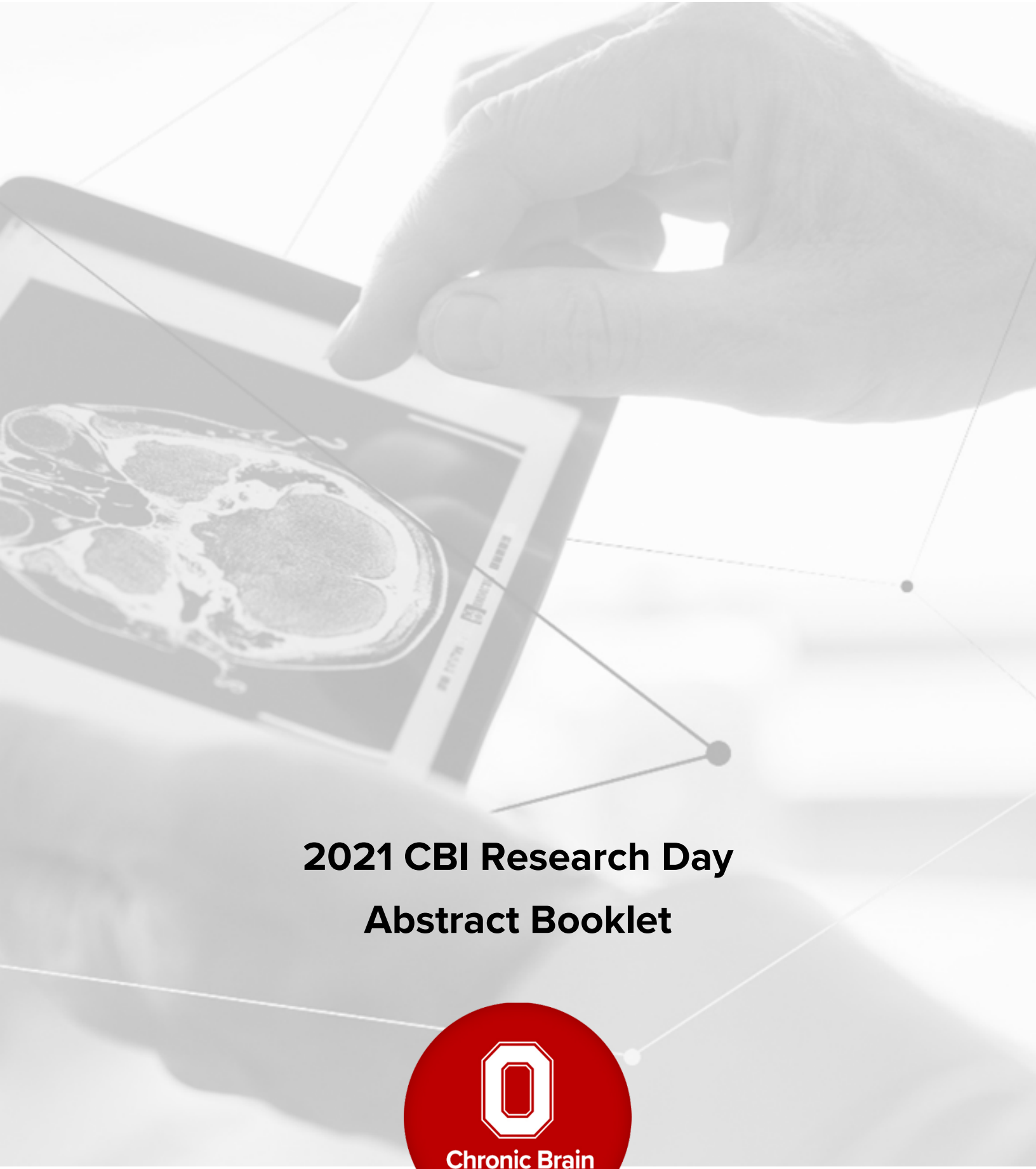

2021 CBI Research Day

Abstract Booklet

Chronic Brain Injury Program

1. **Chronic cortical inflammation and cognitive impairment associated with diffuse brain injury is ameliorated by forced turnover of microglia**

DATA BLITZ

Chelsea E. Bray, Kristina G. Witcher, Dunni Adelkunle-Adegbite, Michelle Ouvina, Mollie Witzel, Fangli Zhao, Titikorn Chunchai, Emma Hans, Julia E. Dziabis, Zoe M. Tapp, Olga N. Kokiko-Cochran, Candice Askwith, and Jonathan P. Godbout
Presenting Author: Chelsea Bray –Research Staff, Department of Neuroscience

Traumatic brain injury (TBI) is associated with cognitive, psychiatric, and neurodegenerative complications that may develop years after injury. Increased microglial reactivity following TBI may set the stage for chronic neuroinflammation, neuropathology and exaggerated responses to secondary immune challenges. Therefore, the goal of this study was to force the turnover of microglia sub acutely post-injury and determine if microglial reactivity was reversed 30dpi. Here, mice were injured by midline fluid percussion injury and 7 d later were subjected to a forced turnover paradigm using the CSFR1 antagonist, PLX5622. At 30 dpi, cortical gene expression was determined using Nano String's Neuropathology panel (760 genes). Myriad neuropathology-related genes were increased 30 dpi in the cortex, and these genes were reversed by forced microglia turnover. In terms of neuroplasticity, reduced neuronal connectivity (N1 and N2 compound action potentials) was evident 30dpi and these deficits were attenuated by microglia turnover. Dendritic remodeling in the cortex, however, remained 30 dpi and was independent of microglia turnover. Assessment of functional recovery showed depressive-like behavior and cognitive impairment 30 dpi, which were ameliorated by microglia turnover. A secondary immune challenge elicited by peripheral LPS challenge 30 d after TBI caused amplified neuroinflammation and prolonged sickness behavior. We provide novel evidence that microglia repopulation after TBI alleviates prolonged sickness behaviors associated with microglial priming. Together, these data suggest microglia are a potential therapeutic target to treat persistent neuroinflammation and improve functional impairments sustained by TBI.

2. **DHA prevents diet-induced memory impairments in aged rats and microglial inflammatory gene expression.**

SPOTLIGHT

Michael J. Butler, Nashali Massa, & Ruth M. Barrientos. Institute for Behavioral Medicine Research, Ohio State Wexner Medical Center, Columbus, OH. Postdoctoral Researcher

It is known that diets high in refined carbohydrates can lead to impairments in brain aging and cognitive performance, but the underlying mechanisms of these impairments are not well understood. Our lab has previously demonstrated that aging is associated with a decrease in the omega-3 polyunsaturated fatty acid docosahexaenoic acid (DHA) in the brain. DHA is involved in many beneficial functions in the brain including neuronal signaling, altering membrane structure and function, lipid mediator production, and regulating immune cells to resolve inflammation. Thus, this age-dependent decrease in DHA may contribute to the refined diet-induced memory impairment. Here, we studied the impact of a refined-ingredients diet with and without DHA on learning and memory in aged rats. In addition, we examined the impact of DHA on microglia-mediated inflammation in vitro. Our data indicate that consuming a diet high in refined ingredients for one month led to memory impairments in aged, but not young rats, relative to control rat fed the standard chow diet. In contrast, the same processed diet supplemented with DHA produced no changes in memory in either young or aged rats, suggesting that DHA may mitigate the impact of diet-induced memory deficits in aged rats. It is important to note that in addition to reduced complex carbohydrates and fiber, processed foods are also often high in saturated fatty acids, (SFAs) such as palmitic acid (PA). In vitro, BV2 microglial cells treated with PA exhibited increased inflammatory and mitochondrial stress gene expression relative to vehicle-treated cells. Furthermore, DHA pretreatment prevented these SFA-induced responses. Together, these data suggest that DHA can prevent diet-induced behavioral and cellular changes elicited by processed ingredients and SFAs, respectively.

3. **Resilience through a new lens: Leveraging photo elicitation methods to define resilience among adults with TBI and opioid use disorder**

DATA BLITZ

Kathryn A. Coxe, MSW; Erica K. Pence, MSW Audrey Begun, PhD, MSW Affiliation: College of Social Work, The Ohio State University, 1947 College Road, Columbus, OH 43210Corresponding Author: Kathryn Coxe (PhD Candidate)

Background: Traumatic brain injury (TBI) and opioid use disorder (OUD) are debilitating conditions presenting unique challenges for adults with these comorbidities. Although deficits associated with TBI and OUD are often focal to rehabilitation and recovery, treatment paradigms are shifting to strength-based models that emphasize resilience. Centering resilience around outcomes rather than fixed traits may illuminate modifiable factors in the recovery process. However, resilience outcomes are poorly researched and difficult to ascertain through quantitative metrics due to memory and communication problems post-injury. Visual methods are a powerful mechanism to engage adults in research to establish a deeper understanding of resilient outcomes from the individual's perspective. Objective: This study aimed to investigate resilience outcomes among adults with co-occurring TBI and OUD, and to identify risk factors contributing to continued vulnerability. Methods: Using qualitative phenomenology, participants were purposively recruited through an urban, hospital outpatient program that specializes in TBI and substance misuse treatment for adults. Participants were included who had lifetime history of TBI identified through the Ohio State University TBI Identification method, DSM-5 diagnosed OUD, and Orientation Log score≥25.Photographs, descriptive text messages, and semi-structured interviews were collected between December 2019 and March 2020 using photo elicitation methodology. Data were co-coded and analyzed using document analysis. Themes were developed according to tenets of Resilience Theory. Results: A total of N =126photographs,47 text messages, and four interview transcripts were included for analysis. Resilience was demonstrated through psychological flexibility, use of existing resources, and compensatory strategies to overcome stressors. Specifically, participants reported:1) commitment to cognitive, physical, and emotional growth; 2) the ability reframe negative experiences associated with the injury, opioid use, pain, and daily stressors into a positive appraisal of the circumstances; 3) social support from family, friends, and peer supporters; and 4) healthy coping skills and feelings of empowerment through physical activity, technology use, and the arts. Participants unanimously documented chronic pain as a major barrier to daily functioning. Participants also reported that lack of transportation and difficulty navigating urban city transportation systems were primary barriers to accessing available health services. Yet, while supportive services specific to TBI and OUD were desired, participants described these as largely unavailable. Conclusion: This study is a first step toward a better understanding of resilience outcomes among adults with comorbid TBI and OUD. Results can inform the development of future strengths-based interventions in TBI and OUD care that promote resilient outcomes post-injury.

4. **Post-surgical morphine prolongs hippocampal dysfunction in aged rats: Implications for neuroinflammation and neuronal structure**

Nicholas P. Deems (1,2), Stephanie M. Muscat (1,3), Heather D'Angelo (4), Meagan M. Kitt (4), Peter M. Grace (5), Nathan D. Andersen (4), Shaelyn N. Silverman (4), Kenner C. Rice (6), Linda R. Watkins (4), Steven F. Maier (4),Ruth M. Barrientos (1, 7, 8, 9)

Post-operative cognitive dysfunction (POCD) is a constellation of impaired cognitive symptoms that can occur following surgery, most typically in elderly individuals. Cognitive impairment can last days to months with more persistent durations associated with greater susceptibility to mortality and dementia. Mechanisms driving susceptibility for persistent POCD are not well understood. Preclinical models have only recapitulated shorter-durations of post-surgical memory impairments and these models overlook the common use of post-operative opioids. Here we report that treatment with post-surgical morphine robustly impairs hippocampal function for at least eight-weeks in aged rats that underwent an exploratory abdominal surgery (i.e., laparotomy). Short-term memory remained intact, suggesting that these three factors (age, surgery, and morphine) combine to compromise memory processes critical for long-term memory formation. Furthermore, we provide evidence that this is driven through a neuroinflammatory mechanism independent of the -opioid receptor. It is well known that excessive neuroinflammation in brain regions such as the hippocampus can have deleterious consequences on neuronal structure & function which can ultimately undermine learning, memory, and cognition. In support of this, we found gene expression of synaptophysin and PSD95, two markers found in pre-and post-synaptic structures, respectively, to be significantly dysregulated in the hippocampus of aged, laparotomized, morphine-treated rats. Moreover, preliminary histological data suggests that dendritic spine density may also be altered in these animals. These data tentatively suggest that aging, surgery, and morphine may compromise neuronal structure and play a role in this persistent memory deficit. Altogether, this rat model of POCD closely mirrors the timeline of persistent forms of POCD in humans and is useful for studying the unique biology underlying this long-lasting dysfunction; thus providing insight into future treatments for patients suffering from POCD

5. **Defining the adult hippocampal neural stem cell secretome**

SPOTLIGHT

Jiyeon K. Denningera, Xi Chenb, Altan M. Turkoglu c, Pearlly Yan b,d, Elizabeth D. Kirbya,e,f a Postdoc in Department of Psychology, College of Arts and Sciences, The Ohio State University, United States b Comprehensive Cancer Center, The Ohio State University, United States c College of Arts and Sciences, The Ohio State University, United States d Division of Hematology, Department of Internal Medicine, College of Medicine, The Ohio State University, United State se Department of Neuroscience, The Ohio State University, United States f Chronic Brain Injury Initiative, The Ohio State University, United States

In addition to generating new functional neurons, adult hippocampal neural stem cells (NSCs) secrete a wealth of bioactive factors. While this NSC secretome has therapeutic potential for many neuropathological conditions, little is known about its composition and how it changes with injury. Studying NSCs in vivo is challenging due to their relatively small population size and integration within a complex niche consisting of several other cell types. To elucidate the adult hippocampal NSC secretome, we have adapted traditional tools and methods that are used to study more readily accessible or abundant cell types. First, to identify potentially secreted proteins at the transcriptional level, we used a novel workflow combining prospective FACS isolation of NSCs with limiting cell RNA sequencing (lcRNA seq) and a data filtering algorithm (coverage-based limiting-cell experiment analysis for RNA sequencing) that generates population-level transcriptional profiles from a few hundred cells. This protocol enabled inclusion of biological replicates and deeper sequencing, yielding a more comprehensive transcriptomic profile than those generated from bulk or single cell-based techniques. From this data, we identified putative NSC-secreted factors. For protein-level study of the NSC secretome, we used cultured NSCs as current proteomics approaches are less adaptable to the small population of size of in vivo NSCs. Comparison of global transcriptomes of cultured adult hippocampal NSCs with in vivo NSCs showed a high degree of correlation, indicating that cultured NSCs are suitable surrogates. To specifically identify NSC-secreted proteins in culture and exclude proteins from culture supplements, we used affinity selection of noncanonical amino acid tagged NSC-synthesized proteins in NSC conditioned media followed by liquid chromatography with tandem mass spectrometry. In addition to identifying numerous NSC-secreted proteins, we also discovered that secreted protein abundance was not always predicted by gene expression levels, suggesting that transcript omics should be used in tandem rather than as proxy to proteomics. Collectively, our data contribute to the comprehensive characterization of adult hippocampal NSC secretome, providing the foundation for future endeavors studying NSC secretome response to injury and potential for therapeutic application.

6. **Acquired pneumonia leads to functional deficits after SCI**

Angela R. Filous, Jan M. Schwab, Department of Neurology

Patients become severely immunocompromised after spinal cord injury (SCI), making them vulnerable to infections. One of the most severe of these infections is pneumonia, which is the leading cause of death after SCI. Additionally, patients that acquire infections have reduced recovery potential compared to SCI patients without infections. We have developed a translationally relevant model to study the effects of acquired infections after SCI. Mice with acquired infections have impaired functional recovery, as assessed with the Basso Mouse Scale and activity box, after SCI compared to SCI mice without infection. Using immunohistochemistry we have identified some of the underlying effects leading to functional impairment after infection. Together this model can be used to develop future therapies for SCI patients in order to preserve rehabilitation potential.

7. **Effects of reproductive experience on acute neuroimmune outcomes following traumatic brain injury in mice**

SPOTLIGHT

'Rachel Gilfarb | Department: Psychology | Level: Graduate Student
Co-Authors: Elise Lemanski, John Velasquez, Zoe Tapp, Sydney Cornelius, Dr. Olga N. Kokiko-Cochran, Dr. Benedetta Leuner

Intimate partner violence (IPV)is a leading cause of traumatic brain injury (TBI)in women, with pregnant women or women with children in the home at the highest risk for acquiring a TBI. Although pregnancy induces profound acute and long-term physiological changes, the consequences of such changes on brain injury susceptibility and outcomes are unclear. Here, we examined the effects of parity (previous pregnancy and maternal experience) on the acute neuroinflammatory response to TBI induced by lateral fluid percussion injury (FPI). Multiparous females (2-3 pregnancies and motherhood experiences) and age-matched nulliparous (no previous pregnancy and motherhood experience) females received either FPI or sham injury. Brain tissue was collected 3 days post-injury and immunohistochemically labeled with: 1) Iba1, a marker of microglia, the brain's innate immune cells; 2) GFAP, to identify astrocytes;3) CD68, a marker of macrophages; 4) CD45, to label a subset of hematopoietic immune cells; and 5) aquaporin 4 (AQP4), a water transport protein integral to the maintenance of the blood brain barrier. We show that corticalIba1immunolabeling increased following injury independent of parity. Near the site of injury, the number of de ramified Iba1+cells, a morphological type of microglia associated with enhanced inflammatory signaling and mitigation of injury, did not differ between TBI groups. Similarly, TBI increased cortical GFAP immune labeling independent of parity. While no differences in cortical CD68 immuno labeling were observed between TBI groups, an interaction between parity and injury was evident in corticalCD45 labeling. Specifically, the number of CD45+ cells near the site of injury was higher in nulliparous compared to multiparous animals. Additionally, an interaction between parity and injury was evident in the extent of AQP4 labeling at the perivascular wall compared to the neuropil in nulliparous females, an effect not observed in multiparous females. Together these data suggest that previous parity can influence the acute neuroinflammatory response to TBI. These data confirm that FPI induces a cortical immune response independent of parity in microglia and astrocytes. However, these are the first data to demonstrate that previous parity may act as a factor in attenuating CD45+cell recruitment to the site of injury and maintaining AQP4 localization to the perivascular wall following TBI. As head injury can be a lifelong condition, parsing the effects of TBI in women with reproductive history —a population particularly vulnerable to IPV and associated TBI—can further develop treatments to improve quality of life following injury.

8. **Flexible, implantable biosensors allow precise measurement and recording of physiologic events**

Samuel Gillespie
Advisor: Jinghua Li

Flexible, implantable biosensors allow precise measurement and recording of physiologic events. Passive radio-frequency transmission could enable wireless neurotransmitter concentration sensing for brain injury diagnosis, treatment, and non-invasive monitoring. In-situ brain ion and neurotransmitter concentration changes have been shown as accurate diagnostic criteria for neuro-trauma and neuro-disorders. This research aims to investigate the feasibility of aptamer-functionalized gold interfaces in future implantable biosensors. Specifically, this experiment examines the field effect of serotonin aptamer functionalized gold interacting in known concentrations of serotonin in various solvents. If physiologically sound, the interface could be used in existing biosensors for brain ion and neurotransmitter concentration information. Information could be transmitted wirelessly for in-situ brain monitoring and diagnosis using existing flexible biosensor technology.
Serotonin Aptamer (1E-5M) is a specific chain of oligonucleotides known to bind to serotonin ligand sites. Functionalization of the 1E-5M aptamer was done via reduction with a thiol group that forms a covalent bond with the gold electrode. When serotonin enters the gold- aptamer interface, the binding and folding of 1E-5M aptamer around the serotonin deviates the existing electric field on the surface of the gold electrode.

After aptamer functionalization of the gold electrode, initial open circuit potential (OCP) testing of the gold electrode in known-concentration, aqueous and phosphate buffered saline (PBS) solutions showed concentration sensitivity greater than baseline OCP tests. Experimental repeatability established the field effect could be used to test for neurotransmitter concentration repeatedly. Field effect transistor (FET) testing was used post-OCP for wireless sensitivity verification. These results suggest aptamer-gold interfaces able to accurately test a range of neurotransmitter concentrations in aqueous and PBS solutions. Physiological feasibility and integration into existing biosensors are ongoing research work.

9. **Short-term high-fat diet consumption impairs long-term potentiation in the aged hippocampus**

Gonzalez Olmo, B.M.1,2, Zhao, F.4, Barrientos, R.M.2-5, & Askwith, C.

More Americans are consuming diets higher in saturated fats and refined sugars than ever before, and obesity rates among older adults alone have doubled since 1980. These trends could have serious consequences for the older population because in addition to the gradual memory declines observed with normal aging, high-fat diet (HFD) consumption, known to induce neuroinflammation, has been shown to aggravate and accelerate memory declines. Because obesity is a complex disease with many comorbidities, making the study of underlying mechanisms difficult and confounded, we employ a short-term diet manipulation protocol. We have previously demonstrated that short-term consumption (3 days) of a HFD among aged rats produced profound impairments to contextual and emotional/fear memories, which depend on an intact hippocampus and amygdala. These impairments were precipitated by increases in proinflammatory cytokines, primarily interleukin-1 beta ($IL-1\beta$), in both brain regions. Here, we explored the extent to which HFD consumption amongst aged rats disrupts hippocampal long-term potentiation (LTP), the form of synaptic plasticity thought to underlie long-term memory consolidation in mammals. Young adult (3 months old) and aged (24 months old) F344xBNF1 rats were assigned to either chow or HFD (containing 60% saturated fat) for three days. Using transverse hippocampal slices, we examined the individual and combined effects of age and diet on several forms of synaptic activity. Specifically, excitatory post-synaptic potentials were induced in the stratum radiatum of CA1and LTP expression was triggered with a theta-burst stimulation protocol. Our preliminary data demonstrate that late-phase LTP was particularly compromised by the combination of aging and HFD while LTP maintenance was robust in chow-fed young and aged rats. These findings suggest that the previously observed neuroinflammation-mediated hippocampal memory impairments in aged HFD-fed rats occurs, at least in part, through deterioration of synaptic plasticity, as measured by LTP, in the hippocampus. Future studies will examine LTP in the amygdala.

10. **Partial Least Squares analysis of Alzheimer's disease biomarkers, modifiable health variables, and gray matter volume in older adults with Mild Cognitive Impairment**

Alexander N. Hasselbach1, JessicaStark1, Kelly Hiersche1, Daniela J. Palombo3, Scott M. Hayes

To date, there is no pharmacological cure for age-or Alzheimer's-related cognitive decline, highlighting the need to identify modifiable variables that may protect against neurodegeneration or cognitive decline. The present study examines the relationships between modifiable physical/health variables and grey matter volume in a cohort of 142 older adult participants ages 55-88(mean = 74.3years, SD=7.5years) from the Alzheimer's Disease Neuroimaging Initiative. Participants were classified as having mild cognitive impairment (MCI). Gray matter volume was assessed using voxel-based morphometry ofT1-weighted MR images. Modifiable health variables associated with cardiometabolic risk (e.g., cholesterol), stress (e.g., cortisol), inflammation (e.g., c-reactive protein), and growth factors (e.g., brain-derived neurotrophic factor) were assessed, as previous research has shown a role for these variables in brain aging. To examine the relationship between modifiable health variables and gray matter volume, a Partial Least Squares Correlation (PLSC) analysis was employed. PLSC is a model-free multivariate technique which defines latent variables(LVs)in a dataset. Two LVs were identified, accounting for 18.82% and 11.68% of the cross-block covariance (ps < 0.05). The first LV had significant contributions from multiple AD biomarkers and several brain regions. Cerebrospinal fluid(CSF)Aβ1-42had a negative relationship to LV1, while CSF total tau, CSF phosphorylated tau181(p-Tau181), and the ratios of CSF total tau/ Aβand CSF p-tau181/Aβhad significant positive associations with LV1. Gray matter volume was positively associated with LV1in the cerebellum, precuneus, and prefrontal cortex and negatively associated with LV1 in the thalamus. The second LV had significant positive contributions from triglycerides, plasma a polipo protein E, interleukin-6 receptor, vascular endothelial growth factor, and plasma tau.LV2 was significantly negatively associated with gray matter volumes in the insula, striatum, medial temporal lobe, and anterior cingulate cortex. These results highlight the relationship between gray matter volume, modifiable health variables, and AD biomarkers.

11. **Examining the Relationship between Modifiable Health Variables and Cognition in Healthy Older Adults**

Kelly J. Hiersche1, Jessica Stark1, Alexander Hasselbach1, Scott M. Hayes1,21 Department of Psychology

Aging is marked by declines in cognitive functioning, yet there is significant variability in cognitive aging. Previous studies have linked individual differences in modifiable fitness metrics to a variety of cognitive functions. The current study aims to identify the relative contributions of physical health variables to cognitive performance in healthy older adults recruited through the Health and Retirement Study (HRS). HRS recruits a representative sample of adults over age 50 to complete a variety of cognitive, medical, and physical health assessments. Individuals who completed the 2016 core appointment and the 2016 harmonized cognition assessment protocol were included in the current analysis. Individuals with any of the following were excluded: diagnosis of Alzheimer's disease or dementia, prior stroke, Mini-Mental State Examination score < 24, endorsing yes on at least 4 of 10 depressive symptom questions, a previous psychiatric diagnosis, or excessive binge drinking (rate of at least 1 time per week over last three months). The analysis sample included 644 older adults (ages 64-98years, $\bar{X}$= 74.8, SD= 7.0). Hierarchical linear regression models were used to assess the relationship between modifiable physical health variables (body mass index, average time to walk 8 feet, dominant hand grip strength, and maximum air expelled in a puff breathing test), and composite measures of episodic memory, executive function, processing speed, and fluid reasoning. Modifiable health variables accounted for variance in each cognitive domain above and beyond demographic variables (age, sex, education, and a chronic disease score). These modifiable health variables explained the most variance in executive function and processing speed. Normal gait speed was the most important modifiable variable within this model. Results suggest that after accounting for effects of education, modifiable health variables are associated with performance in multiple domains of cognition in a large sample of healthy older adults. These findings support previous studies examining the relationship among modifiable physical health variables and cognition and extend the literature by demonstrating the relative strength of the relationship between gait speed and cognition.

12. **Functional reorganization of the visual word form area in an individual born without the left superior temporal lobe**

Jin Li, Evelina Fedorenko, Zeynep Saygin

The visual word form area (VWFA) is a highly experience-dependent region in left lateral ventral temporal cortex that responds selectively to visual words. Studies have shown that this region is preferentially connected to the left frontotemporal language network in literate adults. Strikingly, this pattern of preferential connectivity is already present in neonates, suggesting that connectivity to the language network may be critical for the formation of the VWFA and any neural specialization for reading. However, what happens in the absence of a typical language network at birth? We explored this question in an individual (EG) born without the left superior temporal lobe but with normal reading ability. We used fMRI to record brain activation to visual words, objects, faces, and scrambled words in both EG and typical adults (N=25). We first examined activation to words vs. other categories in the canonical left VWFA (lVWFA) with a univariate approach. No word-selective response was observed in EGand the response magnitude was significantly lower than that in typical adults. This anomaly was only observed for visual words in the lVWFA: face selectivity in the adjacent fusiform face area was typical. Moreover, we did not observe word selectivity in the right homologue of the VWFA (rVWFA)in EG. Next, we investigated whether EG had a distributed pattern of orthographic selectivity using a multivariate pattern analysis (MVPA). We applied MVPA searchlight analyses to compute split-half correlations between two runs of data and compared within-and between-category correlations across runs. In contrast to univariate analyses, we found a set of voxels in both the lVWFA and rVWFA that showed distinctive response patterns to words vs. other categories (i.e., words-words correlations were higher than words-faces) in EG. Further, within-category patterns were stronger for words than other categories (e.g., words-words correlations were higher than faces-faces). Interestingly, while the magnitude of correlations was comparable between EG and typical adults in both lVWFA and rVWFA, the size of these clusters was larger in the lVWFA in typical adults, while EG showed a larger cluster in the rVWFA; this larger recruitment of the rVWFA may reflect are mapping of the language network to the right hemisphere in EG. Overall, the current study suggests that in the absence of a left-lateralized language network, neural selectivity to visual words is highly atypical and that orthography may depend on a more distributed neural representation than that observed in typical literate adults.

13. **The effects of aging and high fat diet on intestinal inflammation and mitochondrial homeostasis**

Nashali Massa1,2, Michael J. Butler, PhD.2, and Ruth M. Barrientos, PhD

Emerging evidence has shown the impact of the immune system and gut dysfunction on neurodegenerative disorders, including Alzheimer's disease. Previous work from our lab has shown that short-term consumption of a high-fat diet (HFD) leads to memory deficits in aged, but not young, rats and that this behavioral change is driven by a potentiated neuroinflammatory phenotype that characterizes aging. That said, growing evidence suggests that alterations in gut homeostasis can impact the brain through different mechanisms, including neuroimmune signaling. Additionally, HFD consumption is known to induce activation of the TLR4/NF-kB signaling pathway and alter tight junction proteins in the gut, but little is known about the role of aging in this process. The proinflammatory phenotype present in aging has been highly associated with mitochondrial dysfunction, particularly in the brain. However, the role of mitochondrial homeostasis in the gut has not been extensively studied in rodents. Therefore, in this study, we investigated the effects of HFD on gut inflammation, permeability, and mitochondrial homeostasis in ileum and colon tissues of adult and aged rats. We will present data on pro-inflammatory markers such as interleukin 1 (IL-1), interleukin 6 (IL-6), and Tumor Necrosis Factor (TNF-a) measured via ELISAs. Gut permeability was assessed by quantifying the tight junction proteins, occlude in and claudin-1, through Western blots. This technique was also used to quantify mitochondrial homeostasis markers PTEN-induced kinase 1 (PINK-1), Mitochondrial E3 ubiquitin-protein ligase 1 (MUL-1), Peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PCG1a), Mitofusin-2 (MFN2), and Dynamin related protein 1 (DRP1).

14. **Speed and Straightness of Reach Change with Different Functional Tasks in Typically Developing Children**

Julia Mazzarella, DPT, PhD Candidate1, Daniel Richie, MA1, Ajit Chaudhari, PhD1, Eloisa Tudella, PhD2, and Jill Heathcock, MPT, PhD11School of Health and Rehabilitation Sciences

Background: Children reach for objects 100's of times daily, a skill that is challenging for many children with motor disabilities. 3D motion capture is frequently used to measure coordination of reach in children with motor disabilities. It would be beneficial to have normative values for variables of reach coordination in typically developing children. In this study, we measured average speed and straightness of hand movement in 3 functional reaching tasks in typically developing children. We hypothesized that there would be significant differences in speed and straightness between tasks and task phases. Methods: 71 (38 M, 33 F) typically developing children, 7-10 years old (mean 8.77 +/-.48) participated. Children were seated at a table, with reflective markers placed on their hands and arms. An object (cup of water, cracker, or ball) was positioned in front of the child. The task followed 4 phases: (1) hand to object (two hands for ball); (2) object to mouth; (3) object to the table; and (4) return hand(s) to start position. Participants completed 2 repetitions per object and per hand for the unilateral tasks. Movement was recorded by a 10-camera VICON system at 120 Hz and filtered with a low-pass Butterworth filter at 4 Hz. Dependent variables were average speed (mm/s) and straightness (length of hand path/length of movement) of hand movement. Linear mixed models for repeated measures were used to compare the variables by task and phase. Results: There were significant main effects for type and phase of task for speed. The unilateral reach for a cookie was significantly faster than the reach for the cup ($p<.05$). Phases (1) hand to object, (2) object to mouth, and (3) object to table were faster than (4) return to rest ($p<.05$). There were significant main effects for type and phase of task for straightness ratio ($p<.05$). The unilateral reach for a cup was straighter than the bilateral reach for a ball. Phases 2 and3were straighter than 1 and 4 ($p<.05$). Phase 1 was also straighter than phase 4 ($p<.05$). Conclusions / significance: Differences by task and phase might be due to prior experience, constraints of the task, or motivation to complete the task. These results provide insight into how coordination and timing of reach and grasp changes with different tasks in typically developing children. With a larger N, this data could be used as a normative comparison for age-matched children with motor disability.

15. **Innate organization of the human brain**

DATA BLITZ

Fiona Molloy, Saygin, Zeynep M. Department: Psychology
Presenter: Fiona Molloy
Level: Graduate Student

The human brain is composed of a multitude of areas with distinct roles in mental function; these regions connect and interact with a set of other brain regions, forming functional networks which are the basis of large-scale information processing in the brain. These functional networks can be reliably identified in human adults as well as other species, and small individual differences in connectomes may contribute to individual differences in behavior. Here, we aim to characterize these functional networks in neonates scanned within one week of life. We use unsupervised learning to uncover underlying patterns in resting-state functional connectivity data from a large cohort of neonates (N = 267 full-term infants from the Developing Human Connectome Project). First, we present the neonate networks determined by optimal solutions in terms of fit to data and generalizability. We found symmetrical and hierarchical networks associated with sensorimotor, visual, default mode, ventral attention, and high-level vision areas. Second, we explored the inter- and intra-subject variability—finding that some networks, such as sensorimotor, were more homogeneous than other networks, such as ventral attention, across and within neonates. Fourth, we compared the neonate networks to those in adults (Yeo et al., 2011) and found similarities with sensorimotor, visual, dorsal and ventral attention, and default mode networks. However, frontoparietal and limbic networks were not discernable in the infant data. Finally, we investigated differential gene expression, determined by the Allen Human Brain Atlas, as a potential explanation for the emergence of these distinct networks, and quantified the similarity within and between networks. These results suggest that the basic network structure that is present in adults also exists at birth, but that there are some important differences, particularly in association cortex, that suggest a role for maturation and experience in developing adult-like networks.

16. **TLR4 Antagonism Ameliorates Persistent Post-Operative Cognitive Decline**

DATA BLITZ

Stephanie M Muscat*, Nicholas P Deems, Ruth M Barrientos
*Graduate Student, Institute for Behavioral Medicine Research

Premise: Post-operative cognitive decline (POCD) is a complication experienced by many surgical patients. POCD is characterized by cognitive impairments ranging from mild confusion to difficulty with executive functions to inability to form long-term memories to dementia. Persistent POCD, lasting weeks to months, is most commonly experienced by older individuals and is associated with an increased vulnerability to developing Alzheimer's Disease. Our previous work demonstrated that, in older rats, surgery alone evoked a neuroinflammatory response and hippocampal-dependent long-term memory dysfunction lasting 4 days. Treating the rats with morphine, often administered post-operatively for pain management, exaggerated and prolonged this surgery-induced inflammatory response, leading to persistent POCD lasting at least 8 weeks. Here, we explored the role of toll-like receptor 4 (TLR4) in this process. TLR4 is an innate immune pattern recognition receptor expressed by microglia. Importantly, activation of TLR4 initiates a proinflammatory cytokine cascade. With age, microglia naturally become sensitized, exhibiting greater expression of TLR4, and increasing the likelihood of exaggerated neuroimmune responses following a challenge. Of note, exaggerated neuroinflammation potently inhibits synaptic plasticity necessary for long-term memory. Interestingly, morphine has recently been shown to have an inflammatory role via TLR4 activation. We hypothesized that surgery, aging, and morphine synergize via TLR4 activation to cause persistent POCD. Methods: We subjected 24-month-old male rats to laparotomy as a model of POCD and administered analgesic morphine for 1 week. Two separate experiments were performed: 1) a single, central pre-operative injection of the TLR4-specific antagonist lipopolysaccharide from the bacterium Rhodobacter sphaeroides (LPS-RS) was administered, 2) LPS-RS was centrally administered 1x/d x7d beginning the day after the last morphine injection post-operatively. For both experiments, hippocampal-dependent long-term memory was assessed 4 weeks after surgery using a contextual fear conditioning paradigm. Results: While a single pre-operative injection of the TLR4 antagonist LPS-RS was insufficient to prevent persistent POCD, the post-operative injection regimen was found to ameliorate the POCD memory impairments in a dose-dependent manner. These results indicate that TLR4 plays a mediating role in the development of persistent POCD, although the dynamics of this process remain to be elucidated. These data also suggest that blocking central TLR4 activation may be a promising therapeutic to treat POCD.

17. **Brain Injury, Regulating Cognition and Affect in Response to Stressors, Food Insecurity, and Pro-smoking Social Situations: factors to consider in cessation intervention targeted to the needs of homeless youth**

Julianna Nemeth, PhD, Assistant Professor, The Ohio State University, College of Public Health Additional Authors: Alice Hinton, PhD; Joseph M. Macisco, MPH; Amy Wermert, MPH, Allison Glasser, MPH; Hannah Kemble, BSPH; Joanne G. Patterson, PhD, MPH; Carra Gilson, MPH; Jacob Caponi, BSPH; Emma Bolkovac; Lucas Hatzer

Abstract Body: 70%+of homeless youth (14-24 yrs. old) smoke combustible tobacco. Most try to quit without success. Study Aim. Identify mechanisms to target in intervention impacting homeless youths' engagement and success with cessation. Methods. Past-week combustible tobacco users were recruited from a homeless youth drop-in center for interviewer-administered survey in January-February2020. Sample. Participants (n=96) were on average 22 years old, persons of color (84.4%), and heterosexual (74.0%). Findings.87% of participants reported at least one exposure to blunt force head trauma that can result in traumatic brain injury (TBI), and 64.9% to oxygen deprivation that can lead to Hypoxic Anoxic Injuries (HAI). 60.4% of participants reported exposures to BOTH blunt force head trauma and oxygen deprivation AND to symptoms indicating probable TBI/HAI. Probable TBI/HAI was associated with higher perceived stress, self-blame for housing situation, affect regulation and anger control difficulties, including dysregulated-expression—all mechanisms associated with behavioral change intervention failure. Among the entire sample, the odds of 30-day quit interest were lower for those motivated to smoke for affect regulation, higher for those in denial about or disengagement from coping with one's housing situation, and higher for those who endorsed smoking as an excuse to get out of a dangerous situation. Whereas more temptation to smoke socially, due to habit, or to keep hands busy, using 2+ tobacco products rather than eating when hungry, and lower confidence in quitting were associated with higher nicotine dependence. Discussion. Factors identified need to be addressed in cessation targeted to the needs of homeless youth.

18. **Impaired Glial IL-10 / TGFβ Signaling Underlies the Exaggerated Sickness Response in Aged Mice**

DATA BLITZ

Shane M. O'Neil1,2,3, Emma E. Hans3, Starr Jiang3, Lynde Wangler1,2,3, Jonathan P. Godbout2,3,4 (1) Neuroscience Graduate Program, (2) Department of Neuroscience (3) Institute for Behavioral Medicine Research (4) Chronic Brain Injury Program, The Ohio State University

Microglia and astrocytes, cells with major immune functions in the central nervous system, exhibit a robust pro-inflammatory phenotype as a function of aging. Microglia develop a pro-inflammatory, "primed" profile with age, which is characterized by increased expression of inflammatory mediators. With aging, this altered neuro-immune communication results in heightened risk of mortality and co-morbidity of depression or dementia. For instance, bacterial infection in elderly patients often presents as acute cognitive impairment and altered mood. Moreover, these individuals are at an increased risk for progressive dementia and cognitive impairment after the infection resolves. Moreover, this age-associated phenotype persists in mice when microglia are renewed with young cells, implicating a microglia-extrinsic mechanism for priming. Therefore, we used single-cell RNA-sequencing (scRNA-Seq) to identify cell- and time-specific responses to a peripheral immune response in both adult and aged mice.

After immune activation, microglia have a differential transcriptional trajectory based on age. In adults, microglia produce interleukin (IL)-10, an anti-inflammatory cytokine. In response to IL-10, astrocytes produce transforming growth factor beta (TGFβ), which completes a negative feedback loop and attenuates microglial activation. Using data gathered from our scRNA-Seq approach, we hypothesized impaired glial interleukin IL-10 / TGFβ signaling underlies the exaggerated sickness response in aged mice. As a result of normal aging, astrocytes express decreased levels of IL-10R and, as a result, produce decreased levels of TGFβ in response to IL-10 signaling. This impaired negative feedback results in exaggerated and prolonged neuroinflammation after peripheral immune activation in aged mice compared to adults. Moreover, our results show genetic knock-out of IL-10R on astrocytes recapitulates these effects in adult mice, as shown by increased social avoidance for an extended period of time and increased pro-inflammatory cytokine expression in the brain after peripheral lipopolysaccharide (LPS) administration.

These data indicate impaired IL-10 / TGFβ signaling between microglia and astrocytes is sufficient to produce an exaggerated and prolonged neuroinflammatory sickness response to a peripheral immune challenge. Our data provides a novel therapeutic target for treating the cognitive dysfunction affecting the elderly population after a peripheral infection, such as a respiratory or urinary tract infection. Furthermore, our novel scRNA-Seq data elucidates the temporal and cell-specific sickness response to peripheral infection in adult and aged mice, giving us further insight into the molecular mechanisms underlying the age-associated neuroinflammatory response to peripheral infection.

19. **Chronic inflammation and Cognitive Deterioration after Diffuse Brain Injury are dependent on activation of the Stimulator of Interferon Genes (STING) and increased type I interferon signaling.**

Jonathan M. Packer, Chelsea E. Bray, Mollie Witzel, Michelle Ouvina, Nico Beckman, Dunni Adelkunle-Adegbite, and Jonathan P. Godbout

Neuropsychiatric complications including depression and cognitive decline develop, persist, and even worsen in the years after traumatic brain injury (TBI), negatively affecting the quality of life and lifespan. Mounting evidence indicates that chronic inflammatory processes are elevated post TBI, but the mechanism that drives this response is unclear. We previously reported that microglia, innate immune cells in the brain, were the primary drivers of chronic inflammation following diffuse TBI in mice. Moreover, the subacute phase of cortical inflammation 7 days post-TBI was dominated by a robust type 1 interferon (IFN) response. Thus, we hypothesize that increased type I interferon signaling is critical in promoting microglial dysfunction and the subsequent transition from acute inflammation to chronic neuroinflammation after brain injury. In the current study, we targeted a key upstream regulator of IFN signaling, the stimulator of Interferon Genes (STING), for intervention. In these experiments, WT and STING knockout (KO) C57Bl6 mice received a diffuse brain injury (induced midline fluid percussion) and indicators of neuroinflammation and functional recovery were determined7 and 30 days post injury (dpi). As expected, inflammatory (Cd68, Tlr4, C1q) and type-1 interferon associated genes (Tmem173, Irf3, Ifi27) were increased 7 dpi in the cortex of TBI mice compared to controls. Moreover, these TBI associated increases in IFN signaling 7 dpi were attenuated in STING KO mice. Furthermore, attenuation of the IFN associated genes in these STINGKO mice was paralleled by reduced chronic inflammation 30 dpi. At 30 dpi, there were deficits in both cortical and hippocampal dependent memory. These cognitive deficits at 30 dpi, however, were ameliorated by STING KO. Taken together, these data provide evidence that reducing type I IFN signaling after TBI with a STING-dependent intervention was effective in reducing chronic inflammation and improving functional recovery.

20. **Resolving Misalignment Limitations of Wireless and Batteryless Brain Implants**

DATA BLITZ

Mihir Patil (Graduate student) and Asimina Kiourti
ElectroScience Laboratory, Dept. of Electrical and Computer Engineering

Deep brain neuropotential monitoring offers unprecedented opportunities for patients with epilepsy, Alzheimer's, Parkinson's, etc., in addition to the advancement of neural modeling [1]–[4]. Traditional neurosensing technologies employ intracranial wires, but these devices inhibit the activities of daily life (thus limiting the testing environment) and are prone to infection [2], [4]. To overcome these issues, wireless implants have been reported but utilize batteries or energy harvesters for operation [5]. These battery-powered devices require replacement/recharging and can damage the surrounding neurons due to heat generation [6]. As an alternative, we proposed a new class of wireless, batteryless brain implants. In [7], we introduced a wireless, batteryless brain implant with a footprint of only 8.7 mm × 10 mm and sensitivity up to 20 µVpp in in vitro settings. This sensitivity was an improvement of up to 25 times compared to previous works and achieves the goal of detecting low voltage neural signals, viz. local field potentials (LFPs). However, the implant and wearable interrogator (antenna used to receive the neural signal) pair [7] is highly prone to misalignment. Slight shift of the interrogator/implant in the 3D space introduces significant losses into the system. These losses become a significant source of error in sensitivity because of the lack of an implanted battery and hence an implanted amplifier in the first place. Thus, in scenarios when the antennas are not in line of sight, the sensitivity is degraded, and the local field potentials are no longer detectable. To overcome this limitation, we propose a new brain implant with a footprint of 8 × 8 mm and a new wearable interrogator of 16 × 16 mm. This antenna pair can detect local field potentials up to 20 µVpp and is robust to misalignment losses: maximum loss introduced for ±4 mm shift is reduced to 2 dB as compared to 15 dB in [7]. Our next steps are to verify the obtained results in vivo. This will be a significant move towards our final goal of designing wireless and batteryless brain implants for operation in the individual's natural environment.

21. **Minocycline is ineffective in treating brain injury-induced impulsive and attention deficits**

Kristen Pechacek | Neuroscience | Graduate Student Pechacek, K.M., Reck, A.M., and Vonder Haar, C.

Traumatic brain injury (TBI) affects nearly 2.8 million in the United States alone and often results in psychiatric impairments such as impulsivity and inattention. Moreover, chronic neuroinflammation is linked to both TBI and various psychiatric disorders that present with similar symptoms (e.g., ADHD). Thus, treatments targeting neuroinflammation may relieve post-injury psychiatric-like symptoms. Minocycline is a broad-spectrum antibiotic that has anti-inflammatory properties. The purpose of this study was to determine if minocycline could be used to treat TBI-induced impulsivity and attention deficits. Rats were trained on an operant task, the five-choice serial reaction time task, a measure of impulsivity and attention, then received a severe bilateral frontal controlled cortical impact injury or sham injury. Minocycline or saline was given via intraperitoneal injections at 45 mg/kg every 12 hours for 5 days and started at either 1 hour or 9 weeks post-injury. TBI induced chronic impairments in impulsivity and attention deficits ($p < 0.001$;$p < 0.001$). Minocycline at both the early and late time points was ineffective in reducing post-TBI impulsivity and attention deficits ($p = 0.672$;$p = 0.903$; 0.654;$p = 0.075$). TBI had no effect on IBA-1+ cells at 13 weeks post-injury in the prelimbic, orbital frontal cortex, or hippocampus ($p = 0.817$;$p = 0.172$;$p = 0.094$). Overall, minocycline failed to treat TBI-induced impulsivity and attention deficits, and alternative treatments should be explored.

22. **Using video footage to characterize potential concussive events in soccer**

DATA BLITZ

Tara Porfido, PT, DPT Department: Rehabilitation and Movement Sciences Level: PhD candidate Co-authors: Jessica Gutt, BS, SPT, Conor Wentworth, BS, SPT, Jaclyn Caccese, PhD, Kerry Peek, PhD, PT, Abigail C Bretzin, PhD, ATC, & Carrie Esopenko, PhD

Background: Soccer is the only sport in the world where players purposefully use their heads to redirect the ball, leaving them at risk of experiencing sports-related concussions (SRCs). Understanding the mechanism of SRCs in soccer can aid in identifying individuals and situations that increase risk of SRC. Video observation has been suggested to be a valuable tool to characterize mechanisms of injury. Our aim was to develop a standardized tool to characterize potential concussive events (PCEs) from soccer match video footage, assess the tool's reliability, and examine PCE characteristics. Methods: An existing tool with established reliability for characterizing mechanisms of SRCs (Heads-Up Checklist [HUC]) was modified to include soccer-specific match characteristics (soccer HUC). Two trained reviewers used the soccer HUC to characterize PCEs in 38 male and female collegiate soccer matches. Cohen's Kappa was used to assess interrater reliability. Consensus values were examined using frequency analyses. Chi-square analyses were used to determine whether the distribution of characteristics for each PCE were consistent between male and female soccer athletes. Results: Using the soccer HUC with 2 reviewers did not yield acceptable reliability for all PCE characteristics. However, when a third reviewer was included, high reliability and consensus were achieved for the majority of PCE characterizations (96.7%). All PCE characteristics were consistent between the male and female athletes (p's>0.05). Conclusion: Our results suggest that the soccer HUC can be used as a standardized method to characterize PCEs from video footage of male and female soccer matches.

23. **Bio-Matched Antennas for Non-Invasive Brain Temperature Sensing**

Allyanna Rice, Katrina Guido, Alexandra Bringer, and Asimina Kiourti Electro Science Laboratory

Edu Various studies have shown potential links between an increase in brain temperature following traumatic brain injury and worsened histopathological outcomes, as well as the efficacy of maintaining hypothermic conditions in the brain to decrease such negative effects [1-3]. As such, monitoring brain temperature over the course of an injury could detect inflammation that could otherwise go undetected. Unfortunately, current standards of care to determine brain or core temperature (defined as the temperature of blood at the hypothalamus [4]) are either inaccurate or highly invasive. Non-invasive microwave radio meters have been proposed as a solution, but the technological limitations inherent to previous systems (e.g. narrowband antennas and unrealistic models) reduce measurement accuracy and efficacy below what is considered clinically acceptable[5-9].To address shortcomings in the state of the art, we build on prior work performed by our team on: (a) bio-matched antennas to enable broadband, into-body measurements [10], (b) radiative transfer models [11], and (c) microwave radiometers [12] that have non-invasively and accurately retrieved the temperature profiles of layered ice sheets (similar to how human body tissues are layered).We are designing and testing a wideband microwave radiometry system to non-invasively and accurately determine a temperature versus depth profile of the human brain. To date, we have combined the broad band bio-matched antenna and radiometer to perform repeatable measurements on single-layer brain phantoms. Thus far, the calibrated radiometer data shows good agreement with our coherent modeler presentation of a given experiment. Additionally, we have performed a fabrication and reproducibility study of our antennas to determine shortcomings and guide improvements. We are currently exploring thermal isolation between the antenna and phantom to further improve accuracy of the coherent model, stable high-permittivity materials for more long-term and robust implementation of the antenna in the system, and optimization of the antenna for our target frequency range.

24. **Sleep Fragmentation Enhances Inflammation and Compromises Stress-Responsive Neuronal Activity following Traumatic Brain Injury**

Zoe Tapp, Julia Kumar, Sydney Cornelius, Alexa Oberster, Ravi Atluri, Kristina Witcher, Sam Houle, Chelsea Bray, John Velasquez, Zachary Zimomra, Juan Peng, John Sheridan, Jonathan Godbout, Olga Kokiko-Cochran

Traumatic brain injury (TBI) impairs the body's ability to restore homeostasis in response to stressors, indicating dysregulation of the hypothalamic-pituitary-adrenal (HPA)-axis. We hypothesize that sleep fragmentation (SF) is a physiologically relevant stressor that engages the dysfunctional HPA-axis after TBI and exacerbates post-injury neuroinflammation. To test this, male and female mice were given moderate lateral fluid percussion TBI or sham injury and left undisturbed or exposed to daily, transient SF for 7- or 30-dayspost-injury (DPI). At 7 DPI, cortical gene expression of interferon (Irf7, Ifit2)-and stress (Bcl6, Tnfaip3)-associated genes were uniquely increased in TBI SF mice compared to controls. This occurred in conjunction with increased phosphorylated glucocorticoid receptor (GR) and disrupted neuronal activity in the hippocampus, a key intersection of the stress-immune axes after TBI. By 30 DPI, cortical microgliosis was enhanced in a region dependent manner with TBI SF and pro-inflammatory signaling genes (Hspb1, Ccl2, Tgfb1) were distinctly elevated compared to controls. Within the hippocampus, TBI SF mice displayed exaggerated microgliosis as well as an imbalance of neuronal activity in the CA1 and CA3. Moreover, integration of the stress response to post-injury SF was further disrupted in the bed nucleus of the stria terminalis and PVN in TBI mice compared to controls. Together, these data demonstrate that post-injury SF engages stress-responsive brain regions and alters the neuroinflammatory environment, potentially through GR-mediated pathways. Further elaboration on stress-immune consequences of sleep disruption after TBI may be critical in improving chronic outcome.

25. **Brain Injury in Female Rats Increases Impulsivity on the Rodent Gambling Task but is not Treated by Neuromodulation Neuromodulation**

Sarah Wampler, Department of Neuroscience Graduate Student Wampler, S. and Vonder Haar, C.

Traumatic brain injury (TBI) often results in chronic deficits in decision making and impulsivity. Impaired dopaminergic neuron function is a potential contributor to these impairments. Cathodal transcranial direct current stimulation (tDCS), a form of neuromodulation, has been shown to increase dopamine levels in the brain. Therefore, it may be an effective treatment strategy for long-term cognitive deficits in patients with TBI. Our lab previously demonstrated that tDCS reduced impulsivity in male rats after TBI. The purpose of this study was to determine how TBI affected female rats' decision-making and impulsivity and to evaluate if tDCS could treat such deficits. Rats were trained on the Rodent Gambling Task (RGT) which measures risk-based decision-making and motor impulsivity. During the task, rats chose between options of varying probabilities and magnitudes of reinforcement and punishment. Once responding stabilized, rats were given a bilateral frontal controlled cortical impact injury. After establishing a new baseline of responding following injury (7weeks), tDCS (cathodal, 10 min, 800 μA) was delivered two hours prior to testing for seven days in a cross-over design. There was an increase in impulsivity after injury similar to the effect seen in males; however, unlike in males, there were no changes in decision-making. Treatment with tDCS had no effect on impulsivity or decision-making. Given the behavioral differences after injury and the different effects from tDCS, it is important to continue to investigate the effects of TBI in females to better understand why differences occur between males and females.

26. **Harnessing structural and functional reorganization of neuronal circuits after stroke**

Antonia Zouridakis, Department of Neuroscience, Undergraduate, Co-authors: Larson, M., Moon, L.D.S., Tedeschi A.

Axon growth and regeneration failure causes neurological deficits and long-term disability after a variety of central nervous system trauma including brain and spinal cord injury (SCI). We recently found that the α2δ2 subunit of voltage-gated calcium channels negatively regulates axon growth and regeneration of corticospinal neurons, the cells that originate the corticospinal tract. Increased α2δ2 expression in corticospinal neurons contributed to loss of corticospinal regrowth ability during postnatal development and after SCI. In contrast, α2δ2 pharmacological blockade through gabapentinoids administration promoted corticospinal structural plasticity and regeneration after SCI in adulthood. We now provide evidence that the same treatment strategy effectively promotes corticospinal plasticity after stroke in adult mice. We demonstrated sprouting corticospinal axons form synapses and functionally integrate into spinal circuits, effectively contributing to recovery of forelimb functions in mice administered gabapentinoids. Thus, targeting α2δ2 with a clinically relevant treatment strategy aids repair of motor circuits after stroke.