DIRECTORY OF GRANT AWARDS
2023 GRANT CYCLE

NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH

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MARCH 2023

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 2023 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.

2023 MEMBERSHIP INFORMATION

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NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH

GRANT AWARDS

PILOT RESEARCH GRANT RECIPIENT:

CBIR23PIL0003
David Devilbiss, Ph.D.
Rowan University
$177,665

Project Title: *Activation of cMet signaling as a novel treatment for cognitive deficits and neuroinflammation after traumatic brain injury.*

We will assess the efficacy of a novel candidate treatment that may be neuroprotective, reduce neuroinflammation, and act as a cognitive enhancer in a rat model of repetitive mild TBI.

Concussion and mild Traumatic Brain Injury (mTBI) represent nearly 90% of 15,000 TBIs in New Jersey and approximately 3 million Americans a year. One in 5 patients experiencing a single, mild TBI will exhibit memory, attention, and motor symptoms for more than a month. Repeated mTBI frequently occurs in athletes and military personnel, placing these family members at greater risk for persistent brain impairments and increased vulnerability to additional TBIs. Impaired brain function is central to difficulties returning to work and other activities affecting quality-of-life. However, there has been no consensus on the treatment of mTBI, and no FDA-approved treatment exists for TBI. A critical need exists to fund and develop treatments for post-injury mental impairments and underlying brain injury.

This study will test the hypothesis that activating the cMet receptor with the drug, dihexa will result in significant and enduring reduction of inflammation in the brain and improvement in cognitive/motor function after repeated mTBI. We will also determine whether cMet activation can prevent the cumulative effects of repeated mTBI and assess if females and males respond differently to dihexa treatment.

The PI and other groups have shown that dihexa can improve learning and memory in rodent models and humans with neurodegenerative disease. Additionally, dihexa and similar cMet receptor activators can act as a neuroprotectant to promote neuron survival. cMet activators are in clinical trials for Alzheimer's disease and exhibit similar procognitive and neuroprotectant activities as dihexa. This proposal is highly significant as it will be the first to characterize the efficacy of c-Met activation in a model of TBI. Furthermore, if successful, there is an accelerated path to the clinic using similar therapeutics already in clinical trials.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR23PIL010
Peii Chen, Ph.D.
Kessler Foundation
$173,949

Project Title: *Telerehabilitation to Restore Upper Limb Function in Chronic TBI*

The pilot study aims to inform the subsequent large-scale clinical trial focused on using telerehabilitation techniques and technologies to improve upper limb function and quality of life.

Upper limb (UL) function is often impaired and not fully recovered after moderate-to-severe traumatic brain injury (TBI), leading to devastating consequences and reducing quality of life. Clinicians have been encouraged to include UL rehabilitation, but existing evidence is insufficient to inform specific treatments for the TBI population. There is urgency to broaden the scientific evidence critical to advancing UL rehabilitation for TBI survivors, especially those living in the community with chronic UL impairment.

The proposed Pilot Research Project will examine two UL exercise programs through tele-rehabilitation (TeleRehab) techniques. Both programs are focused on functional tasks and daily activities. One program is implemented directly in the real-life home environment, the home-based arm and hand exercise (HAHE) program. The other program is delivered through simulated real-world scenarios, the exercise video game (Exergame) program. The HAHE program consists of UL exercises based on real-life activities that involve materials and objects readily available at home or easily obtained in regular stores. The Exergame program packages UL exercises into game-like activities delivered through a non-immersive virtual reality device.

Individuals with chronic UL impairment after moderate-to-severe TBI will participate in the proposed study. They will be randomly assigned to the HAHE or the Exergame program. Patients will complete 30 sessions of the assigned program over 6 weeks at home, with no immediate supervision. An occupational therapist will review the progress, assist in goal setting, and provide consultation to patients at the beginning of each week via a video call. We will determine which of the programs is effective, and whether the programs lead to similar or different outcomes.

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FELLOWSHIP RESEARCH GRANT RECIPIENT:

CBIR23FEL005
Nicole Katchur
Princeton University
$82,500

Project Title: *A Novel Model of Chronic Traumatic Brain Injury - CTE*

This project is investigating the function of dodo and dTau in rTBI and the link between injury force and activation of protein networks that may contribute to the transition of rTBI to CTE.

In 2014, approximately 155 individuals in the United States died each day from injuries induced by a traumatic brain injury (TBI). In New Jersey, an estimated 32-41 individuals suffer brain injuries from traumatic events each day and approximately 175,000 New Jersey residents currently live with disabilities from traumatic brain injury. A previous head injury increases risk for a subsequent head injury, especially in children. Studies have found an association between repetitive traumatic brain injuries (rTBIs) and mild cognitive impairment and clinical depression, suggesting that rTBIs have a cumulative effect on health. rTBIs that are closely spaced, without symptoms fully clearing from the first impact, may result in death. Likewise, chronic traumatic encephalopathy (CTE), which is a progressive neurodegenerative disease associated with repetitive head trauma, may lead to memory loss, personality changes, depression, and suicidality. While both rTBI and CTE have similarities and have limited therapeutic options and no cure, CTE may have critical points at which clinicians and policy makers may intervene; these points may occur before head trauma and before repetitive brain trauma transitions to chronic traumatic encephalopathy. While experts recognize the association between repeated head trauma and CTE, this transition is not sharply defined. Therefore, understanding the link between repetitive head trauma, often experienced by athletes and military personnel, and its progression to CTE, will inform both clinicians and policymakers as they treat head injuries and think about sports-regulations and global action plans, respectively.

One of the main proteins involved in CTE is a protein called tau, which we propose to study in a fly model of rTBI and CTE that we have developed. Tau is important for neuronal function in the brain and abnormal tau may have a direct role in damaging neurons and other brain cells. In neurodegenerative diseases such as CTE, tau accumulates into tangles (so-called neurofibrillary tangles). This protein is further regulated by another protein, PIN1, in humans, yet their interactions are poorly understood in the context of CTE. We chose to study these proteins and model CTE in the fruit fly as use of Drosophila melanogaster mitigates ethical concerns around repetitively injuring vertebrate animals (such as cats, monkeys, mice, the usual models), facilitates longitudinal disease analysis due to their short lifespan, and allows for vast laboratory tools to manipulate our proteins of interest. Our central hypothesis is that repeated head trauma leads to changes in tau and its related proteins, potentially initiating the transition to CTE. This research will inform health and research policy makers as they deploy resources to prevent and potentially treat CTE. Overall, CTE remains a pressing New Jersey and global health problem in critical need of effective therapeutic interventions and global action plans. Therefore, investigating the relationship between tau and its related proteins in a CTE fly model, may ultimately contribute to therapeutic targets for clinical management of head injuries and policies to reduce risk associated with repetitive head injuries.

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INDIVIDUAL RESEARCH GRANT RECIPIENT:

CBIR23IRG008
Ying Xu, M.D., Ph.D.
Rutgers, The State University
New Jersey Medical School,
$540,000

Project Title: *Defining phosphodiesterase 2A directed mitochondrial dysfunction in traumatic brain injury-related Alzheimer's disease.*

This proposal will investigate the causal involvement of aberrant PDE2A, particularly PDE2A2 signaling in mitochondrial dysfunction in traumatic brain injury related Alzheimer's disease.

Traumatic brain injury (TBI) causes memory loss in the progression of Alzheimer's disease and related dementia (AD/ADRD). Mitochondrial dysfunction is an early pathological change in affected neurons of patients with TBI related AD/ADRD. However, the underlying mechanism of TBI-induced memory loss is still unknown. Phosphodiesterase 2A (PDE2A) plays a crucial role in the mediation of cognition due to its primary role in hydrolyzing cyclic AMP (cAMP) and cGMP. Our pilot studies found that the increased PDE2A expression in the brains of AD patients and mice subject to TBI prior to AD-associated cognitive deficits, and decreased cAMP and cGMP in both the cytosol and mitochondria, suggesting the involvement of aberrant PDE2A-cAMP/cGMP signaling in the pathogenesis of TBI related AD/ADRD. Importantly, TBI-induced mitochondrial nucleoid DNA (mtDNA) leakage and respiratory deficits could be rescued by a PDE2A inhibitor, indicating a novel role for PDE2A in mediating mitochondrial dysfunction in the cognitive processing. PDE2A is encoded by three isoforms, PDE2A1, 2A2 and 2A3. Only PDE2A2 is expressed in mitochondria, where it is the primary regulator of cyclic nucleotide signaling. PDE2A2 represents a promising drug target. We have generated PDE2A conditional knockout in the forebrain and functional PDE2A2 knockout mice. They have been crossed with AD mice and carefully characterized.

We will determine how aberrant PDE2A, particularly PDE2A2 signaling, affects mitochondrial homeostasis and function. Our studies will provide mechanistic insights into molecular signaling underlying mitochondrial dysfunction in TBI associated with AD/ADRD and deepen our understanding of PDE2A in the regulation of cognition in the brain. The successful completion of this study will likely pave the way for future drug development of PDE2A inhibitors, specifically for the mitochondrial PDE2A2 isoform, as a promising treatment for brain injury related AD.

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INDIVIDUAL RESEARCH GRANT RECIPIENT:

CBIR23IRG011
Francois Berthiaume, Ph.D.
Rutgers, The State University of NJ
$540,000

Project Title: *Control of Neurovascular Endothelial Dysfunction via vRAGE-ELP-PEC to Improve TBI Outcomes*

We aim to block a molecule released very early after traumatic brain injury (TBI), that is thought to be responsible for causing delayed secondary damage to the brain, to improve outcomes post-TBI.

Traumatic Brain Injury (TBI) - mediated deficiencies in cognitive and motor functions are initiated by the primary mechanical injury to the brain, which in turn triggers a secondary cascade that ultimately dominates over intrinsic protective measures and results in inflammation, brain cell death and tissue degeneration. While current treatments aim to stop or slow the progression of secondary injury, to date, there are no FDA approved pharmacological therapies that result in significant functional improvement, especially after severe injury. Prior attempts to decrease inflammation have not targeted the molecules that are released at the earliest time points after injury. We aim to block a molecule released very early after TBI, which is deemed to represent a master regulator of inflammation, to improve outcomes post-TBI. The proposed research will ultimately develop a new and effective intervention to prevent or decrease the disabilities associated with TBI, which fits with the mission of the NJCBIR. Additionally, this research is a collaboration between a group of scientists at Rutgers University, combining expertise in biomedical engineering and neuroscience. New Jersey is not immune to the consequences of TBI, and the development of new therapies will benefit citizens of New Jersey. Finally, this project promotes the generation of new ideas, and the combination of different expertise, among investigators at Rutgers, which enhances the footprint of TBI research in our institution and in New Jersey.

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INDIVIDUAL RESEARCH GRANT RECIPIENT:

CBIR23IRG017
Bryan Pfister, Ph.D.
New Jersey Institute of Technology
$539,702

Project Title: *Targeting mechanisms of chronic inflammation, progressive neuronal loss and electrophysiological dysfunction initiated by specific biomechanical loading of mild and repeated traumatic brain injury.*

Determine the mechanisms of mild blunt and blast TBI that induce chronic inflammation that perpetuates regulated cell death leading to long-term neuronal loss and electrophysiological dysfunction.

Mild traumatic brain injury (TBI) is a public health concern with particular awareness in sports-related concussions and blast exposure in the military and law enforcement. While both are considered mild TBIs, the types of insults on the brain are quite different. Little is known about the long-term consequences of mild TBI or blast exposure on brain function. While one mild TBI may not lead to readily identifiable deficits, it may induce changes leaving the brain vulnerable to significant injury after a repeated TBI event. We have created unique experimental models to show that mild TBI can result in chronic inflammation that perpetuates loss of neurons and brain activity that is equivalent to a moderate injury. Based on preliminary results, the proposed mechanism of cell loss is a spectrum of immediate and long-term cell death pathways that shifts with the characteristics of TBI event. This proposal will interrupt injury induced inflammation to prevent neuronal loss and avoid the development of post-traumatic dysfunction. In the first aim, the spatial and temporal development of long-term cell loss in the hippocampus will be determined from a single blast and mild fluid percussion injury in the rat. The neuroinflammatory pathway, mode of cell death and the cell types involved in the cell loss will be determined. In aim 2, the findings will be extended to demonstrate that the chronic inflammatory cell death mechanisms initiated by a mild blunt or blast TBI contributes to exacerbated outcomes from a second injury and blocking the RCD pathways can prevent this effect. Finally in aim 3, functional alterations that correlate with injury related cell loss will be analyzed and if blocking cell loss can recover normal function. The successful completion of the aims of this proposal will elucidate the activation of regulated cell death pathways as targets for the prevention of progressive cell loss and dysfunction associated with mild and repeated mild TBI.

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INDIVIDUAL RESEARCH GRANT RECIPIENT:

CBIR23IRG019
Helen Genova, Ph.D.
Kessler Foundation
$528,824

Project Title: *Using my Strengths: Evaluation of a Strength-Based Intervention in Adults with TBI*

The current study will evaluate a strength-based intervention to improve self-concept in adults with TBI.

One of the most devastating effects of TBI is the loss of one's identity: individuals with TBI can experience marked changes in personality, emotional functioning, behaviors, and interests following their injury compared to before. This change in identity can be difficult and can be associated with depression, anxiety, and reduced quality of life. Thus, identity reconstruction has been identified as a critical rehabilitation goal for TBI. Historically, interventions for TBI have taken a deficit-based approach (in which the purpose of treatment is to fix weaknesses). However, a growing belief is that an overemphasis on deficits (with diminished emphasis on strengths) may result in individuals with TBI having a limited sense of what their strengths are, and how to use them to improve their lives. Further, a focus on deficits may lead to the perception that individuals with TBI are "broken," a belief which leads to stigma, loss of hope, reduced quality of life, reduced self-efficacy, and reduced well-being. Thus, the current study will do the opposite: it will evaluate an intervention which takes a strength-based approach to improve identity reconstruction following a TBI. Signature Strengths is a web-based behavioral intervention based on principles of Positive Psychology which emphasizes the cultivation and use of strengths in everyday life. This intervention has significant clinical benefit in other populations, but it is not well-studied in TBI. Thus, the current study will be the first to evaluate the Signature Strengths intervention in TBI with a randomized controlled trial (RCT) to determine whether Signature Strengths improves identity reconstruction, as well as positive emotions, life satisfaction and well-being. The long-term goal of this study is to implement a scalable, accessible and effective strength-based intervention in the TBI community, in order to empower individuals to use their inherent strengths to lead a meaningful life.

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INDIVIDUAL RESEARCH GRANT RECIPIENT:

CBIR23IRG021
Ekaterina Dobryakova, Ph.D.
Kessler Foundation
$452,366

Project Title: *The Effects of Effort on Fatigue and Brain Activity in Individuals with TBI*

Current research evaluates the impact of effort on cognitive fatigue and brain activity during attainment of rewarding outcomes in participants with moderate-to-severe TBI.

Up to 80% of individuals with traumatic brain injury (TBI) report cognitive fatigue. Hence, it is important to identify factors that impact cognitive fatigue and its reduction. Identification of such factors can lead to effective treatments that reduce cognitive fatigue and improve the quality of life after TBI. The goal of the current study is to examine one such factor: effort. We will examine how effort impacts cognitive fatigue in people with TBI and help develop strategies to improve cognitive fatigue symptom management. This proposal combines behavioral experimentation, neuropsychological assessment, and functional magnetic resonance imaging (fMRI). Such unique and innovative approach of the proposed study allows to examine non-pharmacological factors that contribute to cognitive fatigue reduction and will allow development of inexpensive interventions without unwanted side effects that may come with pharmaceutical treatments. We will conduct an experiment in which individuals with TBI and healthy participants undergo a fMRI while performing an effort-based learning task that with low and a high effort conditions. Participants will have to learn through trial-and-error to associate abstract images with one of the four response options. During both conditions, participants will be presented with either a positive or negative outcomes, reflecting their accuracy. We expect to observe increased activation in the striatum (a brain region that is sensitive to effort demands) to outcomes that after high effort vs. the low effort condition. We expect that striatal activation during a low effort task will be associated with lower levels of cognitive fatigue, while striatal activation during a high effort task will be associated with higher levels of cognitive fatigue. We will also look at individual differences with the goal of identifying individuals who are likely to experience low levels of fatigue even when faced with high effort demands.

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