental health, emotional health, and participation in social activities. However, the impact of the SMs TBI was substantially higher. Although the reasons for this decline are likely multifactorial, these results are alarming and call for much needed attention to be focused on the impact of TBI and deployment on children of U.S. military SMs.

Traumatic Brain Injury Alters Physiologic, But Not Subjective, Responses to Emotional Stimuli

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Impairments of emotional function are a common, yet sub-optimally understood, sequelae of TBI. Current clinical measures of assessing emotion rely largely on subjective self-report measures. Converging lines of evidence from behavioral and cognitive neuroscience have identified neural systems for processing multiple aspects of emotion that are independent of explicit awareness, such as involuntary reflexive autonomic outputs or reflexive behaviors. Thus, assessing autonomic activity may represent a novel method of identifying objective changes in the emotional function of TBI patients that are not otherwise captured by current self-report measures. This study was performed to test the hypothesis that alterations in emotional function can be characterized by differences in autonomic activity in patients with traumatic brain injury (TBI) compared with controls. In this study, subjects watched a series of film clips normed to elicit specific emotions. Surface electrodes measured cardiac and respiratory signals, which were used to compute heart rate variability (HRV), from which measures of parasympathetic activity (RFA, Respiratory Frequency Area) and sympathetic activity (LFA, Low Frequency Area) were derived. The subjective intensity of the emotional response to the film-clips was also captured via questionnaires. Twelve healthy subjects, ranging in age from 21 to 67 years (mean \pm SD = 35.8 \pm 13.5 years), with no history of psychiatric disease or complicating medical problems, such as uncontrolled hypertension, diabetes, neurological illness such as stroke, epilepsy, or demyelinating disease participated in the study. Six of the subjects were female. Sixteen subjects with mild to moderate traumatic brain injury (TBI), ranging in age from 25 to 81 participated in the study. Electrocardiographic and respiratory signals were sampled at 250 Hz and 50 Hz, respectively and collected using ANSAR ANX 3.0 software while subjects watched emotional film clips. HRV was computed every 0.25 seconds and time-frequency spectral analysis was performed to quantify ANS activity. Parasympathetic activity was assessed by obtaining the RFA signal, which was measured from higher frequency areas of the HRV spectrum. These higher frequency areas are associated with respiratory sinus arrhythmia, known to be a cardio-vagal response that is reflective of parasympathetic activity. Sympathetic nervous system activity was assessed by obtaining the LFA signal, which is defined as the area under the heart rate spectral curve over the lower limit of RFA range. By localizing and omitting the parasympathetic influence from the low frequency range of HRV, LFA primarily corresponds to activity from the sympathetic nervous system. There was no difference in subjective ratings of emotional intensity between TBI and control groups across all emotional film clips. However, when examining autonomic activity, the TBI group displayed significantly decreased sympathetic nervous system activity when viewing amusing stimuli compared to controls, but significantly increased sympathetic nervous system when viewing sad stimuli.

Efficacy of IncobotulinumtoxinA in Treatment of Lower Limb Spasticity in Adults

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Objectives: Use of incobotulinumtoxinA has been shown to be safe and effective for the treatment of upper limb (UL) spasticity in adults. In the TOWER study (NCT01603459), escalating fixed total doses of incobotulinumtoxinA were used to treat 155 adult subjects with spastic hemiparesis, including both UL and LL clinical patterns. The objective of this post-hoc analysis from the TOWER study was to assess the effectiveness of incobotulinumtoxinA for treating key clinical patterns of lower limb (LL) spasticity (eg, pes equinovarus).

Methods: Subjects in the TOWER study received increasing doses of incobotulinumtoxinA over 3 injection cycles (400U, 600U, and 600-800U, respectively). Muscle tone was assessed using the Ashworth Scale (AS); additional outcome measures included AS responder rates (defined as patients with ≥ 1 point improvement at 4-weeks) and Resistance to Passive Movement Scale (REPAS)

Results: A total of 109 subjects received treatment for any LL clinical pattern in cycle 1. The most frequently treated pattern was pes equinovarus (N=100); however, 9 different LL clinical patterns were treated over the course of the study. During the first cycle, the mean \pm standard deviation [SD] dose for pes equinovarus was 166.3 ± 94.9 U. At 4-weeks post-injection, the mean improvement (\pm SD) in ankle joint AS score was 0.63 ± 0.76 among subjects treated for pes equinovarus, compared with 0.16 ± 0.63 among subjects not treated for this pattern. Multiple regression analysis (adjusting for AS baseline value) revealed a significant effect of pes equinovarus dose on AS improvement ($P=0.0096$). AS responder rates were higher for treated subjects compared with untreated subjects (55.0% vs 12.7%; $P<0.0001$; Mantel-Haenszel Chi-Square test). At the 4-week post-injection visit, the mean improvement (\pm SD) from baseline in REPAS LL scores was 1.6 ± 2.0 in subjects with LL treatment, compared with 0.3 ± 1.5 in subjects without treatment. Multiple regression analysis on LL REPAS baseline value and LL dose demonstrated a significant effect of LL dose administered ($P=0.0022$).

Conclusions: Results suggest that incobotulinumtoxinA is safe and effective for the treatment of LL spasticity.

Escalating Doses of incobotulinumtoxinA (400U-800U) Lead to Increasing Improvements in Muscle Tone and Functional Outcomes Due to Multifocal Spasticity

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Objectives: Patients with severe multifocal spasticity may benefit from treatment using botulinum toxin at higher-than-labeled doses. The objective of this study was to evaluate the safety and efficacy of increasing incobotulinumtoxinA doses (400–800U) for subjects with spasticity.

Methods: This prospective dose-escalation study (TOWER; NCT01603459) included 155 subjects (18-80 years) with spastic hemiparesis who were deemed to require up to 800U total body doses of incobotulinumtoxinA. Subjects received treatment with increasing incobotulinumtoxinA doses during 3 injection cycles (ICs) (400U, 600U, and 600-800U, respectively). Each cycle was followed by 12-16 weeks of observation. Outcomes measures included: Ashworth Scale (AS) responder rate (≥ 1 -point improvement 4 weeks post-injection), Disability Assessment Scale (DAS), Functional Ambulatory Classification (FAC), and Investigators Global Efficacy Assessment (IGEA). Adverse events were monitored throughout the study.

Results: Escalation of incobotulinumtoxinA doses enabled treatment of an increasing number clinical patterns of spasticity in each subject. A total of 364/608 (59.9%) treated patterns were responded to treatment in IC1 (N=155 subjects), 431/743 (58.0%) responded in IC2 (N=152 subjects), and 537/811 (66.2%) responded in IC3 (N=140 subjects). Reporting DAS scores of 0 or 1 (corresponding to “no” or “slight” disability) for the principal target domain increased after each treatment (baseline: 0.7%; study end: 42.9%). The proportion of ambulator-independent subjects (FAC level 5) also improved (baseline: 24.5%; study end: 40.6%). The proportion of IGEA scores of “good” or “very good” increased with escalating doses (IC1: 55.5%; IC2: 72.4%; IC3: 89.3%).

No increases in proportions of subjects reporting AEs overall (IC1: 36.1%; IC2: 37.5%; IC3: 25.7%) or treatment-related AEs (IC1: 4.5%; IC2: 5.3%; IC3: 2.9%) were observed with escalating doses of incobotulinumtoxinA. There were no treatment-related serious AEs or cases of clinical non-responsiveness due to antibodies.

Conclusions: Escalating doses of incobotulinumtoxinA (400-800U) enabled treatment of an increasing number of spasticity patterns without affecting safety or tolerability. Increased doses of incobotulinumtoxinA were also associated with greater efficacy, determined on the basis of improved muscle tone and physician global assessments, reduced upper-limb disability, and greater ambulator independence.

Response Inhibition Deficits Are Associated with Disrupted Intrinsic Connectivity of the Cortical Motor Network after Pediatric Traumatic Brain Injury

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Background: Poor response inhibition is a hallmark of pediatric traumatic brain injury (TBI). The neural correlates of response inhibition are relatively well-established in uninjured individuals, with the cortical motor network playing an important role, but little research exists exploring the neural underpinnings of response inhibition deficits after pediatric TBI.

Methods: We compared 17 children (6 females; mean age: 16.0) with chronic (> one year post-injury) mild, moderate, or severe TBI to 14 uninjured peers (3 females; mean age: 16.2). We assessed response inhibition via commission errors on Simple (minimized cognitive demands) and Motivation (monetary reward) Go/No-Go tasks. Resting State fMRI (rs-fMRI) data were used to assess intrinsic connectivity (IC) of the cortical motor network as derived from the averaged time course of bilateral primary motor cortex seeds. A motor network map was created for each subject and used in between-group connectivity contrasts in SPM 12 with voxel-level threshold $p < 0.001$, family-wise error (FWE) correction, and cluster-level threshold of $p < 0.05$. The location of peak activated voxels from significant between-group clusters was used to identify regions of interest (ROI) for examining brain-behavior relationships with motor network IC. Independent sample t-tests compared Go/No-Go performance and IC at the ROI-level. Pearson correlations examined relationships between IC at the ROI-level and Go/No-Go performance.

Results: There were no significant between-group differences in age ($p = .74$) or sex ($p = .52$). Children with TBI had poorer performance on Simple ($p = .02$) and Motivation Go/No-Go tasks ($p = .03$). In whole-brain contrasts, the TBI group showed reduced cortical motor network IC with one cluster which was located in the left caudate ($p = .02$). The TBI group similarly had reduced functional connectivity between the cortical motor network and left caudate ROI ($p = .02$) and a trend toward lower connectivity between the cortical motor network and right caudate ROI ($p = .07$). In the TBI group, lower cortical motor network to left caudate ROI connectivity was associated with higher commission errors on the Simple Go/No-Go task ($r = -.56$, $p = .03$), whereas lower cortical motor network to right caudate ROI connectivity was associated with higher commission errors on the Simple ($r = -.67$, $p = .01$) and Motivation ($r = -.60$, $p = .02$) Go/No-Go tasks. No brain-behavior relationships existed among controls.

Conclusions: In this cohort of children with chronic TBI, we observed that disrupted intrinsic connectivity of the cortical motor network was associated with deficits in response inhibition. If this finding is replicated in future work, rehabilitation efforts towards optimizing motor network integrity, even in individuals without gross motor deficits, may provide a means of addressing disinhibition after pediatric TBI.

Mild Traumatic Brain Injury is Associated with Reduced Cortical Thickness in Those at Risk for Alzheimer's Disease

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Moderate-to-severe traumatic brain injury is one of the strongest environmental risk factors for the development of neurodegenerative diseases such as late-onset Alzheimer's disease, although it is unclear whether mild traumatic brain injury, or concussion, also confers risk. This study examined mild traumatic brain injury and genetic risk as predictors of reduced cortical thickness in brain regions previously associated with early Alzheimer's disease, and their relationship with episodic memory. Participants were 160 Iraq and Afghanistan War veterans between the ages of 19-58, many who carried mild traumatic brain injury and posttraumatic stress disorder diagnoses. Whole-genome polygenic risk scores for the development of Alzheimer's disease were calculated using summary statistics from the largest Alzheimer's disease genome-wide association study to date. Results showed that mild traumatic brain injury moderated the relationship between genetic risk for Alzheimer's disease and cortical thickness, such that individuals with mild traumatic brain injury and high genetic risk showed reduced cortical thickness in Alzheimer's disease-vulnerable regions. Among men with mild traumatic brain injury, high genetic risk for Alzheimer's disease was associated with cortical thinning as a function of time since injury. A moderated mediation analysis showed that mild traumatic brain injury and high genetic risk indirectly influenced episodic memory performance through cortical thickness, suggesting that cortical thinning in Alzheimer's disease-vulnerable brain regions is a mechanism for reduced memory performance. Finally, analyses that examined the apolipoprotein E4 allele, posttraumatic stress disorder, and genetic risk for schizophrenia and depression confirmed the specificity of the Alzheimer's disease polygenic risk finding. These results provide evidence that mild traumatic brain injury is associated with greater neurodegeneration and reduced memory performance in individuals at genetic risk for Alzheimer's disease, with the caveat that the order of causal effects cannot be inferred from cross-sectional studies. These results underscore the importance of documenting head injuries even within the mild range as they may interact with genetic risk to produce negative long-term health consequences such as neurodegenerative disease.

The Influence of Caregiver Burden on Health Status and Perceived Role Efficacy in Caregivers of U.S. Military Service Members with Traumatic Brain Injury

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Background: Following a traumatic brain injury (TBI), some family members assume the role of “caregiver” for their loved one who is injured. Caregivers often experience significant burden from the demands placed on them in this role. The purpose of this study was to examine the influence of caregiver burden on overall health status and perceived efficacy of functioning in caregiver’s of U.S. military service members (SM).

Methods: Participants were 283 caregivers (female=96.1%) of SMs who sustained a mild-severe, or penetrating TBI. The majority of the sample was Caucasian (92.6%) and was caring for a spouse/partner (86.2%). The mean age was 38.7 years (SD=10.3) and the mean number of years caregiving was 4.1 years (SD=2.9). Caregivers were recruited through community outreach initiatives and from multiple DoD Medical Treatment Facilities nationwide. Participants completed the Caregiver Appraisal Scale (CAS) and the SF-36v2 Health Survey (SF36) that included 11 measures of interest. The sample was divided into three Caregiver Burden groups using the CAS Perceived Burden scale: High (n=138); Neutral (n=106); Low (n=139).

Results: The percentage of participants who reported that their caregiving duties were a high burden was 48.8%. Caregiver burden was not associated with age ($p=.779$), number of years caregiving ($p=.924$), or time post-injury ($p=.317$). Using ANOVA, there was a significant main effect across the three Caregiver Burden groups on all 11 CAS and SF36 subscales ($p=.010$ to $p<.001$). Pairwise comparisons revealed a significant linear relation between caregiver burden and outcome on 7 of the 11 measures (all $ps <.05$; i.e., High > Neutral > Low). As caregiver burden increased, there were increasingly worse scores on the SF36 Role Physical ($d=.44-1.02$), SF36 General Health ($d=.51-1.03$), SF36 Vitality ($d=.66-1.44$), SF36 Social Function ($d=.54-1.31$), SF36 Role Emotional ($d=.53-1.15$), SF36 Mental Health ($d=.64-1.40$), and CAS Caregiver Mastery ($d=.33-.91$) scales. In addition, participants in the High Burden group had significantly worse scores (all $p<.05$) on the SF36 Physical Functioning ($d=.40$ and $.51$), SF36 Bodily Pain ($d=.64$ and $.82$), and CAS Caregiver Satisfaction ($d=.61$ and $.82$) scales compared to the Neutral Burden and Low Burden groups (i.e., High > Neutral & Low). Using Stepwise Regression Analysis, the SF36 Social Functioning, SF36 Vitality, CAS Caregiver Satisfaction, and CAS Caregiver Mastery scales were significant predictors ($p<.001$) of CAS Caregiver Burden total scores, accounting for 43.3% of the variance.

Conclusions: In this sample, there was a strong linear relation between increased perceived burden and (a) poor overall health status, and (b) negative self-appraisal of their efficacy as a caregiver. These findings suggest that many caregivers may benefit from training programs designed to increase their caregiving skills in addition to increased support allowing them time to improve their physical, mental, and social functioning.

Self-Reported Social Communication of Older Adults with Traumatic Brain Injury

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Objective: Traumatic brain injury (TBI) can result in chronic social communication problems that negatively affect social, vocational, and quality of life outcomes. Older adults are at particular risk for TBI, yet little is known about communication effects of TBI in this population, limiting the extent to which individualized communication treatment approaches can be developed. To address this gap, we examined self-perceived social communication of older adults with TBI and compared their reports to those of (a) older adults with no history of TBI; and (b) younger adults with TBI.

Methods: Participants were recruited as part of a larger study on social communication after TBI and included 13 adults (8 men, 5 women), aged 60 years and older, who had sustained a moderate-severe TBI at least six months prior to study enrollment (TBI Old); 13 adults matched for age, sex, and education to the older adults without TBI (TBI Comparison); and 13 younger adults (aged ≤ 35 years) with moderate-severe TBI who were matched to the TBI group for sex and education (TBI Young). Participants completed the La Trobe Communication Questionnaire, Self-Report version (LCQ-S; Douglas, Bracy, & Snow, 2007), a 34-item questionnaire developed to measure perceived frequency of cognitive-communication behaviors and problems in daily life. We calculated Total LCQ-S scores, with higher scores indicating more frequent communication problems. We further examined LCQ-S responses by communication factors (Initiation/Conversational Flow, Disinhibition/Impulsivity, Conversational Effectiveness, and Partner Sensitivity; Struchen, et al., 2000).

Results: The TBI Old group's mean LCQ-S score was 61.69. Across communication factors, the TBI Old group reported that problems with Conversational Effectiveness and Emotion Recognition occurred most frequently. The TBI Old group's LCQ-S Total scores were similar to those of the TBI Old ($t(12) = 1.63, p = 0.13$) and TBI Young groups ($t(12) = 0.32, p = 0.76$). The TBI Old group was also similar to the Comparison Old and TBI Young groups in all LCQ-S communication factors, with the exception that the TBI Old group reported more frequent emotion recognition problems than the Comparison Old group ($t(12) = 3.56, p < 0.01$).

Conclusions: Results of this preliminary analysis suggest that older adults with TBI report experiencing a similar frequency of social communication problems as peers without TBI and younger adults with TBI. This is in contrast to findings reported by Struchen and colleagues (2011) that age was negatively correlated with LCQ scores. This study's small sample size and relatively young older adult sample may account for this difference. These early results also suggest that older adults with TBI may have particular difficulty with conversation and inferring communication partners' emotions. If replicated in larger samples, these aspects of communication may be important treatment targets for older adults with TBI.

Windows to the Brain: Visual Systems, Rehabilitation, and Research in Concussion

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In this presentation, we provide a functional overview of the visual system and the unique ways in which vision may be useful for evaluating, managing, and understanding concussion. We will expand on visual therapeutic measures for the rehabilitation of visual dysfunction after concussion, as well as present emerging research identifying the underlying physiology of commonly used, as well as more novel, diagnostic measures. We will provide an interdisciplinary perspective, with lectures and perspectives from both clinicians (occupational therapy, neuro-ophthalmology, and physiatry) as well as research investigators. Case reports will be presented to facilitate synthesis and retention of the presented information.

The Hull-Ellis Concussion and Research Clinic: The Sleep and Concussion Questionnaire©; A Preliminary Longitudinal Analysis of Sleep and Day-time Wakefulness

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Background: Alterations in sleep and wakefulness are commonly reported symptoms following concussion. During the acute stage, increased sleep need, complaints of less restful sleep and reduced activity have been reported clinically while objective measures of sleep have identified that acute concussions are associated with day-time wakefulness problems rather than sleep disturbances per se.

Objectives: We aimed to conduct: 1. A cross sectional examination of sleep and daytime wakefulness during the acute stage of concussion 2. A longitudinal examination of the trajectory of sleep and daytime wakefulness throughout the recovery period.

Methods: A prospective sample of 83 adults with acute concussion completed the Sleep and Concussion Questionnaire© (SCQ) at baseline (immediately post injury). Serial administration of the SCQ continued at weeks 2: (N=62), 3: (N=50) 4: (N=46), 8:(N=33) and 12 weeks (N=19). Selective attrition occurred as participants recovered. The SCQ is a self-report measure designed to describe and quantify perceived changes in sleep in response to injury.

Results: A. Acute stage: Greater than 80% of participants reported immediate changes in sleep compared to pre-injury, with 68% reporting mild-moderate change, and 15% reporting significant change. 67 % reported sleeping less than usual, 9%, sleeping the same amount but described their sleep as 'less restful'. 25 % reported sleeping more than usual. Greater than 90% reported feeling more tired during the day and 78% needed to nap. The most commonly endorsed factors impacting sleep were pain and psychological symptoms including feelings of restlessness, worrying, bad dreams and mood. B. At week 2, 20% reported that sleep had returned to normal and 43% that sleep was 'returning to normal', however, 10% reported deteriorations in sleep. The percentage of those sleeping more decreased dramatically to < 2% and, 0% by week 3. At week 4, 76% of remaining participants (N=46) reported their sleep was either returning or returned to normal. 19 % reported their sleep was still different from pre-injury, and 5 % reported deteriorations in sleep. Feelings of restlessness, worrying, mood and pain, continued to interfere with sleep. 76% continued to report feeling tired and needing naps. By weeks 8 and 12, our sample included a decreasing subset of patients continuing to report disturbances, characterised by poor sleep maintenance, daytime tiredness and need for naps.

Conclusions: Objective 1: Our data endorse an immediate change in sleep following concussion with increased sleep need, daytime sleepiness and need for naps. By week 2, sleep is returning to normal for some. Pain and psychological symptoms are factors perceived as impacting sleep. Objective 2: Over time, sleep improves with recovery however there continue to be a small sub-set whose sleep disturbance endures or worsens. The SCQ was effective in describing and quantifying changes in sleep following concussive events.

Preliminary Data of the First Post-Traumatic Brain Injured (TBI) Cognitive Rehabilitation Out-Patient Center in Brazil (University of São Paulo, School of Medicine)

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Background: The incidence of TBI is rising worldwide and it is associated with the increased use of motor vehicles, particularly in middle-income and low-income countries. Estimates of TBI incidence show substantial variation between countries. Each year in the USA, 1.7 million people sustain a TBI. In Brazil, this number is between 700,000 and 1.1 million people.

Aim: To introduce and describe the layout and functioning of the first post-TBI cognitive rehabilitation out-patient center in Brazil and to analyze the profile of a sample of patients assisted.

Methods: Data were collected from patient charts retrospectively. Basic statistics were done with Microsoft Excel® 10.0.

Results: There were 143 patients in our sample. Eighty percent were man (115), in contrast to 28 women (20%). The age ranged from 15 to 82 years (average 39.6 years). TBI type were classified into civil (n=135, 95%), sports and military ones. TBI circumstances were divided into 12 categories and the most frequent ones were: traffic accidents, where the patient was in the car as a driver or a passenger, accounted for 31% (42 patients), domestic accident (mainly falls) accounted for 21% (28 patients), hit by a vehicle accounted for 13% (18 patients). The average interval of time the patient took to be referred to our service after TBI was 7.6 years.

Conclusion: The main causes of our TBI sample are similar to international literature: traffic accidents and falls. The demand to Post-TBI Cognitive and Behavioral Rehabilitation in Brazil is enormous, since the number of TBI patients grows in geometric progression each day. In order to plan, organize and enhance our center, it is important that we know the epidemiological characteristics of patients we receive. Information about aspects of rehabilitation as the use of illicit drugs, medications used, neuropsychological evaluations and other issues, will be brought in further congresses and publications to complete the current analysis.

The Relationship Between Perceived Burden and Health-related Quality of Life in Caregivers of Military Service Members with Traumatic Brain Injury

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Background: Family members often assume the role of “caregiver” and bear primary responsibility for assisting a service member (SM) with long-term physical, emotional, and social care following a traumatic brain injury (TBI). The purpose of this study was to examine the influence of self-reported caregiver burden on overall health-related quality of life in caregivers of military SMs who have sustained a TBI.

Methods: Participants were 85 caregivers (female=96.1%) of U.S. military SMs who sustained a penetrating, severe, moderate, or mild TBI. Caregivers were recruited from multiple DoD Medical Treatment Facilities nationwide and by using community outreach initiatives and social media. The mean age of the sample was 39.8 years (SD=8.2) and the mean number of years caregiving was 5.5 years (SD=3.0). The majority of the sample was Caucasian (95.3%) and caring for a spouse/partner (88.2%). Participants completed 12 sub-scales from the Patient Reported Outcomes Measurement Information System (PROMIS), four sub-scales from the TBI-Caregiver Quality of Life (TBI-CareQOL) scale, and the Caregiver Appraisal Scale (CAS). Using the CAS, the sample was divided into three Caregiver Burden groups: High Burden (n= 40); Neutral Burden: (n=35); Low Burden: (n=10).

Results: There were significant differences across the three Caregiver burden groups on all 16 measures ($p=.001$ to $p<.001$). Pairwise comparisons revealed significant differences ($p<.05$) and large to very large effect sizes for the vast majority of measures/comparisons. For all measures, higher caregiver burden was consistently and significantly associated with worse overall functioning (i.e., High > Neutral > Low). The largest effect sizes were found when comparing High vs. Low burden groups ($d=1.24-2.90$), followed by Neutral vs. Low ($d=.79-2.16$), and High vs. Neutral ($d=.44-1.26$) groups. Using a series of regression analyses to determine whether CAS Perceived Burden total scores could predict each of the 16 measures separately, caregiver burden was a significant predictor of all measures (all $ps<.001$). Those measures accounting for the highest variance were TBI-CareQOL Feelings of Loss (58.3%), followed by TBI-CareQOL Caregiver Strain (51.9%), TBI-CareQOL Feeling Trapped (45.1%), PROMIS Anxiety (42.7%), TBI-CareQOL Specific Anxiety (42.9%), PROMIS Ability to Participate in Social Roles and Activities (39.6%), and PROMIS Global Health-Mental Health (38.8%). When combined, these variables account for 70.8% of the variance towards the prediction of CAS Perceived Burden total scores.

Conclusions: These results suggest that high caregiver burden is associated with a substantial decline in overall physical, mental, and social functioning (i.e., anger, general anxiety, caregiver worry, depression, fatigue, poor sleep, stress/strain, social isolation, social dissatisfaction, feelings of being trapped, feelings of grief and loss, and a lack of emotional and informational support). Given that almost half of this sample reported high caregiver burden (i.e., 47.1%), there is an urgent need to increase attention and resources to help this underserved population.

Comparison of the Buffalo Concussion Treadmill Test (BCTT) and Buffalo Concussion Bike Test (BCBT) for the Evaluation of Exercise Intolerance

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The Buffalo Concussion Treadmill Test (BCTT) is a tool that provides an objective measure of exercise intolerance after concussion. The BCTT has been used in the evaluation and treatment of both acutely concussed patients and those with post-concussion syndrome (PCS). Although the BCTT has been successfully administered to a variety of patient populations, the nature of the test makes it infeasible for use with patients with limited mobility, and in physiologic studies of exercise intolerance requiring minimal core body movement. We sought to develop an alternative to the BCTT using a stationary bicycle - the BCBT – which would provide a comparable assessment of exercise intolerance, and be appropriate for a broader patient base.

We created the BCBT by calculating the energy cost, or metabolic equivalent (MET), expended at each stage of activity during the BCTT and calculating the resistance against pedaling required during each stage of exercise on the stationary bike that would result in a comparable MET expenditure. Thirty-eight healthy participants (mean age, 19.2 years) completed both the BCTT and BCBT within seven days. Time to exhaustion was measured, and the rating of perceived exertion (Borg RPE) and heart rate (HR) after each stage of exercise intensity over the duration of both tests were compared to determine if the tests were equivalent.

A repeated measures ANOVA found no significant difference between the change in HR over 10 minutes of exercise on the BCTT as compared to the BCBT ($p>0.05$). A similar comparison of change in the rating of perceived exertion (RPE) over the same 10 minutes of exercise approached significance ($p=0.07$). Sex of the participant was not a factor. Time to exhaustion was significantly affected by participants' age and athlete status ($p<0.02$), with older, non-athletic participants reaching exhaustion significantly earlier. During the BCBT, the average HR at point of exhaustion (RPE of 19) was significantly lower during the BCTT (172 bpm for the BCTT as compared to 155 bpm for the BCBT; $p<0.01$).

The BCTT and BCBT are comparable in terms of the impact of increased exertion on HR. This suggests that the BCBT could provide an acceptable alternative to the BCTT. The bike requires less full-body movement, which is ideal for patients for whom the BCTT is contraindicated, or for the incorporation of physiological monitoring devices which require patient stability for the purposes of research. However, the BCBT appears to be more challenging for patients that do not exercise regularly due to the dependence on lower body strength; as a result, it is possible that some patients may quit the test before reaching a HR that elicits exercise intolerance.

Comparative Effectiveness of Inpatient TBI Rehabilitation Interventions: Impact of More Time in Contextualized Treatment

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The benefit of acute rehabilitation has been the target of research for several decades, but identification of the active and effective ingredients has remained elusive. The difficulties in conducting RCTs in this multidisciplinary environment are widely acknowledged. Studying the effects of rehabilitation using rigorous statistical methodologies for causal inference including propensity score methods (PSM), has been gaining ground.

The current study utilizes PSM to identify inpatient rehabilitation approaches that may have the greatest impact on outcomes within the year post-discharge. It employs data from the TBI Practice-Based Evidence database, a multicenter study of 2130 participants that includes detailed documentation of interventions, patients, and injury characteristics. Patient-reported outcomes, including community participation (Participation Assessment with Recombined Tools-Objective, PART-O), functional independence (FIM-TM), life satisfaction (Satisfaction with Life Scale), and depressed mood (Patient Health Questionnaire-9), were collected at 3 and 9 months post-discharge.

The following hypothesis was tested in the current study: “Patients who receive a greater proportion of therapy that consists of contextualized treatment (versus decontextualized) will achieve better outcomes than similar patients who receive a lesser proportion of time in contextualized treatment.” Contextualized treatment involves tasks that are meaningful to the patient, which can improve motivation and better generalize to daily life. Contextualized treatment relies heavily on procedural memory, which following TBI tends to be more intact than explicit learning. Decontextualized treatment often seeks to improve very specific impairments with tasks that can systematically build and strengthen a particular function, and oftentimes uses a trial and error approach to learning (with feedback and guidance).

From analyses utilizing PSM to control for observed covariates and multiple imputation for missing outcomes, we found that provision of an increased percentage of contextualized treatment (in occupational, physical and speech therapies) during inpatient rehabilitation is significantly associated with better community participation 3 and 9 months post-discharge, especially in regard to activities that involve being out and about in the community. If contextualized treatment were increased for a given participant by 30 percentage points, it is expected that the PART-O score would be increased by 0.12 (95% CI: 0.03, 0.18) and .09 (95% CI: 0.003, 0.17) at 3 and 9 months. The PART-O Out and About score would be increased by .014 (95% CI: 0.03, 0.24) at 3 and 0.15 (95% CI: 0.04, 0.26) at 9 months. Social relations would also be significantly improved with more contextualized treatment, though this effect is only observed at 3 months. The small effects were consistent with important improvements that consumers identified a priori. We also present findings on the effects of quasi-contextualized treatment (training in the use of compensatory strategies applied to simulated real-life activities) and on the heterogeneity of treatment effects relative to level of disability at admission and age.

CROCFLAME - Chronic Neuroinflammation and its Role for Cognitive Decline and Long-Term Sequels following Traumatic Brain Injury

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Traumatic Brain Injury has been considered as an acute brain injury since decades. Recent animal studies and a small number of clinical case reports have brought up a new concept of chronic neuroinflammation following TBI, which may last up to 17 years. Cognitive decline and long-term sequels such as chronic fatigue, posttraumatic stress disorders, anxiety, depression, sleeping disorders and dementia are often underdiagnosed in post-TBI patients, thereby restricting patients' quality of life, independency and daily activities. Currently, it is assumed that the initial trauma abuts neuroinflammation by microglial activation resulting in consequent neurodegenerative processes. So far, the underlying mechanisms are still insufficiently understood and indispensable for the development of new and innovative treatment options. To investigate the correlation between chronic post-TBI neuroinflammation and neurodegeneration, we analyzed medical records of 1266 patients, who suffered from mild, moderate or severe TBI and were neurologically rehabilitated between 2005 to 2015 in Schoen Klinik Bad Aibling, Germany. 439 of 1266 patients were contacted due to our defined inclusion and exclusion criteria. The response rate was 43% (n = 188). The demographic data of our study population was representative per age (45 ± 19 yrs. (mean \pm SD)), gender (75% male, 25% female), TBI severity (13% mild, 12% moderate, 37% severe TBI, 39% no information) and etiology (52% traffic accidents, 38% falls). Neurorehabilitation significantly improved functional outcome (mRS at admission/discharge: 4/3). 135 of 188 patients (72%) made disclosures on their current TBI-specific quality of life (QOLIBRI) up to 10 years following their mild, moderate or severe TBI. 65% indicated a reasonably good quality of life with a score of 61 out of 100. 120 of 188 patients (64%) gave consent to participate in the longitudinal observational study investigating post-TBI neuroinflammation, cognitive decline and long-term sequels. Currently, data analysis on the influence of acute interventions as tracheostomy, decompressive craniectomy, length of ICU and neurorehabilitation treatment as well as patients' functional outcome on the TBI-related quality of life up to 10 years after the acute brain injury is carried out. In conclusion, most patients had a reasonably good quality of life up to 10 years after mild, moderate and severe TBI. This large and representative study population allows the characterization of chronic post-TBI neuroinflammation and its role for cognitive decline, dementia and long-term sequels to further elucidate the pathophysiology and the new paradigm shift from acute to chronic TBI.

Incidence of Associated Gastrointestinal Disorders and Impact on Outcome following Moderate to Severe Traumatic Brain Injury

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Background: Currently, traumatic brain injury (TBI) and the human microbiome are two prominent but separate concerns in research. There is a growing body of evidence that the gut microbial ecosystem is linked to brain physiology and neurochemistry via what the U.S. National Institute of Mental Health calls the 'microbiome-gut-brain axis.' Research in this area is still exploratory, and the incidence of co-existing gastrointestinal medical conditions and associations with TBI outcome has not been well characterized.

Objective: To assess incidence of acutely-occurring gastrointestinal (GI) medical conditions associated with outcome for survivors of TBI.

Methods: Patients with moderate to severe TBI enrolled in the TBI Model Systems (TBIMS) National Database (NDB) were evaluated. Medical conditions identified by ICD-9 code recorded during the acute hospital phase of treatment were selected and grouped in a total of 75 Healthcare Cost and Utilization Project (HCUP) categories or groupings of categories. HCUP category 155 "Other Gastrointestinal Disorders" (which included all gastrointestinal disorders except, for example, Gastrointestinal Hemorrhage, Diverticulosis and Diverticulitis, and Gastroduodenal Ulcer) was analyzed. Outcome measures included FIM™ and Disability Rating Scale (DRS) at the time of inpatient rehabilitation discharge, and rehabilitation length of stay (LOS). Predictors of outcome were assessed using general linear models, controlling for age at injury, sex, cause of injury (high vs. low velocity), Glasgow Coma Scale motor score (following vs. not following commands), subcortical damage, and intracranial mass effect (Bonferroni alpha = 0.0007).

Results: For the study period from May 2007 to December 2013, there were 3,686 patients with complete data. Seventy two percent were male, and 66% white/Caucasian, with a mean age of 46.1±20.6 years. Forty-four percent of injuries were caused by high velocity events, 46% of patients followed commands at initial presentation, 20% had subcortical damage, and 40% intracranial mass effect. Incidence of other gastrointestinal disorders was 25%. Other GI disorders predicted worse outcome by all measures (p<0.0001) except FIM™ Cognitive score (p=0.0602).

Conclusions: Other gastrointestinal disorders were observed in one-fourth of TBI patients at rehabilitation discharge and predicted worse outcome by almost all measures assessed. The findings point to a need for further research on the gut-brain axis in TBI survivors.

Trajectory of Caregiver's Service Needs and Health Status from Inpatient to Home in a Sample of Caregivers of Service Members who have sustained a Traumatic Brain Injury

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Objectives: For many family members of US military service members (SM) who have sustained a traumatic brain injury (TBI), the adoption of the caregiver role begins while the injured SM is an inpatient in hospital. The purpose of this study was to examine long-term service needs and health status in caregivers of SMs following TBI as they transition from hospital to home.

Methods: Participants were 54 caregivers (90.7% female; 64.8% caring for a spouse/partner) of U.S. military SMs who had sustained a mild (51.1%), moderate-severe (23.4%), or penetrating TBI (25.5%). Caregivers were recruited from multiple DoD Medical Treatment Facilities nationwide, and via caregiver events and social media. The mean time caregiving was 5.2 years (SD=3.2; range 1-12 years). Participants completed a questionnaire designed for this study that evaluated five service needs and health status. At the time of the baseline evaluation, participants were asked to retrospectively rate their needs/health when [a] the SM was a hospital inpatient (Time 1), [b] the SM first moved home from hospital (Time 2), and [c] 'within the past 3 months' (Time 3). A subgroup of 42 caregivers also completed a follow-up evaluation on average 8.2 months later (SD=4.2, range=3-20) and again rated their needs/health [d] within the past 3 months (Time 4).

Results: Over time, there was a decrease in the proportion of the sample that reported the need for [a] instruction and coaching to be a caregiver (T1=61.1%, T2=50.0%, T3=27.8%, T4=33.3%; $p<.05$), [b] guidance with how to provide emotional support (T1=66.0%, T2=62.3%, T3=49.1%, T4=51.2%; $p<.05$), [c] finding information about programs and services (T1=81.5%, T2=79.6%, T3=70.4%, T4=54.8%; $p<.05$), and [d] navigating the DoD/VA medical system (T1=70.4%, T2=74.1%, T3=64.8%, T4=57.1%; n/s). However, the need for these services remained high. Of those that needed help, less than 50% received the help they needed initially (25.7-54.5%), when they returned home (20.9-40.7%), at Time 3 (6.7-47.4%), and at Time 4 (14.3-34.8%). A large minority of the sample rated their emotional health and medical health as fair/poor over time. From Time 1 to Time 4, there was a slight increase in ratings of poor emotional health (T1=39.6%, T2=39.6%, T3=49.1%, T4=46.3%; n/s) and a more pronounced increase in ratings of poor medical health (T1=20.4%, T2=24.1%, T3=35.2%, T4=42.9%; $p<.05$).

Conclusions: Overall, these results suggest that a substantial number of individuals require help in their new role as caregiver acutely, when the SM transitions home, and for many years after the SM has returned home. Some caregivers report adequate help initially and when they first return home, but few caregivers receive this help long-term. Long-term follow-up of caregivers should be considered the norm, not the exception.

Anxiety Symptoms and Their Correlates in Adolescents with Mild Traumatic Brain Injury

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Objective: The aim of the current study is to examine correlates of anxiety symptoms in adolescents with mild Traumatic Brain Injury (mTBI) receiving interdisciplinary care. Additionally, qualitative variables including demographics, injury characteristics, and observed symptoms of anxiety are explored. This study serves to further the assessment and understanding of anxiety in adolescents with mTBI, as untreated psychological symptoms in this population are known to contribute to protracted recovery.

Methods: A retrospective chart review of 78 adolescents (ages 13-18; M=14.73) was conducted among those referred for psychology services within an interdisciplinary urban pediatric mTBI clinic. Demographics and injury characteristics were gathered via clinical interview to provide an overall context for the population. Anxiety symptoms were assessed via clinical interview and the Revised Children's Manifest Anxiety Scale -2 (RCMAS-2, Reynolds & Richmond, 2008).

Results: Participants were primarily female (71.8%) and Caucasian (74.4%). Most injuries were sports-related (61.5%). In 76.9% of participants, mood concerns warranting psychological intervention were identified at initial evaluation. Many (43.6%) denied premorbid mental health diagnoses; however, 24.4% of participants endorsed a history of undiagnosed mood symptoms. Of participants with premorbid mental health diagnoses, 33.3% had anxiety disorders. Few were receiving outpatient psychiatric (5.1%) or psychological (6.4%) services. On the RCMAS-2, cumulative number of injuries was correlated with higher levels of response defensiveness, lower report of total anxiety symptoms, and lower report of somatic anxiety symptoms. Time since injury was not correlated with self-report of anxiety symptoms. A substantial percentage of participants endorsed clinically significant levels of overall anxiety (25.6%), somatic symptoms of anxiety (29.5%), and socially related anxiety (16.7%).

Discussion: Within this sample, cumulative number of injuries was significantly correlated with a lower report of anxiety, whereas time since injury was not correlated with level of anxiety symptoms. Specifically, adolescents who sustained more than one injury were likely to respond defensively to the RCMAS-2, appearing to underreport anxiety symptoms, particularly related to somatic functioning. Adolescents with only one injury may be more likely to endorse more anxiety complaints. One hypothesis is that those with multiple injuries may be attempting to present themselves in a more favorable light in order to quickly return to sports and other activities. Conversely, given these findings, it could be hypothesized that adolescents who are new to mTBI may be more likely to attribute mood concerns to the mTBI itself as opposed to pre-morbid anxiety. Regardless of number of injuries or time since injury, participants endorsed more symptoms of anxiety within the context of mTBI recovery than would be expected when compared to normative peers, emphasizing the need for psychology services in mTBI treatment. Overall, anxiety and its correlates following injury warrant further study to clarify symptomatology and unique risk factors associated with mTBI.

Brain Network Analysis of EEG Data in the Service of Clinical Assessment: Utilizing Big Data and Prior Theoretical Knowledge to Make EEG Accessible to Clinicians

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For many years human electroencephalogram (EEG) and Event-Related Potential (ERP) data are being collected and studied around the world. However, extracting clinically meaningful neuro-cognitive information remains extremely challenging. EEG/ERP data suffer from substantial inherent variability and instability compared to other physiological metrics, and are highly sensitive to gender and age differences. Finally, EEG data are extremely complex, hiding a theoretically endless number of possible measurable features, making it hard to be used as a standalone clinical tool in the domain of cognitive function evaluation.

To overcome these challenges, we have developed a framework which combines large datasets, novel signal processing technology and academic knowledge, in the following steps: Initially, we collected 15,100 EEG recording files of healthy individuals aging 12 to 50 years-old, performing various computerized cognitive tasks during several visits. We then analyzed the data and extracted a large number of advanced spatiotemporal features in response to the cognitive tasks (see Stern, Y., Reches, A., and Geva A. "Using Spatiotemporal Features in the Brain Network Activation Analysis for Improved Data Classification". *Frontiers in computational neuroscience*, In Press). Next, using a "hybrid" approach combining machine learning and prior knowledge from the wide ERP literature, we assembled an optimal set of brain network models from these features. We thus obtained a stable cohort of functionally meaningful networks representing the various cognitive functions such as attention, memory, motor control and sensory processing.

Finally, to render this method useful in the clinical setting, we created a normative distribution for each cognitive function, compared to which we can then score and graphically illustrate the functional network activity of individual participants. Furthermore, since the brain develops substantially throughout the aforementioned ages, and differently for men and women, we used our large database to study and refine the functional networks' scoring process by delineating age and gender bins with coherent neuronal network activity. The end result of this process is an age- and gender-matched, literature-based, set of scores of a person's neural-network activity, which map the individual's neuro-cognitive state across a variety of important cognitive functions, in relation to the norm. This map of functional brain network activity (BNA) can assist clinicians as a general neural assessment tool when evaluating a patient for neuropsychological functioning.

Under Diagnosed Traumatic Brain Injury in Traumatic Spinal Cord Injury Patients Admitted to Acute Rehab

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Background: Traumatic spinal cord injury (SCI) typically is the product of high kinetic accidents. Such accidents have also been a factor in the cause of Traumatic brain injury (TBI). These neurotraumas can often be assumed to occur concomitantly, but due to the enormous physical injury that is sustained in a patient with SCI being the focus of concern, some of the basic indicators of TBI may go undetected and therefore undiagnosed.

Objective: To investigate the occurrence of under diagnosed TBI in traumatic SCI patients who were admitted to an acute rehab facility and how detection of cognitive impairments was identified.

Design: Retrospective chart review

Setting: Acute rehabilitation hospital

Participants: Seventy-eight patients with SCI admitted to the SCI unit in an Acute rehabilitation facility

Methods: A chart review was conducted of patients admitted to the SCI unit in an acute rehabilitation facility with primary diagnosis of SCI between November of 2014 to August of 2016. Patients with a primary diagnosis of SCI and no prior history of TBI or any cognitive deficits were included in the study. Additionally, the medical record was also reviewed to identify the personnel who identified the deficits (eg. physician, therapist, etc.).

Results: Seventy-seven patients were admitted to the SCI unit. 15 (19%) patients did not meet the inclusion criteria. Out of the remaining 62 patients who met the inclusion criteria, 7 (9%) patients were found to have a degree of cognitive deficits that was not diagnosed in the acute care setting. Out of these 7 patients, 3 (4%) were found to have mild cognitive deficits while 4 (5%) were found to have moderate cognitive deficits. Out of the 7 patients with newly identified cognitive deficits, 5 (71%) were detected by the admitting physician and 2(28%) were detected by the therapists.

Conclusion: All patients with a traumatic SCI should receive a cognitive evaluation by qualified personnel to identify any potential co-occurring TBI.

Dopamine Imaging in Traumatic Brain Injury (TBI): Association with Functional Outcomes

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Background: Drugs enhancing dopamine (DA) signaling are widely used off label in patients recovering from TBI in an attempt to augment vigilance or accelerate cognitive recovery and rehabilitation. Although there are anecdotal reports and small case series supporting this practice, there is varied effectiveness seen in studies of DA re-uptake inhibitors in TBI, and only amantadine demonstrated efficacy in a single clinical trial. One possible explanation for the variation in outcomes is the heterogeneity of the injury and differential injury to DA circuits. Direct knowledge of the integrity of DA circuits in severely injured patients after TBI should allow more targeted therapy to supplement DA neurotransmission. To address this issue, we employed Single Photon Emission Computed Tomography (SPECT) imaging of the presynaptic DA transporter (DAT) as patients begin rehabilitation in order to assess damage to the DA system.

Objectives:

1. To measure presynaptic DAT expression in severe TBI upon admission to inpatient rehabilitation using SPECT imaging with the DAT imaging agent 123I-iodoflupane.
2. To correlate the binding potential of 123I-iodoflupane in the striatum with deficits and subsequent rehabilitation functional outcomes.

Study Design: Prospective cohort

Methods: Thirteen subjects were consented by proxy and participated with imaging and functional assessment. Baseline SPECT imaging was performed within two weeks of admission to rehabilitation and 3 hours after injection of 5 mCi 123I-iodoflupane tracer. Images were transformed into common space and striatal binding potentials (SBP) calculated using a striatal template with whole extra-striate brain used as a reference for non-specific binding. Baseline and four week outcome measures included Functional Independence Measure (FIM), Disability Rating Scale (DRS), Coma Recovery Scale Revised (CRS-R), and Functional Assessment Measure (FAM).

Results: Subjects were mostly male (n=9, 69%), mean age of 31.32 ± 8.88 with severe TBI. At baseline imaging, SBP was significantly associated with CRS-R Total ($p=0.006$; $r=0.717$), Total FIM self-care items ($p=0.007$, $r=0.707$), Total FAM communication items ($p=0.0003$; $r=0.845$), and Total FIM+FAM cognitive items ($p=0.004$; $r=0.740$). There were no correlations with FIM bladder/bowel control or FIM/FAM mobility items. At the four week follow up, SBP was significant correlated with DRS ($p=0.009$; $r=0.687$), FIM+FAM self-care items ($p=0.006$; $r=0.719$), FIM+FAM communication items ($p=0.006$; $r=0.713$), and FIM+FAM cognitive items ($p=0.008$; $r=0.684$).

Conclusion: Baseline SBP is significantly correlated with a number of rehabilitation functional measures at baseline as well as outcomes achieved after 4 weeks of rehabilitation. These data suggests that damage to the nigrostriatal dopaminergic system explains 50-70% of the variance seen in several functional measures at baseline and 45-50% of the variance in these functional measures achieved after 4 weeks of therapy. A better understanding of dopaminergic dysfunction in TBI, and how best to treat it, has the potential to make a large impact on achievable outcomes.

Factors Affecting Burden in Family Caregivers of Military Service Members with Traumatic Brain Injury

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Background: Family members often assume the role as “caregiver” for a service member (SM) following a traumatic brain injury (TBI) to help with rehabilitation and community reintegration. Caregivers often experience significant burden from the demands placed on them. This study aimed to identify factors that increase caregiver burden.

Methods: Participants were 214 caregivers (95.8% female; 92.5% Caucasian; Age: M=38.6 years [SD=10.4]) of U.S. military SMs who sustained a penetrating, severe, moderate, or mild TBI. The majority of the sample was caring for a spouse/partner (86%) and had been caregiving for 4.1 years (SD=2.9). Caregivers were recruited from medical treatment facilities nationwide and via community outreach. Participants completed the Caregiver Appraisal Scale (CAS), Mayo-Portland Adaptability Inventory (MPAI; significant other ratings), and a structured interview designed to evaluate a variety of caregiving issues (e.g., time spent caregiving, caregiving responsibilities). Only select variables were included that were hypothesized (a priori) to have an impact on caregiver burden. Using the CAS Caregiver Burden subscale, the sample was divided into two groups: High Burden (n= 138) and Low Burden (n=76).

Results: There were no significant group differences for age, gender, household income, number of dependents living in the household, or the number of years caregiving ($p>.05$). However, there were significant group differences on the majority of remaining measures. High caregiver burden was significantly associated with a decrease in the SMs (i) sensory-motor and cognitive abilities; (ii) mood and interpersonal interactions; and (iii) initiation and social contact/activities (MPAI Ability, Adjustment, and Participation scales [all $ps <.001$; $d=.77$ to $d=1.30$]). In particular, high caregiver burden was associated with a SMs symptoms of anxiety, posttraumatic stress, depression, inappropriate behavior in social situations, and verbal and physical expressions of irritability, anger, and aggression (all $ps <.001$; OR=4.81 to 15.36). High caregiver burden was further associated with the caregiver’s: [1] lack of mastery in their role (CAS Caregiver Mastery, $p <.001$; $d=.77$) and need for instruction/coaching to provide care ($p <.001$, OR=3.79); [2] loss of income due to lack of employment or inability to work or find work (all $ps <.006$, OR=2.78 to 14.57); [3] need for help managing medical appointments, navigating the medical health system, and finding information about available services/programs (all $ps <.001$; OR=3.70 to 10.32); and [4] providing care 7 days per week for more than 80 hours p/week; and a lack of time to devote to themselves (all $ps <.001$, OR=3.74 to 10.36).

Conclusion: These results suggests that caregiver burden among family caregivers providing care to SMs following TBI is very high. There is a significant need for increased focus on this population. In order to reduce burden, caregivers would benefit from (a) education programs, (b) assistance with caregiving duties, (c) respite, (d) support groups, and (e) increased financial support.

Thalamocortical Dysrhythmia Following Mild Traumatic Brain Injury: A Working Hypothesis

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Traumatic brain injury (mTBI) is one of the most common neurological disorders affecting up to 500,000-1,000,000 individuals in Europe and US per year. Individuals with mild TBI (mTBI) are characterized by great heterogeneity in terms of etiology, pathology, and severity, with injuries that can be elusive to standard clinical techniques, thus mTBI diagnosis is a challenging problem. mTBI patients may suffer from chronic disabilities that can progress over days, weeks, and even years. Previous electrophysiological studies reported reductions in alpha band activity during resting state in mTBI patients relative to healthy non-head trauma controls that can be observed over extended periods of time after injury (Arakaki, 2016). A reduction in alpha-band power can be attributed to mechanisms affecting the thalamocortical network (Nuwer, 2005), possibly associated with deficits in cholinergic neurotransmission (Tenovuo 2006). Disrupted large-scale intrinsic connectivity has been also observed following TBI (Sharp, 2014). We have recently shown that stroke-related cortical lesions induce pathological alterations to the thalamo-cortical interactions, or thalamocortical dysrhythmia (TCD); this arises by attenuating the cortical drive onto the thalamus and driving it into a low bursting regime, which further propagates to the neocortex through divergent intrathalamic circuits (van Wijngaarden, 2016). This low-frequency TCD dynamics can account for a variety of non-specific symptoms (e.g., post-stroke pain and fatigue, mood-related disorders, etc.) that are apparently dissociated from the lesion's site and temporal onset. Here we investigate whether the same signatures of TCD emerges acutely following mTBI. We examine the resting state EEG recordings of 12 mTBI patients with those of non-head trauma controls within one week of injury. Preliminary results over aggregated data in the acute phase show a pattern of increased delta-band power in the frontal areas relative to healthy controls with no differences in the alpha band. The patterns of spectral power distribution unmasked at the individual level show high heterogeneity that depends on the lesion site and severity, suggesting that diagnostically relevant EEG patterns could be revealed taking into account those specific individualized features.

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Five Year Headache Trajectories after Moderate to Severe Traumatic Brain Injury

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Objective: To determine whether patterns or trajectories of headache occur over five years following moderate to severe traumatic brain injury (TBI) and to identify demographic and injury characteristics that may be related to these trajectories. In addition, we also examined whether trajectory was related to employment and satisfaction with life at 5 years post injury.

Methods: 316 individuals were enrolled during inpatient rehabilitation after moderate to severe TBI and were followed by telephone at 3, 6, 12 and 60 months post injury. At each follow up, Individuals who reported headache during the prior 3 months were asked to rate their headache pain on a 0 to 10 scale (0=no pain, 10=worst pain) and to complete the Headache Impact Test-6 items (HIT-6). Discrete mixture modeling was used to estimate trajectory groups based on both pain rating and impact score.

Results: Four different 5 year trajectories were found for headache pain: minimal (25%), worsening (37%), improving (7%), and chronic (30%) pain. Three trajectories were found for headache impact: minimal (48%), worsening (27%), and chronic (24%). The chronic pain trajectory membership was higher for females, those injured by violence, those unemployed prior to injury, and who had a history of headache or mental health problems. Those in the chronic pain trajectory had significantly lower satisfaction with life at 5 years post injury compared to the other trajectory groups. Chronic impact trajectory membership was higher for women, those injured by violence, who had a history of headache, or were unemployed at the time of injury. At 5 years post injury, the chronic group was significantly more likely to be unemployed and also significantly less satisfied with their lives compared to the minimal or worsening trajectory groups. Those who were employed before injury were more frequent members of the worsening group for both pain and impact compared to those who were not employed prior to injury. No relationship was found between other demographic and injury characteristics including age, post traumatic amnesia or substance use prior to injury.

Conclusions: Trajectory analysis revealed a relatively large (24-30%) group of individuals with chronic headache pain and significant headache functional impact over 5 years post injury. The identification of members within this group may be important in targeting more intensive treatment to improve satisfaction with life and post injury employment opportunity.

Battered & Brain Injured: Identifying and Supporting Brain Injured Survivors of Intimate Partner Violence

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Every year thousands of Canadian women experience intimate partner violence (IPV), receiving injuries such as battery to the face, head, and neck, a pattern of violence potentially causing permanent traumatic brain injury (TBI). Despite preliminary investigation identifying elevated rates (35-80%) of potential TBI among women survivors of IPV it remains a connection left largely unexplored. We carried out a pilot project that surveyed existing TBI- specific knowledge and services in the Toronto IPV survivor support community to better understand the current knowledge of TBI in the IPV support community and identify ways to improve the health and wellbeing of women survivors, and developed a knowledge-to-practice network to address this issue. A scoping review of existing literature was conducted prior to embarking on the research project and the results of that review served to inform project design. Phase one consisted of an online survey sent out to IPV service providers located within the Greater Toronto Area asking about their understanding of TBI in their client population and their ability to offer TBI sensitive services. Phase two expanded the project with a networking/education workshop hosting both provincially and nationally based service providers, brain injured women survivors of IPV, and other key stakeholders to disseminate findings, generate recommendations for 'next steps' in research and practice, and offer relevant TBI/IPV education. This project is the foundation for an extensive program of research intended to significantly improve TBI/IPV survivors' health and wellbeing. Results from the scoping review discuss the limited body of existing literature, identify specific research concerns, and highlight practice and policy recommendations. Study data indicates a need for increased knowledge and awareness of TBI among IPV service providers, emphasizes the need for development of a TBI assessment tool suitable for use in an IPV context, and identifies facilitating factors and barriers to service provision and uptake. We present these findings and provide recommendations for future research agendas and service development.

Epidemiology of Head and Face Injuries in National Collegiate Athletic Association Student-Athletes

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Objectives: The incidence of and outcomes from concussions in National Collegiate Athletic Association (NCAA) student-athletes is well studied. However, little is known about the incidence of other head injuries among NCAA student-athletes, especially those of greater severity. The objective of this study was to determine the proportion of all head and face injuries that are concussions and identify other head injuries, especially those requiring emergency transport or surgery.

Methods: Data from the National Collegiate Athletic Association (NCAA) Injury Surveillance Program (ISP) during the 2009/2010 to 2013/14 academic years were used for this descriptive epidemiology study. Athletic trainers reported the incidence and characteristics of injuries and athlete-exposures (AEs) from 145 schools across 27 sports and 1,614 team-seasons. All injuries to the head and face were examined. Proportions of diagnoses for all injuries, those that required surgery, and those that required emergency transport are reported, as well as national estimates for the number of each diagnosis per year.

Results: There were 2,255 injuries to the head and face, for a rate of 0.50/10,000 AEs (95% Confidence Interval [CI]:0.48, 0.52). Of these, 1678 (74.4%) were concussions, 263 (11.7%) were facial lacerations, and 79 (3.5%) were facial contusions. Only 1 subdural/epidural hematoma was reported (rate=0.0027/10,000 AEs [95% CI:0.0,0.0079]), for a national estimate of 4/year across all sports, though this estimate is imprecise. Additionally, only 1 skull fracture was reported, and only 7 orbital fractures (rate= 0.0187/10000 AEs [95%CI:0.0048, 0.0325]; national estimate 57/year). Thirty (1.3%) head and face injuries required surgery, 13 (43.3%) of which were facial lacerations, 4 (13.3%) were concussions, 4 (13.3%) were scalp lacerations, and 4 (13.3%) were orbital fractures. Sixty (2.7%) head and face injuries required emergency transport, 44 (73.3%) of which were concussions.

Conclusions: Severe brain injuries are rare among NCAA student-athletes. Among head and face injuries that required surgery, the majority were lacerations. Further research is needed into possible misclassification of diagnoses, as it is unlikely that surgery was required for a concussion, and this may represent more severe brain injuries that are misclassified. Additionally, most of the head and face injuries that required emergency transport were concussions. This may indicate that the severity of the brain injury is not clear at the time of presentation. Further research is needed to determine better ways to identify, triage, and manage brain injuries at the time of injury.

A Novel Self-Guided Rehabilitation Task Reduces Somatosensory Sensitivity and Preserves Cognitive Performance Following Experimental Traumatic Brain Injury

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Traumatic brain injury (TBI) is not a transient event from which all people recover; the resulting damage can evolve into neurological disease. In rats, TBI disrupts neural circuits, with functional consequences such as cognitive impairment and sensory sensitivity to whisker stimulation. Experimental rehabilitation strategies across TBI models, such as enriched environment and exercise, have reported varying levels of success in alleviating a broad-range of symptoms. The persistent symptoms of TBI are heterogeneous and therefore require therapies focused on specific symptoms and the associated brain regions with the symptomology. Our model of brain injury leads to sensory sensitivity and cognitive deficits at 28 days following a TBI; therefore, the current study sought to establish a rehabilitation task that was effective in maintaining somatosensory and cognitive function after diffuse TBI in rats. The Peg Forest task takes place in a box with a peg board floor (60 cm X 60 cm) that allows for 10 cm plastic pegs to be inserted at 2.5 cm intervals anywhere across the board. The random configuration of pegs promotes spatial navigation and whisker stimulation as rats complete tactile exploration of the environment. Rats were exposed to the rehabilitation paradigm by allowing them to freely navigate through a random peg-filled arena (92 pegs) or they were exposed to an open field arena for 10 days over 2 weeks. Additional groups of sham and injured rats served as caged controls. All rats were then tested for sensory sensitivity on the whisker nuisance task and cognitive performance in 3 tasks: 1) novel object recognition (short-term memory), 2) novel location recognition (long-term) and 3) temporal object recognition (working memory) starting 28 days post-injury. Brain-injured animals exposed to the Peg Forest showed no sensory sensitivity, performing similar to sham animals on the whisker nuisance task. On all three object recognition tasks, these brain-injured animals exposed to the Peg Forest performed at similar levels to sham rats. Brain-injured rats exposed to the open field task also showed no sensory sensitivity, but performed significantly worse than the sham animals on all three object recognition tasks. As expected, brain-injured caged-control rats exhibited both sensory sensitivity and impaired cognitive performance compared to uninjured animals. The results indicate that self-guided, intermittent rehabilitation personalized to specific neurological impairments can mitigate symptomatology and that the Peg Forest is a viable rehabilitation strategy to explore the cellular and molecular mechanisms that positively impact neurological function after TBI.

Brain Deformation of Youth Athletes During Subconcussive Head Impact

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Introduction: There are 1.6 to 3.8 million sport-related concussions each year, the majority in football [1], but an increasing interest in subconcussive impacts, particularly in the youth population. Biomechanical factors like impact location and direction and their relationship to brain motion and injury must be well characterized. Brain response directional dependence has been reported using animal and finite element (FE) models [2]. For example, Zhang et al. (2001) observed decreased brain tolerance to lateral impact versus frontal impact.

Materials and Methods: On-field head impact data was collected during practices and games for three youth teams over four football seasons using the Head Impact Telemetry (HIT) System. Each impact was characterized based on azimuth from back to front of head (θ) and elevation from nose to top of head (α). Six impact locations were studied: front helmet, front facemask, side facemask, anterior side, posterior side, and rear – A-F) [3, 4]. Normalized load curves for 5%, 50%, and 95% percentile magnitude impacts were created using this data and previously measured six degree of freedom (6DOF) data. These drove a finite element simulation of an anatomically accurate finite element model with gyri and sulci, the atlas-based brain model (ABM) [5]. Brain deformation was analyzed using maximum principal strain (MPS) for each element. Decreasing peak MPS by element was used to compute total brain volume exceeding five (5) percent MPS threshold value.

Results and Discussion: A total of 40,538 impacts from 119 individual athletes were recorded. 50th percentile linear accelerations ranged between 14.8 and 31.2 g's, rotational accelerations between 765 and 1,269 rad/s², and angular velocities between 5.1 and 8.8 rad/sec for the six locations A - F. Volume percentage of brain exceeding 5% MPS ranged broadly between impact severities and by location of impact within each impact severity. For 5th percentile impacts it ranged from 0-6%, for 50th percentile impacts it ranged from 6-53%, and for 95th percentile impacts it ranged from 80-97%.

Conclusions: This study demonstrates brain deformation varies widely by impact location and by impact severity. The location generally resulting in the largest brain deformation was location B, frontal facemask. Locations resulting in lower deformations were location A, a frontal top, and F, rear. Broad variation in volume of the brain exceeding 5 percent strain is worth extensive further investigation. This may have important implications for quantifying concussion risk and long term exposure to subconcussive impacts. Quantifying the relationship between impact location, magnitude and brain deformation will aid researchers, equipment manufacturers and rulemakers in head injury prevention and mitigation.

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Augmentative and Alternative Communication Intervention in Patients with Aphasia

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Background: Over one million individuals in the United States are affected by aphasia annually, in which approximately 180,000 of those cases are newly acquired. The development of efficient and effective treatment is therefore crucial in such population.

Objective: To determine whether an augmentative and alternative communication (AAC) intervention (i.e., GoTalk Now) improves communicative abilities, quality of life but also brain functioning in patients with aphasia. **Methods and Participants.** Nineteen patients were recruited at least three months post injury (age range: 29-78) and were given 6 hours of therapy with a Speech and Language Pathologist, using GoTalk Now. Patients were evaluated prior and after intervention using the Western Aphasia Battery (WAB), the Satisfaction and Success Questionnaires but also using an electroencephalogram (EEG) at rest (for 5 minutes with eyes closed). **Data Analysis:** Paired T-Test and Wilcoxon Signed Rank were used to compare behavioral data pre and post intervention. EEG power spectrum was also estimated pre and post intervention for each patient.

Results: A positive mean difference was found across all subjects of the WAB. Spontaneous speech scores increased significantly for all 3 groups. We also saw an increase in the aphasia quotient when excluding patients with global aphasia (i.e., Broca/Other aphasia). Patients reported higher satisfaction in their communication abilities after AAC therapy. In parallel, they rated higher on the Satisfaction and Success Questionnaires on their success of communicating medical information after therapy. The power spectrum for 6 subjects with artifact free EEG data was estimated. All patients with Broca showed a decrease in delta frequencies post-intervention at left temporal sites as compared to only half of the patients with Global/Other aphasia.

Conclusion: The intervention significantly improved the patients' abilities and satisfaction in communicating with their surroundings. An improvement in brain functioning was also observed with decreased delta frequencies (particularly in Broca's aphasia), suggesting a reduction in aphasia severity after intervention.

The Multiple Roles Families Play, Including Unpaid Healthcare Providers, after Severe Brain Injury

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Objectives: To capture the multiple roles family members of patients in a vegetative state (VS), minimally conscious state (MCS), or with locked-in syndrome (LIS) have while caring for a loved one. Through qualitative interviews, we explored the roles caregivers play and the potential for conflict among them.

Methods: We conducted semi-structured qualitative interviews with twelve substitute decision-makers of individuals who have been diagnosed to be in a VS, MCS, or LIS. Using a constructive grounded theory design, family members were interviewed twice to capture the different roles they play, the relationship among these roles, and the burdens experienced.

Results: Twelve family members participated in the interviews for a total of 21 in-depth interviews to date. Family members described undertaking a wide variety of different roles. The roles include being a caregiver to the patient, caregiver to other family members, advocate, household provider, and financial and legal gatekeeper. The caregiver role included unpaid health care work in caring for a loved one with a severe brain injury, whose needs are often not met completely by the health system. Family members described in detail the physical, emotional, social and economic burdens experienced by them and the impact of these burdens on personal relationships and family dynamics.

Conclusions: Family members caring for a loved one who has been diagnosed to be in a VS, MCS, or LIS undertake a variety of roles. Prominent among these is the role as unpaid health care provider, as families fill gaps in care that exist within the health care system. The complex relationship among the roles is a source of strain and burden for family members. Our findings suggest an urgent need to improve the support family members receive, including strategies to care for themselves.

ISG15 Required for BBB Integrity and Nutrient Homeostasis Following TBI in Young Mice

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Introduction: Recently we have shown that ISG15, an ubiquitin like protein forms a protein-protein interaction with MLCK, claudin5 and GLUT1. Here we show that ISG15 is also likely responsible for the phosphorylation of GLUT1 (p-GLUT1). ISG15 is increased following focal ischemia and is neuroprotective. The significance of ISG15 TBI is still unclear.

Methods: PND21 and PND24 WT and ISG15 ^{-/-} mice were anesthetized with avertin, mechanically ventilated, physiologically regulated, and subjected to lateral closed-skull injury model with impact depth of 2 or 2.25 mm (bregma level - 0.10mm). Mice were sacrificed from T0, through 7D. ISG15, GLUT1 and p-GLUT were analyzed by western blot, BBB disruption with Fluorescein sodium salt and 4Kda Dextran. Wire Hand and Two Object Novel Recognition were performed per protocol to evaluate motor strength and memory.

Results: Protein expression

PND21 Free ISG15 down-regulation: normalized to actin T<2min Sham: 14.83 2.00mm:

9.83, 2.25mm: 3.83 and T4h Sham: 4.5 2.00mm: 5.5, 2.25mm: 6.5, T6h Sham: 4.5, 2.00mm: 9, 2.25mm: 15. 72h Sham: 4.33, 2.00mm: 6.883, 2.25: 15.5.

PND24 Free ISG15 up-regulation: T<2min Sham: 5.167, 2.00mm: 9.167, 2.25mm: 14.17 and T4 Sham: 4.5, 2.00mm: 9.5, 2.25mm: 14. 6h Sham: 6.83, 2.00mm: 7.5, 2.25mm: 14.83, 72h Sham: 6.87, 2.00mm: 7.5, 2.25: 14.33.

PND21 p-GLUT1 decreases: T<2min Sham: 4 2.00mm: 4 2.25mm 3.33 and T4h Sham: 7.167 2.00mm: 10.33 2.25mm: 11.00

PND24 p-GLUT1 increases: T<2min Sham: 4.5 2.00mm: 9.5 2.25mm 14.5 and T4h Sham: 6.5 2.00mm: 8.33 2.25mm: 15.17

ISG15 and p-GLUT1 develop protein-protein interactions on co-immunoprecipitation at 4h following TBI.

Evaluation of the blood brain barrier

PND21 mice brains 72h:

WT

TR- Sham: brains 3.50. 2.25mm: 16.83.

FITC- Sham: 3.50, 2.25mm: 12.67.

EB- Sham: 3.50, 2.25mm: 21.

ISG15^{-/-} 12.17, mice brains 72h: 19.50.

TR- Sham: 2.25mm:

FITC- Sham: 16.17, 2.25mm: 19.50.

EB- Sham: 11.50, 2.25mm: 13.50.

Overall the amount of dyes in the brains are similar in the shams of WT and ISG15 brains and there is no significant difference in the ISG15^{-/-} Sham and TBI brains.

Co-IP-ISG15 shows a protein-protein interaction between ISG15 and P-Glut.

Motor and Neurocognitive Outcomes: The PND21 sham WT mice show preference for the new object: 72.90 over the old object: 34.40 and a decrease in the latency to fall between sham: 20.33 and 2.25mm: 3.50. The

PND21 ISG15^{-/-} shams show a significant decrease in the preference for the new object: 17.13 compared to the old object: 28.32 and no difference between the sham: 12.17 and 2.25mm: 14 in latency to fall.

Conclusion: ISG15 appears to be developmentally regulated and important for nutrient homeostasis and neurological recovery following TBI.

Molecular and Functional Biomarkers of Mild Traumatic Brain Injury

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Traumatic brain injury (TBI) is a major cause of death and disability worldwide, with at least 1.7 million individuals affected annually in the US. Mild TBI (mTBI) alone accounts for 85% of total TBI cases and is associated with serious long-term sequelae including second impact syndrome, post-traumatic epilepsy, and possibly chronic traumatic encephalopathy (CTE). mTBI often goes undiagnosed due to under-reporting, delayed onset of symptoms and the limited sensitivity of conventional assessment techniques in detecting mild brain injury, thereby hampering diagnostic, prognostic, and therapeutic approaches. To overcome these limitations, we have been evaluating the utility of microRNAs (miRNAs) to serve as sensitive and specific peripheral biomarkers of mTBI. miRNAs are small non-coding RNAs that suppress protein expression and that have emerged as useful biomarkers in cancer, diabetes, neurodevelopmental, and neurodegenerative disorders. Notably, although miRNAs are made in all tissues and organs of the body, many of them show tissue-specificity. Moreover, miRNAs can act within the cells that synthesize them or be released into the extracellular space (EC) and travel in biofluids to affect other cells. Numerous studies have shown that miRNA expression profiles differ between healthy and diseased states, and that the release of miRNAs into the EC appears elevated following tissue damage. Our goals in the present study were to establish the relationship between peripheral measures of miRNA, objective assessment of likely mTBI severity, and sensitive indices of balance and cognitive function. To this end, a cohort of adult amateur MMA fighters was recruited for testing. After obtaining informed consent, we obtained a thorough medical history, blood and saliva samples, and baseline performance of balance, cognitive function, and dual-task performance using a newly developed inertial sensor system that was worn during the assessment of 16 different tasks. The blood and saliva samples and performance tests were obtained pre- and immediately post-fight, and in the days and weeks following each competition. miRNA profiling was performed using next generation RNA-sequencing. Using both tool sets, we established that 1) several sets of miRNAs show acute changes in expression after injury in the blood and saliva, although the two biofluids differ in the specific biomarkers that are released; 2) the miRNAs that are altered affect numerous cellular pathways involved in inflammation or cell death in putative concussion subjects; and 3) many of the miRNAs in the two fluids show strong correlations with changes in functional measures that occur in the short and longer term interval following the MMA competition. We conclude that specific subsets of miRNAs show strong preliminary evidence of potential utility as sensitive and specific indicators of mTBI in adult athletes. Ongoing studies are validating the changes seen using more rapid techniques and also determining their utility in replication cohorts.

Subconcussive Head Impact History as a Factor in Concussion Onset

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The science of injury biomechanics often associates a single event with injury onset. However, peak accelerations associated with concussion in football players as measured using the Head Impact Telemetry system are often associated with low risk for concussion onset. This analysis focused on each concussed player's recent head impact history as a factor in concussion onset. The current study enrolled 337 NCAA Division I football players who sustained 147,800 recorded head impacts. Seventeen players sustained concussion. Significant head impact history was assessed as the number of severe head impacts sustained by the player and the number of sessions (games/practices) with an elevated number of head impacts until the injury date. Severe subconcussive head impacts had a magnitude greater than the 75th percentile linear (>31.9g) or rotational (>1,405rad/s/s) acceleration for all recorded head impacts (n=147,800). An elevated number of head impacts per session was defined as any session with the number of head impacts exceeding the 75th percentile (>17 impacts). Head impact exposure for each concussed player was compared to his position- and team-matched controls. There were an average of 4.2 controls for each concussed player (range:2-7). Determination of the concussive impact for each player was achieved by a group of researchers incorporating head impact data, event video, and injury report data from the local study staff. Seventeen concussive impacts were captured, which were associated with linear accelerations of 29-106 g's and rotational accelerations of 1,617-7,805 rad/s/s. Peak linear and rotational accelerations from 16/17 concussive impacts were associated with <25% risk and 8/17 were associated with <1% risk according to a previously defined risk curve. In comparison to the average head impact history until the day of injury from their position- and team-matched controls, six concussed players had greater than 75% more severe head impacts and an additional three concussed players had greater than 35% more sessions with an elevated number of head impacts. Five of those nine concussed players had the most severe head impact history of their team position group. The mean concussive impact for this subset of nine players was 72.6 g's and 4,718 rad/s/s, which is associated with less than 5% risk of concussion. Over the entire collection period, non-concussed players sustained 722 head impacts more severe than the mean concussive accelerations of this subset, indicating that the concussive impact event may not be the sole determinant of concussion onset. This analysis highlighted a subset of concussed players for which recent subconcussive head impact history appeared to play a role in injury onset. While this represents a limited sample, if replicated in a larger study, implications may include the need to limit total head impact exposure during the course of a football season to reduce concussion risk.

Race/Ethnicity Predicts Retention in Traumatic Brain Injury Outcomes Research: A Traumatic Brain Injury Model Systems National Database Study

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Objective: To determine the relationship between race/ethnicity and retention in a longitudinal study at 1 or 2 years after traumatic brain injury (TBI) in the Traumatic Brain Injury Model Systems National Database (TBIMS NDB)

Design: Prospective data from a multicenter national database

Methods: Participants were Whites (n=5548), Blacks (n=1347), and Hispanics (n=790) enrolled in the TBIMS NDB with dates of injury between October 1, 2002 and March 31, 2016. Follow-up was attempted via phone or mail at 1 (\pm 2 months) and 2 years (\pm 3 months) post-injury. Retention was defined as contact with and completion of at least one question on the follow-up interview by the enrolled participant or a proxy. The probability of being retained was initially modeled as a function of race/ethnicity using logistic regression unadjusted for other patient characteristics. Multivariate logistic regression was then used to model the relationship between race/ethnicity and retention status controlling for 12 patient characteristics (age, sex, marital status, education, residence at rehabilitation discharge, pre-injury incarceration, pre-injury problem substance use, violent versus non-violent cause of injury, PTA, FIMTM motor and FIMTM cognitive scores at the time of rehabilitation discharge, and job stability for the year prior to injury). Significant interactions between race/ethnicity and patient characteristics were also examined and included in the adjusted model if significant.

Results: There was a significant interaction between race/ethnicity and pre-injury problem substance use, such that Hispanics were less likely to be retained in the TBIMS NDB among the subset of persons with no history of problem substance use. There was no difference in retention between Whites and Blacks. Other variables associated with not being retained included young age, low education, violent cause of injury, and discharge to an institution versus private residence.

Conclusions: The findings emphasize the importance of looking at retention rates among Blacks and Hispanics separately rather than combining them or grouping either with other races or ethnicities. Improving cultural sensitivity in research staff may improve retention of Hispanics in longitudinal TBI research.

Age and Gender Effects in Response to Repetitive Mild TBI in hTau Transgenic Mice at Two Weeks Post-Injury

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Introduction: Traumatic brain injury (TBI) is a serious illness which on average strikes one person every 15 seconds in the US. Even mild TBI, which comprise as many as 75% of all TBI cases, carries long term consequences. In particular, repetitive mild TBI can result in chronic traumatic encephalopathy, which is characterized by the deposition of phosphorylated tau protein. We have investigated the effects of repetitive mild TBI in young and aged hTau transgenic male and female mice.

Objectives: This study examined the neurobehavioral and neuropathological effects of age and gender on the outcome from repetitive mild traumatic brain injury in mice transgenic for human tau (hTau). These mice express the six human isoforms of tau but do not express endogenous murine tau and they develop tau pathology and memory impairment in age-dependent manner. We sought to determine whether the presence of established tau pathology would significantly interact with the pathological and behavioral effects of head injury.

Methods and Materials: Male and female hTau transgenic mice at either 4 months or 1 year of age received 5 hits with an inter-mTBI injury interval of 48 hours. Briefly, an electromagnetic impactor generated a midline mTBI on the mouse scalp with a 5.0mm diameter flat face tip, at a 5m/s strike velocity, with a 1.0mm strike depth, and a 200msec dwell time. Anesthesia controls were matched for time spent under anesthesia. In the week after the completion of all injury or sham procedures, mice were assessed for motor performance using the Rotarod. Spatial learning and memory were assessed during the second post-injury week using the Barnes maze. Two weeks after the final impact the mice were euthanized for neuropathological analyses.

Results: Rotarod testing of hTau mice in the first week following r-mTBI reveals no significant gender differences in young mice, but a significant interactive effect of gender and injury in aged hTau mice. Female r-mTBI mice exclusively show significantly impaired rotarod fall times on days 1, 5 and 7 after injury compared to their sham counterparts by repeated measures ANOVA ($p < 0.05$), and though we have not yet found the pathological source of these differences, impairments in motor and balance may be driven by brain regions that have not yet been examined in our studies. Barnes maze data show a similar differentiation between young and aged mice, with young mice showing no significant effects between genders. In aged mice, male sham mice did not learn the Barnes maze task as well as female sham mice, obscuring an injury effect in male shams ($p > 0.05$ by non-parametric Mann-Whitney U test). Female mice showed the expected injury effect, but there were no significant differences between the two genders in the injured groups.

Effect of Cranberry Oil Supplementation Following Traumatic Brain Injury, for Neurorehabilitation and Health: A Case Report

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Objective: Case Report of a 23-year old man with traumatic brain injury, suffering neurologic symptoms, responding with noticeable improvement following cranberry seed oil supplementation.

Methods: Case study involved neuro-cognitive testing and dietary supplementation with 500mg purified cranberry seed oil softgel capsules. Dosage: 4gm/day or 1gm qid for 7 days; followed by 2gm/day or 1gm bid thereafter. Neuropsychological tests completed and psychometric characteristics recorded.

Results: Brain injuries are common in sports, combat, assault, motor vehicle accidents, falls and those with substance abuse. Intracranial trauma can cause neurologic limiting and life-threatening conditions. According to the CDC, the number of TBIs is estimated at 1.7 million adults annually. In Afghanistan, incidence is unknown; treatment and rehabilitation is not often available. There is an increase in TBI-related emergency visits and hospitalizations due to falls, motor vehicle accidents and assault. Cranberry seed oil is known for beneficial unique balance of omega-3, -6, and -9 fatty acids, tocotrienols, tocopherols, phosphatidyl choline and beta-sitosterols. This is the first report of cognitive impairment from a street fight, in post-war Afghanistan responding to cranberry seed oil. The patient presented with 2-week impairment and reduced neurologic assessment. Measurement of auditory-visual response time, number recall forward-backwards, were part of cognitive function tests. Patient had a headache and nausea the initial week post trauma. Imaging scans were normal, no vertigo, no gait ataxia, and no visual deterioration. Minor brain injury scaled by GCS: E4 + V4 + M5 = 13/15, with verbal confusion and difficulty with commands, no cranial nerve palsies, no cerebellar signs, BP 120/76, pulse 72/min, temp 37 degrees C. Following initial supplementation 4 grams/day of cranberry seed oil for one week, then 2 grams daily. On post-exam day 5, patient showed some improvement in cognitive function and headache free, and on 10th day examination, noticeable cognitive improvement. Patient was followed up monthly and in retest showed improvements in attention, memory, reasoning, and processing speed. Family also reported subjective improvement in brain function and response time.

Conclusion: Dietary supplementation with cranberry seed oil, rich in omega fatty acids and anti-inflammatory phytonutrients, is an option for patients with brain injury to improve the recover providing improvement in cognitive performance and neurologic deficits. Cranberry seed oil is a safe and affordable adjunct therapy that can be provided globally to help in TBI patient recovery. This study opens discussion for the health benefits of cranberry oil strengthening neurologic health, with suggestive anti-inflammatory effects, hypoxia protection and cerebral blood flow as an immediate intervention and low-cost approach for traumatic brain injury patients to attain health.

Pharmaceutical-grade cranberry seed oil softgel provided by NUTRATIVA Global. Shipments to Afghanistan provided by NATO-led ISAF, and a donation from United States Navy Lieutenant Commander Stanley Ormbrek.

An Alternative Approach to Interpreting Baseline Neurocognitive Performance in High School Athletes with Attention-Deficit Hyperactivity Disorder and Learning Difficulties

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Background: Baseline preseason computerized cognitive testing is often used as a component of sport concussion management programs. There is growing evidence that high school students with attention-deficit hyperactivity disorder (ADHD) or academic difficulties perform more poorly on baseline computerized neurocognitive tests, which suggests the need for separate normative data. We investigated an alternative approach to interpreting cognitive performance in these populations using multivariate base rate analysis (i.e., considering multiple test scores simultaneously).

Method: Participants were adolescent student athletes (ages 13-18 years) from the state of Maine who completed baseline preseason testing using ImPACT[®] and had not sustained a concussion in the past 6 months. Extreme outliers (i.e., > than 3 SD below the mean) for each composite score were removed and only valid tests were used. Participants were divided into four groups: ADHD only (n=1,496), ADHD and learning difficulties (n=751), learning difficulties only (n=2,837), and healthy controls (n=31,838). ImPACT[®] Online normative data was used to identify percentile ranks for performance on the four composite scores and to calculate multivariate base rates. Rates of low scores were examined separately for girls and boys.

Results: Means and standard deviations [M (SD)] of percentile ranks for the entire sample were as follows: Verbal Memory [48.0 (29.2)]; Visual Memory [47.2 (29.3)]; Visual Motor [34.3 (27.8)]; and Reaction Time [39.9 (27.0)]. Of the control subjects, 52.7-59.2% obtained one or more scores below the 16th percentile. Adolescents with ADHD had a higher frequency of one or more scores below the 16th percentile compared to healthy controls, regardless of age group and gender (58-66.7%; p<.05). Similarly, high school students with learning difficulties (73.7-80.2%; p<.001) and those with learning difficulties plus ADHD (71.9-83.0%; p<.001) obtained a higher frequency of scores below the 16th percentile. Furthermore, low scores were more common in those with learning difficulties, and those with learning difficulties and ADHD, compared to high school students with ADHD only (ps<.05).

Conclusions: This study used a multivariate base rate approach to characterize performance on computerized neurocognitive testing (i.e., ImPACT[®]). Using a large sample of high school students from Maine, we found lower scores than expected, overall, on the speed and reaction time composites of ImPACT[®]. Healthy high school students obtained a larger number of low scores than has been previously reported. Furthermore, students with neurodevelopmental difficulties obtained a higher frequency of low scores compared to healthy controls. This study illustrates the utility of using a multivariate approach to interpret neurocognitive test performance (i.e., expected vs. obtained number of low scores) in students with ADHD and/or learning difficulties.

Endpoint Scores of Executive Functioning for Acquired Brain Injury Studies

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Introduction: Deficits in executive functioning are common in people with neurological problems and traumatic brain injuries. This study examined two new cognition endpoint scores that summarize deficits in executive functioning. These scores were designed to overcome possible limitations associated with the Global Deficit Score (GDS), such as ceiling effects, restricted range, and reduced sensitivity to cognitive impairment in people with above average intellectual abilities. Compared to the GDS, it is hypothesized that the new composite scores will have a greater distribution of values, less skew, and minimal ceiling effects.

Method: The sample consisted of 854 healthy individuals (ages 20-89; 47% male; 81.4% ≥ 12 years of education) from the standardization sample for the Delis-Kaplan Executive Function System (D-KEFS). A subsample (n=707) were administered the Wechsler Abbreviated Scale of Intelligence, with the two-test FSIQ used to estimate intellectual ability. Seven individual test scores from the Trail-Making Test, Color Word Interference Test, and Verbal Fluency Test were analyzed. The GDS was calculated by converting age adjusted scaled scores (SS; M=10, SD=3) of 6 or less to deficit scores, as follows: SS 6=1, 5=2, 3-4=3, 2=4, and 1=5. The deficit scores were summed and divided by seven to derive the GDS. Two new neuropsychological deficit scores were calculated by raising the ceiling for the deficit scores to scaled scores of 10 or lower. The Neuropsychological Deficit Score (NDS) starts at SS 10 and has seven gradations (SS 10=0.25, 9=0.5, 8=1.0, 7=1.5, 6=2, 5=3, 1-4=4), whereas the Neuropsychological Deficit Score Extended (NDS-E) also starts at SS 10 but has ten gradations to lower the floor effect (i.e., SS 5-9 deficit scores were equivalent to the NDS, but SS 4=4, 3=5, 2=6, 1=7).

Results: The GDS, NDS, and NDS-E increased with lower levels of education and lower intellectual ability. The distributional characteristics of the GDS in the total sample were as follows: M=0.32, SD=0.49, Skew=1.94, Kurtosis=3.70, and percentage scoring zero=51.8%. The distributional characteristics of the NDS were as follows: M=0.67, SD=0.50, Skew=1.25, Kurtosis=1.31, and percentage scoring zero=6.3%. The distributional characteristics of the NDS-E were as follows: M=0.74, SD=0.50, Skew=1.54, Kurtosis=2.29, and percentage scoring zero=6.3%. The percentages of people with above average intelligence who obtained scores of zero were as follows: GDS=73.9%, NDS=14.2%, and NDS-E=14.2%. The percentages of people with below average intelligence who obtained scores of zero were as follows: GDS=22.1%, NDS=0%, and NDS-E=0%.

Discussion: The two new executive functioning composites had a wider range of scores and more symmetric distribution in healthy adults compared to the GDS, perhaps making them better suited as clinical trial endpoints. The reliability, sensitivity, and specificity of these composite scores need to be examined in future studies with people with acquired brain injuries.

The Prognostic Value of the Coma Recovery Scale – Revised

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Objective: According to the American Congress of Rehabilitation Medicine (2010), the Coma Recovery Scale-Revised (CRS-R) meets the highest psychometric standards for the evaluation of severely brain-injured patients. Nevertheless, no data has yet been published on its prognostic value. This study therefore aimed to provide psychometric data as regards the prognostic validity of the scale.

Design: Prospective longitudinal study. Setting. Neurosurgery unit of Ronald Reagan Hospital (University of California, Los Angeles, CA, USA).

Interventions and Main Outcome Measure(s): Twenty one patients with severe traumatic brain injury (Age: 43y ± 19; time post-injury: 25d ± 11) have been assessed off sedative drugs using the CRS-R. The outcome has been documented in each patient at 6 months post-injury, using the Glasgow Outcome Scale – Extended (GOS–E).

Results: A linear regression showed that the CRS-R explained most of the variance of the outcome at 6 months (Beta: 0.79; t: 5.68; p<.001) as compared to other demographics variables such as age and time post-injury (Beta: 0.15; t: 1.05; p=0.31). A clear cut-off CRS-R score of 13 with a sensitivity of 93% and a specificity of 100% has also been obtained for differentiating patient with good outcome (mild to moderate disabilities) from patients with bad outcome (severe disabilities).

Conclusions: Our results suggest that the CRS-R has excellent prognostic value and could be used by clinicians to predict the outcome of patients with severe brain injury, at 6 months. These results have now to be confirmed in a larger sample.

The Effect of Sleep Disruption on Mild Traumatic Brain Injury in an Animal Model

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Introduction: Mild traumatic brain injury (mTBI) is one of the most common injuries across all age groups. There is often concern in the acute setting on whether interruption of normal sleep cycles will have a lasting effect on neurological function. It is common practice for a physician to keep a patient awake to prevent a lapse into a coma, however it is believed the sleep following a mTBI may aid in healing of brain function.

Objective: To determine the role sleep deprivation plays in rodent neurological function following a mTBI via a unique rotational model.

Methods: There are 4 groups of rodents each composed of 3 animals: Sham with sleep deprivation (SD), mTBI with SD, Sham with no SD, mTBI with no SD. The animals will be given their treatment and then according to their assigned group be kept awake for 48 hours in a shaker cage. Following that SD they will be given 24 hours of rest and then tested for neurological function in an elevated plus maze. They will be tested on a weekly schedule to determine change in function.

Results: The results following 2 weeks after treatment showed a mTBI dominated response. The mTBI and mTBI with SD each showed decreases of 50% in total open arm time following the injury treatment. The decrease in open arm stabilized heading into week 1 and week 2 post treatment. Meanwhile the sham group showed a more consistent open arm response. In addition the mTBI and mTBI with SD had the great decrease in open arm entries following the treatment with decreases in 33% and 37% respectively.

Conclusions: The decrease in open arm time is consistent with increased neurological damage and anxiety in the rodents. The dominant mTBI response in both open arm time and entries may indicate that the injury process may have a greater effect on neurological function than sleep deprivation. However, because of the small sample sizes, more testing with larger groups may better elucidate the effects on the brain processes following treatment.

Describing Weight Loss History Among Individuals with TBI

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Objective: To describe the (1) weight loss history, (2) perceptions about making lifestyle changes, and (3) reported physical activity among a sample of individuals with a TBI prior to starting a 12-month lifestyle change program. TBI is a critical public health issue, as individuals experience higher incidence of obesity and increased risk for co-morbid conditions compared to the general population; yet lifestyle behaviors remain largely understudied.

Methods: Participants included individuals who were enrolled in a weight loss program, ≥ 6 months post-TBI, body mass index (BMI) ≥ 25 , between 18-64 years old, and had physician's clearance to participate. Self-report data was collected prior to beginning the lifestyle change program. Participants answered quantitative and qualitative questions related to their weight loss history, motivation and confidence in losing weight, perceived benefits of lifestyle change, and physical activity behaviors.

Results: The final sample included 22 participants (M age = 46), who were primarily Caucasian (68.2%), had completed post high-school education (86.4%), and experienced their injury a median of 8 years ago. Mean weight was 208.5 lbs (SD=40.2) with an average BMI of 31.84 (SD=4.4) which is considered obese. The majority of participants (72.7%) reported prior weight loss attempts and 50% reported gaining ≥ 10 pounds since injury. All participants indicated they were highly motivated and ready to make lifestyle changes (numeric rating scale 10 out of 10), although confidence to successfully make lifestyle changes was lower (8 out of 10). The most frequently reported perceived benefits for making lifestyle changes included feeling better or increasing one's personal drive, improving overall health, and being more active and energetic. The most commonly reported barrier to weight loss was physical health complications. Typical types of physical activity completed included walking (68% of sample) and swimming (32%), although the duration of activity was only reported to be 180 and 79 minutes per month respectively.

Conclusion: Though the tenets of weight loss to eat less and be more physically active are equally relevant for individuals with TBI, they are less easily accomplished due to the myriad of functional characteristics associated with TBI. Results indicate that the majority of individuals have gained weight since injury and attempted weight loss, demonstrating a need for evidence-based lifestyle interventions. This is emphasized by the finding that participants reported low activity levels and health complications were a barrier to weight loss. Future research is needed to determine if individuals with TBI are able to achieve and maintain weight loss using modified programs and how weight loss affects chronic disease.

Disorders of Consciousness Family Education Materials: Information, Gaps and Dissemination

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Objective: The DOC-Family Education Committee identified a need to get information out to families/caregivers about Disorders of Consciousness and how to manage and address the complex needs of these individuals. Three tasks were selected:

- a) Identify the materials being used currently by DOC programs nationally and internationally,
- b) Identify gaps in the educational materials, and
- c) Identify strategies for organizing and disseminating this material to families effectively.

Data Sources: Over 1100 surveys went to National and International CARF Accredited Brain Injury Programs and to 22 past and current TBI Model Systems Programs. 37 programs responded to the survey where services for people in DOC ranged acute to long-term care. 23/37 programs said they had specific information about DOC, and 15 said they would share their information for purposes of this project. The number of patients served from the 15 facilities ranged from 5-65 DOC patients per year with the majority serving 15 patients per year.

Study Selection

Data Extraction: Programs reported providing information to families on the following topics: General Information, Medical Complications, Pharmacology Management, Nursing-Health and Safety Needs, Neuropathology/Brain Anatomy, the Rehabilitation Process, Assessment and Treatment, Prognosis, Extended Care Needs, Financial, Legal Guardianship/POA, Family Adjustment, Self-care for caregivers, Family Interaction with DOC, Resources and/or Local Supports. Copies of handouts, web links, PowerPoint presentations, booklets and pamphlets were obtained from responding programs.

Data Synthesis: Several challenges were identified in disseminating the assembled information to family members. An organizational model, Timing It Right, used in other diseases involving chronic care described by Cameron, et al in working with stroke family caregivers was proposed. This model encourages different forms of informational, emotional, instrumental and training support based on the phase of treatment/recovery of the patient (Event/Diagnosis, Stabilization, Preparation, Implementation, and Adaptation). The assembled informational material was further organized into 4 headings: Body, Mind, Taking Care of Myself, and Resources for more family friendly language.

Conclusions: There is an array of quality educational material available to families and caregivers of severe TBI/DOC patients; however there are gaps in the available information that need development. It is also evident that the amount of material can be overwhelming to families and the material should be organized in a manner that makes it accessible as needs for information evolves over the course of the patient's recovery. Also, noted were the organization and health literacy issues in the materials. The panel will discuss the above issues, the challenges for family/caregivers, minimal guidelines for programs serving DOC patients in regards to family training and the need for ongoing review and study.

Hormonal Alterations and Outcome Following Stroke in Women

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Introduction: Hormonal alterations have been demonstrated to play a substantial role in functional recovery following stroke. The objectives of this study were to determine the incidence of neuroendocrine dysfunction in female stroke survivors and to determine if these alterations had an influence on disability and responsiveness to rehabilitation following stroke.

Methods: Hormone levels were evaluated in 54 female stroke survivors (mean latency: 98.8 days, SEM \pm 23.06). Age differences in hormone levels and disability were evaluated according to younger (Y; M=39.3, SEM \pm 1.5) and older (O; M=58.4, SEM \pm 1.2) age categories. Additionally, 49 women were evaluated for insulin growth factor 1 (IGF1) and growth hormone (GH) deficiency. GH levels were evaluated via glucagon stimulation testing. Functional ability was assessed with the Disability Rating Scale (DRS), Independent Living Scale (ILS) and the Mayo-Portland Adaptability Inventory IV (MPAI). All patients underwent post acute rehabilitation.

Results: The Y group had significantly higher levels of estradiol, prolactin and IGF1 compared to the O group. Alternatively, follicle stimulating (FSH) and luteinizing hormones were higher in the O group ($p < 0.05$). No differences between GH were observed between Y and O groups. Forty percent of women showed a GH deficiency (20%: ≤ 3.0 ug/L; 20%: 3.1-5 ug/L). The Y group had significantly lower disability according to DRS, MPAI, and ILS (activities of daily living subscale). High levels of prolactin were correlated with better performance in ADL's. Estradiol correlated with lower disability as measured by MPAI. High values of FSH were associated with lower initiation as assessed by a subscale of the ILS. Analysis of changes in outcome measures before and after rehabilitation showed that both Y and O groups benefited equally.

Conclusions: Hormones are predictive of levels of disability and independence in ADL's. Sex hormone levels in post-stroke patients should be considered for prognostication. In spite of hormonal differences both Y and O groups benefit from rehabilitation.

Modulation of ER Stress and Oxidative Stress Improves Outcome after Traumatic Brain Injury

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Endoplasmic reticulum (ER) stress and oxidative stress are major contributors to the secondary neuronal damage and in turn the neurological deficits associated with traumatic brain injury (TBI). In our study, we have shown that treatment with salubrinal and TBHQ/apocynin helps in the inhibition of ER stress and oxidative stress thereby improving outcome after traumatic brain injury. Following a moderate controlled cortical impact (CCI) injury in adult mice, an increase in the phosphorylation of PERK and eIF2 α and the expression of the downstream CHOP and ATF4 were observed indicating the activation of PERK signaling pathway contributing to ER stress that leads to neuronal cell death. We further show that treating mice with salubrinal (an inhibitor of PERK pathway) leads to a significant decrease in the contusion volume with an effective time window of efficacy (5 min to 4h after injury). Also, mice treated with salubrinal at 2h after TBI showed a significant improvement in the motor function based on the performance in the rotarod and beam walk test. Oxidative stress also plays a major role in TBI pathophysiology through the action of NADPH oxidase subunit NOX2 (gp91phox) which promotes formation of reactive oxygen species and the transcription factor Nrf2 which induces downstream anti-oxidant enzymes. This was demonstrated by testing the action of apocynin (an inhibitor of NOX2) and TBHQ (an activator of Nrf2) on post-TBI outcome. We treated mice subjected to CCI injury with apocynin (10 mg/kg) and TBHQ (25 mg/kg) alone or in combination. The results indicated that either apocynin or TBHQ treatment alone significantly improved the motor function after TBI compared to vehicle control. The drug treated mice stayed longer on rotarod and made fewer foot faults in beam walk test between day 1 to 7 after injury. A combination of both the drugs (apocynin + TBHQ) also significantly improved the post-TBI motor function compared to vehicle control, but there was no additive effect of the 2 drugs. The combination of both the drugs also significantly increased the time spent in the platform quadrant with higher frequency in comparison with the vehicle-treated control mice when tested for cognition by Morris water maze test at 3 weeks after injury. The cortical contusion volume was also significantly lower in the combo therapy group compared to vehicle control. In conclusion, these studies show that modulation of ER stress or oxidative stress significantly improves the functional outcome and attenuates tissue damage post TBI.

Psychological Symptom Course from the Acute to Post Acute Phases of Concussion in Patients Referred from the Emergency Room: Preliminary Data from The Hull-Ellis Research and Concussion Clinic at the Toronto Rehabilitation Institute

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Introduction: Assessment of psychological symptoms is important in the acute post-concussive period given that level of psychological symptoms immediately post-injury has been found to predict poorer outcomes¹ and moreover, the presence of psychological difficulties may in turn exacerbate symptoms in other domains² and impede recovery³. In order to assess for psychological symptom course in the acute to post-acute phases of concussion, the Brief Symptom Inventory-18 (BSI-18), a brief screen of psychological distress with a Global Severity Index (GSI) and 3 clinical subscales (Somatization, Anxiety and Depression) was administered at repeated time points post-concussion in order to monitor recovery.

Methods: An ongoing prospective cohort of individuals with physician confirmed concussion diagnosed in the Emergency Report was enrolled in the project within 1 week of injury. Participants were not eligible if there was evidence of skull fracture, haemorrhage or contusion on CT scan. All participants were tested on the BSI, as part of a larger battery of demographic, clinical and neuropsychological measures at 2, 4, 8, 12 and 16 weeks post-concussion.

Results: N=81 acute concussion patients (44 females and 37 males with average ages of 33.2 (SD=14.0) and 33.1 (SD=3.69), respectively) were recruited from the Hull Ellis Concussion Clinic at Toronto Rehabilitation Institute. This study is ongoing with preliminary results demonstrating scores on all BSI subscales showing steady decline across the acute to post-acute concussive period from moderately high to lower levels. Symptomatic individuals (i.e., requiring ongoing physician follow-up) at week 4 demonstrated higher albeit still declining levels on all BSI subscales than those deemed recovered and discharged at that point.

Significance: Results suggest that at least some psychological gains are made even in those judged still symptomatic. This finding is a first step in better understanding the acute to post-acute psychological symptom recovery trajectory. The next step in this line of research is to more closely define the associated course of other symptoms (e.g., cognition, pain, sleep) and possible pre-disposing factors (e.g., pre-injury psychological history, adverse child events) between patients that recover and those who go on to develop long term disability. Better understanding in this regard can help to better inform appropriate treatment options and timing.

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Comprehension of Legal Language and Legal Concepts by Individuals with and without Traumatic Brain Injury: Implications for the US Legal System and Public Policy

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Traumatic brain injury (TBI) is increasingly associated with an elevated risk of arrest and incarceration (Elbogen et al., 2012; Schofield et al., 2015), but navigating criminal proceedings requires advanced communication abilities (Wszalek & Turkstra, 2015), an area of impairment for many individuals with TBI (Catroppa & Anderson, 2004; Ferstl, Guthke, & von Cramon, 2002; McDonald, 2007). Additionally, linguistic and conceptual themes associated with legal processes may be particularly challenging to understand (Wszalek, 2016; Rogers et al., 2013), in order to better understand the nexus between TBI and the comprehension of these themes, we developed a testing battery to broadly assess three legally relevant skills: (1) legal-language comprehension, operationalized as the comprehension of language stimuli modeled on judicial colloquies (2) legal-concept comprehension, operationalized as the comprehension of legal rules modeled on the social-exchange task (Ermer et al., 2010); and (3) working knowledge of the US legal system, operationalized as a structured interview. Preliminary data suggest that individuals with TBI have poorer comprehension of legal language and of legal rules and require longer time to complete the tasks, trends that pose worrisome questions about fundamental legal rights under US law. We also obtained structural MRI scans to examine the relationship between white-matter integrity in anatomical network likely recruited during language comprehension (Ferstl et al., 2008) and the language-comprehension behavioral data. I will discuss the results of this analysis and the importance for future TBI research. In addition, I will discuss the relationship between language comprehension and other measures of cognitive function (working memory and executive functioning, e.g.), and I will identify implications that these findings have for the US legal system and for public policy.

Do Children and Youth with Concussion Really Follow Return to School and Return to Activity Guidelines?

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Objectives: Mild Traumatic Brain Injury, also known as concussion, is a serious public health issue in the pediatric population. A key component of evaluating the effectiveness of Return to School (RTS) and Return to Activity (RTA) guidelines is being able to determine if children and youth with concussion are adhering to guideline recommendations. Paediatric specific, evidence-based concussion management guidelines on RTS and RTA were developed in 2012 at CanChild. The primary objective is to explore the rates and predictors of adherence to these RTS and RTA guidelines for children and youth diagnosed with concussion.

Methods: Children and youth aged 5-18 diagnosed with concussion were followed for up to 6-month post recruitment in a prospective cohort. Children's self-reported Post Concussion Symptom Scale (PCSS) scores, stage of RTS and RTA guidelines, level of cognitive and physical activity, were collected every 48 hours. At study completion the children and parents completed a quiz evaluating their knowledge of the guidelines. Research personnel also rated their perception of the child's adherence to guidelines using symptom profiles and the child's and parents' ratings of stage advancement and actual knowledge of the guidelines. Pearson correlations were used to examine the total PCSS score versus RTS and RTA stage of guidelines. Logistic regression was used to determine which factors significantly contributed to adherence to guidelines.

Results: Eighty-five youth, mean age of 13.4 years with 46% (n = 39) male, were included in this analysis. The correlation between the total PCSS score and the stage of RTS guideline ($r = -0.448$, $p < 0.005$) and the stage of RTA guideline ($r = -0.389$, $p < 0.005$) indicated that lower symptom scores were correlated with higher stages guidelines. Overall, approximately 50% of children and youth adhered to each guideline. This proportion appeared to increase with time post injury. More children appeared to have adhered to the RTA guideline than the RTS guideline. Children's scores on the knowledge quiz at 1 week for the RTS guidelines was the only variable able to significantly predict adherence. For every one-point improvement in children's scores on the knowledge quiz, the odds of a child adhering to the RTS guidelines at 1 week increased by a factor of 1.995 ($p = 0.049$, 95% CI= 1.004 to 3.965). Parents knowledge was not a significant predictor.

Conclusion: As symptoms go down stages are advanced, RTA more than RTS suggesting that children are following guidelines to a degree. Further investigation is needed, to confirm these findings and to triangulate with accelerometry readings of activity. Children's knowledge of guidelines may be more important than parent knowledge in predicting adherence to guideline recommendations during recovery from concussion.

Binocular Occlusion Turns the Head of a Patient with Severe Right-Facing Postural Deviation After an Acquired Brain Injury

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Background and Objective: Following a brain injury, patients may present with spatial neglect and severe postural impairment, making it difficult to engage in rehabilitation activities. This poses a significant barrier to progress. Research has shown that eliminating visual input may increase attention toward the contralesional side. This case study illustrates the use of binocular occlusion as a treatment technique.

Case Description: A 53-year-old female, K.L. was admitted to an inpatient rehabilitation facility (IRF) 16 days after a hemorrhagic stroke with lesions involving the right basal ganglia and subcortical areas in the right inferior frontal lobe. K.L. presented with poor function from IRF admission to discharge (FIM = 18 to 29), spasticity in the left extremities, severe right gaze preference, and an asymmetrical resting head position due to a flexed and right-rotated cervical spine.

Methods: A series of measures were administered to investigate potential sources of K.L.'s presentation and facilitate treatment planning. Passive range of motion of the neck was normal. Integrity of the visual field was inconclusive due to impairments in communication and cognition. Contraversive Pushing was ruled out (SCP=0). Spatial neglect was severe at IRF admission and improved to moderate at discharge (KF-NAP=27/30 to 12.5/30). To examine the effect of binocular occlusion, K.L. was seated at the edge of a mat and the following measures were administered including visual inspect of trunk posture and head position and left-right asymmetry in sitting surface contact and weight distribution. Right-sided bias was noted with a positive sign, and left-sided with negative.

Results: Observed and recorded with photographs in 4 sessions over 32 days, K.L. showed no apparent change in trunk posture before, during or after blindfolding. However, changes of head position were noticeable: K.L. faced toward her right shoulder before blindfolding, and once blindfolded, she almost immediately faced forward in all 4 observations and even turned to the left side in 2 observations. In the last observation, 69 days post stroke, her head position (nose relative to sternum in degrees) was +35 before blindfolding (BB), -6 during blindfolding (DB), +6 immediately after removing blindfold (imA), and +14 three minutes after removing blindfold (3minA). Within a single session, buttock-mat surface contact bias changed: BB= +5%, DB= -5%, imA= no difference, and 3minA= +6%; weight distribution (indexed by average pressure) changed: BB= +20mmHg, DB= -18mmHg, imA= no difference, and 3minA= +23mmHg.

Discussion: Binocular occlusion demonstrated an immediate, albeit transient, improvement in the patient's head position, weight and pressure distribution in a seated position. We hypothesize that the technique helped disengage attention from ipsilesional visual information and led to the observed change, which could facilitate therapy activities as many require patients to sit-up straight or face forward, independently.

Internalizing Behavior Problems and Sleep Disturbances Follow Unidirectional Pathways Following Traumatic Injury

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Rationale: Pediatric traumatic brain injury (TBI) and extracranial bodily injury (EI) are glaring public health concerns. Although sleep disturbances (SD) are one of the most common complaints following TBI, the association between pediatric TBI, EI, and SD is vastly understudied. Importantly, SD in children and adolescents has been linked independently to a number of adverse health outcomes, such as internalizing behavior problems, which also occur after injury.

Objective: The current study aimed to investigate links between internalizing behavior problems and chronic sleep disturbance (SD) after TBI and (EI) in children and adolescents, and to better characterize longitudinal relations between such sequelae.

Participants and Methods: Participants (N=87) aged 8-15 included those with TBI, EI, and typically developing children (TD) who were assessed at pre-injury/baseline, 6-months, and 12-months. Internalizing behavior problems were measured via the parent-report subscale in the Child Behavior Checklist. The parent-report Sleep Disturbance Scale for Children was used to assess overall SD. Orthogonal planned comparisons examined longitudinal relations of internalizing and sleep scores in 1) both injury groups versus the healthy group and 2) the TBI versus the EI group.

Results: Internalizing problems and SD were comparable across all 3 groups at the preinjury assessment. Controlling for age, the combined TBI and EI group experienced significantly higher levels of SD ($p=.042$) and internalizing problems ($p=.024$) than the TD group across the 1 year follow-up, but injured groups did not differ from each other. Injury severity was not significantly related to SD or internalizing problems in the TBI group, but was positively associated with SD at 6 months and internalizing behavior problems at 6 and 12 months in the EI group. Cross-lagged panels examining longitudinal relations between internalizing and SD identified unidirectional paths in which internalizing predicted later SD but not vice-versa. Mediation analyses demonstrated 6 month internalizing significantly mediated level of SD one year after injury for both injury groups.

Conclusions: Traumatic injury predicted higher SD and internalizing problems. Injury severity was only positively significantly associated with SD and internalizing problems in the EI group after injury. Although bidirectional relations between SD and internalizing disorders have been reported, the current study only identified significant pathways from internalizing to SD. Longitudinally, early internalizing problems predicted chronic SD. This study provides further evidence that internalizing problems should be a focus of intervention and highlights the importance of injury comparison groups in TBI study design. R01NS046308

The Utility of Computerized Neurocognitive Testing and Symptom Evaluation in Predicting Outcomes for Children Following Concussion

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Introduction: Computerized neurocognitive tests (CNTs) are increasingly used to assess cognition post-concussion. This includes baseline testing, assessment during the acute period, and also assessing cognitive change to determine recovery. These data are often used to help clinicians determine when an individual has recovered from their injury and can return to school and return to sport. The clinical utility of CNTs has been examined in adult populations, with fewer studies conducted in pediatric samples. The aim of the present study was to observe CNT performance in a pediatric sample from the acute period (1-4 days post-injury) through recovery (2-weeks and 3-months post-injury) and to examine whether CNT performance in the acute period can predict delayed recovery at 2 weeks post-injury.

Method: Participants were recruited through the Emergency Department for the Take CARE (Concussion Assessment and Recovery Research) study, a pediatric concussion study based at the Royal Children's Hospital in Melbourne, Australia. Data were collected 1-4 days, 2 weeks, and 3 months post-concussion. Measures include the Post Concussion Symptom Inventory (PCSI), and CogSport (now Axon Sports), a computer-based neurocognitive assessment. The sample consisted of 139 paediatric concussion ED patients (mean age = 10.4 yrs, range = 5-17 yrs). Concussion recovery, determined at 2-weeks, was established via two methods: clinician diagnosis (n=28, 21%), or by the Post Concussion Symptom Inventory with 2 or more items with worsened severity from pre-injury (n=79, 57%).

Results: Linear latent growth models showed no significant difference in log-transformed RT trajectories between recovered and symptomatic groups. Moreover, no significant differences were found between groups in mean RT at 1-4 days post-concussion, or at 2 weeks post-concussion (adjusting for baseline). Negative binomial models similarly found no significant differences between groups in number of errors, nor error count trajectories over time. Given that the PCSI cut-off errs on the side of inclusion, a sensitivity analysis using clinical-determined symptom/recovery status was carried out. Results were not different to PCSI cut-off models.

Discussion: The present study did not identify any significant difference in CNT performance from the acute period through recovery. Further, CNT performance in the acute period did not predict recovery at 2 weeks post-injury. The findings of the present study raise questions about the potential clinical utility of CNTs in younger children and adolescents. Considering the widespread adoption of CNTs in schools and sporting clubs around the world specifically for concussion management, additional research is necessary.

Do We Need to Rethink Screening for Post Traumatic Hypopituitarism (PTHP)?

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Introduction: PTHP has a reported prevalence of 15-68% [1] after traumatic brain injury (TBI) [2-4]. We established a screening protocol based on consensus guidelines [5] and evaluated its impact after 3 years.

Methods: Protocol required screening within 3-12 months to include serum sodium; thyroid function; short-synacthen test (SST) or early-morning cortisol (EMC); FSH/LH; testosterone and prolactin. From a referrals database, we identified patients, diagnosis, and screening outcomes.

Results: Between March 2013 and May 2016, 132 patients were referred for admission to our service. 20 cases were excluded from analysis: 5 were mis-coded; 9 had pre-existing TBI; 6 transferred to units local to home. Of the remainder: 24 were discharged home; 15 to other specialist services in our region; we admitted 73.

36 of 73 admissions were screened: Of 37 whose total (acute plus rehabilitation) inpatient stay exceeded 90 days, 28 were screened; 5 of 7 whose stay was in range 60-89 days were screened; 3 of 29 whose stay was less than 60 days were screened. Of 37 not screened, 15 had some endocrine assay performed, 3 as a partial compliance to screening protocol.

Of the 24 discharged home, 2 were screened, and 6 had other endocrine assay. Of the 15 discharged to other services, 1 was screened, and 6 had other assay. With one exception, all screenings were performed within 12 months of injury

Of 39 deemed to have a complete screen, 15 had SST, and 24 had EMC. EMC was intended for primary care if discharged prior to 3 months post-injury, but was used for inpatients following synacthen production shortage.

Two patients developed clinical features of PTHP in their acute post-injury phase. 7 others had abnormalities requiring further assessment, 4 having low testosterone (1 resolved spontaneously), 2 with other deficit subsequently deemed insignificant, and 1 with an unrelated TSH rise. As testosterone replacement in patients older than 50 was not proposed, we have not recorded low values in this age-group in our analysis.

Conclusion: PTHP screening revealed treatable testosterone deficits in 3 of 39 cases. The prevalence of PTHP was much lower than suggested in literature [1]. This challenges the value of screening, particularly in a patient group in which screening compliance would be difficult.

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Epidemiology of Associated Medical Conditions and Treatment Complications in Patients Receiving Inpatient Rehabilitation for Traumatic Brain Injury in The U.S.

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Background: Traumatic brain injury (TBI) leads to 2.2 million annual emergency department visits and 20,000 admissions to inpatient rehabilitation in the U.S. Incidence of co-existing medical conditions, acute treatment complications, and associations of these factors with outcome, in a general TBI rehabilitation population have not been well characterized.

Objective: To estimate the extent of co-occurring medical conditions and acute hospitalization complications, and their role in short-term outcomes, in a population of patients with a full range of injury severities who receive inpatient rehabilitation following TBI.

Methods: Data for patients with moderate to severe TBI enrolled in the TBI Model Systems National Database (NDB) were evaluated for patient, injury, co-existing medical condition, and outcome characteristics. Medical conditions recorded by ICD-9 codes during the acute hospital phase of treatment, were grouped in a total of 75 Healthcare Cost and Utilization Project (HCUP) categories for analysis. Outcome measures were FIM™, Disability Rating Scale (DRS), and rehabilitation length of stay (LOS). The NDB data set was raked and weighted according to annual population characteristics obtained from UDSMR and eRehabData to produce estimates that are more representative of the overall population of TBI patients admitted for rehabilitation in the U.S. Predictors of outcome were assessed using general linear models, controlling for age at injury, sex, cause of injury (high vs. low velocity), Glasgow Coma Scale motor score (following vs. not following commands), sub-cortical damage, and intracranial mass effect (Bonferroni alpha = 0.0007).

Results: For the study period (05/2007–12/2013), there were 3,686 patients with complete data; 63% were male, 79% white/Caucasian, with a mean age of 60.3±22.4 years. One-third of patients had high-velocity injuries, 66% followed commands at initial presentation, 17% had sub-cortical damage, and 37% intracranial mass effect. Mean outcome scores were 61±17 for FIM™ total score, 6.5±3.5 for DRS, and 18±16 days for LOS. Commonly co-occurring medical conditions were: other nervous system disorders (44%), fluid and electrolyte disorders (30%), respiratory failure (27%), crush injuries (24%), hyperlipidemia (23%), and gastrointestinal disorders (22%). Predictors of worse outcome and extent of effect on FIM™ total score (β) include: aspiration pneumonia (-13.3), acute myocardial infarction (-10.8), paralysis (-9.6), pneumonia (-9.1), spinal cord injury (-8.1), nutritional deficiency (-7.6), and diabetes mellitus (-7.5).

Conclusions: Co-existing medical conditions and treatment complications are estimated to occur frequently in TBI survivors receiving inpatient rehabilitation, based on a weighted analysis. Trauma-related injuries

such as paralysis and spinal cord damage predict poorer functional outcome, as do general conditions such as diabetes mellitus and conditions potentially related to treatment such as aspiration pneumonia. The findings point to the value of incorporating associated medical conditions and treatment complications in TBI outcomes models.

Evaluation of Time-Varying Aspects of Head Impact Exposure in Youth Athletes

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There is increasing evidence demonstrating a potential link between subconcussive head impacts and brain alterations related to neurodegenerative diseases. Associations between changes in pre- to post-season imaging and cognitive measures and subconcussive head impact exposure over a single season of play have been observed. In order to better characterize cumulative exposure to subconcussive head impacts and understand the critical windows of exposure with respect to clinical outcomes, it is important to understand how head impacts are accumulated over the course of the season.

Head impact exposure was measured by instrumenting the helmets of youth football players (age 9-13) participating in a single youth football organization with the Head Impact Telemetry System (HITS) over four seasons of data collection. Head impact data was collected at each practice and game during the 3-4 month football season. Data were grouped into pre-season, regular season, and playoffs based on the respective team's season. Mean number of impacts and mean 95th percentile linear and rotational acceleration were computed within each time-frame and compared using a non-parametric Wilcoxon test of each pair. Next, aggregate exposure data, including number of head impacts and summed linear and rotational acceleration, was quantified on a daily and weekly basis to capture how exposure changes as the season progresses. Athletes were grouped into four quartiles (Q1-Q4) representing a range of high and low exposure groups based on the respective exposure metric to examine the variability observed in head impact exposure measured at this age.

Sixty-seven (67) seasons of head impact data were evaluated with 4,023 impacts measured during pre-season, 18,585 impacts measured during regular season, and 4,085 impacts measured during playoffs. The lowest exposure group (Q1) had significantly great impacts per practice measured during pre-season compared to playoffs ($p=0.0394$), while the highest exposure group (Q4) had significantly greater impacts per game measured during playoffs compared to pre-season and regular season ($p=0.0015$, $p = 0.0362$, respectively). The mean 95th percentile linear acceleration measured during practice did not differ greatly between the four exposure groups, however there was a trending increase in the mean 95th percentile linear acceleration measured between the four exposure groups, with values decreasing from pre-season to playoffs for Q1-Q3, and increasing for the highest exposure group (Q4). Additionally, the highest exposure group (Q4) resulted in 4x the number of impacts per week and summed linear acceleration compared to the lowest exposure group (Q1).

These data demonstrate wide variations in head impact frequency and magnitude measured throughout the season within the youth population. Studying the time-based measures of head impact exposure or late-season exposure is potentially important when studying the effects of head impact exposure on pre-to-post season imaging/cognitive changes.

Development of A Curriculum for Concussion Management Training in Schools

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All 50 states have laws stipulating that those involved in concussion assessment and management for youth sports must undergo some form of training. However, there are no specific curricula for directing such training and education. Based on previous work creating school-based concussion management programs, we developed a set of specific content areas (competencies) were identified to guide trainings and an assessment tool for assessing the effectiveness of a training curriculum was developed. The objectives of this study were to provide initial validation of specific domains of knowledge, and to assess the relevance of those domains for concussion management in schools. Additionally, the project provided an opportunity for initial validation of test questions for assessing knowledge regarding concussion management from a non-medical (behavioral) perspective.

The ten competencies were: basic neuro-anatomy, biomechanics of injury/ definition, concussion basics, risk factors, prevention, evaluation what and when, assessment practices, treatment approaches, individual recovery, and programmatic concussion management.

Trainings were conducted at four schools (public and private schools, all grades). 99 school personnel with various levels of self-reported experience and knowledge of concussions participated in the full training. No demographic factors accounted for test score variance.

A pool of test questions were developed that reflected the important knowledge from these competencies. A pre-post test design was used to determine knowledge gain regarding the identified competencies. A repeated measures within-subjects ANOVA found significant pre- to post-test difference in percent score change with medium effect size: $F(1,94) = 67.48, p < .001, \eta^2 = .418$. Relative to self-report rating of perceived knowledge of concussion management (group by change score) showed a linear trend in improvement, with those self-reporting the least pre-training knowledge improving 7%, those with medium knowledge improving by 6%, and those with the highest knowledge levels improving by 4%.

Participants' rankings of competencies were completed immediately after training ('How important is each topic to your work?'), and then 5 months later ('In retrospect, how important has each topic been to your work?'). The top four competencies from each rating were: individual recovery, concussion basics, risk factors and treatment approaches.

General feedback and satisfaction surveys showed that 92 percent of participants endorsed agreeing or strongly agreeing that the presentations improved their understanding of concussion management, with overall satisfaction a 4 out of 5.

As a first step in defining an effective training curriculum, this study supports the use of a set of topic areas (competencies), and provides validation for questions regarding knowledge needed in this domain. Results from the test of knowledge and ratings of topic importance will inform a standardized test of concussion knowledge.

Investigation of Neuroinjury and Inflammatory Biomarkers after Sport-related Concussion: From the Subacute Phase to Clinical Recovery

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The pathophysiology of sport-related concussion (SRC) is not well defined. While experimental animal studies suggest inflammation is an important contributor to secondary injury, scarce evidence exists in humans. Blood biomarkers have emerged as a viable, non-invasive tool to evaluate the experimental findings in human injury, and have potential utility in mild brain trauma. This study characterized a number of circulating biomarkers of inflammation and neurological injury in athletes with SRC, from the subacute phase through to medical clearance. Participants included 38 inter-university athletes from 16 sports (n = 19 SRC; n = 19 healthy matched-controls). Blood samples were taken within one week of SRC and again at medical clearance. Blood was also sampled from 88 healthy athletes before the start of the competitive season as a baseline control group. Twenty-eight immunoinflammatory and 11 neuroinjury biomarkers were analyzed using commercially available V-PLEX® and prototype MULTI-ARRAY® Human Immunoassay Kits. At both the subacute and medical clearance time points, circulating peroxiredoxin (PRDX)-6 concentrations were elevated in SRC athletes compared to healthy matched-controls. Interferon gamma-induced protein (IP)-10 and total-tau were higher at medical clearance compared to matched controls. In addition, neuron-specific enolase (NSE), PRDX-6, monocyte chemoattractant protein (MCP)-1, macrophage inflammatory protein (MIP)-1 β and eotaxin were inversely correlated with total reported symptoms subacutely in athletes with SRC. Lastly, total-tau, PRDX-6, neurogranin (NRGN), von Willebrand Factor (vWF), tumor necrosis factor (TNF)- α , interleukin IL-16, MCP-4, MIP-1 β , thymocyte and activation regulated chemokine (TARC) and eotaxin, varied in healthy athletes throughout the academic year. Collectively, blood biomarkers may be useful in elucidating secondary injury pathophysiology after SRC. However, their implementation requires mindfulness of extracranial factors, such as academic stressors and exercise training, as well as the inherent heterogeneity of concussive injury. Our findings are consistent with others who have found physiological perturbations at clinical recovery, and further support continued use of blood biomarkers in elucidating the biology of brain restitution after SRC.

Hippocampus and Cingulate Gyrus Volume Reductions are Associated with Neurobehavioral Dysfunction in Former NFL Players

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Background: Chronic traumatic encephalopathy (CTE) is a neurodegenerative disease associated with exposure to repetitive head impacts. Neuropathological studies have shown that as the disease progresses atrophy is pronounced in limbic brain structures. Furthermore, CTE is related to life-altering dysfunction in mood, behavior, and cognitive functioning, and may progress to dementia. The aim of this study is to investigate the volumes and neurobehavioral correlates of the amygdala, hippocampus, and cingulate gyrus in symptomatic, former National Football League (NFL) players.

Methods: With high-resolution structural 3T Magnetic Resonance Imaging, we contrasted the volumes of the amygdala, hippocampus, and cingulate gyrus between former NFL players (n = 86) and same-aged control subjects who had no history of contact sport involvement or history of brain injury (n = 22). We contrasted the groups' neurobehavioral functioning across four neurobehavioral domains: mood and behavior, attention and psychomotor speed, verbal memory, and visual memory. Within the NFL group, we examined the associations between neurobehavioral functioning and regional limbic brain volumes.

Results: The NFL group evinced volume reductions in the bilateral amygdala, hippocampus, and cingulate gyrus, relative to the control participants (all $p < .05$). Additionally, the NFL group demonstrated significantly lower scores for mood and behavior, as well as reduced attention and psychomotor speed (both $p < .05$). Within the NFL group, reduced volumes of the bilateral cingulate gyri were associated with impairments in attention and psychomotor speed, while volume reductions within the right hippocampus were associated with impairments in visual memory performance (both $p < .05$).

Conclusion: Our findings demonstrate that reduced volumes in the amygdala, hippocampus, and cingulate gyrus may serve as candidate biomarkers of CTE. Overall, limbic system structures seem especially sensitive to repetitive head impact in living, former NFL players, which is consistent with neuropathological studies of CTE.

Concussion Recognition and Management in the Pediatric Urgent Care Setting

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Purpose of Study: Historically, the evaluation and management of concussion in the pediatric urgent care setting has been inconsistent, and concussion often goes unrecognized. In 2010 the Acute Concussion Evaluation- ED (ACE-ED) and ACE-ED Care plan, a psychometrically validated concussion diagnostic tool and management plan, were developed and integrated into the electronic health record (EHR) at a level 1 urban pediatric emergency department (PED) and onsite urgent care. Our objective is to assess the effect of integration of these diagnostic and management tools into the EHR.

Methods: Patients <21 years old presenting with a chief complaint of head injury were included in this analysis. Patients triaged to the PED had the ACE-ED diagnostic tool utilized by the nursing staff at the time of triage. Patients triaged to onsite urgent care had the ACE-ED completed by their clinician during the assessment. This electronic decision support tool uses built-in conditional logic in order to generate an ICD-10 code and recommendation. For patients meeting diagnostic criteria for a concussion, the tool launched a brain icon on the patient tracking board to inform staff that the patient has been diagnosed with a concussion and should receive the ACE-ED Care Plan upon discharge.

Results: In 2015, 2,326 patients presented with chief complaint related to head injury and 18.1% were diagnosed with concussion. Of the 2,326, 443 (19%) were seen in the urgent care and subsequently 13.4% were diagnosed with a concussion. We were more likely to diagnose concussion in the PED. (OR 1.5 (95%CI: 1.1-2.1) A quality improvement (QI) intervention to facilitate workflow decision support to improve the diagnosis and management of concussions in the pediatric urgent care population is warranted. Future analysis will include the adherence rates in urgent care to utilization of the diagnostic tool and management plan in pre-and-post QI intervention. We will evaluate the percentage of ICD-10 codes generated as well as the rate of receipt of the ACE-ED Care Plan to patients discharged home from urgent care with a diagnosis of concussion.

Conclusions: The clinical decision support tool for concussion diagnosis (ACE-ED and Care Plan) is feasibly integrated into the electronic health record for urgent care. This clinical decision support tool results in fewer concussion diagnoses in the urgent care setting when compared to the emergency department. Quality improvement for provider education and workflow integration may increase the number of patients correctly diagnosed with a concussion, decrease practice pattern variation, and improve patient education for concussion management after discharge from urgent care.

Vestibular and Vision Deficits Following Concussion in Children Under 12

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Vestibular and oculomotor visual (VOM) deficits are emerging as key characteristics of youth concussion. Reported rates of these deficits following concussion in older children can be as high as 80% for balance and 69% for gaze stability. These vestibular oculomotor deficits can have a significant impact on children in return to school and activities in that presence of such deficits has been associated with longer return to school and sports compared to those without these deficits. However, since most studies of pediatric concussion focus on adolescents, little is known about the extent to which younger children experience this deficit. To address this gap, we utilized an electronic health record (EHR) system across a large pediatric healthcare network to quantify the presence of VOM deficits following concussion in patients under age 12.

Data were collected from all primary (n=31) and specialty care (n=4) settings within the healthcare network. We identified all patients aged 5-11 years who had ≥ 1 clinical visit for concussion at a network primary or specialty care site from 7/1/2014 through 6/30/2015. We included the 82% of these patients for whom a concussion electronic clinical decision support tool within the EHR was used during their initial visit. All patients had a vestibulo-oculomotor vision examination performed as part of their routine clinical care for concussion. Deficits assessed included balance, saccades, gaze stability, dysmetria, smooth pursuits, nystagmus, and convergence.

871 patients were included (median [IQR]: 10 [8, 11] years). On physical examination, 58% had at least one VOM deficit. 44% had balance abnormalities, 39% had saccadic dysfunction, 13% had deficits in gaze stability, 11% had dysmetria, 10% convergence insufficiency, and 2% had nystagmus.

In conclusion, vestibular oculomotor visual deficits following concussion in young children were common. Improved recognition of the deficits will lead to timely diagnosis and appropriate management, including school accommodations for oculomotor visual challenges and vestibular therapy for balance and motion sensitivity issues.

Improving the Clinical Management of Traumatic Brain Injury through the Pharmacokinetic Modeling of Peripheral Blood Biomarkers

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Background: Blood biomarkers of neurovascular damage are used clinically to diagnose the presence, severity or absence of neurological diseases, but data interpretation is confounded by a limited understanding of their dependence on variables other than the disease condition itself. These variables include half-life in blood, molecular weight, and marker-specific biophysical properties, as well as the effects of glomerular filtration, age, gender, and ethnicity. To study these factors, and to provide a method for markers' analyses, we developed a pharmacokinetic model that allows the integrated interpretation of these properties.

Methods: The pharmacokinetic behaviors of S100B (monomer and homodimer), Glial Fibrillary Acidic Protein and Ubiquitin C-Terminal Hydrolase L1 were modeled with relevant chemical and physical properties, using MatLab software; modeling results were validated by comparison with data obtained from healthy subjects or individuals affected by neurological diseases. Brain imaging data were used to model the passage of biomarkers across the blood-brain barrier.

Results: Our results show the following: 1) changes in biomarker serum levels due to age or disease progression are accounted for by differences in kidney filtration; 2) a significant change in the brain-to-blood volumetric ratio, which is characteristic of infant and adult development, contributes to variation in blood concentration of biomarkers; 3) the effects of extracranial contribution at steady-state are predicted in our model to be less important than suspected, while the contribution of blood-brain barrier disruption is confirmed as a significant factor in controlling markers' appearance in blood, where the biomarkers are typically detected; 4) the contribution of skin to the marker S100B blood levels is directly correlated with pigmentation, rather than ethnicity; the contribution of extracranial sources for other markers requires further investigation.

Conclusions: We developed a multi-compartment, pharmacokinetic model that integrates the biophysical properties of a given brain molecule and predicts its time-dependent concentration in blood, for populations of varying physical and anatomical characteristics. This model emphasizes the importance of the blood-brain barrier as a gatekeeper for markers' blood appearance and, ultimately, for rational clinical use of peripherally-detected brain protein.

Appraisal of Knowledge-To-Practice Gaps to Facilitate the Implementation of a Clinical Practice Guideline for Adults with Moderate-To-Severe Traumatic Brain Injury

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Introduction: Clinical practice guidelines (CPG) derived from scientific knowledge are more likely to be implemented if they fill practice gaps deemed important by clinical teams. Through a collaborative partnership, the Institut national d'excellence en santé et en services sociaux du Québec and the Ontario Neurotrauma Foundation developed a CPG aimed at supporting the rehabilitation of adults with moderate-to-severe traumatic brain injury. In order to promote implementation of a CPG, the first step in the process must be identification of knowledge-to-practice gaps which highlight areas for improvement.

Methodology: An email survey was conducted with acute and rehabilitation sites (N=55) across each province (Quebec (QC) and Ontario (ON)). For the 109 fundamental and priority CPG recommendations, clinical teams were asked to 1) indicate the actual level of implementation of the recommendations in their site; 2) prioritize recommendations not yet implemented and 3) indicate the feasibility for recommendations considered priority. Respondents also identified perceived obstacles for those recommendations not fully implemented.

Results: The survey was completed by 44 sites (26 from QC and 18 from ON). Overall, a vast majority of recommendations (82% in QC and 93% in ON) were rated as at least "partially implemented" by the majority of facilities, while only four 4% in Québec and 5% in Ontario were rated as "occasionally" or "not implemented".

In both provinces, recommendations related to education of patients and the public were the most likely to be perceived as implemented. However, in Québec, respondents identified practice gaps relating to dysphagia and nutrition as these recommendations were less likely to be rated as implemented, while in Ontario the practice gaps related to the use of medication for arousal and attention problems and heterotopic ossification, and the use of strategies to enhance reasoning skills.

In Québec, two recommendations relating to coordinating the management of comorbid conditions were rated as high priority and feasible by both acute and rehabilitation respondents. In Ontario there were differences observed between the acute and rehabilitation sites with regard to recommendations not fully implemented that were a priority and feasible, and notable the rehabilitation sites were more similar to the QC findings. There were two recommendations in common across the ON acute and rehabilitation respondents: consistent training in behaviour management skills and access to specialized oral and dental care.

Discussion: The knowledge-to-practice gap analysis highlights that clinical teams generally believe many recommendations are already adopted in their clinical settings. It also identifies areas where improvement

is deemed important and feasible. Despite the same clients and federal healthcare system in these two provinces there are different perceived priorities, and this work shows the importance of considering clinical settings' perception when designing implementation.

The Effect of Augmentative and Alternative Communication Display Type on the Theme Identification Abilities of Adults with TBI

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Purpose: Adults with who have sustained severe traumatic brain injuries (TBI) may present with motor speech disorders that limit their ability to functionally communicate through speech. In these instances augmentative and alternative communication (AAC) supports as often implemented to allow these individuals to functionally communicate. A variety of visuographic aids are utilized as AAC supports; however, limited research is available to guide speech-language pathologists as they select and design these supports. The purpose of the current study was to compare the speed, accuracy, preference, and cognitive processing necessary for adults with severe TBI to identify two types of AAC displays: grids composed of decontextualized images and visual scenes displays composed of a single contextual image.

Method: Seven adults with severe TBI viewed 20 AAC displays (i.e., 10 grids and 10 visual scenes) presented individually on an eye-tracker monitor. Content between images was matched such that each visual scene contained the same content as its matching grid display. Accuracy and speed of theme identification were both measured. Eye-tracking technology was also employed to measure the number of visual fixations and average visual fixation duration (i.e., two measures that have been shown to reflect both on the interest and difficulty of processing level of image regions; Poole & Ball, 2004) necessary to process each of these image types. After completing the eye-tracking portion of the experiment, participants completed a brief survey and participated in discussion regarding their preferences for and opinions relating to visual scenes and grids.

Results: Participants accurately identified all displays presented. Data analysis revealed a significant differences for average fixation duration, $F(1,6) = 31.003$, $p = 0.001$, and number of fixations, $F(1,6) = 40.394$, $p = 0.001$, between grids and visual scenes. Inspection of these results revealed that participants required significantly greater numbers of fixations and lengthier fixation durations to identify grids as compared to visual scene images. In addition, participants reported greater ease of identification of visual scene displays than grid displays.

Discussion: The results of the current study are preliminary in nature; however, analysis of the existing data indicates that individuals with TBI do differ in the manner in which they interact with and make meaning from visual scene displays composed of contextualized images and grid-based displays composed of decontextualized photographs. Clinicians working with individuals with TBI should consider these differences when determining which types of displays will be most effective for their clients.

Understanding Neonatal Hydrocephalus Using an Ex Vivo Model of Pressure-Induced Neural Injury

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Objectives: Neonatal hydrocephalus is a progressive disorder of pathologic elevation of intracranial pressure (ICP) and ventriculomegaly, which frequently produces devastating neurological deficits. The diverse initial injuries associated with neonatal hydrocephalus (infection, inflammation, hemorrhage, or congenital abnormalities) are well documented, and seldom preventable. The secondary injury of neonatal hydrocephalus is related to the pathophysiology of elevated ICP, and is responsible for ongoing, long-term damage. These secondary mechanisms are poorly understood. To date, the lack of a model to study the cellular pathways associated with elevated ICP-induced cellular injury has impeded progress. Identifying the cellular biomarkers associated with elevated ICP will advance our understanding of the pathologic sequence of events leading to brain injury, and may provide earlier and greater predictability of patient outcomes and potential therapeutic targets for the treatment of hydrocephalus.

Methods: To simulate pressure-induced brain injury, we developed an ex vivo model of neonatal hydrocephalus, which combines 3D neural cell cultures and a newly developed Pressure Controlled Cell Culture Incubator (PC³I). Human cells (microvascular endothelial cells, astrocytes and neurons) maintained in 3D peptide-conjugated alginate hydrogels were subjected to pressures that mimic both physiologic and pathologic conditions of untreated hydrocephalus. Culture media bathing the cell-laden hydrogels was analyzed for injury/inflammatory biomarkers (bioluminescent ATP assay, and magnetic bead-based multiplex assays for cytokines, chemokines, and growth factors), while cellular viability was determined using an assay that measured intracellular esterase activity and plasma membrane integrity.

Results: Intracellular release of ATP following exposure to pathologic pressure was dependent on the time of exposure, amount of pressure, and type of exposure (sustained v. pulsatile) when compared to control conditions. Inflammatory biomarkers were measurable in the media bathing the 3D cellular constructs following both sustained and pulsatile pressure exposures. We demonstrated the ability to maintain greater than 50% cellular viability in 3D alginate hydrogels for up to 4 weeks. The percent of viable cells exposed to different pressure paradigms was not different from controls.

Conclusions: Using a novel ex vivo model of neonatal hydrocephalus, these data indicate the cellular release of ATP is an important signal associated with elevated pressure, and may be a key early secondary injury response to elevated ICP in the developing neonatal brain. Further experiments using this model system will be valuable to determine other cellular biomarkers associated with pathological ICP.

Characterizing Head Impact Exposure in Youth Female Soccer

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While many research efforts have focused on the consequences of concussion and head impact exposure at the professional level of female soccer, there have been few studies characterizing sub-concussive impacts in youth female soccer. The aim of this study is to characterize the head impact exposure for youth female soccer players and investigate the differences in impact sources and ball delivery methods.

Seven athletes from a local soccer organization were enrolled in an IRB-approved study. Polyvinyl acetate (PVA) dental impressions were collected from the upper dentition of each athlete. Dental molds were poured from each PVA impression and used to create a custom-fit instrumented mouthguard. Each mouthguard features a tri-axial accelerometer and gyroscope embedded within a rigid retainer material for improved coupling and measurement of head impact kinematics during practices and games. To obtain head kinematics at the head center of gravity (CG), the raw mouthguard output was transformed from the sensor location using subject-specific measurements.

Detailed video analysis was conducted to identify impact time and characteristics of head impact events that were paired with the kinematic data. Impact characteristics describing impact source (last contact the ball had before the observed header) and ball delivery method (details describing how the ball was delivered for the header) were collected for each impact. Possible impact sources include: bounce from ground, as well as headed, kicked, and thrown from another athlete. Possible ball delivery methods include: bounce from kick, short kick, long kick, overhead throw, and underhand throw. A non-parametric Wilcoxon test of multiple comparisons was used to assess differences in impact source and ball delivery method in the associated linear accelerations and rotational velocities.

Head impact data was collected over 32 practices and 9 games and a total of 764 mouthguard impacts were paired with video analysis and used to evaluate the differences in impact source and ball delivery methods. The median/95th percentile linear accelerations and rotational velocities of all collected head impacts were 9.32/19.91g and 4.09/10.11 rad/s, respectively. Pairwise comparisons resulted in statistically significant differences in mean linear acceleration and rotational velocity among impact source. Significantly greater mean linear acceleration and mean rotational velocity was measured when the ball was headed from a kicked ball compared to when the ball was headed after another headed ball ($p=0.0001$, $p<0.0001$, respectively). Also, significantly greater mean linear acceleration and mean rotational velocity was measured when the ball was headed after a long kick compared to after a short kick ($p<0.0001$, $p<0.0001$, respectively). This is the first study to evaluate head impact exposure in adolescent girls' soccer using an instrumented mouthguard. This study also quantified differences in head linear acceleration and rotational velocity when heading the ball based on impact source and ball delivery method.

Expression Profiling of Tau-Positive Cholinergic Neurons Within the Nucleus Basalis of Meynert in Brains from Veterans and Athletes with A Postmortem Diagnosis of Chronic Traumatic Encephalopathy (CTE): A Chronic Effects of Neurotrauma Consortium Study

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Military personnel in the battlefield and athletes in contact sports (e.g., boxing, American football, and hockey) are exposed to mild repetitive traumatic brain injury, which can result in chronic traumatic encephalopathy (CTE). The neuropathology of CTE is characterized by the intracellular accumulation of abnormally phosphorylated tau proteins (p-tau), the main constituent of neurofibrillary tangles (NFTs) in Alzheimer's disease (AD) and related tauopathies. Recently, we found that cholinergic basal forebrain (CBF) neurons within the nucleus basalis of Meynert (nbM), which provide the major cholinergic innervation to the cortical mantle and their degeneration results in memory impairments in AD display an increasing number of NFTs across the pathological stages of CTE. However, molecular mechanisms underlying CTE neurodegeneration within CBF neurons remain unknown. Here, we assessed the genetic signature of cholinergic neurons within the nbM containing the p-tau pretangle marker pS422 obtained from subjects who came to autopsy and received a neuropathological staging assessment for CTE (Stages II (n = 7), III (n = 5), and IV (n = 6)) using a combination of laser capture microdissection and custom-designed microarray analysis. Quantitative assessment revealed that between CTE Stages II and III there was significant downregulation of select genes associated with cholinergic {nicotinic acetylcholine receptor subunit beta-2 (Chrn2)} and catecholaminergic neurotransmission {Catechol-O-methyltransferase (Comt) and dopa decarboxylase (Ddc), intracellular signaling (Prkca), and tau/apoptosis {calpain 2 (Capn2) and dipeptidyl-peptidase 10 (Dpp10)}. By contrast, comparing Stage II to IV, we found upregulation of select genes associated with autophagy (Atg4c) and tau {microtubule-associated protein 2 (Map2)} and downregulation of transcripts related to cell homeostasis/neurotransmission {chloride channels (Clcn4 and Clcn5), endocytosis {Caveolin1 (Cav1)}, mitochondrial biogenesis/transcript factor (Ssbp1) and intracellular signaling {adenylate cyclase 3 (Adcy3)}, as well as Dpp10. Comparing Stage III to IV revealed downregulation of Clcn5, Cav1, Adcy3, and cortical development/intracellular signaling lissencephaly 1 (Lis1) transcripts, as well as upregulation of Capn2. These data suggest genes related to cell homeostasis, intracellular signaling, endocytosis, and tau biology are differentially regulated within p-tau-containing vulnerable cholinergic nbM neurons during the pathological progression of CTE. Based on these single population microarray findings, a molecular signature of CTE is emerging that may be exploited for therapeutic interventions. These data support CTE drug discovery related to the molecular pathogenesis of cholinergic nbM neurons, and that drug targets should emphasize neuronal homeostasis/neurotransmission therapies and concomitantly reducing pathological tau.

Obesity Among Individuals with Moderate-Severe Traumatic Brain Injury (TBI): A Large Scale Examination of Weight Classification Prevalence and Factors Associated With Problem Weight Across 1, 2, 5, 10, 15, and 20 Years Post TBI Using the TBI Model Systems National Database

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Objective: Obesity has become one of the United States' most significant public health problems. Results from the National Health and Nutrition Examination Survey in 2010 revealed that among Americans, the mean Body Mass Index (BMI) was 28.7, which is classified as overweight. Furthermore, the prevalence of individuals classified by the Centers for Disease Control (CDC) as overweight or obese is 70.7% among adults. These statistics refer to able-bodied person; an understanding of problems with weight management among people with a traumatic brain injury (TBI) is noticeably lacking. Such studies are needed given research showing that persons with disabilities are at greater risk for obesity, sedentary lifestyles, and unhealthy behaviors. Thus, this study aims to examine the distribution of weight classifications and factors related to obesity/overweight among persons with moderate-severe TBI at 1, 2, 5, 10, 15, and 20 years post-injury using a large-scale database, the TBI Model Systems (TBIMS) national database.

Methods: The current study is both a cross-sectional and prospective design. Height and weight (BMI), demographic, and psychosocial information was collected from survivors at 1, 2, 5, 10, 15, and 20 years after sustaining a moderate-severe TBI or their proxy. Weight categories were coded according to the World Health Organization Classification for underweight, normal, overweight, and obese. The sample consisted of 7,287 TBIMS participants: 5,347 adult males (73.4%) with 4,971 non-Hispanic Caucasians (68.2%), and 1,217 non-Hispanic African Americans (16.7%). Mean age at injury was 40 years (SD = 18.4). Prevalence rates across time points were examined. Standardized effect sizes (Cohen's h and Cohen's d) were used to assess relative importance of sociodemographic and medical factors related to weight categories given the large sample size. "Very important" (0.3 – 0.4) and "substantial" (> 0.4) effect sizes are summarized for the purposes of this abstract but others will be included in the formal presentation.

Results: The percentage of patients who fell within the obese classification was 18.6%, 19.8%, 23.6%, 24.7%, 25.7%, and 30.3%, respectively across time-points showing an increase for prevalence rates of obesity further out post-injury. This trend was also observed for the overweight classification: 36.4%, 35.0%, 36.3%, 37.9%, 35.5%, and 37.1% respectively. The trend was opposite for normal and underweight categories. "Very important" effect sizes were observed between obesity/overweight and age at injury, hypertension, heart failure, general health, and diabetes. "Substantial effects" between obesity/overweight were observed for post-injury age and vegetative state.

Conclusions: Survivors recovering from TBI are at risk for obesity and overweight problems and health conditions particularly during long-term recovery. The findings indicate a need for further identifying factors related to unhealthy weight management and the design of health promotion, prevention, and/or treatment programs.

Development of Intravenous Imatinib Treatment for Traumatic Brain Injury

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Objectives: Traumatic brain injury (TBI) poses a serious public health challenge with the Centers for Disease Control estimating that in the United States there are approximately 53,000 TBI related deaths and 283,000 hospitalizations annually. However, at present, there is no proven effective pharmacological therapy for treating TBI patients. The development of improved therapies for the treatment of TBI depends upon understanding the underlying mechanisms of the pathologies associated with TBI. One of the hallmarks of TBI is the opening of the blood brain barrier (BBB) which leads to an influx of plasma proteins, increased inflammation, and the development of cerebral edema, all of which can affect outcomes and exacerbate the recovery processes. Our recent studies have shown that tissue type plasminogen activator (tPA) activates latent platelet derived growth factor CC (PDGF-CC), which in turn binds to platelet derived growth factor receptor- α (PDGFR α) and regulates the opening of the BBB in a number of CNS pathologies. Blocking this pathway reduces BBB opening and improves outcomes in stroke and spinal cord injury. Recently we also showed Imatinib protects against TBI-related injuries. In the study presented here we have developed an intravenous formulation of Imatinib for the treatment TBI in patients who may be unconscious and unable to swallow.

Methods: We performed a dose escalation study with an intravenous formulation of Imatinib in a well-established model of TBI—controlled cortical impact (CCI) in mice.

Results: We show that intravenous Imatinib treatment in mice (15mg/kg, 60mg/kg, 120mg/kg, 150mg/kg) begun 1h after TBI and given twice daily for 5 days, significantly reduced lesion size and edema in a dose dependent manner at 24 hours, 7 days, and 21 days after TBI.

Conclusions: Our data suggests a novel strategy for the treatment of TBI with an existing FDA approved antagonist of the PDGFR α .

Barriers to Physical Activity Among Individuals with Traumatic Brain Injury (TBI) One Year Post-Injury: A TBI Model Systems Study

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Objective: Obesity represents a significant public health problem according the Centers for Disease Control and Prevention (CDC). While there is a large body of evidence examining factors related to weight management among adults without disabilities, an understanding of these factors among people with TBI is noticeably lacking. This limited understanding is made more poignant given the impact a TBI has on risk for sedentary lifestyles, mobility limitations, and poor quality of life, all of which impact participation and activity as well as morbidity and mortality. In order to design effective programs to prevent or treat unhealthy lifestyle habits associated with obesity/overweight problems post-TBI, we need to understand the amount of physical activity survivors engage in post-injury as well as the barriers to physical activity and exercise post-injury. Thus, the goal of this study was to identify physical activity levels and barriers among patients one year post moderate-severe TBI.

Methods: Participants included 208 adults (75% male, 59% Caucasian) recruited from three participating TBI Model Systems Centers (TBIMS). Mean age at injury was 40.69 (standard deviation (SD) = 17.02). Participants were asked to complete measures assessing demographic, medical, weight (Body Mass Index score: BMI), dietary, and lifestyle information upon discharge from inpatient rehabilitation and during follow-up interviews at 6-month and 1-year intervals post-injury.

Results: The mean BMI for patients upon discharge was 25.8 (SD=5.6), and by 12-months post-injury, this index increased to 26.2 (SD=5.4). Accordingly, while 50.7% of individuals were considered overweight or obese upon discharge, approximately 57.4% of participants fell into these categories by 12-months post-injury. The number of days per week spent engaging in vigorous activity significantly differed between self-reported pre-morbid functioning (M=2.19, SD=2.04) and 6-months post-injury (M=1.01, SD=1.73), as well as pre-morbid functioning and 1-year post-injury (M=1.44, SD=2.19), $p < .05$. The five most common barriers to regular exercise/physical activity prior to TBI included: 1) lack of time (62.6%), 2) lack of interest (54.8%), 3) lack of motivation (52.2%), 4) cost of exercise programs (51.3%), and 5) finding exercise boring (40.9%). In contrast, 1-year post-injury, the five most common barriers were 1) health concerns (51.9%), 2) lack of energy (50.9%), 3) lack of motivation (48.1%), 4) body pain (47.2%), and 5) cost of exercise programs (46.2%). The most common barriers to physical activity 1-year post-injury were consistent across participants, irrespective of weight classification.

Conclusions: Survivors recovering from a moderate-severe TBI are at risk for sedentary behaviors and obesity. Our findings suggest that individuals' pre-morbid vigorous physical activity levels significantly decrease over the course of 6- and 12-months post-injury. Given the role that physical activity plays in recovery, more research is needed to determine how to effectively promote physical activity among individuals recovering from TBI in light of barriers.

Rehabilitation Interventions for Improving Health-Related Quality of Life After Stroke: A Systematic Review and Meta-Analysis

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Background: The ultimate goal of stroke rehabilitation is to regain optimal health-related quality of life (HR-QoL). However, rehabilitation interventions are usually targeted to specific goals, such as improvement of physical functioning, cognitive problems, or symptoms of depression. This raises the question whether rehabilitation interventions may also improve HR-QoL as a global outcome measure after stroke. Furthermore, different study designs are used to evaluate outcome of rehabilitation interventions: randomized controlled trials (RCT's) and studies that use a pre-post design, which may lead to different conclusions.

Objective: To present a systematic review and meta-analysis of rehabilitation intervention studies for improving HR-QoL after stroke and to compare the evidence from RCT's and pre-post designs.

Methods: PubMed and Web of Science were searched for studies that evaluated the effects of a rehabilitation intervention on HR-QoL after stroke. The following inclusion criteria were used: 1) study population of at least 10 patients with stroke; 2) intervention study; 3) SF-36 outcomes reported; 4) RCT or pre-post design; and 5) in- or outpatient rehabilitation or community setting. Primary outcomes were the Mental Component Score (MCS) and Physical Component Score (PCS) of the SF-36 at first follow-up. A random-effects meta-analysis was performed on all RCT's and on the pre-post studies. PRISMA guidelines and GRADE quality assessment were followed.

Results: In total, 32 articles were selected, including 18 RCT's and 14 pre-post design studies. A total of 1,744 patients were included, of which 968 in the RCT's and 776 in the pre-post designs. In the RCT's the MCS improved significantly over the intervention time (effect size (ES)=0.2, p=.001), but PCS did not improve significantly (ES=0.1, p=.058). In the pre-post studies, both MCS and PCS significantly improved over the intervention time (ES=0.3, p<.001).

Conclusions: Evidence was found that rehabilitation interventions may be effective in improving the mental component of HR-QoL after stroke. Studies that use pre-post designs may overestimate the effect of rehabilitation interventions, especially on the physical component of HR-QoL.

Application of Virtual Environments in a Multi-Disciplinary Day Neurorehabilitation Program to Improve Executive Functioning Using the Stroop Task

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Introduction: Virtual reality (VR) technology has demonstrated its potential usefulness as a tool for diagnosis, education, and training. To date, application of VR in neurorehabilitation is not systematic and studies supporting the use of VR as a therapeutic treatment in medical rehabilitation settings remains limited. This study endeavors to address some of these limitations by using VR in a treatment capacity.

Objective: To determine whether immersive VR treatment interventions improve executive dysfunction in patients with brain injury as stimulus demands within a virtual apartment and a classroom/office environment gradually increase across treatment sessions. To determine whether performance is stronger on a VR version of the Stroop compared with traditional paper-and-pencil, unimodal computerized, and bimodal VR Stroop formats.

Setting: Outpatient neurorehabilitation program.

Participants: 15 patients with brain injury (traumatic brain injury, stroke, brain neoplasm) admitted to a day neurorehabilitation programs.

Design: Correlational study.

Main Outcome Measures: Reaction time, inhibition, and accuracy indices on VR Stroop measures (compared baseline Session 1 to final Session 8); Automated Neuropsychological Assessment Metrics (ANAM) Stroop, Delis-Kaplan Executive Function System (D-KEFS) Stroop, Golden Stroop, Woodcock-Johnson, 3rd Edition (WJ-III): Pair Cancellation, Simulator Sickness Questionnaire (SSQ).

Results: Participants demonstrated significantly reduced response time on the word-reading Stroop condition (Session 1 = 553ms; Session 8 = 502ms; $p = 0.03$) after receiving a VR classroom/work setting treatment intervention. A non-significant improvement in accuracy (total number of correct responses: Session 1 = 70ms; Session 8 = 71ms; $p = 0.08$) and inhibition (omission errors: Session 1 = 1.1 errors; Session 8 = 0.6 errors; $p = 0.08$) was demonstrated on the color-naming Stroop condition of a VR apartment treatment intervention.

Participants achieved significantly higher accuracy on the word-reading trial of the unimodal ANAM Stroop after 8 sessions of VR intervention compared with baseline performance, when time constraints were considered (Session 1 = 61 items correct; Session 8 = 70 items correct; $p = 0.02$). Participants committed significantly fewer commission errors on the ANAM Go/No-Go subtest by session 8 compared with baseline (Session 1 = 95 impulsive responses; Session 8 = 92 impulsive responses; $p = 0.04$).

The presence of distractors in the VR intervention was more cognitively taxing than any other Stroop version, resulting in longer response times for correct and incorrect responses. By conclusion of the VR treatments, patients demonstrated improved inhibition, sustained attention, and selective visual attention on outcome measures.

Conclusions: Implementation of immersive VR interventions during neurorehabilitation is effective in improving specific executive functions and information processing speed in brain injured patients during the subacute period. No adverse events were associated with use of a head-mounted display for VR interventions. Further research is necessary to determine frequency and length of sessions to optimize cognitive rehabilitation gains using VR.

Astrocyte Contribution to the Extracellular Matrix Environment Following Traumatic Brain Injury

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Introduction: Astrocytes play an essential role in neuronal survival. Yet, the mechanobiology of astrocytes and in particular how their neuro-supportive role is affected by the mechanical stimuli that are generated during traumatic brain injury (TBI) is not well understood. Our group is exploring the hypothesis that the extracellular matrix environment produced by astrocytes following traumatic brain injury is influenced by mechanical stimuli. The objective of this project was to characterize the regulation of extracellular matrix genes and cytokines by astrocytes in response to TBI mimetic mechanical loading.

Materials and Methods: A novel cellular drop/crash tester (Figure 1) was used to (1) precisely apply TBI mimetic impacts (strain + deceleration) to populations of astrocytes in culture and (2) concentrate and collect the soluble (cytokines) and insoluble (extracellular matrix) molecules released in response to TBI mimetic loading. Primary astrocytes were isolated from 1-2 day old neonatal rat pups. Experimental groups were subdivided into cultures receiving a single 150G impact with or without 20% strain, or two 150G impacts with or without 20% strain (n=8/group). Cell culture supernatants were collected 48 hours after the last impact for ELISA analysis of TGF β -1, TIMP-1, and MMP-2 concentration. Cells were isolated 6 hours after initial impacts to quantify gene expression of collagen I, versican, and neurocan using qPCR.

Results and Discussion: ELISA analysis for TGF β -1, MMP-2 and TIMP-1 showed that protein concentrations were decreased in cultures that received 150G impacts with 20% strain compared to the control (Figure 2). Cultures receiving a single 150G impact without strain also had decreased MMP-2 concentrations. There was no difference in protein concentrations for TIMP, TGFB, or MMP between cultures receiving a single impact or two impacts. qPCR analysis for cultures receiving a single impact did not significantly effect collagen expression. A trend of decreased neurocan and versican expression was observed for single impact cultures. A significant difference was seen in cultures receiving a second impact. The expression of collagen, versican, and neurocan were each down regulated.

Conclusions: Astrocytes receiving TBI mimetic impacts suppressed ECM gene expression and ECM regulatory cytokine production. Both the nature of the impact (strain versus no strain) and dose (one versus two impact) influenced astrocyte mechanobiology. A possible explanation for the lowered expression of ECM molecules is a shift in astrocytes to a survival state or apoptotic pathway. Going forward, we will isolate the ECM secreted by cultures receiving impacts and grow neurons on the material to explore whether the ECM collected from mechanically stimulated cultures impairs neurite outgrowth.

Computerized Cognitive Rehabilitation Outcome in Neurological Populations: A Systematic Review of Recent Research

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With increasing frequency, people with brain injury encounter popular computerized exercises of cognitive functioning. It is estimated that consumers spent \$715 million on computer applications for brain training in 2013, and may spend as much as \$3.38 billion by 2020 (Yong, 2016). Clinicians need guidance in how to respond to inquiries about these applications but available literature reviews are incomplete and do not offer a systematic approach that allows comparisons between studies. One recent comprehensive literature review concluded that outcome studies do not support marketing claims that computerized training generalizes to other cognitive tasks or to real-life functioning (Simons et al. 2016). But people with brain injury and their clinicians may not find relevant data in that comprehensive review, since the authors restricted their scope to studies of neurologically intact samples. Another review of older articles focused specifically on computerized remediation of attention and executive functioning in people with acquired brain injury and concluded that there is preliminary evidence of modest benefits (Bogdanova et al., 2015). But computerized clinical treatment of other aspects of functioning has also been addressed in studies that have yet to be surveyed. Similarly, the literature is growing rapidly and recently released studies have not yet been summarized. For these reasons, there is a need for a broader, updated review.

We identified studies of the clinical efficacy of five of the most promising, commercially available computerized cognitive rehabilitation interventions (CogMed, Lumosity, Brain HQ, IREX and the APT-III). These applications involve the newest technologies (including the use of virtual environments) to treat not only attention impairment and executive dysfunction but also deficits of memory and visuospatial abilities. We included articles published as recently as October, 2016.

Similar to previous reports, our review showed modest benefits of computerized cognitive rehabilitation. Computerized cognitive rehabilitation results in improvement in abilities measured by tests that are very similar to the exercises included in the therapeutic applications. There is limited evidence of “far-transfer” or generalization to improvement in real-life functioning and to neuropsychological abilities that are dissimilar to rehabilitation exercises.

In contrast to previous reports, we discuss in detail recent suggestions that patients’ expectation effects, their emotional status and other nonspecific factors may play a role in self-reported benefits of computerized interventions. It is especially notable that gains are greatest when the computerized exercises are supervised by a human therapist or complemented by conventional rehabilitation that includes human interaction. This finding challenges the rationale that computerized rehabilitation applications have promise as labor-saving devices.

We conclude with exploration of interpersonal factors that maximize the efficacy of technological interventions and discussion of implications for clinical care and future research.

Characterization of Diffused Traumatic Brain Injury using an Automated Functional Eye Movement Assessment as related to Clinical Neurocognitive Testing

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Purpose: We proposed to characterize post-concussion symptoms in persons with diffused traumatic brain injury (dTBI) using standardized clinical assessment tools including a computerized neurocognitive assessment in combination with an automated functional eye movement assessment (FEMA) using eye tracking technology.

Methods: 26 volunteers (12 females/ 14 males) age 18 years and over with a history of dTBI were recruited for this study. Inclusion criteria included binocular vision with visual acuity at least 20/200, status post a head injury classified as 13-15 on the Glasgow Coma Scale, no spine abnormalities, and unremarkable imaging studies post injury.

Participants received a physical screen including visual acuity measured by the NeuroCom® InMotion™ computerized test and convergence eye test, the ImpACT® neurocognitive testing and an automated functional eye movement assessment using the Eyelink® 1000 laser eye tracking technology. Eye track recorded data were analyzed offline using an automated computer program to identify saccadic, fixation and glissadic oculomotor behaviors. A reference database (Controls) including 298 participants without head injury from a previous study was used for comparisons.

Variables included: Visual Acuity LogMAR (VA), Perception Time (PT), Near Point Test (NPT) convergence score, Visual Memory (ViMEM) score, Verbal Memory (VeMEM) score, Visual Motor (VMOT) score, Cognitive Reaction Time (CRT), Vertical Saccade Speed (VSS), Saccade Rate (SR) and Fixation Drift Velocity (FDV).

Data Analysis: Descriptive statistics using SPSS (vs. 24.0, IBM Inc.) help describe test outcomes. Variable comparison analyses included a MANOVA for outcome differentials using Gender and Group as fixed factors and Spearman Rho Correlation Coefficient analysis to test relationships. Alpha levels were set at $p < 0.05$.

Results: Participant average age was 23.15 (+/- 3.77) years range from 1 to 5 head injuries with an average onset of injury 31.52 (+/- 27.02) weeks, previous night's sleep = 7.44 (+/- 1.28) hours, NPT convergence score = 7.61 (+/-4.93) cm. Vision scores for PERCEP = 38.40 (+/- 10.28) msec.

There was a significant positive relationship between NPT and TSYMP ($r = 0.427$, $p = 0.033$), VeMEM and ViMEM ($r = 0.425$, $p = 0.030$), PT and VeMEM ($r = 0.445$, $p = 0.026$), VSS and ViMOT ($r = 0.555$, $p = 0.021$). FDV was significantly related to both VSS ($r = -0.500$, $p = 0.041$) and SR ($r = 0.498$, $p = 0.042$).

There was a significant difference in SR = -0.61 (+/-1.16) compared to Controls (-0.02 +/- 0.993, $p = 0.001$) saccades/sec and FDV (0.46 +/- 0.70) compare to those without dTBI (0.053 +/- 0.99, $p = 0.019$) m/sec.

Conclusion: Results indicate that there is a significant relationship between functional eye movements and prolonged symptoms after diffused traumatic brain injury. We propose that functional eye movement

testing in combination with neurocognitive testing is crucial to document treatment response and long term symptom recovery.

A Novel Approach to Intensive Cognitive-Communication Rehabilitation for Young Adults with Acquired Brain Injury

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Objective: To assess the effects of a novel intensive therapy program for individuals with acquired brain injury (ABI) on their language, cognitive, and academic skills, and ultimately on their ability to return to a post-secondary education setting.

Participants: This study included four individuals with ABI, two as a result of traumatic brain injury (TBI) and two as a result of stroke (CVA). Three individuals participated in this 15-week intensive intervention. Treatment was deferred for the fourth individual, since they served as a control.

Intervention: This intensive intervention integrated classroom-style lectures with individual and group therapy, which targeted participants' cognitive-communication skills to bolster academic performance. Individuals attended three hours of classes per day (e.g., Psychology, Economics), simulating a typical college semester. They participated in daily speech-language therapy addressing specific impairments and daily group therapy targeting metacognitive strategies. Participants were given a Skill Book, consisting of schedules, cognitive-linguistic strategies, group exercises, and daily home activities to encourage therapeutic carryover. Individuals also participated in guided app-based work to apply cognitive-linguistic skills in functional contexts. Many of the foundational principles and materials were derived from the models of SCORE (DVBIC, 2015) and CogSMART (Twamley, Noonan, Savla, Schiehser, & Jak, 2010).

Design: Three individuals participated in a case-control series design, with an assessment battery at three time points: baseline (T1), mid-point (T2), and post-intervention (T3). The control subject was assessed on the same battery at T1 and T3, only, to monitor change without intervention. Experimental subjects were also measured on individual speech therapy goals and changes in classroom performance.

Main outcome measures: Weekly quiz and classroom performance, WAB-R, RBANS, SCCAN, SLP goal performance.

Results: Students are significantly more accurate in their responses to class discussion questions. They also demonstrate more spontaneous use of cognitive-communication strategies in the classroom. At mid-point testing, participant one (P1) demonstrated improvements on both the RBANS (+3 Total Scaled Score-TSS) and the SCCAN (+6 TSS); P2 demonstrated improvements on the WAB-R (+4.4 Language Quotient-LQ, +3.8 Cortical Quotient-CQ, +1.6 Aphasia Quotient-AQ); and P3 demonstrated improvements on all three measures (WAB-R: +4.3 LQ, +4.43 CQ, +9.2 AQ; RBANS: +2 TSS; SCCAN: +11 TSS). Individual short-term speech-language therapy goals are reviewed weekly and are met when a participant demonstrates criterion performance on three consecutive days. P1 partially met 11 weekly goals and fully met one; P2 partially met eight; P3 partially met 13 and fully met five. All participants are making steady incremental progress towards long-term goals.

Conclusions: Individuals with ABI demonstrated improved speech, language, and cognitive-communication skills as a result of this novel intensive cognitive-communication rehabilitation program (ICCR). They showed substantial improvements in standardized and qualitative performance as a result of this intervention.

BrainEx90: An Effective, Combined Physiotherapy and Occupational Therapy Treatment Group for Adults with Persistent Symptoms Post-Concussion/Mild Traumatic Brain Injury

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Introduction: There is a lack of evidence on effective treatment strategies for individuals with persistent symptoms after concussion/mild traumatic brain injury (mTBI). BrainEx90 is an innovative 90-minute group circuit training program involving physiotherapy and occupational therapy treatment strategies for adults with persistent symptoms post-concussion/mTBI. Seven participants at a time rotate to different 5 minute stations to complete balance, vision/vestibular, cognition, and self-management tasks as well as participate in a 20-minute education session. The BrainEx90 program runs for 16 sessions. The purpose of this research project was to evaluate the effectiveness of BrainEx90 in improving patient-reported and objective outcomes. The study was approved by the Western's Research Ethics Boards (REB) office of Human Research Ethics, London, Ontario, Canada.

Methods: Pre and post intervention assessment data was extracted from charts of patients who provided consent to the chart review. Pre and post scores were extracted from patient-reported measures: Canadian Occupational Performance Measure (COPM), Rivermead Post Concussion Symptoms Questionnaire (RPQ-3 and RPQ-13), Brain Injury Vision Symptom Survey (BIVSS), Headache Impact Test (HIT) and Generalized Anxiety Disorder 7 (GAD-7). Pre and post assessment data was extracted for selected objective outcome measures: Functional Gait Assessment (FGA), 10-Metre Walk Test (10MWT) self-selected and maximum speed, Modified Clinical Test of Sensory Interaction and Balance (mCTSIB) which was completed with feet together, single leg stance left and right and tandem stance. The extracted data was compared using a Wilcoxon or paired t-test.

Results: Pre-post assessment data was collected for 99 participants who completed 12 or more group sessions. Mean age = 44 years and mean time since injury = 746 days. There was significant improvement in patient-reported COPM Performance ($p < .001$) and Satisfaction ($p < .001$) scores. There was a reduction in symptoms scores on the RPQ-3 and RPQ-13 scores ($p = .002$, $p < .0001$) and anxiety as measured by the GAD7 ($p = .04$). Significant objective improvements were observed in FGA ($p < .001$), normal and maximum walking speed during the 10MWT ($p < .001$, $p = .003$) and feet together, tandem, right single leg and left single stance scores of the mCTSIB ($p = .004$, $p < .0001$, $p = .002$, $p < .001$). No other outcomes demonstrated a significant difference.

Discussion: This study is the first of its kind to demonstrate a group circuit training model that addresses the multiple systems affected by mTBI can effectively improve balance, walking speed, patient-reported symptom severity and performance and satisfaction with activities of daily living in adults with longstanding persistent symptoms post-concussion/mTBI.

Comparison of the Sensory Organization Test and the Balance Evaluation Systems Test in Traumatic Brain Injury

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Chronic balance deficits are often reported after traumatic brain injury (TBI). These deficits contribute to increased risk of falls, more limited community participation, and decreased quality of life. It is important for clinicians to be able to accurately describe balance deficits experienced by these patients in order to appropriately prescribe plans of care, justify treatments to payers, and to adequately track improvements or changes with treatment. The purpose of this study is to examine correlations between the Balance Manager Sensory Organization Test (SOT) and the Balance Evaluation Systems Test (BESTest) sensory orientation subscale in individuals with chronic TBI. Participants (n=44) are taking part in a larger randomized controlled trial in which the Balance Manager SOT and the BESTest are tested at baseline. All are living in community settings, and testing is completed in a rehabilitation hospital. Participants all have a previous history of TBI demonstrating balance impairments. All consented to the study and completed both outcomes. The primary outcome measures are the Balance Manager SOT and the sensory orientation subscale of the BESTest. The purpose of this report is to evaluate correlations between the baseline data provided by the BESTest and the SOT and to examine whether or not advanced technologies can provide insight into balance impairment that a standard clinical measure may not. To date, 44 individuals have completed both measures at baseline. There was a moderate and statistically significant correlation of 0.54 between the SOT and the BESTest (95% CI = 0.28, 0.72, $p = 0.0002$, $R^2 = 0.29$). Although there is a positive correlation between the Balance Manager SOT and the sensory orientation subscale of the BESTest, 70.8% of the variability in balance remains unexplained in this data. There are multiple potential explanations for this variability. The SOT includes additional conditions of altered vision that are unable to be tested with the BESTest and the force plate used with the SOT may be more accurate and precise than clinician observation. These two tools may be providing different information about the balance impairments in this population, despite the common clinical assumption that performing both tests is redundant.

Does Concussion Affect the Sense of Smell? Preliminary Data from A Longitudinal Prospective Study of Patients with Acute Concussion Referred from the Emergency Room

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Introduction: Up to 60% of adults with traumatic brain injury (TBI) present with olfactory impairments. Estimated rates of olfactory dysfunction in mild TBI and concussion are not well established, and little is known about the early effects of concussion on smell. The objectives of this study were to: 1) Measure the proportion of patients with evidence of smell dysfunction as measured by the University of Pennsylvania Smell Identification Test (UPSIT) scale at <1 week post-concussion and 2) Measure recovery of smell from <1 week to 8-12 weeks after injury.

Methods: An ongoing prospective cohort of individuals with physician confirmed concussion diagnosed in the Emergency Report were enrolled in the project within 1 week of the injury. Participants were not eligible if they had evidence of skull fracture, haemorrhage or contusion on CT scan. All participants were tested on the UPSIT, as part of a larger battery of demographic, clinical and neuropsychological assessments, within 1 week of injury. Each patient followed was followed biweekly for up to 12 weeks. A subset were tested at a second time between 8 and 12 weeks post-injury.

Results: N=81 acute concussion patients, comprising of 44 females and 37 males with average ages of 33.2 (SD=14.0) and 33.1 (SD=3.69), respectively, were recruited from the Hull Ellis Concussion Clinic at Toronto Rehabilitation Institute. At time 1, the average smell score for the full group was in the mild microsmia range (Mean=33.4, SD=3.4; mild microsmia), with 59% falling in the mild microsmia range. There were no significant differences or trends towards significance between males and females.

For the 23 patients with data at two time points, the mean smell at Time 1 was 33.1 (SD=2.9), mild microsmia), with no significant differences or trends towards significance between males and females. A significant improvement was observed ($t(23)=-2.35$, $p < 0.05$; Cohen's $d=-0.549$), with scores increasing to a mean level of smell within the normal range. This also represented a decrease in the proportion of individuals in the mildly impaired range or lower, from 74% at time 1 to 48% at time 2.

Significance: This is the first study to examine smell impairments longitudinally within the first three months of concussion. These early findings suggest that disrupted smell might be a supplementary biomarker for the detection of concussion and its resolution across time.

(This is part of a larger research study at the Hull-Ellis Concussion and Rapid Access Research Clinic in Toronto, which offers acute concussion care. This model is an innovative one in that it allows patients early access to concussion care, hopefully mitigating the risks associated with the psychological aspects concussion. It also helps us to better understand what functions are impacted in concussion).

Examining the Relationship Between Anxiety Symptoms and Mild Head Injury: Does Dispositional Mindfulness Play a Role?

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Introduction: Mild head injury (MHI) accounts for the majority (70 to 90%) of all brain injuries and represents a significant public health issue, given the potential for long-lasting impairments (Cassidy et al., 2004; Konrad et al., 2011). Anxiety symptoms are particularly prevalent following MHI, with 53% of individuals reporting clinically significant cases of anxiety (Osborn et al., 2016). Since self-reported anxiety is a strong predictor of long-term psychosocial outcomes post-injury, it is especially important to develop rehabilitation techniques to target anxiety symptoms (Draper et al., 2007). Mindfulness strategies may be relevant in this context, since higher dispositional mindfulness is associated with fewer psychiatric symptoms, including anxiety (Short et al., 2016). The purpose of the present study was to investigate the association between dispositional mindfulness and self-reported anxiety in an MHI population.

Methods: The relationship between anxiety, MHI, and mindfulness was examined in 138 Brock University undergraduates (M age = 20.51, SD = 4.29). The State-Trait Anxiety Inventory (STAI; Spielberger et al., 1983) was used to assess current anxiety symptoms (state) and the general propensity to be anxious (trait). A modified version of the Post-Concussion Symptom Scale (PCS; Gouvier et al., 1992) was also used to assess anxiety symptoms. The Everyday Living Questionnaire (ELQ; Brock University, NCR Lab, 2008) was administered to determine a history of MHI. The Five Facet Mindfulness Questionnaire (FFMQ; Baer et al., 2006) was used to assess levels of dispositional mindfulness.

Results: Dispositional mindfulness significantly predicted levels of state anxiety, $F(1, 85) = 61.10, p < .001, r = .65$, trait anxiety, $F(1, 85) = 77.12, p < .001, r = .69$, and PCS anxiety scores, $F(1, 120) = 16.97, p < .001, r = .35$, such that higher mindfulness was associated with less anxiety. Moreover, individuals with a history of MHI who had high levels of mindfulness reported significantly fewer symptoms of state anxiety, $t(32) = 2.65, p < .05$, trait anxiety, $t(32) = 2.69, p < .05$, and lower PCS anxiety scores, $t(41) = 2.65, p < .01$, than individuals with low levels of mindfulness. Further analyses revealed that the non-judgment subscale of the FFMQ was the best predictor of state ($\beta = -.44, p < .001$) and trait anxiety, ($\beta = -.49, p < .001$), while the non-reactivity subscale was the best predictor of PCS anxiety scores, ($\beta = -.32, p < .001$).

Discussion: These findings suggest that higher levels of dispositional mindfulness may mitigate anxiety symptoms following MHI. Additionally, it appears that the fewest anxiety symptoms are experienced by those who attend to the present moment experience with a non-judgmental and non-reactive approach. Therefore, interventions that foster these types of mindfulness skills may be useful in an MHI rehabilitation setting.

Increased Gray Matter Fractional Anisotropy in the Left and Right Occipital Lobe in Symptomatic Former Professional Football Players

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Introduction: Chronic traumatic encephalopathy (CTE) has been linked to a history of repetitive head impacts (RHI) for both concussive and subconcussive levels. Exposure to RHI has been shown to result in decreased fractional anisotropy (FA) in white matter. Of note, increased FA has been reported following concussion in gray matter of the brain. However, to date only a small number of studies have investigated diffusion parameters in gray matter following RHI, as seen in contact-sports such as football. To what extent exposure to RHI at concussive as well as subconcussive levels affects long-term gray matter integrity remains to be elucidated.

Methods: We included 87 former professional football players (mean age = 55.2 ± 8.2 years) and 21 controls (mean age = 56.3 ± 7.3 years) without contact sport or brain injury history who participated in the Diagnosing and Evaluating Traumatic Encephalopathy using Clinical Tests (DETECT) study. We analyzed diffusion weighted (DWIs) and T1w images acquired on a 3T scanner, applied a free water correction to the DWIs, and used FreeSurfer 5.3 to parcellate the T1w images. We registered the FreeSurfer parcellation to DWI space and extracted FA values for the four cortical lobes by combining all corresponding FreeSurfer regions of interest (ROIs) using Matlab. We conducted a MANCOVA to investigate overall group differences in FA across all four lobes while controlling for age. If significant, we used post hoc ANCOVAs to analyze each of the four cortical lobes as well as to differentiate between left and right hemispheres. All analyses were controlled for age and multiple comparisons.

Results: Results from the MANCOVA indicated significant group differences in FA between former NFL players and controls ($p = 0.010$). The four post hoc ANCOVAs revealed a significant group difference in the occipital lobe ($p = 0.001$; Bonferroni corrected, $p < 0.013$). The final two post hoc ANCOVAs showed that there were significant group differences in FA for both left and right hemispheres in the occipital lobe (left, $p = 0.021$; right, $p = 0.015$; Bonferroni corrected, $p < 0.025$).

Conclusion: In our sample we report that former professional football players who are at high risk of developing CTE showed significantly higher FA in bilateral occipital lobe gray matter compared with controls. This study provides initial evidence that exposure to RHI can lead to abnormally increased FA in posterior gray matter, possibly due to loss of dendrites or other cellular processes. Future studies are needed to examine whether these findings reflect long-standing chronic injury from the time of RHI exposure or are indicative of the neurodegenerative process associated with CTE.

Age at First Exposure to Repetitive Head Impacts Is Associated with Smaller Thalamic Volumes in Former Professional Football Players

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Background: Chronic traumatic encephalopathy (CTE) is associated with a history of repetitive head impacts (RHI). Reduced thalamic volumes have been reported in neuropathologically confirmed cases of CTE. Further, younger age at first exposure (AFE) to RHI has been linked to long-term white matter alterations and greater later-life cognitive impairment. However, to date there has been only one study that has investigated thalamic volume in a sample of professional fighters. To what extent these findings can be generalized to athletes exposed to RHI in other contact sports such as football remains to be elucidated. Further, whether AFE to RHI affects thalamic volume is unknown.

Methods: We included 86 former professional football players (mean age = 54.9 ± 7.9 years) who participated in the Diagnosing and Evaluating Traumatic Encephalopathy using Clinical Tests (DETECT) study. In this study we analyzed T1w data acquired on a 3T scanner and used FreeSurfer 5.3 to analyze thalamic volumes. We evaluated results from a neurocognitive testing battery assessing mood and behavior, psychomotor speed, as well as visual and verbal memory. We investigated the association between thalamic volumes and AFE and total years of play with mixed effects regression models while controlling for age, body-mass index, estimated total intracranial volume, and years of education. Further, we adjusted for total years of play in the AFE analysis. We computed partial correlations to examine the relation between neurocognitive test results and thalamic volumes, while adjusting for age, body-mass index, estimated total intracranial volume, and years of education. All analyses were corrected for multiple comparisons.

Results: Right and left thalamic volumes were associated with total years of play (right, $p = 0.03$; left, $p = 0.012$), indicating that the longer a player participated in football the more prominent his thalamic volume loss. Further, younger AFE to RHI was associated with lower right thalamic volume ($p = 0.014$). This association remained significant when adjusting for total years of play. Correlations with neurocognitive assessments revealed that left thalamic volume was negatively associated with visual memory, whereas right thalamic volume showed a positive association with mood and behavior.

Conclusion: In our sample of former professional football players at high risk for CTE, both total years of play and AFE to RHI had a significant effect on thalamic volume. The effect of AFE was almost twice as strong as the effect of total years of play. Our results correspond to previous reports that describe reductions in

thalamic volumes in neuropathologically confirmed cases of CTE. Our results also suggest that younger AFE to RHI may constitute a risk factor for greater reduction in thalamic volume.

The Impact of Age on Functional Outcome and Mortality in Patients Admitted to Traumatic Brain Injury Rehabilitation

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Objectives: The effect of age on functional outcome after admission to traumatic brain injury rehabilitation (TBI-RH) remains uncertain. Some studies suggest worse functional outcomes with increasing age, while other studies demonstrate no difference in functional outcomes. Few recent studies have specifically examined functional improvements after TBI-RH in a Medicare population.

Methods: All patients admitted between 2008-2012 to the regional TBI-RH were identified from the TBI-RH database and matched to the state death index. Patients were divided into a less than 65 years non-Medicare (NMC) age group and a 65 years and above Medicare (MC) age group. Functional Independence Measure (FIM) score gains from TBI-RH admission to discharge were compared between groups.

Results: A total of 414 TBI-RH patients were identified in the database, 315 patients in the NMC group and 99 patients in the MC group. NMC patients had a lower acute hospital median admission Glasgow Coma Scale score (10 vs. 15; $p < 0.0001$) and had more severe traumatic injuries as measured by the acute hospital median Injury Severity Score (21 vs. 17; $p = 0.02$). The rate of surgical procedures and the presence of polytrauma was similar between groups. Length of stay in TBI-RH was similar between NMC and MC groups (16 days vs. 15 days; $p = 0.06$). However, the percentage of NMC patients discharged to home was higher (76% vs. 50%; $p < 0.0001$) and the six-month mortality rate for NMC patients was lower (0.6% vs. 9%; $p < 0.0001$). Larger median gains in FIM scores were observed in the NMC group for the overall median FIM score (39 vs. 25; $p < 0.0001$), the median FIM motor sub-score (31 vs. 21; $p < 0.0001$), and the median FIM cognitive sub-score (6 vs. 4; $p < 0.0001$).

Conclusion: MC patients admitted to a regional TBI-RH have less severe brain and systemic injuries and a similar length of stay in rehabilitation. However, MC patients demonstrate less improvement in median FIM score and sub-score gains at discharge from TBI-RH. Future research should focus on the development and implementation of more age-specific rehabilitation therapies.

Economic Burden of Illness for Patients with Traumatic Brain Injury Resulting in Chronic Motor Impairment

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Objectives: Traumatic brain injury (TBI) can result in motor impairment that persists indefinitely. Longitudinal follow-up of patients with severe TBI with motor impairment suggests that recovery occurs primarily within 6 months post-trauma, suggesting that patients who do not recover within this period may endure substantial long-term burden. At present, the economic burden of severe TBI resulting in chronic motor impairment is poorly understood. This study examined medical resource use and healthcare costs for patients with TBI with chronic motor impairment compared to similar patients without TBI in the US.

Methods: Patients (aged 18-75) diagnosed with a head injury (ICD-9-CM 800-804, 850-854) in 2006 or later (index date) were selected using de-identified administrative claims data for commercially-insured patients (1999-2015). Included patients had initial evidence of motor impairment <6 months post-index and subsequent evidence ≥6 months post-index. Patients with evidence of motor impairment during baseline were excluded. Additionally, patients had ≥1 diagnosis for personal history or late effects of TBI (ICD-9-CM V15.52, 905.0x, 907.0x). Patients were required to have continuous healthcare insurance coverage for ≥6 months before (baseline) and ≥12 months after index; a subset of patients with ≥24 months of continuous coverage was also identified. Patients with TBI were matched 1:2 with controls without TBI using propensity score matching that accounted for baseline patient demographics, comorbidities, and resource use. Post-injury healthcare costs and medical resource use were assessed during successive 6-month periods and compared between patients with TBI and controls using signed-rank tests and McNemar tests.

Results: 297 patients with TBI and 594 matched controls were analyzed. The majority (84%) of patients with TBI was diagnosed with a head injury in an inpatient or emergency setting; median age at index was 51.0 years, and 67% were male. Mean direct costs to payers (2015 \$USD) during the first 6 months post-index were \$268,676 for patients with TBI and \$5,865 for controls (excess \$262,811; p<0.001); excess costs gradually declined to \$12,457 (p<0.001) during months 18-24 of follow-up. The majority of excess costs were attributed to inpatient and emergency services (0-6 months: 90.2%; 18-24 months: 58.6%). Rates of resource use were substantially higher among patients with TBI in the first 6 months (emergency: 90.9% vs. 21.2%; inpatient 81.1% vs. 9.9%; physical therapy/rehabilitation: 86.2% vs. 18.9%; all p<0.001); after 1 year, patients with TBI exhibited sustained, elevated use of medical services (>20% difference, except inpatient; all p<0.001).

Conclusions: TBI with chronic motor impairment was associated with substantially increased use of medical services and healthcare costs. Excess costs and resource use were highest during the acute phase post-injury (\$262,811) – reflecting the severity of injuries – but remained significantly elevated throughout the 2-year study period, highlighting the significant unmet need for effective care in this population.

DTI in Orthopedic Injury Patients Differs From Uninjured Participants But Not From mTBI Patients

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The rationale for recruiting orthopedic injury (OI) patients as controls for mild TBI (mTBI) patients includes similar risk factors (e.g., impulsivity, attention deficit hyperactivity disorder, substance abuse) for traumatic injury which are not shared by uninjured community residents recruited based entirely on demographic features. We recruited 80 mTBI, 55 OI (with mild injuries documented by the Injury Severity Score) and 34 typically developing (TD), uninjured participants. All participants were 12 to 30 years old. We compared diffusion tensor imaging (DTI) data for the three groups to test the hypothesis that findings in both the OI and mTBI groups would differ from the TD participants. mTBI and OI groups were recruited from the same emergency departments at three Level 1 trauma centers and imaged within 96 hours and at 3 months post-injury; TD participants were recruited by advertising in the community and imaged on a single occasion. The three groups did not significantly differ in age, gender, socioeconomic level, race, or education. Severe psychiatric disorder, neurologic disorder and substance dependence were exclusion criteria. The two patient groups did not differ in the time since injury when they were imaged. DTI was acquired on a 3 T Philips system using a 32 direction protocol. Quantitative tractography was used to analyze DTI data without knowledge of group status. Inter-rater and intra-rater reliability in the DTI analysis was confirmed, $p < 0.01$. A higher percent of the mTBI group were injured in motor vehicle crashes (45%) than the OI group (11.1%), $\chi^2 = 17.21$, $p < 0.0001$. All of the DTI metrics were normalized by the TD group's DTI metrics for corresponding regions. Both patient groups had higher mean diffusivity (MD) than TD participants (range from $p < 0.0001$ to $p < 0.0008$) in multiple regions including the genu of the corpus callosum, uncinate fasciculus, inferior frontal occipital fasciculus, cingulate bundle, and frontal white matter. The mTBI and OI groups did not significantly differ on MD for any region. Our results raise issues to consider in selecting a comparison group for imaging studies of mTBI patients. TD participants provide a normative reference, whereas OI patients share risk factors with mTBI patients and ostensibly traumatic stress. Our findings provide a rationale for recruiting both OI and TD groups for comparison with mTBI patients. Friends of mTBI patients have also been recruited as a comparison group in studies by Drs. Sureyya Dikmen and Nancy Temkin. This approach mitigates to some extent the concern about risk factors for traumatic injury, but it does not address injury-related stress which is controlled by recruiting OI patients.

Resting State Functional Connectivity Evidence of Familiar Auditory Sensory Stimulation Promoting Plasticity in Disordered Consciousness

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Objectives: To characterize the mechanism of therapeutic effect for a familiar auditory sensory training (FAST) protocol (Pape 2012 & 2015) among severe traumatic brain injury (TBI) participants by assessing functional neural connectivity relative to neurobehavioral function.

Methods: We previously reported that the FAST protocol was efficacious in improving arousal and awareness among persons remaining in states of disordered consciousness after a severe TBI (Pape 2015). The FAST is a standardized passive auditory stimulation intervention where the participant listens to familiar auditory stories (active) or silence (placebo) for 10min four times per day for six weeks. Four participants from the active and four from the placebo groups completed and had structural and functional magnetic resonance imaging (MRI) data meeting standard quality and assurance standards. MRI sequences completed prior to (baseline) and after the FAST intervention (endpoint) included three-dimensional magnetization-prepared rapid gradient-echo (MPRAGE) and resting state functional MRI sequences. A total of 26 brain regions associated with default mode (DMN), salience, attention and language networks were analyzed using within and between group analyses. Correlations between neuroimaging data and neurobehavioral function using the following assessments were also made Disorders of Consciousness Scale-25 (DOCS-25), the auditory-language subscale of this test and the Coma-Near-Coma scale (CNC).

Results: Connectivity within the DMN, language and salience networks was significantly decreased between baseline and endpoint within the FAST group. Connectivity between the attention and salience network was significantly increased between baseline and endpoint within the FAST group. Connectivity within the salience network was significantly increased in the placebo relative to the FAST group at endpoint. At endpoint, better CNC performance was significantly associated with decreased connectivity between the attention and DMN networks. At endpoint, better DOCS auditory-language performance was significantly associated with decreased connectivity between the attention and language networks.

Conclusions: FAST engaged long-term memory circuitry, which in turn engaged interactions between other regions and networks thereby promoting compensatory processing. The FAST is also thought to promote concurrent plasticity, as evidenced by correlations between attention and DMN networks with gains in non-trained neurobehavioral modalities. These findings support the concept that this patient population has potential for recovery and the need for more research to develop treatments that optimize this potential.

Sleep-Disturbances and Fatigue Predicts Post-Concussive Symptoms 12 Months After Mild Traumatic Brain Injury

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Objectives: I) To examine the frequency of clinically significant levels of fatigue, sleep-disturbance, sleepiness, and symptoms of depression and anxiety during the first year after mild traumatic brain injury (mTBI). II) To investigate whether such symptoms at 3 months after injury can predict post-concussive symptoms (PCS) at 12 months after injury.

Methods: In this large prospective cohort study 379 patients (65.2% men, median age: 25.1, minimum: 16.1 maximum: 59.7) with mild TBI were recruited from St. Olavs Hospital and the municipal clinic in Trondheim, Norway. Falls (35%), violence (17.4%) and bicycle accidents (15.3%) were the most common injury mechanisms. Fatigue, sleep-disturbances, sleepiness, PCS, as well as symptoms of anxiety and depression were measured at 2 weeks, 3 months and 12 months after injury. Assessment tools included the Insomnia Severity Index (ISI) (selected items), Fatigue Severity Scale (FSS), the Epworth Sleepiness Scale (ESS), Brief Symptom Inventory-18 (BSI-18) and the Rivermead post-concussion symptoms questionnaire (RPSQ). Conventional cut-off values defining clinical significance for the various assessment tools were applied.

Hierarchical multiple regression was performed in order to investigate the effect of the independent variables FSS, ESS, BSI18-depression, BSI18-anxiety and ISI at 3 months on PCS at 12 months. The regression model was adjusted for age, sex, and injury mechanisms. Only patients who had completed questionnaires at both 3 months and 12 months (n=173) were included in the analyses.

Results: Clinically significant levels of fatigue were observed in 32, 27 and 26 % of the patients at 2 weeks, 3 months and 12 months, respectively. For insomnia and sleepiness, the frequency was highest at 2 weeks (ISI:14%, ESS:19%), and lower but relatively stable from 3 months (ISI:12%, ESS:12%) to 12 months (ISI: 11%, ESS: 12%) after injury. Frequency of clinically significant symptoms of anxiety declined from 2 weeks (15%) to 3 months (13%), and further to 12 months (9%). An identical proportion of patients reported clinically significant symptoms of depression at 2 weeks and 3 months after injury (13%), with increased numbers at 12 months (15%). The full hierarchical multiple regression model explained 51% of the variance in RPSQ at 12 months after injury. Moreover, the independent variables explained 42% of the variance in RPSQ at 12 months, after controlling for age, injury mechanism and sex. Insomnia, sleepiness, fatigue, sex and injury mechanism, made a unique statistically significant contribution, with insomnia recording a higher standardized beta value (beta 0.4, $p < 0.001$) than fatigue (beta 0.2, $p < 0.002$), and sleepiness (beta 0.1, $p < 0.04$).

Conclusion: The results from this study indicates that both fatigue and sleep-disturbances may be primary symptoms of long-term PCS and can potentially predict symptoms the first year after mild TBI, either independently or in a combination.

Concussive TBI Produces Deficits to the Blood Brain Barrier and Perineuronal Nets in Rats

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Concussive traumatic brain injury (cTBI) can produce long-term deficits that result in life-long impairments in cognitive functions. Most human TBIs consist of mild, closed head, frontal impacts in which the brain undergoes both lateral and rotational acceleration; conditions that are represented in a novel rat model of TBI ("Maryland model", Kilbourne et al. 2009). Here, we further characterize this model by investigating the effects of a single concussion on aspects of normal brain integrity; the blood brain barrier (BBB), key regulator of the blood-born access of materials into the CNS, perineuronal nets (PNNs), extracellular matrix molecules that shape the development of synapses and regulate the plasticity of neural pathways and the activation of microglia, early indicators of inflammatory and immune response. Adult male Sprague Dawley rats were anesthetized and received a frontal, closed-head cTBI. Controls received no cTBI. Brains were collected 1, 7 and 28 days post injury. cTBI-induced BBB breakdown was measured by quantitative assessment of the influx of serum protein normally excluded by the BBB within rostro-caudal sections of brain. Active BBB permeability was further measured by assessing the spatial distribution of exogenously applied IV dextran at all 3 time points. Integrity of the PNN was assessed by measuring binding/distribution of wisteria floribunda lectin in brain sections. Activation of microglia was examined using Isolectin B4 labeling. Preliminary analysis suggests cTBI increases the amount of albumin labeling at 24 hours, but not 7 days post injury. Similarly, cTBI also produced a decrease in cortical PNN distribution at 1, but not 7 days. Together these data show that this model of cTBI is associated with BBB permeability and reduced PNN integrity. The Maryland model represents a novel tool with which to better understand the pathophysiology of concussive TBI.

Post-Traumatic Stress After Severe Traumatic Brain Injury in Patients Impacts Their Close Relatives' Health-Related Quality of Life

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Background: Post-traumatic stress (PTS) symptoms after severe Traumatic Brain Injury (TBI) may affect the health-related quality of life (HRQoL) of the close environment. The present study investigated the relationship between PTS symptom severity and HRQoL of close relatives after severe TBI.

Methods: A total of 190 patients from a prospective cohort study on severe TBI in Switzerland were evaluated (2007-2011). Outcome measures: a) HRQoL (SF-12, physical and mental component scales, respectively), b) PTS symptom severity (Short Screening Scale for DSM-IV PTSD [SSS-PTSD]) and time (evolution across time). Covariates: a) Injury severity (Abbreviated Injury Score of head region [HAIS]), b) age. Analyses were run separately for individuals ≤ 50 and > 50 years (i.e., bimodal distribution). Longitudinal assessments were done at 3, 6, and 12 months post-injury.

Results: Multilevel models for both age groups revealed significant negative associations between PTS symptom severity and a) mental HRQoL ($p_{\leq 50} = .033$; $p_{> 50} = .017$).

Limitations: Inconsistent participation across follow-ups may have impacted the results.

Conclusion: Findings indicate that PTS symptoms after severe TBI are negatively associated with HRQoL in relatives

Keywords: post-traumatic stress disorder; severe traumatic brain injury; quality of life; recovery; trajectories of recovery.

Cerebral Waste Accumulation and Glymphatic Clearance as Mechanisms of Human Neurological Diseases

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The brain is a complex system that requires continual regulation of parenchymal pressure, osmolarity, and waste removal for optimal function; despite this, human brain lacks any obvious extension of lymphatic circulation for moderating fluid and waste regulation. We recapitulate herein a recent analysis of proteinaceous waste deposition in the human brain, its observed route of clearance, and the implications of abnormal accumulation along this clearance pathway as a potential mechanism of neurological diseases. This study uncovered an analogous staining pattern of cerebral phosphorylated tau in temporal lobe epilepsy (TLE) and chronic traumatic encephalopathy (CTE). Regardless of the underlying physiopathology, p-tau elimination occurred via circulation through the perivenous space, as predicted by a glymphatic route of clearance. Remarkably, we demonstrated that p-tau is associated with a neurological disease that can develop independent of head trauma, since in both CTE and TLE: 1) Extracellular p-tau followed unidirectional, fluid-driven pathways that led toward the space bordering large (>100 μm diameter) blood vessels; 2) Tau-positive staining occurred within astroglial cells adjacent to blood vessels, which signified transcellular transport of p-tau as a potential secondary efflux route; 3) P-tau frequently appeared clustered within the perivenous space. This waste aggregation bears significant implications in the disruption of interstitial fluid circulation, which may contribute to exacerbation of disease states. A better understanding of waste elimination in the human brain may prove significant as a therapeutic target to improve parenchymal fluid circulation, and consequently, mitigate the hydrostatic, osmotic and oncotic imbalances that often cause or exacerbate brain diseases.

Do Ways of Coping Vary with Respect to Resilience Among Family Members Supporting Relatives with Traumatic Brain Injury?

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Introduction: Resilience contributes to the individual adjustment of family members providing support to relatives with a traumatic brain injury (TBI). Contemporary formulations suggest that rather than being a personality trait, resilience is a set of skills that can be learned. The study investigated whether there are resilience-based differences in patterns of coping in family member.

Method: A multi-centre prospective cross-sectional study was undertaken across six rehabilitation centres located in the states of New South Wales and Queensland Australia. Family participants (n=131) completed the Resilience Scale and the Ways of Coping (WOC) Questionnaire. The WOC-Q comprises eight scales (Confrontive Coping, Distancing, Self-Controlling, Seeking Social Support, Accepting Responsibility, Escape-Avoidance, Planful Problem Solving and Positive Reappraisal) and two summary scales (Emotion Focused Coping and Problem-Focused Coping). Demographic and injury data were also collected.

Results: Family members were principally parents (58/131, 44%) or spouses (59/131, 45%), with an average age of 53.8±11.4 years. Their relatives with TBI were 41.4±14.3 years of age, had sustained extremely severe injuries (average duration of post traumatic amnesia 71.7±64.3 days) and were 3.0±3.9 years post injury. There were no gender-based differences among family members (females n=106, males n=25) in either resilience or ways of coping scores. Similarly, there were no differences among parents and spouses on resilience or ways of coping.

Families were divided into two groups (low or moderately low resilience, LRS, n=49 vs. moderately high to high resilience, HRS, n=82) based on Resilience Scale scores. Between groups analysis (t-tests) found that the HRS group were significantly more likely to use Confrontive Coping (p=.005) Planful Problem Solving (p=.005) and the overall Problem-Focused Coping summary scale (p=.004). There were also trends for the HRS group to have higher scores on Distancing (p=.009) and the Seeking Social Support (p=.028) scales compared to families in the LRS group. There were no differences on the Emotion-Focused Coping summary scale or other remaining scales.

Conclusion: The results suggest that families with higher resilience scores display a range of coping skills that are not as frequently employed by families with lower resilience scores. The results can help guide the development of skills-based interventions to strengthen resilience among all families supporting relatives with TBI.

12-Month Prospective Cohort Study of Patients with Severe Traumatic Brain Injury and Their Relatives: Coping, Satisfaction with Life, and Neurological Functioning

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Objective: Examine the associations between the functioning of patients with severe traumatic brain injury, and their relatives' coping style and Quality of Life across 12 months post-injury.

Design: Longitudinal, prospective, population-based cohort-study assessing 188 patients with severe traumatic brain injury (Abbreviated Injury score of the head region >3), and their relatives. Data were drawn from a larger national study run in Switzerland (2007-2011). Mixed linear models were run separately for ages > 50, and ≤ 50 (i.e., bimodal distribution).

Setting: Assessments took place at the patients' location at the time (i.e., home, rehabilitation clinic, hospital, etc.).

Interventions: Patients Data were collected as a part of the assessments of patients and their families at the time of the accident, 3, 6, and 12 months post-injury.

Main measures: Patient: Glasgow Coma Outcome Scale Extended (neurological functioning), Patient Competency Rating Scale for Neuro-Rehabilitation (reported emotional, interpersonal, cognitive, and total functioning), Abbreviated Injury Score of head region. Relative: Health Related Quality of Life, Coping with Stressful Situations.

Results: Patients' neurological functioning predicted the relatives' reported mental Health Related Quality of Life across age ($p < 0.01$). Relatives' coping strategies predicted patients' functioning among patients > 50 years: Total and cognitive functioning decreased as a function of emotion-oriented coping ($p = 0.01$), while interpersonal functioning increased as a function of task-oriented coping ($p = 0.01$) and decreased as a function of avoidance-oriented coping ($p = 0.02$).

Conclusion: Patients' neurological functioning predicts relatives' mental Health Related Quality of Life, relatives coping strategies predicts the patients reported functioning.

Keywords: Severe TBI, coping, Quality of Life, recovery trajectory, relatives

Post-concussive Symptoms the First Year after Mild Traumatic Brain Injury: Preliminary Results from A Large Prospective Cohort Study

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Background: Symptoms after mild traumatic brain injury (mTBI) typically resolve within the first weeks, and previous studies report persisting symptoms in 10-20% of the patients.

Objectives: Objectives were to study occurrence, characteristics and evolution of post concussive symptoms during first year after mild traumatic brain injury (mTBI) in a large prospective cohort study, in Trondheim, Norway.

Methods: 379 patients (65% men) between 16-60 years old (mean age: 31±13) who met WHO criteria of mTBI were included in the study. Patients were recruited from a regional level 1 trauma center and Municipal Emergency clinic in Trondheim, Norway in the period April 2014 - December 2015. The most common injury mechanisms were falls (35%), violence (17.4%), and bicycle accidents (15.3%).

Patients were asked by telephone interview at two weeks, 3 months and 12 months after injury, whether they had noticed any symptoms related to their head injury. Rivermead Post Concussion Symptoms Questionnaire (RPSQ) was returned by mail or filled during direct contact at the same time-points.

Items from the RPSQ were divided into 4 symptom groups after the ICD-10 PCS syndrome criteria, describing unpleasant sensations and pain (question 1-4, 6, 13-15), emotional changes (questions 7-9,16), subjective cognitive changes (question 10-12) and sleep disturbances (question 5). A repeated measures GLM was performed on patients who had completed RPSQ at all three time points (n=140).

Results: In the telephone interview 50% (159/318) of the patients reported that they had noticed symptoms after their head injury at two weeks, 25,5% (83/326) after 3 months, and 19,1% (54/282) after 12 months. Total RPSQ score showed a change over time ($F = 21.5$, $p < 0.0001$). Total RPSQ score was highest after 2 weeks (mean 9.8±10.9), as compared to both after 3 months (mean 6.4±9.3, $p < 0.0001$) and 12 months (mean 5.1±8.1, $p < 0.0001$). The difference between 3 and 12 months was not significant ($p=0.18$). All RPSQ score groups were influenced by time ($F = 4.3$ to 24.4 , $p = 0.02$ to < 0.0001). We found a decrease in unpleasant sensations and pains ($p < 0.0001$) and subjective cognitive changes from two weeks till 3 months ($p=0.0028$), while emotional changes ($p=0.009$) and sleeping disorder ($p=0.007$) only showed a significant decrease from two weeks till 12 months. Women had higher RPSQ score compared with men ($p < 0.001$), however, this difference decreased over time ($F = 4.1$, $p = 0.021$).

Conclusions: In this cohort study we found that post concussive symptoms were frequent two weeks after mTBI, and less so after 3 and 12 months. The decrease from 3 to 12 months was modest and did not reach statistical significance.

Assessing Depressive Symptoms and Their Correlates in a Sample of Adolescents with mTBI

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Objective: Prior research shows that youth sustaining mild traumatic brain injuries (mTBI) can be at risk for post-injury symptoms of stress, depression, and anxiety, which can impact recovery. This study's aim is to assess symptoms of depression and their correlates in a sample of adolescents referred for psychology consultation following mTBI. Qualitative variables including demographics, injury characteristics, and symptoms of depression will also be presented.

Method: Participants were 78 adolescents (age range: 13-17; M=14.73) with mTBI seen in a pediatric mTBI clinic and referred for outpatient psychology consultation in an urban pediatric hospital in the United States. Participants were initially seen by an interdisciplinary team of medical providers, neuropsychology, and nursing. Based on presenting problems, they were referred for additional psychological assessment and intervention. Assessment consisted of clinical interview, review of medical records, and completion of questionnaire battery, including the Children's Depression Inventory 2nd Edition: Self Report (CDI-2; Kovacs, 2011). Data for this study were gathered via retrospective chart review.

Results: Data related to referral concern, symptom presentation, and standardized measures were analyzed. Average time since injury was 11.36 weeks, and most adolescents (73.1%) had sustained only one mTBI. Most participants (56.5%) displayed prior psychological symptoms, and 42.3% had a co-occurring medical condition. At assessment, 6.4% had current counseling services, 23.1% had prior counseling, and 5.1% had current psychiatry services. The majority of the sample (76.9%) was referred for psychology consultation to address post-injury mood or coping concerns. Regarding mood, 24% self-reported a significant amount of depressive symptoms on the CDI-2. Significant correlations with CDI scores were not found for referral concern, loss of consciousness, or history of mental health services. However, significant correlations were found between time since injury and the CDI Negative Self-Esteem subscale. Additionally significant correlations were found between number of sustained concussions and the CDI total, the CDI Emotional Problems scale, the CDI Functional Problems Scale, and the CDI Negative Mood/ Physical Problems subscale.

Conclusions: Given the current attention to mTBI in the medical and athletic communities, this study highlights the need for behavioral health assessment and screening for depressive symptoms following injury. Findings showed that in a sample of adolescents referred for psychology consultation, higher rates of self-reported overall depressive symptoms, emotional and mood-related functional problems, and negative mood/ physical symptoms were associated with sustaining fewer mTBIs. Additionally, longer time since injury was associated with lower self-esteem. While additional research is needed, this study is a promising first step towards identifying depressive symptoms associated with mTBI in adolescents.

Structural Neuroimaging Characterization of U.S. Military Veterans and Retired National Football League Players with Mild Traumatic Brain Injury: Gray Matter Density and Diffusion Tensor Imaging Analyses

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Objectives: To characterize gray matter density and white matter integrity among U.S. Military Veterans and retired National Football League (NFL) players with a history of mild traumatic brain injury (mTBI).

Methods: This was a preliminary, prospective study including 9 Veterans and 9 retired NFL players with a history and current symptoms of mTBI. 9 healthy participants were also studied as controls. mTBI was classified using a symptom attribution and classification algorithm (SACA, Pape, Herrold et al., 2016), which encompasses the American Congress of Rehabilitation Medicine definition of mTBI (ACRM, 1993). Veterans and retired NFL players completed structured interviews, self-report questionnaires and neuropsychological tests in order to classify mTBI using the SACA. All participants completed a magnetic resonance imaging (MRI) scan including three-dimensional magnetization-prepared rapid gradient-echo (MPRAGE) and diffusion tensor imaging (DTI) sequences. The MPRAGE images were processed using SPM8 and VBM8 to assess for gray matter density differences within a mask comprised of the bilateral dorsolateral prefrontal cortex (DLPFC), anterior insulae, and anterior cingulate cortex (aCC). Two sample T-tests using small volume correction were used to compare paired groups ($\alpha=0.01$). DTI data were eddy current corrected and fractional anisotropy (FA) maps were created using FMRIB Software Library (FSL) version 5.0.1. FA maps for all participants were entered into a voxelwise statistical analysis using Tract-Based Spatial Statistics (TBSS). A general linear model was constructed and t-tests were completed ($p<.05$ two-sided) between groups. The JHU white matter atlas was used to extract FA values in 48 white matter tracts from the skeletonised FA maps. Age and time since injury were used as covariates as appropriate.

Results: Gray matter density results indicate that retired NFL players had less gray matter in the aCC and Veterans had significantly less gray matter in the left insula relative to healthy controls. Furthermore, retired NFL players had significantly less gray matter density than the Veterans throughout the mask, particularly in the aCC. DTI results indicate that retired NFL players had higher FA values in 42/48 and Veterans had higher FA values in 13/48 white matter tracts assessed relative to healthy controls. No significant differences in FA values were found between Veterans and retired NFL players.

Conclusions: mTBI regardless of etiology had significant effects on gray matter density and white matter integrity. However, a different pattern of gray matter density results was found for Veterans relative to retired NFL players among the brain regions important for working memory, executive function and emotional processing. Results also indicate that white matter integrity was more greatly affected for retired NFL players than for the Veterans. Additional research on characterizing the relationships between structural morphometry and behavioral assessments is warranted in future research.

Symptom Reduction in Young People (15 – 30 Years) After a Brief Behavioral Intervention for Persistent Post-Concussion Symptoms: An Uncontrolled Study

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Background: About 5 – 15 % of patients with concussion experience persistent post-concussion symptoms (PCS) longer than 3 months post-injury. Currently, treatment options are limited, and no evidence-based intervention is available. Recent studies suggest that cognitive and behavioral processes may be involved in symptom maintenance.

Aim: To explore in an uncontrolled study design: 1) the overall outcome of a newly developed, brief behavioral intervention in young patients (15 – 30 years) with persistent PCS 3 – 6 months after concussion, and 2) the hypothesised mediators, i.e. illness perceptions and illness behaviors.

Methods: Thirty-two patients, consecutively recruited from an epidemiological study or referred by primary care physicians, received an 8-week interdisciplinary intervention carried out by a physiotherapist, an occupational therapist and a neuropsychologist. The intervention was based on principles from cognitive-behavioral therapy and gradual return to activities. The primary treatment objective was to reduce PCS and prevent chronification of symptoms by reducing negative illness perceptions (eg. beliefs that one cannot control the symptoms and that they will persist), and reducing maladaptive illness behaviors (eg. excessive rest, exertion or oscillation between these opposites). Self-report measures were completed pre-intervention, post-intervention, and at 3 and 12 months post-intervention. Change after intervention was measured by the Rivermead Post-concussional Symptoms Questionnaire (RPQ) (primary outcome). Hypothesised mediators were measured by the Brief Illness Perception Questionnaire (B-IPQ) and the Behavioural Response to Illness Questionnaire (BRIQ). Patients' experiences were evaluated by Experience of Service Questionnaire (ESQ).

Data was analysed using an unadjusted mixed model.

Results: Mean age was 23.3 years, and 81 % were women. Patients showed a reduction in PCS from 35.2 points pre-intervention to 25.6 points post-intervention (N=23, $d=9.6$ (95% CI 5.2 - 13.9), $p < 0.001$, ES = 1.04), as well as a reduction in negative illness perceptions (N=23, $p < 0.001$) and maladaptive illness behaviors (N=23, $p < 0.05$). Improvements were maintained at 3 months (N=20) and 12 months (N=26) follow-up. Furthermore, patients' responses to the ESQ post-intervention showed that 95% rated the intervention as good, and 100 % would recommend the intervention to a friend (N=23).

Conclusion: Based on uncontrolled data, this new intervention was associated with significant symptom reduction as well as more adaptive illness perceptions and illness behaviors. Thus, it may have the potential to prevent chronification of PCS. In addition, the intervention was feasible and well received by the patients. An RCT is currently performed to evaluate the effect of the intervention and to further test the hypothesised mediators, i.e. illness perceptions and illness behaviour.

Diffusion Imaging Findings in US Service Members with Mild Traumatic Brain Injury and Post-Traumatic Stress Disorder

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Mild traumatic brain injury (mTBI) is a common public health concern, particularly in military service members returning from combat deployment. Though most mTBI patients demonstrate a rapid improvement in symptoms, approximately 20% go on to develop persistent symptoms that affect troop readiness and safety. Additionally, psychiatric disorders such as post-traumatic stress disorder (PTSD) complicate diagnosis and recovery from mTBI due to the high prevalence in deployed military populations. The current study utilized a clinical diffusion MRI (dMRI) scan to investigate diffusion associated with a diagnosis of mTBI or PTSD. Research suggests that changes to dMRI metrics of fractional anisotropy, mean diffusivity, axial diffusivity, and radial diffusivity may yield unique information about diagnosis and/or post-acute recovery following mTBI, but examination of these measures is limited, especially when contrasted with other recently deployed control groups.

A total of 147 (74 mTBI, 18 PTSD, 55 Orthopedic) individuals recruited from a large military treatment facility between the ages of 19 and 60 participated in the study. Participants underwent structured interview and medical record review to determine group classification. mTBI diagnosis was made according to VA/DoD criteria and all participants sustained their injury while on active duty two to 24 months prior to enrollment. Deployment related PTSD diagnosis was confirmed using the CAPS. The Orthopedic group was cleared of any history of head injury or PTSD and had returned from deployment within the past three to 24 months after sustaining orthopedic injury. A clinical 3T Siemens Verio Syngo scanner was used for data acquisition, including 64 direction dMRI scan processed using ENIGMA protocols for extraction of scalar metrics.

Analyses covaried for demographic group differences and corrected for multiple comparisons revealed a consistent pattern of lower white matter integrity in the PTSD group for FA, MD, and RD. Regions affected included primarily right hemisphere areas of the internal capsule (anterior, retrolenticular, posterior limbs), posterior corona radiata, as well as the splenium of the corpus callosum. These differences were observed in comparison to both the mTBI and Orthopedic groups, while the mTBI group did not exhibit notable white matter abnormalities compared to the Orthopedic group.

These results suggest that low-resolution scan sequences are sensitive to post-acute abnormalities associated with PTSD. Interestingly, the regional distribution of findings seen here is relatively consistent with right hemisphere-centric models of PTSD. While the mTBI group did not exhibit white matter changes, research suggests that PTSD severity may exert a more consistent signal on diffusion outcomes, particularly considering the diffuse injury nature of mTBI and limited scanner resolution used in this study. Future studies should utilize additional imaging methodologies to verify these findings and assess white matter changes associated with mTBI and PTSD in a prospective manner.

Clinician Training Competency Protocol for Administering and Interpreting CRS-R (Coma Recovery Scale- Revised)

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Intro: The CRS-r assessment is increasingly utilized and thought to be the gold standard with assessing minor changes with disorders of consciousness patients. JFK previously facilitated training of this protocol, however, to date it has become a self-study course with only an educational DVD and scoring forms. Without proper training on administration and interpretation of results, the potential to have variable scores and decreased interrater reliability exist. In our inpatient rehabilitation facility, a new program for Disorders of Consciousness was created. It was recognized that CRS-r training was needed for the clinicians. Therefore, formalized training for the CRS-r was initiated to improve the administration and understanding of the CRS-r.

Method: The following training protocol was created after review of the literature and experience.

- 1) Clinician self-study of CRS-r training DVD and reading three specified articles (“The JFK Coma Recovery Scale-Revised, Measurement characteristics and diagnostic utility” Giacino 2004, “Recent advances in behavioral assessment of individuals with disorders of consciousness” Giacino 2007, “The vegetative and minimally conscious states: Consensus based criteria for establishing diagnosis and prognosis” Giacino 2004)
- 2) Complete pretest case study of DOC patient
- 3) Observed 5 CRS-r administrations, scoring, interpretation write up, and family education from seasoned clinician
- 4) Participate in 5 CRS-r administrations, scoring, interpretation write up, and family education with supervision of seasoned clinician
- 5) Lead 5 CRS-r administrations, scoring, interpretation write up, and family education with close supervision of seasoned clinician
- 6) Lead 2 CRS-r administrations, scoring, interpretation write up, and family education with distant supervision of seasoned clinician

Pre and post-training comfort level and understanding of the CRS-r was monitored by the training clinician.

Results: More clinicians were able to administer the CRS-r and there was more comfort with performing the CRS-r and education of the family.

Discussion: This protocol has been beneficial for training experienced clinicians with minimal experience with DOC population; clinicians meet with mentors regularly during this training phase to discuss concerns, modify training, and receive feedback. In addition, clinician confidence has improved with this training protocol. Future testing of this protocol is warranted to evaluate for improvement in interrater reliability.

Conclusion: A strict training protocol involving self-study, observation, and hands on experience is needed to assure clinicians are competent to administer, score, and interpret CRS-r.

Potential of Acetylcholinesterase Inhibitors in Eliciting Visual Hallucinations When Added to Amantadine and Provigil in an Elderly TBI Patient: A Case Report

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Neurostimulant medications have often been used in off-label forms for alertness and arousal in traumatic brain injury patients. Amantadine has been shown to accelerate recovery from states of decreased consciousness after a severe traumatic brain injury. The side effects of amantadine including GI upset, blurred vision, and headaches are well-known. Due to the dopaminergic agonist properties of Amantadine, it is feasible to elicit side effects of hallucinations and psychosis.

The case reported here is of an elderly 87-year-old man who had an emergent craniotomy evacuation of a right subdural hematoma several days after a fall from a standing position at home. He presented to our brain injury acute inpatient rehabilitation unit roughly 2 weeks after his surgery. He underwent the normal phases of brain injury recovery, including post-traumatic agitation and disturbed sleep/wake cycles. With the addition of Amantadine and Provigil during the day and Trazodone for sleep at night, he improved significantly in his agitation, wakefulness and alertness. He began participating well in therapies, but continued with post-traumatic amnesia and forgetfulness.

It was with the addition and increase of Galantamine for memory impairment, and a likely underlying dementia, that he began having mental status changes and visual hallucinations. When the Amantadine and Galantamine were stopped, he began having extrapyramidal symptoms of tremor and cogwheel rigidity, suggesting dopamine withdrawal. This unique case details the possible potentiation of acetylcholinesterase inhibitors with the commonly used Amantadine in elderly traumatic brain injury patients to elicit dopaminergic toxicity.

30 Year Outcomes after Severe Traumatic Brain Injury in a Pediatric Population

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Background: The pediatric traumatic brain injury (TBI) population may have pronounced and persistent deficits in neuropsychological, behavioral, adaptive and academic outcomes. Interruption of normal developmental capabilities may occur in a pediatric TBI patient as they age, which is not appreciated in the adult TBI patient. However, long term follow up of pediatric samples has been limited. The question remains whether these deficits continue to be more pronounced and persistent years after the injury. The purpose of this study is to describe the functional outcomes of subjects less than or equal to 18 years old at the time of severe TBI (pediatric-onset) relative to those subjects greater than 18 years old at time of severe TBI (adult-onset) approximately 30 years after injury.

Methods: Thirty-two patients with severe traumatic brain injury (GCS \leq 9) who were previously enrolled in a study at a Level One Trauma center during the 1980s were re-contacted. Participants completed a detailed health questionnaire and underwent the Telephone Interview for Cognitive Status-modified (TICS-m) to evaluate cognitive function. Statistical analyses were calculated for group differences using a Pearson's Chi-Square test where all cell values remained five or above, and where this was violated Fisher's Exact test was used instead. Statistical significance was accepted as p value < 0.05 ; all tests were two-tailed.

Results: Of the 32 participants, 19 (56.25%) were over 18 years old at time of injury (mean age 30.5 years) and 14 (43.75%) were less than or equal to 18 years old at time of injury (mean age 13.7 years). Follow-up duration was 30 years (mean 29.66, median 29.00) from date of injury. Fifty-three percent of the population had abnormal cognitive status (TICS-m score \leq 32) with the mean TICS-m score for the pediatric-onset group being 29 and the adult-onset group being 34 (p=0.0852). With regard to the pediatric-onset participants, 62% had completed at least some college, 50% reported working either full or part-time, 64% handled their own finances (vs 83% of adult-onset), and 79% could climb one flight of stairs (vs 94% of adult-onset). However, patients with adult-onset TBI were more likely to report at least one arrest compared to pediatric TBI patients (p=0.048, 66% vs 31%).

Conclusion: This study provides functional outcomes of severe pediatric TBI patients 30 years after injury and compares them to their adult counterparts. Of the two groups, pediatric-onset TBI patients reported more severe functional outcomes. Though within the margin of error, the overall trend suggests there may be a difference between pediatric-onset TBI patients and adult-onset TBI patients 30 years after injury. Certainly, further research is needed to help clarify long term functional outcomes of severe pediatric-onset TBI patients and how they differ from the adult-onset TBI patient.

Disrupted Functional Connectivity in Emotional and Executive Networks in Chronic Symptom Traumatic Brain Injury

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Recent work indicates that changes in brain connectivity may partly explain the alterations in brain function after mild to moderate TBI in its chronic stage. Two separate models were constructed here to investigate the networks responsible for the most debilitating problems in chronic stage TBI.

Executive Function Network: Fifty-seven individuals were recruited from Santa Clara Brain Injury center and VA Palo Alto. There were 23 TBI patients with chronic symptoms, such as self-report memory complaints, (mean age = 46.6 yrs +/- 12.8 yrs, 9 females) and 34 control subjects (mean age = 38.6 +/- 13.9 yrs, 17 females); median time since injury 11 - 27 years. We hypothesized that chronic symptom status would correlate with altered functional connectivity within the dorsolateral prefrontal and lateral parietal cortices (executive control network). Regression analyses demonstrated that subject-reported chronic symptom status was a significant predictor of decreased connectivity in the left executive control network. Additional between-group analyses showed decreased connectivity between the left dorsolateral prefrontal cortex and the left medial temporal lobe, the left superior parietal cortex and the right superior parietal cortex of the chronic symptom group. White matter integrity, as estimated based on fractional anisotropy obtained from a diffusion MRI scan, correlated with initial injury severity but not chronic symptom status.

Emotional Network: Prior work has shown aberrant connectivity BETWEEN networks (e.g., default mode and central executive networks) in patients with TBI as compared to control groups. We hypothesized that patients with TBI would demonstrate aberrant connectivity between amygdala networks that in healthy people are normally loosely if at all connected. To examine this, we acquired discovery and replication samples from two independent datasets (Santa Clara Brain Injury Center and University of Maryland) containing resting-state fMRI in patients with moderate to severe TBI (n = 30 discovery, 14 replication) and healthy controls (n = 29 discovery, 20 replication). We first computed resting-state connectivity strength in each of the amygdala's networks using previously published networks for each participant and then compared connectivity strength within and between networks for TBI versus control groups. Overall, we found that the amygdala's connective architecture demonstrates aberrant connectivity in TBI, a finding that replicated across two independent samples. The present work illustrates two important findings: 1) A decrease in functional connectivity in the left executive control network, particularly connections with the left dorsolateral prefrontal cortex, hews more closely with chronic symptom status following TBI than injury severity, and 2) the corticolimbic circuit might be vulnerable to the chronic effects of TBI, which could help explain the social and emotional changes seen in post-concussive syndrome.

Exploring the Relationship Between Repetitive Subconcussion and Risky Behaviour

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The incidence of subconcussions in sport is exceedingly high – the average football player sustains as many as 1400 of these impacts over a single athletic season (Crisco et al., 2010). Defined as any impact to the head or torso that is below the threshold for, and without sufficient symptoms of, concussion (Bailes, Petraglia, Omalu, Nauman, & Talavage, 2013), subconcussions have become increasingly implicated in emotional and behavioural dysfunction, given the orbitofrontal cortex's susceptibility to disruption following mild trauma (Morales et al., 2005). Accumulated subconcussion has also been associated with long-term neuropathological changes, such as Chronic Traumatic Encephalopathy (CTE; Stern, Riley, Daneshvar, Nowinski, Cantu, & McKee, 2011); however, the relationship between repetitive subconcussion and behavioural symptomatology has not been adequately studied. Although early neuropathologic changes of CTE have been observed in individuals in their teens or early twenties, it remains unclear if any behavioural symptoms present at that time can be directly linked to subconcussive disruption. Indeed, athletes are found to have riskier personalities than non-athletes (Goswami et al., 2015), which may increase their risk of sustaining a head injury and account for this relationship.

To address this issue, the current study examined the relationship between subconcussive impact exposure (SIE) and risky behaviour, independent of athletic status. Using a cross-sectional design, participants completed a questionnaire package in the Jack and Nora Walker Lifespan Development Centre testing facilities. Specifically, 230 Brock University students completed the Self-Report Psychopathy Scale III (SRP-III; Paulhus, Hemphill, & Hare, 2009), the Sensation Seeking Form 3 (SS-F3; Zuckerman, Eysenck & Eysenck, 1978), and the Everyday Living Questionnaire (ELQ; Baker & Good, 2008). SIE (a composite measure derived from indicators such as athletic participation history) was found to significantly predict scores on the Erratic Lifestyle subscale of the SRP-III, over and above athletic status (athlete vs. non-athlete), indicating that greater subconcussive exposure is associated with more reckless and impulsive behaviour. Moreover, SIE significantly predicted Thrill and Adventure-Seeking on the SS-F3, independent of athletic status; and predicted how many drinks per week students consumed on average. That is, those with greater SIE endorsed more thrill-seeking behaviour and reported greater alcohol consumption per week. Taken together, these findings indicate that cognitively competent university students with a protracted history of SIE engage in riskier activities than those with less SIE. This is consistent with research showing that SIE is associated with physiological underarousal (i.e., reduced electrodermal activation; Gallant, Alcock, & Good, 2016) – a profile similar to that of mild head injury (Baker & Good, 2014). These differences in risky behaviour may be indicative of early neurodegeneration; however, further research is needed to elucidate whether the relationship between SIE and behavioural symptoms is mediated by arousal mechanisms.

Development of a Best Practice Model in Acute Concussion Care: The Hull-Ellis Concussion and Research Clinic at the Toronto Rehabilitation Institute

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Introduction: Research in the area of Sport Related Concussion has yielded a wealth of translational research data over the past 10 to 20 years. However, there is a lack of research relevant to patients with acute concussion who are not athletes. The Hull-Ellis Concussion Care and Research Clinic at the Toronto Rehabilitation Institute was designed from the outset to prospectively characterize and understand factors associated with concussion in a cohort of the general population. Variables collected include: mechanism of injury (MOI), symptoms at first visit, the 'normal' recovery trajectory, gender differences, modifiers of recovery, neurocognitive and psychological dysfunction and recovery, balance impairment, etc. Data collection occurs simultaneously providing participants with routine medical care, monitoring and follow-up.

Methods: Patients/study participants diagnosed with concussion from 3 partnered ERs in downtown Toronto who meet specific inclusion criteria (e.g., GCS=15; 17-85 years, not admitted to hospital, no positive imaging findings) are referred to the Hull Ellis Clinic immediately after attending the ER. Each patient is contacted by the Clinic Coordinator within 72 hours of referral, with admission to the clinic within one week of referral. Comprehensive multifactorial NIH common data elements are collected at the first visit. Patients are then offered an opportunity to participate in a prospective research REB-approved study, where data on multiple variables are collected at 2, 3, 4, 5, 6, 7, 8, 12 and 16 weeks. Data elements specific to cognitive functioning, balance, psychosocial variables, symptoms, physician related assessments and date of discharge are captured. During the data collection sequence, each patient also receives treatment by a physician, including medical assessment, education, symptom management support, routine monitoring and regular follow-up. Participants are reviewed at 8 weeks; those who remain symptomatic beyond 16 weeks are offered further treatment outside of the research paradigm.

Preliminary Results: 269 patients have been referred to the Clinic since February 5, 2016, of whom n=126 (Female=69; Male= 57) met admission criteria and were admitted for a first visit within one week of referral (Mean=5.9 days). 91 patients (F=49, M=32) with an average age of 32.9 years (SD=3.4 years) agreed to participate in data collection beyond Week 1. Falls (33%) were the most frequent MOI followed by Sports (30%), MVAs (20%), Assaults (8%) and Other MOI (9%). Most frequently reported symptoms include headache, fatigue and poor concentration at Week 1 compared to headache, sleep disturbance and fatigue at Week 8. Of n=34 patients enrolled in the study at Week 8, only 4 (12%) remained symptomatic and/or had objective findings related to concussion. Reduction in symptoms, not objective cognitive measures is associated with recovery.

Future Directions: Continued subject enrollment in this prospective study will help further characterize concussion in a general population who present to the ER.

Neurocognitive Effects of NMDA Receptor Encephalitis: Case Study of an 11 Year-old Female

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Abstract: Areas of the brain that are responsible for language, memory, movement, and emotional functioning are commonly affected in patients with NMDA receptor encephalitis. Early diagnosis and rehabilitation are essential for the long-term optimal recovery of these patients. In this presentation, we will review the symptoms and rehabilitation course of a young girl affected by NMDA receptor encephalitis. Our discussion will focus on her neurocognitive functioning at illness onset, as well as at follow-up visits.

Proposal: Anti-N-Methyl-D-Aspartate (NMDA) receptor encephalitis is a relatively new disorder that was first recognized in 2007 as an autoimmune disease. It impacts both sexes and all ages, although it is most common in young adults and children (Moura et al, 2016). Most patients affected by this disease develop a complex syndrome, initially presenting with behavioral disturbances and rapidly progressing to develop speech problems, memory deficits, movement disorders, seizures, dysautonomia, and respiratory dysregulation (Macafferri et al, 2016). Several studies indicate that despite substantial clinical remission after anti-NMDA encephalitis, most patients continue to exhibit persistent cognitive deficits several years later (Carsten et al, 2012).

We present the case of an 11-year-old girl who was healthy prior to presenting acutely to the emergency department with symptoms of fever, nausea, vomiting, respiratory distress, progressive muscle weakness, and altered mental status. The patient had an extensive workup, including MRI and CT scans of the brain, which were unremarkable. She underwent multiple EEGs, which revealed slow wave activity over the left central region. CSF was positive for anti-NMDA receptor antibody IgG. In addition to her altered mental status, the patient also experienced behavioral changes, decline in her expressive language skills, and social withdrawal. She completed immunotherapy and steroid treatment with positive effects in her presentation before being transferred to a rehabilitation hospital.

Upon admission to our rehabilitation unit, the patient presented with considerable cognitive and motoric challenges. Specifically she exhibited severe expressive aphasia characterized by an inability to use fluent speech to communicate. She was able to utilize one-word utterances at first and her speech had a dysarthric quality. Although the length of her speech utterances improved over the course of treatment in the acute rehabilitation, she continued to have difficulty with complex discourse and pragmatic language skills. Additionally, she demonstrated short-term memory difficulties, as well as struggles with attention and associated executive functioning skills. Motorically, she was noted to have challenges with initiating and stopping movements. In this presentation, we will be discussing the patient's language, behavior and cognitive changes over the course of her rehabilitation stay, as well as her status at follow-up appointments after discharge.

Trajectory of Functional Independent Measurements During Five-Years Following Moderate and Severe Traumatic Brain Injury

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Objectives: The disability following traumatic brain injury (TBI), particularly for persons with moderate-to-severe injuries, could be multidimensional including cognitive and physical difficulties that could potentially last for lifetime. To better understand the long-term functional recovery and facilitate effective rehabilitation interventions in this population, this study intends to identify and characterize the trajectory of functional recovery in the first five-years after injury for patients with moderate-to-severe TBI.

Methods: Patients with moderate-to-severe TBIs who were admitted at Oslo University Hospital between 2005 and 2007 were included in the study. Inclusion criteria were age 16 - 55 years, residing in the east region of Norway, and admitted with ICD-10 diagnoses S06.0–S06.9 within 24 hours of injury. Patients' baseline characteristics and lengths of acute/post-acute hospital stays were documented, and the Functional Independence Measure cognitive (FIM-Cog) and motor (FIM-M) subscales (5 and 13 items respectively, scores 1-7; the higher scores representing more independence) were recorded at 3 months, 1 year, and 5 years. SAS Proc Traj procedure was used to identify the subgroups of patients who shared the same trajectory of functional profile during the 5-year period. Combinations of substantive knowledge and Bayesian Information Criterion (BIC) and logged Bayes factor ($2\Delta\text{BIC}$) were used to determine the trajectory groups. Chi-square Test or ANOVA was used to compare the characteristics of the trajectory memberships. Bonferroni correction was applied to reduce type I errors due to multiple comparisons.

Results: The original study included 133 eligible participants. This study excluded 12 subjects who later withdrew or were lost to follow-up. For the FIM-Cog measures, four trajectories of functional recovery were identified over time: 4.1% and 54.6% patients had a steady total assistance needed ($5.0\pm 0 - 5.0\pm 0$) or modified or completely independence ($32.8\pm 2.3 - 34.7\pm 1.0$) cognitive measurements at all three follow-up points; 12.6% patients who started with low 3-month FIM-Cog measurements (8.9 ± 3.5) had a speedy improvement at 1-year (20.6 ± 4.6) and 5-year (28.3 ± 3.8) follow-ups; and 28.7% patients who began with supervision needed (27.0 ± 3.8) 3-month measurements also had improvement to modified independence at 1-year (29.9 ± 3.1) and 5-year (31.1 ± 2.3) follow-ups. Similarly, for the FIM-M measures, three trajectories of physical recovery were identified over time: 8.2% patients who started with total assistance needed 3-month FIM-M measurements (13.6 ± 1.5) had some improvement at 1-year (17.9 ± 8.8) and 5-year (21.0 ± 17.9) follow-ups; 9.2% patients with moderate assistance 3-month measurements (35.8 ± 14.5) had a speedy improvement at 1-year (75.5 ± 12.4) and continued to 5-year (85.5 ± 8.1) follow-ups (modified or completely independence); and the majority of patients (82.6%) had relative stable FIM-M measurements ($89.0\pm 3.6 - 90.8\pm 1.0$) over the three follow-up points.

Conclusion: Patients following moderate-to-severe TBI could have different recovery trajectories. Identifying and characterizing the trajectory memberships will better enable effective rehabilitation programs to meet the long-term needs of this patient population.

Social-Cue Perception and Mentalizing Ability Following Traumatic Brain Injury: A Human-Robot Interaction Study

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Research studies and clinical observations of individuals with traumatic brain injury (TBI) indicate marked deficits in perceiving social information and integrating it into judgments about the affective and mental states of others. Prior research has primarily relied on video-based, third-person paradigms to study these processes, and whether or not individuals with TBI are able to recognize and integrate second-person social information in dynamic interactions remains an open question with significant research and clinical implications. Studying mentalizing in dynamic interactions, however, requires overcoming the methodological challenge of achieving sufficient experimental control in a realistic dynamic interaction setting. To overcome this challenge, the current study utilized a human-robot-interaction paradigm in which study participants were expected to make judgments about a robot's mental state from the precisely controlled behaviors of the robot and integrate these judgments into their performance in the experimental task. We hypothesized that individuals with TBI would display impaired judgment, and thus worse performance in the task, compared to their healthy controls.

To test our hypothesis, we collected data from 153 participants, including 74 individuals with moderate-severe TBI and 79 demographically-matched healthy comparisons (HC). Participants played nine rounds of a guessing game in which a NAO humanoid robot selected one of several household items and asked the participant to guess its selection by asking questions that it can only answer with "yes" or "no," such as "Is the item red?" In four of the trials, the robot signaled its selection by producing a short glance toward the item before answering the participant's first or second question. The number of questions that the participant asked to correctly guess the robot's selection served as a behavioral measure of mentalizing ability. Our analysis showed a significant main effect of our manipulation in the number of guesses, but, contrary to our hypothesis, there was no significant interaction between our manipulation and group. Comparisons within each group showed that individuals with TBI asked marginally fewer questions when the robot's gaze "leaked" information, while the robot's behavior did not affect the performance of healthy controls. Our data provides some evidence that individuals with TBI can perceive, correctly recognize, and integrate social information, particularly isolated gaze cues, in dynamic situations. Our findings highlight a need for further research to understand why the social-cue perception and mentalizing abilities shown by participants in our study may not translate into social interactions in day-to-day settings.

Biomechanical Modeling of Youngsters Head Impact by Sporting Balls

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Sports-related head impacts have led to many brain injuries. Although such impacts by a sporting ball may not be counted as a concussion for adults, however it might be more damaging for youngsters. In this study, a biomechanical simulation is to be conducted to analyze brain damages of different ages subjected to basketball hits. Employing a finite-element biomechanical head model technique, an adult and a teenager head and brain are modeled subjected to impacts by basketball hits from front and side directions at different speeds. The response of the brain will be monitored and assessed. In particular the head acceleration, brain intracranial pressure (ICP) and shear stresses and strains under impact speeds of 10, 15 and 20 m/s will be measured. The results show basketballs of equivalent impact speeds cause significant effects to the youth brains than the adult ones. The findings indicate that the condition of mild head impact for the adult could be considered as somehow severe head impact for youngsters which possibly could lead to brain injury. The study can ultimately correlate the deformation of the brain with the brain size impacted by sporting balls. In particular, impacts to youngster heads particularly with multiple sub-concussive head impacts by sporting balls might be recognized as a cause of brain injury or malfunction.

Keywords: finite-element method, sub-concussive head impact, brain injury, biomechanics.

Sex Differences in the Effects of Exposure to Repetitive Subconcussive Head Impacts in Collegiate Ice Hockey Players

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Objective: Previous research has shown worse neurocognitive and clinical outcome after repetitive subconcussive head impacts (RSHI) among female athletes when compared to males; yet, a structural correlate has not been identified. The aim of this study is to identify and to characterize sex differences in the effects of exposure to RSHI during a season of collegiate ice hockey on brain structure.

Methods: 25 collegiate ice hockey players (14 males and 11 females, 20.6 ± 2.0 years) were part of the Hockey Concussion Education Project (HCEP). Study participants underwent diffusion-weighted magnetic resonance imaging (dMRI) before and after the Canadian Interuniversity Sports (CIS) ice hockey season 2011/2012. Whole-brain tract-based spatial statistics (TBSS) were used to compare pre- and postseason imaging in both sexes. In this context, postseason dMRI was subtracted from preseason dMRI in each subject to create individual delta maps, which were then compared between male and female players to evaluate sex differences in fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD).

Results: After one season of play, a significant decrease in FA values in females (0.0268; $p=0.0010$) and a statistically insignificant increase in males were observed ($p=0.2$). Furthermore, females showed a significant increase in MD over one season (0.0002; $p=0.0011$) whereas males showed no change in MD ($p=0.9$). Significant differences in FA and MD changes between sexes were primarily located within the superior longitudinal fasciculus, the internal capsule, and the corona radiata of the right hemisphere. Importantly, none of the enrolled subjects suffered from a concussion during the 2011/2012 CIS season.

Conclusions: Previous research has shown that RSHI during a single ice hockey season can result in significant alterations of the brain's white matter. The results of this study further suggest sex differences in response to RSHI at a microstructural level. Future studies need to investigate the association with previously observed neurocognitive deterioration and poorer clinical outcome among female athletes, which may be the result of increased vulnerability of the female brain to RSHI.

Disrupted Sleep Predicts Next Day Agitation in Moderate to Severe Traumatic Brain Injury

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Objectives: The present study is part of a larger ongoing exploration of the impact of disrupted sleep in the recovery from moderate to severe brain injury. The purpose of this study is to investigate the relationship among nighttime wakefulness after sleep onset (WASO), sleep efficiency (SE), number of wake bouts (NWBs), and daytime agitation.

Methods: All individuals admitted for TBI rehabilitation were clinically monitored with actigraphy for the first 72 hours (Actiwatch Spectrum Phillips-Respironics). The actigraph default settings were used to collect the data (30-second epochs with medium sensitivity, 40 activity counts per epoch). Retrospectively, actigraphy data was abstracted from 40 patients. Each patient's average WASO, SE, and NWBs for the 3-day period was calculated using the device software (Respironics Inc - Actiware version 6.0) for the sleep interval of 2100-0700. WASO is the product of the total number of epochs over the sleep interval and the epoch length in minutes. NWBs is the total number of continuous blocks of epochs where each epoch is scored as wake for the interval. Twice daily Agitated Behavior Scale (ABS) scores were obtained and the average 3-day score was calculated for each patient. Linear regression analyses controlling for length of stay in rehabilitation (LOS) and time from head injury to rehabilitation were conducted to determine whether 3-day averages of WASO, SE and NWBs predicted 3-day average ABS scores.

Results: Seventy-seven percent of the participants were male and the mean age was 37 years (range, 17-68 years). The mean time since injury was 38 days and the mean LOS was 53 days. The mean 3-day average for WASO was 83.5 minutes, mean SE was 71.9%, mean NWBs was 43 and mean ABS score was 19.7. Average 3-day WASO significantly predicted 3-day average ABS scores above and beyond LOS and time since injury ($R^2=.43$, $F(1,28)=5.59$, $p=.025$). Average 3-day NWB also significantly predicted the mean 3-day average ABS scores above and beyond LOS and time since injury ($R^2=.48$, $F(1,28)=7.64$, $p=.010$). As WASO and NWBs increased, agitation also increased. Sleep efficiency was not significantly correlated with ABS scores.

Conclusion: Disrupted sleep is highly prevalent during acute rehabilitation. This study supports our previous findings that poor sleep is associated with increased agitation scores and additionally suggests that WASO and NWBs may be better predictors of agitation than SE. Future studies should consider using WASO and NWBs when investigating the effect of sleep quality on agitation in the TBI population.

Long-term Health Outcomes Associated with Traumatic Brain Injury in Post-9/11 Veterans: TBI Severity or Comorbidity?

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Objectives: To determine how long-term outcomes relate to self-reported symptoms, health status, and measures of community reintegration differ among Iraq and Afghanistan veteran (IAV) with and without traumatic brain injury (TBI).

Methods: A prospective longitudinal survey was conducted with individuals from a longitudinal cohort of IAV who entered VA care between 2007 and 2009, and who had at least three years of care at the end of 2011. TBI severity was classified based on a hierarchy with data sources that have more clinically rich data prioritized as follows: 1) Department of Defense Trauma Registry (Glasgow Coma Scale, ICD-9-CM codes), 2) VA Comprehensive TBI Evaluation (duration of loss of consciousness, alteration of consciousness, and post-traumatic amnesia), and 3) ICD-9-CM codes included in VA care. Comorbidity was defined using latent class analysis which identified 5 latent classes that were similar for men and women (Healthy, Chronic disease, Mental Health, Pain, Polytrauma Clinical Triad [PCT; TBI, Mental Health and Pain]) and two latent classes that were identified in men only: Minor Chronic (low but not trivial proportion with hypertension, obesity, lung disease) and PCT+Chronic disease. We selected a random sample stratified by these trajectories with approximately 800 individuals sampled from each trajectory (N = 9358). Surveys were administered using a Dillman methodology in September 2014-April 2015. Measures included current health, somatization (PHQ-15), current pain, mental health symptoms, and measures of combat exposure. We used analyses of variance with Bonferroni adjustment for multiple comparisons to compare outcomes among individuals across TBI severity, and generalized linear models to determine if there were differences on these outcomes after controlling for comorbidity trajectories.

Results: Response rate for the survey was 23% (n = 2046). Individuals with TBI had significantly lower scores on all measures than individuals without TBI; individuals with moderate/severe TBI had scores indicating significantly more pain, depression, and PTSD than those with mild TBI. After controlling for comorbidity and combat exposure, depression scores were significantly higher for those with moderate/severe TBI compared to those with no TBI and mild TBI, and somatization was significantly higher for those with moderate/severe TBI compared to no TBI.

Conclusions: After adjusting for comorbidity and combat exposure there were no differences between those with mild TBI and no TBI on mental health or physical health measures, but significant differences persisted between no TBI and moderate/severe TBI for depression and somatization which suggests that TBI related depression for those individuals. More severe injuries in those with moderate/severe TBI may result in broad somatic pain that cannot be distinguished in a simple pain score.

Treatment Efficacy for TBI In Children: Importance of Detailed Evaluation and Individualized Family-Based Rehabilitation Program

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Objectives: With the target of accessing treatment efficacy for TBI, we recognize the importance of a detailed evaluation and description of each stage of recover, planning on an individual program for the child and its family.

We also aim to find a correlation in between radiological, neurophysiological, functional and psychological aspects.

Methodology: We are going to describe a case from a series of children who are being studied prospectively: a 7 years old boy who was severely brain-injured on a car accident on February 2016. Initially, Glasgow coma scale was 7; he needed decompressive craniectomy and a ventriculoperitoneal shunt. He was discharged from the emergency hospital 3 months later and came to SARAH 5 months after the accident.

Results: At first, GMFM scale was IV, WISC at the average and we decided for an internal and intensive 8 weeks rehabilitation program with an experienced interdisciplinary team. He also was evaluated by Vineland and PEDI scales, besides PegBoard. Pictures and videos register his improvement.

Now, he is on an external program 3 times a week, in group or individual activities that include physiotherapy, daily activities training, swimming, electronic games, psychomotricity sessions, with pscopedagogical support. He is visibly improving his motor function, and follow-up is showing impulsivity, low self-regulation, disinhibition and impaired memory function.

"His MRI, including DW, CSD tractography and spectroscopy showed frontal and parietal hemorrhage, parenchymal contusions, areas of reduced levels of Naa and less fibers of right corticospinal tract and of the corpus callosum". His VEEG showed global waves lentification.

On the next weeks his evaluation will be completed with sequential images, evoked potential responses and blood markers (APOE, MAPT, BDNF).

Once his locomotion is improving, and since December 2016, he is able to use a walker, part of the time, on the next months we probably will do a complete Gait Analysis and Computerized Dynamic Posturography.

One year after the accident, he is able to return to regular school, and his mother will be back to work. Our team will continue following them closely, to increase the chances of success.

Conclusion: Tests selected by an experienced team are able to identify the points that better need to be addressed and reinforce strong and potential aspects, that will increase treatment efficacy and help to rebuild the patients self-esteem. Family participation and support are essential to develop strategies that will reduce the stress level for everyone, increasing quality of life.

Still is necessary a long way before we understand the total correlation in between neuroimage, neurophysiology and all the aspects above.

Reactions to Traumatic Brain Injury: A New Post-Concussive Symptoms and Observations Checklist for Early Childhood

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Traumatic brain injury (TBI) sustained in early childhood can have detrimental effects on development and result in adverse outcomes. Converging evidence suggests that children below the age of 5 (i.e., preschoolers) are at risk for persistent problems following TBI because of the vulnerability of the developing brain. Post-concussive symptoms (PCS) are common after TBI and may include physical (e.g., headache), cognitive (e.g., forgetfulness) and behavioral (e.g., irritability) changes. These symptoms are challenging to identify in preschoolers because of their limited verbal abilities. Typical manifestations of PCS may also differ from those known to occur in older individuals. Adequate documentation of PCS after early TBI is currently limited by the absence of validated PCS measures for children 0-5 years. To address this, we developed REACTIONS (Report of Early Childhood Traumatic Injury Observations & Symptoms), a parent-report questionnaire designed to document the presence and severity of PCS and their associated manifestations in preschool children.

Methods: Domain content was partially derived from three existing PCS measures (PCS-Interview, Mittenburg et al., 1997; HBI, Barry et al., 1996; PCS-Inventory, Sady et al., 2014) validated in older children. Items not applicable to preschoolers were discarded and others were adapted to reflect non-verbal and age-appropriate manifestations. New items, specific to young children, were also created based on parental observations derived from empirical studies of preschool TBI and from clinical observations. To ensure content validity, REACTIONS was reviewed by an expert consultation committee composed of parents of preschoolers with TBI, clinicians, researchers, research assistants and nurses from two urban paediatric hospital centers. The resulting inventory is composed of three main domains: Cognitive (3 subscales: attention/concentration, memory, reduced speed of processing), Physical (8 subscales: headache, nausea, balance, fatigue, sleep, vision, sensitivity to light and noise) and Behavioral (5 subscales: irritability, mood/motivation, anxiety, regression, comfort) symptoms.

Validation process: Preliminary results from a pilot study with preschoolers presenting with TBI indicates that parents endorsed the new items, and that they attributed higher PCS scores than parents of children without TBI. Current validation work aims to use REACTIONS in ongoing preschool TBI cohorts, perform factor analysis to discard non-pertinent items, and evaluate internal consistency and reliability. Correlations between REACTIONS and existing measures of PCS suggest initial construct validity. REACTIONS has the potential to contribute to research and clinical follow-up pertaining to TBI in children 0-5 years by providing accurate profiles of PCS in the acute and long-term phases post-injury.

Predicting Mortality after Traumatic Brain Injury: A Prognostic Model Based on Admission Characteristics

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Introduction: Traumatic Brain Injury (TBI) is a public health problem. It is a pathology that causes significant mortality and disability. Different models have been developed in order to predict the neurological outcomes. Marshall computed tomographic (CT) classification is widely used as a predictor of outcome. However, this grading system lacks useful variables to predict the outcome of the patient, which are subarachnoid/intraventricular hemorrhage, extradural haematoma, and extent of basal cistern compression. We aimed to develop and validate a practical prognostic model that include all the variables above and predict death at six months after TBI.

Methods: Prospectively collected individual patient data were analyzed. The CT model included midline shift over 5 mm, normal, compressed or absent basal cisterns, subarachnoid bleeding, basal bleeding, intraventricular bleeding, contusion and epidural, subdural or intracerebral haematoma. We considered predictors available at admission in logistic regression models to predict mortality at 6 months after TBI. The performance and accuracy of several model was assessment using the Spearman's rank correlation coefficient and the area under the receiver operating characteristic curve (AUC).

Results: A total of 145 patients were recruited for study, median age 33 (15 -85) years, and 86.89% were male. The overall mortality was 24.82%. The median GCS of patients was 6 (3-12). The Marshall CT classification discrimination was AUC= 0.646, Helsinki CT Score discrimination was AUC= 0.724, Rotterdam grading discrimination was AUC= 0.735, all these with a low correlation with the outcome (Spearman's rho <0.40). Our model showed the best performance and correlation with 6-month mortality: AUC= 0.7755, Spearman's rho 0,4201, p= 0.000.

Conclusions: Our prognostic mortality CT model showed a great performance and accuracy and can be used to obtain valid predictions of relevant outcomes in patients with TBI.

Treating Disrupted Sleep on a TBI unit with a Sleep Hygiene Intervention: A Feasibility Study

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Objective/Method: This pilot trial is an attempt to ameliorate disrupted sleep following moderate to severe brain injury via a sleep hygiene intervention during inpatient rehabilitation. The primary purpose of the study is to test the feasibility of implementing a controlled trial with minimization allocation targeting sleep hygiene in an inpatient rehabilitation setting. As such, the intent of this pilot trial is to test the process, resources, management, and scientific basis of the study, rather than test hypotheses with inferential statistics.

Consenting individuals with sleep efficiency $\leq 75\%$ on initial actigraphy screening were assigned to either a sleep hygiene protocol (SHP) or standard of care (SOC). The sleep intervention was developed based on the work of Moran and colleagues employing concepts of both sleep restriction and stimulus control. The SHP consists of five principle components: (1) improved nighttime sleep environment, (2) increased daytime activation, (3) enhanced circadian stimuli, (4) consistent morning wake time and ADL routines each day, and (5) no caffeine intake after 12:00pm. The SOC undergoes all typical rehabilitation care with no specific attempt to influence sleep or circadian patterns. In both groups, participants' sleep is monitored with 24-hour actigraphy and bi-hourly staff ratings on the Makley Sleep Scale (MSS). Nursing staff rates agitation twice daily and cognitive function is monitored three times per week until emergence from post-traumatic amnesia.

The overall feasibility of this pilot trial is evaluated on multiple levels. To assess the process of the study, we look at recruitment rates, refusal rates, and eligibility criteria. To assess time and resource problems, we evaluate capacity and issues related to use of the study equipment (i.e., Actiwatch). To address potential human and data management problems, we continually monitor challenges experienced by clinical staff, data management, fidelity of the treatment protocol, and variability in our outcome measures. Finally, to continually evaluate the scientific rigor of our sleep hygiene intervention, we assess whether or not patients are responding to the sleep hygiene protocol and the fidelity of the intervention.

Results: Over the course of six months four participants have been enrolled in the study, with two participants in the SHP and two participants in the SOC. To date, there have been no withdrawals from the study. Current fidelity for the SHP is 89%. Due to an insufficient recruitment rate, the eligibility criteria were recently expanded.

Conclusion: Based on the current findings, a controlled trial of a SHP is feasible with modifications. Given the inherent nature of feasibility studies, adaptation of the study protocol is possible to ensure that it can be conducted while maintaining scientific rigor. Most importantly, this study exemplifies why it is necessary to conduct a pilot trial prior to implementing a fully powered randomized controlled trial.

Headache Prevalence 30 Years After Severe Traumatic Brain Injury

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Background: Headache is the most common pain complaint following traumatic brain injury (TBI), and has been reported in up to 30-90% of patients. However, the time course and contributing factors for headache following severe head trauma are not well established. Most clinical studies report that headaches occur less frequently after severe TBI as compared to mild TBI. This inverse relationship is often attributed to under reporting of symptoms by patients with severe TBI due to associated higher rates of cognitive impairment. However, supporting evidence of this claim is limited. Here we describe subjects' report of headache three decades after severe TBI and examine potential association with cognitive status and psychological comorbidities.

Methods: Thirty-two patients with severe traumatic brain injury (Initial GCS \leq 9) who were previously enrolled in a hyperbaric oxygen study at a Level One Trauma center during the 1980s were re-contacted. Participants completed a detailed health questionnaire and underwent the Telephone Interview for Cognitive Status-modified (TICS-m) to evaluate cognitive function. All analyses were done using a Pearson's Chi-Square test except when one cell dropped below a value of five then a Fisher's Exact Test was used. Statistical significance was accepted at a p value $<$ 0.05 and all tests were two-tailed. All analyses were completed with SAS version 9.4.

Results: Follow-up duration was on average 29.66 years (median=29.00) from date of injury. Headache was reported in 39% of patients and those with headache were significantly more likely to have comorbid depression (p=0.02, 66% vs. 22%) and insomnia (p=0.008, 92% vs. 42%). Self-reported anxiety was not associated with headache (p=0.184) but was present in 33% of those with headaches vs. 11% of those without. Nearly 53% of the subjects had abnormal cognitive status (TICS-m score \leq 32). There was no correlation between complaint of headache and level of cognition (p=0.55). Level of cognition did not correlate with patient report of depression (p=0.52), anxiety (p=0.67) or insomnia (p=0.65).

Conclusion: Headache is a prominent pain complaint decades after severe TBI and may be more chronic and persistent than previously thought. Previous studies report that headaches occur less frequently after severe TBI, as opposed to mild TBI, and may be attributed to impaired cognition. However, our analysis demonstrates the level of cognition following severe TBI does not correlate with report of headache, depression, anxiety or insomnia. Headache was correlated with depression and insomnia, and may lead to the development of these comorbid conditions within this population. Further research is needed to examine mechanisms of pain processing and perception following severe TBI to help facilitate management and functional recovery.

Risk factors to Predict Mortality for Patients with Spontaneous Subarachnoid Hemorrhage

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Introduction: Subarachnoid hemorrhage (SAH) is a pathology associated with high mortality and unfavorable neurological outcome, lifestyle and other factors can be relevant in the prognostic for this pathology, identified which are the most important factors, prevent and resolved some of these factors could improve the outcome of the patients. We aimed identified the most important risk factors for mortality in patients with SAH.

Methods: This is a retrospective study of patients with spontaneous SAH who presented to our hospital in the period from 2014 to 2015. All the patients were followed in order to determine the mortality at 28 days and neurological unfavorable outcome at 6 months. For statistic analysis were used the Shapiro Wilks, Chi2, MannWhitney tests and the ORs were calculated by logistic regression models for the multivariate analysis.

Results: A total of 101 patients with spontaneous SAH were recruited for the study, the median age was 62 (47-71) years old and 66% of the patients were women. The overall mortality was 39%, the risk factors associated with mortality were female (OR=3,64 p=0,025), glucose over 180mg/mL at hospital ingress time (OR=1,01 p=0,043), non-reactive pupils (OR=13,33 p= 0,001), midline shift over 5 mm (OR=11,79 p=0,002) and hydrocephaly (OR=3,36 p=0,044) and the risk factors associated with an unfavorable neurological outcome were midline shift over 5mm (OR=5,265 p=0,038), intraventricular hemorrhage (OR=4,67 p=0,000) and cerebral edema (OR=6,50 p=0,018).

Conclusions: Spontaneous SAH is a heterogeneous pathology associated with poor outcome for the patient, we found that the most important risk factors for mortality in patients with spontaneous SAH are glucose over 180mg/mL at hospital ingress time, be female, have nonreactive pupils, hydrocephaly and midline shift over 5 mm and the most important risk factor to an unfavorable neurological outcome are shift midline over 5mm, have a intraventricular hemorrhage and cerebral edema.

Neural Mechanism Underlying Facial-Affect Recognition Deficits in TBI: An fMRI Study

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Facial-affect recognition is a complex cognitive process, requiring both the detection and interpretation of salient perceptual cues. Although deficits in facial-affect recognition have been reported in up to 40% of individuals with moderate-severe traumatic brain injury (TBI), it remains unclear whether the breakdown occurs at the perceptual level, at the interpretative level, or at both, and little is known about the underlying neural mechanisms. In the current study, we used functional magnetic resonance imaging (fMRI) to measure patterns of brain activity while individuals with moderate-severe TBI and demographically-matched healthy comparison (HC) participants engaged in a facial affect recognition task including an emotion matching condition (aimed at measuring the ability to detect salient facial configurations) and an emotion labeling condition (designed to measure the ability to connect perceptual cues with semantic emotional knowledge). We hypothesized that individuals with TBI would perform worse than the HC group overall and that the disruption in emotion-affect recognition may be reflected in altered brain activity in brain regions important for high-level visual perception and/or affective processing.

Analysis of behavioral data indicated that individuals with TBI significantly underperformed HC on both labeling and matching emotion recognition tasks. Analysis of fMRI data revealed that while engaging in both emotion matching and emotion labeling individuals with TBI displayed significantly higher activation than HC in prefrontal regions, including the bilateral ventromedial prefrontal cortex and frontal pole. Interestingly, in both conditions individuals with TBI showed significantly lower activation than HC in primary and secondary occipital visual regions, including the left fusiform face area. Our data suggests that both perception and interpretation of facial emotional cues are impaired in individuals with TBI. In addition, our results reveal that facial affect recognition impairment following TBI is associated with abnormal patterns of activation in brain areas that have been found to be involved in emotion recognition in healthy populations, and indicate a possible neurobiological mechanisms underlying emotion recognition impairment following TBI.

Brain Vital Signs Demonstrate Sub-concussive Impairment after A Single Season of Ice Hockey

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Background: While concussions occur frequently during contact sports such as ice hockey, there is increasing awareness regarding the consequences of repetitive sub-concussive impacts. We have recently focused on translating well-established event-related potentials (ERPs) derived from electroencephalography (EEG) into a portable platform for objective longitudinal monitoring of brain function. Brain vital signs is an integrated hardware and software framework that involves a linear transformation of the N100 ERP for auditory sensation, the P300 for basic attention, and the N400 for cognitive processing. This framework was applied in the current study to assess potential changes in brain function of non-concussed athletes over the duration of a regular hockey season.

Methods: Ten healthy ice hockey athletes (age 17-21) were scanned once at baseline (prior to season) and again after their season ended. None received a diagnosed concussion during the season. At each session, binaural auditory stimuli were presented while the athletes were scanned using a portable 8-channel EEG system. ERPs were derived from the data using standard processing approaches including filtering (1-20Hz), ocular artifact correction, segmentation, and conditional averaging. Three brain vital signs were evaluated for both response time and amplitude (6 total measures). Independent two-tailed paired t-tests compared the changes in each measure from baseline to post-season. P-values were adjusted with Bonferroni correction to account for multiple comparisons.

Results: Results showed significant changes from baseline to post-season in 4 brain vital signs measures. The N100 index of auditory sensation showed a delay in response time ($p < 0.05$) and reduction in amplitude ($p < 0.05$). The P300 index of basic attention showed reduced amplitude ($p < 0.05$). The N400 index of cognitive processing showed a response delay ($p < 0.001$).

Discussion and Conclusion: In the absence of a diagnosed concussion, the brain vital signs framework captured significant group-level changes in brain function after a single season of ice hockey. This is a quantitative demonstration of the cumulative effects of repetitive sub-concussive head impacts, undetected concussions, or potentially a combination of both. The findings show that the brain vital sign framework provides a clinically relevant approach to evaluate the effects of sports-related brain injury. Ongoing work is exploring the brain vital sign characterization between sub-concussive and concussive events to better understand the conceptual distinction, including comparisons with existing concussion management protocols. Future work will incorporate machine learning techniques to delineate patterns of injury and subsequent return-to-play protocols.

Comparison of Predictability of Marshall, Rotterdam and Helsinki CT Scan Scoring System in Determining Early Mortality after Traumatic Brain Injury

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Introduction: Traumatic Brain Injury (TBI) is a public health problem. It is a pathology that causes significant mortality and disability. Different models have been developed in order to predict the neurological outcomes. Marshall computed tomographic (CT) classification is widely used as a predictor of outcome. However, this grading system lacks useful variables to predict the outcome of the patient, which are subarachnoid/intraventricular hemorrhage, extradural hematoma, and extent of basal cistern compression. Newer classifications like Rotterdam and Helsinki CT scores include the above variables and seem to be very similar, however these classifications have not been validated widely. We aimed to compare the discriminatory power of all the grading systems in a university hospital in Colombia.

Methods: This is a retrospective study of patients with moderate and severe TBI (Glasgow coma scale (GCS) 3–12) who presented to our hospital. All the patients were followed up for 6 month to determine early mortality and neurological unfavorable outcome. The discriminatory power of each grading system was determined using area under the receiver operating characteristic curve (AUC).

Results: A total of 145 patients were recruited for study, median age 33 (15 -85) years, and 86.89% were male. The overall mortality was 24.82%. The median GCS of patients was 6 (3-12). There was good correlation between Marshall, Rotterdam and Helsinki CT Scores. The Marshall CT classification had reasonable discrimination (AUC - 0.646), Helsinki CT Score had good discrimination (AUC - 0.724). Rotterdam grading had best discrimination (AUC - 0.735).

Conclusions: Rotterdam and Helsinki classification systems are good in predicting early mortality after moderate and severe TBI at 6 months, however Rotterdam show the best discrimination.

Cerebral Blood Flow Correlates of Acute Symptoms after Sport Concussion

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Concussion is defined by acute disturbances in brain function following direct or indirect contact to the head, in the absence of gross anatomical lesions. The associated functional complaints vary, and encompass numerous symptom clusters, including somatic (e.g., dizziness, headache), cognitive (e.g., confusion, memory problems) and emotional (e.g., anxiety, irritability). In the sport domain, the cornerstone of concussion diagnosis and management involves careful evaluation and monitoring of post-concussion symptoms. However, it has not yet been established whether there are consistent neurobiological changes associated with subjective symptom complaints. It is critical to identify brain biomarkers, to better understand how brain injury leads to post-concussion symptoms, and develop better, more objective assessments of concussion.

It has been previously established that cerebral blood flow (CBF) is a sensitive marker of brain injury. In the current study, we used Arterial Spin Labelling to measure the CBF correlates of symptoms at acute injury, for 26 varsity athletes and matched controls. For acutely injured athletes, total symptom severity was associated with elevated subcortical CBF in the hippocampus. An examination of symptom clusters also showed that athletes with high cognitive symptoms and relatively low somatic complaints had decreased CBF, compared to other concussed athletes. Thus, CBF may be a robust biomarker of symptom severity at acute injury, where different patterns of CBF change are associated with specific symptom clusters. These novel findings will help to improve our understanding of the neurobiological basis for post-concussion symptoms.

External Validation of the Modified Fisher Scale in the Prediction of Mortality and Prognosis in Patients with Subarachnoid Hemorrhage

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Introduction: Subarachnoid hemorrhage (SAH) is a disease that has been the target of several investigations and discussions because of its high mortality and significant morbidity. Different classifications have been developed in order to predict the neurological outcomes. The Fisher scale (FS) is the most commonly employed method of assessing SAH on CT scans. The Modified Fisher scale (MFS) presents an alternative for evaluating patients with subarachnoid hemorrhage (SAH). In this study, we compared the FS versus MFS in the prognosis of patients with SAH in a University Hospital in Colombia.

Methods: This is a retrospective study of patients with subarachnoid hemorrhage who presented to our hospital between January 2014 to December 2015. All the patients were followed up for 6 months to determine early mortality and neurological outcome. We evaluated the Fisher scale and Modified Fisher scale. The discriminatory power of each grading system was determined using area under the receiver operating characteristic curve (AUC) and Spearman's rank correlation coefficient.

Results: A total of 101 patients were enrolled in the study, median age 62 (47-71) years, and 65.35% were female. The overall mortality was 38.61%, the unfavorable neurological outcome was in 55.44%. The FS (3) Mortality was 40% vs MFS (3) 43.48%, The FS (4) mortality was 51.06% and MFS (4) 52.16%. Spearman's rho 0,31 and 0.54 and AUC 0,679 and 0,798 for MFS in mortality and unfavorable neurological outcome respectively.

Conclusions: The behavior of two scales was similar, but the modified scale Fisher has better performance and correlation with mortality and worse prognosis of neurological outcome in patients with subarachnoid hemorrhage.

Predicting Outcome after Subarachnoid Hemorrhage: Prognostic Model Based on Admission Characteristics

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Introduction: Subarachnoid hemorrhage (SAH) is a disease that has been the target of several investigations and discussions because of its high mortality and significant morbidity. We aimed to develop and validate a practical prognostic model for death at 28 days and for unfavorable neurological outcome (death or severe disability) six months after subarachnoid hemorrhage.

Methods: Prospectively collected individual patient data were analyzed. We considered predictors available at admission in logistic regression models to predict mortality and unfavorable outcome according to the Glasgow Outcome Scale at 6 months after SAH. The performance, precision, accuracy and prediction power of the model were assessment through the area under the receiver operating characteristic curve (AUC), sensitivity and specificity with probability cutoff graph, proportion of correctly classified and detection of specification error.

Results: The model included nine predictors: age, sex, pupil reactivity, glucose, shift midline over 5mm and hydrocephaly, we also included three SAH scales: Hunt and Hess, Modified Fisher and WFNS scale. The model showed excellent discrimination (area under ROC curve= 0.9284), overall correct classification of 90.48%, with a sensibility of 88% and specificity of 92%.

Conclusions: Our prognostic model showed an excellent performance with a great precision, accuracy and prediction power and can be used to obtain valid predictions of relevant outcomes in patients with SAH.

Disorders of Consciousness Due to Anoxic Brain Injury: A Case Series Of 8 Patients

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Disorders of consciousness (DOC) can occur after severe acquired traumatic or non-traumatic brain injury. Anoxic brain injury (ABI) is a type of non-traumatic brain injury that may result in DOC. Presently, the literature regarding clinical manifestations, treatment paradigms, and prognostic information of patients with DOC focuses primarily on patients with traumatic brain injuries, while research focused on the unique characteristics of patients who suffer ABI is limited. The goal of our study is to begin to characterize common medical complications, treatments, and recovery in patients with DOC due to ABI. The present study is a retrospective case series at a single academic inpatient rehabilitation facility. Patients who suffered DOC due to ABI and were admitted to inpatient rehabilitation (IPR) from 2015-2016 were considered for inclusion. Patients were excluded if there was associated head trauma. History and clinical course were obtained from review of the electronic records. Uniform Data System data was used to determine Functional Independence Measure (FIM) scores. JFK/Coma Recovery Scale – Revised (JFK/CRS-R) scores were obtained for all vegetative patients. Eight patients were identified (6 male, 2 female) with average age of 30 (range 22–42) years. On admission to inpatient rehabilitation, 5 patients were vegetative and 3 had recently emerged from minimally conscious state (MCS) prior to admission to IPR. During IPR course, 2 vegetative patients emerged, 1 became minimally conscious, and 2 remained vegetative. FIM scores on admission were 18 or below for all patients, and improved in 4 patients by an average of 40 (range 19–59) points. Scores did not improve for the remaining 4. Where applicable, JFK/CRS-R scores improved for all patients. All patients were given neuropharmacologic medications to improve arousal and attention. Paroxysmal sympathetic hyperactivity (PSH) affected 6/8 patients and clinically resolved for 2 of these patients prior to discharge. Six of 8 patients had spasticity, resolving in 3 by discharge. Six of 8 patients exhibited movement disorders, primarily myoclonus. No patients developed seizures while at IPR, but 2/8 patients experienced status epilepticus during acute hospitalization. Two of 8 had MRI evidence of focal ischemic strokes, and 7/8 had urinary tract infections during IPR. Overall, 6/8 patients were discharged to home with the other 2 patients being discharged to a skilled nursing facility. In IPR, patients with DOC due to ABI presented with prominent neurological and cognitive deficits, for which they were prescribed neuropharmacologic agents in conjunction with therapies. Common limitations to rehabilitation include the severity of deficits in arousal and cognition, PSH, spasticity, movement disorders, and a high rate of infection; however, a high number of patients were able to be discharged to the home setting. Further investigation into predictors of outcome and optimal medical management for this population is warranted.

Model of Traumatic Brain Injury Using Imaging, Physiological and Psychosocial Parameters: Pilot Study

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Background: Recovery of function from traumatic brain injury (TBI) is of great value for rehabilitation interventions, yet the mechanism of brain injury and recovery remain poorly characterized. The purpose of this study was to measure the size and location of TBI lesions creating perfusion and metabolic statistical parametric maps using Tc99m ECD SPECT/CT and F-18-FDG PET/CT in patients with TBI, while assessing neurophysiologic parameters using Somatosensory Evoked Potentials (SSEP). The magnitude of the association between brain perfusion defects, brain metabolism impairments and brain electrical disturbances was correlated with quality of life measured by functional status, activities in daily living and depression. In addition, the study aimed to describe the psychosocial experiences of veterans with TBI and model the relationship between the neuro-imaging and neurophysiologic characteristics in the studied population.

Methods: This was a cross sectional, pilot study to characterize the brain injuries of OIF/OEF veterans and categorize them based on these characteristics. The study population included males and females returning soldiers older than 21 years of age who were diagnosed with TBI and had not received rehabilitation. The participants underwent a SPECT/CT and PET/CT scan within 2 weeks of TBI diagnosis confirmation by a Polytrauma expert. The subjects completed a neurological exam and a SSEP. Quantitative data on functional status, activities of daily living and depression was obtained using Functional Independence Measure (FIM), Barthel Index and Beck Depression Inventory-II (BDI-II).

Results: Six-patients were enrolled in the pilot. The correlation between FIM and the imaging data showed a 0.87 Spearman-coefficient in both SPECT and PET. The correlation coefficient between SPECT and BDI-II and PET and BDI-II was 0.74 and 0.63, respectively. An increased severity and number of perfusion defects compared to metabolic defects were observed. The most common site of perfusion abnormalities was the frontal lobe and of metabolic abnormalities was the temporal lobe. Perfusion and metabolic findings were detected in the presence of negative CT. SSEP showed that the patients had an abnormally increased Central Time from cervical to cortical response. Qualitative data on the daily activities and experiences were obtained using a semi-structured interview methodology.

Conclusions: The data showed that higher trauma severity is accompanied by greater rates of depression and low level of independence. Damage to the Basal-Ganglia correlated with the presence of severe depression (.89-Spearman). The mismatch between perfusion and metabolic defects suggested up-regulation of cerebral glucose-transporters/receptors to compensate for diminished perfusion. The etiology of TBI may be related to impaired vasomotor response or endothelial dysfunction. SPECT/CT and PET/CT have an add-value in the diagnosis of patients with mild and moderate TBI. However, a larger clinical trial is required in order to develop new predictive TBI model-systems and proposing algorithms to target rehabilitation interventions.

Local Tissue Metabolism Impairment Correlates with Brain CT After Brain Injury

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Introduction: Patients with severe traumatic brain (TBI) or vascular brain injury (VBI) in coma require brain monitoring due to limited possibilities of clinical assessment. Much research interest has been focused on association between multimodal monitoring (MMM) and clinical outcome. This is, however, a rather rough parameter, which may be influenced by several factors. The goal of our study was to correlate brain metabolism with the final tissue outcome at the end of monitoring, which in our opinion has a much tighter relationship.

Materials and Methods: Multimodal brain monitoring, including an ICP, a brain tissue oxymetry and a microdialysis probe, was applied in comatose patients (GCS < 9) with severe TBI or VBI. The probes were implanted via a tripple-lumen bolt or percutaneously. In the majority of the patients, brain CT was performed before implantation of probes, during monitoring and at the end of the monitoring period. We correlated the signs of local tissue hypoxia (below 15mmHg on brain tissue oxymetry) or metabolism impairment (the LP ratio above 40, glycerol above 150 umol/l and glucose below 0.8mmol/l) with tissue outcome on CT surrounding the monitoring probes.

Results: We evaluated 72 patients with severe TBI or VBI. 58 were males and 14 females. The average age was almost 50 years and the mean monitoring time 9 days. In our study we found that low tissue oxymetry and tissue metabolism impairment are associated with tissue hypoxia on brain CT around the probes at the end of MMM.

Conclusion: Signs of focal tissue metabolism impairment or hypoxia using brain MMM correlate with local brain tissue outcome. It still needs to be determined whether therapeutic decisions based on MMM would lead to prevention of brain tissue damage.

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WATCH Me Go: Activity in Children Following Concussion and Its Association with Outcome

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Introduction: Following a mild traumatic brain injury (mTBI) one of the management strategies for children is absolute rest until symptoms subside, but this is now perceived to have limited benefits. The effect of physical activity on exacerbating post concussive symptoms and the social impact of prolonged rest for children recovering from an mTBI is under-evaluated in current literature. Considering one in five children will sustain an mTBI by 16 years of age, improving effectiveness of care for children suffering from Post Concussive Syndrome (PCS) should be of major concern. A correlation between activity levels during the recovery period and PCS outcomes could potentially vastly improve current treatment methods for mTBIs. These findings will drastically change how the medical community perceives idle physical rest following a concussion.

Objective: To examine activity levels during the recovery period following an mTBI and its role in determining injury outcome and symptom exacerbation.

Methods: This prospective cohort study examined activity levels of children aged 8-18 years with mTBI who were symptomatic at one month post injury, and compared them to children who were asymptomatic at one month post injury and uninjured healthy control children. This was conducted as part of the Play Game Trial (www.playgametrial.ca). Physical activity was monitored using Actiwatch 2 (a validated, objective, wristwatch-like device) over a period of 3-7 days. Respironics Actiware software was used to measure time awake and activity levels throughout the day. The Actiware software quantified activity count values for 15-second epochs throughout the active interval. This was used to determine the duration of time per day spent in each activity level: low (1-80 activity counts), moderate (81-262), high activity (263-406), and very high (>406). Post-Concussion Symptom Inventory (PCSI) was used to measure symptom severity.

Results: Data from 27 control, 28 asymptomatic, and 70 symptomatic participants were analyzed. No significant differences were seen between the three groups in duration the watch was worn, or in time spent in each measured activity level. PCSI scores at one month post injury in the injured group could be predicted by moderate activity levels (Beta -3.03, $p=.003$). Good or poor outcome (based on PCSI) at 2-3 months post-injury could not be predicted by activity levels (at one month post-injury) in the symptomatic group $\chi^2(3) = 2.232, p = .526$.

Conclusion: Higher levels of moderate activity in injured participants were associated with lower PCS symptoms after controlling for the effect of high and low activity levels. Activity at one month post-injury did not predict recovery at two months post-injury. Further analysis is needed to understand the role of activity and how it influences outcome in cases of post-concussion syndrome. We hope this work will later assist in developing management strategies for mTBIs.

From Paper to Practice - Developing and Implementing Sports Injury Prevention Interventions That Make a Difference

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There has been much written in the last five years, in science publications and in the press, on the importance of reducing the number of youth sport concussions and finding ways to manage concussion recovery better in children. And for all the clamor to create or change school and youth sport concussion policies, there are very few examples of how to take theory laid out in these scientific papers and implement low-cost programs in children's day to day lives across an entire city.

This presentation will highlight an on-going three year project in Norwalk, Connecticut, USA, where RE-AIM Sports Setting Matrix (RE-AIM SSM), a health promotion planning and evaluation framework, was used to develop and implement a city-wide concussion education and management policy targeted at the 11,000 children in all schools and all city youth recreation sports programs. In 2014, researchers were concerned the newly updated CT State Concussion Law only applied to 1,145 high school students participating on official high school teams. The project launched in the 2014-2015 school year to investigate how many of the 9,855 non-children not covered by the state law were having concussions and how many student-athletes were having concussions.

For the last three years, all concussions reported to the school nurses and athletic trainers in all the Norwalk Public School were recorded by age, sex, mechanism of injury, and where injury occurred. All children, aged kindergarten to 12th grade, could be considered involved in sports if sports are considered in a range from peer organized games at recess, school gym class, official sports teams and also solo sports outside of school. Specific data was also captured on the ratio of sports to non-sports injuries, and if concussions happened at school or home.

Researchers then used the RE-AIM Sports Setting Matrix (RE-AIM SSM) to guide the development, implementation and evaluation of sports injury prevention interventions across this entire city by involving the schools, the city hospital, city government, youth sports organizations and the city parks and recreation department.

The proposed presentation on this project will discuss how to use RE-AIM SSM to develop interventions and accompanying implementation plans targeted at a multi-layered implementation context to maximize the adoption and overall impact of sports injury prevention interventions. The presentation will also provide a unique opportunity for participants to share the challenges they face and explore practical solutions in planning and implementing sports injury prevention interventions in complex settings.

NOTE: While the RE-AIM SSM was used in this case was modified to be specific to the community sports setting context, this framework could be used to optimize the impact of future sports safety, and other health promotion, interventions in complex real-world settings.

Identifying Exemplars of Meaningful Functional Change seen in Patients with Disorders of Consciousness Following Severe Traumatic Brain Injury

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One important reason for the lack of successful clinical trials in the treatment of traumatic brain injury (TBI) is the paucity of clinically meaningful indices of change for the major assessments of neurobehavioral function (NBF). Anchor-based minimally clinically important differences (MCIDs) are considered the most clinically relevant indicator of responsiveness for TBI clinical trials because they connect change on the endpoint of interest to an already established and valued indicator of important change. Consequently, anchor-based MCIDs rely heavily on the quality of the selected anchor. Typically, an anchor-based MCID is created by associating the amount of change in a known measure (i.e., change in total score), with the amount of change in the target measure. For example, we recently demonstrated that patients who made a 2-point change in the Glasgow Coma Scale, on average, made a 10-point change in DOCS-25 score. We recognized this was far from ideal, as it reflects a very gross indicator of change.

Instead, we argue that taking the notion of “meaningful” change seriously requires a radical rethinking of both what constitutes an anchor and how those anchors are identified. Consequently, we describe a qualitative, narrative approach to uncover clinicians, family members and caregivers “typifications” of meaningful change. Typifications refer to the language participants use while interacting with patients in states of disordered consciousness (DOC) following brain injury to make sense of what they perceive patients are exhibiting as ‘change’.

Thematic and content analyses were used to analyze interview data and understand perceptions of change related to improvement, decline and stability of function in people with DOC. To promote rapport, we conducted the interviews, whenever possible, in neutral spaces in a manner that has been referred to as “kitchen-table talks”. Participants are 10 clinicians actively treating adults with DOC in post-acute rehabilitation facilities. Two clinicians trained in narrative interview techniques conducted the interviews which were audiotaped and transcribed verbatim. Data were analyzed using several narrative approaches. Two members of the team examined transcriptions to gain familiarity with the data. Thematic analysis involves reviewing transcripts for themes both within and across individual participant interviews. We used a systematic process to code data and generate themes with subsequent team meetings to check codings and interpretations of the data. Because we expect examples of meaningful change in NBF will be narratively structured, we specifically examined data for “illness narratives” and “treatment stories”.

This novel approach provides rich information that takes taking into account the unique perspectives of clinicians, family members, and caregivers. These will be used to develop exemplar narrative vignettes of small, medium, and large amounts of NBF change – textual visuals that can serve as anchors of clinically meaningful change.

Status Report on Magnetic Resonance Imaging (MRI) Quantification in the Chronic Effects of Neurotrauma Consortium

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The Chronic Effects of Neurotrauma Consortium (CENC;

https://en.wikipedia.org/wiki/Chronic_Effects_of_Neurotrauma_Consortium) is a large-scale multi-site study of traumatic brain injury (TBI) examining a host of demographic, deployment, medical and biomarker variables, including neuroimaging. Imaging data from 263 participants across four CENC sites will be described and used in this presentation. All participants are Veterans or Active Duty Service Members with combat exposure and a history of TBI associated with blunt-force trauma or blast injury or are from a mixed control group of healthy participants (with or without post-traumatic stress disorder (PTSD)). The neuroimaging core uses magnetic resonance imaging (MRI) and a multi-modality approach to assess various sequences that incorporate both structural and functional techniques. As part of the neuroimaging core, structural MRI studies are undertaken on the majority of participants where image quantification of the T1-weighted images is accomplished using FreeSurfer (<http://freesurfer.net/>) and various measures of volume, thickness and/or surface area can be derived for numerous regions of interest (ROI). The structural image analysis performed in CENC provides individualized quantitative information for each participant as well as investigating group-wise differences that relate to the various demographic, medical, deployment and biomarker findings. One challenge in undertaking such an investigation is that across the CENC image acquisition sites, different MRI platforms are used to acquire the images; this adds another level of variance to the quantitative findings actively being explored by our group (Wilde et al., 2016). This presentation demonstrates the efforts used to illustrate the variability between CENC sites so appropriate conclusions are made from group analyses while describing the development of precision medicine methods/tools that can be used to explore the volumetric data of the individual CENC patient. This presentation will overview standardization methods across multiple imaging platforms, describe data analyses reliability, as well as delineate the methodological corrections necessary to harmonize the data in group analysis. In addition, we will illustrate the utility of a new method for mapping individual patient FreeSurfer quantitative image information into a 3-D image display using a portable document format (PDF) that permits simultaneous viewing of cortical and subcortical anatomical detail and any ROI analyses that reveal significant regions that differ from normative standards. We will discuss the diagnostic, clinical, and prognostic value of these methods and implications for future use.

Observational Study of Autonomic Dysfunction after Traumatic Brain Injury in Neurorehabilitation

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Objective: Few studies have characterized autonomic dysfunction in the acute rehabilitation stage after moderate to severe traumatic brain injury (TBI). Even fewer have measured parasympathetic and sympathetic dysfunction at this stage after TBI. Characterization is clinically relevant because changes in the sympathetic and parasympathetic systems after TBI may contribute to various systemic abnormalities including metabolic, cardiac, immune, musculoskeletal, cognitive and psychological manifestations and may hinder recovery after TBI patients or serve as a marker for poor prognosis. Previous outpatient studies have found associations between autonomic dysfunction and executive dysfunction, behavioral dysfunction and posttraumatic stress disorder. The heart is innervated by both the sympathetic and parasympathetic systems branches of the autonomic nervous system (ANS). Beat-to-beat variation in the heart rate, termed heart rate variability (HRV), is determined by the balance between these systems. HRV can be evaluated by a non-invasive technique to assess autonomic modulation and judge parasympathetic versus sympathetic tone and influence. Normative values exist for each based on the subjects age and gender. This pilot study evaluates the physiologic parameters of HRV in TBI patients in the acute rehabilitation period compared to control aged-matched data in order to better characterize ANS dysfunction type and incidence.

Methods: This is a prospective pilot study of twelve subjects with moderate to severe TBI who were inpatients in a brain injury rehabilitation center, at least two weeks post injury, and met inclusion and exclusion criteria. Demographics, injury characteristics, medications, and medical history were obtained from the inpatient chart. Participants underwent autonomic function testing in the first two weeks after admission using the ANX-3.0 autonomic monitoring system to evaluate sympathetic and parasympathetic function. The ANS testing was carried out by a certified ANS testing specialist in the participant's room and consisted of two parts: cardiovagal function testing and sweat testing.

Results: A spectrum of sympathetic and parasympathetic abnormalities were found. Overall, parasympathetic dysfunction was found in 75% of subjects. Overall, sympathetic dysfunction was found in 33% of subjects. Decreased heart rate variability was found in 67% of subjects. Orthostasis syndromes were seen in 75% of subjects.

Conclusion: This pilot study found high rates of autonomic dysfunction after moderate to severe TBI. Future studies are needed to characterize the change in autonomic function during acute rehabilitation and to correlate this with functional changes. Prospective studies are needed to evaluate the association of long early autonomic dysfunction and the long-term incidence of cognitive, behavioral and psychiatric sequelae of TBI.

Immediate Head CT following Emergency Craniotomy or Craniectomy for Trauma

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Background: There is no neurosurgical standard of care of when a follow-up head CT scan (HCT) should be performed after craniotomy/craniectomy (Crani) for acute trauma. When patients require a second Crani based on a delayed post-operative (post-op) HCT, there is always a question of whether the new HCT findings could have been detected earlier. The purpose of this study was to see how frequently immediate post-op HCT following Crani for acute trauma detected new findings prompting immediate repeat or additional Crani for evacuation of new intracranial hemorrhage.

Method: All patients at one Level II Trauma Center requiring Crani for acute trauma were studied from November 2014 through September 2016. All patients went directly from the OR suite to the CT suite for HCT following Crani. The neurosurgeon (NS) reviewed the HCT while the patient was on the CT table and determined whether the patient needed to return to the OR for immediate second Crani. Demographic data, coagulation parameters, HCT findings, re-operation, and hospital outcome data were collected prospectively. Protocol violators were excluded from analysis.

Results: There were 61 total patients undergoing emergent Crani for acute trauma with eight protocol violators which were excluded from analysis, two of which were assessed as having a fatal brain injury at time of initial Crani and died shortly after Crani. The study population included 53 patients that underwent 59 Crani's. Mean age was 48 years with 66% males with mortality of 21%. Indication for initial Crani was subdural hematoma (SDH) in 34 patients, epidural hematoma (EDH) in 12 patients, intraparenchymal hematoma (ICH) in two patients, contusions with edema (C/E) in four patients and significant edema alone (E) in one patient. Immediate post-op HCT following Crani for acute trauma detected new intracranial findings requiring another immediate Crani in five patients with one patient requiring two additional Crani (total 6 immediate reoperations). The findings on immediate HCT which prompted immediate reoperation were SDH in three cases, EDH in two cases and ICH in one case. Four of the six subsequent Crani's were at a different location from the first Crani. None of the patients requiring immediate second or third Crani were coagulopathic or on blood thinners. There were no deaths in the patients who had additional immediate Crani.

Conclusion: Significant surgical findings were identified in 10% (6/59) of all immediate post-op HCT in this study. Immediate post-op HCT following Crani for acute trauma may be warranted to detect ongoing or new intracranial hemorrhage requiring second Crani to avoid delays in management and progression of brain injury.

Quantifying Cerebral Perfusion Changes Over Time During Recovery from a Mild Traumatic Brain Injury in Children

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Introduction: Mild traumatic brain injury (mTBI) during the period of critical brain maturation in childhood is likely to impair outcomes due to varied pathophysiological response. Although post-concussion syndrome (PCS) is a common consequence of mTBI, there is limited understanding of its pathophysiological mechanism. We and others have recently shown abnormalities of cerebral blood flow (CBF) following mTBI.

Objective: To explore changes in CBF during recovery from pediatric mTBI and its relationship to post-concussion syndrome and cognitive function.

Methods: This was a prospective controlled cohort study of children ages 8-18 years presenting to a Pediatric Emergency Department with mTBI. Symptomatic and asymptomatic (clinically recovered) participants were imaged at approximately 1 and 2 months post-injury, and compared to a healthy control group. Pseudo-continuous arterial spin labeling (pcASL) MRI was used to quantify CBF. Outcome measures: Global and regional CBF change, and Post-Concussion Symptom Inventory (PCSI). Analysis: SPM12 was used for preprocessing and creation of the statistical model. An inclusive 40% Grey Matter Mask was applied. Regional CBF maps were created using voxel clusters ≥ 100 at a 5% significance level.

Results: 56 symptomatic, 33 asymptomatic, and 20 healthy controls (mean age = 13.9 ± 2.7 , 46.8% male) were scanned; 48 symptomatic and 10 asymptomatic participants had repeated neuroimaging. Groups did not differ in terms of sex, age, handedness, or socioeconomic status. At one month post-injury, regional CBF maps demonstrated that symptomatic participants had increased CBF whereas asymptomatic children had decreased CBF compared to healthy controls. Over time, there were no significant changes in CBF for asymptomatic participants, whereas symptomatic participants experienced an overall decrease in CBF that was correlated with recovery. Recovery by two months post-injury was associated with decreased global CBF at one month post-injury when compared to symptomatic participants who showed no recovery.

Conclusion: After mTBI, there are regional CBF differences which are dependent on symptom status. These regional differences change over time and a model will be demonstrated. Ongoing changes in CBF in the asymptomatic group suggest that recovery is not yet complete despite the absence of clinical symptoms. CBF may be a prognostic indicator of recovery in children who have post-concussion symptoms at one month post injury.

The Utility of SPECT-CT and PET-CT in the Diagnosis of Traumatic Brain Injury at the VA Caribbean Healthcare System (VACHS): Retrospective Descriptive Study

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Objectives: The main objective of this study was to characterize brain injuries among Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn VACHS veterans using functional Nuclear Medicine neuron-imaging (SPECT and PET CT). **Aims:** (1) Describe size and location of Traumatic Brain Injury (TBI) lesions using Tc99m-ethyl-cysteinate-dimer-SPECT/CT and F-18-Fluorodeoxyglucose-PET/CT; (2) Assess symptomatology (Physical, cognitive and psychological) in TBI veterans patients; (3) Estimate the association between brain perfusion defects and brain metabolic impairment versus physical, cognitive and psychological symptomatology; (4) Create a socio-demographic and health-characteristics profile of Puerto Rican Hispanics veterans diagnosed with TBI. Data is intended to support rehabilitation strategies for future studies.

Methods: This was a retrospective-descriptive study. CPRS records of all subjects that underwent a SPECT/CT and/or PET/CT for TBI during 01/01/2007-03/30/2012 were reviewed. Objectives 1, 2 and 3 variables included: results of SPECT/CT, PET/CT, CT and MRI, trauma mechanism, symptoms, motor FIM score, Barthel Index, Cognistat Assessment and Mental Status Exam. Objective 4 variables included: age, gender, marital status, race/ethnicity, income, education, TBI severity, co-morbidities, hospital admission, bed days of care, any Occupational/Physical/Speech Therapy use, clinic nurse/doctor visits and use of prosthetic devices.

Results: 150 records were eligible for the study. Preliminary results on the first 100 records analyzed (94% were males with an average age of 40 years, 73% had mild TBI, 80% were White/Hispanics, 9% were Black/Hispanics and 11% had no reported race/ethnicity) showed that the most common physical, cognitive and psychological symptoms were headaches, forgetfulness and irritability, respectively. 96 subjects had only SPECT/CT, 4 had only PET/CT and 3 had both. 39% of the SPECT/CT studies were abnormal. Most common location for TBI lesions was the frontal lobe. 51% did not have MRI or CT and 49% had CT and MRI all with normal results or showing minor abnormalities. Socio-demographic trends showed that 76% of veterans received some level of college education (51% did not graduate), 76% were married, and the average annual-income was \$27,949. Service utilization during the first year after TBI diagnosis confirmation showed: 31% hospital admission, 15 average bed days of care, 88%, 85% and 46%. Occupational/Physical/Speech Therapy usage respectively, 53 average visits per year to providers, and prosthetics usage: 73% eyeglasses, 45% equipment and 51% bath equipment)

Implications: SPECT/CT and PET/CT have an added value in the diagnosis of TBI. The study provided a profile of Post-deployment population of Puerto Rican veterans with TBI.

Impacts: This line of research provides the basis to develop new predictive TBI model-systems and proposing algorithms to target rehabilitation interventions.

Neural Substrate of Working Memory Improvement Following Methylphenidate and Cognitive-Behavioral Therapy for Cognitive Symptoms after Traumatic Brain Injury (TBI)

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Objectives: Cognitive symptoms are among the most common and troublesome sequelae of traumatic brain injury (TBI). In particular, persistent deficits in working and episodic memory are frequently reported. We recently tested the comparative effectiveness of a cognitive-behavioral therapy intervention (Memory and Attention Adaptation Training; MAAT), with and without pharmacological augmentation with methylphenidate (MPH), for treatment of post-injury cognitive symptoms. Patients treated with MAAT showed greater improvement in verbal learning, while patients treated with both MAAT and MPH showed greater improvement in nonverbal learning and auditory working memory and divided attention. Here we report on the use of fMRI to characterize the neural substrate of differential treatment effects associated with cognitive-behavioral and pharmacological interventions.

Methods: Participants included adults with a history of TBI of any severity at least four months prior to study entry, with cognitive deficits on a neuropsychological screening battery and/or significant cognitive complaints as measured by the Multiple Abilities Self-Report Questionnaire (MASQ). In a 2x2 design, participants were randomized to receive MPH or placebo, and MAAT or Attention Builders Training (ABT), a manualized repetitive practice intervention with no cognitive-behavioral component. This resulted in four treatment combinations: MAAT/MPH (N=10), ABT/MPH (N=10), MAAT/placebo (N=10), and ABT/placebo (N=12). fMRI was conducted pre-treatment (baseline) and after six weeks of treatment (post-treatment) using a visual-verbal “N-back” working memory task. Statistical analyses used SPM12 to compare difference images (post-treatment – pre-treatment) for a high working memory load contrast (3-back > 0-back), controlling for study site.

Results: At baseline groups did not differ statistically on gender, age, education, estimated premorbid intellect, injury severity, time post-injury, or medication adherence. Patients receiving treatment (MPH, MAAT, or both in combination) showed significantly greater activation at post- relative to pre-treatment than patients receiving ABT/placebo in bilateral dorsolateral prefrontal and anterior cingulate regions ($p < 0.001$, uncorrected). Increase in anterior cingulate activation showed a trend toward correlation with improved task performance post-treatment.

Conclusions: Increased frontal lobe activation during working memory processing was seen following treatment with MPH and/or the MAAT cognitive-behavioral therapy intervention for cognitive symptoms after TBI. Clusters of increased activation post-treatment were observed both within and beyond typical working memory circuitry, suggesting that additional brain circuitry may be recruited to support cognitive functioning after TBI. Findings are consistent with the hypothesis that MPH and cognitive-behavioral therapy may improve working memory after TBI via increasing frontal brain activation. Given the modest sample size of this study, these results should be interpreted cautiously, and require replication. However,

these findings suggest that interventions targeting frontal circuitry, particularly dorsolateral prefrontal and anterior cingulate regions, show promise for improving cognitive function after TBI.

Evaluation of Modifiable and Non-Modifiable Risk Factors Associated with Readmissions in Patients with Acute Traumatic Brain Injury Routinely Discharged from Inpatient Care Using a Nationwide Database

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Objective: Early readmissions have been identified as a viable metric for evaluating patient outcomes and quality of patient care. Apart from its impact on overall patient well-being, it also leads to significant increase in direct and indirect healthcare costs amplifying its toll on the healthcare system. Here, we evaluate 30-day readmission and identify risk factors associated with readmission after moderate to severe traumatic brain injury (TBI) in a convenience sample of patients hospitalized with TBI.

Methods: Data was obtained from the 2013 nationwide readmissions database. Patients with a diagnosis of TBI were included in our study if they had moderate and/or severe TBI without significant injury to any other body region. Discharge dispositions among patients were examined and factors associated with the likelihood of readmission in those routinely discharged from index hospitalization were studied. Retrospective review was performed using standard descriptive techniques and multivariate regression analysis was used to explore the odds ratios of likelihood of readmissions.

Results: Overall, 96,210 TBI patients meeting the inclusion criteria were studied. The mean age of patients was 65.58 years (SD±22.31). The median abbreviated injury score (AIS) was 4 [interquartile range (IQR=3-4)], with males representing 75% of cases. Insurance coverage types were as follows: Medicaid (59.83%), Medicare (9.92%), private insurance (19.02%), self-pay (5.77%), and other/unqualified insurance types (5.46%). Most cases were treated at teaching hospitals (71.58%), and falls represented the most prevalent external cause of injury (71.47%).

Fatalities were present in 10.19% of index TBI cases. Overall discharge disposition of survivors were as follows: routine discharge (50.11%), short term hospital (1.85%), skilled nursing care (32.11%), home health care (14.46%), against medical advice (1.28%), and unknown (0.18%). Of the patients that were routinely discharged, 7,196 patients (16.62%) were readmitted within 30 days following discharge from the index hospitalization. Multivariate regression analyses identified independent risk factors associated with an increased likelihood for readmission after initial routine discharge including increasing patient age (OR=1.01; 95%CI=1.00-1.01), presence of Medicaid insurance coverage (OR=1.15; 95%CI=1.00-1.35), and AIS 4-5 (OR=1.44; 95%CI=1.32-1.57). Similarly, TBI associated with falls (OR=1.24; 95%CI=1.03-1.49), patients with multiple medical comorbidities (OR=1.67; 95%CI=1.43-1.96), and patients having major surgery (OR=1.13; 95%CI=1.01-1.28) were also at increased risk of readmission after initial home discharge. However patients with private insurance (OR=0.88; 95%CI=0.78-0.99), patients who underwent decompressive craniectomy (OR=0.79; 95%CI=0.64-0.97), and patients who underwent post-acute care rehabilitation (OR=0.80; 95%CI=0.64-0.99) were less likely for 30-day readmission after routine discharge.

Conclusion: We have implemented a critical evaluation of modifiable and non-modifiable factors associated with an increased risk of readmission after moderate to severe TBI using a national database. Modifiable factor(s) including decompressive craniectomies for persons in whom it is indicated was found to be protective. These findings however warrant validation in a prospective cohort.

Impact of Comorbid Conditions on Persistent Concussion Symptoms

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Background: Concussion is the most common form of brain injury. Most symptoms resolve spontaneously within weeks of the injury however up to 20% of people can have persistent symptoms that require multiple physician visits for treatment. We hypothesized that pre-existing conditions such as migraines, vestibular problems, or mental health problems would increase the likelihood of development of persistent symptoms.

Methods: Administrative databases available at the Institute for Clinical and Evaluative Sciences (ICES) were used to identify residents in Ontario diagnosed with concussion between 2008 and 2013. Comorbid conditions were identified by examining physician and health system utilization for 5 years prior to injury. The cohort was then tracked using their unique health card identifier for 2 years after the index concussion to determine those with persistent symptoms as defined by those requiring 2 specialist visits i.e. neurology, psychiatry, otolaryngology 3 months after index date for concussion symptoms.

Results: 888 472 people were diagnosed with concussion from 2008 to 2013. Of these 305 665 had persistent symptoms. People with the following pre-existing conditions were more likely to require persistent symptom care after concussion: neurological disorder (Odds Ratio 3.1), vestibular conditions (2.1, OR) and sleep disorders (2.2 OR) ($p < 0.0001$). This group receive an average of 6.5 specialist visits ($p < 0.0001$), and visit more than 2 types of specialists for their treatment. Other comorbidities that were associated with increased health care utilization were mental health conditions (2.1 OR), pain disorders (2.1 OR), headaches (1.7OR), and prior concussions (1.3 OR). Individuals with multiple premorbid conditions have an average conditional Odds Ratio of 3.8 for developing persistent symptoms i.e. mental health with pain disorders (4.4 OR), headaches with pain disorders (4.1 OR), mental health with headaches (3.8 OR), sleep disorders with mental health (3.9 OR), headaches with vestibular disorders (3.7 OR), mental health and vestibular disorders (3.6 OR), sleep disorders and vestibular disorders (3.5 OR), and pain disorders with mental health and sleep disorders (3.4 OR).

Conclusions: These findings identify a high-risk post-concussion group that clinicians can proactively target for earlier intervention to potentially reduce the duration of symptoms. Future research will develop a decision algorithm.

Disorders of Consciousness: A Focus on Program Evolution in the Civilian Population

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Background: In the state of Ohio there are no dedicated Disorders of Consciousness (DOC) programs. All literature pertaining to creation of DOC program have been focused in the Veterans Administration Medical Systems. 5 year functional outcomes in DOC patients have been reported across all systems of care from the TBI-MS DOC special interest group. Patients with DOC are deemed to not be able to participate in 3 hours of therapy per day because of minimal ability to interact with the environment and follow commands. Therefore, they are usually transitioned to a skilled nursing facility with limited medical expertise of Brain Injury and DOC management. Studies have shown comprehensive inpatient rehabilitation programs are essential to assist patients with their emergence to consciousness. Barriers included a lack of a formalized program and training in our facility to manage these patients. Additionally, it was difficult to convince insurance payors to cover treatment due to a lack of understanding the unique needs of these patients; preventing admission to inpatient rehabilitation.

Methods: A focus group was created with representation from an interdisciplinary team: Psychiatrist, Rehab Psychologist, Speech Language Pathologist, Occupational Therapy, Physical therapy, and Rehabilitation Manager with Therapy and MBA background. The initial program proposal was created to gain support from stakeholders and administration. Once support was secured, the program was further developed to include a formalized program structure, clinical interventions, educational training, and research goals.

Results: A comprehensive Rehabilitation program was developed that included: specific admission criteria to utilize with families and insurance carriers, formal intake process for the team, structured schedules for the patients, clinical interventions for each therapy specialty, and educational programming for family training. Staff training was also developed for direct service staff and affiliated staff. Additional resources were created for referring facilities, insurance companies, and other interested parties. In the two years, 9 patients were admitted (of about 20 referrals). Length of stay in rehabilitation was 21-56 days. 6 patients emerged, 4 discharged to home, 3 discharged to SNF and 2 patients were readmitted to acute care for medical complications.

Discussion: A formalized program for DOC was created and launched with strong backing from the administration. Staff was educated on management of DOC patients and formalized education was provided to referring hospitals. The results included an increase in the number of referrals, consistent approval from insurance companies, and better outcomes in emergence to consciousness and community discharge.

Conclusion: Formalized programs and documentation of results is essential in creating a program with specialized care, administrative support, and education of families and insurance companies.

Return to School and Return to Play - Are they Compatible?

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Objectives: Concussion has become an epidemic problem for children and youth, and there are still controversies in pediatric concussion management. Return to School (RTS) and Return to Activity /Play (RTA) are considered important, but there is debate as to sequence and whether they can be achieved simultaneously or that one, usually RTS, must be achieved before beginning RTA guidelines. Being a student is the primary role for children and youth and participation in school is vital in their overall development. However, the emphasis in post-concussion management has been on RTA, mostly sports. This study investigates the recovery trajectories of children and youth while following RTS and RTA guidelines, with the following objectives: 1) to examine symptom trajectories compared to patterns of RTS and RTA; 2) to determine if integration of RTS and RTA guidelines can be done effectively.

Methods: In a 3-year prospective cohort study of 126 children and youth aged 5-18 years with concussive injury, four main factors are being examined to measure their compliance with the RTS and RTA guidelines. These are: i) Symptoms – every 48 hours, ii) accelerometry, iii) Self report Cognitive and Physical activity levels, iv) Stage of guidelines. Cognitive, physical emotional and quality of life outcomes are evaluated at study entry, symptom resolution and 3-month post symptom resolution.

Results: Sample mean age is 13 yrs, 45% male. On average, youth are returning to school with accommodations by 8 days post injury and fully back to school by 1 month with 25% of youth still symptomatic at full return. The average return time to full sport competition is 52 days and 10% are still symptomatic. Sixty seven percent of youth report problems at school with 32% reporting a drop in grades. While many (84%) received various academic accommodation such as shortened days, altered courses, or delayed exams; falling of grades and other academic challenges are still noted, months after the injury.

Conclusion: Youth return to school faster than they return to play despite symptom profiles. Adherence with RTS guidelines appears to be less than RTA guidelines. RTS can be integrated with RTA in the early stages 1-3 of the guidelines. Considering the numbers of youth having school difficulties post concussion, full contact sport, stage 6, of RTA, should be delayed until full and successful reintegration back to school has been achieved. Balancing symptoms with cognitive and physical demands is still the challenge for each individual child and there is much to be learned with further research needed in this area.

Exploring the Biological and Clinical Effect of Depressive Symptoms in Youth Following Concussion

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Background: Concussion increases risk for depression both immediately after injury as well as later in life. The overlapping symptoms between concussion and depression (such as irritability, sadness, emotionality), however, can make depressive symptoms difficult to detect. Executive dysfunction is prevalent in youth following concussion. Evidence suggests a link between cognitive performance and emotional regulation in both healthy and concussed populations. The impact of emotional stimuli on executive control performance has yet to be explored in individuals with concussion who are displaying depressive symptoms.

Objectives: Primary: to explore the effect of depressive symptoms on executive function in youth with concussion in the presence of emotional stimuli using fMRI. Secondary: (1) to investigate overlapping symptoms of concussion and depression, (2) to explore locations of injury in individuals with depressive symptoms.

Methods: 30 adolescents diagnosed with concussion between 10-17 years were recruited. Levels of depressive symptoms were collected using the Children's Depression Inventory (CDI) self-report questionnaire, which identified youth with elevated depressive symptoms. All participants completed the Post-concussive symptom scale (PCSS), neurocognitive test (ImPACT), and an Emotional Go/No-Go task, which assessed emotion-mediated inhibitory control in a 3T MRI scanner.

Results: The group as a whole had impaired performance on cognitive performance demonstrated by ImPACT. Faces activated regions associated with both facial and cognitive processing. Youth with elevated levels of depressive symptoms were more likely to engage frontal regions that subserve evaluative processes. In concordance with CDI depression reporting, youth with elevated depressive symptoms were more likely to endorse emotion-related symptoms on the PCSS and with greater severity. However, fatigue and sadness was common between depression and concussion. The occipital lobe was the primary location of injury in 72% of youth with elevated depressive symptoms.

Conclusion: There are deficits in cognitive function following concussion. Youth with elevated depressive symptoms were more likely to engage brain regions subserving evaluative processing of social interactions, which might suggest that depressive symptoms display differences in physiology when emotional stimuli are present. This provides insight into the role the environment plays in contributing to the cognitive demands placed on adolescents recovering from concussion.

Protocol for The Creation of GIttools Supporting Evidence Based-Practices for The Rehabilitation of Moderate to Severe Traumatic Brain Injury

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Poor adherence to clinical practice guidelines (CPG) is a critical issue in health care delivery. Since 2012, the National Institute for Clinical Excellence recommends that guideline implementation tools (GIttools), defined as information helping users to adopt and apply recommendations included to or provided with CPGs, accompany each CPG. Although many quality CPGs have been produced to support best practices of rehabilitation for adults who sustained a traumatic brain injury (TBI), none include such tools.

The main goal of this project is to facilitate the adoption of evidence based practices presented through a CPG for the rehabilitation of adults who sustained a moderate to severe TBI. The objectives are: 1) to create GIttools for selected recommendations from the CPG-TBI, including summary sheets, training capsules, self-training modules, and complementary tools; 2) to ensure the dissemination of these GIttools in Quebec concerned clinical settings; 3) to measure the effectiveness of these GIttools in increasing the knowledge of clinicians and the level of implementation of selected recommendations.

The general methodology of the project follows the steps for GIttool development proposed by Gagliardi et al. (2015). A consultation will first be carried out with potential users from rehabilitation settings to select the recommendations for which GIttools will be produced. A rapid review of literature will then be carried out for each of them to find information on existing tools that could facilitate the adoption of the recommendations. Then, to create the clinical and theoretical content necessary to the development of the implementation tools, 20 leader clinicians will participate in intensive two-day workshops with the research team. Ten prototypes of summary sheets (pocket-cards), ten training capsules and ten self-administered modules will be produced. Complementary GIttools (checklists, decision algorithms to be added to the patient's file, or user-friendly versions of assessment tools) will also be created. The initial versions of the GIttools, validated by an Implementation committee, will be submitted to a sample of 20 pilot clinicians who will assess their acceptability and clinical utility. The tools will be revised with leader clinicians and members from the Implementation committee until a final version are considered suitable.

The inclusion of GIttools to the CPG-TBI represents an important « first » for the field of traumatology. The dissemination of these tools to Quebec clinical settings will improve the CPG's use and provide users with an opportunity for training, especially to those who will not have participated to the implementation process, including clinicians from other Canadian provinces (especially Ontario) and countries. By giving continuing education opportunities to new users, the created GIttools will contribute to the sustainability of evidence based practices promoted by the CPG-TBI.

Role of Subconcussive Head Impacts Exposure in Onset of Concussion on Day of Injury

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An estimated 300,000 sports-related concussions occur each year with high school and collegiate football players reporting higher rates of concussions compared to other contact sports. With increasing rate of sports related concussion, the role of subconcussive head impacts has received increased attention in recent years. The number and magnitude of subconcussive head impacts have been theorized to influence concussion tolerance. Subconcussive head impacts exposure during routine participation has also been associated with decreased cognitive abilities among non-concussed football players at the end of the season. Therefore, it is important to characterize role of subconcussive head impact exposure in onset of a concussion. One hundred and ninety-five athletes from four NCAA Division III football teams and 36 football athletes from two high schools participated in the study during 2015 season. All athletes were issued helmets containing the Head Impact Telemetry (HITS) system designed to measure head impacts biomechanics during games and practices. The system consists of 6 single-axis accelerometers mounted inside the helmet using modified liner. A total of 120,985 impacts and 12 concussions were captured with the system. The number and magnitude of head impacts sustained by players during each activity was compared between concussed (n=12) and non-concussed (n=213) athletes. Non-concussed athletes sustained an average of 13 impacts per session with average linear acceleration of 26 ± 18 g and rotational acceleration of 1126 ± 816 rad/s². The average peak linear (PLA) and peak rotational acceleration (PRA) of concussive impacts was 99 ± 29 g and 4506 ± 1674 rad/s² respectively. The system recorded 1,224 impacts among non-concussed players with magnitudes greater than average PLA or PRA of concussive impacts that did not result in a concussion. In order to further understand role of head impacts resulting in a concussion, the number of head impacts sustained by a concussed player on day of injury was compared to the significant number of head impacts sustained by non-concussed players at each activity throughout the season. Significant number of head impacts was defined as the 75th percentile (17 impacts) of average number of impacts sustained by non-concussed players during each session. Concussed players sustained an average of 27 impacts on day of injury, which was considerably higher compared to 13 impacts per session sustained by non-concussed players. Eight out of twelve concussed players also sustained significant number of head impacts (>17) on day of injury compared to non-concussed players. The data from present study show that number of subconcussive head impacts may influence the onset of concussion on day of injury. Further investigation is needed in order to study the role of magnitude and frequency of subconcussive head impact exposure leading up to the day of injury in influencing concussion tolerance.

Gender-Related Characteristics of Traumatic Brain Injury Patients: Data from A Tertiary-Care Hospital in Kampala, Uganda

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Background: Traumatic brain injuries (TBIs) are an important cause of death and disability in Sub-Saharan Africa. This study assesses the gender-related characteristics of TBI patients presenting to a tertiary-care hospital in Kampala, Uganda.

Methods: This prospective study is being conducted at Mulago National Referral Hospital, Kampala, Uganda since May 2016. The current analysis is on data from May – October 2016. Patients of all age groups presenting to the emergency department of the Mulago Hospital with suspected or documented TBI are enrolled. Gender differences in patient demographics, TBI characteristics and outcome in the emergency department (ED) were compared using Chi-square test for categorical and t-test for continuous variables. Ethical approval was taken from all three institutions.

Results: Of 1332 patients enrolled, 84.68% were males. Mean age of females was 25.2±18.6 years and of males 28.9±13.2 years. Among females, 62.3% were single, about a quarter were married, while among males 48.5% were single and 44.8% were married (p-value<0.001). The proportion of TBI patients with primary education was higher among females compared to males (71.6% vs 65.3%, p-value<0.001). Among males, 82.3% were working while only about 45.1% of the females was working. A quarter of the working males were boda boda (motorcycle taxi) drivers while females were mostly small business owner (29.4%). Seventy percent of males and a quarter of females were breadwinners of their families. The most common place of injury was road for both males (77.6%) and females (74.0%). Second common place of injury for females was home (16.7%) while workplace for males (7.9%). Road traffic crash (RTC) was the common cause of TBI in both males and females (56.7% and 69.1%) while assault (30.6%) in males and falls (13.7%) in females were second common cause (p-value<0.001). Among RTC victims, most males were motorcycle drivers (37.1%) and females were pedestrians (56.7%). Most of male assault victims were assaulted by bodily force (28.7%). The proportion of deaths in ED was higher in males compared to females (3.8% and 2.5%). Most of the TBI patients were admitted to wards for further care (males 42.4% and females 43.1%).

Conclusions: Compared to males, females with TBI are younger and single. Most of the males sustaining TBI are young, married and are breadwinners of the family. The results point towards the importance of road safety measures and violence prevention to reduce the burden of TBIs as well as burden on health care services.

Physiological Under-Arousal and Anxiety Following Mild Head Injury

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Objective: Anxiety disorders are one of the most common psychiatric complications following mild head injury (MHI; concussion). Further, anxiety has been reported as the most significant predictor of poor psychological and social outcomes after injury. Yet the types of symptoms these individuals endorse may differ from a non-MHI population, possibly reflecting a unique underlying neural mechanism.

Method: This study investigates self-reported anxiety symptoms, state and trait levels of anxiety, and overall physiological arousal in 300 university students with and without MHI. The Anxiety subscale of the Personality Assessment Inventory (PAI) was used to measure general feelings of tension, worry, and nervousness as well as physical signs of stress. In order to detect differences in anxiety symptoms reported between these two groups, anxiety components were classified into three subtypes: cognitive, affective and somatic features. The State-Trait Anxiety Inventory (STAI) was used to provide an index of frequency and intensity of both current and long-term anxiety levels. Electro dermal activation (EDA) and pulse rate were measured as indicators of overall physiological arousal.

Results: Those with head injury reported higher levels of cognitive and somatic relative to affective anxiety symptoms, in comparison to a healthy control group. These individuals also reported higher levels of trait rather than state anxiety relative to their cohort. Moreover, pulse rate and EDA levels were found to be lower in students who reported sustaining a MHI possibly reflecting a psychological and physiological unpreparedness to external stimuli.

Conclusion: It is our belief that this outcome may be due to disruption between the ventromedial prefrontal cortex (VMPFC) and subcortical structures involved in regulating autonomic arousal levels, thereby reducing the ability to incorporate emotional and physiological feelings from the viscera into the context of the present situation. This lack of information both diminishes the individual's reasoning and decision making processes and inhibits their ability to accurately perceive the situation, ultimately negatively affecting their ability to anticipate a likely course of action or outcome. A decreased capacity for appropriately anticipating future events may lead to frequent unexpected outcomes for these individuals, which may leave them feeling frustrated, irritable and in a state of constant worry. Moreover, given the lower baseline level of physiological arousal individuals with MHI exhibit, their reaction to stressful events may seem further exacerbated. This may be interpreted and reported as ongoing cognitive and somatic symptoms of anxiety despite these individuals being physiologically underaroused. This theory is further reflected as persons with MHI report lower levels of state relative to trait anxiety. Acknowledging and understanding the unique underlying neural architecture following MHI can provide a distinction from affective, somatic and cognitive symptoms of anxiety disorders, ultimately leading to better treatment paradigms.

Longitudinal Follow up of Cortical Excitability in Pediatric Traumatic Brain Injury

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Introduction: Recovery from mild traumatic brain injury (mTBI) is variable, with symptoms persisting past 3 months in 10-15% of children. Mechanisms of neurotransmission in mTBI recovery are poorly understood, however prior evidence suggests neurotransmission mechanisms are altered after an mTBI. The role of altered neurotransmission in post-concussive symptom persistence in children is unknown. Transcranial Magnetic Stimulation is a non-invasive brain stimulation technique that can be used to investigate neurotransmission post-injury by measuring alterations in cortical excitability in the superficial layers of the cortex.

Objective: The aim of this study was to determine if cortical excitability is altered following mTBI in children, and compare its relation to symptomatology at one and two months post injury.

Methods: This was a prospective controlled cohort study of children (aged 8 to 18 years) with mTBI. The Post-Concussion Symptom Inventory (PCSI) was used to determine recovery status (symptomatic vs. asymptomatic). Control group: Healthy children without a history of neurotrauma and of similar age, sex and socioeconomic circumstance.

Procedure: Cortical excitability was measured using single and paired pulse TMS paradigms at one and two months post injury. Outcome measures: The primary outcome was long interval cortical inhibition (LICI), a measure of GABA mediated cortical inhibition. Secondary outcomes included alternate TMS paradigms.

Results: Ninety-five children with mTBI (62 symptomatic, 59% female, mean age 14.07, SD=2.51, 33 asymptomatic, 45% female, mean age 13.71, SD = 2.57) and twenty-nine healthy controls (48% female, mean age 14.25, SD=2.97) were enrolled. Long interval cortical inhibition (LICI) values decreased (showing greater inhibition) between session one (40 days post injury) ($F(1, 59) = 5.70, p = 0.020$) than at session two (70 days post injury).

Conclusions: TMS measures of cortical excitability are altered at two months post injury. Long interval cortical inhibition is reduced in children with persistent symptoms after two months.

Assessing Recovery of Acute Mild Traumatic Brain Injury Patients Using Diffusion Tensor Imaging

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Objectives: In the present study we investigated whether Diffusion Tensor Imaging (DTI) can be used to assess recovery in patients with mild traumatic brain injury (mTBI).

Methods: Eleven acute mTBI patients 18-50 years of age and seven age- and sex-matched controls with no head injury were recruited from the emergency department of Huntington Memorial Hospital in Pasadena, CA. Images were acquired on three different visits, two weeks and four weeks, respectively, after the first recording, using a 3.0 T scanner for approximately 12 min of total imaging time. Diffusion images were collected along 32 directions with an isotropic voxel size of 2.5 mm³. An additional image with no-diffusion weighting was used as a reference. Image distortions, resulting from susceptibility-induced and by eddy current-induced off-resonance fields, were corrected using routines from the software package FSL. An affine linear registration routine part of FSL was also used to align the 32 images to the reference image. For each DTI dataset, diffusion Fractional Anisotropy (FA), Mean Diffusivity (MD), Apparent Diffusion Coefficient (ADC), and probabilistic tractography were estimated using FSL and the software package MedInria, with an FA threshold of 200, a minimum length for the detected fibers of 20 mm, and volume sampling every 5 voxels. To perform a quantitative analysis across the two groups, we first used the Johns Hopkins University tractography atlas to define 20 regions of interest (ROI), and the scans from the control subjects to create a reference database that included the mean and standard deviation values in each ROI. Then we computed z-scores for each subject's data and compared the groups using MANOVA with p value set at 0.05, corrected for multiple comparisons, considering group and visit as the independent variables.

Results & Discussion: The two groups were significantly different in FA values, but not in ADC or MD. Furthermore, FA values were significantly different only on the first visit, but not the second or third. The ROIs with the largest differences were the left and right superior longitudinal fasciculi. These areas, and their four distinct components, are involved with motor behavior and association tasks, perception of visual space, spatial attention, language articulation, and working memory.

Conclusions: Our results indicate that FA is a sensitive measure to detect injury in patients with mTBI during the acute phase, and it can also quantify improvement over time that correlate well with clinical measures and subjective patient-reported symptomatology. These findings suggest that FA may be used as a reliable biomarker of mTBI that can help with the diagnosis, prognosis, and assessment of treatment effectiveness.

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Impact of Head CT Findings on Parental Report Scoring of the Post Concussive Symptom Inventory in Children after Traumatic Brain Injury

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Objective: To describe deficits following an acute pediatric traumatic brain injury (TBI) utilizing a standardized tool in the subpopulations that receive brain imaging, specifically head CT, at time of injury. We hypothesized that there would be an increase in symptomatology following more significant injury as described by positive intracranial imaging findings on head CT.

Methods: Retrospective chart review on pediatric patients that attended a TBI follow-up clinic at a Level I trauma center. Inclusion criteria included having undergone CT brain imaging, age 3-21 years, and Post Concussive Symptom Inventory-Parent Rating (PCSI-PR) completion. 265 unique patients were identified. Of those, 84 were excluded due to age <3 years, 8 were excluded for non-acute TBI, and 4 were excluded for no imaging, for a total of 169 eligible records.

Results: ANOVA indicated significant differences were noted between the subpopulations of children with and without head CT findings (CT negative and CT positive). These data indicated that those in the CT negative category had a significantly greater mean total PCSI-PR score of 32 than those in the CT positive category of 16.6. ($p=0.001$) This held true for all subscales, including physical, cognitive, emotional, and fatigue.

Conclusions: Although positive CT is often considered a risk factor for worse injury severity and symptom persistence, these findings suggest that children with TBI without head CT findings may actually be at significant risk for increased symptomatology at follow-up. Reasons for this unanticipated finding will be discussed.

Clinical Characteristics of Traumatic Brain Injury Patients: Data from A Tertiary-Care Hospital in Kampala, Uganda

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Background: The clinical characteristics of traumatic brain injuries (TBIs) depend on severity of injury. This study assesses the clinical characteristics of TBI patients presenting to a tertiary-care hospital in Kampala, Uganda.

Methods: This prospective study is being conducted at Mulago National Referral Hospital, Kampala, Uganda since May 2016. The current analysis is on data from May – October 2016. Patients of all age groups presenting to the emergency department (ED) of the Mulago Hospital with suspected or documented TBI are enrolled and followed up till discharge. Patient demographics, circumstances causing TBI, pre-hospital management, injury characteristics, treatment, and outcome was noted. TBI was grouped into mild, moderate and severe categories based on Glasgow Coma Scale (GCS).

Results: Of the 1332 patients enrolled, 84.7% were males giving a male female ratio of 5:1. Mean age was 28.4±14.2 years. Road traffic injury (58.6%), assault (27.0%) and falls (7.9%) were the common mechanisms. Among all patients, most common presenting complaints of TBI were headache (67.0%), scalp wound (64.0), head swelling (58.4%), vomiting (29.7%) and drowsiness (20.3%). Most patients had closed TBI (69.4%). About a quarter of patients had no history of loss of consciousness (LOC) and 6.7% patients had LOC for >24 hours without return to baseline. Common modes of arrival at Mulago Hospital were private vehicle (32.0%), police vehicle (30.9%), and ambulance (24.7%). About 52.2% received care prior to presenting to the ED of Mulago Hospital; half of these patients (54.8%) received treatment in another health care facility. Use of alcohol was suspected in 32.9% and drugs in 11.9% of the TBI patients at the time of initial presentation. More than a quarter had associated injuries in other body regions with 6.1% patients having two or more of serious injuries. Mean heart rate was 86.0±22.4 beats per minute, respiratory rate was 22.3±7.1 per minute, systolic blood pressure was 122.0±20.6 mmHg. About 61.9% patients had mild TBI (GCS 13-15), 25.2% had moderate (GCS 9-12) and 12.9% had severe TBI (GCS ≤8) at the time of ED presentation. CT scan was done in 55.0% patients. Thirty four percent patients were sent home while 42.5% patients were admitted to wards. Only 6 patients were admitted to ICU and all had severe TBI. There were 48 deaths in the ED; 7 among mild TBI patients, 12 in moderate group and 29 in severe TBI group.

Conclusions: Young male patients, with the history of road traffic crash or assault are the most common victims of TBI. More than half of the patients receive first aid elsewhere and are subsequently transferred, which may contribute to the delays in definitive treatment. Majority patients had mild TBI but poor outcomes like ED death were observed within all categories of TBI patients.

Impact of Early Craniectomy on Mortality following Severe Blunt Traumatic Brain Injury in Children

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Background: The purpose of the study was to evaluate the impact of early craniectomy on mortality following severely blunt traumatic injury in children.

Method: First four years of data files from National Trauma Data Bank (2007-2010) was used. Data was then extracted using Current Procedural Terminology (CPT) procedure code for decompressive craniectomy (Pcode=1.25). Only severe head injury was included in the study. All children' age \leq 17 years and sustained blunt mechanism of injury were included in the study. Other key variables included in the study were, sex, injury severity score (ISS), initial Glasgow Coma Scale (GCS), transit time from scene to hospital \leq 60 minutes and craniectomies performed within 24 hours of admission. Patients were classified into early group if craniectomy was performed \leq 4 hours and late group >4 & \leq 24hours. Data were summarized using median for continuous variables, and frequency (percentage) for categorical variables. The Wilcoxon rank sum test was used to compare the continuous variables. The chi-square test was used to compare the categorical variables. A p-value of 0.05 or less was considered an indication of statistical significance.

Result: Total of 104 patients satisfied our inclusion criteria. Of that 84 patients had craniectomies performed within the 4 hour of hospital admission. There were no significant differences between the groups regarding age (P=0.511), male proportion (P=0.775), race (P= 0.996), pre-hospital transportation time (P=0.769), pulse rate (P=0.739), initial systolic blood pressure (P=.973), ISS score (P=0.305), subdural hematoma (P=.638) and epidural hematoma (P=0.707). In early group, there was a significantly lower GCS score (3 [3, 6] versus 3[3, 14], P<0.001). There was no significant difference in early versus late group related to overall mortality (18 [21%] versus 4 [20%]).

Conclusion: No significant difference seen in mortality whether the craniectomy was performed within 4 hour or between 4 hours and 24 hours following severely blunt traumatic brain injury in children.

Treatment for PTSD May Normalize Functional Connectivity Patterns in Veterans with mTBI and PTSD

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Background: Mild traumatic brain injury (mTBI) and posttraumatic stress disorder (PTSD) is a common comorbidity in veterans from the Iraq and Afghanistan wars. However, the literature on how mTBI and comorbid PTSD affect each other is sparse. Treatment recommendations specific to veterans with both mTBI and PTSD are in flux, and while treatments address each disorder independently, they may not be effective when the two disorders co-occur. Further, few studies focus on how co-morbid mTBI and PTSD present neurally. The aim of this project is to characterize the neural changes accompanying a novel treatment for PTSD, Group-Based Prolonged Exposure Therapy (GBET). We hypothesized that veterans with mTBI and PTSD in the GBET group would show reductions in PTSD symptoms compared to the Veterans with mTBI and PTSD in a treatment as usual (control) group, and that they would demonstrate altered functional connectivity (FC) in regions associated with PTSD.

Methods: Thirteen veterans participated (7 GBET, 6 Control). Measures included the Clinician Administered PTSD Scale (CAPS), the PTSD Checklist (PCL), and Beck Depression Inventory (BDI). Seed-based correlational analyses, FDR corrected for multiple comparisons across the whole brain and with correction for inflated cluster extent, and graph theoretic analyses FDR-corrected, were performed. Changes in PCL scores were related to FC changes.

Results: There were significant decreases in PTSD and depression symptoms (PCL and BDI) and a trend toward decreased symptoms in the CAPS in the GBET group, relative to the control group. In the seed-based analysis, the GBET group demonstrated increased FC between precuneus and the right ventral medial prefrontal cortex (VMPFC) and between the left amygdala and right supramarginal gyrus, relative to the control group. Additionally, the GBET group showed increased local efficiency around the lingual gyrus, relative to the control group. In regressions, people who benefitted the most from GBET showed greater FC between PCC and thalamus before treatment compared to after treatment, while people who did not benefit as much from GBET had greater FC between PCC and cerebellum before treatment.

Conclusions: Treatment with GBET was associated with reduction in psychiatric symptoms in patients with co-morbid mTBI and PTSD. Relative to the control group, these patients also demonstrated increased FC between regions associated with PTSD (precuneus and amygdala) and regions associated with emotion regulation (VMPFC) and executive control (supramarginal gyrus), respectively. Treatment with GBET also increased efficiency in neural connections around the lingual gyrus, known to have reduced FC in PTSD. Regressions of changes in PCL scores onto changes of FC revealed patterns that may serve as individualized indicators of patients who would benefit the most from this treatment. This study is limited by small samples, and larger groups are needed to explore how treatment influences brain activity.

“Look at our Concussion Protocol!”: A Case Study of Changes in TBI identification of School Students in Colorado

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Background: Nationwide a long-standing argument is that thousands of students are struggling in school, due to an undiagnosed brain injury or misdiagnosis with an incorrect disability. The Colorado Department of Education (CDE) made two major changes to increase the identification of students with previously unidentified traumatic brain injury (TBI), thus facilitating their eligibility for an IEP or 504 plan. 1) revised their IEP documents so that TBI was pulled out of the Other Health Impaired category of the IEP forms and given its own category. No longer hidden, it now appears y - and placed along side of among the other more- familiar special education categories, such as Intellectual Disabilities and Specific Learning Disabilities. 2) brought changes to the educational law in Colorado, so that students with no medical documentation of a TBI, can become “educationally identified” with one, opening the door for appropriately supportive related services.

The purpose of this study was to explore whether screening and identification processes have changed in Colorado school districts in response to this new category and educational identification. We also asked how these changes have facilitated the process of gaining eligibility for IEP services or 504 plans.

Methods: Design/Approach: Qualitative Case Study approach, with the “case” encompassing Colorado’s school districts.

Participants: Purposive sample of 10 rural, urban, and suburban school districts from the four quadrants of Colorado were recruited. The districts included those who had sent educational team members to attend two levels of training from the state educational agency and TBI program.

Data Collection and Procedures: Districts’ special education staffing professionals (e.g. - psychologists, special education teachers, occupational therapists, nurses, speech/language therapists), were given the choice of individual interviews or focus groups. Eight of the 10 school districts chose to gather in focus groups.

Data Analysis: We used analysis strategies developed for large case studies. Each district’s data were content coded, then re-coded for themes describing how each district identifies and supports students with TBI. We compared each district’s described process, use of terminology, geographic variables, and identified common statements.

Results: Common statements from school districts:

- Look at our Concussion Protocol!!
- We did attend state trainings on TBI changes
- Rural Districts – We’re too far from Denver!
- We don’t feel equipped for students with TBI – need more training..
- 504s are tolerable but IEPs are taboo for sports-related concussions and mild brain injuries
- Outlier District – We have used the new ED-ID protocol successfully with several students

Discussion: Why have districts developed a dichotomous view of TBI – sports concussion related TBI versus TBI bound for special education? How can we build a bridge from concussion to TBI identification for IEP development in special education?

The Clinical Course of Children Younger than 3 Years of Age with Anti-N-methyl-D-aspartate Receptor Encephalitis

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Objective: To describe the presentation, clinical course, and outcomes of children younger than 3 years of age with Anti- N-methyl-D-aspartate Receptor (Anti-NMDAR) encephalitis, specifically highlighting unique features within this specific age group, as little is known about Anti-NMDAR encephalitis in very young children.

Methods: Retrospective chart review of children younger than 3 years of age who were diagnosed with Anti-NMDAR encephalitis at a single pediatric tertiary referral hospital during a 2 year period (2015-2016). Data collected included demographics, presentation at admission, diagnostic evaluation, clinical course, immune suppression and other treatments, and exam at discharge and last follow-up appointment.

Results: Three children aged 18 – 23 months were admitted with Anti-NMDAR encephalitis. All presented with predominantly motor (not walking) and language (talking less) complaints with initially mild abnormal movements and irritability. CSF and other studies were consistent with the diagnosis, though one child had concomitant positive PCR for Epstein Bar Virus in CSF. Choreiform and other movement disorders markedly worsened in all 3 children early during acute hospitalization, requiring intubation, ICU admission, and continuous medication for control of movements in 2 children. All 3 received IV Methylprednisolone, IVIG, and Rituximab within the first 2 weeks of admission; the 2 children requiring critical care also underwent plasmapheresis, during which one child developed a left inferior cerebellar stroke. One child received a dose of cyclophosphamide after all other treatments due to lack of clinical improvement. One child required tracheostomy and two required gastrostomy tube placements. None had clinical or electrographic seizures; 2 of the 3 children developed autonomic instability. Clonazepam was started and continued at discharge in all 3 children; Tetrabenazine was prescribed for 2 of the 3. All 3 children were significantly functionally impaired (non-verbal, non-ambulatory) at acute hospitalization discharge. Only 1 of the 2 children made notable functional gains during subsequent inpatient rehabilitation; however, at last follow-up evaluation, all 3 demonstrated ongoing developmental gains with gross motor skills more improved than language skills (all 3 walking but without verbal communication). None had ongoing movement disorder at follow-up evaluation.

Discussion: As highlighted in this case series, the initial presentation and clinical course of children younger than 3 years of age is different than older children and adults with Anti-NMDAR encephalitis. Follow-up is ongoing for the children yet it appears that even with early and aggressive immune suppressive therapies, all 3 children still have ongoing developmental delays, especially language impairment, within the first year of insult. Considering the underlying neurodevelopmental pathophysiology, young children may be uniquely vulnerable to deleterious effects following Anti-NMDAR encephalitis.

Depression Post-Head Injury: Severity of Somatic Depressive Symptoms Associated with Sympathetic Underarousal

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Objective: Depressive symptoms post-traumatic brain injury (TBI) are one of the most common and challenging barriers for survivors, with estimates as high as 70 to 80% reporting symptoms (Chrisman & Richardson, 2013). Despite the high prevalence, minimal treatment strategies have been shown to be efficacious, with the most common treatment for depression in the non-neurally compromised population (i.e., SSRIs) linked with detrimental effects to neurocognitive capacity within the TBI population (Lee et al., 2005). The orbitofrontal cortex (OFC) has been implicated in the TBI literature as being both highly vulnerable to injury and important for modulation of sympathetic arousal through its connections with the brain stem via the limbic system (Wallis, 2007); and in the non-TBI literature for its connection in the etiology of depression (Maller et al., 2010). Our prior work has shown that individuals with mild head injury (MHI) are sympathetically underarousal at rest and in anticipation of decision-making, similar to what has been observed in OFC lesion populations (Bechara et al., 1996; 2004). Recently, we have demonstrated in several studies that MHI endorse more somatic depressive symptomatology relative to affective (sadness, hopelessness, etc.), despite having the same summary depressive score as their no-MHI cohort. This has provided preliminary evidence for individuals with head injury to potentially have a phenomenologically different “type” of depression. We then sought to replicate this finding in a larger sample.

Methods: 300 participants (35% with MHI) were recruited from the University setting to complete a series of neuropsychological, self-report psychopathology measures (SCL-R-90, BDI, PAI) and measures of sympathetic arousal (e.g., pulse, respiration, blood pressure, and electrodermal activation [EDA]). Further, we have developed a double-blind cross-over randomized control trial utilizing a psychostimulant medication to increase arousal in individuals with mild-TBI and determine if this will subsequently impact measures of neurocognition and depressive symptomatology.

Results: As observed in prior studies, individuals with MHI displayed a pattern of physiological underarousal as measured by EDA and systolic blood pressure. Furthermore, they endorsed more somatic symptoms of depression relative to their non-injured cohort and the severity of these symptoms was predicted by their underarousal. This pattern of results was not observed in the no-MHI cohort, whereby they endorsed more affective symptoms and there were no relationships between depression and sympathetic arousal. Although not yet complete, preliminary results of the RCT will be discussed, highlighting a discussion about whether dopaminergic agonists will be potentially helpful in the treatment of underarousal sequelae.

Conclusions: These findings replicate our prior work, suggesting that depressive symptoms post-head injury are phenomenologically different than typical MDD and are mediated by physiological underarousal. Moreover, a potential treatment target may include elevating arousal with psychostimulants as a treatment approach for targeting depressive symptomatology in TBI populations.

Development of a Semi-Interpenetrating Network Hydrogel to Study the Effects of Mild Traumatic Brain Injury on Astrocyte Remodeling

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There are over 1.7 million cases of traumatic brain injury (TBI) that are reported each year; the vast majority of which are considered mild injuries, commonly referred to as concussions. In all cases of TBI, the contact and/or inertial forces experienced by the brain result in the rapid deformation of the tissue and ultimately a cascade of pathological events. In this study, an alginate/laminin semi-interpenetrating network (sIPN) was constructed to encapsulate and maintain viable astrocytes in an environment with a biomaterial stiffness similar to the brain parenchyma. This sIPN was then used to study the mechanisms behind astrocyte remodeling following mechanically-induced mild traumatic brain injury (mTBI). First, primary neonatal rat astrocytes were encapsulated in alginate or alginate/laminin hydrogels. Laminin was incorporated in the hydrogel to investigate the importance of ECM proteins in combating cell injury. The cell encompassing hydrogels were then placed in our custom-made TBI bioreactor which imposed rapid impact and inertial loading to the hydrogels to simulate a mild TBI. Effects of the TBI were examined 1 and 7 days post-injury. 1 and 7 days post-mTBI, cell proliferation was evaluated via MTT Assay, expression of reactive astrocyte markers was measured via RT-PCR, and cell viability was assessed using Calcein and ethidium homodimer-1 fluorescent staining. MTT assays showed that there was an increase in proliferative astrocytes 1 and 7 days post-TBI and the presence of the laminin protein also increased astrocyte proliferation. These results lead us to believe the cells were being activated by the mTBI. To further investigate this hypothesis, we used RT-PCR to look at the gene expression markers for astrocyte injury (S100B) as well as reactive astrocytosis (GFAP, Vimentin, IL-6, and TNF). Our results showed an increase in S100B and significant increases in the reactive astrocyte markers. Lastly, we assessed cell viability. Initial experiments showed an increase in dead cells post-TBI compared to the control. Furthermore, adding laminin decreased the number of dead cells compared to the TBI no laminin counterpart. In summary, our study showed that the mechanical forces exerted on astrocytes during a mTBI can lead to not only cell injury and death but also cell activation to repair the damaged microenvironment.

Acetazolamide Mitigates Astrocyte Cellular Edema Following Mild Traumatic Brain Injury

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Mild traumatic brain injury (mTBI) is the most common type of traumatic brain injury and is often experienced by those in car accidents, on the battlefield, and in full-contact sports. One of the major factors that lead to the high morbidity and high mortality rates post-TBI is cellular edema in astrocytes. Studies have shown that Aquaporin-4 (AQP4), a water-permeable protein channel highly expressed on the membranes of astrocytes, is upregulated following brain injury. In this study, we investigated the use of the antiepileptic drug and known inhibitor of AQP4, Acetazolamide (AZA), as a therapeutic to mitigate mTBI-induced cellular edema. We hypothesized that mTBI-mediated astrocyte dysfunction, initiated by increased intracellular volume, could be reduced when treated with AZA. We tested our hypothesis in a three-dimensional in vitro astrocyte model of mTBI. Samples were subjected to no stretch (control) or a single high-speed uniaxial stretch (mTBI) injury. Immediately following the mTBI, the cells were analyzed under a multi-photon microscope in which Z-stack images were acquired every 10 minutes for 1 hour for volumetric analysis. 24 hours post-mTBI, AQP4 expression was analyzed via western blotting and immunofluorescent staining, S100B expression was observed via immunofluorescent staining and cell vitality was assessed using a commercially available cytotoxicity assay (LIVE/DEAD Cell Vitality Assay Kit, C12-Resazurin/SYTOX Green; Molecular Probes, Eugene OR). AQP4 expression in the astrocytes was significantly increased 24 hours post-TBI. Notably, there was also a 4.6-fold increase in cell volume immediately following the mild TBI. The addition of AZA to the model significantly reduced the observed increase in AQP4 expression and there was only a 1.7 fold increase in cell volume post-TBI. Cell death and injury, quantified via flow cytometry and S100 β expression, was also significantly decreased when AZA was added shortly before the mTBI stretch. Overall, our findings point to the occurrence of astrocyte swelling immediately following mTBI and AZA as a promising therapeutic strategy to mitigate downstream mortality.

Low Frequency of Cognitive Decline or Impairment in Acutely Concussed Patients

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Introduction: Concussion is frequently accompanied by subjective cognitive symptoms that usually resolve spontaneously in most adults within 7 to 14 days. (e.g., McCrea et al, 2003). The 'baseline' neuropsychological (NP) model allows a clinician to compare pre- to post-concussion data to determine if any NP changes might be due to brain trauma. This approach has been criticized for a variety of reasons (see Echemendia et al, 2013). In the absence of baseline NP data, determination of a patient's normal or abnormal cognitive functioning can be established using group normative data.

Methods: Patients who are referred to the Hull Ellis Clinic are NP assessed at their first visit and subsequently at specified intervals using several neurocognitive tests from the NINDS Common Data Elements suggested list for assessment of Traumatic Brain Injury. These include those designed to measure processing speed, reaction time, simple and divided attention, visual scanning, 'set' shifting, verbal learning and verbal memory. Although NP data are collected for research purposes, patient feedback on NP scores is provided. In the absence of baseline NP data, a very liberal clinical determination of cognitive decline or impairment - operationalized as any score lower than the 10th percentile – is used.

Preliminary Results: 91 patients (F=49, M=32) with an average age of 32.9 years (SD=3.4 years) agreed to participate in data collection beyond Week 1 and were admitted to Clinic at an average of 5.9 days after referral. Cognitive test data obtained at 3 time points (1st visit, Week 2 and Week 12) indicate in general a very low frequency of cognitive decline or impairment for most measures, at time of 1st visit, for the vast majority of participants, even when 'impairment' was liberally defined as any score placing lower than the 10th percentile. For example, only 1 participant (< 1 percent) scored less than the 10th percentile using normative comparative data on the Trails B test at 1st visit. The most clinically sensitive measure proved to be Symbol Search test; but the frequency of scores less than the 10th percentile was still only 8 percent. All participants' scores on all NP measures improved from 1st visit to Week 2; but it is unclear if this was due to practice/learning effects or 'recovery'.

Conclusion: The very low frequency of cognitive decline or impairment observed in a sample of acutely concussed patients suggests that such tests may be of very limited clinical value in determining, objectively, whether a patient's subjective complaints of cognitive dysfunction may be verified using a normative approach more than 1 week post-injury.

References: McCrea, M., et al (2003) Acute Effects and Recovery Time Following Concussion in Collegiate Football Players. *JAMA*, 290: 2556-2563

Echemendia, R. et al (2013) Advances in neuropsychological assessment of sport-related concussion. *Br J Sports Med* 2013; 47:294-298

Objective Assessment of Auditory Hypersensitivity in Acute Concussion: A Case Series

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Background: One-third of individuals who have sustained a concussion reportedly suffer from noise sensitivity (Potter, Leigh, Wade, & Fleminger, 2006). By exacerbating cognitive and fatigue symptoms, noise sensitivity (hyperacusis) can significantly limit function post-concussion, and has been suggested as a predictor of post-concussive syndrome (Dischinger, Ryb, Kufera, & Auman, 2009). Importantly, while hyperacusis has been evaluated in various pathologies (Sheldrake, Diehl, & Schaette, 2015), the nature and underlying mechanisms of hyperacusis in patients with concussion is “under-researched” (Landon, Shepherd, Stuart, Theadom, & Freundlich, 2012). Only one preliminary study investigated auditory dysfunction in concussed athletes, and concluded that concussion may lead to prolonged auditory dysfunction, suggestive of pervasive pathology (Assi et al., 2015). Further research is necessary to characterize post-injury symptoms, and document objective changes associated with abnormal auditory sensitivity, a critical step prior to consideration of assessment and rehabilitation. The purpose of this study is to identify and document auditory hypersensitivity in young adults with acute sport-related concussion.

Methods: Three university students who had received a medically documented sport-related concussion were recruited. In order to track possible rapid changes in hypersensitivities, participants were assessed as soon as possible after their concussion, and again at 2 weeks and at 10 weeks post-evaluation. **Procedures:** Participants completed a subjective symptom checklist, including psycho-affective symptoms and degree of noise sensitivity. The test battery for auditory sensitivity included tests routinely used in the field of clinical and vestibular audiology: Dynamic Range of Hearing, Uncomfortable Loudness Levels (UCLs), Speech-In-Noise, and Acoustic Reflex Thresholds (ARTs), as well as the King-Devick Test of Concussion for visual-vestibular function and the Sway balance test. In addition, each participant had P300 event-related potentials collected using an auditory oddball paradigm.

Results: Initial results indicate a reduction in sound tolerance in the acute phase, as evidenced by decreased dynamic range of hearing and decreased UCL – with decreases of 9 - 24 dB across participants. Reduction in UCL was present even when the participant did not complain of hypersensitivity to noise. Hearing thresholds, Speech-In-Noise testing and ARTs were all within normal limits. Further analysis will examine to what extent subjective symptoms and objective measures of noise sensitivity and vestibular functioning correlate and change over time.

Discussion: Preliminary findings give early objective support to the common patient complaint of hyperacusis and suggest that noise sensitivity has a perceptual basis. Additionally, these results offer early, but important, consideration that objective measures of hypersensitivity may be present even without subjective complaints. This case series adds to the understanding of auditory dysfunction in concussion and serves as a pilot for future research for expansion of adult and pediatric populations.

Ready to Be Steady: Correlation of Balance Measures Commonly Used in Traumatic Brain Injury (TBI)

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Purpose: The purpose of this report is to evaluate the correlation of three balance measures commonly used in individuals with traumatic brain injury (TBI).

Subjects: Subjects for this report were recruited from a larger RCT comparing the effect of two interventions on balance after TBI. All subjects met the following criteria: \geq one year post TBI; \geq three months beyond completion of formal PT; and able to independently ambulate in the home environment. To be enrolled, subjects also needed to self-report ongoing balance challenges and demonstrate deficits on standard outcome measures for balance.

Materials and Methods: After an initial phone screening, all appropriate individuals participated in a baseline assessment completed by a blinded physical therapist to determine overall severity of balance deficits and the underlying balance systems impaired. The Community Balance and Mobility total score (CB&M), the BESTest and the Activities Balance Confidence scale (ABC) were all measured in 45 subjects with TBI who met the inclusion criteria previously described.

Results: Evaluation of the 45 subjects demonstrated statistically significant ($p < 0.01$) positive correlations at baseline between balance measures to include the following: BESTest and CB&M $r = 0.847$; ABC and BESTest $r = 0.474$; ABC and CB&M $r = 0.399$.

Conclusions: The CB&M and BESTest demonstrate a very high positive correlation while the ABC (self-report) is only moderately correlated with both the CB&M and the BESTest.

Clinical Relevance: The CB&M and BESTest may provide similar information when clinically evaluating individuals with TBI who have balance dysfunction. Although self-report scales may be beneficial when assessing balance dysfunction in this population, clinical measures such as the BESTest and CB&M are likely also needed to provide a more in depth clinical picture.

A Qualitative Study on the Experiences of Caregivers of Individuals in a Locked in, Minimally Conscious, or Vegetative State with the Health Care System

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Objective: The objective of the current study was to understand the experiences of caregivers of individuals in a locked-in state (LIS), minimally conscious state (MCS), or vegetative state (VS) with the health care system when caring for their family member. The context for the current study is the Canadian health care system. It is publicly funded and administered on a provincial or territorial basis, within guidelines set by the federal government.

Methods: A qualitative descriptive approach was used and involved telephone interviews. Semi-structured telephone interviews were conducted with family members of individuals in a LIS, MCS, or VS. Participants were recruited between June 2014 and December 2016. Analysis was conducted using inductive thematic analysis as described by Braun and Clarke.

Results: A total of 21 interviews were conducted and included spouses, parents, and a sibling of individuals in a LIS, MCS, or VS in Ontario, Canada. We organized our findings in relation to the emergent theme of caregivers' experiences with the health care system: importance of a respectful attitude on the part of health care providers towards the individual in a LIS, MCS, or VS and their family members; experiences of abuse towards the individual in a LIS, MCS, or VS or their family members; lack of flexibility in health care policies; inappropriate care settings; and, jurisdictional challenges in the care/policies between provinces.

Conclusion: To the best of our knowledge, this is the first study on the experiences of caregivers' of individuals in a LIS, MCS, or VS with the health care system. We identified micro-, meso-, and macro-level health care system barriers to the delivery of high quality care. The findings from this study should be used to develop policies and/or interventions aimed at improving these aspects of the health care system and ultimately providing patient and family-centred care.

Tape Walking Improves Gait after Stroke

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Background: Walking impairments are common after stroke, and are strong predictors of poor community integration, health-related complications, and even death. Improving ambulation is the most commonly stated goal in stroke rehabilitation. Physical therapy efforts to improve ambulation can be categorized into (1) neurodevelopmental techniques, (2) strength training, and (3) task-specific training within the context of an intensive multi-modal approach. The latter is associated with the most robust outcomes. This study aims to examine the effectiveness of a visually guided gait-training intervention within the context of a comprehensive interdisciplinary brain injury rehabilitation treatment plan.

Design: Case-series design.

Method: Seven patients who have experienced a cerebrovascular accident (CVA) (three right CVA, four left CVA) received thirty minutes of this intervention five days a week for four weeks (i.e., 20 sessions) as part of an interdisciplinary milieu-oriented brain injury rehabilitation program. The intervention was comprised of assisting patients as they walk over-ground with pieces of tape placed horizontally at a specified distance apart from each other. Patients were encouraged to lengthen their steps by extending one leg at a time to reach the next piece of tape. Treatment outcomes were measured using the GAITRite Electronic Walkway.

Results: Patients' with left hemiparesis demonstrated increases in step length and velocity after the intervention. Patients with right hemiparesis demonstrated the same increases. Step length differential between left and right lower extremities decreased among both patient groups as well.

Conclusion: The results of this case-series investigation suggest a tape walking intervention within the context of an interdisciplinary multi-modal approach to physical therapy improves gait after strokes.

Inpatient Rehabilitation for Traumatic Brain Injury Patients: Content of Interventions and Functional Outcomes by Age

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Introduction: Although several population-based studies have been conducted on demographic and clinical characteristics of Traumatic Brain Injury (TBI) patients, there is a paucity of evidence on the influence of age on components of treatments and outcomes of IR in patients who were treated in Canadian settings.

Objectives: Exploring differences in occupational and physical Therapy treatments and functional outcomes by age in TBI patients at Toronto Rehabilitation Institute-University Health Network.

Methods: Data on 149 adult TBI patients between 2008 and 2011 were obtained from Practice-Based Evidence data-set. Patients were stratified by their age into three sub-groups (<30, 30-65, ≥65). Point of care forms and Functional Independence Measure (FIM) were used to document activities and motor/cognitive functions.

Results: Males (108, 72.5%) and middle age group (78, 52.3%) made up the main proportion of TBI patients. Rehabilitation length of stay was significantly longer for older adults than youngest counterparts ($p < .05$). Regarding content of treatments, number of Occupational and physical therapy sessions was higher in older patients than their youngest counterparts. However, older patients received less intensity (minute/week) of treatments with respect to OT interventions (i.e., cognitive activity and community reintegration) and PT interventions (i.e., therapeutic exercise and stairs training). Regarding functional outcomes, youngest patients had significantly higher FIM cognitive and motor function score at admission, discharge and 3 months post-discharge than other two groups. This up-ward trend remained significant to 9 month post-discharge for motor function ($p > .05$) but not for cognitive function.

Conclusion: Youngest patients showed significantly greater motor and cognitive recovery from admission to 3 months post-discharge than the other two age groups. However, this upward trend did not stay significant to 9month post-discharge for cognitive function. This result could be attributed to the lower pace of cognitive recovery than motor recovery in patients with TBI. Furthermore, older adults received more number of therapy sessions with fewer duration of occupational therapy (i.e., cognitive and community reintegration activities) and physical therapy (i.e., therapeutic exercise and stairs training) interventions. This could be explained by the lower tolerance of older adults in performing activities.

The Ketogenic Diet and Brain Injury: A Scoping Review

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Introduction: Traumatic brain injury (TBI) is a leading cause of injury-related morbidity and mortality worldwide. It is estimated that 3.2-5.3 million persons in the United States are living with a TBI-related disability and approximately one third of injury-related deaths are attributable to TBI. The pathophysiology of TBI involves an immediate primary injury by direct trauma to brain tissue, and a delayed secondary injury. Secondary brain injuries arise from subsequent complications including inflammation, cell-receptor mediated dysfunction, free radical and oxidative damage and ion-mediated cell damage. Recently, the ketogenic diet, a long-standing metabolic therapy for children with intractable epilepsy, has been shown to have neuroprotective effects, including the inhibition of the pathophysiologic pathways of secondary injury. The purpose of this study was to synthesize the evidence surrounding the role the ketogenic diet in TBI recovery.

Methods and Analysis: The methodological frameworks used by Arksey, O'Malley and Levac et al. were employed. Literature search strategies were developed using medical subject headings and text words related to traumatic brain injury and the ketogenic diet. The search was peer-reviewed, and involved EMBASE, Cochrane Central Register of Controlled Trials, MEDLINE, PUBMED, CINAHL and Web of Science databases. Two reviewers independently screened titles, and abstracts for inclusion, followed by screening of the full texts of potentially relevant articles to determine final inclusion. 6634 articles were screened; 11 articles were included for scoping review.

Results: All articles included for review noted significant differences between ketogenic and control groups in cerebral metabolism. Nine out of the 11 articles identified in the review investigated the effects of the ketogenic diet on TBI in rat models. Rat models demonstrated that the ketogenic diet when compared to a standard diet reduced injury-related nitrosative stress, oxidative stress, cerebral edema, cellular apoptosis and contusion volume. Furthermore, significantly better motor, cognitive and anti-epileptic recovery was demonstrated in rats with an age-dependent effectiveness. Human trials did not investigate recovery outcomes, however, noted significant changes in cerebral metabolism markers including blood glucose, lactate and pyruvate concentrations, in addition to protein sparing effects with a ketogenic diet.

Conclusions: Current literature suggests a ketogenic diet contributes to significantly improved outcomes for cellular, metabolic and behavioural end-points in rats with TBI. Unfortunately, there is a lack of human trials investigating the role of the ketogenic diet in TBI at present. Existing animal study findings are compelling and the explained target mechanisms involved correlate well with established mechanisms for human TBI. The ketogenic diet is a tried, safe and widespread metabolic and weight therapy used by people everyday. Therefore, it is strongly recommended that human RCTs be conducted to further investigate the role of the ketogenic diet in TBI outcomes and recovery.

Nutrition and Meal Preparation Among Survivors of Moderate-Severe Traumatic Brain Injury (TBI): A TBI Model Systems Study With Implications for Weight Management and Health

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Objective: Proper nutrition and healthy dietary intake has been linked to improved health (e.g., prevention of high cholesterol or high blood pressure; reduced risk for diseases such as diabetes, hypertension, and obesity), weight management, greater energy, neuroplasticity, and growth/development. Given the impact of a moderate-severe traumatic brain injury (TBI) on cognitive, motor, and/or emotional functioning, one's ability to independently participate in healthy dietary intake behaviors and activities (e.g., meal preparation) may be temporarily compromised. Upon injury, nutrition and dietary intake are often controlled by medical intervention (e.g., feeding tubes, prepared foods) until medical issues are stabilized. However, less is known about potential changes in dietary intake and nutrition along with activities related to healthy eating (e.g., meal preparation) over the course of recovery. Thus, the aims of this study were to 1) examine nutrition and meal preparation patterns among individuals with a moderate-severe TBI upon discharge from inpatient rehabilitation and at 6-months and 1-year post-injury and 2) identify nutrition-specific weight management practices post-injury.

Methods: Participants include 208 adults (75% male, 59% Caucasian) recruited from three participating TBI Model Systems Centers (TBIMS). Average age at injury was 41-years old (SD=17.02). Participants were asked to complete measures assessing sociodemographic, medical, weight, nutrition, and lifestyle information upon discharge from inpatient rehabilitation and at 6-months and 1-year follow-up.

Results: While 57.2% of individuals reported preparing their own meals prior to their TBI, this rate significantly decreased to 38.0% by 6-months post-injury ($p < .05$) and down to 32.7% at 1-year post injury ($p < .05$). Contributing to this decrease is the proportion of individuals reliant upon another individual for meal preparation (2.9% of individuals upon discharge; 20.7% at 6-months; 21.6% at 1-year; $p < .05$). There was a statistically significant effect of time since injury on self-reported healthy nutrition habits, $F(2, 278) = 4.41, p < .05$. Specifically, TBI survivors reported engaging in healthier nutrition patterns at 6-months following TBI than they did prior to the injury and 1-year post-injury ($p < .05$). However, there was no significant difference in nutrition patterns prior to the injury and 1-year post-injury. Among those attempting to lose weight, significantly more people reported eating fruits and vegetables ($p < .05$) and reducing their junk food intake ($p < .05$) at 6-months post-injury than at discharge or 1-year post-injury.

Conclusions: Survivors of TBI tend to rely on a caregiver 6-months and 1-year post injury for assistance with meal preparation. They also appear to engage in behaviors to attempt to manage their weight (e.g., gain weight back from time of injury or lose weight). Given the role that proper nutrition plays in healthy weight management, personalized health promotion programs for survivors and caregivers are warranted as part of routine rehabilitation, particularly given the risk for sedentary lifestyles and ultimately obesity.

Source Connectivity Analysis Can Assess Recovery of Acute Mild Traumatic Brain Injury Patients

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Objectives: In this study we investigated whether source connectivity analysis of resting state Magnetoencephalographic (MEG) activity can detect patients with mild traumatic brain injury (mTBI).

Methods: Thirteen acute mTBI patients 18-50 years of age and eight age- and sex-matched controls with no head injury were recruited for the study. Approximately 5 minutes of continuous MEG was acquired on three different visits, two weeks and four weeks, respectively, after the first recording, using a CTF whole-head system with 66 axial gradiometer sensors. Data were sampled at 625 Hz and bandpass filtered between 0.1–80 Hz. Linear drifts, line noise, and eye movement artifacts were minimized using a notch filter at 50 Hz, and a blink detection procedure based on signal-space projection. Estimation of intracranial sources for each subject was based on dynamical Statistical Parametric Mapping (dSPM). The Desikan-Killiany atlas, consisting of 68 brain regions of interest (ROIs), was used for common co-registration of sources. Functional connectivity brain networks among the intracranial sources, including connectivity strength and directionality, were measured using Granger causality (GC). After co-registration of all data onto the same atlas, the intracranial sources, their activation, and the resulting connectivity networks were averaged across all subjects of the same group. The two groups were compared using MANOVA with group and recording session as the independent variables and number of ingoing (IN) and outgoing (OUT) connections in each ROI as dependent variables. The level of statistical significance was $p=0.05$, corrected using the false discovery rate (FDR) method. Our analysis focused on the delta band, source activations between 0.1-4 Hz.

Results & Discussion: We found that mTBI subjects had a larger number of stronger connections compared to controls. The IN connections were significantly different in two regions, (a) the right entorhinal cortex of the medial temporal lobe and the (b) supramarginal gyrus of the left parietal lobe. The OUT connections were significantly different in five regions, (a) the isthmus of right cingulate gyrus, (b) the pars triangularis of the left inferior frontal gyrus, (c) the right precentral gyrus, the (d) right postcentral gyrus, and (e) the precuneus of the superior parietal lobule. These areas are involved with spatial memory, perception of visual space, emotion formation and processing, learning, and memory, regions also known to be affected in Alzheimer's disease.

Conclusions: Our results indicate that GC can detect injury in patients with mTBI during the acute phase and correlates well with clinical symptomatology, and suggest that GC may be used as a reliable biomarker of mTBI that can help with the diagnosis, prognosis, and assessment of treatment effectiveness.

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Community based Cognitive Training of Executive Functions with Motion Based Video Games

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Background: Deficits in executive functions are common following acquired brain injury (ABI). Computerized software for cognitive training is becoming more popular as a rehabilitation tool for ABI, however there is limited evidence for effective transfer of the improvements to real-life performance. Moreover, patients often do not continue to receive cognitive rehabilitation when discharged home, and clinicians lack tools to effectively monitor patients' conditions once released from the clinic. Computerized cognitive training using motion-interaction software offers a training environment that is more realistic and natural, therefore may facilitate transfer to everyday-life performance. The software adapts in real-time to the patient's behavior and therefore may potentially enhance usability by these individuals. It further bridges the gap between the clinic and home, providing a tool for continuous training.

Objectives: The goal of this study is to assess the potential benefits as well as the experience and safety of community-based cognitive training of executive functions (EF) with motion based video games, for individuals with ABI, training at their place of residence.

Methods: Individuals with ABI living in the community were screened to have executive dysfunction using the Montreal Cognitive Assessment (MoCA). Eligible participants were instructed to use the adaptive motion-based video games for 15-20 sessions, at home. Before and after training assessments were also conducted at their homes, and included the Dysexecutive Questionnaire (DEX), functional EF assessments (EFPT), Computerized Neuropsychological EF assessments (NIH EXAMINER) and a measure of dual tasking (Walking While Talking). Once completing the intervention, participants filled in a satisfaction questionnaire at their home. Within games performance was recorded throughout the training.

Results: Participants successfully used the program at home, did not report any adverse effects, and reported enjoyment from the training. Preliminary results show that participants were challenged by the games and were able to perform increasingly more challenging EF tasks within the game environments. Preliminary results show improvements in multiple functional tasks and most executive neuropsychological tests following intervention.

Conclusions: These findings demonstrate the potential of community-based cognitive training of executive functions with individuals with ABI. Additional participants are currently being trained to power the effectiveness of this novel training for improving executive functions in individuals with ABI living in the community.

Understanding Inconsistent Implementation of Stroke-specific Screening in Emergency Departments: Findings from a National Audit of Acute Services

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Background: The assessment and treatment of acute stroke is time-critical. Clinical guidelines recommend prompt assessment in emergency settings for early identification of stroke and implementation of hyperacute interventions. Unfortunately the Australian National Stroke Foundation recently reported that only 38% of stroke cases in their national audit adhered to clinical guidelines regarding assessment in the emergency department. This study reports patient and clinical factors associated with stroke-specific assessment in emergency departments among patients hospitalised with a stroke.

Methods: The Australian National Stroke Foundation, National Stroke Audit of Acute Services included unique patient stroke cases (n=4087) from 112 hospitals across all states and territories of Australia. Clinicians completed the Australian Stroke Data Tool for at least 40 consecutively admitted acute stroke cases. This included reporting whether a stroke-specific assessment was completed in the emergency department. Reliability and program data logic checks were undertaken (using sub-sample audits by a second clinician at each site and statistical software, respectively). Hospital and patient identity information was removed. Patients were excluded from analyses if they did not present via an emergency department (e.g., in-hospital stroke). Generalised linear modelling (Bernoulli family) was used to examine patient and clinical factors associated with whether a stroke-specific assessment had been completed. Findings were presented as odds ratios (OR) and (95%) confidence intervals. To examine the proportion of variance attributable to differences between hospitals (versus between individual patients) the final linear model was repeated with hospital as a random effect (random intercept, 2-level model, patients clustered in hospitals).

Results: The single-level model indicated that a stroke-specific assessment was more likely to be completed for patients with an ischaemic stroke OR1.53 (1.24, 1.88) or transient ischaemic attack OR2.05 (95%CI 1.28, 3.28) in comparison to hemorrhagic stroke, for patients requiring a language interpreter OR1.33 (1.00, 1.77) and arriving by ambulance OR1.44 (1.21, 1.71). Stroke specific assessments were less likely to be completed for patients who arrived on a weekend OR0.78 (0.68, 0.90) and for Indigenous Australians OR0.63 (0.39, 1.01). The multi-level model indicated 58% (95%CI 50%, 67%) of the variation in screening practice was attributable to differences between hospitals rather than individual cases. Adjusting for the effect of clustering within hospitals eliminated the effect of language interpreter OR1.03 (0.71, 1.50) and being an Indigenous Australian OR0.99 (0.55, 1.80); all other effect estimates were similar across single-level and two-level models.

Conclusions: The clinical and patients factors associated with screening practices could be used to improve outcomes for people with stroke through targeted implementation of better early screening in emergency care settings. Given the substantial proportion of variation explained by differences between hospitals, targeted improvements in care models at facilities that are currently least aligned with best practice recommendations may yield the greatest benefits.

Morbid Thoughts Decrease on Individuals with Concussion History After An 8-Week Educational Program

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Introduction: Head trauma can have an impact on mental health, increasing risk of depression and suicidal thoughts. This study documents the response of an 8-week program on the morbid thoughts of individuals with a history of significant hit to the head.

Methods: Participants from 4 continents who finished a depression and anxiety educational program were studied. Those who chose to participate met once a week for 8 weeks for a 2 hour program. It consisted of a 45 minute DVD presentation by a physician experienced in the treatment of depression and a facilitated small group facilitated discussion together with weekly practical assignments. The program was available in Spanish and English. No doctor patient relationship was established. The program was offered by previously trained facilitators that were certified. This program focused on educating participants on healthy behaviors such as exercise, plant-based diets, sleep hygiene and others. Each participant answered at the beginning of the program and at the end of the program the Depression and Anxiety Assessment Test, a 77 question questionnaire that measured depression based on DSM-5 [The Diagnostic and Statistical Manual of Mental Disorders Volume 5], patient history, demographic and evaluated the presence and frequency of morbid thoughts. Morbid thoughts were defined as thinking about death often, considering harming yourself or others. The depression was classified according to DSM-5 into 4 categories as none (0-6), mild (7-10), moderate (11-19) or severe (20 or more).

Results: From 5997 participants that finished the 8 week program, n=297 participants reported having a history of head trauma. That group mean age was 52.1, SD 15.7, minimum 13, maximum 90, median 54 and 89.9% were Caucasian, 3% black and 5% were Hispanic. From this group, n=130 (43.7%) participants reported having some degree of morbid thoughts the last two weeks before the program (i.e. having them 1/4 of the days, 1/2 of the days or almost every day in a period of 2 weeks). Those with a history of head injury and that reported morbid thoughts had at baseline a mean depression of 18.7 SD 6.3 while those with a history of head injury but without morbid thoughts had a baseline mean depression of 11.7, SD 6.7. At the end of the 8-week program only 55 out of the 130 (that originally had morbid thoughts) continued with some level of morbid thoughts. At the end of the program the mean group depression of the original group that had the history of head trauma and morbid thoughts was 11.3, SD 7.2.

Conclusion: The intervention effectively improves depression and decreases morbid thoughts in most of the participants. This model should be studied further and a long term follow up should be done.

Which Patients Hospitalised with Acute Stroke Receive Risk Modification Advice: Findings from A National Audit of Acute Services

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Background: People who have experienced a stroke are at an elevated risk of another stroke. Evidence based recommendations suggest that advice and education about modifiable risk factors should be provided while patients are still in hospital following an acute stroke. The Australian National Stroke Foundation highlighted in their 2015 Acute Services Report that the provision of risk factor advice only in only 56% of cases in their audit. The present analyses examined patient and clinical factors associated with the provision of risk factor modification advice (risk advice) to patients during a hospitalisation for an acute stroke.

Methods: The Australian National Stroke Foundation, National Stroke Audit of Acute Services included (n=4087) cases from 112 hospitals across all Australian states and territories. Clinicians reported whether (or not) patients received risk factor modification advice before being discharged from hospital using the Australian Stroke Data Tool. Facilities were invited to include at least 40 consecutive admitted acute stroke cases. Re-audits of a subset of cases by a second clinician and program data logic checks were used to ensure the reliability and validity of data, with discrepancies clarified with each facility prior to analyses. Cases were excluded from this analysis if the patient had died in hospital or were not discharged from hospital directly (e.g., patients transferred to another hospital facility). Multi-level generalised linear modelling (Bernoulli family, random intercept, 2-level model, patients clustered in hospitals) was undertaken to examine factors associated with whether or not patients received risk advice with findings presented as odds ratios (OR) and 95% confidence intervals (95% CIs). The intra-class correlation coefficient from the final multi-level model was used to examine the proportion of variance attributable to differences between hospitals (rather than between individual cases).

Results: Patients were less likely to have received advice about risk factor modification if they were older OR 0.85 (0.78, 0.93) per additional decade, female OR 0.77 (0.61, 0.97), presented with a cognitive deficit OR 0.53 (0.39, 0.71), required a language interpreter OR 0.47 (0.28, 0.77), required a carer OR 0.65 (0.47, 0.89) or were discharged on a weekend day OR 0.60 (0.39, 0.91). They were more likely to have received this advice if they received treatment on a specialised stroke unit OR 1.98 (1.44, 2.74). Approximately 39% (95%CI 31%, 48%) of variation was attributable to differences between hospitals (rather than individuals).

Conclusions: The aforementioned clinical and patient factors associated with provision of risk modification advice among people hospitalised with stroke may be used to target improvements in clinical care models to help patients (and their families) reduce the risk of further stroke events.

A Case Study of Rehabilitation Outcomes Post Acquired Brain Injury in An Indigenous Central Australian Cultural Context

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Background: There is limited research into culturally appropriate assessments and rehabilitation services for Indigenous Australians post brain injury. The health needs of remote communities and adequate health service provision in Central Australia specifically are also challenged due to geographic, social, economic and cultural contexts.

The purpose of this case study is two-fold: 1) to describe clinical experiences faced in providing culturally and contextually appropriate clinical practice in Central Australia and 2) to add to a professional evidence base that can contribute to the development of culturally competent health professionals.

Method: A single case study from a speech-language pathology (SLP) rehabilitation approach of a 21 year old Indigenous Australian male admitted to a remote primary hospital with an acquired hypoxic brain injury post attempted suicide.

Results: Initial case history: 1) multiple social stressors leading up to incident, 2) previously independent in activities of daily living, 2) participated in a community work programme, 3) unknown level of literacy, 4) reported to speak Pitjantjara and some English.

Initial cognitive and language assessment results: 1) daily fluctuating levels of orientation, 2) difficulties with attention, short-term memory and problem solving, 3) difficulties in following verbal instructions in both languages and 4) expressive communication in both languages limited to keywords, short phrases and some gestures.

Initial challenges: 1) lack of culturally appropriate cognitive and language assessments, 2) patient's limited literacy levels; 3) patient's limited family support due to cultural issues and geography; and 4) the lack of awareness and understanding of rehabilitation.

The rehabilitation objective was to facilitate patient participation and independence in functional activities of daily living as well as support family for his ongoing care within the community.

Rehabilitation outcomes: 1) For the patient: able to use visuals (photos, menu board) and concrete objects (money, key card) to facilitate both culturally appropriate and practical approaches for functional daily living skills. 2) For the speech – language pathologist: able to use a person-centred, practical approach in holistically facilitating therapy.

Discussion: This case study describes multiple challenges in the provision of culturally appropriate rehabilitation post brain injury complicated with the challenges of remote health service provision. Culturally appropriate and safe rehabilitation practices need to be developed with adequate clinical education and training for speech-language pathologists and other health professionals. This case-study provides an insight from a speech-language pathologist to help initiate the expansion of our knowledge of effective cultural practice in context.

Emotional Intelligence Improves in 8 Weeks in Participants with History of Head Injury

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Objective: The study assesses the improvement of emotional intelligence (EQ) in participants with a history of significant head injury after an eight week community based educational depression program.

Design and Methods: The educational intervention consisted of weekly meetings. Participants watched a lecture by a mental health professional follow by small group discussion, weekly assignments were given. The participants meet once a week for 8 weeks for a 2 hour session. Healthy lifestyle principles of nutrition, exercise, rest, bright light, sleep, and other lifestyle changes were encouraged. All the facilitators were previously trained and certified. Organizers were professional and lay persons. The programs were organized as a service to the communities in 4 continents and each program was encouraged not to profit from the activity. Each program was organized independently. The programs took place in doctor's offices, hospitals, libraries, schools, churches and community centers. No patient physician relationship was established. Each participant at baseline and at the end of the program completed a 75 question questionnaire, the Depression and Anxiety Assessment Test, which measured levels of depression, anxiety, emotional intelligence, history (such as head injury) and demographics. Participants that finished the 8-week program were retrospectively included in the study. EQ can greatly impact work life and career and has been linked to better social intercourse and success in life. The 5 components of EQ are knowing their emotions, managing their emotions, recognizing emotions in others, managing relationships with others and motivating themselves to achieve their goals.

Results: From 5997 participants that finished the program, 297 self reported that they had suffered a significant head injury the last two years at baseline. The demographics of this 297 participants consisted of Caucasian n=267 (89.9%), African American 9 (3%), Hispanic 16 (5%), Asian 4 (1%). Average age was 52.1 (SD 15.7). The sample consisted of 28.6% male and 71.4% female. At baseline, participants had a group average EQ of 95.9 (lower than normal average), SD 14.9, minimum 54, maximum 144, median 96 and mode 102. At completion of the eight-week program participants had a group average EQ of 104.7 (above normal), SD 15.4, minimum 54, maximum 152, median 104, mode 112.

Conclusion: The program was beneficial to victims of recent head injury. Patients with a recent history of head injury had a below average EQ but increased after the 8-week educational intervention. It would be interesting to see how the increase of EQ affects important aspects of their lives. A follow up study is being planned.

Educational Intervention on Participants with Head Injury Improves Depression by Indirectly Improving Frontal Lobe

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Background: It is our hypothesis that there are 10 groups of causes that may trigger depression and anxiety. The 10 causes or hits are (1) Genetic, (2) Developmental, (3) Lifestyle, (4) Circadian Rhythm, (5) Addiction, (6) Nutrition, (7) Toxic, (8) Social/Complicated Grief, (9) Medical Condition, and (10) Frontal Lobe. There seems to be a correlation between negative behaviors towards the frontal lobe and depression. We consider a negative hit on the frontal lobe:

Anyone who is on a low carbohydrate diet, high meat diet, or high junk food diet.

Anyone that consciously suppresses frontal lobe activity.

Anyone that does not do regular abstract thinking or acts against their conscience or known value system.

It is hypothesized that changing key behaviors may potentially affect the frontal lobe and may improve depression.

Methods: An 8 week educational program was organized by certified facilitators which ran a two hour once week for 8-weeks program. The first hour, a DVD is watched followed by a facilitated small group discussion about improving various lifestyle factors. The Depression and Anxiety Assessments Test (DAAT) was used at baseline and at the end of the 8-weeks, it measured depression level based on DSM-5 [The Diagnostic and Statistical Manual of Mental Disorders Volume 5], demographics, history of significant hit to the head and included the questions of behavior that potentially affect the frontal lobe. The depression was classified according to DSM-5 into 4 categories as none (0-6), mild (7-10), moderate (11-19) or severe (20 or more).

All participants learn healthy behaviors and one session was focused on behaviors that may improve the frontal lobe. The program did not establish a doctor patient relationship. Programs were not run for profit.

Participants that finished the 8 week program and that had a history of significant hit to the head were included in the study.

Results: From 5997 participants that finished the 8-week program, 203 individuals reported that they had behaviors that were negative to the frontal lobe and had a history of head trauma. This group mean age was 52, SD 15.7, minimum 13 and maximum 90. These 203 individuals had a group mean baseline depression of 14.7, SD 7.4.

By the end of the 8 weeks, only 124 (61%) out of the original 203 individuals continued with behaviors that potentially affected the frontal lobe. Those without a negative behavior towards the frontal lobe had an end depression level of 7.1, SD 6.8, while those who continued with negative behaviors towards the frontal lobe had an end depression of 10.7, SD 6.2.

Conclusion: Certain behaviors that potentially affect the frontal lobe translate into higher levels of depression. The program seems to be an effective tool to encourage healthy behaviors.

Hippocampal Vulnerability After Diffuse Traumatic Brain Injury: Histological Analysis

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Introduction: Traumatic brain injury (TBI) is a public health problem due to the high morbidity and mortality in young and adult people, cause by traffic accidents and falls, which involves mechanical forces generating focal or diffuse brain injury in different degrees. The highest incidence corresponds to moderate trauma which does not imply death but cognitive and behavioral changes. The most susceptible region is the hippocampal formation, structure located deep in the temporal lobe and whose connectivity with other limbic structures and cortical areas is involved in processes such as learning, memory, spatial location, face recognition and attention. It is considered that post trauma amnesia whose duration is variable is the result of stretching and axonal edema which in severe cases can lead to deafferentation.

Objective: The aim of this work was to identify changes expression of especific cell, neurogenesis and neurodegeneration markers in the hippocampus of Wistar rat after traumatic brain injury.

Materials and Methods: Adult Wistar rats (300-360gr) were subjected to traumatic brain injury by Marmarou's weight-drop model (Impact acceleration model) and survival periods of 24 (n=6) 48 (n=6), 72 (n=6) hours, were compared with its respective controls (n=30). Fixed frozen brains were sectioned coronally at 30 micrometers using a cryostat. The sections collected from hippocampus were used for multi-histological analysis such as immunohistochemistry and immunofluorescence reaction with antibodies against NeuN, PV, GFAP and Beta-III Tubulin. Fluoro Jade C stain was also used. Sections were observed under a confocal laser scanning and light microscope. In the murine model of diffuse TBI free-fall weight of moderate intensity performed at the Centro de Estudios Cerebrales, and using immunohistochemical procedures we analyzed the cellular behavior in the lesion tissue.

Results: Temporary changes were observed in the immunoreactivity to NeuN; at 48 and 72 hours it was found a redistribution of NeuN without nuclear immunoreactivity and fragmented appearance. We also observed an increased in GFAP positive cells in the hippocampus, which showed larger bodies with thick and tortuous processes from 24 hours. B-III Tubulin expression predominated in the hippocampus with a peak at 48 hours. It is important to note that PV+ neurons were found to be significantly decreased compared to control. Fluoro Jade positive neurons was observed in dentate gyrus at the firts 24 hours. These results showed an early response of both neurons and glia to the diffuse brain trauma. The hippocampus showed major expression of cell deth and neurogenesis markers, which will indicate its susceptibility, last aspect associated with memory disturbances and epilepsy. Understanding the pathophysiological mechanisms in subacute period of trauma may allow to elucidate the processes that regulate cell survival and may help to find therapeutic approaches.

Gender Differences in Neurobehavioral Functioning in Chronic TBI

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Objectives: The majority of survivors of moderate to severe traumatic brain injury (TBI) suffer chronic cognitive, behavioral, and emotional problems. Challenging behaviors, change in personality, and lack of awareness can be the most disabling sequelae, negatively impacting socialization, employment, and quality of life. Behavioral manifestations may vary by gender and differentially affect functional outcomes. Thus, in order to understand risk factors for outcomes after TBI, it is critical to identify and discriminate differences in gender-specific neurobehavioral dysfunctions.

Methods: Participants included 39 males and 12 females with moderate to severe chronic (8.67 ± 7.42 years since injury) TBI. Average age was $41.80 (\pm 12.80)$ years, and average education was $14.47 (\pm 1.9)$. Primary measures included the Neurobehavioral Functioning Inventory (NFI), Beck Depression Inventory (BDI), Fatigue Severity Scale (FSS) and the Everyday Memory Questionnaire (EMQ). 2×2 (gender: male, female; rater: patients, family) repeated-measures ANOVAs were performed for each of the six NFI scales (depression, somatic, memory/attention, communication, aggression, motor). Pearson correlations were conducted to examine the relationships between NFI scales and the BDI, FSS, and EMQ.

Results: Mean t-scores for the NFI scales for patients and family members fell entirely within the average range for both genders. However, within the range of scores reported, 15%-26% of male patients and 3-24% of their family reported clinically significant problems, whereas 17-50% of female patients and 10-40% of their family reported clinically significant problems. For males, there was general agreement between patients and family regarding the most frequently reported problems. In contrast, female patients' report of most common problems was discordant from that of their family. Paired samples t-tests revealed no statistically significant differences between male patients and their family's scores on any of the scales. For females, a significant patient/family score differences emerged just on the aggression scale, $t(9) = 3.63$, $p = .006$; this difference score was found to be moderately correlated with fatigue ($r=.37$) and quality of life ($-.31$), and strongly correlated with depression ($r=.58$) and everyday memory ($r=.57$).

Conclusions: The results demonstrate preliminary support for distinct patterns of neurobehavioral symptoms in males versus females with chronic TBI. Clinically significant problems were reported in all domains of the NFI for both males and females. However, the order of importance of the problems differed by gender and, within gender, the rate of patient/family agreement differed by domain. These discrepancies did not result in statistically significant findings, except for females, where patient/family discrepancies in evaluation of aggression behaviors were related to psychosocial functioning and memory functioning awareness. Although generalization of these the study findings is limited by the small number of females in this sample, results offer initial support for gender differences in TBI outcomes.

An Investigation of Lipid Lowering Medication Prescription Among Ischaemic Stroke Survivors at Discharge from Hospital: Findings from a National Audit of Acute Services

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Background: Ischaemic stroke survivors are at an elevated risk of experiencing another stroke. A report from the Australian National Stroke Foundation highlighted that only 64% of ischaemic stroke survivors in their acute stroke national audit were receiving appropriate secondary prevention medications on discharge from hospital. This study aimed to identify patient and clinical factors associated with ischaemic stroke survivors being discharged on lipid lowering medications (when not contraindicated or futile).

Methods: The Australian National Stroke Foundation National Stroke Audit of Acute Services included (n=3121) patients with an ischaemic stroke from 112 hospitals across all states and territories of Australia. Clinicians reported whether (or not) patients were receiving lipid lowering medications at hospital discharge, using the Australian Stroke Data Tool for consecutive acute stroke cases admitted to their facility. Reliability of the data was enhanced by re-audits of a sub-sample of cases by a second clinician at each facility and program data logic checks. Discrepancies were clarified with each facility. Cases were excluded from this analysis if they did not have an ischaemic stroke, deceased in hospital, secondary prevention was considered futile (e.g., palliative), or the patient transferred to another hospital facility. Clinicians from each facility also reported whether lipid lowering medications were contraindicated for each case (and if so, those patients were excluded from analyses). Multi-level generalised linear modelling (Bernoulli family, random intercept, 2-level model, patients clustered in hospitals) was used to address the study aim with findings presented as odds ratios (OR) and 95% confidence intervals (95%CI). The intra-class correlation coefficient from the final multi-level model was used to examine the proportion of variance attributable to differences between hospitals (rather than between individual cases).

Results: Patients were less likely to be taking lipid lowering medication when discharged from hospital if they were discharged on a weekend OR 0.46 (0.28, 0.76), had a cognitive deficit OR 0.57 (0.40, 0.87), female OR 0.79 (0.58, 1.08), or had experienced a fever during their admission OR 0.52 (0.26, 1.01). Patients were more likely to be discharged on lipid lowering medications if they received treatment on a specialised stroke unit OR 1.37 (0.92, 2.01), and if had been prescribed lipid lowering medications prior to their current admission OR 9.36 (5.92, 14.82). Approximate 18% (95%CI 10%, 29%) of variation was attributable to differences between hospitals (rather than individual cases).

Conclusions: Correlates identified during this investigation may assist those seeking to improve rates of prescription of lipid lowering medications during acute hospital admissions for ischaemic stroke survivors. Ensuring ischaemic stroke survivors receive treatment on a specialised stroke unit, and targeting patients who may be at risk of not receiving appropriate preventative medications may yield benefits to patients but require health-service level interventions.

Variation in Whether Anti-thrombotic Medications Were Prescribed for Acute Ischemic Stroke Survivors: Findings from a National Audit of Acute Services

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Background: Ischaemic stroke survivors may be at an elevated risk of experiencing another stroke. A recent report from the Australian National Stroke Foundation highlighted that only 64% of ischaemic stroke survivors in their national stroke audit of acute services were receiving appropriate secondary prevention medications at discharge from hospital. This analysis examined patient and clinical factors associated with whether or not patients being discharged from hospital following an ischaemic stroke had been prescribed anti-thrombotic medication.

Methods: The Australian National Stroke Foundation, National Stroke Audit of Acute Services included 112 hospitals across all states and territories of Australia and comprised (n=3121) unique patients with an ischaemic stroke. The Australian Stroke Data Tool was completed for consecutive acute stroke cases admitted at each participating facility. This included recording whether each patient had been prescribed anti-thrombotic medication prior to being discharged from hospital. A sub-sample of cases were re-audited by a second clinician at each facility to enhance data reliability and program data logic checks were undertaken using statistical software. This investigation only included patients with ischaemic stroke; patients were excluded from analyses if anti-thrombotic medication was considered futile (e.g., dire prognosis) or contraindicated, as were those who died in hospital, and those who transferred to another hospital facility. Multi-level generalised linear modelling (Bernoulli family, random intercept, 2-level model, patients clustered in hospitals) was used to examine patient and clinical factors associated with prescription of anti-thrombotic medications. Findings were presented as odds ratios (OR) and 95% confidence intervals (95% CIs). The intra-class correlation coefficient from the final multi-level model was used to describe the proportion of variance attributable to differences between hospitals (rather than between individual cases).

Results: Patients who had received care in a specialised stroke unit were more likely to have been prescribed anti-thrombotic medication OR 1.86 (0.98, 3.56) as were patients taking anti-thrombotic medication prior their acute stroke 2.35 (2.35, 4.43). Patients identified as having a cognitive impairment OR 0.16 (0.08, 0.30), and patients who experienced a fever during their hospitalisation OR 0.29 (0.12, 0.71) were less likely to have been prescribed anti-thrombotic medication. The proportion of variation attributable to differences between hospitals (rather than individual cases) was approximately 11% (95%CI 1%, 43%).

Conclusion: Prescription of anti-thrombotic medications (where indicated) for people who have experienced an ischaemic stroke is an important secondary prevention activity that can be initiated in the hospital setting, but unnecessary variation away from best practice guidelines may contribute to risk of further stroke. Understanding patient and clinical factors associated with prescription of anti-thrombotic medications may be useful for developing targeted practice-change interventions to improve adherence with evidence based clinical practice guidelines in the field.

Effects of Concussion History on Driving Behaviors

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Background: Research has found deficits in gait, reaction time, and processing speed years to decades after experiencing a concussion. However, it is unclear whether these deficits translate to activities of daily living. The purpose of the current study was to examine whether a concussion history increases poor driving behaviors and increases risk for driving violations and/or accidents.

Methods: Young adults (age 18-29) were recruited and classified into concussed and non-concussed groups based on self-report. Previously concussed participants were required to have a diagnosed sport-related concussion a minimum of 2 years prior. Non-concussed subjects had no history of concussion. All subjects completed questionnaires on their health, athletic, concussion, and driving history prior to starting a driving simulation. The driving simulation contained an acclimation drive, a drive without a cognitive task, and a drive with a cognitive task (ie texting, phone call, directions). The non-cognitive demanding and cognitive demanding drives were randomized across subjects. Research staff administering the driving simulation were blinded to the concussion status of the subject.

Results: Subjects (N = 53) participated in the study, 49% (n = 26) were female, averaging 22 (SD = 3.3) years old. Concussed subjects (n = 26) were on average 4.6 (SD = 3.3) years removed from their most recent diagnosed concussion. There was no effect of concussion history on the Manchester Driving Behavior questionnaire. There was no effect of concussion on likelihood for any car accident, at fault accident, or moving violation. However, there was a greater likelihood for at fault car accidents among females who were concussed relative to females who were not concussed (OR = 17.4).

Conclusions: Concussion history alone did not appear to be associated with increased car accident or moving violations. Sex appears to modulate this relationship with concussed females having greater risk for an at fault car accident. Future research should prospectively track driving records post-concussion to determine whether concussion increases risky driving behavior.

Outcome of Children after Traumatic Brain Injury - First Results of the CREATKids Study (On Behalf of the CREATIVE Consortium)

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CREACTIVE multinational project, follow patients with moderate-to-severe traumatic brain injury (TBI), as part of the global InTBIR initiative. Patients outcome are measured in terms of injury-related disability and quality of life at six months post injury. CREATKids is the pediatric sub study which is led by a team from Ben Gurion University of the Negev in Israel. The Pediatric ICU at Soroka University Medical center is the first to fully implement the study tools and we present our methodology and center's results.

Materials and Methods: Common Data Elements endorsed by InTBIR are collected, along with items required to develop a sensitive prognostic model. Clinical data is collected via computerized software built and maintained by the CREATIVE study center situated in the Department of Clinical Epidemiology of Mario Negri institute, Ranica, Italy. Patients outcome are followed-up with separate Tool-box built for CREATKids study. The tool-box assesses impairment and disability in sleep, behavioral, emotional and neurocognitive dimensions and is distributed via the computerized software using both questionnaires and computer based neurocognitive tasks on designated touch screen. We present the first CREATKids results from our PICU: Two years descriptive results, Tool-box assessment pilot study and TBI-patients outcome assessment.

Results: Descriptive data: 1280 patients were admitted to our PICU during 2014-2015, 105 (8.2%) due to TBI. Mean age was 5.1 years, 68% were male. 95% came from the emergency room; 94% came from our hospital. Co-morbidity from other diseases was rare. Most head injuries were closed (84%) from low energy falls or traffic accidents; 58% of cases had focal injury, half of them with subarachnoid hemorrhage. 7.5% had diffuse injury. Overall ICU mortality was 2.8% and average length of PICU stay was 2.5 days (median 1 day (1-23)). Tool-box pilot study: the aim was to assess the feasibility of our toolbox to be submitted and complete follow up in diverse PICU patients. 52 PICU patients were approached and 49 consented to participate. 36 (73%) completed phone-call follow-up and 18 arrived to the face to face meeting. We concluded that our Tool-Box is a practical and easy to distribute tool. CTRACTKids 6 month follow up outcome preliminary results: Recruitment rate was 50% of TBI parents consenting to participate in the study of them 86% completed the follow-up procedure. Half of the patients that completed the procedure presented symptoms of PTSD in mild to severe manifestation. More than 60% of the patients presented sleep disorder that were not present before the injury. All but three patients completed the computer tasks. All patients passed a short physical examination, physical disability was rare.

Conclusions: We present the first pediatric results of our CREATKids study which brings important information on Post TBI outcome in children.

A New Comprehensive Tool-box for Assessment of Children's Outcome After Pediatric ICU Admission due to Traumatic Brain Injury (On Behalf of the CREATIVE Consortium)

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Traumatic Brain Injury (TBI) necessitating admission to pediatric ICU (PICU) is a dramatic experience both from physical and emotional perspectives. CREATKids is the pediatric sub-study of the CREATIVE consortium, investigating TBI as part of InTBIR initiative. We aim to study how TBI affects children wellbeing and long term outcome. Expert group (developmental psychologists, pediatric sleep, psychiatric trauma, neurosurgeons, rehabilitation, epidemiologists) led by PICU specialists, developed a comprehensive tool-box assessing impairment and disability in these children.

Methods: Patients are assessed at three time points: Time-0: On admission, parents describe their child's pre-injury sleep, emotional and behavioral characteristic using structured questionnaires; phone call interview 5 months' post injury - assessing use of rehabilitation, child's outcome and quality of life; Time-1: face to face meeting six months post injury, parents fill in same questionnaires as in T0 and also, children are tested with computerized, age-specific, tasks aimed to detect impairments in inhibition, working memory, numerical cognition and attention. The child undergoes a short physical examination.

Questionnaires: All tools are age specific as standard in pediatric research. Temperament: (36/37 items each) IBQ (ages 3months – 14months), ECBQ (ages 14months – three years) and CBQ (3-7 years). Sleep: BISQ (ages 0-3 years), CSHQ (3-12 years) and "school sleep habit survey" (13-18 years). Other: SDQ (2-18 years) behavioral emotional and social problems and their effect on the family. PTSD-RI symptoms of post-traumatic stress disorder (PTSD). PedsQL - measures Physical, emotional, social, and school functioning and quality of life. GOS-E Peds. provide an age-appropriate, measurement of outcome post TBI.

Neuro-Cognitive Tasks: Go/NoGo – assesses inhibition. N-Back - working memory assessment. Corsi - assesses visual (spatial) working memory. Dot Comparison – assess the sensitivity of patients' numerical perception. ANT - providing separate measures for the three different attention networks: Orienting, Alerting and conflict resolution.

Platform: All the assessment tools are computerized and based in a central server (Mario Negri Institute, Milan, Italy). Participating centers access the tools in a secured on-line connection. Computerized tasks are performed with a dedicated touch-screen monitor (Lilliput UM 1010T) in order to create standardization and an intuitive approach to the tasks among participants. Data is saved (anonymously) and analyzed on a centralized server. The Tool-box is currently translated to all participants' native languages (English, Italian, Arabic and Hebrew) and easily can be further translated to others using our online web translator.

Conclusion: The CREATKids tool-box is a novel comprehensive toolbox that uses age specific, state of the art measures to assess sleep, neurocognitive, behavioral, physical and emotional dimensions after TBI. It is

distributed using secured internet connection and is centrally analyzed. The tool-box achieves high compliance rates among patients, with each session taking less than one hour to complete.

Assessing the Clinical Usefulness of Three Tablet-Based Visuomotor Tasks to Evaluate Closed Head Injury (CHI)

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Closed head injury (CHI) varies in severity, and although severe cases have obvious and devastating effects on behaviour, milder cases can also have unexpectedly disruptive and long-lasting consequences. Research suggests that visuomotor deficits are amongst the last symptoms to resolve, taking longer than other cognitive processes such as memory. Given the sensitivity and possible importance of visuomotor processing as an index of recovery from CHI, the current study aimed to assess and validate the clinical usefulness of three tablet-based tasks that assess visuomotor function. Specifically, three common laboratory tasks measuring different aspects of visuomotor control and sensitive to brain damage were formatted for a portable tablet. Stop-Signal is a test designed to measure how well people can inhibit an already-signalled movement (Logan et al., 2014). Interception is a test that measures how well people can perceive velocity and acceleration of a moving target to accurately intercept that target (e.g., Brown et al., 2007). The Double-Step task measures movement updating in response to the changing position of a reaching target (Prablanc et al., 1986). Participants included a group of individuals who had suffered a closed head injury within the past three years (CHI: n = 30), a group of individuals who had suffered an orthopaedic injury within the past three years (IC: n = 30), and a group of age-matched healthy controls (HC: n = 30). It was predicted that the CHI group would perform worse on all three tablet-based tasks compared to the IC and HC groups and that performance would correlate with time since injury. All participants completed the three tablet-based tasks along with a battery of neuropsychological tests assessing visual and verbal memory and estimating verbal and performance IQ. The results suggest that the CHI group demonstrated a pattern of decreased performance on the Stop-Signal and Double-Step tasks compared to the two control groups but not on the Interception task. Specifically, participants with a CHI were less likely to accurately inhibit a movement as SOA increased and were less able to update movements when target position changed. A positive relationship was also found between performance on the Stop-Signal task and time since injury, however, testing is continuing. With visuomotor processing taking longer to restore following CHI than other cognitive functions, having tablet-based visuomotor tasks that are sensitive to mild brain injuries would be beneficial in assessing recovery.

Work-Related Traumatic Brain Injury Due to Assault: What is the Impact on Return to Work? Analysis of Workers' Compensation Claims in Victoria, Australia

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Background: Workplace violence is not only an occupational health and safety hazard but its consequences also carry a substantial economic loss burden (i.e., worker absenteeism, low productivity, increased care costs). As per the Canadian literature, up to 10% of all TBI admissions are a result of physical assault. There is evidence to suggest that individuals who have sustained physical assault score significantly lower on scales measuring reintegration into normal life.

Objectives: The aim of this study was to explore the contribution of intentional TBI (assault) versus non-intentional TBI on the outcomes related specifically to days off work while controlling for potential confounding factors such as age, sex, employment status and injury severity.

Methods: The dataset (n=3173) utilized for this study is based on claims made to WorkSafe Victoria (Australia) from 2004 to 2012; a nine year timeframe. Descriptive statistics were computed by generating frequency distributions for categorical variables. Chi-square test was used to examine the significance of association between and vocational variables of interest.

Results: Amongst all the workers who sustained wrTBI (n=3173), assault contributed to 9% as a mechanism. The distribution of sex in the sample population was balanced, i.e., there were 59% males and 42% females. The majority (70%) of the sample was aged 25 to 54 years of age; nearing approximately 20% for each of the three decades. A multivariate logistic regression analysis was performed to predict whether time off work was required (yes/no) for workers who had sustained wrTBI as a result of assault versus those who did not. Additional covariates included in the model were hospitalization (hospitalized versus not hospitalized as a measure of severity), sex, age (grouped by decades) and employment status (full-time, part-time and others). Workers who sustained their injury as the result of an assault were more likely to have days off work (OR = 1.694, 95% confidence interval 1.23, 2.32) compared to those who did not.

Conclusion: The results have policy-related implications for workplace safety and prevention of workplace violence. Work injuries due to assaults are associated with a greater likelihood of time off away from work, independent of injury severity (as measured by hospitalisation). Future work should explore other reasons that may explain this observation examining workplace and individual level factors.

Supporting Factors for Follow-Up Care in TBI Patients Post-Inpatient Discharge

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Background: Outpatient rehabilitation provides an important piece of the continuum of care for traumatic brain injury (TBI) patient recovery soon after discharge from inpatient rehabilitation. Studies indicate that the initial period (6 months to 1 year) following discharge is critical to successful adjustment to community life with a TBI for patients and their caregivers.

Objective: The purpose of this study is to investigate post-inpatient discharge awareness of, attitude toward, and attendance in outpatient rehabilitation at 1-year post-injury.

Methods: n = 86 participants diagnosed with moderate to severe TBI enrolled in the TBIMS who received inpatient rehabilitation services in a New York City public hospital completed a post-discharge care interview; however only those who did not live in a sub acute hospital or nursing home post-injury were included in primary analyses (n = 56). These patients were compared based on whether they returned for a follow-up appointment or not. Utilized data collected through TBI Model Systems (TBIMS) Form I (pre-injury, medical record abstraction) & II (year one follow-up) interviews and additional post-discharge care interview at first year post-injury follow up. The post-discharge care interview was designed to assess reasons why patients return or fail to return to their rehabilitation hospital within one year of their injury, the services they receive, and level of social support/care they have at home.

Results: Results showed that patients who failed to return for outpatient appointments were significantly younger and reported greater anxiety and depression during their first year follow-up interview. The primary reasons reported for failing to return included the patient reporting they did not need to (22.7%), patient moved/relocated (18.2%), patient went to another facility instead (13.6%), or the patient experienced additional medical complications (9.1%). Other reasons included insurance/financial issues, cost of transportation, or that they forgot they had an appointment. Furthermore, results showed that patients who were given an appointment at discharge were more likely to return, $\chi^2 = 9.8$, $p > .01$.

Conclusions: These results support previous research demonstrating that the initial transition phase from hospital to home is associated with worse emotional well-being (i.e., depression, anxiety, etc.), and suggest that worse emotional states are associated with a reduced likelihood to participate in outpatient services. Implications for clinical care include ensuring that discharge planning discussions address common issues TBI patients experience in the initial transition phase. Discussion topics can include emotional changes resulting from the injury itself, expectations of progress during this transition time, and the importance of continued therapy. Additionally, these findings show that appointment-making at the time of discharge contributes to the likelihood of attendance in outpatient rehabilitation. This further supports the case for discharge planning discussions to review the importance of and to set up appointments for continued therapy.

SMARTraining: A Novel Approach for Teaching Clinicians, Family Members, and Caregivers to Conduct Neurobehavioral Assessments

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Assessment of neurobehavioral function is important for developing targeted, person-centered, rehabilitation plans for individuals with severe traumatic brain injury. Accurate, reliable assessment of neurobehavioral function (NBF) is a critical component of conducting clinical trials in this vulnerable population. NBF assessment is usually the purview of licensed professionals. But we hypothesize that caregivers can also be effectively trained to conduct NBF assessments of family members with disordered consciousness. By engaging learners interactively at their own pace, online training provides a model for creating consistent learning experiences and ensuring minimal levels of competency in score. Online training is gaining popularity, yet little is known about its effectiveness for teaching skills such as NBF assessment relative to traditional approaches. We are not aware of any literature that has examined teaching caregivers to evaluate NBF. In this presentation, we describe the theory and design principles for this approach to teaching clinicians, family-members and caregivers to conduct neurobehavioral assessment of individuals with severe traumatic brain injury (TBI).

This novel strategy, called SMARTraining (ST) is an online, individualized training that engages learners in interactive instruction with immediate specific feedback on their performance. This interactive training includes animated slides with narration, video and audio cases with personalized feedback, and access to resources. Learners practicing scoring skills throughout the training and progress through the training at their own pace. ST is housed in a Learning Management System (LMS) that monitors learners' progress through the training, time on pages, attempts on test questions, and number of logins.

Merriam & Caffarella (1999) identified seven principles that contribute to successful learning for adults. These include: learning as a process, variable rates and styles of learning, readiness to learn, life experiences, application, knowledge of progress, and repetition. In this presentation we describe how these principles can be applied to teaching NBF assessment to both clinicians and family members. For example, using the principle of variable rates of styles and learning, training is designed to be self-paced, enables learners to review material multiple times, and to present the information in several formats. SMARTraining enacts this principle by giving learners the ability to access the material at any time, repeat modules, and providing spoken, video, and written versions of the information. Finally, we describe our framework for evaluating the effectiveness of the training based on Kirkpatrick's Four-Level Training Evaluation Model. This model proposes 4 levels to evaluating training effectiveness, of which we will evaluate three: reaction, knowledge, behavior change, and health outcomes.

If this approach proves successful, this model could dramatically change the role of assessment as a way of communicating between caregivers and clinicians. It could also provide greater flexibility, and significantly reduce burden and costs in clinical trials.

Children with Traumatic Brain Injury Have a Right to Specific Care in the Netherlands

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In the Netherlands 15.000 children between 0 and 24 years are treated with traumatic brain injury (TBI) in Dutch hospitals each year (de Kloet et al, 2013). In mild TBI 10-20% of these children experience no long term consequences (Eastvold, A.D., 2013; Yeates K.O. et al, 2009). The other 10-20 % does not always find the pathway to the right care. Moderate to severe TBI leads in general to moderate to severe decline in physical functioning, neurocognitive functioning and communication and speech (Anderson, V. et al, 2001; Babikian, T., 2009). After a year children with moderate to severe TBI also have a higher risk to develop emotional, behavioural, social problems and psychiatric disorders. In adolescence all groups of TBI with long term consequences have a risk to develop behavioural problems, substance abuse, mood disorders and other psychiatric disorders (LaxPericall, M.T. et al, 2014; McKinlay, A. et al, 2009; Rosema S. et al, 2012).

The chain of care in children with TBI is very important because problems are often not immediately recognised as TBI and also arising on the long term. Every professional in healthcare, education and mental care needs to know how to identify the (late) consequences of TBI, the visible as well as the invisible ones. This is necessary to assure that every child has the opportunity to the right care in all regions of the country.

In the Netherlands we have a good quality of care, but there are still a lot of differences in which care a child receives, among others depending on the region it lives in in the country. The consequences of TBI are several and influence all domains of the ICF-CY.

On behalf of the Dutch brain foundation, the Dutch pediatric brain injury network (in which medical specialists, psychologists, teachers and (social) workers in long term care are gathered), patient associations and adolescents with TBI and parents of TBI-patients made a standard of care for children and youth with TBI in the Netherlands (Gijzen, R., Zadocks, J., 2016).

This standard describes the signaling of (the assumption of) TBI and aspects of diagnostics, prognostics, therapy and guiding in the acute phase, recovering phase and chronic phase. It further describes how the organisation of care should be in a realistic way. Finally the standard describes the agenda to realise this and unroll the standard care in the whole country.

4 regions in the Netherlands now got a small grant to realise a part of this care and describe it for other regions so that it can be easily implemented there.

Apolipoprotein E epsilon 4 (ApoE-ε4) Genotype Is Associated with Decreased Six-month Verbal Memory Performance after Mild Traumatic Brain Injury: A TRACK-TBI Pilot Study

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Background: Mild traumatic brain injury (mTBI) is a major cause of cognitive impairment, which may be modulated in part by genetic susceptibility. The apolipoprotein E (ApoE) gene encodes a lipoprotein with three common isoforms (ε2, ε3, ε4); presence of the ε4 allele associates with memory impairment in neurodegenerative diseases. However, its association with memory function after MTBI remains unclear.

Methods: MTBI patients (Glasgow Coma Scale (GCS) score 13-15, no acute neurosurgical intervention, extracranial Abbreviated Injury Scale (AIS) score ≤1) aged ≥18-years with ApoE genotyping results were extracted from the Transforming Research and Clinical Knowledge in Traumatic Brain Injury Pilot (TRACK-TBI Pilot) study. Cohorts were determined by ApoE-ε4(+) vs. ApoE-ε4(-), and assessed for associations with six-month verbal memory, measured by five subscales of the California Verbal Learning Test, Second Edition (CVLT-II): Immediate Recall Trials 1-5 (IRT), Short-Delay Free Recall (SDFR), Short-Delay Cued Recall (SDCR), Long-Delay Free Recall (LDFR) and Long-Delay Cued Recall (LDCR). Multivariable regression controlled for age, years of education, sex, race, prior medical history (PMH) of seizures, loss of consciousness, posttraumatic amnesia, and acute intracranial pathology on head computed tomography (CT) scan. Mean differences (B) with 95% confidence intervals (CI) are reported. Statistical significance was assessed at p<0.05.

Results: Multivariable analysis demonstrated in 114 mTBI patients (ApoE-ε4(-)=79, ApoE-ε4(+)=35) that ApoE-ε4(+) was associated with long-delay verbal memory deficits (LDFR: B= -1.17 points, 95% CI [-2.33, -0.01], p=0.049; LDCR: B= -1.58 [-2.63, -0.52], p=0.004), and a marginal decrease on SDCR (B= -1.02 [-2.05, 0.00], p=0.050). ApoE-ε4 did not associate with IRT or SDFR. CT pathology was the strongest predictor of decreased verbal memory on all subscales (IRT: -8.49, SDFR: -2.50, SDCR: -1.85, LDFR: -2.61, LDCR: -2.60; p<0.001). PMH of seizures was associated with decreased short-term memory (SDFR: -1.32, p=0.037; SDCR: -1.44, p=0.038) but not long-term memory.

Conclusions: Presence of the ApoE-ε4 allele may confer an increased risk of rapid forgetting and impaired retrieval on six-month verbal memory outcomes for patients suffering mTBI, with implications for heightened surveillance and targeted therapies. Acute intracranial pathology remains the driver of decreased six-month verbal memory performance. Future studies are needed to confirm these findings.

The Relationship Between Moral Injury and Persistent Mental and Physical Health Symptoms Among Veterans with Mild Traumatic Brain Injury

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Objective: This study aims to explore the relationship between moral injury and the mental and physical health symptoms in Veterans with deployment related mild traumatic brain injury (mTBI).

Design: This was an observational study of Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) Veterans with mTBI.

Setting: All participants were recruited from the Veterans Health Administration Eastern Colorado Health Care System.

Participants: OEF/OIF Veterans with mTBI (N=145). The majority of participants were male (92.4%) with a mean age of 33.1.

Measures: Clinical interviews were used to assess lifetime history of mTBI and post-traumatic stress disorder (PTSD). Questionnaires included the Moral Injury Events Scale (MIES), Short Form Health Survey (SF-36), Brief Multidimensional Measure of Religiousness/Spirituality (BMMRS), and PTSD Checklist – Civilian Version (PCL-C).

Results: The transgression score on the MIES was predictive of persistent psychological symptoms. For every 1 point increase in transgression score there was a decrease of 0.36 points in the SF-36 Mental Health factor t-score, after adjusting for covariates ($p=0.001$) such that increased moral transgression is associated with worse persistent mental health symptoms after mTBI. The betrayals score was predictive of SF-36 general health ($p=0.006$), however this relationship was also found to be moderated by self-reported religiosity ($p=0.02$). For those who reported high levels of religiosity, there was a negative relationship between betrayal score and physical health score such that increased betrayal is associated with worse physical symptoms. As self-reported religiosity decreases, this relationship is attenuated.

Conclusions: Among OEF/OIF Veterans with a history of deployment-related mTBI, moral injury was predictive of persistent mental and physical health symptoms. These findings suggest that for some Veterans moral injury may play an important role in the maintenance of physical and mental health symptoms post mTBI. That is, acting or observing others act in a way that violates one's own morals or values may have lasting effects on Veteran's psychological and physical health. Results highlight that moral injury may be a novel area for intervention among those with mTBI.

Moving Beyond the Bottom Line: Importance of Inter-Agency Collaboration in Client Success

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The Brain Injury Alliance of Washington (BIAWA) has developed a true client-centered support system for individuals with Brain Injury, their families, and caregivers throughout the state of Washington. Our state-wide network operates independently of any one health network, group, or agency. As such, we are able to provide consistent telephone and in-person support to connect survivors and family members to the services and activities necessary in achieving the highest quality of life attainable. BIAWA develops relationships ongoing with all medical and non-medical systems to achieve the best possible outcome for client success. Since 2010, BIAWA has incorporated national standards and practices to reorganize its infrastructure in a manner which not only increases the value of its services and the numbers of individuals served, but also ensured long-term sustainability of collaborative relationship with medical and non-medical sectors. We continue to recognize the importance of bringing all public and private sector parties together to provide the best comprehensive services to the individuals who need services. Those needs will always go beyond what one hospital, one system, or one provider can engage in independently for the survivor and their family. In this presentation, BIAWA will depict successful partnerships between a private, human service agency and hospitals, government agencies, and other support programs and the way these collaborations benefit both the organizations involved and the communities they serve. The presentation will review the implementation of services provided by BIAWA and discuss its approach to expand and improve relationships with other organizations to effectively assure more comprehensive and widespread support to assist clients with reintegration after injury in all areas of life.

Evaluation of A Visuospatial N-Back Task in fMRI To Examine Working Memory Network Activation in Children Following a Mild Traumatic Brain Injury

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Aim: Mild traumatic brain injuries (mTBI) are most common in childhood. Working memory (WM) complaints are often reported in the absence of measurable impairments. Our aim was to examine cortical activation with fMRI during a WM task and its relationship to cognition in children with and without post-concussion symptoms.

Methods: This was a controlled prospective study of children 8 to 18 years with mTBI. Exclusion criteria were loss of consciousness greater than 30 minutes, Glasgow Coma Scale score lower than 13, previous mTBI within 3 months and MRI contraindications/intolerance. Symptom persistence (symptomatic vs. asymptomatic) was determined by family responses at one month post-injury. An age and sex matched control group with no history of head injury was recruited. A visuospatial n-back WM task was developed for fMRI, with three cognitive loads, 0-back, 1-back and 2-back. Outcome measures: included Post-concussion symptom inventory; Neurocognitive index, complex attention and WM scores on computerized cognitive testing (CNS Vital Signs). Pre-processing of fMRI data, single-subject and group-level analyses were performed using FSL FEAT, cluster-corrected for multiple comparisons ($p < 0.01$).

Results: 37 symptomatic patients, 25 asymptomatic and 19 controls were included. Groups were similar in age (14.8, 14.5 and 13.8 years; $F=0.872$, $p=0.422$), sex (19, 13 and 9 males; $\chi^2=0.107$, $p=0.948$), socioeconomic status ($F=1.636$, $p=0.201$) and time since injury (35.6, 38.4 days; $p=0.116$). Accuracy decreased with increasing difficulty of n-back task (n-0, n-1, n-2), and showed a high degree of correlation (1, 778; $F=153.854$; $p < .001$) although there was no effect of group. Reaction times also increased with task difficulty, were highly correlated within subjects although there was no effect of group. Performance on the n-2 task showed a significant correlation with complex attention ($r=.337$; $p=.002$), neurocognitive index ($r=.315$; $p=.004$) and composite memory ($r=.234$; $p=.035$). Differences in complex attention scores between symptomatic and asymptomatic groups approached significance ($F=2.940$, $p=0.051$). WM network activation increased with task difficulty in all 3 groups, particularly in the bilateral dorsolateral prefrontal cortex (DLPFC), dorsal anterior cingulate cortex and parietal cortex. Group differences in activation were noted for the n-1 > n-0 contrast. Specifically, the asymptomatic group showed greater activation than the symptomatic group in the left DLPFC, hippocampal subdivision of the temporal lobe and the supramarginal gyrus of the parietal cortex. Similarly, the control group demonstrated greater activation than the symptomatic group in the supramarginal gyrus of the parietal cortex.

Conclusions: This visuospatial n-back task is valid for use in children with mTBI. Despite the absence of objective performance differences on cognitive testing and the n-back WM task, the symptomatic group showed decreased activation in regions that coordinate WM, compared to children that are asymptomatic and healthy. This research may provide further insight into the reported WM difficulties in mTBI.

Use of Force Platform and Visual Feedback in Home Based Therapy of Patients with Brain Injury

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The use of technological devices in controlled home based therapy forms part of modern neurorehabilitation. An interactive system for home based balance training after brain injury was developed at the 1st Faculty of Medicine of Charles University in Prague. The developed system Homebalance consists of two lightweight parts – a tablet and a force platform, connected through a wireless Bluetooth connection. The patient is asked to move an object which appears on the screen. This is done by shifting their center of gravity. The tasks are combined with exercises targeted at attention and memory. The system was tested in home environment of patients with acquired brain injury. A total of 12 subjects underwent four weeks of home based therapy using an interactive system Homebalance. The control group of 12 subjects underwent home based balance training without any technological equipment. Patients participated in the initial examination, home based therapy and final examination. As an evaluation of the therapy Mini-BESTest and diagnostic dynamic scene in Homebalance software have been used. After the therapy both groups improved in Mini-BESTest and diagnostic dynamic scene. The research group had statistically better results in both tests when compared to the control group.

A Center-specific Demographic Analysis of Barriers to Retention in Traumatic Brain Injury Model System (TBIMS) Research

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Objective: This analysis examines barriers affecting participant follow-up in longitudinal studies, specifically the Rusk Rehabilitation Traumatic Brain Injury Model System (TBIMS). While longitudinal designs allow researchers to study clinically-meaningful outcomes, high rates of participant loss to follow-up (LTFU) are a common problem. This study examines possible factors associated with LTFU.

Design: Utilized data collected through TBIMS Form I interviews and abstraction from acute and rehabilitation medical records.

Setting: Two urban New York City TBIMS hospitals.

Participants: Participants (N=143) enrolled in TBIMS between April 2013 and June 2016, primarily male (79.7%), White (39.3%) or Hispanic (28.0%), English-speaking (67.4%), an average of 48.4 years old (SD = 19.1) and had an average of 12.6 years of education (SD = 4.3).

Intervention: None

Main Outcome Measures: Variables from TBIMS Form I (pre-injury, medical record abstraction).

Results: Descriptive and inferential statistics were used to analyze the demographics, psychosocial variables, injury-related variables, and other jeopardizing factors one year post- injury. The attrition rate was 14.7%. Chi-square analysis showed participants lost to follow-up were more likely to report binge drinking, $\chi^2(1) = 9.05$, $p < 0.01$. Binge drinking was defined as drinking more than five alcoholic drinks on any one occasion during the month prior to their injury.

Additional chi-square analyses showed no relationship between LTFU and any demographic variable (gender, race, marital status, residence after discharge, language spoken at home, employment status, or country of birth).

Incarceration history and having a history of housing instability showed a trend towards significance, but lacked enough participants with complete data to achieve sufficient power.

Conclusion: Unlike previous studies, results did not demonstrate an association between LTFU and race. This may be due to the homogeneous, less diverse samples commonly found in the literature, leading to biased results.

Results also identify substance abuse and binge drinking as risk factors for LTFU. Literature in this area has demonstrated that individuals with TBI do not engage in drinking behavior for the first year post- injury, however, further investigation is needed to determine if this trend is skewed by not including these LTFU individuals who endorsed pre-injury problem substance use. These results support the need to encourage patients with a history of problematic substance use and their clinicians to explore and utilize substance abuse related resources.

Data collection will continue to further investigate the association between LTFU and clinically-related variables. In addition, associations between LTFU and incarceration and housing instability history will be explored as this research continues.

Learning Objectives:

1. To recognize the impact of participant loss to follow-up in longitudinal research studies.
2. To identify variables associated with loss to follow-up.
3. To develop strategies to minimize loss to follow-up based on identified variables.

Quality of Life 10-12 Years after Recovery from Prolonged Disorder of Consciousness in Young Patients

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Evidence is growing about the possible effectiveness of stimulation and rehabilitation therapies on recovery of disorders of consciousness (DOC). Most studies show the effects in the short term: months or a couple of years. Recently, we published the 10-12 years outcome of a group of 34 children and young adults, who had received an early intensive rehabilitation program (EINP) to resolve the DOC, within 6 months after severe brain injury (Eilander, 2016). Eleven of them have died, four still were classified with DOC, the remaining 19 had recovered to full consciousness.

In the Netherlands, there is concern about the quality of life (QOL) of the long-term survivors. The mainstream opinion is of people who live 'as a vegetable' with a lot of suffering, both by the patients themselves as well as by the closest family members. In the long-term follow-up study we showed that 12 of 19 patients with recovered consciousness at the moment of discharge EINP live (semi-) independently 10-12 years later. The patients or their relatives responded in a positive way on some simple questions about their social networks, the daily activities and the living situations. But what about the experienced quality of life? What aspects are important in order to let them feel comfortable? And what is the burden on family members? What aspects make them feel fine?

In general, QOL is investigated by means of a 5- or 7-point Likert-scale or a continuous 0-100 scale. These kinds of investigations give only limited information about the real experiences and feelings. We want to investigate QOL in a more qualitative, narrative way.

As a pilot, in order to investigate the possibilities of in-depth qualitative research, we interviewed three patients of the above mentioned cohort and/or their closest relatives thoroughly and captured it on film. We will present a 10-minute movie in which the most important aspects of their situations will be elaborated. The full interviews (over 28 minutes in total) have been processed by using the software program Atlas.ti, a digital tool to analyze the interviews qualitatively. The aim of this exercise is twofold: first to identify the topics mentioned by the patients and/or their family members and secondly to explore whether this way of analyzing is suitable.

After the movie, we will present the first results of the analyses and discuss with the audience the pros and cons of this research method. The results of the analyses, combined with the results of the discussion will form the base for a more comprehensive study amongst all conscious survivors of the cohort.

Factors Influencing Parental Return-to-Play Decisions in Post Adolescent Sport-Related Concussions: A Mixed Methods Exploratory Study

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Background: Annually, an estimated 3.8 million concussions occur in recreation and sports in the United States. All 50 states have return to play (RTP) laws in place for youth athletes and require medical clearance prior to RTP. The factors that determine clinical RTP have been well described. There have been several studies on parental, child, and coach knowledge regarding concussions, concussion legislation, and RTP protocols. Moreover, there is a significant body of literature on concussion epidemiology, RTP procedures, and RTP timelines for providers. Despite this knowledge base, to our knowledge there are no studies investigating parental decision-making in sports-related concussion (SRC) to guide provider education for patients.

Objective: The objective of this pilot study is to obtain a better understanding of parental concerns regarding concussion, SRC recovery, and RTP.

Hypothesis: This study is exploratory and we have no direct hypotheses that we will be testing. Our aims are to: 1) identify parental concerns regarding sports-related concussions (SRC); 2) to determine the feasibility of our study design; and, 3) use the results of this study to guide future work on decision-making in SRC, non-sports concussion, and mild traumatic brain injury.

Methods: Institutional review board approval has been obtained prior to the start of data collection. It is expected that 100 participants will complete the quantitative study. An expected 30 participants will participate in the qualitative study to achieve saturation. Both quantitative and qualitative data will be analyzed prior to the presentation.

Results: We anticipate that parents may be making RTP decisions based on concerns of rare and severe negative outcomes (e.g. chronic traumatic encephalopathy, second impact syndrome) and underestimating more likely outcomes (e.g. academic issues, reactive mood disorders).

Discussion: It is expected that results of this study will provide a clearer understanding of parental concerns regarding concussion and RTP decisions. These results will immediately aid providers in regards to patient education and the production of educational materials for parents, athletes, sports leagues, and administration. Future studies based on this work will allow us to increase understanding regarding the differences in decision-making for other sub-populations of concussion patients.

Late Recovery or Late Discovery?

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Introduction: Recovery of consciousness in patients in vegetative state/unresponsive wakefulness syndrome (VT/UWS) is considered unlikely beyond 12 months after traumatic brain injuries (TBI) and 3-6 months in non-traumatic brain injuries (non-TBI). In recent years, various cases of recovery of consciousness beyond these prognostic boundaries have been described.

The aim of our study was to provide insight into the clinical course of patients in VT/UWS who showed improvement in consciousness beyond the prognostic boundaries for recovery. This is important to improve the medical care and decision-making in those patients and to contribute to realistic expectations of recovery.

Methods: A retrospective descriptive study was conducted between February-April 2016 by using the clinical records of patients who were included in an ongoing dynamic cohort study on patients in VS/UWS in the Netherlands. Informed consent was given by the patients' proxies. All patients met the following criteria: diagnosis of VS/UWS after acute brain injury, confirmation of this diagnosis by an independent expert using the Coma Recovery Scale-revised (CRS-r) and detection of signs of consciousness after the expected prognostic boundaries were passed. Data about the context of the recovery of consciousness, patient and care characteristics and the present functional behavior of the patients were extracted. In addition information about the recovery verbally given by family members was used.

Results: Four patients met the inclusion criteria and were included (4/4). A minimally conscious state (MCS) was diagnosed respectively 10 months, 9 months and 5.5 year after non-TBI and 1 year and 2 months after TBI. In all patients the medical files contained a description of a sign corresponding with MCS before reaching the prognostic boundaries for recovery. However, either these signs were not recognized as a sign of consciousness and/or did not lead to change the diagnosis. In two patients the level of consciousness improved after reducing sedative medication and in one patient after treatment of hydrocephalus. All patients remain severely disabled. We found incorrect terminology in the description of the level of consciousness.

Conclusions: Rather than late recovery of consciousness, the patients investigated in this study did show signs of consciousness within the expected period after their injuries, but were not recognized in doing so; in every case there seems to be late discovery of signs of consciousness instead of late recovery. The poor recognition of signs of consciousness, diagnosing the level of consciousness without a validated scoring scale and the presence of factors that negatively influence the level of consciousness, might contribute to this delay. To recognize signs of consciousness in time it is important to improve the knowledge of caregivers, to use validated diagnostic scales at the time of changes in patients' behavior and to use correct terminology in communication and files

The Dying Process of a Patient in Unresponsive Wakefulness Syndrome After Withdrawing Tube Feeding: Medical Facts and Reflections of Family and Caregivers

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Introduction: In the Netherlands, authoritative reports to allow the withdrawal of futile medical treatment, including artificial nutrition and hydration (ANH), from patients in an irreversible vegetative state/unresponsive wakefulness syndrome (VS/UWS) were published in the nineties. Still national and international debates reflect different opinions about the dignity of the dying process after withdrawing ANH. The experiences and opinions are mainly depicted in lay press and empirical data are scarce.

In this study, reflections from the physician, nurse and the relatives involved are compared with the medical facts registered in the files, after withdrawal of ANH from a patient in VS/UWS. The aim is to explore the quality of the dying process and to contribute to a realistic picture of what happens after discontinuation of ANH in a patient in VS/UWS.

Methods: Explorative, descriptive case report of a 75-year old patient in a post-anoxic VS/UWS for nine months in a nursing home, at which time the decision to withdraw ANH was made by the physician after consultation of the patient's family.

Twenty months after the patient had died, we reviewed the symptoms and events after the withdrawal of ANH as registered in the multidisciplinary records. We compared these medical data with the reflections of the responsible physician, nurse and two sons, collected in semi-structured interviews. The interviews were recorded on tape and transcribed for qualitative analysis.

Results: In the clinical records, one short moment of possible discomfort was reported on the 11th day after withdrawal, relieved with palliative care. Medical notes from the 13th day testified that the patient had died peacefully, without further medical interventions.

In the interviews all participants indicated this was a dignified death under the given circumstances. We found different opinions concerning the impact of the length of the dying process. The physician and nurse thought a slow passing away would be preferable for the family. However, the family would have preferred a shorter deathbed, based on the intense emotions they experienced during this period and an anxiety for suffering of the patient.

Looking back, all participants supported the decision to withdraw ANH in this context. In discussing alternatives, the sons, with hindsight, would have preferred euthanasia by a lethal injection if that had been a legal option.

Conclusion: The findings show that the dying process in a patient in VS/UWS after withdrawal of ANH can be peaceful and dignified according to both family and medical staff. Regular, but intensive and pro-active palliative care is essential in these extraordinary circumstances, in particular to inform caregivers about

what to expect in the terminal phase. Options and wishes of families on end-of life decisions concerning patients in VS/UWS deserve further exploration in future studies.

Lifetime History of TBI Among Soldiers Returning from OEF/OIF Deployments

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Background: It is well-known that a signature injury from Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) conflicts is mild traumatic brain injury (mTBI). Yet, only a handful of studies have reported lifetime history of traumatic brain injuries (TBIs) among military populations. Researchers have suggested that sustaining a TBI earlier in life may have long-term negative effects, even when the injury is mild, and that this relationship is more pronounced the younger the age of initial injury; thereby suggesting potential short- and long-term health risks associated with multiple TBI among military personnel.

Objective: To describe the lifetime history of TBI among OEF/OIF Soldiers. Given the limited knowledge of lifetime history of TBI among Soldiers who have deployed to OEF/OIF, no hypotheses will be tested. Instead, descriptive analyses of the complete lifetime history of TBI, including information on mechanism of injury and severity of TBIs, among Soldiers returning from OEF/OIF will be presented.

Methods: During the post-deployment health assessment process, Soldiers returning from OEF/OIF between 2009 and 2014 were invited to participate in the study. Participants completed the Ohio State University TBI Identification Method (OSU TBI-ID), a standardized, structured interview for eliciting lifetime history of TBI. The analytic sample consists of 1,489 Soldiers who completed the OSU TBI-ID.

Results: Almost three-quarters of the sample reported a lifetime history of TBI. Full descriptive analyses are currently underway and will be completed prior to the conference. These results will include information related to number of TBIs, deployment-related TBI, age at time of TBI, frequencies of mechanism of injury, and severity of TBI.

Discussion: Given the potential risks associated with multiple TBIs, descriptive analyses will provide valuable and novel information regarding OEF/OIF Soldier's lifetime history of TBI. This knowledge will help to inform the development of future studies exploring the potential cumulative effect of multiple TBIs, and may identify treatment targets to facilitate improvement in recovery after multiple TBIs.

Burden of Paediatric Traumatic Brain Injuries: Single Centre Experience Over 3 Years

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Introduction: Paediatric traumatic brain injury (TBI) is a significant management issue with morbidity and mortality higher than in adults, especially in developing countries. However, epidemiological data is lacking from India.

Aims & Objectives: To see the demographic, clinical and outcome data on paediatric patients with TBI.

Materials & Methods: In this retrospective study over 3 year period (January 2012- Dec 2014) in a single trauma centre, a prospectively maintained neurotrauma database was queried for all paediatric patients (Age ≤ 18 years) with TBI (GCS ≤ 15). Demographic, clinical and outcome data (in hospital mortality) was reviewed in all cases

Observations: A total of 10625 were admitted in Neurosurgery in the study period. Of these, there were 2238 (21.1%) paediatric patients. The mean age was 8.46 years (range 4 months -17 years) with an M: F ratio of 2.31:1. There were 1951 (87.2%) minor TBI (GCS 13- 15) patients, 111 (4.9%) moderate (GCS 9-13) TBI and 176 (7.8%) severe TBI (GCS ≤ 8) patients. 7.8%, 25.2% and 46.5% of mild, moderate & severe TBI respectively underwent surgery. The mean hospital stay was 1.49 days 4.0 days and 10.1 days in mild, moderate & severe TBI respectively. In hospital mortality was 0.30%, 3.60%, 28.4% in mild, moderate & severe TBI respectively.

Conclusions: This is the largest studies from the Indian subcontinent on pediatric TBI and shows that children constitute almost one quarter of all TBI. In-hospital mortality rates compare very favourably with published literature from developed countries.

Thromboelastometry: Utility in Diagnosing of Infection in Neurosurgery Intensive Care Unit

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Introduction: Commonly known biomarkers for the diagnosis of sepsis are procalcitonin, interleukin 6, and C-reactive protein lack adequate sensitivity or specificity. Sepsis is associated with coagulation defects and these alterations can be detected by thromboelastometry (TEG).

Aims & Objectives: Whether TEG variables can be used for the early detection of infection in Neurosurgery Intensive care unit (ICU) as compared to established biomarkers.

Methods: In the observational cohort study over two years (June 2012- June 2014), blood samples were obtained from patients who admitted to the neurosurgery ICU on admission day 0 and subsequently samples were collected at day 3 and day 5. TEG variables such as clotting time, clot formation time, maximum clot firmness, alpha angle, and lysis index were measured at the all three-time points. In addition, procalcitonin, interleukin 6, and C-reactive protein levels will also be determined simultaneously at all three points for comparison. Based on a combination of clinico-microbiological diagnosis, patients were divided into two groups, who developed infection at day 3 and who did not developed infection till day 5.

Results: There were 60 patients in non-infectious group vis-a-vi 40 patients in infectious group. (71.7%) patients with infection showed significantly prolonged clot-formation time (R time) on the admission (Day0) as compared with noninfectious group (28.3%) ($p=0.00$). Procalcitonin, interleukin 6, and C-reactive protein concentrations were tested; there was no difference between patients with and without infection group at different time of interval (Day0, day3, and day5).

Conclusions: Clot-formation time (R time) on TEG proved to be a more reliable biomarker of severe sepsis in critically ill adults than procalcitonin, interleukin 6, and C-reactive protein and can be used as a very cost effective marker for sepsis development. The results also demonstrate that early involvement of the hemostatic system is a common event in infection.

Moral Dilemmas Concerning Patients in Unresponsive Wakefulness Syndrome: Shared or Non-Shared Decision-Making?

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Objectives: Ethical dilemmas and conflicts have been described regarding patients in a vegetative state (VS/UWS). Many conflicts are about end-of-life decisions. This study aims to gain more insight into conflicts and ethical dilemmas experienced by professionals of patients in long-term-care in order to solve or prevent conflicts.

Method: The design was an explorative, qualitative case study of two moral deliberations (MD) of patients in Dutch nursing-homes. Both patients survived long after recovery of consciousness could be expected. The cases were selected because of the conflicts between the professionals and the families.

The MDs were transcribed. The data were thematically coded and systematically charted, following the principles of framework analysis. The software program Atlas-ti was used for coding and analyzing.

Result: This study showed 6 main themes: 1) Vision on VS/UWS; 2) Treatment and care-plan; 3) Impact on relationships; 4) Feelings/attitude; 5) Communication; 6) Organizational aspects. These themes were related to professionals as well as to what families of these two patients had expressed to the professionals. We found conflicts as well as contradictory feelings and thoughts to be a general element in all themes and in both professionals and families. Conflicts were found: within families and with physicians concerning all themes, with nursing-teams concerning daily activities.

Conclusion: A patient in VS/UWS is alive, but the actual meaning or even worth of such a life is hard to establish. Different interpretations by all involved are inevitable. Conflicts even persevere these views and there are no criteria available to challenge the opposing interpretations. Realizing and being aware of all these paradoxes and different views might give a better understanding of each other.

Real shared-decision-making can only be done in case of: as much clarity as possible about the wishes of the patient through AD, clarity upon the role of the physician in the decision-making process after consulting the family, competent physicians with knowledge about VS/UWS, excellent communication skills and medical leadership, a supporting organization with stability and the use of a MD to explore and solve the dilemmas.

Recommendations: We recommend education of all professionals regarding: diagnosis, prognosis and treatment-plans and medical ethical considerations of patients in VS/UWS; excellent communication skills, insight in the effects of inner-contradictory feelings/thoughts. And that these patients are more clustered in order to enhance the expertise and knowledge.

We further recommend organizations provide stability in the teams and support their personnel. And give the opportunity to have MD's.

This study emphasizes need for more insight in the role of the family as caregiver and on what they think is the best way to deal with the (ethical) dilemmas and decision-making. We recommend indepth interviews.

A Comparative Study of the Glasgow Coma Scale (GCS) with the Reaction Level Scale (RLS85)

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Objectives: The GCS was introduced in 1974 and, having three components, progressively became an international standard for determining the severity of brain injuries. The RLS85 is an eight grade single line scale, designed for assessment of overall responsiveness and consciousness level in patients with acute brain disorders, constructed near the year 1985 by Scandinavian investigators with the important objective that even intubated patients and patients with swollen eyelids could be reliably assessed. The aim of our study was the comparison of GCS and RLS85 in a sample of brain – injured patients admitted to a regional trauma center.

Methods: This prospective study included 106 patients with severe, moderate, or minor brain injury. Patients with associated spinal cord injury and major chest/abdominal trauma were excluded. The consciousness levels were assessed using both GCS and RLS85 scales. Assessments were made by five physicians who performed 162 pairwise ratings. The segments 1, 2 – 3, and 4 – 8 of RLS85 were thought as approximately corresponding to the GCS sum score level 15 – 13, 12 – 9, and 8 – 3 respectively. Neurological outcome was evaluated according to Glasgow Outcome Score (GOS).

Results: The Spearman's rank correlations between the GCS sum score and the RLS85 indicated that the two scales have the same ranking order of severity. The results of the 162 paired observations showed that the physicians agreed as to the assessments using both the GCS and the RLS85 only on 70 test occasions, not clearly indicating which scale shows the best reliability. The two scales demonstrated a high percentage agreement on severely head – injured patients and on patients with minor head injury, but were less effective in determining the conscious level of patients with moderate brain injury. The "sign test" showed that the GCS motor response and the RLS85 had coverage of 100%. Finally, both scales demonstrated similar GOS for the patients allocated to the three severity categories.

Conclusions: The majority of physicians reported that RLS85 is simpler than GCS, but the latter is ten years older and more widespread in use. The principle limitation of the RLS85 is that it is used almost exclusively in Scandinavia. Both compared scales proved reliable for patients in the extremes of minor and severe head injury, but demonstrated weakness when defining moderate brain injury. In this intermediate level the discriminative power of both scales was reduced. GCS and RLS85 values are ordinal scale data and do not incorporate brainstem reflexes or the size and reactivity of patients' pupils. Therefore, the author's recommendation is that the final adoption between them might remain a matter of departmental preference. Full knowledge of these scales' strengths and limitations is essential for both physicians and their patients.

Post-Traumatic Brain Injury Behavioral Management

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Post-Traumatic Brain Injury behavior management is crucial in the treatment of its survivors. Types of behaviors were examined in both children and adults. Behavior impacts were considered as well as a variety of treatments. Younger individuals that are diagnosed with a brain injury are more likely to make complete recovery. Although specific causes of behavior and treatment may work for one individual with a sustained injury, these findings for each person is different from the other. Together, these studies suggest that immediate care be taken and education be provided to the individual and family involved.

Smell Disorder in Chronic Severe Traumatic Head Injury Patients

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Purpose: Disorder of higher brain function or multiorgan failure in severe traumatic head injury patients make it difficult to do nutrient intake for the patients. Although traumatic smell disorder is considered as one of the reasons, little is known.

Method: Our hospital, Chiba Ryogo Center, specialize hospital for the long-term treatment and care of chronic severe brain-injured patients by motor vehicle accident in Japan. This is a cross-sectional, observational study from the 2013 to 2016 in our hospital. Inclusion criteria of this study included understanding of simple words, expression of YES or NO. We examined by using odor stick identification test for Japanese, which included 12 odorant (india ink, wood, perfume, menthol, orange, curry, city gas, rose, cypress, sweaty socks, condensed milk and fried garlic). Smell disorder was defined as ≤ 8 points of this test. Traumatic lesion of brain and sinusitis were examined by CT or MRI. Clinical manifestation was assessed by Coma Recovery Scale-Revised (CRS-R) scoring.

Results: Thirty eight participants included 9 healthy volunteers and 29 patients, male 30 and female 8, age 38.3 ± 15.3 (standard deviation; SD). All patients suffered severe traumatic brain injury at accident (Glasgow Coma Scale score ≤ 8) and CRS-R score was 22.3 ± 1.5 (SD). Among them, 5 patients could communicate only YES or NO (17.2%). Interval period between traffic accident and examined day was 870 ± 380 (SD). Twenty six patients were diagnosed as smell disorder (89.7%). These patients statistically significant increase in smell disorder compared with healthy volunteers ($p < 0.001$). The smell disorder patients included anosmia 7 patients, parosmia 13 patients and both 6 patients. In 12 odorants, fried garlic and curry were well recognized and perfume and city gas were not.

Conclusion: Most of chronic severe traumatic head injury patients were severely impaired in olfactory sensation. Some kinds of foods might have potency of improve of alimentation. And, we must warn the control of fire using city gas for home-care patients.

Head Injury in Motorcycle Accidents: First Rider vs. Second Rider- In Perspective of a Developing Country

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Introduction: We all know that head injury is the main cause of death in motorcycle accidents. Motorcycle riders are much more vulnerable than vehicle drivers, however, their use is increasing given the increase in auto- and fuel prices, hence making motorcycle an important vehicle for transportation, especially in a third world country like Pakistan. Many studies have shown that wearing a helmet decreases the head injury as well as the mortality rate in motorcycle accidents, but little has been done to explore the injury pattern sustained by the first and the second rider, or to compare their outcome.

Objective: To compare the rate and pattern of head injury sustained by the first vs. second rider and mortality rate and functional outcome of the two groups.

Place and Duration of Study: DHQ hospital, Rawalpindi from 1st Oct., 2014 to 30th Sep., 2016.

Methods: All adult patients presenting to DHQ Hospital, with head injury from a motorcycle accident, during the study period were enrolled after informed consent. Performas were filled by the on-duty doctor, including the demographic details, details regarding helmet and first or second rider, neurological status, additional injuries and radiological pattern of injury. These patients were divided into two groups: Group-1 (First riders) and group-2 (Second Riders) and both groups were compared for the above details, and followed. All patients received the standard treatment for their respective injuries and the two groups were compared for the mortality and functional outcome(EGOS).

Results: A total of 360 patients were included in the study- 234 (65%) patients were in group-1 and 126 (35%) were in group-2. All (100%) of the patients in group-1 were males while 61.9% in group-2 were males. Majority of the riders in both groups were not wearing helmets at the time of accident. Major injury in both the groups was facial injury but its frequency was significantly higher in group-1 as compared to group-2 i.e. 20.5% vs. 11.9% ($p = 0.040$). CT brain showed normal scan in 15.4% patients in group-1 and in 2.4% patients in group-2. CT brain showed high frequency of traumatic brain contusions in group-1 (24.4%) and group-2 (35.7%). Complete recovery was significantly higher in group-1 as compared to group-2 ($p = 0.011$).

Conclusion: Although economical, motorcycle is a dangerous and risky vehicle and head injury is a potential threat not only to the 1st rider but also to the 2nd rider as well. This study has also brought into light the public violation of the helmet regulations, whereby a person jeopardizes not only his own safety but that of his family also.

Strategies and Public Health Impact of Head Injuries Prevention

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Objectives: Traumatic brain injury (TBI) constitutes a major health problem globally, and is a leading cause of death and long – term disability. There are many reports on TBI, but in view of methodological shortcomings the epidemiological data are not always easily comparable. Only at last decades our interest in TBI has changed from clinical intervention to prevention. However, there is a lack of data to estimate the contribution of TBI to the world's health burden so that reasonable priorities and strategies can be developed for prevention.

Methods: The main causes of TBI are road traffic accidents (RTA), falls and violence. Exposure to these hazards varies considerably from region to region and this must be taken into account by health planners who design prevention programmes. A schematic model associated with primary, secondary, and tertiary head injury prevention might include the key points of opportunity for intervention actions in the natural history of TBI. Primary prevention is aimed at reducing the frequency and degree of exposure to potential hazards (improvements in road conditions/vehicles design, seat belts, air bags, helmets, medical check – up of drivers, zero blood alcohol concentration level for all drivers, changes in architectural designs to prevent falls, ban handguns). Secondary prevention focuses on reducing mortality and morbidity following TBI (establishment of regional trauma centers with an effective emergency medical service, time of arrival and transportation). Finally, tertiary prevention includes physical, psychological, and vocational rehabilitation for head – injured patients (changes in rehabilitation practice, novel neuromodulation techniques).

Results: A technically feasible prevention strategy does not imply automatically that the intervention will succeed, as public response may be poor or the cost may be too high. On the other hand, a low – cost strategy might be potentially beneficial for only a small fraction of the possible TBI exposures. A technically achievable strategy may have no viability because of cost and public acceptability reasons. Although educational strategies have been attempted for many years, they have shown limited success in modifying the behaviors that predispose to TBI. Legislation and environmental measures together probably will make a larger impact on reduction of TBI.

Conclusions: There is an urgent need for the development of global and national policies in order to minimize the risks and the consequences of RTA, particularly in the developing countries. This should be a joint effort between different government agencies, medical societies, motor vehicle manufacturers and nongovernmental organisations. Policies to improve the outcome of TBIs must aim primarily at improving the research – based knowledge of regional epidemiology, preventive programmes, and the acute management of TBI in pre – hospital and inpatient settings. Prevention based upon robust data on risk factors involved in TBI might have a greater impact.

Investigating the Effects of Repetitive Head Impact Exposure in Youth Football Using Neurite Orientation Dispersion and Density Imaging (NODDI)

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Introduction: Although diffusion tensor imaging (DTI) has dominated the traumatic brain injury literature, there are more advanced and physiologically relevant biophysical models of white matter microstructure that can be elucidated by acquiring diffusion data using multi-shell magnetic resonance imaging techniques, such as neurite orientation dispersion and density imaging (NODDI). Unlike DTI directional diffusivities, NODDI allows modeling of parameters, such as orientation dispersion index (ODI) and neurite density (ND) that are more biologically interpretable, as they correspond to known axonal characteristics. The purpose of this study was to determine the effects of cumulative subconcussive head impact exposure associated with youth football on white matter microstructural complexity and dispersion using NODDI.

Methods: Thirty-eight male football players (age: 8-13) without a history of concussion prior to or during the football season participated in this Institutional Review Board approved study. Head impacts were measured via HITS, which recorded kinematic data during all practices and games. HITS biomechanical data were used to compute cumulative combined (linear and rotational) RWE. All subjects received pre- and post-season MRI, including NODDI. ODI and ND were obtained using the NODDI fitting procedure. Diffusion image pre-processing and TBSS analysis was performed on ND and ODI using programs from the FMRIB Software Library (FSL). TBSS linear regression analysis was conducted using age and time between delta-season MRI scans (post-season minus pre-season) as covariates to determine the association between RWE and change in white matter diffusion parameters (ODI and ND). Results were corrected for multiple comparisons using threshold free cluster enhancement at $p < 0.025$.

Results: TBSS linear regression analyses revealed statistically significant linear relationships between RWE and increased ODI (post-pre season) within the inferior fronto-occipital fasciculus, inferior longitudinal fasciculus, and uncinate fasciculus. There were no statistically significant associations between cumulative head impact exposure and change in ND over the season of football.

Conclusions: Our findings suggest that cumulative head impact exposure is associated with ODI multicompartamental biophysical changes in white matter after a single season of youth football, even in the absence of concussion. ODI is thought to reflect the bending and fanning of axons. In the setting of non-concussive head impact exposure, an increase in white matter ODI may indicate deformation of fiber directionality due to cumulative head impact-associated mechanical strain, however, with no change in ND to indicate fiber loss. NODDI may represent a new biomarker for characterizing changes in white matter associated with sports-related head impact exposure. However, more research using a longitudinal design across different contact sports in a larger population, including females, is necessary to generalize these findings to a broader population of youth athletes.

Methyl – Methacrylate Cranioplasty After Head Injuries: A Single Center Experience of 144 Cases

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Objectives: Cranioplasty is the surgical intervention to repair cranial defects in both cosmetic and functional reasons. Although a variety of grafts have been previously used for the treatment of calvarial defects with varying success rates, there is still no consensus on which method is better. Methyl methacrylate is a relatively cheap and easily available material. Its main advantage is that it's completely malleable in the initial stages of hardening and can be molded easily during operation to fit the contour defects. It is biologically inert and does not interfere with computed tomography or magnetic resonance imaging studies. This article describes our experience of cranioplasty in a series of head – injured patients using methyl methacrylate.

Methods: From 1990 till 2015, 144 cranioplasties with methyl methacrylate were performed at Asclepeion Hospital for head – injured patients. In all patients the indication for craniectomy was brain trauma mainly due to road traffic accidents. Our reasons for performing a cranioplasty were the protection of the brain, restoration of cosmetic appearance, and improvement of neurological status if the defect caused a “trephined syndrome”. Mean age at the time of cranioplasty was 38 years and majority was males. Cranioplasty was performed from 4 up to 19 months after head injury. We delayed the operation in cases of delayed primary wound healing or communication with air sinuses.

Results: 60% of patients with neurological disability showed some improvement in postoperative status. All patients with “trephined syndrome” showed improvement of their initial symptoms. In twenty three patients were noted minor or major complications. Nine patients had subgaleal collections and five patients had superficial wound infection. Three patients had a deep wound infection and two others had wound dehiscence requiring surgical debridement and removal of plate. Postoperative epidural hematoma appeared in two patients who required reoperation. One patient developed a small temporal contusion and was managed conservatively. In another one, a broken methyl methacrylate material was detected two months postoperatively. An adequate aesthetic restoration was noted in most cases.

Conclusions: There will always be a need for cranioplasty in neurosurgery. Methyl methacrylate cranioplasty continues to be used by neurosurgeons, is a relatively safe and cheap method, provides an acceptable aesthetic reconstructive option, and contributes to neurological improvement in the treatment of cranial defects in spite of the use of other expensive materials. A disadvantage of methyl methacrylate is that autopolymerization may cause thermal damage to the underlying brain. Moreover, when the cranial defect is large or complex, obtaining a good cosmetic result is often difficult.

Even though considered as simple procedure, cranioplasty is often associated with complications. Independently of the selected cranioplasty material, physicians should know that a seemingly minor neurosurgical operation requires thorough surgical approach to minimize morbidity.

Performance and Symptom Validity Testing as a function of Medical Board Evaluations in U.S. Military Service Members with a History of Mild TBI

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Objective: Military service members sustaining a mild traumatic brain injury (mTBI) are often referred for neuropsychological testing. Standard of care for neuropsychological evaluations includes administering performance validity tests (PVT) and symptom validity tests (SVT), indicators that the patient's presentation and the obtained scores are credible for interpretation. Previous research has demonstrated services members have an elevated rate of failing PVTs, particularly within the context of medical board (i.e., disability) evaluations (MEB). The current study sought to evaluate whether the reason for the MEB was a relevant factor in failure rates of PVTs and SVTs.

Methods: The sample consisted of 231 active duty service members with a history of mTBI. Of these, 61 were in the midst of a medical evaluation board (MEB) for either behavioral health and/or physical health conditions. A full neuropsychological battery was administered, which included measures of performance validity (Word Memory Test; WMT) and symptom validity (MMPI-2-RF). Failure of the WMT was defined as scoring below the published cutoff scores for the Immediate Recognition, Delayed Recognition, and Consistency subtests. An invalid MMPI-2-RF was defined as F-r >99 or Fp-r >79 or Fs >99 or FBS-r >99 or RBS >99.

Results: The overall PVT failure, per the WMT, was 57.4% for those in an MEB and 30.6% for those not in an MEB ($X^2 = 13.7, p < .001$). SVT failure for those in an MEB was 57.4%, and 22.4% for those not in an MEB ($X^2 = 25.1, p < .001$). Of the 61 participants in an MEB, 19 were related to behavioral health conditions (BH), while 45 were related to physical health conditions (PH). Three participants had both BH and PH conditions. The PVT and SVT failure rates for those being evaluated for BH were 56.3% and 62.5%, respectively. The PVT and SVT failure rates for those being evaluated for PH were 52.4% and 54.8%, respectively. There were no statistically significant differences between SVT and PVT failure rates as a function of the reason for MEB (i.e., BH vs PH).

Conclusions: The current findings support previous research highlighting the notable rate of invalid cognitive and psychological testing among military service members with a history of mTBI. These rates are even higher in service members with a pending MEB. However, the current data did not demonstrate significant differences in PVT or SVT failure rates as a function of the reason for MEB (i.e., behavioral health versus physical health). Therefore, regardless of disability claim status, the current data emphasizes the importance of using both performance and symptom validity testing when evaluating military service members with a history of mTBI in order to ensure the accuracy of cognitive and psychological test data.

Cognitive Test Performance and Evaluation Context in U.S. Military Service Members with a History of Mild TBI

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Objective: Mild Traumatic Brain Injury (mTBI) is a frequently experienced injury among U.S. Service Members, many of whom are ultimately referred for neuropsychological assessment. However, factors outside of neurologic insult can influence cognitive testing, with one such factor being “performance validity.” Performance validity refers to the patient taking the tests in such a way (e.g. putting forth adequate effort) that the scores obtained are credible for drawing conclusions about neurocognitive functions. It is standard of care for neuropsychological evaluations to include measures that assess performance validity. In civilians, individuals being evaluated for disability claims have higher rates of poor performance validity. The current investigation evaluated performance validity testing and cognitive test scores in the context of a pending disability evaluation (Medical Evaluation Board) or a clinical/non-disability evaluation.

Methods: The sample consisted of 231 active duty military service members with a history of mTBI, 61 (26.4%) of which were being evaluated in a disability context (e.g. Medical Evaluation Board). All patients underwent a full neuropsychological assessment that included cognitive ability measures, as well as performance validity testing (PVT). Testing occurred at least 6 months post-injury, when complete or nearly complete recovery of cognitive functions would be expected. PVT failure rate was compared between disability and clinical evaluations and cognitive test performances were compared between those that passed and failed performance validity testing.

Results: 57.4% of those involved in a disability evaluation demonstrated invalid cognitive testing, while 30.6% of those in a clinical evaluation evidenced PVT failure ($\chi^2 = 13.7$, $p < .001$). Those who demonstrated invalid test performance had significantly lower cognitive test scores across all measured domains (attention, processing speed, memory, visual and verbal reasoning, executive functioning, and overall test battery mean), with all p values $\leq .001$. Effect sizes for each of these comparisons ranged from medium ($d = 0.4$) to large ($d = 1.3$).

Conclusions: The current data demonstrate the high incidence of invalid testing in neuropsychological assessments in U.S. service members with a history of mTBI, particularly those engaged in a disability examination. The effect sizes for PVT performance on cognitive testing were generally large and highlight the importance of using PVTs in this population. If such factors are not considered, there is a notable risk of inaccurate test conclusions owing to cognitive test scores that are artificially suppressed.

Moderate Head Injury: An Outcome Prediction Analysis in a Series of 126 Consecutive Patients

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Objectives: Most of the literature on brain injury has focused on the outcome prediction of severe head injuries, in contrast with the few studies that have been dedicated to patients sustaining moderate head injuries (MHI). An analysis of these patients reveals a significant percentage of morbidity, or even mortality. Deterioration in these patients is generally the result of factors that could be treated, such as intracranial hematoma, cerebral edema, or ischemia. This study aims to develop an estimation of the probability of outcome in a series of patients with MHI including early prognostic variables.

Methods: This study included 126 patients with MHI (GCS 9 – 12). Data collected on admission included age, sex, GCS score, cause of injury, duration of loss of consciousness, duration of post traumatic amnesia, anisocoria, presence of skull fracture, brain CT result, and prior consumption of alcohol.

The sample population was composed of 79 males and 47 females, aged 14 to 87 years. 21.64% of the patients had a history of alcohol intake. 53 patients had a GCS score of 9 to 10, and 73 patients of 11 to 12. Anisocoria was presented in 6% of the patients, while 43 patients had a skull fracture. All patients had brain CT on admission and results were simplified to the presence or absence of a hematoma. There was a 15% overall incidence of operated hematomas.

Depending on the neurological examination and findings of CT scan, patients were taken to the operating room, to the Intensive Care Unit, or to the High Dependency Unit. Outcome was assessed at 6 months according to Glasgow Outcome Score.

Results: A preliminary study was conducted in a first group of 70 patients using ten possible variables. By separating outcome into favorable and unfavorable categories, logistic regression analysis identified four statistically significant prognostic factors: age, GCS score, anisocoria, and presence of hematoma.

External validation of the above model was carried out prospectively in the group of the next 56 patients, showing good discrimination and adequate calibration, but with a tendency to be pessimistic about more severely injured patients.

Conclusions: Several studies have constructed predictive models for survival after severe injury, but there is not enough published research based on outcome from MHI. Since the majority of patients admitted to hospitals is not severe, reducing mortality and morbidity in patients suffering MHI would have a significant impact.

We have derived, checked, and validated a predictive model of survival after MHI. Based upon our results, a four variables model was developed; all variables are simple and easy to measure rapidly in a center with access to 24 hour CT. However, further studies recruiting larger number of patients are needed for validation of statistical models in MHI.

The So - Called Oval Pupil and its Importance in Severe Head Injury

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Objectives: Pupillary size and light reaction are routinely recorded in all patients with severe brain injury. Pupillary abnormalities are accurate predictors of neurological outcome. They may be present from the time of injury, or may appear later. Irregularities of pupil shape are not uncommon in terminal stages of cerebral compression. The finding of an oval pupil is often associated with intracranial hypertension and is a sign of impending herniation. This study aims to describe our experience in the so – called oval pupil and its association with intracranial pressure (ICP) and outcome in a series of severely head – injured patients.

Methods: During a 3 – year period, the ICP was monitored in 114 patients suffering severe head injury who were admitted to Asclepeion Hospital. An intraventricular ICP catheter was inserted and ICP was continuously monitored for five days. Patients were considered to have intracranial hypertension when their mean ICP reached levels ≥ 20 mm Hg despite aggressive therapy.

Results: An oval pupil was observed in 9 of the 114 patients; in these patients the ICP was elevated, ranging from 26 to 47 mm Hg at the time the oval pupil was first noted. In three patients with intracranial hypertension at the time that the pupillary abnormality was first noted, the oval pupil returned to a normal shape when the ICP was reduced to below 20 mm Hg. In the remaining six cases, the ICP could not be satisfactorily controlled and the oval pupil became progressively larger and finally fixed and unreactive. There was a significant difference on outcome between patients with an oval pupil that returned to normal and those whose pupillary abnormality became fixed and unreactive.

Conclusions: The oval pupil has been well described in the ophthalmological literature. Historically, it has been shown that intracranial hypertension in severe brain injury results more frequently in unfavorable outcome.

In this study, we analyzed a group of nine severely head – injured patients with an oval pupil whose ICP was elevated at the time the pupillary abnormality was first noted. The oval pupil represents a potentially transitional stage between the normal and the fixed pupil indicating transtentorial herniation. The facts that in one – third of our cases the oval pupil returned to normal shape after controlling of intracranial hypertension, and, failure to control ICP was associated with the development of a dilated and unreactive pupil, on the other hand, support this argument, in spite the small number of patients. The presence of such a pupil suggests depletion of compensative reserves and impending herniation. The above observed appearance of the oval pupil with relatively moderate increased ICP values might indicate a time window to begin early therapy at lower ICP levels.

Clinical Features and Outcomes of Bilateral Decompression Surgery for Delayed Intracranial Hematoma After Craniectomy Following Acute Subdural Hematoma

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Objective: Delayed contralateral epidural hematoma (EDH) and traumatic intracerebral hematoma (T-ICH) after craniectomy for traumatic subdural hematoma (SDH) are rare but devastating post-operative complications. Their clinical features and outcomes are not well studied. In this report, we present the clinical features and outcomes of delayed contralateral acute hematoma cases requiring a second operation.

Methods: This study includes 10 cases of delayed contralateral EDH and T-ICH following bilateral craniectomy for the evacuation of traumatic SDH and contralateral hematoma between 2004 and 2015. Their medical records and radiographic findings were reviewed and analyzed retrospectively.

Results: Ten of the 528 patients (1.89%) who underwent craniectomy for the evacuation of traumatic SDH developed post-operative EDH (n=5), T-ICH (n=5). The trauma was caused by a fall in 5 patients and by a traffic accident in 5 patients who suffered trauma due to pedestrian accidents died. Seven patients had a low admission GCS (GCS≤8) score in the preoperative state (average admission GCS, 7.7; average discharge GCS, 4.9; average discharge GOS, 2.0). Severe intra-operative brain swelling was noted in all patients, while skull fracture was observed in 8. Multiple associated injuries and medication for heart disease were characteristic of patients who died.

Conclusion: The prognosis of delayed contralateral hematoma was very poor. Multiple associated injuries, medication for heart disease, Traffic accidents, especially pedestrians, were associated with higher mortality rates. Finally, skull fractures can indicate high risk of delayed contralateral acute intracranial hematoma.

Multimodal Evidence of Cognitive Impairment in Former NFL Players

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Introduction: Forty-nine (49) former NFL players were evaluated in my neurology clinic due to progressive cognitive complaints which were attributed to prior multiple concussions. In addition to cognitive problems many subjects reported behavioral dysfunction including depression, anxiety and even aggressive behavior. Most of the former players were initially evaluated by psychologists and completed an extensive battery of neuropsychological testing. Structural brain imaging (MRI or CT) and functional electrical imaging (quantitative electroencephalogram-QEEG) were completed in most of subjects in addition to neurological examination.

Results: An average age of former players was 42 (range between 28 to 62). Average Full Scale IQ was 64 (range between 53 to 86). The most frequently detected cognitive impairment was the Learning and Memory domain (43 of 48 subjects or 89.5%), and Executive Function (39 of 48 subjects or 81%) followed by the Complex Attention/Processing Speed (24 of 48 subjects or 50%), Visual/Perceptual (23 of 48 subjects or 48%) and Language (13 of 48 subjects or 27%). Approximately 23% of former players were identified with white matter abnormalities on the brain MRI testing. Most of players were found to have also functional abnormalities detected with QEEG (Brain Mapping) testing which frequently included increase in frontal and temporal delta and theta power.

Conclusions: These data confirmed findings from prior studies reporting a major cognitive decline of former NFL players who sustained multiple concussions while playing for NFL. In addition, brain mapping (QEEG) analysis showed evidence of functional brain impairment in most of former football players subjected to testing. Regular MRI testing detected white matter brain abnormalities in only smaller fraction of subjects. Most of former NFL players tested are currently unemployed and unable to secure any type of employment due to advanced cognitive problems despite having a college degree or even graduate education.

Extremely Severe Head Injury (GCS = 3): Defining the Limits of Neurotraumatology?

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Objectives: Head injury remains the leading cause of death and severe disability in young adults. The most important prognostic factors are age, level of consciousness, presence of intracranial hematomas, pupillary reactivity, and intracranial pressure (ICP) monitoring. Mortality significantly increases with lowering of GCS score, and with a GCS of 3 there are practically no chances of favorable outcome. This study was performed in order to find if there are patients with a GCS of 3 who have a chance of survival in a series of severely head – injured patients.

Methods: This study included 59 patients with severe brain injury admitted to the Asclepeion Hospital of Athens. All of them were assessed on presentation according to the GCS score as 3 points. The sample population was composed of 49 males and 10 females, ranging in age from 16 to 84 years. 62.7% of patients exhibited an abnormal pupillary response (unilaterally or bilaterally absent). All patients were examined by brain CT scan as soon as possible. An ICP monitoring catheter was inserted in 34 patients and neurological outcome was assessed at 6 months after injury according to Glasgow Outcome Score.

Results: 42 patients underwent craniotomy within the first three hours, including 5 epidural, 28 acute subdural, and 9 intracerebral hematomas/contusions. In the remaining 17 patients, a diffuse brain injury was detected; four of them classified as having a diffuse injury type I. The overall mortality rate was 73%. However, seven patients had a favorable neurological outcome. Of these patients, four were operated on for an epidural hematoma, and three had no abnormalities on initial CT scan. An analysis of these patients' age revealed that all patients who survived with a favorable outcome were younger than 54 years.

The mortality rate was 15.2% in the presence of bilaterally reactive pupils and 57.6% in the case of unilaterally/bilaterally unreactive pupils. A further analysis revealed that patients who survived were younger and had lower ICP levels than those who died.

Conclusions: Advances in the early diagnosis and treatment of severe head injury have led to major improvement of outcome, but a GCS score of 3 has been recognized as a bad prognostic factor, and questions have been raised as to whether these patients have any chance of a meaningful recovery.

Our study shows that the successful management of a very severe head injury still remains rare. With a GCS of 3 only patients with a promptly evacuated epidural hematoma or a normal initial CT scan have a chance to survive. Within the population of very severely head – injured patients, the simple combination of age, pupillary reactivity, and CT scan findings appears to predict accurately non – functional outcome in almost 50% of patients.

Brain Injuries from Falls on Stairs of Children and Youth in Canada: Epidemiology & Prevention

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Background: Stairs and steps have in some countries become the leading specified source of brain injury, with children and working age adults as the main populations at risk. Risk factors and trends were assessed for hospitalizations of children and youth ≤19 years in Canada.

Methods: Non-nominal hospital admission data were obtained from the Canadian Institute of Health Information for the years 1994-2009. Hospitalizations of children and youth 0-19 years of age due to falls on stairs and steps were extracted using appropriate ICD 9 and 10 codes. Trends by age group were analyzed and hospitalizations cross classified using external cause and nature of injury codes. Statistical evaluation included χ^2 for univariate and bivariate analysis and Poisson or negative binomial regression for trend analysis of hospitalizations and injuries.

Results: There were 13,500 hospitalisations from falls on stairs and steps among 0-19-year-olds. Rate of hospitalization decreased by 55% over the study period from 16.8/100,000 to 7.5/100,000. Infants less than <1 year old had the highest rate at 33.2/100,000, and the greatest improvement correlating in time with banning of baby walkers in Canada. Males represented 55% of patients. The home was the site of 60% of incidents, with 60% of falls resulting in a fracture and 30% in intracranial injury. For infants <1 year, 50% of stair falls resulted in an intracranial injury. Income quintiles were highly correlated ($p < 0.001$), especially for lowest, at 25% of total, versus highest 16%.

Conclusions: Home stairs present serious hazards, especially for infants and children. While rates of stair falls have declined in the last two decades, much work remains to make stairs safer and prevent injuries, especially of the brain. Home stairs and stairs in the workplace can be made less steep by adopting the 7-11 configuration widely mandated for public places, and other building code measures to correct frequent design and construction hazards. Banning of baby walkers can eliminate most infant brain injuries on stairs, while stair safety gates can prevent many injuries of toddlers as children begin to walk.

Keywords: stairs, falls, brain injury, intracranial injury, children, youth, social epidemiology, built environment

Written Materials in A Brain Injury Network in Northern France Improve Information and The Quality of The Health Course

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Aim: After traumatic Brain injury and Stroke, the way is long and difficult. Patients and families describe a lot of difficulties to understand what is happening and to know what they should do and where they should go, from early stage in hospital to late stage of social and professional reintegration. Professionals give oral explanations to patients and families but it represents a lot of informations to understand and assimilate. Therefore, we propose materials to improve information quality.

Method: The regional network proposes to make written information materials for patients and families. Thematic working groups gather professionals who are working in different stages of course. Working groups have made multiple information sources to explain coma, awakesness, reeducation, physical and neuropsychological difficulties, social reintegration. These booklets explain symptoms and propose advice (for example, what to do about selective attention difficulties...). Booklets are proposed about specific neuropsychological difficulties (memory and specific attention disorders, aggressiveness, apathy...). Working groups have realized booklets about physical activity, car driving, swallowing disorders....

These booklets are used in resuscitation, rehabilitation services and after return to home in the follow-up multidisciplinary consultations, and in social services. So, in different stages of course, patients hear the same words and explanations, see the same booklets. Different booklets are given when the professionals think that it is the appropriate time.

Furthermore, the TBI and Stroke Network has a website in which the booklets are available. Some booklets can be seen by the general public and some other can only be accessed by the professionals. (www.reseautcavc5962.org).

Results: Patients and families are reassured. They know better what to do and where to go to improve family, social and professional integration. There are less breaks in the health course. Moreover, thanks to the working groups, professionals know better the other stages of the course and the other professionals. Finally, we can use the booklets for students, trainees and new professionals to introduce to them the specific difficulties of brain injury.

To conclude, written supports help patients, families and professionals in different stages of course after brain injury.

Health Professionals' Perception on the Traumatic Brain Injury Care Pathways: A SWOT Analysis

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Background: The quality of care after traumatic brain injury (TBI) may be compromised during complex pathways of care. Numerous transitions, lack of capacity, lack of expertise, and lack of appropriate follow-up are possible challenges to the quality of care in pathways after a TBI.

The aim of this study was to describe the main challenges in the pathways of TBI care from the perspective of health providers in four different European countries.

Methods: Four work shops were conducted in 2014/2015 in the institutions participating in The Collaborative European NeuroTrauma Effectiveness Research study in Traumatic Brain Injury -CENTER-TBI (Oslo University Hospital, Trnava University, University of Versailles Saint Quentin, and Oxford Brookes University). In total 74 healthcare professionals of TBI care from different disciplines (medical administrators, medical doctors across specialties, nurses, physiotherapists, occupational therapists, speech therapists, psychologists /neuropsychologists, social workers, TBI researchers) from both the public and private healthcare sectors participated in the workshops. The output of each workshop reflected the local systems and structure of TBI care, pathways of care, and their bottlenecks. The SWOT charts (Strengths, Weaknesses, Opportunities, Threats) were used to assess the key points that emerged during each workshop.

Results: The main strengths of the pathways of TBI care identified across the countries were as follows: well-organized pre-hospital and acute TBI care with the coverage of the whole population within the public healthcare system, good technology to support patients with acute rehabilitation needs, and multidisciplinary evidence-based treatment approaches. The main recognized weaknesses concerned the fragmentation of care following an acute TBI hospitalization, where the subsequent settings of care may function as a silo, lacking formal relationships with other settings of care as well as having poor communication and information transfer. This in turn may disrupt the continuity of care. In addition an insufficient bed capacity – especially for acute and sub-acute rehabilitation, and long waiting times for most services were identified as major weaknesses.

Conclusion: The continuity in health care service delivery from acute to post-acute/rehabilitation TBI phases as well as rehabilitation capacity could be improved. Improving communication and collaboration across different TBI care facilities will break down borders in healthcare and improve patients' pathways of care.

Systematic and Automated Algorithms for Detecting Cortical Spreading Depolarizations Using EEG and ECoG to Improve TBI Diagnosis and Treatment

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Rationale: Cortical Spreading Depolarizations (CSDs) are waves of depolarization that spread across the cortical surface and are known to cause secondary brain insults after TBI. Because they have been shown to be reliably detected only through surgically placed Electrocorticography (ECoG) arrays on the brain surface, they can go undetected in many injured brains. In severe cases, CSDs are known to cause neuronal death [Pietrobon'2014 NatureReviews Neuroscience;15;379-393], and thus motivate our work on engineering and algorithmic tools for reliable detection/diagnosis of CSDs.

We pose two questions fundamentally important to detecting CSDs:

- 1) Can one develop systematic automated algorithms for detecting CSDs without visual inspection while providing explicit guarantees on the algorithms' success?
- 2) Can high-density noninvasive Electroencephalography (EEG), coupled with advanced data processing, improve noninvasive detection of CSD waves?

Recent studies show that EEG can indeed detect some CSDs [Hartings, AnnNeurol2014 Nov;76(5):681-94]. However, because of the diffusive effect of the layers between brain and the scalp (which act as spatial low-pass filters), EEG detection reliability was observed to be substantially smaller than ECoG's. We expected that the diffusive effect of head layers can be compensated to a degree by increasing the EEG electrode count.

Methods: ECoG: We use wavelet-based edge-detection as a pre-processing step, followed by stitching together data from different time-steps to maximize detection probability under constrained false-alarm probability (Neyman-Pearson formulation). The algorithms are made robust to changes in wave propagation velocity across different areas of cortex by using composite hypothesis testing.

EEG: We first propose and use a spatial equalization-based approach that appropriately inverts the brain-to-scalp spatial low-pass filter, with improved inversion as the number of electrodes increase. The key difficulty lies in performing this inversion with a finite number of sensors. By paying attention to the highest spatial frequency that can be recorded with a given electrode count, we partially invert the spatial low pass filter. Once on the cortical surface, the algorithm is similar for EEG and ECoG.

Results/Conclusions: ECoG: with sufficient electrode density, the algorithm successfully detects CSDs as expected, with low false-alarm and missed-detection rates.

EEG: We expected that the accuracy of recovering the cortical signal from scalp measurements improves with increasing number of electrodes [Grover, Venkatesh, Proc. IEEE'17], and this is indeed what we see. Consequently, our algorithm (for high-density EEG measurements) enables improved detection using EEG in cases when visual inspection might fail (e.g. when the data is noisy or when the spreading depression causes only a mild depression on the brain surface). As an example, we consider a simulated CSD on a 4-sphere

head model where the depression causes loss of 80% energy. Visual reading of unprocessed EEG error-prone, but signal projected onto the brain surface brings out the hidden depression!

Attention and Visuo-Spatial Function in Children Aged 6-8 Years Without Cerebral Palsy, Who Were Cooled for Neonatal Encephalopathy; Preliminary Evidence of Dorsal Stream Vulnerability

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Background: Neonatal encephalopathy (NE) after asphyxia affects 1-3/1000 live births in the UK each year. Therapeutic hypothermia (TH), significantly cooling infants with NE within 6 hours of birth for three days, reportedly improves outcome and reduces incidence of cerebral palsy (CP) in survivors. As such it is now standard-care for infants with NE. Previous research attests to the vulnerability of the dorsal cortical stream of the visual system in perinatal brain injury. Measures of visuo-spatial ability, and control of attention are reportedly indicators of the integrity of the dorsal cortical stream (Atkinson & Braddick, 2010). Children aged 6-7 years who underwent TH for NE are reported to have cognitive impairments even in the absence of cerebral palsy (CP) (Pappas et al, 2015). It is unknown whether visuospatial and attention abilities are affected in early school age children cooled for NE that do not have CP.

Objective: In children aged around 6-to-8 years without CP who were cooled for NE we (i) compared visuospatial and attention abilities with a contemporary control group, and (ii) investigated the relation between attention abilities and cognitive function.

Design/Methods: Twenty-seven children aged 6-8 years cooled for NE, and 18 controls matched for age, sex and socio-economic status were administered an attention test (the Connor's Performance Test-2) utilizing measures of average speed of correct responses, response speed consistency, and change in reaction time across test-duration. The block construction test from the NEPSY-II was used as a measure of visuo-spatial processing. The WISC-IV-UK was used to generate Full-scale IQ data. We assessed the relation between response times <50th percentile on Full scale IQ (FSIQ<85).

Results: In considering attention, children with NE were found to have significantly reduced abilities in sustaining attention over time, their reaction-times were slower and there was greater inconsistency in response speed compared to controls. They were also found to have significantly reduced visuo-spatial processing performance. Response times <50th percentile were found to have 100% specificity and positive predictive value in predicting FSIQ<85.

Conclusions: Our results provide preliminary evidence to support dorsal stream vulnerability in children with NE after cooling, and further indicate that difficulties with attention and visuo-spatial processing may contribute to cognitive impairments in cooled children without CP. We discuss negative early neuro-cognitive effects as potentially predictive of later executive function difficulties.

Blood Based Mitochondrial Targeted Diagnostic Test for Traumatic Brain Injury

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Background: Most of the consequences of mild TBI are due to the progression of secondary cell injury cascade due to the depletion of cellular energy (ATP), increased free radicals and enhanced neuronal cell death due to the damaged mitochondria. [1] Depletion of cellular ATP in injured brain can be identified by 1). Defect in substrate utilization- by measuring pyruvate dehydrogenase enzyme (PDH), and 2). Defect in electron transport chain (ETC) enzymes- by ETC enzyme activities of complex I,II, III and IV. When and how mitochondria get damaged, and cause secondary cell injury following TBI is not known, because we don't have biomarkers of mitochondrial damage? One of the key mitochondrial enzymes is pyruvate dehydrogenase (PDH), which supply reducing equivalents to complex I through the oxidative decarboxylations of pyruvate. Complex I is the first enzyme of the electron transport chain (ETS) required for ATP generation. Depletion of complex I increases free radicals. Our aim was to develop blood based mitochondrial biomarkers of brain injury severity.

Methods: Mild TBI was induced in male Sprague dawley rats by lateral fluid percussion injury. At day 7 post injury, serum and hippocampus lysate were used to measure PDH and complex I by dipstick test according to our established procedure. [2]

Results: There was an inverse correlation between serum and hippocampus PDH. In contrast, there was a positive relation between serum and hippocampus complex I. Measurement of serum complex I can provide an estimation of mitochondrial ETC damage in brain, while increase in serum PDH indicate a compensatory mechanism to meet the growing demand of substrate supply for ATP production in injured brain.

Conclusions: Use of blood based mitochondrial dipstick test for the diagnosis of TBI severity can hold a promising future in the development of mitochondrial targeted therapeutic strategies for the treatment of TBI.

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Case Report: Post-Concussion Syndrome Following Mild Traumatic Brain Injury

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A 43 year-old white, right-handed female was involved in a car accident in July 2016; referred to our center for evaluation of the slurring speech and headache since after the accident. After the accident she was evaluated in the hospital; works ups were negative. In addition, she was having left sided headache with dizziness almost everyday and feeling depressed as well. The headache was tension type, not associated with photophobia or sonophobia; and the headache lasted over 4 hrs. Medications didn't relieve the headache.

Review of system: Negative.

Past Medical History: Right breast Cancer.

Past Surgical History: S/P Right Mastectomy.

Family History: Breast cancer.

Allergy: Not Known Drug Allergy.

Physical exam: Unremarkable.

Neurological Exam: alert, awake and oriented time, place and person.

Cranial Nerves: II to XII -intact.

Motor: Tone: normal, Power: 5/5.

DTRs: +2 Biceps, triceps and Brachioradialis. knees and ankles: +1.

Coordination: Intact.

Sensory exam: Pin prick and Temp: Intact.

Planters: Mute bilaterally.

Gait: Unstable sec to knee pain.

Investigations: Labs: CBC & blood chemistry: Normal.

CT & MRI brain: Normal.

Diagnosis: Likely Post concussion syndrome.

Treatment: Her headache was improved with Gabapentin; and depression was treated with Amitriptyline. In addition, she had CBT (Cognitive Behavioral therapy for depression).

The patient responded well; and her symptoms were resolved in November, 2016.

Determination of the Efficacy of the Patient Global Impression of Change as an Outcome Measure to Assess Improvement in mTBI/PH Symptoms

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Background: The Patient Global Impression of Change (PGIC) is an outcome scale used to evaluate patients' perception of treatment efficacy. In an effort to identify standardized outcome measures that can be used at all military health system TBI centers, a DVBIC Health Outcomes Standardization Working Group selected the PGIC as a core assessment tool. Here, we sought to determine whether the PGIC could be used to measure change in response to treatment in patients with mild traumatic brain injury (mTBI) and psychological health conditions (PH) who are enrolled in the interdisciplinary outpatient program (IOP) at the National Intrepid Center of Excellence (NICoE) at Walter Reed National Military Medical Center (WRNMMC).

Methods: To determine whether PGIC can be used to assess change in response to treatment in patients with mTBI/PH, we compared PGIC scores at discharge with several independent outcome measures. First, we compared PGIC scores with the change in scores from admission to discharge of several commonly used self-report scales (NSI, PCL-M, GAD-7, PHQ-9, ESS, HIT, SWLS, and AUDIT-C). In addition, we compared PGIC scores with improvement of individual symptoms that patients identified as areas of chief concern at admission.

Results: Our data indicate a significant negative correlation between PGIC scores and the change in most scales. AUDIT-C showed a weak relationship with PGIC ($r=0.02$). Multiple regression analysis indicated that the GAD-7, PHQ-9, and ESS significantly explain 21.34% of the variance of the PGIC ($p<0.001$). Analysis of patient complaints indicated that patients who reported PGIC scores of 6-7 (representing meaningful improvement) were significantly more likely to report improvement in areas of concern than were patients with PGIC scores of 1-5 ($p=0.016$), and were significantly more likely to report improvement than worsening of symptoms ($p<0.0001$). There was a significant relationship between PGIC scores and changes in headache ($p<0.001$), sleep disturbances ($p=0.007$), cognitive disturbances ($p=0.012$), and visual disturbances ($p=0.016$).

Conclusions: It is likely that multiple factors contribute to patients' perception of improvement in response to the NICoE IOP. Analysis of patients' complaints suggests that patients are more likely to report improvement when symptoms that they consider to be most disruptive are addressed. Correlation analysis between PGIC and other self-report scales indicates that PGIC scores reflect change that is represented across the range of outcome metrics but do not correlate significantly with any single scale. These data suggest that patient perception of change can be measured with a scale influenced by multiple domains. Therefore, the PGIC may be an accurate metric to reflect patient change in response to a multidimensional treatment paradigm.

Disclaimer: The views expressed in this abstract/poster are those of the authors and do not reflect the official policy of the Department of Army/Navy/Air Force, Department of Defense, or U.S. Government.

KPT-350, a Potent and Selective Inhibitor of XPO1, Reduces Neuronal Injury and Regulates Expression of Genes Associated with Neuroprotection and Inflammation after TBI

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Objective: Traumatic brain injury (TBI) accounts for approximately 230,000 hospitalizations and 50,000 deaths in the US annually. Currently, there are no effective therapies available to reduce or reverse the damage caused by TBI. Recently, Exportin 1 (XPO1) – a nuclear export protein that trafficks over 200 cargo proteins to the cytoplasm – has surfaced as an attractive target for the treatment of neurodegenerative and inflammatory disorders because it facilitates certain pro-inflammatory pathways. KPT-350 is an oral Selective Inhibitor of Nuclear Export (SINE) compound, which covalently binds to XPO1 and blocks its function. KPT-350 is well-tolerated, brain penetrant and therapeutically active in preclinical models. This study sought to determine the effect of KPT-350 on physical and biochemical endpoints in a rat model of TBI.

Methods: TBI was induced in adult male Sprague-Dawley rats via a unilateral controlled cortical impact (CCI). The rats were treated with 15 mg/kg KPT-350 or vehicle orally 2 hours after injury and sacrificed 24-72 hours later. Brains were collected and sectioned for histological analysis to examine the effect of KPT-350 on TBI-induced neuronal injury. Brain tissues, whole blood cells and plasma were isolated to allow a comparison of gene expression profiles between treated and untreated rats. Microarray and bioinformatic analyses were used to determine the genes and pathways that were altered in response to TBI and KPT-350 treatment. Molecular pathways that were associated with the altered gene expression profiles in brain tissues following TBI and KPT-350 were identified using Ingenuity Pathway Analysis (IPA) software.

Results: KPT-350 significantly reduced the size of the injury and the number of fluoro jadeB (FJB)-labeled injured neurons after TBI compared to vehicle treated animals. In addition, KPT-350 blocked microglial activation as measured by Iba1 and ED1 labeling and reduced reactive astrogliosis as determined by GFAP immunoreactivity. Expression levels of >500 genes were significantly altered by TBI and many of these expression changes were reversed by KPT-350. Predicted upstream regulators of the TBI- and KPT-350-regulated genes included NFκB, IL12, MAPK, CREB1, STAT1 and STAT6. The overall analysis of expression changes in networks associated with cell death and apoptotic pathways suggested that KPT-350 reduced the secondary injury in TBI by a neuroprotective and anti-inflammatory mechanism.

Conclusions: These findings demonstrate that in the CCI model of TBI, KPT-350 has a significant impact on neuronal survival and on the expression of genes in networks associated with neurodegeneration and neural damage. This study also suggests that KPT-350 acts through a combined neuroprotective and immunomodulatory mechanism to prevent neuronal injury following TBI.

Neuropsychological Outcomes for Children Referred for HIV-Related Difficulties to a Local Pediatric Neuropsychology Clinic in Cape Town, South Africa: Attention Vs Memory Problems?

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Introduction: Human immunodeficiency virus (HIV) is a serious public health concern, which is the leading cause of morbidity and mortality in South Africa. Children are unduly affected and experience both direct and indirect effects associated with the disease, seen in a range of domains including medical, developmental, psychosocial, academic and cognitive spheres.

Aim: The main aim of this study was to describe neuropsychological profiles of children referred to the Red Cross War Memorial Children's Hospital's (RXH) pediatric neuropsychology clinic (PNC), over a one-year period for HIV-related neuropsychological difficulties.

Methods: We adopted a case series approach, reporting on all children referred to the RXH's PNC in 2015 in the first instance, and then all children referred for HIV-related difficulties more specifically. The study design was retrospective and quantitative, based on medical (including PNC) records at the RXH.

Results: A total of N=41 children were referred to and seen at the RXH PNC in 2015 for a range of neuropsychological difficulties based on various etiologies. We focused on the subsample of children who were referred specifically for HIV-related difficulties, who constituted almost 50% of that sample of referrals (n=20) to the PNC for 2015. The mean age of the subsample was approximately 10 years. Most children were male, isiXhosa-speaking, and from low socio-economic backgrounds. The results of the neuropsychological assessments showed that, on average, the children scored quite poorly across the domains of attention, executive functions (including working memory and abstraction), language, processing speed and general intellectual functioning. However, what was inconsistent with previous literature is that children performed in the average range for memory.

Discussion and Conclusion: In and amongst the range of neuropsychological difficulties reported for children referred to the PNC for HIV-related difficulties, memory problems were common. However, the neuropsychological reports suggest that these difficulties may be a function of attentional problems rather than pure memory problems per se. The interrelationship between these domains is discussed. Future research is important to substantiate this finding as it can begin to inform new, and revise existing, intervention strategies.

Safety, Acceptability and Outcomes Following Early Active Rehabilitation for Concussion Recovery in Youth: An Exploratory Randomized Clinical Trial

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Background: One third of youth experience persisting symptoms following concussion lasting upwards of one month. The traditional approach of physical rest has not been shown to alleviate symptoms for this unique group of patients. Active Rehabilitation approaches are gaining traction by exploring the utility of individualized physical activity as a management strategy.

Objectives: Evaluate the safety and acceptability of implementing early Active Rehabilitation (AR) for concussion management in youth with symptoms persisting more than 2 weeks post-injury. A secondary and exploratory objective was to estimate the extent to which early AR contributed to changes in post-concussion symptoms when compared to standard AR.

Design: Single centre, randomized clinical trial examining early AR (initiated 2-weeks post-injury) compared to standard AR (initiated 4-weeks post-injury) over a 6 week follow-up period.

Setting: Mild Traumatic Brain Injury Program/Concussion Clinic at a tertiary care paediatric university teaching hospital and Trauma Centre.

Participants: Twenty youth (9-17 years old) with post-concussion symptoms for at least two-weeks were randomized to early AR (n=10) or to standard AR (n=10), out of 50 screened consecutively for eligibility.

Intervention: Active Rehabilitation (aerobic exercise, coordination drills, visualization, education/reassurance) was administered by physiotherapists in-person, and then continued as a home program. The AR was provided in addition to usual recommendations and activity management post-concussion (school and general/physical activities). Content was similar in both groups, only timing of initiation was different (early vs standard).

Outcome Measures: Safety was ascertained with a daily online survey to monitor changes in post-concussion symptoms, adverse events, and aerobic exercise details (type, frequency, duration & intensity). Adverse events were defined as an exacerbation of post-concussion symptoms during or immediately following aerobic exercise. Acceptability to patient and patient families was inferred based on reasons for declining participation, as well as based on clinician willingness to provide early rehabilitation. Post-concussion symptom severity, measured with the Post-Concussion Symptom Inventory, was documented 2, 4, 6, and 8 weeks post-injury to address our secondary objective.

Results: No adverse event was reported by participants in either group in the first 2 weeks of intervention. Two adverse events (one in each group) were identified through the online survey more than one-month post-concussion. Early AR was acceptable to all but one parent and one patient (not related), who declined participation due to concern of possibly being randomized to the early AR group. Other reasons for not participating included scheduling difficulties and lack of interest. Post-Concussion Symptoms decreased over time for both groups.

Conclusions: The results from this pilot study indicate that early Active Rehabilitation (starting 2-weeks post-injury) is an acceptable and safe approach for the management of persisting symptoms after a concussion. Further study is needed to determine the superiority of this strategy over current treatment approaches.

Investigating Emotional and Behavioral Sequelae and Concussive Injury in a Sample of Adult Rugby Players in Cape Town, South Africa

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Introduction: Given its rising incidence rates and potentially debilitating neurodegenerative outcomes, sports-related concussion has received dramatically increased attention over recent years. Rugby is among the highest-risk contact sports for diagnoses of concussion or mild traumatic brain injury. The occurrence of rugby-related concussion mirrors the repetitive, high impact nature of the game. This research forms part of a larger research project that aims to investigate the long term neuropsychological outcomes of repeated concussions and sub-concussive injuries in rugby players.

Aim: The current project explores the relationship between concussion and emotional and behavioral disturbance in rugby players and non-contact sportsmen.

Methods: Questionnaires measuring depression, anxiety, general health, anger, impulsivity and alcohol usage were administered to a sample of 114 participants including rugby players (n = 88) and non-contact sport participants (n = 26), matched on age and intelligence.

Results: 45 rugby participants (51%) reported 1 to 5 previous formally diagnosed concussions and 30 (34%) reported potential undiagnosed concussions ranging from 1 to multiple incidents. In total, 68% of the rugby players in the sample reported previous concussive injury. We conducted a discriminant function analysis with three groups (rugby players with concussion, rugby players without concussion and non-contact sport control participants) using measures of emotional and behavioral disturbance as predictors. Results indicated that the groups did not differ on emotional and behavioral disturbance and that discriminant functions could not be used to significantly predict group membership.

Discussion and Conclusion: The findings of this study suggest that emotional and behavioral disturbance after concussion might dissipate altogether in the acute phase of concussive injury or may only surface later in life. In addition, it appears that outcomes of emotional and behavioral disturbance after mTBI cannot be predicted solely by injury-related variables. Further considerations including the possible implications of self-report measures on the reliability of emotional and behavioral disturbance in the sample are discussed.

Combining rTMS and Amantadine to Enable Neurobehavioral Recovery for Persons Living in Chronic States of Disordered Consciousness after TBI

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Objective: Characterize effects of repetitive Transcranial Magnetic Stimulation (rTMS), Amantadine (AMA), and rTMS+AMA among persons living in chronic vegetative (VS) and minimally conscious (MCS) states after TBI according to changes in neurobehavioral function and functional connectivity of the dopamine network.

Methods: In this trial (registry #NCT02025439), four participants first received rTMS-alone (30 sessions, right Dorsal-Lateral-Prefrontal-Cortex) or AMA-alone (100mg BID, at least 28 days) after which all received TMS+AMA. To increase size of rTMS-alone group, two participants from a previous trial were added.

The Disorders of Consciousness Scale (DOCS-25) was collected weekly during treatments and at 6-week follow-up. Resting state functional connectivity (rsFC) was assessed at baseline and after each treatment. Treatment effects on rsFC of the dopamine network (16 regions) and the three pathways comprising this network were examined separately and relative to neurobehavioral outcomes.

Results: AMA-alone group (n=2) made an average neurobehavioral gain of 4.2 (SD: 3.7), but it is not meaningful because it is less than the DOCS-25 minimally detectable change (MDC) of 4.6. rTMS-alone (n=4) and rTMS+AMA (n=4) groups made clinically meaningful gains respectively of 11 (SD: 4.8) and 15 (SD: 10.1) exceeding the MDC and Minimally Clinically Important Difference (MCID) of 6.

To examine treatment differences according to sustainability of gains, we identified peak neurobehavioral performance during treatments. Each group made clinically meaningful gains from baseline to peak (AMA-alone: 18, SD: 0.54; rTMS-alone: 19, SD: 10.6; rTMS+AMA: 19, SD: 8.8). From peak to treatment endpoint, however, only rTMS+AMA sustained gains (3.3, SD: 18.1) (AMA-alone: -12.0, SD: 1.3; rTMS-alone: -9.6, SD: 11.3).

rsFC of the dopamine network (mean z-score) decreased for all groups (AMA-alone: -0.12; rTMS-alone: -0.07; rTMS+AMA: -0.22), but correlations with neurobehavioral measures increased (rTMS-alone: Baseline $r = -0.65$; Endpoint $r = 0.35$; rTMS+AMA: Baseline $r = -0.36$; Endpoint $r = 0.42$). Differential rsFC change within the dopamine network was examined by computing the proportion of z-scores changing for all region-region pairs comprising each pathway and by computing correlations between neurobehavioral measures and these z-scores. rTMS-alone and rTMS+AMA each evoked more than 90% change in each of the three pathways. Both treatments also had positive correlations between neurobehavioral measures and region-region z-scores within the nigrostriatal (rTMS-alone $r=0.55$; rTMS+AMA $r=0.60$) and mesolimbic (rTMS-alone $r=0.82$; rTMS+AMA $r=0.65$) pathways. For the mesocortical pathway, however, rTMS-alone correlations were positive ($r=0.91$) and rTMS+AMA were negative ($r=0.70$).

Conclusions: Findings suggest that rTMS+AMA may support sustained neurobehavioral gains possibly enabled by differential modulation within the dopamine network that could reflect a trade-off between subcortical processing and higher-level processing mediated by the mesocortical pathway. Findings also suggest that persons living in chronic VS and MCS provided with targeted treatments can recover meaningful function highlighting the need for research to optimize this potential.

Does Amantadine Have a Role in Maintaining Function in Long-established Brain Injury? A Single Subject Research Study

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Research into dopamine agonist (DA) use in traumatic brain injury (TBI) has focused on acute or recovery phase consciousness or cognition (1-5). The role of DA in later rehabilitation or in functional outcome is less well defined. We report a single case experimental design demonstrating amantadine associated functional improvement, six years following TBI with bifrontal & bitemporal contusions, traumatic subarachnoid haemorrhage and intraventricular bleeding.

The subject was initially given Amantadine two years post injury when in a low awareness state. Due to associated infrequent seizures, repeated attempts were made to discontinue or use alternative stimulants, but with loss of function on each occasion.

To justify continuation with amantadine, a non-blinded trial of withdrawal using an ABA format was performed. Based on the subject's ability to participate in dressing, personal care, oral hygiene, feeding, mobility, comprehension, vocalisation and musical ability, 41 individual activities were graded in a range of 1-4 according to complexity or degree of prompting required. At baseline, his grades were skewed towards upper end of range (21 "4"s; 10 "3"s; 1 "2" and 9 "1"s) possibly reflecting impact of learning effect from task repetition in preparation for the trial. Score on Disability Rating Scale (6) at baseline was 11.

At 25 and 36 days post withdrawal, deterioration was recorded in 21 and 26 respectively of the 41 graded activities, and deterioration by 2 or more grades in 11 and 12 activities respectively. By 17 and 31 days following reintroduction, most grades returned to baseline or better (higher in 10, lower in 2).

This is the first comparable report of DA associated improvement in late phase rehabilitation following TBI. Were this pattern is to be researched further, client specific scales, rather than standardised outcome measures, may be required if trials are to be sufficiently sensitive to quantify change in function or quality of life.

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The Quest for Data in a State Without Significant Brain Injury Resources

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Decisions are being made every day about TBI patients in the state of South Carolina. Decisions are being made by patients, families, providers, schools, insurance carriers, hospitals, and legislators. South Carolina has no TBI Model System Center. The Brain Injury Association of South Carolina, although committed to serving this population, only has the limited financial resources to maintain a small staff for community outreach and education. Without specific data about what is actually happening in this state, future efforts to support and advocate for brain injury patients were at risk for being driven only by national trends and locally available resources.

Some states are fortunate to have medical and educational institutions funding multidisciplinary teams with the time to seek large grants and engage in impressive research. Many, like ours, are not. A significant risk associated with this discrepancy is that much of the research being published is coming from the states in which patients may already have the greatest access to data-driven services, and these patterns may be dramatically different in states without those types of resources.

Already a year into this quest by the South Carolina Brain Injury Leadership Council, there are as many unanswered questions as answered ones. As expected, small amounts of data have been gathered fairly easily from the SC Department of Education and regional emergency departments. Conversations are ongoing with Blue Cross Blue Shield of South Carolina and local hospitals, but no promises have been made to grant access to their records. Our greatest success has been in collaboration with SC Medicaid. Although Medicaid-funded services are only a portion of those being provided in our state and target a very specific demographic of the population, these efforts have provided the first ever actual (but very preliminary and with significant limitations) global data set on the numbers of brain injury patients in South Carolina and the services being provided. Ultimately, the goal is to gather data from other payer and provider sources and to place this state-wide data into a national context, but even the latter has been daunting and complex as well. BIAA and NASHIA publish national data, but many states configure this information differently making direct comparisons challenging and potentially unreliable. Access to commercially managed Medicaid data would require exactly the kinds of financial resources that our committee is without.

While the SCBILC plans to publish and present the limited data we have been able to collect, it has been the time, effort, and obstacles faced during this process that are worthy of attention as well. In fact, sharing these experiences may be one of the greatest contributions this committee can make to the ongoing research on this population around the world.

Teleneuropsychology Rehabilitation Services for Regional Inpatients with Stroke: Development and Evaluation of a Novel Pilot Program

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Over two-thirds of survivors of stroke exhibit cognitive impairment and over one-third experience clinical levels of mood disturbance. If left untreated, these neuropsychological impairments can result in protracted inpatient admissions, poor response to rehabilitation and compromised long-term recovery and quality of life. Unfortunately, access to neuropsychology services in remote and regional settings is extremely limited. The overwhelming majority of patients with stroke do not have access to cognitive or mood assessment and treatment. The aim of this research program is to develop and evaluate a new teleneuropsychology rehabilitation service for a regional Australian hospital. In particular we seek to determine the feasibility and effectiveness of this service model, including the critical success factors to support sustainability and upscale. A pilot model of neuropsychological assessment and rehabilitation service provision has been developed since July 2016. Clinical services are provided to an Echuca Regional Health inpatient rehabilitation unit by an experienced clinical neuropsychologist based at a Monash University clinic located in metropolitan Melbourne, Australia, one day per week. The service includes comprehensive assessment of patient cognition, mood and behaviour in addition to provision of cognitive rehabilitation and psychological interventions for mood. Consultations are also provided to medical, nursing and allied health clinicians to assist them to manage patient neuropsychological impairments within therapy sessions. An education program is also being delivered to build team capacity regarding detection and management of neuropsychological dysfunction. Furthermore, the neuropsychologist attends weekly team meetings via telehealth to identify appropriate referrals and for ongoing team communication and advice. The service is provided using various telehealth information communication technologies, with Zoom the primary software program utilised. Within the first three months of service implementation, six team education sessions, five neuropsychological assessments, and three team consultations for patient management have been successfully provided via telehealth. A pre/post service implementation design is utilised to evaluate the feasibility and effectiveness of this service. Initial pilot evaluation data of the first three months of service implementation will be provided.

Key Areas of Evaluation Include: medical and allied health clinician knowledge and confidence; proportion of patients receiving cognitive and mood assessments and associated waiting times; proportion of patients receiving cognitive rehabilitation and psychological therapy and associated waiting times; number of interdisciplinary rehabilitation goals set relating to neuropsychological function; and changes in patient cognition and mood function during inpatient rehabilitation admission. A cost description analysis is also planned and will be used to describe the potential economic benefits of a teleneuropsychology rehabilitation service, compared to other service options. These analyses will be used to support a business case for ongoing application of this new model of care.

Discrepancies Between Patient and Clinician Reports of Disability Following Stroke Differ Across Functional Domains and Time Points

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Background and Aims: Reduced self-awareness of impairments following stroke is well-acknowledged in existing literature; however, studies to date have predominately focused on physical impairments. Self-awareness of functional activity limitation and participation restriction, which incorporate both physical and cognitive abilities, is less well understood. Furthermore, most studies have examined self-awareness of current impairments during inpatient rehabilitation, with limited focus of function post-discharge. Thus, the primary aim of this study was to examine discrepancies between patient and clinician reports of disability post-stroke (commonly referred to as “self-awareness”) across activity limitation and participation restriction domains and across current and predicted functioning 3-months post-discharge. A secondary aim was to compare patient and clinician predicted functioning with close other reports at 3-months post-discharge.

Methods: Fifty subacute inpatients with stroke (Age M = 70.3 SD = 15.80, 56% female) and their treating occupational therapist independently completed three measures assessing patient motor, cognitive and instrumental activity limitations (Functional Independence Measure Motor subscale; Functional Independence Measure Cognitive subscale; Patient Competency Rating Scale respectively), and participation restrictions (Mayo Portland Adaptability Inventory-4). Measures were completed twice, for current inpatient functioning and predicted functioning three months post-discharge. Close-others completed measures at three months post-discharge.

Results: Patients reported higher levels of functioning than clinicians across all functional domains and time points; however, patient-clinician discrepancies were greater for cognitive ($p < .001$, $r = .510$) and instrumental activity limitation ($p < .001$, $r = .606$) compared to motor activity limitation ($p = .182$, $r = .136$) and participation restriction ($p = .195$, $r = .130$). Patient-clinician discrepancies were greater for current function, compared to predicted function, for cognitive ($Z = -4.21$, $p < .001$) and instrumental ($Z = -4.00$, $p < .001$) activity limitations. In contrast, patient-clinician discrepancies were smaller for current, compared to predicted, participation restriction ($Z = -4.03$, $p < .001$) while no differences were found between current and predicted motor activity limitation discrepancies ($Z = -1.35$, $p = .177$). Finally, clinician predictions of function were highly correlated with close other reports of function at 3-months post-discharge across all activity limitation and participation domains, while patient predictions were only significantly correlated for motor activity limitation.

Conclusions: Discrepancies between patient and clinician appraisals of function vary across disability domains and time points, with patient-clinician discrepancies particularly evident for current cognitive and instrumental activity limitations. Furthermore, clinician predictions of post-discharge function appear to be more reliable than patient predictions. These findings support the concept of awareness as a multidimensional construct and emphasise the importance of considering the object of appraisal when making assessments regarding insight. The results can be used to inform discharge planning and post-discharge support plans and to develop future measures of self-awareness.

Neuroimaging of Tauopathy in Chronic TBI

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Introduction: Although several studies have used PET with [11-C] Pittsburgh Compound-B to examine A β deposits after TBI, at present, there is no specific, noninvasive assessment of trauma-related tau pathology that can be performed in vivo. Tau imaging via [18F] AV-1451 PET has been recently reported in Mild Cognitive Impairment, Alzheimer's Disease, and normal aging. We imaged a cohort of TBI subjects in the chronic phase and control subjects with [18F] AV-1451 as an indicator of trauma-related neurodegeneration.

Methods: Seven chronic TBI subjects (all males, mean age 47yrs) and six healthy controls (three males, mean age 30yrs) underwent PET imaging after i.v. injection of 10 mCi [18F] AV-1451. PET data were acquired on a Siemens mCT-Flow Biograph PET/CT 75 minutes after injection. Structural T1-weighted MPRAGE MR images were acquired on a 3T Siemens TIM Trio scanner. PET images were normalized to Montreal Neurological Institute template space using the coregistered MR. Cerebellar grey matter activity was sampled and SUVR PET images were generated by dividing the image by cerebellar grey matter activity. Normalized SUVR PET images were visually inspected for abnormal uptake and asymmetry and quantitative regional SUVR analyses were performed.

Results: Various degrees and patterns of uptake were observed in the TBI subjects whereas controls showed more uniform results. We present results for 3 TBI subjects and 1 control that span observed uptake patterns.

There was absence of uptake in both gray and white matter and minimal uptake in the brainstem and substantia nigra in the normal control (24y/o).

TBI subject 1 (39y/o) had multiple blast injuries and severe neuropsychiatric symptoms, but the [18F] AV-1451 was overall minimally above background levels (1.10 SUVR in cerebral gray matter). There was slightly increased substantia nigra uptake.

TBI subject 2 (21y/o) had a single severe TBI and prolonged coma. The [18F] AV-1451 uptake in much of the brain was only minimally above background levels. But specific lacunar encephalomalatic regions (predominately left pallidum (2.25 SUVR), left medial temporal cortex (1.33 SUVR), and bilateral orbitofrontal cortices (1.54 and 1.40 SUVR respectively) showed focal intense uptake.

TBI subject 3 (60y/o) sustained multiple TBIs and received a diagnosis of early dementia. The most striking areas of uptake are in the bilateral occipital, parietal, and precuneus regions (3.09 – 3.48 SUVR), diffusely in the orbitofrontal (1.94 left and 1.83 right SUVR), lateral temporal (2.66 left and 2.50 right SUVR), and hippocampus (2.34 left and 2.35 right SUVR) brain regions.

Conclusion: Overall, the prevailing pattern on the [18F] AV-1451 PET images is notable for a absence of specific uptake in controls and regions of intense uptake in two of three chronic TBI subjects with lasting sequelae. The importance of focal [18F] AV-1451 uptake has been suggested to mirror clinical and neuroanatomical functional variability in chronic TBI subjects.

Outcome Research of Head Injury Patients Undergoing Emergency Air Medical Transport (EAMT)

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Emergency air medical transport (EAMT) has become a major part of the modern trauma care system and is frequently used to transport patients from remote islands to a tertiary center. Data of all patients with traumatic brain injury and underwent EAMT were retrospectively retrieved from National Aeromedical Approval Center (NAAC), Taiwan. Patient data were analyzed by using the following parameters: age, gender, injury of severity score, and outcome within three days after air transport.

Between Oct 01, 2002 to Dec 31, 2016, there were 4236 EAMS requests from the four major remote islands to Taiwan Main Island. Among them, 3701 were approved. Brain injury patient has been a major component of patient group. Male predominates in the head injury patient populations (M:F =2.8:1). Patients between 21 and 30 years old comprised the majority (25%). There was higher percentage of moderate to severe head injury patients compared with ground transport. Moderately injured patients comprised 31% and severe head injury patients comprised 35%. Of these moderate and severe injury patients, 29% were intubated. Mannitol (or Glycerol) was routinely used. Thirty-eight patients expired within seven days after air medical transport. These findings demonstrated that proper preflight assessment and airway maintenance is a key factor for traumatic brain injury patient transport both in air and ground.

Do Individual Domains of Cognitive Functioning Predict Community Participation At 1, 2, and 5 Years After Moderate to Severe Traumatic Brain Injury?

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Background: Given the breadth of adverse long-term sequelae that can follow a moderate to severe traumatic brain injury (TBI), it is crucial that early predictors of optimal and suboptimal outcomes are identified. Community participation is a meaningful way to measure how individuals reintegrate into their lives after an injury, but few studies have examined rehabilitation outcomes using this construct. Five domains of cognitive functioning are commonly measured during inpatient rehabilitation: language expression, language comprehension, memory, problem-solving, and social interaction. It is not yet known whether cognitive functioning in these domains predicts participation after TBI.

Objective: Identify whether the individual domains of cognitive function measured by the FIM at inpatient rehabilitation discharge predict participation outcomes at one, two, and five years after TBI.

Methods: Secondary data analysis was performed on a sample of 1000 individuals with moderate to severe TBI from the TBI Model Systems National Database. All participants were over the age of 16 and received acute inpatient rehabilitation treatment from a facility in the TBI Model Systems of Care. Hierarchical linear regression analyses were conducted in block format on follow-up data collected at one, two, and five years post-injury. Scores on the five Cognitive FIM subscales served as independent variables and scores on the Participation Assessment with Recombined Tools – Objective (PART-O) served as the dependent variable.

Results: Of the five cognitive domains that were examined, only memory scores were found to be a significant predictor of participation over and above the contribution of demographic and injury severity predictor variables, and only at two years post-injury ($p < .05$). At two years, higher memory scores were associated with more participation. Language expression, language comprehension, problem-solving, and social interaction scores were not found to be significant predictors of participation at one, two, or five years after injury.

Conclusions: Based on these findings, rehabilitation interventions that incorporate memory training may have positive implications for participation after discharge. Cognitive impairments that are isolated to a specific domain may not have a significant impact on community participation if injured persons can use preserved abilities to compensate after TBI. Participation is a meaningful measure of health care outcomes that should continue to be utilized in future studies. Future studies should also examine the relationship between participation and objective neuropsychological assessment, which may provide a more comprehensive measure of cognitive functioning.

Involvement of Connexin40 in the Protective Effects of Ginsenoside Rb1 Against Traumatic Brain Injury

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Ginsenosides are the major active components of ginseng, which have been proven to be effective in therapies for neurodegenerative diseases. Ginsenoside Rb1 (GS-Rb1) is the most abundant among all the identified ginsenosides and has been shown to exert neuroprotective effects, although the underlying molecular mechanisms remain unclear. Connexins are a family of transmembrane proteins that form gap junctions, which are important for diffusion of cytosolic factors such as ions and second messenger signaling molecules. Previous studies have shown that a subset of connexin proteins is involved in neuroprotection. We investigated the protective effects of GS-Rb1 against traumatic brain injury (TBI) and the potential mechanism using TBI mouse model. We discovered that TBI-induced brain injury and up-regulation of connexin40 (Cx40) protein expression as early as 6 h post-TBI, which was reversed by administration of GS-Rb1. In addition, we found that the protective effects of GS-Rb1 are dose and time dependent and are partially mediated through phosphorylation of ERK1/2 signaling pathway, as evidenced by the abolishment of GS-Rb1-mediated elevation of p-ERK1/2 expression and inhibition of Cx40 expressions when ERK inhibitor U0126 was used. Our study provides evidence that Cx40 is implicated in TBI induced brain injuries, and GS-Rb1 exerts neuroprotective activity against TBI involving down-regulation of Cx40 expression.

Keywords: TBI Connexin40 Ginsenoside Rb1 Neuroprotective activity

Deficit in Memory for Faces in Delayed Recall Condition in Children with Hypoxic-ischemic Encephalopathy

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childhood. The investigation of these deficits can shed light on the nature of neurodevelopmental abnormalities in these children.

The goal of this research was to examine the hypothesis that preschool children, born with perinatal Hypoxic-ischemic Encephalopathy, have deficit in memory for faces in delayed recall condition.

Participants and Methods: The experimental group included 26 children aged 6-8 years old (mean age = 6.8) with ADHD, born full-term with perinatal Hypoxic-ischemic Encephalopathy. The control group included 26 typically developing children. The children from experimental and control group were matched for IQ, gender and age.

Children from both groups were assessed with NEPSY using Memory for Faces subtest. This subtest is designed to assess the ability to learn and recall 16 faces in immediate and delayed recall conditions. Each child was asked to recall 16 faces immediately after first presentation and 30-min later.

Results: Two-way ANOVA was used to reveal group differences in reproducing the faces in immediate and delayed conditions. We have not revealed significant differences between children from experimental and control group in the recalling the faces in immediate condition. However, the interaction of condition type and group was significant. Children from experimental group were less successful in recalling the faces in delayed condition.

Conclusion: This research has shown that preschool children, born with perinatal Hypoxic-ischemic Encephalopathy, have deficit in memory for faces in delayed recall condition. It can be assumed that perinatal Hypoxic-ischemic Encephalopathy can cause specific (not global) memory deficit in childhood – the deficit in recall in delayed condition.

The research was supported by Russian Foundation for Basic Research, grant № 15-06-06491A.

Impact of Motor Sequencing Training on Executive and Motor Abilities in Children with Hypoxic-ischemic Encephalopathy

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It is known that children with hypoxic-ischemic encephalopathy (HIE) have a risk for neurodevelopmental disorders. Particularly these children often develop ADHD. It is of great significance to receive the evidence for efficiency of different training programs that are aimed to help children with perinatal trauma.

The goal of this study was to assess the impact of 12 weeks of motor sequencing training on the executive and motor abilities in children who were born at full-term with perinatal hypoxic ischemic encephalopathy.

Participants and Methods: The participants were 24 children aged 5-7 years old (mean age = 5.9) with ADHD, born full-term with perinatal hypoxic-ischemic encephalopathy. Children were randomly assigned to the intervention and comparison group. Children from intervention group participated in 12 weeks of motor sequencing training. This program trains the child to plan, sequence, and process information more effectively through repetition of goal-directed movements. This program is built on the conceptual framework derived from the work of Luria's theory of restoration of neurocognitive functions (Luria, 1963, 1974).

The Luria's child neuropsychological assessment battery was administered before and after the intervention period.

Results: Analysis of covariance tested the effect of motor training program on four scales of the Luria's child neuropsychological assessment battery: Executive scale; Motor scale; Visuospatial scale; Memory scale. Group differences were found for the Executive scale and Motor scale. Post-test mean for the intervention group were significantly greater than the control group.

Conclusion: Motor sequencing training in children with ADHD who were born at full-term with perinatal hypoxic ischemic encephalopathy benefits both motor abilities and executive functions.

The research was supported by Act 211 Government of the Russian Federation, agreement № 02.A03.21.0006.

Impact of Preterm Birth on Early Cognitive Development in Infants At 5 Months of Corrected Age

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It is known that brain injury in premature infants has serious and diverse effects on subsequent brain and neurocognitive development [Anderson & Doyle, 2008; Inder et al., 2005; Volpe, 2009]. However, the impact of prematurity on the neurocognitive abilities during early stages of development is not investigated thoroughly.

The aim of this research was to reveal the differences in the neurocognitive development in premature infants and full-term infants at 5 months of age using the Bayley Scales of Infant and Toddler Development. This research is a part of longitudinal study designed to track the developmental trajectory in cognitive and brain measures as preterm children transition from 5 to 36 months of age using multidisciplinary approach.

Participants and Methods: The participants were 26 premature infants and 26 gender matched healthy full-term infants at 5 months of age. The gestational age of preterm infants was between 29 and 35 weeks.

The Bayley Scales of Infant and Toddler Development (3rd Edition) were used to evaluate the neurocognitive abilities in infants.

Results: The one-way ANOVA has revealed that premature infants performed significantly ($p \leq 0,05$) more poorly than the full-term infants on cognitive scale, receptive language and gross motor. No significant differences were found between preterm and full-term infants on expressive language and fine motor. Two-way ANOVA with age and gender as between-subjects factors has revealed no significant ($p \leq 0,05$) differences between female premature infants and full-term female infants on gross motor in comparison to male infants.

Conclusion: It can be assumed that the prematurity has specific (not global) negative effect on neurocognitive development at 5 months of age with gender effect on development of gross motor.

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Neurocognitive Outcome at the Age of 5 Months after Perinatal Hypoxic-ischemic Encephalopathy

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Hypoxic-ischemic encephalopathy (HIE) in the full-term newborn is a major cause of neurodevelopmental abnormalities in childhood (Haataja, 2001; Levene, 1995). However, the impact of HIE on the neurocognitive abilities during early stages of development is not investigated thoroughly.

The aim of this report is to compare the early neurocognitive outcome of infants from two groups – infants at 5 months of age who were born at full-term with perinatal hypoxic ischemic encephalopathy and healthy infants. This research is a part of longitudinal study designed to track the developmental trajectory in cognitive and brain measures as children with HIE transition from 5 to 48 months of age using multidisciplinary approach.

Participants and Methods: The participants were 17 surviving children, born full-term with perinatal HIE, and 17 gender matched healthy full-term infants at 5 months of age.

At 5 months of age, neurocognitive abilities in infants were assessed with the Bayley Scales of Infant and Toddler Development (3rd Edition).

Results: The one-way ANOVA has revealed that infants with perinatal HIE performed significantly ($p \leq 0,05$) more poorly than the infants from control group on cognitive scale, receptive language, expressive language and gross motor. No significant differences were found between preterm and full-term infants on fine motor.

Conclusion: It can be assumed that hypoxic-ischemic encephalopathy has specific (not global) negative effect on neurocognitive development in infants at 5 months of age. We expect to reveal the impact of HIE on neurocognitive abilities during next stage of development in the framework of longitudinal study – in 10, 14, 24, 36 and 48 months.

The research was supported by grant of the Russian Foundation for Basic Research №15-06-06491A.

Arterial Ischemic Stroke In Children: Whether or Not Procoagulant And Prothrombotic Genes Are Able to Predict the Outcome?

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Introduction: Paediatric Arterial Ischemic Stroke (PedAIS) is rare and severe disorder, which leads to severe palsies, epilepsy, mental retardation, etc. At the same time disability as PedAIS outcome is poorly investigated and poorly predictable state.

Methods: Series of clinical cases, the forecast cohort study. The assessment of outcomes in 142 children after 4 and more years later PedAIS has been held in November and December 2016 – whether or not there was disability. 67 patients were recognized as disabled (Dis), 75 children – as nondisabled (NotDis).

Disability was interpreted as the state that is required constant external support and replacement of irreversibly lost functions of the nervous system.

PedAIS in both groups was confirmed by brain CT (MRI) scan; all patients signed informed consent form.

All the children has been tested of 12 single nucleotide polymorphisms (SNP) in 8 thrombophilic genes (FGB:-455G>A, F2:20210G>A, F5:1691G>A, F7:10976G>A, F13:103 G>T, ITGA2:807C>T, ITGB3:1565T>C, PAI-1:-675 5G>4G), 4 genes of folic acid enzymes (MTHFR:677C>T, MTHFR:1298A>C, MTRR:66A>G, MTR:2756A>G), by polymerase chain reaction.

Results: Quantitative analysis showed that the carriage of 4 thrombophilic genes SNP raised the risk of disability (OR = 2,03, 95%CI 0,92-4,47, Fisher 0,05) as well as the carriage of 4 SNP genes of folic acid enzymes (OR = 8,69, 95%CI 1,00-75,77, Fisher 0,02).

As a result of stepwise discriminant function analysis and logit regression the prognostic rule for disability outcome after PedAIS has been created: $Z = 0,381 - 0,0214 * \text{FGB:-455G>A} + 1,09 * \text{F2:20210G>A} - 0,99 * \text{F5:1691G>A} + 0,228 * \text{F7:10976G>A} - 0,704 * \text{F13:103 G>T} - 0,116 * \text{ITGA2:807C>T} + 0,569 * \text{ITGB3:1565T>C} - 0,126 * \text{PAI-1:-675 5G>4G} + 0,172 * \text{MTR:2756A>G} - 0,381 * \text{MTRR:66A>G} + 0,471 * \text{MTHFR:677C>T} + 0,286 * \text{MTHFR:1298A>C} - 0,0665 * \text{StrokeAge}$. Each variable of 12 genes could take 3 values: 0, 1, 2 - depending on the number of SNP (not wild) alleles; "StrokeAge" takes the value of the number of full years old when stroke occurred. If the summation obtained a positive (greater than zero) result, disability is predicted, negative (less than zero) – absence of disability. Sensitivity and specificity for the training set rules has amounted to 0.73 and 0.55, accordingly.

Conclusion: Disability has a close relationship with the number of 12 detected procoagulant and prothrombotic genes' SNPs. There are no clear genes which inevitably lead to disability after PedAIS in children, but we consider that evaluating the number and the condition of those thrombophilic genes and genes of folic acid enzymes seems to be good applicants to become such genes-candidates combinations.

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GFAP and UCH-L1 As Predictors of Outcome in Mild and Moderate Traumatic Brain Injury

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Objectives: To correlate the levels of glial fibrillary acidic protein (GFAP) and ubiquitin C-terminal hydrolase-L1 (UCH-L1) in patients with computed tomography (CT) positive and CT-negative mild and moderate traumatic brain injury (TBI) with outcome during the first three post-injury days.

Methods: 191 patients with mild or moderate TBI [Glasgow Coma Scale (GCS) ≥ 9] having the blood samples for GFAP and UCH-L1 available on the day of arrival or day 1 were included in this study. In some patients, also day 2 and day 3 samples were available, and these were included in the analyses. Patients with TBI were divided into CT-positive and CT-negative groups based on Marshall classification. Glasgow Outcome Scale (GOS) or its extended version (GOSE) was used to assess the outcome. Outcomes were defined as, full: GOSE 8 or GOS 5, incomplete: GOSE < 8 or GOS 1-4; favorable: GOSE 5-8, unfavorable: GOSE 1-4; good: GOSE 7-8, and compromised recovery: GOSE 1-6.

Results: Patients with full recovery had significantly ($p=0.030$) lower GFAP levels on day 1 compared with patients with incomplete recovery. The levels of GFAP and UCH-L1 were significantly lower in patients with favorable recovery on arrival day, day 1 and day 2 than in patients with unfavorable recovery ($p=0.014$, $p<0.001$, $p=0.026$ and $p=0.008$, $p=0.020$, $p=0.039$, respectively). Patients with good recovery had significantly lower levels of GFAP and UCH-L1 on arrival day and day 1 and 2 than in patients with compromised recovery ($p=0.015$, $p=0.001$ and $p=0.019$, $p=0.039$, respectively). For predicting favorable recovery, the area under the receiver operating characteristic (ROC) curve for GFAP 0.676, 0.718, 0.643 and for UCH-L1 0.691, 0.637, 0.633 on arrival day, day 1 and day 2, respectively. The biomarkers predicted good recovery on day 1 with the area under ROC curve for GFAP 0.680 and for UCH-L1 0.622. In a multivariate logistic regression model including age, GCS, and posttraumatic amnesia, UCH-L1 on day 1 was an independent predictor for full recovery.

Conclusion: GFAP and UCH-L1 are significantly correlated with the outcome in patients with mild and moderate TBI. UCH-L1 at day 1 has a significant predictive value in mild and moderate TBI also in a multivariate model.

Keywords: 1) traumatic brain injury, 2) GFAP, 3) UCH-L1, 4) biomarker, 5) outcome

White Matter Alterations in Acute/sub-acute Stage after Mild Traumatic Brain Injury

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Objective: To investigate brain white matter alterations in patients with mild traumatic brain injury (mTBI) in acute/sub-acute stage compared to healthy controls using diffusion tensor imaging (DTI).

Methods: Diffusion-weighted (DW) magnetic resonance imaging (MRI) was performed on 86 patients with mTBI (GCS \geq 13) aged 47 ± 20 years within two months post-injury (22 ± 15 days) (acute/sub-acute). In addition, 30 controls aged 50 ± 20 years were scanned for comparison. DW MRI images were acquired using Magnetom Verio 3T (Siemens Healthcare, Erlangen, Germany) in 64 directions and with a b-value of 1000 s mm^{-2} . Images were then analyzed using tract based spatial statistics (TBSS) voxel-wise method in FMRIB Software Library (FSL). Fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD) and radial diffusivity RD were calculated along the white matter skeleton. Statistical analysis was performed using age as a covariate with randomise tool in FSL, and 5000 permutations were performed using threshold-free cluster enhancement and corrected for multiple comparisons using family-wise error rate (FWE). Statistically significant ($p < 0.05$) clusters with more than 10 voxels are examined in more detail in this study. JHU DTI-based white matter atlas was used to define studied brain regions.

Results: FA was found to be significantly lower (FWE-corrected $p < 0.05$) in patients with mTBI at the acute/sub-acute stage compared to controls in many white matter regions: body of corpus callosum (CC), left (L) superior longitudinal fasciculus (SLF), right (R) SLF, anterior limb of internal capsule R, posterior thalamic radiation L, sagittal stratum L, anterior corona radiata (CR) L, anterior CR R, posterior CR L, external capsule R. MD was higher in anterior CR R, SLF L, cerebral peduncle R, fornix, posterior CR R, posterior CR L, sagittal stratum L, posterior limb of internal capsule R, SLF R, superior CR R, superior CR L, cingulum L. Additionally, patients showed higher AD values only in anterior CR R and higher RD in anterior CR R, sagittal stratum R, SLF R, splenium of CC, posterior limb of internal capsule R, sagittal stratum L, external capsule R, fornix, posterior CR R, SLF L, superior CR L, cingulum L, anterior limb of internal capsule L, body of CC, posterior thalamic radiation L, uncinate fasciculus R.

Conclusion: mTBI is associated with widespread white matter alterations in acute/sub-acute stage and patients have significantly lower FA and higher MD, and RD values in several white matter regions compared to controls.

Disorders of Visual Orienting in a Social Context in Premature Children

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Brain injury in premature infants can cause the serious problems in brain and neurocognitive development [Anderson & Doyle, 2008; Inder et al., 2005]. However, the impact of prematurity on the neurocognitive abilities during early stages of development is not investigated thoroughly.

The aim of the study was to investigate the influence of prematurity on development of communication skills related to gaze following behavior in infants.

Participants and methods.

Totally 65 infants aged 5-11 months were participated in this study - 31 preterm infants and 34 full-term infants, who were born in gestation period from 37 to 42 weeks. Participants in experimental group were born in gestation period from 27 to 35 weeks (mean gestational age - $31,86 \pm 2,38$). Infants in both groups were matched by sex and age. Data recorded with eye-tracking were taken for statistical analyses if the eye-tracker was calibrated correctly for participant. Finally we have chosen 18 infants for experimental and 16 infants for control group.

Each trial was divided in four phases: 1- the model sits, looking down; 2- the model is looking straight ahead; 3 – the model is shifting her gaze to the toy; 4 – the residual time. The number of valid trials, the percentage of performed trials, fixation duration (ms) on relevant and irrelevant stimulus, fixation duration (ms) on the model's face were analyzed for each participant.

Results: ANOVA was used to evaluate the influence of prematurity on different parameters of oculomotor behavior. The statistically significant difference between groups in the number of performed trials was found ($p=0,015$). Participants from control group shifted their gaze to the relevant toy in a larger percentage of trials (70%) then participants from the experimental group (49%). The difference in fixation duration on the relevant object during the fourth phase was also obtained ($p=0,007$). The average value of this parameter was 631,96 ms in the full-term, whereas the average fixation duration in children with prematurity was 276,45 ms. There were no significant differences between groups in fixation duration on irrelevant object in this study. There were also no differences in average fixation duration on the model's face during the second phase of the presentation.

This result is consistent with studies that have shown delayed maturation and atypical variants of visual orienting in a social context in children with prematurity [DeSchuymeretal, 2012; Telfordetal, 2016; Imafukuetal, 2016].

Conclusion: This eye-tracking study has shown that premature infants have lower level of gaze following behavior than infants from control group. Received results may indicate that prematurity is a risk factor for disorders of visual orienting in a social context.

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Organized Neurosurgical Care in Ontario

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Intended Level of Audience: All participants

Intended Subspecialty: Neurosurgery/Critical Care

Purpose: The purpose of this paper is to identify the role and responsibilities of the Neurosurgical members within Neurosurgical Education Outreach Network (NEON). Identify the scope of practice of NEON members including the Educator and the Clinical Outreach Nurse.

NEON roles: Neurosurgery Nurse Educators (NNEs) were established in Ontario's 11 adult neurosurgery centres in January 2011 to support the management of the specialized neurosurgical patients. The role of the NNE involves developing and delivering educational material for community hospitals within the LHINs (Local Hospital Integrated network) they serve. They address the needs of the neurosurgical patient throughout the entire continuum of care and provide support and education as required. NNEs can be a great resource for community hospitals they can help mitigate knowledge gaps and identify priorities for neurosurgical educational needs.

NEON roles: Clinical Outreach Nurse (Clinical Nurse Specialist or Advanced Practice Practitioner) has the responsibility to improve patient neurosurgical care at the community hospitals within their region.

Together these two roles will work together to expedite timely access to specialized neurosurgical services and assist with repatriation and transfer across the continuum of care developing tools and providing education to enhance the care of the neurosurgical patient. The two roles will provide expertise in neurosurgical care to aid in access to beds and repatriation including patient care plans, development of protocols and care practice and participate in quality improvement initiatives related to the Neurosurgical population.

Increasing demand for neurosurgical services across Ontario (Neurosurgery Ontario, 2011) is changing the way we provide care. This abstract will describe how neurosurgical centres are bringing specialty care to non-neurosurgical sites throughout Ontario.

The Neurosurgical Outreach Program was established by Critical Care Services Ontario, Provincial Neurosurgery Ontario and Ministry of Health and Long Term Care in 2011. Two roles were developed to support this Program, the Neurosurgical Nurse Educator (NNE) and the Clinical Outreach Role.

Developed in 2015, the Neurosurgical Education Outreach Network (NEON) is comprised of educators, outreach nurses, and administrators. NEON is responsible to increase knowledge and expertise, support equitable and timely access to neurosurgical care, and help maintain the province's neurosurgical capacity. NEON has developed many educational tools provincially and regionally including assessment guidelines for the Neurosurgical population. These tools, in conjunction with outreach activities, are used to improve the healthcare provider's knowledge and skills when assessing and caring for patients. NEON also support real-time decision making by healthcare providers to ensure timely access to neurosurgical care.

A Systematic Review of the Usefulness of Glial Fibrillary Acidic Protein (GFAP) for Predicting Acute Intracranial Lesions following Head Trauma

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Objectives: The extensive use of computed tomography (CT) in acute head injury management has caused concerns in relation to health care costs and cancer risk. Blood-based biomarkers may predict which patients will have acute intracranial abnormalities, thus reducing unnecessary head CT scanning. We conducted a systematic review of the usefulness of glial fibrillary acidic protein (GFAP) for predicting acute CT-positive intracranial lesions following head trauma.

Methods: In this systematic review, we screened MEDLINE, EMBASE, PsychInfo, CINAHL, Web of Science, the Cochrane Database, Scopus, Clinical Trials, OpenGrey, Research Gate, and the reference lists of eligible publications for original contributions published between January 1, 1980, and October 12, 2016. Eligibility criteria included: (i) population: human head and brain injuries of all severities and age groups; (ii) intervention: blood-based GFAP measurement ≤ 24 hours post injury; and (iii) outcome: acute traumatic lesion on non-contrast head CT ≤ 24 hours post injury. Three authors completed the publication screening, data extraction, and quality assessment of eligible articles. The review was registered with PROSPERO and adhered to the PRISMA guidelines. The scientific quality of each article was evaluated with the Newcastle-Ottawa Scale (NOS). The level of evidence was rated according to the Oxford Center of Evidence-based Medicine (CEBM) and GRADE rankings.

Results: The initial search identified 2,394 articles, and 49 were eligible for full-text assessment. Twenty-three full-text articles were excluded because of the following reasons: (i) study population consisted of non-TBI patients (n=4), (ii) no blood-based GFAP sampling (n=3), (iii) no CT data available (n=6), (iv) autopsy or animal study (n=2), (v) editorial (n=1), and (vi) no GFAP-CT analyses included (n=7). A total of 26 articles (all case-control and cohort studies, 4 pediatric studies) were included in the review. The 26 studies included 3,354 TBI patients and 1,533 controls (blood donors, non-TBI trauma patients, and healthy volunteers). Twenty-two (n=22, 85%) studies reported a positive association between GFAP level and head CT trauma lesions. The area under the receiver operating curves were 0.79-0.98 for GFAP to identify CT-positive cases. In four studies, a GFAP cut-off value (range=0-0.2 ng/mL) with a 100% sensitivity for CT-positivity was established. Based on Marshall grading, which was the most common CT head trauma scoring system employed, GFAP seemed to discriminate mass lesions and diffuse injury, with mass lesions having significantly higher GFAP levels. There was considerable variability on the measured GFAP averages between studies and assays (i.e., CT-positive TBIs: range=0.1-2.9 ng/mL and non-trauma controls: range=0-0.3). The average NOS was 4 and CEMB 4. The GRADE score was: "very low".

Conclusions: Intracranial CT-positive trauma lesions were consistently associated with blood-based GFAP levels. Methodological heterogeneity and limitations hinder the level of evidence. However, GFAP holds promise to reduce unnecessary head CT scanning in head trauma.

Postdeployment Prevalence of TBI, PTSD, and Chronic Pain Among OEF/OIF Soldiers Who Utilized Care in the Veterans Affairs Polytrauma/TBI System of Care

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Background: The Department of Veterans Affairs' (VA) Polytrauma/TBI System of Care (PSC) is designed to provide integrated, coordinated rehabilitation services for both Veterans and military members with combat and civilian-related polytrauma (i.e., injuries to multiple body parts and organ systems). Combat-related polytrauma often includes traumatic brain injury (TBI), chronic pain, and psychological health problems such as posttraumatic stress – referred to as the polytrauma clinical triad.

Methods: We conducted a retrospective analysis of soldiers returning from Operation Enduring Freedom or Operation Iraqi Freedom (OEF/OIF) in FYs 2008-11 as a part of the Substance Use and Psychological Injury Combat Study – Pain Management (SUPIC-PM; N=643,205). We determined the proportion of these soldiers who utilized care in the PSC within 12 months after returning from an OEF/OIF deployment by examining VA PSC stop codes for inpatient bed section and outpatient clinic. Among soldiers who used the PSC, we described their demographic characteristics and military history using Military Health System enrollment and Contingency Tracking System deployment records. We utilized VA ICD-9 diagnosis codes to identify the prevalence and co-prevalence of conditions (TBI, posttraumatic stress disorder (PTSD), and chronic pain). Chronic pain was defined as having 2+ pain diagnoses from the same category (e.g., back and neck, headache/migraine) at least three months apart within the postdeployment year. This paper will present findings of opioid utilization and complementary and integrative medicine treatments among this PSC population by condition sub-groups.

Results: Among soldiers returning from deployment, 1.8% (n=11,743) utilized care within the PSC during the postdeployment year. The majority were male (92.6%), white (70.2%), with an average age of 32. A disproportionate share were from the Guard (58.0%), with 25.8% Active Duty and 16.1% Reserve. More than half were junior enlisted (55.1%). More than half (53.5%) were returning from their first deployment. VA data showed that during the postdeployment year, 47.1% were diagnosed with TBI, 49.4% were diagnosed with PTSD, and 66.7% had chronic pain. Among the co-prevalence of these three conditions, the polytrauma clinical triad was the most common (23.1%), followed by chronic pain only (17.0%). Approximately 14% had PTSD and chronic pain only, and more than 12% had TBI and chronic pain only. As expected, few soldiers had TBI only (5.9%), PTSD only (6.4%), or PTSD and TBI without chronic pain (5.7%). Among those with chronic pain, the most common non-mutually exclusive pain conditions were back/neck pain (60.1%), non-traumatic joint pain (56.1%), headache/migraine (50.7%), and musculoskeletal pain (50.0%).

Conclusions: A disproportionate share of those utilizing the VA's PSC were Guard members and the clinical triad was present in about one-quarter of the utilizers. Chronic pain was the most common condition highlighting the importance of incorporating integrated pain management treatment modalities that best support the health of soldiers with polytrauma into the PSC.

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Prevalence and Correlates of Unemployment among Iraq and Afghanistan War Veterans with Deployment-related TBI History Enrolled in the Veterans Health Administration

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Objectives: Over 20,000 Iraq and Afghanistan War Veterans with traumatic brain injury (TBI) use Veterans Health Administration (VHA) healthcare each year. Research has shown relatively high unemployment rates among civilians with TBI, but little is known about unemployment among recent war Veterans with TBI, particularly those receiving VHA care. The purpose of this study was to estimate the prevalence and correlates of unemployment in this population.

Methods: We conducted a mailed survey of 1,800 randomly-sampled Iraq and Afghanistan War Veterans with clinician-confirmed, deployment-related TBI who used VHA care. Veterans with moderate/severe TBI were oversampled. Surveys asked Veterans about their employment and job-seeking status, and select demographic, health, and financial characteristics. VHA databases were also used to identify Veterans' demographics, TBI severity, and healthcare utilization. We estimated the prevalence of unemployment by Veterans' TBI severity and examined Veterans' characteristics associated with unemployment and job seeking status. Multivariable and multinomial logistic regression models were used to compute adjusted odds ratios (aORs) and 95% confidence intervals (CIs) while controlling for age, sex, race, and service connection (disability) status. Results were weighted to account for oversampling of Veterans with moderate/severe TBI and to adjust for potential non-response bias.

Results: Among 616 Veterans with TBI who completed the survey, 389 (63%) had mild TBI and 227 (37%) had moderate/severe TBI history. Nearly half (45%) reported being unemployed at the time of the survey (43% mild TBI; 52% moderate/severe TBI). Among all unemployed Veterans with TBI, 31% were actively looking for work. The most frequent reasons unemployed Veterans with TBI reported for not looking for work were illness/injury/disability (55%); school (26%); retirement (16%); and caregiving (7%). Compared to employed Veterans with TBI, those who were unemployed/not looking for work were more likely to have moderate/severe TBI (aOR=1.5; 95% CI: 1.0-2.3); comorbid diagnoses for posttraumatic stress disorder (PTSD; aOR=2.4; 95% CI: 1.2-4.5), depression (aOR=2.0; 95% CI: 1.3-3.2), or substance use disorder (SUD; aOR=2.4; 95% CI: 1.5-3.7); high levels of anger (aOR=2.9; 95% CI: 1.8-4.9); and annual household incomes \leq \$25,000 (versus $>$ \$25,000; aOR=2.0; 95% CI: 1.1-3.6). Veterans who were unemployed but looking for work were also more likely to have diagnosed PTSD, depression, or SUD, and annual household incomes \leq \$25,000. Additionally, they were more likely to be unmarried (aOR=3.7; 95% CI: 2.1-6.7); living at or below federal poverty level (aOR=2.7; 95% CI: 1.2-6.1); and experiencing financial difficulty (aOR=3.2; 95% CI: 1.9-5.7).

Conclusion: The prevalence of unemployment among VHA-enrolled, Iraq and Afghanistan War Veterans with TBI was high; only one-third were actively looking for work. Mental health-related diagnoses were related to unemployment status, while financial characteristics appeared to drive employment-seeking

status. These factors may serve as indicators of need for vocational rehabilitation services among Veterans with TBI.

Concussion and Return to School: Evaluating A Group Model of Intervention for Secondary and Post Secondary Students with Persistent Post-Concussion Symptoms

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Background: Current research efforts have focused on guidelines for post-concussion return to play/work/learn, and yet there remains relatively little literature that focuses on specific treatment methods.

Hypothesis: This study proposes that a 7-week group intervention will improve self-reported symptom scores.

Methods: Participants (n = 71; 45 females, 26 males) were provided with treatment and novel strategies in reading, writing, study skills, social communication and technology use. Self-assessment of symptoms was obtained weekly, both before and after each session of the treatment program, in an effort to monitor the cognitive demand of each session, and to identify the extent to which the program produced an improvement over the course of seven weeks.

Results: Symptoms were transiently exacerbated by treatment, $F(1, 343) = 255.69, p < .05$, within each week of the program, but overall, the treatment was found to be effective, $F(6, 343) = 2.29, p < .05$. Post-hoc analysis of means (using Tukey's HSD) suggests that there was a significant improvement ($\alpha = 0.05$) of self-reported symptoms when comparing weeks 1 and 6, and between weeks 1 and 7.

Conclusions: Transient exacerbation of symptoms aside, the 7 week Return to School (RTS) Group treatment model produced a statistically significant benefit in patients' reporting of their persistent concussion symptoms pre to post participation in the Group series.

Late Seizures in mTBI: A Prospective Study

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Objective: Persistent symptomatic mild traumatic brain Injury (mTBI) is a focal disease process. Almost 80% for the patients have spontaneous resolution after mTBI, but 5 to 10 % who have persistent mTBI disease presented to our clinic with persistent symptoms. The study was conducted on this group of patients with symptoms after mTBI for more than one month. Abnormal EEG results increase with persistent symptoms as the focal abnormalities increase due underlying focal shear brain cell injury. To study predictor of late complications of seizure after episodes mTBI.

Method: A perspective study of patients who presented to a TBI clinic for 5 years. On initial visit after neurological evaluation and detail questioning about the history of the mTBI and possible seizure semiology with strict inclusion criteria, a Montreal Cognitive Assessment (MoCA) was administered to patients. Following neurological evaluation, a one-hour routine EEG as a standard protocol was performed after 4 weeks of the mTBI.

Results: 202 patients presented and followed over 3 years after mTBI, 105 females:97 males, an average age of 42 years. Total 14 patients (6.9%) had seizures and 12 (5.9 %) late seizures with average time of 22 months. 8/14 (57%) patients experienced complex-partial seizures and 6/14 (42%) encountered partial seizures episodes. 11/14 (78%) had recurrent seizure episodes while 3 patients had single episodes. 111/202 (55%) experienced transient LOC and 35/202 (12.4%) patients had abnormal focal EEG reports. 24/35 (68.6%) patients had an abnormal EEG and LOC. 12/14 (85.7%) patients had abnormal EEG results in predominantly frontal and temporal lobes, but only 10/14 (71.4%) of those also had LOC. On further analysis LOC has a relative risk of 81.8% for future seizure episodes. Abnormal EEG is 37.14% directly correlated with seizures and 20.12% related with memory loss. $p < 0.0392$. LOC is 5.35% related with Memory Loss. $P < 0.0412$. Since the relative risk is 6.15, the patients who experienced seizures after the mTBI were six times more likely to have an abnormal EEG than those who did not experience any seizures. The sensitivity of the EEG at discovering abnormal brain wave-like activity was 85.7% with LOC group.

Conclusion: We do not have any standard protocol for recommendation and follow up after mTBI and to determine the late risk of seizure. From our study loss of consciousness, abnormal EEG and memory loss are directly correlated with each other after mTBI and the abnormal EEG will increase the risk of late seizure in mTBI patients. Persistent symptomatic mTBI needs further testing with EEG to define future risk of seizure or increase risk of memory loss. The late risk of seizure after mTBI from this study was 6.9% and had an onset up to 6 years.

[18F]T807/AV-1451 (flortaucipir) Imaging in Athletes with Post-Concussive Syndromes Including Clinically Probable CTE: Prominence of Psychiatric Clinical Symptoms and Implications for Experimental Therapy

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Chronic post-concussive syndromes are a major source of morbidity and mortality across the lifespan. Methods of assessment and prediction of outcome are major areas of research focus on (1) cognitive, behavioral and emotional assessment; (2) non-cognitive physiology; (3) structural neuroimaging; and (4) measurement of brain-specific proteins in blood following damage to brain and blood-brain barrier, among others. Functional and molecular neuroimaging provide other modalities for noninvasive investigation. Traditionally, imaging has included functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) with [18F]fluorodeoxyglucose. The advent of molecular neuroimaging (i.e., application of ligands that are retained by structural neuropathological lesions such as plaques, tangles, or activated microglia) has led to new insights into the antemortem biomarker support of post-concussive neurodegenerative diagnoses. Among these, the best characterized is chronic traumatic encephalopathy (CTE), a neurodegenerative condition associated with repetitive mild traumatic brain injuries (mTBI) that occur in high-impact collision sports like football, hockey, soccer, and boxing. Pathologically, CTE is characterized by the presence of hyperphosphorylated tau in neurofibrillary deposits. While the rising awareness of mTBI and CTE has galvanized research into the mechanisms and pathology by which mTBI leads to CTE, how to confirm the clinical diagnosis in living persons remains an issue. Advances have been made in diagnosing CTE using the [18F]T807 tau PET tracer that binds to aggregated tau. Our goal in the present study was to examine [18F]T807 uptake in athletes with mTBI resulting from multiple concussions. Out of the twenty-four athletes enrolled, eight have abnormal [18F]T807 ligand retention. None retained [18F]florbetapir, the fibrillary amyloid ligand. While the amount of ligand retention varied, the pattern of tau distribution resembles that observed postmortem in CTE, namely at the white matter-grey matter junction. Our data also show a high frequency of positive tau scans in clinically probable CTE while mostly negative in less severe post concussive states. Our experience also leads us to propose modification of the general awareness of the clinical syndrome associated with CTE. As a tauopathy, CTE is recognized as a dementing disorder and there is growing recognition of behavioral and emotional symptoms often early, across the spectrum of dementing conditions including in Alzheimer's disease. In CTE the presenting symptoms are often irritability, anger, dyscontrol and depression. These behavioral features are present when little or no cognitive decline can be detected. Our study of in vivo PET imaging of tauopathy deposition in the brains of retired athletes can provide insight into the pathogenesis, diagnosis, and potential treatment of tauopathies such as CTE. Whether tauopathy PET imaging can provide useful diagnostic or prognostic screening information and/or clinically important outcome measures for anti-tauopathy therapies, such as tauopathy-reducing interventions, are major questions for the future.

Risk of Depression following mTBI

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Background: Depression is well studied in Traumatic Brain Injury (TBI) but there is scarce data on single episode mTBI with depression and prognosis is clouded by umbrella diagnosis of the postconcussion syndrome. There is no predictor other than well-defined risk of depression with previous history of depression. Lack of follow up with mTBI patients, leaves many at risk for developing post-mTBI depression without proper monitoring.

Method: A retrospective analysis of 174 mTBI patients (87 females and 87 males) presenting at a headache and TBI clinic over a four year was conducted. The criteria for inclusion in this study was a diagnosis of mTBI, with normal radiological findings and persistent physical and emotional symptoms. Participants ranged in age from 14 to 84 years (M = 43.92). Analysis was done to determine risk of depression, post-mTBI, using the Patient Health Questionnaire (PHQ-9). The PHQ-9 scores of 5, 10, 15, and 20 represent mild, moderate, moderately severe, and severe depression, respectively.

Results: Taking into account prior diagnoses of depression, it was found that females developed a two-fold prevalence of depression as compared to males. In addition, it was found that those who had a prior diagnosis of depression (N=105), had a statistically higher PHQ-9 score than those who had not been previously diagnosed (N=69). An independent-samples t-test was conducted to compare the PHQ-9 scores in mTBI patients with depression and mTBI non-depressed conditions. There was a significant difference in the scores for patients with a previous diagnosis of depression (M = 14.981, SD = 5.77) and patients with no previous diagnosis of depression (M = 11.387, SD = 7.52) conditions; $t(127) = -2.943$, $p = .004$. Temporal correlation was established into groups based on the length of time in new onset depression after mTBI ; it was found that incidence of depressive symptoms increased with time since mTBI. In patients with no prior diagnosis before mTBI, it was also found that having an mTBI increased the risk of developing moderate to severe depression was at 25.90% at 3 months.

Discussion: Routine follow-up visits on mTBI patients 2 and 4 weeks post-mTBI, in addition to constant vigilance for the emergence of new symptoms of cognitive impairment and depression disorders and early intervention, are not well adapted in clinical practice. This current study supports the need to monitor the patient following mTBI due to the increased risk of developing depression as time progresses independent of diagnosis of post concussion syndrome.

Conclusion: The results of this study support the need for re-evaluation of current guidelines for psychological monitoring following mTBI. The increased risk of depression as time passes is a serious health issue that should be carefully monitored and prevented in patients with mTBI.

A Large-Scale Study of Brain Injury Survivors Undergoing Technology-Based Cognitive Rehabilitation Shows Potential for Improvement Regardless of Severity

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Objective: Advances in technology has provided a unique opportunity to facilitate rehabilitation in TBI individuals. This project examined the effectiveness of cognitive rehabilitation in adults with TBI to understand factors that predict outcomes.

Methods: 219 patients with TBI, all of whom presented with language/cognitive disorders used a mobile therapy platform, Constant Therapy, which includes over 60 evidence-based tasks. Patients used the program in the clinic with clinicians, at home as homework, and independently if they were not currently receiving therapy. Therapy was designed and administered in a uniform way, but also individualized in that patients were assigned tasks that addressed their individual strengths and weaknesses and dynamically adapted to each individual's progress.

Analysis: Based on an initial baseline assessment, a given task was assigned to a patient if performance was below 90% accuracy and average latency. To account for familiarity effects, the first 3 items of each task were ignored for each individual, and accuracy and latency of the first and last 10 items were compared using a paired T- test. Thus, patients' data were analyzed in case-mix adjusted way controlling for intensity of practice and initial severity to determine which types of patients improved after rehabilitation.

Results: Across patients, problem solving (29%), reading (16%), auditory processing (13%), naming (12.5%), and visual processing (12.4%) comprised the main rehabilitation domains completed. ANOVAs using accuracy and latency as the dependent measures and initial performance (binned from 0-40%, 40-50%, 50-60%, until 80-90%) and the aforementioned domains (and others) showed a significant interaction effect ($F(52, 1077) = 3.8, p < .0001$) indicating that more severe patients (starting accuracy at 0-40%, 40-50%) showed gains (~30-40 points) on targeted domains. Analysis of the interaction between initial severity and intensity of practice was also significant ($F(23, 1077) = 7.24, p < .0001$), indicating that more severe patients improved with increased practice (100 - 1000 trials); and patients with initial accuracy less than 50% could achieve mastery (>80% accuracy with practice of 100 trials or more ($F(23, 1077) = 8.49, p < .0001$)). Importantly, analysis of speed revealed that while severe patients made gains in speed with increased practice, mildly impaired patients (initial accuracy 70-90%) also improved ($F(23, 1077) = 2.5, p < .0001$).

Discussion and Conclusions: To our knowledge, this is the first large scale examination of rehabilitation for patients TBI and show that patients can make strong gains in cognitive and language skills following repeated practice of therapy items. Notably, while all patients show improvements, the severe patients (starting accuracy < 50%) show robust gains across domains with increased practice. Mildly impaired patients also show gains in speed of processing across language/cognitive domains. Ongoing analysis is identifying other prognosticators of outcome.

Relationship of Mental Healthcare Utilization and Suicidal Behaviors and Ideation at 1-Year Post Traumatic Brain Injury (TBI): A VA TBI Model Systems Study (VA TBIMS)

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Objective: To characterize suicide-related ideation and attempts, as well as pre- and post-traumatic brain injury (TBI) mental health utilization among a cohort of individuals who received care within the Department of Veterans Affairs (VA) Polytrauma Rehabilitation Centers (VA PRCs).

Setting: Inpatient VA PRCs facilities.

Participants: VA TBI Model Systems participants enrolled within one-year of TBI and eligible for a one-year, post-injury follow-up (N=284).

Design: Descriptive, prospective observational cohort study.

Main Outcome Measures: Self-reported suicide-related ideation from the Patient Health Questionnaire (PHQ-9) ("Bothered by thoughts that you would be better off dead" in the past two weeks), and suicide attempts between discharge and the 1-year follow-up evaluation.

Results: At the one-year post-TBI evaluation, 13% (N=37) of Veterans and Service Members reported suicide-related thoughts of varying frequency in the previous two weeks: "several days (11%)", "more than half the days (1%)" or "nearly every day (1%)". In addition, eight individuals endorsed a history of a suicide attempt (3%) within the initial year post-TBI. Of those attempting suicide, only one participant had attempted suicide prior to sustaining the TBI. Three of these individuals had mental health treatment over the course of their lifetime (none in the year prior to TBI). All participants who attempted suicide during the time period of interest, received mental health treatment post-TBI primarily for depression (N=8; 100%) or PTSD (N=5; 65%), and a majority (N=7, 88%) reported no suicidal ideation on the PHQ-9 in the two weeks prior to one-year follow-up. Among those not attempting suicide (N=276) during the one-year follow-up period, 88% had a lifetime history of mental health treatment (55% in the year prior to TBI; 53% in the year post-TBI)

Conclusions: Findings suggest that members of this cohort are endorsing concerning levels of suicide-related ideation and attempts. Increased implementation of suicide-prevention strategies pre- and post-discharge is warranted.

Keywords: Suicide attempt, traumatic brain injury, mental health, Veterans

Functional and Cerebral Metabolites Evaluation of Single Episode mTBI with MRS and DTI

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Background: Traumatic Brain Injuries (TBI) are widespread and well documented. However, impact a single episode mTBI has been under-diagnosed, with symptoms and underlying microscopic injuries being ignored. Studies with functional Magnetic Resonance Imaging (fMRI), Diffusion Tensor Imaging (DTI) and reconstruction software are becoming more popular in mTBI diagnoses. These methods have proven problematic and their use as a diagnostic tool for mTBI has been called into question.

Methods: Retrospective study on 250 mTBI patients was conducted in TBI clinic over last 4 years. 160 patients were given WMS-IV standardized test after scoring <26 on MoCA cognitive screening. fMRI/DTI tests were performed within average of 22 months after initial mTBI. 31 patients were further tested with fMRI, SWAN, Flair and DTI with Fractional Anisotropy (FA) on white matter (WM), and the cortical thickness was measured in grey matter (GM) with color representation. Magnetic Resonance Spectroscopy (MRS) was done on bilateral frontal lobe and posterior cingulate consistently in all patients, if decreased cortical thickness was observed with neuronal loss. We identified subject-specific regions of abnormally high and low FA, axial diffusivity (AD), radial diffusivity (RD), and mean diffusivity (MD) across all white matter voxels and several WM regions.

Results: The decrease cortical thickness in Left Frontal Lobe (LFL) and RFL 89% (26/29) patients had MRS with decreased NAA, increased choline and myo-inositol were compared WM tract low FA. Corpus Callosum (CC) WM DTI with decrease FA is 83.33% correlated with LFL GM MRS. Similarly CC is 95% related with RFL with p value<0.05. (23/29) 79% of lesions in the CC, Hippocampus, and SLF are well published in DTI literature as characteristic of mTBI. Immediate and Delayed Memory index is 36.79% related with Rt. Temporal lesion. Decrease probability of Attention Score is 61.25% related with RLF and 64.51% with CC with P value< 0.039. Executive Functioning probability of low score is 100% related with LFL and 82.6% with RFL with P value<0.05.

Conclusion: There was no statistical difference between the areas tested by MRS in GM and DTI on WM, but they compliment each other by detecting the lesions in the same patients in two different places. These tests can be used simultaneously to increase the predictive value. The MRS study with cerebral metabolites changes were seen at an average of 22 months, which was a longer interval than prior studies. WMS-IV findings of delayed recall and executive functioning are hallmarks of TBI and confirm disruptions in the memory circuit pathway. fMRI/DTI study further support the memory loss in patients with cognitive deficits on WMS IV battery. There is a direct correlation between single-incident mTBI to underlying cerebral lesions and cognitive deficits. Strong correlations seen secondary to patient selection, after low WMS-IV scores.

Machine Learning Models Including Biomarkers, Age and Sex Identify Brain-Injured Patients with Greater Accuracy: Results from the HeadSMART Trial

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Head injury brings nearly 5 million patients into emergency departments per year in the US. While many receive a CT scan, only a small percentage show structural evidence of injury. Our purpose was to identify serum biomarkers that objectively identify patients with traumatic brain injury. The HeadSMART prospective clinical trial was conducted at Johns Hopkins University School of Medicine. A total of 500 brain injured patients were enrolled, along with 160 control subjects. Additional healthy control subjects (n=250) were recruited from Baylor College of Medicine. Previously we have reported on preliminary results from HeadSMART in which biomarker panels were shown to accurately predict TBI in objective blood tests. The current analyses present more comprehensive biomarker data analysis across the complete HeadSMART mild TBI cohort and control subjects. Of 8 biomarkers examined, Neurogranin (NRGN), Brain-derived Neurotrophic Factor (BDNF), and Synuclein beta (SNCB) were chosen for superior performance by ROC analysis in and using univariate statistics in distinguishing TBI from healthy control subjects ($p < 0.001$). Serum samples were tested in colorimetric or electroluminescence-based sandwich ELISA assays in all subjects. Extensive clinical data was collected for TBI patients, including functional and neurological outcomes at 1, 3, and 6 months post injury. Models for classification were built in R using logistic regression and in random forest to differentiate between healthy controls and in TBI patients meeting the American College of Rehabilitative Medicine diagnostic criteria (ACRM+). Model performance for single biomarkers and in combinations were compared using ROC curve analysis, minimizing overfitting using extensive cross-validation. To adjust for any imbalances in age and sex between the cohorts, the models were also built using biomarkers with patient age and sex included, and the results compared. Combining biomarkers in panels was associated with an improved C-statistic, with the best performing panel including all 3 biomarkers, age, and sex (AUC= 0.97; Sens=0.986; Spec=0.913; NPV=0.970). The top performing panel built using random forest also outperformed models built in logistic regression. Panel performance was found to differ between male and female subjects, a phenomenon reported with cardiac biomarkers but never before described in TBI. Furthermore, methods were devised to examine stability of the models generated by these methods, providing a useful technique with which to evaluate the reproducibility of model-generated classifications, particularly of different panels of biomarkers that may have similar ROC curves statistics. These results identify a panel of three biomarkers that can accurately classify patients with TBI who may be CT negative or ACRM negative, but have significant injury. In addition, the methods developed further refine the evaluation of reliability in clinically relevant classification models built with machine learning techniques. These methods form the basis of ImmunArray's testing panels for objectively identifying brain injury irrespective of neuroimaging.

An Evaluation of the Effectiveness of Functional Electrical Stimulation (FES) to Improve Upper Limb function in Children with Hemiplegic Cerebral Palsy (HCP)

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Introduction: Functional electrical stimulation (FES) therapy involves the transcutaneous administration of electrical impulses to activate muscles and obtain functionally useful movement (1). FES of the upper limb (UL) has been used widely for patients with a variety of neurological conditions, including stroke, but few studies have been conducted on its use for children with hemiplegic cerebral palsy (HCP) (2). Prenatal or perinatal stroke is often the underlying mechanism of injury in children with HCP (3), it affects one UL, and often results in reduced selective motor control, weakness, decreased sensation, and spasticity. Motivated by a prior successful study showing that FES therapy can be effective at improving voluntary hand function in paediatric chronic stroke patients (1), the aim of this study was to evaluate the use of a new multichannel FES system for improving UL function as measured by the Quality of Upper Extremity Skills Test (QUEST) grasp score (and other secondary outcome measures) in children with HCP.

Method: Case studies of three children with HCP (aged 6 to 13 years; mean= 9; SD= 3.6) completed up to 48 FES therapy sessions (mean= 47.3; SD= 0.5), administered for 1 hour, 3 times per week, for 16 weeks. The study design involved a baseline, and a post-intervention assessment. Primary outcome measure: QUEST (grasp domain) score, which evaluates movement patterns and hand function of the affected UL. Secondary outcome measures: unimanual capacity (Jebsen–Taylor Test of Hand Function), functional goals (Canadian Occupational Performance Measure), bimanual performance (Children’s Hand-use Experience Questionnaire), spasticity (Australian Spasticity Assessment Scale), and different sensory modalities of UL function.

Results: Case 1 and Case 3 improved on the grasp component of the QUEST (>7 points). But, consistent improvement across all subcomponents was present only for Case 1, as demonstrated by the change in the overall score (15.4 points).

Only Case 2 had an improvement in ‘independent execution’ of CHEQ activities after the intervention (20.6%).

The COPM-Performance and COPM-Satisfaction for Case 1 showed a clinically significant increase of 3.7 and 2.1 points between baseline and post intervention, respectively. Proprioception accuracy increased for all three cases after FES therapy. The JTHFT total scores decreased for Case 1 and Case 2, implying improved movement efficiency and dexterity. Case 3 was unable to complete any of the JTHFT subtests within the maximum allowable time of 2 min.

Discussion and Conclusions: The pre–post differences in scores on most measures clearly demonstrated improvement in voluntary hand function following FES sessions for only one child. Interestingly all 3 children improved in proprioception and grip strength. A second follow-up assessment is planned to determine if any effects are maintained at 6 months post-FES to help guide the significance of the immediate gains observed post-intervention.

Development of Neurofilament Light chain (NF-L) Digital Immunoassay for Blood and Cerebral Spinal Fluid (CSF) Samples

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Neurofilament light chain (NF-L) has been shown to be a potential biomarker for traumatic brain injury. Recently ultrasensitive digital ELISA made it possible to measure NF-L in plasma or serum. Here we develop a fully automatic digital immunoassay to reliably measure NF-L in serum, plasma and CSF in both healthy and diseased individuals.

The assay reagents were designed to be used on Simoa HD-1 Analyzer. Conjugated capture beads and biotinylated detection antibody were prepared following homebrew protocol. During the assay, for first step, antibody coated capture beads, biotinylated antibody detector were incubated with calibrator/samples together. After wash, immunocomplex were labeled with enzyme and transferred to an array of microwells. A single labeled NF-L molecule provided sufficient fluorescence in 30 seconds to be detected. The concentration of NF-L is then interpolated from a calibration curve. The assay was evaluated for sensitivity, precision, linearity, spike/recovery etc. Acute Traumatic Brain Injury (TBI) and healthy control samples were evaluated for plasma NFL.

Limit of detection (2.5 SD) was 0.040pg/mL and limit of quantification was 0.171pg/mL. Recovery of NF-L spiked into human serum and plasma averaged 89.5%. Recovery of NF-L spiked into human CSF averaged 100.4%. Mean dilution linearity of spiked serums was 97.4%. Mean dilution linearity of CSF was 89.4%. Precision was determined using 3 native and spiked serum samples across 5 runs. Mean inter-assay and intra-assay CVs were 10.2% and 7.8% respectively. In normal healthy individuals (n=20), median [NFL] was 8.87 pg/mL (Range 2.68-15.4 pg/mL) and 7.57pg/mL (Range 3.23-16.0 pg/mL) in serum and EDTA plasma respectively. Median [NFL] in CSF was 2127 pg/mL (range 258-87559 pg/mL). Acute TBI plasma samples (n=30) had a much higher median [NFL] of 25.18 pg/mL (3.69-892.9 pg/mL).

The Simoa NF-L assay measured Neurofilament Light chain in plasma, serum and CSF samples reliably from both healthy and diseased individuals. Preliminary data suggest plasma NFL level is higher in acute TBI patients than healthy controls. This assay should facilitate the research and diagnostic development of NF-L related diseases, such as TBI and other disease.

Elevated Matrix Metalloproteinase-9 blood Levels after mTBI Decline Over 30 Days Post Injury

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Diagnosis and treatment of mild traumatic brain injury (mTBI) is challenging since there are no clinically validated biomarkers. We hypothesized that the blood brain barrier will be disrupted after mTBI and proteins will leak from the brain into the blood circulation. We studied nine proteins to represent different types of head injury: matrix metalloproteinase 9 (MMP-9) for blood brain barrier integrity; GLUT-1 for endothelial and vascular changes; S100 β and CKBB for astrocytic damage; NSE and UCHL1 for neuronal and astrocytic damage; GFAP for astrocyte integrity; FABP7, a modulator of astrocytic function; and FABPH for fatty acid transport. We developed an assay in which tryptic peptides unique to each protein were identified and standards containing stable isotope amino acids (¹³C, ¹⁵N) were synthesized. A known amount of the stable isotope standards were spiked into the plasma prior to enzyme digestion, and the mixture was analyzed by liquid chromatography mass spectrometry. We recruited 14 patients from the Emergency Department at Huntington Memorial Hospital after their diagnosis with mTBI, and 9 trauma controls without head injury, and collected blood on 3 visits over 30 days post-injury. The levels of peptides specific for MMP-9 increased in blood from mTBI study participants at their first visit (1-5 days post injury) that gradually returned to normal by their third visit (~30 days post injury) compared to controls ($P < 0.05$, Wilcoxon matched-pairs signed rank test). The other eight proteins were not detected in any samples. MMP-9 may be useful as a biomarker after mTBI. Funded by DoD W81XWH-13-1-0005.

Development of Glial Fibrillary Acidic Protein (GFAP) Digital Immunoassay for Blood and Cerebral Spinal Fluid (CSF) Samples

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Objectives: Glial Fibrillary Acidic Protein (GFAP) has been shown to be a potential biomarker for brain trauma related diseases such as Traumatic Brain Injury (TBI), stroke etc. Here we develop a fully automatic digital immunoassay to reliably measure GFAP in serum, plasma and Cerebral Spinal Fluid (CSF) in both healthy and diseased individuals.

Methods: The assay reagents were designed to be used on Simoa HD-1 Analyzer. Conjugated capture beads and biotinylated detection antibody were prepared following homebrew protocol. During first step of the assay, antibody labeled capture beads, biotinylated antibody detector were incubated with calibrator/samples together. After wash, immunocomplex were labeled with enzyme and transferred to an array of microwells. A single labeled GFAP molecule provided sufficient fluorescence in 30 seconds to be detected. The concentration of GFAP was then interpolated from a calibration curve. The assay was evaluated for sensitivity, precision, linearity, spike/recovery etc. Acute Traumatic Brain Injury (TBI) and healthy control samples were evaluated for plasma GFAP.

Results: Limit of detection (2.5 SD) was 0.211pg/mL and limit of quantification was 0.686pg/mL. Recovery of GFAP spiked into serum and plasma averaged 92.8%. Mean dilution linearity in serum was 106.2%. Mean dilution linearity in CSF was 90.1%. Precision was determined using 3 native and spiked serum samples across 5 runs. Mean inter-assay and intra-assay CVs were 10.8% and 8.47% respectively. In normal healthy individuals (n=20), median [GFAP] was 90.6 pg/mL (Range 44.3-152 pg/mL, in serum, n=20) and 88.0 pg/mL (Range 45.9-180 pg/mL in EDTA plasma, n=20). Median [GFAP] in CSF was 10427 pg/mL (range 2013-41757 pg/mL, n=10). Acute TBI plasma samples (n=30) had a much higher median [GFAP] of 1044.5 pg/mL (Range 50.0-18817 pg/mL).

Conclusions: The Simoa GFAP assay can reliably measure glial fibrillary acidic protein in plasma, serum and CSF samples from both healthy and diseased individuals. Preliminary data suggest plasma GFAP level is higher in acute TBI patients than healthy controls. This assay will facilitate the research and diagnostic development of GFAP related diseases, such as TBI and other diseases.

The Hospital Class: A Case Study with Inpatient Patients in A Public Hospital

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Considering that education is a right provided for in the Federal Constitution of 1988 and extends to all, the main objective of this study was to elucidate the importance and necessity of the implementation and implementation of a hospital class in the public hospitals of the Municipality of Fortaleza. Therefore, it is necessary to create a public policy that can guarantee specialized educational services for children and adolescents who are unable to attend classes because of the illness process that requires hospital admission. Thus, it is proposed the partnership with the Municipal Education Department - SME, in order to carry out and ensure this service for the students of the municipal education network that fit into this profile, favoring the continuity of the teaching and learning process of these. The qualitative methodology was used, with two research steps: bibliographic research and interviews, resulting in the absence of a hospital.

Academic Effects Post Concussion in Undergraduate College Students: A Campus-Wide Survey

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Purpose: The purpose of this study was to describe the 'return to academics' experience from a campus-wide online survey in a sample of collegiate students with self-reported concussion injury versus musculoskeletal injury in a large public university in the Midwestern United States.

Background: Current guidelines for return to academics are a product of an expert panel of the 4th International Conference on Concussion in Sport (Zurich, 2012) and focus on elementary and high-school students. College students also are at risk for post-concussion symptoms that can affect academic performance, but there are no guidelines for this population.

Methods: A previously validated survey (Kennedy & Krause, 2009) that assessed the college experience of students with moderate to severe traumatic brain injury was adapted for students with concussion and sent via mass email to 29,195 enrolled undergraduate students. Students who reported concussion or musculoskeletal injury while enrolled at the university were eligible to be included in this analysis. Students who reported being < 18 years, not fluent in written English, reported both a musculoskeletal injury and a concussion, or a history of other intracranial morbidities were excluded. In addition to academic-related effects, the survey also inquired about injury history, reporting behavior, healthcare services utilized, social and behavioral symptoms and knowledge and use of campus-based resources.

Results: 1749 students completed the survey. Of those, 4.2% (n=76) reported a concussion and 9.5% (n=167) reported a musculoskeletal injury while enrolled. Those who reported concussion had an average age of 20 years (Range=18-41), with 72% female; 90% self-identified as white, 12.5% Asian, 1.4% Black and 1.4% American Indian; and 96% self-identified as not of Hispanic, Latino or Spanish origin. The highest percentage of students (35%) had completed 2-3 years of undergraduate coursework. Demographics for those who reported musculoskeletal injury were comparable. Of the students who reported concussion and completed the academic section of the survey (n=64) vs those who reported a musculoskeletal injury (n=154), differences were found. For example: took a break from school (20.3% vs 7.1%); difficulty concentrating (67.9% vs 25.3%); difficulty remembering (86.4% vs 26.1%); felt disorganized (80% vs 37.9%), felt foggy (92.9% vs 25%), forgot what was said in class (21.7% vs 3.2%) and reduced their college credits due to injury (8.3% vs 4.1%). Additional analyses examining relationships are in progress.

Implications: A large number of college students who had sustained a concussion reported adverse academic effects. Students with musculoskeletal injuries reported a much smaller proportion, supporting an argument that these effects are not solely attributable to an injury experience. Future directions for research should address the burden of academic effects with the goal of developing empiric guidelines to support collegiate students.

Communication Problems Reported by College Students with and without Concussion

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Objectives: Individuals with concussion have been shown to be at risk for communication problems. It is important to characterize these problems because they have a significant negative impact on employment opportunities, social integration, and health-related outcomes. The purpose of the current study was to characterize communication problems of college students with concussion, by surveying students with and without concussion in a large public university in the Midwestern United States.

Methods: We used a validated survey (Kennedy & Krause, 2009) that assessed the college experience of students with traumatic brain injury, adapted for students with concussion. The survey was sent via mass email to 29,195 undergraduate students, and we analyzed responses of students who reported concussion or orthopedic (i.e., musculoskeletal) injury while enrolled at the university. In addition to questions about communication, the survey asked questions about history of concussion, students' reporting behavior, services utilized, concerns about prolonged symptoms (academic, social and behavioral), and knowledge about campus-based resources for individuals experiencing prolonged symptoms after their injuries.

Results: 1749 students completed the survey. Of those, 4.2% (n=76) reported incurring a concussion while enrolled. Those who reported concussion had an average age of 20 years (Range=18-41), with 72% female; 90% self-identified as white, 12.5% Asian, 1.4% Black and 1.4% American Indian; and 96% self-identified as not of Hispanic, Latino or Spanish origin. The highest percentage of students (35%) had completed 2-3 years of undergraduate coursework. Sixty of the students who reported concussion completed the communication portion of the survey. Of those, 18% (n=11) reported difficulties with receptive communication (e.g., understanding directions), 27% (n=16) reported difficulties with expressive communication (e.g., difficulty putting thoughts into words) and 15% (n=9) reported difficulties with reading. Of the students who reported orthopedic injuries and completed the communication portion of the survey (n=126), 10% (n=13) reported difficulties with receptive communication, <1% (n=5) reported expressive communication problems and <1% (n=3) reported difficulties with reading. Additional analyses specific to variable relationships and comparisons between concussion vs orthopedic injury are in progress.

Conclusions: A significant portion of college students who had incurred a concussion reported communication problems. These problems were not reported by students with orthopedic injuries and thus were not attributable to the injury experience alone. Future directions for research should address the trajectory of recovery for communication problems related to concussion and characterize underlying mechanisms of these deficits in order to develop sensitive assessments and interventions.

Exploring the Relationship Between Behavioural, Somatic, Cognitive and Emotional Symptoms Following Concussion with Considerations for Treatment

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Introduction: A concussion, typically classified as a mild traumatic brain injury (MTBI), is known to result in various behavioural, somatic, cognitive and emotional symptom constellations with differing degrees of severity. While research related to other health events, such as diabetes or chronic pain, approach questions related to assessment and treatment of these conditions in a more integrated manner, concussion research typically focuses on one symptom category, with little attention given to the relationship between the multi-factorial symptoms associated with concussive events. Cognitive dysfunction, impaired sleep, fatigue, and pain are known to impact mood, yet concussion research tends to focus on each of these symptom areas in isolation, overlooking the interaction between the factors and their relationship to one another in context of mild traumatic brain injury.

Method: Data was collected at Advance Concussion Clinic (ACC), an interdisciplinary outpatient clinic based in Vancouver specializing in the treatment of concussion. Patients completed the Patient Reported Outcomes Measurement Information System (PROMIS-57 and Applied Cognition measures) at intake. This sample included 160 patients—53% female; age range 18-91 with a mean age of 39.79.

Results: A bivariate correlation was calculated using SPSS statistics to identify relationships between symptom categories. Sub-factors within these categories included physical function, fatigue, sleep disturbance, satisfaction with social role, pain interference, pain intensity and subjective cognitive function. All behavioural, somatic, cognitive and quality of life symptoms were positively correlated with anxiety and depression. Fatigue and subjectively impaired cognitive functioning correlated most significantly with anxiety and depression. The correlation between anxiety, depression and fatigue was more significant than anxiety, depression and sleep disturbance.

Implications and Conclusions: Depression and anxiety are commonly identified following concussion, and are frequently the sole treatment targets for physicians or psychologists in treating MTBI sufferers. Our findings suggest that an interdisciplinary approach is needed in the treatment of concussion, as treating mood in isolation may be ineffective if what may be causal symptom factors are overlooked. MTBI patients may require physiotherapy, psychotherapy, sleep management, and exercise tolerance or cognitive training, to effectively treat behavioural, somatic, cognitive and emotional symptoms. Such an aggregate approach would be expected to improve outcomes in this patient population. Medical professionals should refrain from solely prescribing psychotherapy or medication for anxious or depressed mood associated with concussion and consider a broader range of interdisciplinary treatment options to achieve optimal recovery outcomes.

The Use of Functional Near-Infrared Spectroscopy (fNIRS) for Assessing Cognitive Workload After Concussion

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Objectives: Functional near-infrared spectroscopy (fNIRS), a noninvasive and portable neuroimaging modality that detects changes in blood oxygenation related to human brain function, is a promising tool to address the current lack of objective biomarkers to identify pathophysiologic changes associated with concussion. We sought to determine the utility of fNIRS to detect and differentiate cortical brain activity between concussed and healthy subjects when they performed the King-Devick test.

Methods: We conducted a prospective study of 19 concussed subjects and 9 healthy controls who completed the King-Devick test while wearing an fNIRS headband that recorded anterior prefrontal cortex oxygenation changes with 12 channels/4 optodes at 4Hz sampling rate. Linear mixed model analysis was performed to compare oxygenation changes in the two cohorts.

Results: There were significant differences across increasing difficulty of the King-Devick test conditions when comparing concussed subjects with healthy controls in both the left prefrontal cortex ($F_{1,26} = 9.906$, $p < 0.005$) and right prefrontal cortex ($F_{1,25} = 7.965$, $p < 0.01$). Among this pilot cohort, healthy controls showed significantly higher levels of oxygenation changes upon initiation of the King-Devick test compared to concussed subjects, but had decreased oxygenation changes over each successive test card. This pattern was not mirrored in concussed subjects who maintained consistent levels of oxygenation changes in the left prefrontal cortex and increasing levels in the right prefrontal cortex over the course of the test.

Conclusions: Our preliminary experimental results suggest that fNIRS detects changes in cerebral blood oxygenation between concussed and healthy subjects. Further investigation into the utility of this neuroimaging modality for quantifying changes in cognitive workload after injury and over the course of recovery is warranted. fNIRS may be a useful objective tool to assess concussion and aid decision-making in clinic and on the sidelines.

Brain Injury and Gender Differences in Emergency Head Trauma Admissions Among Infants and Young Children: A Data-linkage Study

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Background: Children under the age of two are at elevated risk of non-accidental trauma, including abusive head trauma. Unfortunately, it has historically been difficult to acquire large representative samples to examine rates of brain injury among males and females admitted to hospital with head trauma during the first five years of life, particularly during infancy. This study aimed to examine gender differences (in rates of presentation to hospital for head trauma and head trauma with brain injury, and hospital length of stay) during the first five years of life. This has been enabled by recent data-linkages of trauma-related hospital records.

Methodology: Hospital records (n=205135) for people admitted with head-trauma related primary diagnoses identified from the Queensland Hospital Admitted Patient Data Collection were linked and analysed. This included public and private hospitals that provide inpatient care to people within a 1.85 million km² geographically and ethnically diverse region of an industrialised nation (Queensland, Australia). This study included head-trauma emergency inpatient admissions (children <5 years of age), including both neurological and non-neurological injuries. Primary diagnosis codes (ICD-10) were used to identify relevant head and brain injury diagnostic categories. Elective or planned admissions were excluded. Descriptive statistics, univariate analyses and multi-level modelling (admissions=level-1, individuals=level-2, facilities=level-3) was undertaken to examine gender differences in incidence of presentation to hospital across diagnostic categories and length of stay in hospital.

Results: A total of 27690 (males=15964, 58%) emergency admissions for head-trauma injuries from 12318 unique children (males=7108, 58%) <5 years from 105 hospitals were identified. Of these, 3761 (14%) admissions were for a brain / intracranial injury primary diagnosis: concussion (total=938/3761, 25%), subdural haemorrhage (total=600/3761, 16%), subarachnoid haemorrhage (total=228/3761, 6%) and focal brain injuries (total=168/3761, 4%) were frequently represented primary diagnoses. Males were consistently more prevalent than females (each year-of-age from infancy to the fifth year of life). There was some variation in the extent to which males proportionally exceeded females across brain injury diagnostic categories (chi-square(8)=38.5, p<0.001). Mixed-effects generalised linear modelling indicated that even after adjusting for diagnosis-related factors (fixed effects) and clustering (three-level, random intercept model) the length of stay was slightly longer for males than females (coefficient = 0.08, 95%CI 0.03, 0.13; p<0.001).

Conclusions: Emergency hospital admissions for head injuries, including an array intracranial injury diagnoses, were higher for males than females from infancy onward. The inability to accurately discern accidental from non-accidental trauma is a limitation of this study. However, it is unlikely that contributors to traumatic brain injury often attributed to older males (e.g., aggressive behaviour) are applicable to infants. Both male and female infants and young children are at an elevated risk of abusive head trauma, the risk seems higher for males even during the first year of life.

Oculomotor Treatment in Traumatic Brain Injury Rehabilitation: A Pilot Trial

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Objective: To determine feasibility of a randomized controlled trial examining the efficacy of oculomotor treatment in traumatic brain injury rehabilitation. A protocol of impairment-based oculomotor exercises was compared to activity-based standard of care interventions.

Methods: Twenty individuals with TBI in inpatient rehabilitation who had oculomotor impairments were randomized into an experimental arm (n=10) participating in Six Eye Exercises protocol or into a control arm (n=10) participating in standard of care treatment. Participants in each arm individually worked with an occupational therapist 30 minutes per day, five days per week, for four weeks. Severity of oculomotor impairments and their impact on function were measured at baseline and post-treatment.

Results: Sixteen participants completed the trial. Fatigue was the primary reason for withdrawal. No other negative effects adverse events were reported. The selected outcome measures captured positive improvements in both groups.

Conclusions: The study findings support the feasibility of a powered randomized controlled trial to evaluate efficacy of oculomotor rehabilitation in this population.

Autologous Neural Progenitor Cell Based On 3D Biodegradable Scaffold Improve Long-Term Functional Outcome After Traumatic Brain Injury of C57BL/6 Mice

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Objectives: One of the most promising methods of the treatment of TBI is neurotransplantation of progenitor cells based on 3D scaffolds from synthetic biodegradable materials. However, clinical and experimental effects of cell transplantation creating suitable for tissue regeneration and neurotransplantation environment are not well understood.

Methods: The neurological (mNSS, open field test) and cognitive functions (passive avoidance behavior, novel object recognition test) long-term outcomes were studied during reconstructive therapy of open TBI by autologous neural progenitor cells on the 3D biodegradable scaffold consisting from hydrogel of high molecular weight hyaluronic acid and modified chitosan and performing the role of the basis for transplanted cells and replacement matrix of neural tissue.

Results: It has been shown that transplantation of autologous neural progenitor cells on the 3D scaffold in the brain significantly reduces the neurological and motor functions impairments, lead to the restoration of learning, short-term and long-term memory functions of mice at 6 months of post-traumatic period. MRI data analysis showed the reduction of the volume of the brain injury in comparison with control.

Conclusions: Thus, the transplantation of autologous neural progenitor cells on the 3D biodegradable scaffold promote to maintain the volume of the injured site in the first months after the injury and prevented the disruption of the neural networks of the brain that, in turn, leads to recovery of cognitive and neurological functions of the CNS in the remote period.

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Computational Assessment of Dynamic Interaction of Neural Probes with The Brain Motion Under Mechanical Motion and Impacts

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The improvement of the design of neural probes to monitor neural signals in the brain under mechanical motion and impact is addressed in this study. Novel designs and materials will aid to assess better brain function and damage mechanisms while reducing the risk of injury in the brain under mechanical motion. According to our computational analysis, reducing the stiffness discrepancy between the probe and the brain is the best solution to minimize the impact to neural recordings and injury to brain tissue surrounding the neural probe. Various material stiffnesses were examined for the probe to quantify the degree of injury from the probe when interfaced with surrounding brain tissue using Finite Element Analysis (FEA). The probe stiffnesses examined in the study range from 10^{11} Pa to 10^5 Pa, corresponding to commonly used silicon probes to softer polymers such as hydrogel, respectively. Deformation profiles are assessed along the probe-to-brain interface for mechanical motion typically seen in the brain due to pulsation, breathing, and walking. The study is extended to the dynamic interaction of various tungsten array configurations and is examined using Finite Element Analysis. Specifically, the effects of design parameters such as spacing, probe quantity, and geometry on the deformation buildup within the brain are presented.

Mechanically Flexible and Soft Neural probes for In-Vivo Neural Recordings in the Brain under Mechanical Impacts

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Traumatic brain injury (TBI) is comprised of a continuum of mild to severe brain injuries which may result from linear and rotational accelerations. The physiological and psychological state change during the course of mechanical impact on the brain is becoming recognized as an important variable to understand the impacts of TBI. The design and material improvement of neural probes is addressed in this study to monitor neural signals in the brain under mechanical motion and impact. Novel designs and materials for highly soft and flexible probe structures will aid to record neural signals while reducing the risk of injury in the brain under mechanical motion of brain. We developed neural probe array with nanoelectrodes to measure and image neural networks under mechanical motion and impacts into the brain. Various processing conditions were implemented for flexible and soft multilayer depth probe structures with overall thickness of 50 μm with parylene-C/Polydimethylsiloxane layers. Especially, by applying nanotechnology, we significantly reduced electrode impedance to much less than that of the previously used planar microelectrodes by the order of three. The novel design of soft depth probe and functional advantages of nano-electrodes in neural recording under mechanical motion and impacts will be discussed in this presentation.

Using of Accelerometer in Neurorehabilitation of Brain Damage Patients with Upper Limb Paresis

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Introduction: Neurorehabilitation intervention of patients with brain damage is an interprofessional, complex, intensive, long-term and individual process. Motor disorder of the brain damage patients is often hemiparesis.

Main Text: The main aim of the study was to demonstrate that the monitoring of motor functions in patients after brain damage leads to improved motivation, thereby improving motor functions.

New technological developments have led to the production of miniature accelerometer sensors. The using of accelerometer is possibility for objective functional assessment in rehabilitation.

In neurorehabilitation of the patients with hemiparesis is possible to use accelerometer for monitoring of functional changes of movement pattern. The basic principle is measuring of static and dynamic acceleration. Sensors can be used objectively to quantify amount of movement paretic and healthy upper arm activity. We used 3 different types of sensors: left blue sensor is on the left wrist, right red sensor is on the right wrist and green body sensor on the left hip. Our clinical study was undertaken with selected patients after brain damage with paresis.

25 patients after brain damage with upper arm activity were measured by accelerometer. Data from accelerometer monitoring were analysed in special program WMSAPP (Wrist Motion Sensor APplication software). The following parameter was all-day percentage movement activity of paretic and healthy upper arm activity. The patients were detected at the first and the last week during 4 weeks in a rehabilitation day care center from 9 a.m. to 4 p.m.

Methods: 55 patients after brain damage with upper arm paresis were randomized to an experimental group (A, n=25) and a control group (B, n=25). Patients in both group attended a rehabilitation day care center for 4 weeks. Patients in group A were measured by sensor - accelerometer for 7 hours per day of first week after admission and the last week in the care center. The FIM and Jebsen-Taylor (JT) tests were applied on all patients at the beginning and after 4 weeks of rehabilitation intervention during the final examination. Both tests are used for measurement of quantitative and qualitative changes in activities of daily living during rehabilitation process.

Results: Using of sensor - accelerometer in the experimental group (group A) significantly improved upper arm movement activity, can objectively detected the positive changes in movement spastic pattern. The accelerometer has the role of virtual therapist for the idea of permanent monitoring by the therapist. The patients were more motivated for active cooperation during the whole rehabilitation process.

Conclusion: Sensor – accelerometer can improve motivation (virtual therapists) of patients and also improve movement pattern and functioning of upper extremity. Activities of daily living of the patients with brain damage were also improved.

Developing Symptom Profiles in Depressed Versus Non-Depressed Youth Recovering from Concussion

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Objectives: Concussion and subsequent recovery protocols lead to many losses in children's lives as routines and normal activities are disrupted. Reactions to these losses can range from immediate distress and grief to long-term depression. Distinguishing between normal reactions and potential depression is a clinical dilemma that we sought to explore. The purpose of this study was to investigate the relationship between post concussive symptoms and scores on the Children's Depression Inventory to determine any patterns and associations between those with depression and those with no depression.

Methods: A prospective cohort study was conducted and data collected as part of a bigger study investigating whether adherence to guidelines decreases the duration of symptoms. Depression data was collected for 117 children at 1 – 3 time points during their recovery from concussion using the Children's Depression Inventory-2 (CDI -2). At each of these time points, post concussive symptom inventories were completed. Independent t tests, chi-square and correlational analysis were used to examine the associations between individual post-concussive symptoms and scores on the CDI-2.

Results: Clinically significant depressive symptoms (T score on CDI-2 > 65) were found in 18.8% of the children aged 7-18 years (mean=13.92). Children with evidence of depressive symptomatology had significantly higher mean post-concussive symptom inventory scores (M=35.8) in recovery (p=0.000) than children who were not depressed (M=13.9). While headache, fatigue and concentration were commonly reported in those without depression, there remains a significant difference in the means between the depressed and non-depressed groups (p=0.000) for these symptoms. Sadness, being more emotional and vision problems are also highly discriminating between the groups (p=0.000).

Conclusions: Depression is commonly reported in this cohort of children during their recovery from concussion. The post concussion symptom inventory score is significantly different between the groups of depressed and non-depressed youth reflecting a greater number and intensity of symptoms in the depressed youth. Numerous emotional and cognitive symptoms were reported to be highly different between the two groups. These results begin to build symptom profiles that are associated with depression. Symptom profiles will help in clinical decision-making and assist in early intervention to prevent poor outcomes.

Nutritional status of Traumatic Brain Injury Patients of Oman

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Traumatic Brain Injury (TBI), also known as acquired brain injury or concussion is one of the most serious and challenging health problems worldwide. Emerging economies such as Oman has high rates of traumatic brain injury due to road traffic accidents. Previous studies have focused on pharmacological intervention. There is no study, to our knowledge, on the nutritional status in TBI patients of Oman. Despite this extraordinary incidence, little is known about the nutritional complications followed TBI. The aims of this study were to assess the nutritional status and nutritional adequacy of traumatic brain injury in Oman. In Oman, this study was conducted in Khoula Hospital (national trauma center) – Muscat – Oman from February 2014 to February 2015 among consecutive patient with TBI. Healthy volunteers were recruited as controls. All participants were signed consent. Demographic variables, anthropometric measurements and dietary intake were assessed to assess the adequacy/inadequacy of macronutrients and micronutrients. The results showed that the cohort with TBI tends to exhibit nutritional imbalance, including deficiency in energy, carbohydrate, protein, micronutrients, and fiber respectively when compared with healthy control volunteers. These results indicate that TBI population involved in the study from Oman could be at high risk of developing malnutrition. These factors are likely to impede their road to regaining pre-morbid self. The limitation of this study is less sample size and not representative and further extensive studies are needed to find the exact link to promote the better therapeutic strategies for post traumatic injury status. The support provided by The Research Council (RC/AGR/FOOD/11/01) and Sultan Qaboos University (IG/AGR/FOOD/14/01), Oman are highly acknowledged. The support given by Dr. Ali Al-Mashani and his team from Khoula hospital Muscat, Oman is highly acknowledged.

Alpha Power During Working Memory is Compromised in Acute Mild Traumatic Brain Injury

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Background and Objectives: We aimed to explore alpha power during working memory (WM) processing in a longitudinal study of acute mild traumatic brain injury (mTBI).

Methods: We used quantitative electroencephalography (qEEG) to explore alpha frequency power during WM processing in an ongoing acute mTBI study. Thirteen acute mTBI patients and seven non-head trauma controls, 18-50 years of age, were recruited from the emergency department of Huntington Memorial Hospital in Pasadena, CA. Brain challenges using the N-back (0-back and 2-back) WM test were administered. Behavioral performance and EEG data from 21 recording electrodes were collected at three different recording sessions: within one week, 14 days, and 30 days after injury.

We observed the symptomatic progression of the TBI patients over the three visits and analyzed the EEG alpha power overall (MANOVA) and for specific channels (exploratory approach), relating the analysis results to the patients' symptoms at each visit.

Results & Discussion: During the first visit, mTBI patients did not realize they were not well; they were "a little shaken up," indicating an executive dysfunction. Compared to controls, the 0-back responses of mTBI patients showed excessive alpha event-related desynchronization (ERD) in the frontal areas (Fz) that was not phase locked to the eliciting events, consistent with an executive dysfunction.

At the second visit, mTBI subjects knew they were not well and their experience was described "like a dream." The phase-locked alpha power computed over parietal regions was significantly lower in the mTBI group, consistent with the "dream-like" detached perception of the real world.

At the third visit, they knew they were better, but still they were not back to "normal." However, no different alpha powers were shown during 0-back test. Behavioral responses to the 2-back trials showed initial WM impairment in the mTBI group that improved at the later visits. In response to the 2-back task, the frontal (Fp1) alpha ERD was decreased in the controls between the first and third visits, possibly indicating a learning mechanism. In mTBI patients, however, no decrease was observed over the three visits, indicative of a learning impairment that correlated well with their feelings that they were not back to "normal".

Conclusions: Our results indicate that alpha ERD during WM processing is sensitive and correlates well with the evolution of subjective symptoms occurring in acute mTBI. These results suggest that WM parameters may have significant potential as objective biomarkers that can reliably quantify mTBI symptoms and may also help with the diagnosis, prognosis, and monitoring of treatment efficacy.

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Supramarginal Gyrus to Thalamus Functional Connectivity in Brains of Active and Retired National Football League Players

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Background: There is rising concern that former National Football League (NFL) players may experience onset of cognitive and other neuropsychiatric symptoms linked to history of sports-related head injury. Recently, we showed that brains of active, recently retired, and elderly retired NFL players had higher binding of the PET ligand [11C]DPA-713 to translocator protein 18 kDA (TSPO), a marker of brain injury and repair, compared to healthy controls. Higher binding of [11C]DPA-713 was found in the supramarginal gyrus (SMG) and thalamus of players compared to controls in studies of both younger and older individuals.

Objective and Hypothesis: To conduct a focused investigation of functional connectivity between the SMG and thalamus using resting state functional magnetic resonance imaging (rsfMRI). We hypothesized that NFL players would show evidence of disrupted functional connectivity in the analyzed regions compared to controls.

Methods: NFL and control groups were recruited in two separate studies: one with older (age >55 years) and one with younger (age <55 years) individuals as previously published. Younger NFL players consisted of active or recently retired (within 12 years from last NFL play) individuals. Resting state Bold Oxygen Level Dependent (BOLD) data was obtained and analyzed using a seed-based analysis with 6mm spherical regions of interest placed in bilateral SMG and bilateral thalamus. The comparison was bilateral thalamus to SMG connectivity by side using t test. Results. rsfMRI data from 14 younger NFL players, 15 younger controls, 10 older NFL players, and 6 older controls were analyzed. Mean correlation values (younger NFL, younger control, older NFL, older control, respectively) were as follows: bilateral thalamus to LEFT SMG (0.01, -0.42, 0.11, -0.11) and bilateral thalamus to RIGHT SMG (0.05, -0.39, 0.01, -0.08). Results of t test by age and SMG side as follows (statistic, p value): left younger (-2.3352, 0.0272), right younger (-1.7194, 0.0970), left older (-0.7982, 0.4381), and right older (-0.2642, 0.7955).

Conclusions: The anti-correlation in resting state connectivity between bilateral thalamus and left SMG seen in younger controls was absent in the younger NFL group. Absence of anti-correlation was also seen in both the older controls and older NFL players. These results together with our published PET data suggest that brain injury or repair, marked by higher TSPO PET signal in SMG and thalamus, may be associated with altered thalamus-to-SMG resting state functional connectivity in younger NFL players.