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involves an early hypermetabolic response followed by metabolic collapse. Preserving the metabolic balance after TBI could reduce the impact of secondary damage. In rodent models of TBI, metabolic depression is seen by 6 hours after severe TBI. Hypermetabolism is suspected to occur in humans based on temporal changes in cerebral microdialysis in injured patients. Here, we used a translationally relevant porcine cortical impact model to determine whether glucose hypermetabolism is evident after TBI. Brain tissue was acquired from animals receiving TBI (n = 6) and control animals that underwent anesthesia and non-cranial procedures (n = 6). The survival time was 6 hours. We directly measured enzyme activity of hexokinase (HK), lactate dehydrogenase (LDH), and pyruvate dehydrogenase (PDH) in perilesional cortex and in distal cortical regions using plate-based assays. PDH activity was upregulated in perilesional cortex ($p = 0.009$) we found no differences in either LDH activity ($p = 0.3769$) or tissue lactate levels ($p = 0.2273$) at the injury site. Expression of the astrocytic lactate transporter MCT4 was upregulated near the injury ($p = 0.03$) but not the general monocarboxylate transporter MCT1. We found no differences between TBI and control outside of the perilesional cortex. Our results suggest a clinically relevant window in which providing supplemental energy sources after TBI could preempt later metabolic decline.

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P04.105

BLOOD BIOMARKER ANALYSIS TO STUDY THE EFFECT OF SEX AND MENSTRUAL CYCLE ON THE BRAIN ALTERATIONS DUE TO REPEATED HEAD IMPACTS

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Sport-related repeated head impacts (RHI), although asymptomatic, are linked to cognitive declines over-time. Females have shown higher rate of concussion than their male counterparts in comparable sports. Among the female-male comparable sports, soccer has the highest head impact rate and a high number of concussion occurrence. Therefore, herein, we investigated the potential brain alterations due to RHI in soccer, and the effect of sex and menstrual cycle on the outcomes of RHI. Using a standard soccer heading protocol, we induced 10 head impacts, one-minute apart. Blood was collected prior and at 1-hour, 1-day, and 7-days following the RHIs. The plasma biomarker levels including GFAP, TAU, NFL, and UCH-L1 were analyzed and compared between males (n = 16) and females (n = 17: 8 at follicular phase (FP) and 9 at luteal phase (LP)). The baseline/pre-exposure of these blood biomarkers were not significantly different between females and males, except UCH-L1 which was higher in females. Following RHI, females (FP/LP-combined) showed significantly higher GFAP than males for all time-points post-RHI. In females, GFAP was significantly elevated at 1-hr post-RHI while in males, UCH-L1 was significantly increased at 1-day post-RHI. In addition, higher baseline levels and post-RHIE elevations were observed in female-FP group compared to female-LP. In summary, the results showed that potential brain disruptions may occur during typical soccer headings and LP-females may experience less brain disruption due to RHI compared to FL-females, suggesting that higher progesterone level in LP may have protective effects on the brain alterations acutely after trauma. Funded by UTSA-BHC seed grant.

P04.106

ASSESSING THE IMPACT LOCATION AND PLAYER POSITION IN SEVERITY AND FREQUENCY OF HEAD IMPACT EXPOSURES IN YOUTH FOOTBALL

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Contact sports are associated with high incidence of brain injury with millions reported concussions yearly in US. Herein, we investigated the head impact kinematics and corresponding brain tissue deformations in different player positions (PP) and impact locations (IL) in high school football. The head impacts of players (n = 16) were recorded using instrumented mouthguards (Prevent-Biometrics) and video confirmed over one season. Ten PP including Offensive-Line, Quarter-Back, Running-Back, Tight-End, Wide-Receiver, Defensive-Line, Corner-Back, Kick-Off, Line-Backer, and Safety were studied. The IL were also divided in ten categories including Top-Front, Top-Rear, Front-High, Front-Low, Side-High, Side-Low, Rear-High, Rear-Low, Bottom-Front, and Bottom-Rear. The Global-Human-Body-Model-Consortium head finite element model was also used to simulate the tissue deformation responses. The impacts were categorized to four severity bins ('low' <25th, 'low-mid' 25th-50th, 'mid-high' 50th-75th and 'high' ≥75th) based on all the parameters studied the number of impacts were normalized based on the number of players played in each PP in each game and averaged over the games throughout the season. Offensive-Line and Running-Back showed the highest numbers of total impacts and impacts with 'high' and/or 'mid-high' severity based on all kinematics and tissue deformation parameters including peak linear and angular accelerations, angular velocity, and maximum principal strain, and maximum principal strain-rate. The Front-Low and Front-High IL showed highest number (3-14fold) of impact occurrence compared to other ILs. However, the distribution of ILs were similar between different PPs (P-value >0.05). This study identified the PPs and ILs at highest risk of concussion in high school football. Funded by UTSA-HP-RIG seed grant.

P04.107

DTI-BASED TRACTOGRAPHY STUDY OF THE HUMAN BRAIN: SEX SPECIFIC TEMPLATES AND SEX VARIATIONS

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The human brain is sexually dimorphic and these sex differences have shown to affect brain response to trauma. We investigated the sex differences in the tract structures by studying diffusion weighted (DW) images of 594 females and 506 males from the Human-Connectome-Project dataset. All the female and male DW images were reconstructed in the ICBM152 space using Q-Space diffeomorphic reconstruction technique and their mapped orientation distribution function images were averaged to generate the female- and male-DW-templates. The tract streamlines were generated through tractography for female and male templates and normalized to the total brain volume . The distributions of normalized tract lengths were significantly different between female- and male-templates and the female-template showed to have more longer normalized tracts compared to the male template. For the regional analysis, the templates were parcellated into sixteen regions of interests (ROI) including brain-stem, five subregions of corpus-callosum, and right and

left hippocampus, thalamus, cerebellum white-matter (WM), cerebral WM, and cerebellum cortex using a FreeSurfer-based segmentation atlas. For all the ROIs, the average fractional anisotropy (0.5-5.7%) and normalized tract lengths (1.1-2.7%) were larger in female-template while the average mean diffusion was larger (1.3-5.6%) in male-template. Quantifying brain connectivity by counting number of tracts passing through pairs of ROIs, showed more pairs with a higher connectivity in female-template, and one of the highest percentages of sex differences in right/left cerebellum WM/cortex connections. Our results reinforce the need to continue investigating the sex variations in axonal structure and their effects to brain trauma. Funded by NSF-2138719.

P04.108

SATELLITE MICROGLIA: LOSS OF NEURONAL REGULATION AFTER TRAUMATIC BRAIN INJURY AND ROLE OF P2Y12 RECEPTORS

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Microglia, the primary mediators of innate immune activation in the brain, are increasingly recognized as key modulators of neuronal activity. Prolonged activation of the innate immune system can impede repair in TBI, and it is not understood how microglia's impact on neuronal activity might contribute or protect. One microglial subtype that may be critical in the regulation of neuronal excitability is the perineuronal satellite microglia (Sat-MG). These microglia are juxtaposed adjacent to neurons with their soma and processes entwined around the neuronal cell body. To understand how these microglia modify neuronal excitability and change after injury, we utilized patch clamp recordings, immunohistochemistry, and confocal imaging. We found an increase in the numbers of Sat-MG in the orbitofrontal cortex in both a murine model of TBI that is associated with network hyperexcitability and deficits in reversal learning months after TBI, as well as human tissues from donors with a history of chronic TBI, compared to controls. Our data, utilizing whole cell recordings in transgenic mice with GFP-labeled microglia (Tmem119-EGFP), also indicate that Sat-MG suppress neuronal excitability, in control mice, but lose this ability in chronic TBI with an associated decrease in expression of P2Y12 receptors, which appears more selective for the satellite microglial subtype. Furthermore, preliminary data suggests acute treatment with a P2Y12R antagonist could reverse the Sat-MG associated reduction in excitability and increase network excitability, supporting our hypothesis that reduction of P2Y12Rs may contribute to loss of neuronal regulation and cognitive dysfunction after TBI.

P04.109

INVESTIGATING THE RELATIONSHIP OF ARTAG TO TRAUMATIC BRAIN INJURY

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Astrocytes, in addition to neurons, are vital cells in the brain that contribute to maintaining function. Like neurons, astrocytes can also accrue abnormal deposits of proteins with aging and neurodegenerative disease. However, how these abnormal proteins in astrocytes contribute to cognitive decline has not been well-studied as opposed to neurons. Phosphorylated tau is one protein that can accumulate in astrocytes and is often referred to as tau astrogliopathy. Tau astrogliopathy frequently accompanies the pathology of chronic traumatic encephalopathy (CTE)- a neurodegenerative pathology associated with repetitive head injury. Given this information, we hypothesized that tau astrogliopathy would also occur at a higher incidence and with increased levels of pathology in those with a history of traumatic brain injury (TBI), even without CTE. We evaluated and quantified tau astrogliopathy in brain sections from donors with TBI compared to age-, sex-, and cognitive-status matched controls, in a previously published ACT (Adult Changes in Thought study) brain donor cohort at the University of Washington neuropathology research core. Specifically, the density of thorny shaped astrocytes (TSA) and granular fuzzy astrocytes (GFA) in different tissue locations (white matter, grey matter, etc.) throughout different cortical and subcortical regions was quantified. Our preliminary data found no statistically significant difference in the presence, density or pattern of distribution of ARTAG pathology between the TBI and control groups; but we are currently expanding this analysis to further understand ARTAG deposition across different cohorts.

P04.110

IMPROVED MEMORY FUNCTION IN OLDER ADULTS WITH HISTORY OF TRAUMATIC BRAIN INJURY THROUGH REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION OF LEFT DORSOLATERAL PREFRONTAL CORTEX

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Background: Numerous studies provide evidence for traumatic brain injury (TBI) not only leading to increased risk of cognitive decline, but accelerated onset, as well. Repetitive transcranial magnetic stimulation (rTMS) has been shown to have enhancing effects on memory in older adults with amnestic mild cognitive impairment or in the early stages of Alzheimer's disease, especially in hippocampal-mediated memory tasks. To date, no studies have examined rTMS treatment in older adults with a history of TBI.

Method: In a double-blind randomized clinical trial, we used rTMS treatment on the left dorsolateral prefrontal cortex (l-DLPFC) to improve memory problems in older adults with a history of TBI. We enrolled (n = 19) Veterans and civilians (mild and moderate TBI; mean age = 62.63) in either a placebo or an active trial arm. Participants received neuropsychological assessment at baseline, after 10 treatments, and six month follow-up.