

# The Canadian Concussion Centre

## 6th Annual Concussion Research Symposium Concussions: Cumulative, Persisting and Progressive Consequences Saturday, May 12, 2018 | BMO Education & Conference Centre

### Speaker Presentations

#### **1. If (Almost) Every Athlete has CTE, Why Do We Need Pathologists?**

*W. Stewart, Honorary Clinical Associate Professor at the University of Glasgow*

Recent media headlines would suggest virtually all athletes in certain sports will develop chronic traumatic encephalopathy. Despite this apparent CTE pandemic, the diagnosis is still one that relies on autopsy confirmation. This talk has examined the contradictions and confusion in current understanding of CTE, and underline the need for unbiased neuropathology studies.

Objectives:

- Recognize limitations in current research and reporting in CTE
- Describe current understanding of the neuropathology of CTE
- Appreciate the need for continued and comprehensive autopsy studies to characterize the neuropathology of CTE

#### **2. The Spectrum of Neuropathological Changes in Athletes with History of Repeated Concussions: Are We Chasing the Wrong Lesion?**

*L.N. Hazrati*

Chronic traumatic encephalopathy (CTE) is suggested to be a progressive neurodegenerative disease, characterized by tau deposits in the depth of cortical sulci in glio-neuronal complexes around blood vessels. Based on this pathological criteria, a recent publication showed that most American football players studied had CTE. This is an in depth neuropathological study of donated brains with the objective of evaluating all structural changes in concussed brains. Our aims include the assessment of proportion of cases with CTE and the extent of CTE, the presence and severity of other proteinopathies, non-protein-related structural and cellular changes such as vascular disease, axonal damage, inflammation and DNA integrity. Over the last 6 years, we have collected the brains of about 40 high level professional and amateur athletes with history of repeated concussions. All brains were sampled extensively and studied with standard histological and immunohistochemical tools. Our results indicate that only a small portion of cases have CTE. Moreover, most cases are low stage (stage 1 or 2) and this pathology is mainly seen in some of the younger players. Older players either have no pathological findings or have complex patterns of pathological changes that overlap with different diseases. Additionally, most cases show evidence of DNA damage. Based on these findings, we conclude that CTE is not a predominant brain lesion in our cohort of athletes with history of multiple concussions.

### **3. Cerebrospinal Fluid Biomarkers in Professional Athletes with Multiple Concussions**

**F. Taghdiri, N. Multani, R. Goswami, A. Tarazi, S.A. Naeimi, M. Khodadadi, L. Oliva, L. Levesque, C. Esopenko, R. Wennberg, D. Mikulis, R. Green, B. Colella, K. Davis, B. Levine, C.H. Tator, M.C. Tartaglia**

The lack of an *in vivo* diagnostic tool for chronic traumatic encephalopathy has made the accurate diagnosis and treatment impossible while patients are alive. Since cerebrospinal fluid (CSF) connects directly to the pathological milieu in the central nervous system, it has great potential as a biomarker. CSF biomarkers are commonly being used in the diagnosis of AD. CSF samples were obtained from eighteen retired professional male athletes (9 football players and 9 hockey players) [age (mean±SD): 57.0±10.3 years] and nineteen patients with biomarker proven Alzheimer's disease (AD) [age: 75.5±4.6 years]. Concentrations of phospho-tau181 (p-tau), total-tau (t-tau), and  $\beta$ -amyloid (A $\beta$ 42) in the CSF were measured using ELISA (Innogenetic) assays. Imaging and neuropsychological assessment were completed. CSF concentrations of p-tau and t-tau were significantly lower in the athletes compared to patients with AD (43.8±13.30 pg/ml vs. 120.99±20.15 pg/ml,  $p<0.0001$ ; 368.1±193.1 pg/ml vs. 867.11±286.29 pg/ml,  $p<0.0001$ , respectively) and the concentration of A $\beta$ 42 of the athletes was significantly higher compared to the AD subjects (753.6±185.04 pg/ml vs 442.66±107.72,  $p<0.0001$ ). An apparent bimodal t-tau distribution was observed in the athletes group (8 athletes with normal concentration (NC) of t-tau [167.3±47.8 pg/ml] vs 10 with high concentration (HC) of t-tau [528.7.3±64.1 pg/ml]). Subjects in the NC group scored significantly higher in the trail making test (TMT) part B compared to subjects in the HC group (t-score: 64.3±5.8 vs 43.9±20.2;  $p=0.001$ ). In addition, subjects in the HC group showed evidence of reduced integrity with significantly higher mean diffusivity (MD) of the right superior longitudinal fasciculus compared with the normal tau group (0.00082±0.00003 vs. 0.00079±0.00002,  $p=0.03$ ). CSF total tau may reflect cerebral changes associated with cognitive impairment and loss of white matter tract integrity in athletes with multiple concussions.

### **4. What We Are Learning about the Importance of Concussions in Women and Girls**

**K. Snedaker, Founder and Executive Director, PINK Concussions**

This presentation provides a broad overview of sex and gender differences in brain injury between men and women based on current scientific research and Katherine's experience working with the thousands of women in the PINK Concussions Support Groups. And beyond research data, Katherine has addressed why these differences are important for patients, families and clinicians to consider in care plans for women and girls. The lack of education and awareness about these differences can lead to a patient's unrealistic expectations of recovery time and an underestimation of the need for support from family and school/work. In addition, a lack of training in a medical professional in these differences can inhibit diagnosis and appropriate intervention across the care continuum and affects the development and delivery of appropriate healthcare service.

Objectives:

- Describe three ways in which brain injuries (including concussion) in women differ from males.
- Articulate factors that may account for sex and gender differences in TBI incidences, severity, and recovery
- Understand the urgent need to develop "better" practices in the care and education of women with brain injury to facilitate recovery and positive long-term outcomes.

## **5. Sex-Specific Alterations of the Salience and Fronto-Parietal Networks in Individuals with Post-Concussion Symptoms-Resting-State Functional Connectivity Of Large-Scale Networks.**

*Shafi, R., Crawley, A.P., Tartaglia, M.C, Tator, C.H, Green, R.E., Mikulis, D.J., & Colantonio, A.*

Concussions may be associated with a range of cognitive, neuropsychological and behavioural sequelae that extend beyond the one year post-injury period. While there is evidence that mild traumatic brain injury or concussion can disrupt network-based connectivity, there remains a significant knowledge gap regarding the influence of sex-based differences in resting state functional connectivity (rs-FC) post- concussion. Our primary goal was to investigate the changes in rs-FC across three large- scale neural networks: 1) the Default Mode Network (DMN), 2) the Salience Network (SN) and, 3) the Fronto-Parietal Network (FPN). Our secondary objective was to explore the sex-based differences in network-based connectivity and behaviour post-concussion. Behavioural and 3T MRI data was collected from a sample of 80 individuals (47 males) who reported a history of concussions and 31 participants (17 males) with no known history of concussion. Both seed-to-seed and seed-to-region connectivity maps were used to assess network-based connectivity using the Functional Connectivity (CONN) toolbox. Network based statistics was utilized to understand rs-FC differences post concussion. Concussed participants showed significant differences across both the SN and the FPN. More specifically, a functional subnetwork was observed where the frontal nodes of both the SN and FPN were hyperconnected in a ‘fronto-insular’ component and the posterior nodes were hypoconnected via a “parietal” component when compared to control participants. Seed-to-region analyses revealed significantly reduced rs-FC between the FPN and the association cortices of the temporal, parietal and frontal lobes in concussed females relative to both controls and concussed males. This study provides the first evidence for sex-specific network-based alterations in rs-FC during the chronic stages of recovery post-concussion. Notably, our findings point to a regional sex-specific alteration post-concussion.

## **6. Full-brain Connectivity Analysis in Healthy Aging Remotely Concussed Athletes**

*S. Guay, S. Tremblay, Y. Iturria-Medina, J.M. Mateos-Perez, A.C. Evans, L. De Beaumont*

The interaction between initial brain damage after sports-related concussions (SRC) and the aging process exacerbates alterations of brain structure and function in aging athletes. Diffusion magnetic resonance imaging (dMRI) has proven to be effective in characterizing subtle white matter changes, the predominant structural damage following SRC. In this study, we aimed to characterize white matter integrity and network topology in remotely concussed athletes by conducting full-brain connectivity analysis. A total of 30 former hockey or football athletes between the ages of 51 and 75 were subdivided into two groups based on their SRC history. The concussion group consisted of 15 asymptomatic males who sustained from 1 to 5 SRC that took place at least 30 years prior to testing. The control group consisted of 15 healthy controls. All diffusion images were obtained on a Siemens 3T scanner. After contrasting the connectivity matrices of both groups, six statistically significant differences were observed within the right hemisphere. As for graph theoretical analyses, we found significant differences at local level only, but not at global level. All  $p$ -value < .05 after FDR correction. Our investigation on the interaction between normal aging and sports-related concussions shows that white matter anomalies seem to preferentially affect specific connections within the right hemisphere in remotely concussed athletes. However, it remains to be tested whether these differences indicate efficient compensatory mechanisms following concussions using functional measures. Further studies should investigate specific white matter tracts that appear to be affected after SRC using tractometry.

## **7. Psychological Mechanism Underlying Persistent Symptoms After Concussion**

*N. D. Silverberg, Clinical Associate Professor, Division of Physical Medicine & Rehabilitation, University of British Columbia*

Mental health problems prior to injury and emotional distress soon after injury are among the strongest predictors of concussion outcome. However, it has not been clear which mechanisms underlie the relationship between these proxy psychological variables and concussion recovery. This presentation has synthesized evidence on maladaptive illness beliefs and coping behaviors associated with persistent symptoms after concussion. Implications for psychologically-informed treatment have also been reviewed.

### Objectives

- State the importance of psychological factors in recovery from concussion.
- List specific psychological factors that can complicate recovery from concussion.
- Describe psychologically-informed treatment strategies.

## **8. Remotely Delivered Cognitive Behavior Therapy for Treatment of Mood Disturbance in People with Persisting Symptoms of Concussion**

*B. Budisin, L.M. Jaimes, D. Kwan, L. Meusel, M. Panoso, A. Changoor, A. Tibbles, A. Robertson, B. Colella, M.C. Tartaglia, C.H. Tator, R. Green*

Few treatments have demonstrated efficacy for persisting symptoms of concussion. Cognitive Behaviour Therapy (CBT) is a well-validated talk-therapy for emotional disturbance in neurological populations, with demonstrated efficacy for remote delivery. To date, remote CBT has yet to be employed in adults with persisting concussion symptoms. To assess feasibility and efficacy of remotely delivered CBT for persisting symptoms of concussion in adults. An RCT was undertaken for reduction of emotional distress (and to compare differing formats of booster sessions; findings not presented). Adults with elevated emotional distress on the SCL-90-R were randomized to the CBT arm (including one of three sub-conditions for booster formats) or the concussion education control arm. Eight telephone-administered sessions were administered by trained therapists. Pre- to post-treatment change on mood outcomes were the primary dependent variables. On paired t-tests pre- to post-treatment, 18 CBT patients showed significantly reduced depression ( $p < .005$  Depression, Anxiety, Stress Scale [DASS];  $p < .05$  Beck Depression Inventory II), anxiety ( $p < .05$  DASS;  $p < .05$  Beck Anxiety Inventory), stress ( $p < .01$  DASS), and general emotional distress ( $p < .05$  SCL-90-R). The 6 controls showed very similar means pre- to post-treatment with no significant changes and small effect sizes. Retention was high (89 percent), and 80 percent of completers had zero missed sessions. Preliminary results show encouraging findings for the feasibility and efficacy of remote CBT for mood disturbance in adults with persisting concussion symptoms. The remote delivery modality allows for economic scaling and broad reach, improving equity of access to treatment.

## **9. Concussion Protocol Harmonization: The Who, What, and How of a National Approach to Concussion**

*S. Cowle, P. Fuselli*

In recent years, experts have called for policy development to address sport-related concussion (Frémont et. al., 2014). However, a lack of national-level coordination has resulted in concussion protocols of variable content and quality. Further, patients presenting with concussion are receiving inconsistent messages from healthcare providers, potentially impacting post-injury outcomes (Babul, 2015). Objectives: Provide national leadership to: (1) harmonize sport concussion protocols (2) enhance healthcare provider competencies for concussion best practice. We reviewed current scientific evidence and international expert consensus to develop guidance tailored to the Canadian sport and health contexts (*Canadian Guideline on Concussion in Sport*). We built tools to translate this guidance into concussion protocols and worked with National

Sport Organizations (NSOs) on tailored return-to-sport progressions. Concurrently, we conducted a needs assessment to identify priorities for improving consistency in healthcare practice. Over 40 NSOs were engaged in the harmonization project. Readiness was not dependent on the level of concussion risk in a sport or organizational experience with concussion policy. Using a harmonized template proved effective and required less customization than anticipated. Primary care provider competencies to assess, manage, and refer concussion cases were identified as priorities for improving consistency in healthcare practice, and were targeted in a newly developed online program. This is the first national effort to harmonize concussion protocols. Ongoing, authentic collaboration between the health and sport systems is necessary for concussion outcome optimization in Canada.

## **10. Development of a Best Practices Consensus For Concussions Policy In Schools**

*S. Mylabathula, C.H. Tator*

Concussions are a major public health concern, and policies have been developed for implementation targeting specific vulnerable populations such as school-aged children and youth in the school setting. Currently, policies exist in various jurisdictions in the school setting, such as Canada's first concussion policy, PPM158, and many policies in the United States. However, the content is variable and often not comprehensive. Developing a best practices expert consensus would help in setting a standard for policy on concussion in schools. The aim of this research is to employ a modified Delphi method to develop best practices for concussion policy for schools. Following a pilot study in the Toronto District School Board, which emphasized common missing elements in existing concussion policy, a consensus approach was used to develop best practices for concussion policy in schools. The consensus approach used is an 8-step modified Delphi Method following an integrated knowledge translation method with participation from a diverse stakeholder group of principals, school board directors, physicians, policymakers, public health representatives, and parents. The modified Delphi method allowed the development of a comprehensive policy to address concussions in the school setting from a multidisciplinary expert panel composed of 27 individual recommendations with the following themes: Leadership, Education, Return to Learn, Return to Play, Communication, and Injury Prevention. This policy list reflects diverse perspectives and addresses the role of parents, teachers, coaches, school administrators, referees, trainers, and students. This research promises to enhance the quality of concussion policies in schools across Canada and beyond, by providing a comprehensive framework to guide best practices for policy development and implementation. The policy recommendation list is a tool to help update existing concussion policy in some jurisdictions, and to inform development of new concussion policy in other jurisdictions.

## **11. Mild Traumatic Brain Injury Leads To Sustained DNA Damage and Acquisition of Senescence-Associated Secretory Phenotype by Astrocytes**

*N. Schwab, L.N. Hazrati*

Mild traumatic brain injury (mTBI) is common in contact sports, and can cause brain damage with long-term symptoms, including depression, memory loss, and an increased risk of neurodegenerative disease. Recently there has been increased attention towards concussion in sport, however the nature and pathophysiology of mTBI remain unknown. The objective of this study was to identify early pathophysiological markers of mTBI. This study used a collection of donated postmortem brains with a history of repetitive mTBI in contact sports and controls with no history of TBI. Nanostring ncounter's immune panel was used to quantify gene expression, and results showed that brains with a history of mTBI tended to group with aged brains with no mTBI history. Further analysis of this expression panel revealed that genes associated with senescence and secretory vesicles were upregulated in brains with a history of mTBI. Immunohistochemistry for  $\gamma$ -H2AX (marks double-stranded DNA breaks) showed that TBI brains accumulated a spectrum of DNA damages not present in controls. This damage was

widespread and involved neurons, oligodendrocytes, and astrocytes. Astrocytes showed morphological changes reminiscent of senescence, including soma swelling and process beading. These changes were accompanied by translocation of structural nuclear proteins (including emerin), did not correlate with p-tau distribution in cases with tauopathy, and were seen in cases without any proteinopathy. These results suggest that DNA damage and senescent-like gene expression represent early upstream events in the manifestation of post-TBI symptoms and pathology, representing promising opportunities for discovery of biomarkers for early TBI detection and follow-up of progression.

## **12. A Novel Visual Task As An Indicator of White Matter Integrity and Cortical Thickness in Retired Professional Athletes with Multiple Concussions**

*F. Taghdiri, J. Chung, N. Multani, A. Tarazi, S.A. Naeimi, M. Khodadadi, R. Wennberg, D. Mikulis, R. Green, B. Colella, K. Davis, C.H. Tator, M. Eizenman, M.C. Tartaglia*

The aim of this study was to evaluate the contribution of white matter integrity and cortical thickness to performance on a novel visual scanning task of processing speed in retired professional athletes with a history of multiple concussions. Forty-two retired professional male athletes (age  $53.7 \pm 12.7$  years) underwent imaging, neuropsychological testing, and eye-tracking assessment. In the Matching Familiar Figure Test (MFFT), an eye-tracking assessment for processing speed, subjects were presented with a series of slides. Each slide included a master image and six variants of the master image and subjects were instructed to choose the matching variant. Percentage of first correct selection (PC), latency to reach the correct selection (L), and the ratio of the two (PC/L), a measure of efficiency were recorded. We evaluated the relationship between performance on the MFFT and integrity of the major white matter (WM) tracts (uncinate fasciculus (UNC), cingulum (Cg), superior longitudinal fasciculus (SLF), and corpus callosum (CC)) derived using seed-based probabilistic tractography of diffusion tensor data. The CC, being a large tract, was divided into 5 components. The cortical thickness was measured using Freesurfer v5.3. There was a significant negative correlation between the latency and left UNC fractional anisotropy (FA) ( $r = -0.566$ ,  $p < 0.001$ ). Positive correlations were observed between the PC/L ratio and FA of the left UNC and the fifth component of CC as well as the right entorhinal cortical thickness ( $r = 0.440$ ,  $p = 0.004$ ;  $r = 0.306$ ,  $p = 0.005$ ; and  $r = 0.605$ ,  $p < 0.001$ , respectively). Impaired performance on the MFFT may reflect loss of WM tract integrity and focal atrophy in retired professional athletes with a history of multiple concussions.

## **13. AV1451 Positron Emission Tomography (PET) Tau as a Potential Biomarker in Professional Athletes with Possible Chronic Traumatic Encephalopathy**

*A. Vasilevskaya, F. Taghdiri, C. Burke, A. Tarazi, S.A. Naeimi, M. Khodadadi, R. Goswami, R. Wennberg, D. Mikulis, R. Green, B. Colella, K. Davis, P. Rusjan, S. Houle, C.H. Tator, M.C. Tartaglia*

Repeated concussions can be associated with neurodegenerative disease, in particular chronic traumatic encephalopathy (CTE). There are currently no ante-mortem biomarkers for the tau pathology of CTE.

Objective: Assess the use of [18F] AV1451 PET to detect abnormal tau of CTE in former professional athletes that have suffered repeated concussions and correlate with neuropsychiatric measures. 37 former professional athletes [36 males, 1 female; mean age  $56.27 \pm 13.42$ ; median 4 concussions (range 0-60)] were recruited for this ongoing study. Neuropsychological and neurological assessments were completed. PET tau imaging with 18F AV1451 tracer, structural MRI and diffusion tensor imaging (DTI) was acquired for all participants. The standard uptake value ratios (SUVRs) for regions of interest were calculated using cerebellar grey matter as a reference region. Participants were visually divided into positive [N=7, age  $45.00 \pm 14.00$ ] and negative [N=30, age  $58.90 \pm 12.04$ ] groups based on PET frontal lobe tau burden. The tau positive group had significantly higher personality assessment inventory (PAI) aggression t-scores ( $p = 0.038$ ) when corrected for age, and significantly lower paced auditory serial addition test 2.0

z-scores ( $p=0.039$ ). There was also a trend for higher PAI depression t-scores in the tau positive group ( $p=0.079$ ). Full brain grey matter SUVRs significantly correlated with right superior longitudinal fasciculus DTI mean diffusivity values [ $N=36$ , age  $56.08\pm 13.56$ ,  $r=0.453$ ,  $p=0.006$ ] and radial diffusivity values [ $r=0.445$ ,  $p=0.007$ ], corrected for age. A higher tau burden as measured with [ $^{18}\text{F}$ ] AV1451 PET is associated with greater behavioral and cognitive impairment and decreased white matter integrity.  $^{18}\text{F}$  AV1451 tracer shows promise as a potential in-vivo biomarker of possible CTE.

#### **14. Longitudinal Study of 834 Concussed Patients to Highlight Factors that Contribute to the Development of Postconcussion Syndrome (PCS)**

*E. Boulanger, P. Lakshmi, C.H. Tator*

Most individuals recover from a concussion within 28 days, but some do not recover for months or years after injury, and some never recover. Individuals who do not recover within the usual time are said to have postconcussion syndrome (PCS). The first objective of this study is to determine the demographics and predictors of PCS in a large series of concussed patients. The second objective is to verify if some differences (such as gender, age at time of the concussion, and number of concussion) affect the recovery from PCS. Our long-term aim is to develop strategies to prevent and treat PCS and to determine whether PCS is an antecedent to chronic traumatic encephalopathy (CTE). We conducted a retrospective cohort study of 834 concussed patients, all of whom had PCS on the basis of at least 1 symptom persisting more than 3 months in combination with a negative brain computed tomography (CT) or magnetic resonance imaging (MRI) scan to exclude more severe brain injuries. Patients were seen in consultation at a Toronto Western Hospital Concussion Clinic and mailed a questionnaire to evaluate their PCS. Results are currently being statically analyzed. We will be able to present the results and conclusions at the time of the Concussion Research Symposium.

### **Poster Presentations**

#### **15. Defining Patient Recovery From Concussion Based on Multiple Criteria and Recovery Trajectories**

*L. Rokos, P. Comper, C. Saverino, T. Chandra, M. Bayley*

There is no consensus around when patients with concussion are deemed recovered. The study seeks to develop an operational definition for concussion recovery merging criteria from physician assessment, patient reporting, and performance based tests. We are conducting a longitudinal study of adult patients diagnosed with a concussion referred to the Hull-Ellis Concussion and Research Clinic by local Emergency departments. For up to 8 weeks post-injury, patients will be followed by clinic physicians and will be assessed on sensory, physical and cognitive criteria. Patients will outline their personal recovery goals and will provide self-reports on concussion symptoms. Performance based measures will also be examined. We will assess the percentage of individuals recovered across time based on the different criteria described above. Data from sixty patients were analyzed. There was variation in the number of patients deemed recovered at different timeframes in days depending on which criteria was used. Preliminary results suggest that SCAT criteria is stricter than physician criteria in terms of deeming patients recovered. Variation of when patients were deemed recovered by each criteria suggests a need for more objective tools and a patient-centered operational definition for concussion recovery. The operational definition of recovery will ensure patients receive consistent, objective and evidence-based diagnosis and care. It will help physicians to determine when it is safe for patients to return to sport, work or school and it will help standardize the criteria used in research surrounding factors influencing patients with persistent post-concussive symptoms.

## **16. Effect of Internal Jugular Vein Compression on Intracranial Volume: A Transorbital Ultrasound Study of the Optic Nerve Sheath Diameter**

*M. Dinsmore, Z. Hajat, J. Fisher, L. Venkatraghavan*

Concussions have become a growing epidemic in both competitive sports and recreational activities and incur significant personal and socio-economic costs. It has been shown that mild jugular venous compression causes an increase in intracranial blood volume which may have a protective effect by minimizing brain “sloshing” within the cranium. However, the effect of wearing a cervical neck collar on intracranial volume has not been demonstrated in the upright position. To investigate the effect of IJV compression on intracranial volume using transorbital ultrasound of the optic nerve sheath diameter (ONSD) as a surrogate of changes in intracranial volume. Two independent investigators performed ultrasound measurements on ten healthy volunteers. Ultrasound measurements were performed on the right IJV cross-sectional area, and the change on right eye ONSD before and after application of IJV compression. All volunteers were in the sitting position and ultrasound of the IJVs was performed at the level of the cricoid cartilage cephalad to the neck collar. Mean (SD) cross-sectional area for the right IJV at the level of the cricoid was 0.10 (0.05) cm<sup>2</sup> at baseline with a corresponding ONSD of 4.6 (0.5) mm. After application of the neck collar, IJV cross-sectional area increased to 0.66 (0.40) cm<sup>2</sup> with a corresponding increase of ONSD to 4.9 (0.3) mm, which was significant when compared to the baseline value ( $P = 0.041$ ). We present the first study to demonstrate that mild IJV compression in subjects in the sitting position increases the intracranial volume as demonstrated by an increase in ONSD. Therefore, our finding may support the use of a neck collar in minimizing the harmful effect of concussions.

## **17. Sex-specific Differences in Cerebral Blood Flow for Athletes with a History of Concussion**

*J. Hamer, N. Churchill, M. Hutchison, T. Schweizer*

Growing evidence suggests there are differences in concussion outcome for males and females based on initial clinical presentation, with neuroimaging studies suggesting a physiological basis for these differences. However, it is currently unknown whether there are persistent long-term differences in the effects of concussion on brain function, for males and females. This study evaluated sex differences in cerebral blood flow (CBF) in asymptomatic athletes with and without a history of concussion. 2D pulsed Arterial Spin Labeling (pASL) was acquired for 71 asymptomatic varsity athletes with a history of concussion (36 female), all scanned >9 months post-concussion, and 64 control athletes without prior concussion (30 female). Athlete groups did not differ significantly in age, time since last concussion, recovery time or balance scores. Males with a history of concussion had lower thalamic and cerebellar CBF compared to females with a history of concussion. Concussed males also had lower CBF in the anterior cingulate and supplemental motor area compared to male controls. In contrast, female athlete groups showed no significant differences. This is the first large-scale study to examine sex differences in cerebral perfusion associated with concussion history and suggests subtle differences in neurovascular response, despite a lack of significant symptoms or cognitive impairments.

## **18. The time course of behavioural impairment in mice following mild traumatic brain injury**

*M. Mellerup, L. Gazdzinski, J. Sled, A.L. Wheeler*

Mild traumatic brain injury (mTBI), which includes concussion, causes highly variable physical, cognitive, and behavioural symptoms that are most often transient; however, 10-15% of patients experience persistent symptoms. It is not known what differentiates those who recover quickly from mTBI from those who do not. The objective of this study was to describe the time course of behavioural impairment following mTBI in a mouse model of concussive injury. mTBI was induced in mice using a closed-skull Controlled Cortical Impact model, and behavioural



assessments were conducted at an acute (3 days) and chronic (6 weeks) delay post-injury to characterize the time course of impairment. At each time-point, the open field and light/dark tests were used to assess anxiety-like behaviours, the tail suspension test was used to assess depressive-like behaviours, the Y maze was used to assess working memory, and the pre-pulse inhibition test to assess sensorimotor gating. mTBI mice spent significantly more time in the centre of the arena within the first 5 minutes of the open field test compared to shams across time-points. In the tail suspension test, mTBI mice showed increased mobility compared to shams at the acute time-point. mTBI mice had significantly fewer successful novel arm transitions in the Y maze compared to shams at both time-points. There were no differences between groups in the light/dark test and in the pre-pulse inhibition test. These results reveal an unexpected phenotype whereby mTBI mice displayed fewer anxiety-like and depressive-like behaviours after injury, however these mice appear to have memory deficits that persist over time.

### **19. Does a History of Concussion Matter?**

*K. Dalton, C. Sikorski, T. Simpson*

Acute concussion significantly impacts visual function, however it is unknown whether or not residual vision deficits persist after recovery. This study assessed visual function in athletes with and without a history of concussion to determine if residual vision deficits persist following concussion recovery. Data from 319 varsity athletes (age 17 - 29) at the University of Waterloo, collected from 2013 – 2016 were examined retrospectively. Athletes played a variety of sports, and were healthy at the time of testing. A number of visual functions including visual acuity (VA), contrast sensitivity, stereopsis, and visuomotor reaction time (VMRT) were measured. Athletes also self-reported concussion history and visual symptoms (everyday and in sport). Differences between groups were compared using Student's t-tests. 27% of athletes reported having at least one concussion. Contrast sensitivity was better in athletes with concussion than athletes without concussion ( $p < 0.01$ ); no other visual function differences were found between groups. There was no difference in reported visual symptoms everyday (concussion: 42%, none: 34%,  $p = 0.20$ ) or in sport (concussion: 25%, none: 23%,  $p = 0.22$ ), but athletes with symptoms in sport had significantly worse VA ( $p < 0.01$ ) and slower central VMRT ( $p < 0.01$ ). Visual function deficits do not appear to persist following concussion recovery. This study was limited because athletes did not report how many previous concussions they had or the time since their last injury. The suggestion that athletes with a history of concussion have more visual symptoms warrants further investigation.

### **20. A New Biomarker To Guide Neuromodulatory Treatment For Patients Suffering From Post-Concussion Syndrome and Chronic Pain**

*D.M. Buchanan, T. Ros, R. Nahas*

Quantitative-electroencephalography (qEEG) is a low-cost and non-invasive neuroimaging modality useful for identifying specific subtle electrophysiological changes in the brain after a concussion (Thatcher et al., 2001; Ayaz et al., 2015). The disconnection of networks in the brain results in changes in neuroelectrical transmission (Rapp, 2015). This can be detected in qEEG as abnormal spectral power (amplitude), or phase-locking value (functional connectivity) (Cao et al., 2010). Changes in power and functional connectivity are shown to correlate with changes in neuro-inflammation (Scott et al., 2015), and with cognitive, behavioural, and emotional symptoms exhibited in post-concussion syndrome (PCS) (Zhu et al., 2014; Dunkley et al., 2015). To identify unique pathophysiological biomarkers in patients with PCS and pain to inform evidence based treatments. We conducted a retrospective case-control study using 19-channel resting-state EEG data from 57 patients with PCS and chronic pain following MVAs, and 54 healthy controls matched closely for age and sex. Data were analyzed using MATLAB and SPSS. Independent samples exact Mann-Whitney U tests revealed significant increases in global spectral power across all frequency bands, and a significant increase in delta relative to alpha

power in the patient group vs. control group. Opposing significant decreases in phase-locking value were found in PCS patients in the alpha band. The present study provides evidence of a potential biomarker to guide treatment for people with PCS and pain. Our future research will identify biomarkers specific to PCS independent of chronic pain, and vice versa, to better differentiate their pathophysiology.

## **21. Establishment of Normative Data for Examination of Visual Function in Post-Concussion Syndrome**

*S. Alamri, K. Dalton*

Post-concussion syndrome (PCS) is associated with visual deficits on traditional clinical tests. However, these tests do not adequately describe all of the visual deficits in PCS. The purpose of this study was to establish normative data for novel tests of visual function that may improve the description of visual deficits in PCS. 44 subjects (controls n=33, PCS n=11) completed this study. They attended two visits, where traditional clinical tests (visual acuity (VA), contrast sensitivity (CS), stereopsis, accommodative facility (AF), vergence facility (VF), and NPC) and novel clinical tests (NPC difference (recovery minus break), AF and VF variability (standard deviation of 3 tests), visuomotor reaction times (RT), and King-Devick (KD)) were conducted. Overall, the controls performance on the traditional vision tests was clinically normal (VA:  $0.11 \pm 0.1$  logMAR, CS:  $2.00 \pm 0.06$  logCS, Stereo:  $31.3 \pm 17.1$  arcsec, AF:  $>10$  cpm, VF:  $15.8 \pm 5.0$  cpm, NPC:  $4.9 \pm 3.2$  cm). On novel tests, controls performance was: NPC difference  $1.1 \pm 0.3$  cpm, AF variability:  $2.1 \pm 2.2$  cpm (OD),  $1.3 \pm 1.2$  cpm (OS), VF variability:  $2.4 \pm 2.0$  cpm, RT: Central  $509.1 \pm 115.2$  ms, Peripheral  $960.3 \pm 236.6$  ms), KD:  $48.0 \pm 0.4$  s. Performance of the PCS group was similar to the control group on both the traditional and novel tests; the most pronounced difference between the two groups was that the PCS group had more symptoms. PCS patients appear to have similar visual function to controls, however they also appear to experience more symptoms. Further investigation is needed to understand the relationship between symptoms and visual function in PCS.

## **22. Do Patients With Mild Traumatic Brain Injury Accurately Assess Their Sleep Duration? A Preliminary Report.**

*T.L.C. Yang, A. Colantonio, T. Mollayeva*

Short sleep is linked to dysfunction of restorative function, while long sleep is associated with increased cytokine levels and sickness behaviour. Moderate-severe traumatic brain injury (TBI) patients' responses weakly correlate with objectively measured sleep markers, but little is known about response accuracy in mild TBI (mTBI) patients. Objectives: To determine relationship between patient- and polysomnography (PSG)-assessed sleep duration in mTBI and identify factors associated with both assessments. We hypothesized that mTBI patients underestimate sleep duration and that age, sex, brain injury markers, psychosocial distress, insomnia and mental health disorders influence patients' sleep duration assessment. The study, approved by hospital and university ethics boards, took place in a research- teaching hospital. Thirty-seven participants diagnosed with mTBI (57% male,  $47.54 \pm 11.3$  years old,  $547 \pm 1380$  days post injury) underwent clinical and neuroimaging examinations, full-night PSG, and estimated their sleep duration in the morning following PSG. Mean self-assessed sleep duration was  $342 \pm 93.6$  minutes and PSG-assessed sleep duration was  $382 \pm 76.8$  minutes. The two measures were moderately correlated ( $\rho=0.46$ ,  $p=0.004$ ). Of the hypothesized variables, age and sleep efficiency, as measured by PSG, were significantly correlated with both self and PSG-assessed sleep duration ( $\rho=0.34$  and  $\rho=0.84$ , respectively,  $p$ -values  $<0.05$ ). Self-assessed sleep duration was uniquely associated with insomnia severity ( $\rho=-0.48$ ,  $p=0.002$ ). No other significant associations were observed. Patients with mTBI do not accurately assess their sleep duration, thus reinforcing the importance of PSG. Specific analyses of patients who under-report and over-report will provide greater insight into

sleep perception in mTBI and associated factors.

### **23. Neck strength screening protocol: potential utility for sport-related concussion**

*D. Richards, T. Beach, M. Hutchison*

Neck musculature controls motion of the head, which has led to investigation of neck strength (NS) as a potential modifiable risk factor of sport-related concussion (SRC). Currently, there is inconsistent evidence supporting the association between maximal NS and post-impact head acceleration and/or risk for SRC. Objectives: (1) Utilize a novel neck screen protocol to evaluate multi-directional NS-endurance properties; (2) to evaluate the effect of sex and history of SRC on NS-endurance performance in interuniversity athletes. NS-endurance of 103 interuniversity athletes (49=M, 54=F) was assessed. A load proportional to their body weight (BW) was applied to the head in flexion (10% BW) bilateral flexion (12%BW) and extension (15%BW) for 15 seconds. Head motion was clinically assessed to determine a “pass” or “fail” in each direction. 41% of participants failed in  $\geq 1$  directions of the screen. 50% of those with history of SRC and 30% with no history of SRC failed  $\geq 1$  directions. Similarly, 50% of females and 31% of males failed  $\geq 1$  directions. Differences in failure rates between sex and history of SRC were discovered in this screen, revealing compromised NS-endurance in females and those with history of SRC. Neck pain and weakness are frequent complaints and treatment targets of SRC. Compromised NS may lead to an increased susceptibility to secondary injury if not adequately addressed. Results from the present study shed light on the potential role of NS as a modifiable risk factor of SRC, as well as how it may be identified and targeted for intervention in the athletic population.

### **24. The Effects of Sub-Concussive Impacts on University Hockey Players**

*D. Richards*

Ice Hockey is a popular sport, yet the majority of head impact research has focused on primarily on football. Hockey and football differ in many ways. Hockey players reach top speeds of up to 60mph (30) resulting in greater energy transfer upon impact. There are many fixed boundaries in the sport such as the boards, goal posts and ice playing surface as well as the imbalance from being on a thin blade. (30). Few studies have observed the total number of impacts through a season, and none have done so with an Ontario University Hockey Team. Research looking at the biomechanical forces of sport related impacts found hockey had 1/3 the amount of high force impacts as football. However, they did find the number of total hits per hour of play to be similar. The objectives of this study are to measure the impact accumulation that occurs over the course of a OUA hockey season and to measure the cognitive changes from these impacts. An impact measuring device (GForceTracker) was used to record the number of impacts that each player experienced in a season. Players completed baseline, 2 midseason, and postseason, neurophysiological tests to measure P3b amplitude in response to a visual oddball paradigm. Pro and Anti Saccades were also measured at these time points to measure changed in executive function. Over the course of the season, players accumulated approx 5000 impacts ranging from 10 to 600. Over the first half of the season, players had an increase in P3b latency (23ms) and decreased amplitude (-2mv) eluding to slower cognitive function with less output. During the month of rest, players saw reduced latency and no change in amplitude, suggesting recovery from this initial injury. In the second half of the season, there was an increase in latency again, which further leads to the assumption that subconcussive impacts affect cognition.