DIRECTORY OF GRANT AWARDS
2022 GRANT CYCLE

NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH

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MARCH 2022

NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH

This data was compiled in compliance with the New Jersey Commission on Brain Injury Research's statutory mandate, N.J.S.A. 52:9EE-1" …to compile a directory of brain injury research being conducted in the State."

The information contained within this directory is not all-inclusive. The research projects and researchers listed in this directory are all based in the State of New Jersey and have applied to and received funding during the fiscal year 2022 grant cycle. The research projects are not categorized, or listed in any order.

This directory is not a complete listing of all scientific research being performed within the State of New Jersey due to the proprietary nature of the research being conducted at various institutions throughout the State. In addition, institutions are not obligated to share their research information with the New Jersey Commission on Brain Injury Research.

Please feel free to contact the New Jersey Commission on Brain Injury Research at P.O. Box 360, 369 S. Warren Street, Trenton, New Jersey, 08625. The Commission's office can be reached by telephone at 609-913-5010, by fax at 609-943-4213, or by e-mail at NJCBIR@doh.nj.gov.

For information on the New Jersey Commission on Brain Injury Research's grant award process, grant applications and deadlines, please see: www.state.nj.us/health/njcbir.

2022 MEMBERSHIP INFORMATION

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NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH

GRANT AWARDS

PILOT RESEARCH GRANT RECIPIENT:

CBIR22PIL018
Sona Patel, Ph.D.
Seton Hall University
$180,000

Project Title: *Speech Indicators of Dysfunction and Recovery following Mild Traumatic Brain Injury*

We seek to identify speech changes after mTBI in order to develop a sensitive, fast, and accessible method of detecting the presence of concussion and monitoring changes during the recovery process. The growing concern of brain diseases resulting from repetitive concussions calls for a more sensitive protocol for detecting total symptoms and objectively monitoring recovery of athletes with concussion. Current assessments have improved in recent years to expand beyond physical evaluation with components measuring cognition and psychological status. However, these tests are basic and do not capture the full array of cognitive domains that may be impacted in mTBI. More sensitive assessments have not been adopted in standard of care, due in part to the cost of time and resources associated. The ability to detect changes in the brain using fast and easy measurements, such as speech changes, could radically change concussion evaluation. Acoustic changes for speech also convey emotional and physiological, information beyond what is said. Recent research also shows that speech is a robust indicator of brain damage. Further, speech production is a natural metric for measuring total symptoms in concussion as it is generated through a combination of thought (cognition), movement (physical), and emotion (psychology). The possibility of evaluating whether or not a child has sustained a concussion simply by talking into an iPad or phone is powerful. The goal of this research is to use speech metrics as a means for more precisely detecting concussion symptoms. By obtaining more accurate estimates of injury and progression in recovery, we hope to be able to make recommendations of academic accommodations during recovery, inform the RTP process, and minimize the risk of secondary concussion in our young athletes. Establishment of such metrics for refined assessment of concussions will result in a direct and easily transferable impact on the standard of care, thus improving the health, safety, and rehabilitation outcomes of student athletes with concussion in New Jersey.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR22PIL002
Xiaobo Li, Ph.D.
New Jersey Institute of Technology
$180,000

Project Title: *Early brain predictors for psychopathology progression in adolescents with childhood TBI*

This study will apply the innovative ensemble learning approach in longitudinal data to identify and validate early brain predictors for psychopathology progression in adolescents with childhood TBI.

Traumatic Brain Injury (TBI) in children is a major public health problem. About 35% of children develop severe attention deficits within two years of their TBI, who were found to have heightened risk for developing severe psychopathology in late adolescence. Identification of early brain markers that can precisely predict later psychopathology progression in children with TBI is urgently expected for the development of refined early prevention and long-term intervention strategies.

Our neuroimaging studies in children with post-TBI attention deficits (TBI-A) and matched controls have revealed structural and functional brain abnormalities in frontal and parietal lobes that were associated with inattention problems in children with TBI-A. Functional alterations in fusiform gyrus (FG) have also been observed in TBI-A. FG anomalies have been found to play critical role in severe psychopathology, especially psychosocial and emotional dysregulation and psychosis. Based on these prior studies, we hypothesize that post-TBI structural and functional alterations in FG, frontal and parietal lobes will contribute to severe late adolescence psychopathology, with the FG significantly involved in anxious/depressed, social and thought problems, while frontal and parietal anomalies involved in attention problems.

The proposed project will re-evaluate 153 subjects in our child TBI study cohort at their 16-19 years of age, by re-collecting clinical, behavioral, and age-appropriate psychopathology measures. The baseline and follow-up time point measurements will allow us to assess the longitudinal behavioral changes and their interactions with early markers of anatomical and functional brain abnormalities. By utilizing a machine learning approach, we will identify and validate the most significant early brain markers for precisely predicating severe psychopathology in late adolescence.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR22PIL020
Bonnie Firestein, Ph.D.
Rutgers, The State University of NJ
Dept. Cell Biology & Neuroscience
$180,000

Project Title: *Metabolic Mechanisms for Recovery after mild TBI*

The current studies address whether therapeutics that change metabolism can be used to promote recovery after a single mild TBI or concussion, paving the way for future drug development for humans.

Concussion, or mild traumatic brain injury (mTBI), is the most common neurological condition seen in both children and adults, and the incidence of concussions is increasing with a growing awareness of the possible consequences of repetitive concussions on brain health. After a TBI, there is a loss of coenzymes that are involved in energy metabolism and production in neurons. With previous funding from the NJCBIR, we identified two small molecule compounds that protect neurons from injury, promote nerve cell function, and protect learning and memory in animals with TBI. However, it is currently unknown 1) if these molecules can be used as a therapeutic for concussion and 2) if these molecules replace the lost coenzymes. Experiments will not only test whether our small molecules hold potential but also will elucidate metabolic changes to the brain after concussion and during development, leading to much needed therapies for those who have suffered a concussion.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR22PIL003
Nancy Chiaravalloti, Ph.D.
Kessler Foundation
$169,383

Project Title: *Examining the Long-term Neurological Impact of COVID-19 in Individuals with TBI*

The current study examines the long-term impact of COVID-19 on individuals with moderate-severe TBI as compared with neurologically healthy individuals in cognitive and neurological functioning.

Growing evidence suggests that COVID-19 impacts the brain and neurological symptoms often persist after recovery from the virus. Individuals with underlying neurological impairment, such as traumatic brain injury (TBI), are vulnerable to infection with COVID-19, and those who are infected have worse outcomes. The current study examines the neurological consequences of COVID-19 in individuals with moderate to severe TBI in comparison to those without TBI.

Kessler Foundation (KF, NJ) and the Icahn School of Medicine at Mount Sinai (ISMMS, NY City) have pre-COVID-19, baseline cognitive data for 633 individuals with TBI, and 270 healthy individuals, as well as baseline neuroimaging data on 204 individuals with TBI and 147 healthy individuals. We will identify participants with and without TBI who have been diagnosed with COVID-19 and re-evaluate their cognitive and neurological functioning with annual follow-ups. We will thus be able to directly compare the cognitive and neurological status of those with TBI who had COVID-19, to pre-COVID neurologically healthy individuals.

The proposed work will represent an important contribution to the COVID-19 literature in that we will document changes in cognitive and neurological functioning from pre- to post-COVID-19 in individuals with and without TBI and continue to monitor change over time. Subsequent projects will follow these patients long-term. Additional future directions will examine both the risk for cognitive decline and late-in-life ramifications, such as dementia, and develop and evaluate treatment options for neurological symptoms. Given that individuals with TBI are already at elevated risk for dementia, and that COVID-19 may ALSO serve an independent risk factor for cognitive decline, the longitudinal follow-up of this sample is imperative to manage future cognitive decline, maximize quality of life and facilitate continued inclusion into society.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR22PIL029
Jean Lengenfelder, Ph.D.
Kessler Foundation
$175,996

Project Title: *Improving Social Skills for Young Adults with Brain Injury*

The current proposal will apply an existing treatment to improve social skills, previously utilized in autism, to youth who have sustained a TBI.

Social skills are important in our relationships with others such as friends, family, teachers and employers. As young adults with TBI finish school and enter the workforce, social skills are important to secure a job as well as maintain their job.

The current study applies a social skills program to youth with TBI in the critical age where they will be transitioning from school to work. The program, The Assistive Soft Skills and Employment Training (ASSET), has been used with young adults with autism with very positive results, improving performance of social skills as well as self-confidence, depression and anxiety. The current study would apply ASSET, a 15 sessions treatment, to individuals with TBI between the ages of 15 and 25 in small groups of 4 to 6 people to improve social skills.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR22PIL016
Michael Matise, Ph.D.
Rutgers, The State University of NJ
Biomedical & Health Sciences
$180,000

Project Title: *Role of Hh-responsive astrocytes in restoring homeostasis following acute cortical injury*

The goal of the proposal is to gain a better understanding of the cellular and molecular mechanisms that regulate the response of a sub-population of astrocytes to TBI in a rodent model system.

The goal of the proposal is to better understand of the mechanisms that regulate the response to, and repair of, traumatic brain injuries (TBI) in a rodent model system. We have found that a subset of astrocytes in the brain are under the control of the Sonic hedgehog (Shh) signaling factor that plays a key role in CNS diseases and injuries. Shh sensitive astrocytes respond to traumatic brain injury (TBI) by becoming hypertrophic, re-entering the cell cycle to generate new astrocytes, and contributing to the glial scar and repair of the blood-brain barrier (BBB). We have also found that cortical astrocytes under the control of Shh signaling respond to TBI by first shutting down their sensitivity to the pathway and then re-acquiring sensitivity at later stages during glial scar formation and BBB restoration. Furthermore, our preliminary data shows that the BBB fails to be repaired in the spinal cord of mice in which the Shh pathway has been blocked in reactive astrocytes, suggesting a crucial role in CNS injury repair. Together, these data support our hypothesis that proper modulation of Hh signaling in cortical astrocytes is required for their reactive response and restoration of tissue homeostasis following TBI.

The current pilot study proposal will address this hypothesis by using molecular genetic tools to selectively manipulate the Shh pathway in reactive cortical astrocytes following TBI. The study will comprise two specific aims that will combine conditional mutagenesis (gene inactivation and activation), genetic lineage tracing, and surgically induced TBI.

Results from our work will lay the foundation for future efforts to determine whether manipulation of the Hh pathway could increase the efficacy of CNS repair following TBI. Many small-molecule compounds that regulate Hh signaling both positively and negatively have already been identified, allowing for rapid development of potential new therapies from the bench to the bedside.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR22PIL026
Annika Barber, Ph.D.
Rutgers, The State University of NJ
Waksman Inst of Microbiology
$173,898

Project Title: *Molecular and circuit mechanisms of traumatic brain injury-induced disruption of sleep and circadian rhythms in Drosophila*

This proposal uses a new fruit fly traumatic brain injury paradigm to investigate how traumatic brain injury alters neuronal function to cause sleep and circadian rhythm disorders.

Traumatic brain injury (TBI) contributes to one-third of all injury-related deaths in the United States, and the long-term complications resulting from TBI in survivors are complex and under-reported. These complications include dysregulated circadian rhythms and sleep disorders, which may underlie or exacerbate other elevated risks found in TBI survivors such as mood disorders, endocrine disorders, and neurodegenerative disease.

The goal of this project is to identify the how TBI causes neurological damage that disrupts daily activity patterns and sleep. Molecular circadian clocks in the brain coordinate the timing of biological systems within an animal with respect to each other and the environment. Misalignment of the timing of different biological functions can result in mood, metabolic and sleep disorders. This proposal will test how the time of injury affects health and survival to determine how molecular circadian clocks in the brain contribute to recovery from both single-incident and mild, repetitive TBI. Understanding the role of molecular circadian clocks in TBI recovery will help researchers design interventions that leverage our bodies' natural timing system to improve outcomes for TBI survivors. This project will also determine how TBI alters the function of neurons specialized in controlling daily biological rhythms and sleep to cause sleep and circadian rhythm disorders. After measuring the effects of TBI on daily activity timing and measures of sleep quantity and quality, we will examine how TBI damages the neurons regulating sleep and circadian rhythms. These pilot studies will set the stage for us to identify the processes that occur in the brain after injury that damage circuits, so that we can find new therapeutic targets that prevent progressive neuronal damage. We will also test how environmental and pharmacological treatments that improve sleep and circadian rhythms can improve outcomes for TBI survivors.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR22PIL022
Mark Zimering, MD., Ph.D.
Veterans Biomedical Research Institute
$180,000

Project Title: *Neurodegeneration after Traumatic Brain injury: Protection by Serotonin Receptor Peptide*

The goal is to determine whether a serotonin 2A receptor peptide decreases the risk of anhedonia and impaired pattern separation (dentate gyrus-dependent) after mild traumatic brain injury in adults. Traumatic brain injury (TBI) contributes to substantially increased global disability and has been associated with major depressive disorder through unknown mechanisms. Chronic inflammation increased autoantibodies to a serotonin receptor in the bloodstream of adults suffering with major depression. The autoantibodies were also found in blood of TBI patients having dementia and impaired thinking. A new drug was designed to bind the autoantibodies. Neurons in a specific brain region called dentate gyrus have many serotonin receptors which help in normal thinking and recovery from depression. Depressed patient autoantibodies bind to dentate gyrus neuron serotonin receptor interfering with memory and recovery from depression symptoms such as anhedonia, the inability to feel pleasure.

We propose to test Aim 1 whether the new serotonin peptide receptor drug given 1 day after TBI in rats prevents anhedonia and protects against the loss of pattern separation. In Aim 2, the dentate gyrus will be examined in the rat to determine if number, shape or maintaining proper location of neurons after TBI may explain drug's protective effect on maintenance of normal thinking in pattern separation task. Aim 3 will test whether higher autoantibody in blood in traumatic brain-injury patients predicts worsening performance on a pattern separation thinking task. The knowledge gained from the proposed studies could help validate the utility and advance the development of a new candidate serotonin receptor drug which could prevent a major symptom of depression (inability to feel pleasure) and lessen impaired thinking and memory following TBI. The knowledge and techniques resulting from the study can benefit persons in New Jersey and throughout the United States.

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