



NEW JERSEY COMMISSION ON
BRAIN INJURY
RESEARCH

**DIRECTORY OF GRANT AWARDS
2019 GRANT CYCLE**

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MAY 2019

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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 2019 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 609-633-6465, 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.

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NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH
GRANT AWARDS

INDIVIDUAL RESEARCH GRANT RECIPIENT:

CBIR19IRG033

Rakesh Pilkar, Ph.D.

Kessler Foundation - \$534,045

Improving Anticipatory and Compensatory Postural Responses to Avoid Falls after TBI

This study assesses the roles of anticipatory and compensatory balance strategies and evaluates if a novel, perturbation-based training will improve these strategies and avoid falls after TBI.

Trauma to the brain impairs the ability to determine the body-position in relation to self and the environment. This accompanied by muscle weakness significantly affects TBI survivor's ability to achieve balance during environmental disturbances (slippery floor, standing in a moving bus etc.). In general, humans generate either anticipatory (proactive) or compensatory (reactive) balance strategies before and after the occurrence of such disturbances, respectively. However, populations with balance dysfunction (BDF) have shown to have impaired ability to generate such responses. BDF after TBI is the major contributing factor to falls. Assessing and treating BDF has always been the major focus of post-TBI rehabilitation. However, no study has reported how TBI specifically affects the generation of these essential anticipatory and compensatory responses during standing. For the first time, we propose a study with an objective to specifically enhance these responses to improve balance function and reduce the risk of falls in a dynamic environment. We will provide balance training using a computerized platform along with visual help for anticipating and reacting to upcoming perturbations. We will determine if this training can improve balance and reduce fear of falling after TBI. BDF post TBI and weakened ability to generate aforementioned balance strategies may result in fatal falls. The significance of this study is that it will provide novel information on how TBI affects these in-built balance strategies that are based on anticipation and compensation. It will also provide a strong reasoning to include anticipation-based training along with reactive response strengthening in clinical setting. This study strongly aligns with one of NJCBIR's primary objectives to develop novel interventions that could lead to improved treatment and function after TBI.

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INDIVIDUAL RESEARCH GRANT RECIPIENT:

CBIR19IRG037

Denise Krch, Ph.D.

Kessler Foundation - \$490,379

Life Reentry to Improve Grief and Fear in Partner Caregivers of Individuals with TBI

The goal of this project is to examine whether a web-based grief-counseling program will help partner caregivers of individuals with TBI process feelings of grief and overcome fears of the future.

The occurrence of a traumatic brain injury (TBI) is a life-changing event for people with TBI and their caregivers. Partners of people with TBI often report feelings of grief and fear as they experience the loss of their former life, face changes in their relationship as they take on a caregiver role and juggle multiple new responsibilities. Traditional support groups for caregivers of people with TBI may help them feel less alone in their experience. However, they usually do not help them move past their grief, address fears about the future, and create a new vision for life after TBI.

The proposed study will go beyond traditional support groups to improve quality of life for partner caregivers of people with TBI by examining the potential benefits of a web-based counseling program known as Life Reentry (LR). This 6-week program helps people who are dealing with a major life change to work through their feelings of loss and take actions that will help them live a happy and satisfying life. 92 partner caregivers of people with TBI will be enrolled and randomly assigned to either the LR program or an education series about health and function in people with TBI. Both programs will be delivered online and will be similar in all respects (e.g., time commitment) except for the content of the classes. This design will help determine what benefits the LR program may offer over traditional support groups.

Investing in the well-being of partner caregivers is expected to benefit both them and their loved one with TBI whom they support. In so doing, it is envisioned that the LR program will empower partner caregivers with strategies and skills to move forward with the business of living—truly living— after a great loss.

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INDIVIDUAL RESEARCH GRANT RECIPIENT:

CBIR19IRG025

Barry Waterhouse, Ph.D.

Rowan University - \$533,061

Effects of Repetitive Mild TBI on Flexible Attention and the Norepinephrine Transmitter System

The proposed project will focus on effects of repetitive mild TBI on flexible attention and the functionality of the locus coeruleus-norepinephrine transmitter system.

The proposed project will focus on the effect of repeated concussive events on a specific dimension of cognitive function; flexible attention. The ability to engage and alternate between competing behavioral demands is critical to management of everyday tasks and workflow. Under normal conditions the norepinephrine (NE) transmitter system in the brain regulates attention and other cognitive functions. Following concussion, also referred to as a mild traumatic brain injury (TBI), many executive functions including attention can be compromised for days, weeks, or months following injury leading to poor performance in the classroom and workplace. After experiencing a single concussion individuals are more vulnerable to future head injury and may likely experience more severe and/or more prolonged symptoms following repeated head trauma. Although many studies have focused on the consequences of single concussive events, fewer investigations have examined outcomes following repeated instances of concussion. Experimentally-induced mild TBI in rats serves as a useful model of single and repetitive concussion.

The proposed work will characterize the effects of repetitive mild TBI on a well-established rat model of flexible attention. Additional experiments will use anatomical and electrophysiological approaches to assess the functionality of the NE transmitter system after injury and examine the ability of methylphenidate (Ritalin®), a drug that elevates NE in brain, to attenuate the effects of repetitive mild TBI on flexible attending. As such the project will link concussion-induced deficits in cognitive function to a specific transmitter system in the brain and evaluate drugs that target this system for their efficacy in treating the consequences of repetitive head injury. This work is particularly relevant for treatment of NJ residents who experience multiple concussions as a result of participation in contact sports or military combat.

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INDIVIDUAL RESEARCH GRANT RECIPIENT:

CBIR19IRG029

Anthony Lequerica, Ph.D.

Kessler Foundation -\$411,672

Investigation of Neural Mechanisms Associated with Sleep-Dependent Enhancement of Motor Learning after Brain Injury

This study will examine the neural mechanisms associated with sleep-dependent enhancement of motor learning among individuals with traumatic brain injury using functional neuroimaging.

Studies have shown that a period of sleep, even in the form of a daytime nap, after a period of training on a motor learning task can boost subsequent performance beyond that observed after an equal amount of time spent awake and resting. This leap in performance has been referred to as “off-line” motor learning because it occurs during a period of sleep in the absence of additional practice. Motor learning is an integral part of the physical and occupational therapy that patients receive after traumatic brain injury (TBI) in which various activities of daily living may need to be relearned. Targeted motor skills may include dressing (learning how to zip up a jacket or button a shirt), using a fork and knife to eat, or using technology (tapping touch screen on a cell phone or typing on a computer). Yet the potential of sleep in the form of a strategic nap as a therapeutic tool to maximize motor learning in rehabilitation therapies has not been fully realized. In addition, a growing body of research among healthy individuals has shown evidence of changes in the brain associated with enhanced performance among those who slept following training compared with those who spent the same amount of time awake.

The neural mechanisms of “off-line” motor learning have not been studied among individuals with TBI. Using functional neuroimaging and measurement of brain waves, the current study will examine the mechanisms underlying this sleep-related enhancement of motor learning among individuals with TBI and determine how brain physiology may influence the magnitude of the effect. By understanding how this treatment works and identifying the factors that modulate its effectiveness we can identify which individuals will be most likely to benefit from a nap after training to improve motor learning after TBI. This can provide a more person-centered approach to treatment delivery that can maximize the effectiveness of a simple, but potent behavioral intervention.

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INDIVIDUAL RESEARCH GRANT RECIPIENT:

CBIR19IRG014

Jorge Contreras, Ph.D.

Rutgers University Biomedical & Health Sciences

New Jersey Medical School - \$540,000

Role of Microglia/Monocyte Pannexin-1 in Blood-Brain Barrier Disruption and Leukocyte Infiltration after Traumatic Brain Injury

Microglia/monocyte pannexin-1 is a molecular target to attenuate neuroinflammation after TBI.

Damages to blood brain barrier and leukocyte infiltration to the parenchyma are common pathological events that occur in different brain pathologies, including traumatic brain injury. Yet adequate targeted therapies are lacking.

For example, anti-integrin antibodies were developed to reduce leukocyte infiltration via compromised blood brain barrier, but they showed off-target effects. Results from this proposal can potentially guide the development of a drug target that specifically inhibits pannexin-1 channel activity reducing BBB damage and leukocyte infiltration after traumatic brain injury

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FELLOWSHIP RESEARCH GRANT

CBIR19FEL018

Mr. Anton Omelchenko

Rutgers, The State University - \$100,500

Exosome-Based Delivery of RNAi Therapeutics to Target Traumatic Brain Injury

This project will assess the therapeutic efficacy of exosome-based delivery of NCX1 RNAi in the treatment of Traumatic Brain Injury.

Traumatic brain injury (TBI) is the leading cause of death and disability in the world. While TBI refers to a change in brain function as a result of physical impact to the brain, it encompasses a series of different biological injury mechanisms, which ultimately lead to a multitude of symptoms. The calcium ion plays an important role in the biological mechanisms, which lead to extensive cell damage in the brain after TBI. The sodium/calcium exchanger (NCX) is a protein that regulates the amount of calcium present inside of brain cells (neurons) and the supporting cells (glial cells). Impaired function of NCX contributes significantly to the dysregulation of calcium balance in neurons and glial cells, leading to subsequent cell damage and death.

Targeting proteins, such as NCX, in the brain with standard pharmaceutical drugs is difficult due to the blood brain barrier, a biological system that prevents easy passage of molecules into the brain from the bloodstream. A novel system to introduce therapeutics into the brain is the use of exosomes, nanoscale biological vesicles naturally released by cells for intercellular communication. These vesicles can be harvested from cells, loaded with drugs or other therapeutic molecules, and injected into the bloodstream to deliver the intended therapy to the brain.

Here, we propose to develop such a system to use targeted exosomes to deliver a molecular therapy to reduce the amount of NCX protein in neurons in the brain. Our aim is to develop such a delivery system, test it in cell culture and mice, and ultimately assess the therapeutic potential of the system with respect to learning and memory deficits and cell damage, in an animal model of TBI. Our proposed work will provide key stepping stones for future therapeutic strategies involving novel delivery of therapeutics for TBI.

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FELLOWSHIP RESEARCH GRANT

CBIR19FEL014

Mr. Lucas Corrubia

Rutgers University Biomedical & Health Sciences

New Jersey Medical School - \$100,500

The Role of Adult-Born Neurons in Traumatic Brain Injury Induced Neuropathology

The proposed study will examine circuit connections of aberrant newly born neurons after brain injury to determine their role in neuropathology.

Traumatic brain injury (TBI) is currently a rising epidemic that is increasing in prevalence at an alarming rate. Victims of TBI can suffer from life changing symptoms, such as memory loss and post-traumatic seizures, that drastically hinder quality of life and accumulate unwanted healthcare bills. Throughout life, our brain is constantly producing new neurons, which serve to encode information perceived in the world around us. The phenomenon of the brain's ability to produce these new neurons is called neurogenesis. One of the most well-known sites of neurogenesis is in the hippocampus, which is thought to be mostly involved in specific types of memory function essential for daily navigation of the environment.

Following TBI, there is a massive burst of new-born neurons in the hippocampus, specifically in a sub-region called the dentate gyrus, and these neurons were originally thought to be reparative as injury causes damage to tissue and neuronal death. However, our lab has shown that if you inject a drug in to the brain that inhibits the ability for these neurons to be produced after injury, rats are less prone to developing seizures and experience reversal of abnormal excitability in the circuits where the new-born neurons integrate, ultimately reducing risk for post-traumatic epilepsy. Despite these exciting results, a limitation in our previous studies was the potential for non-specific effects of the drug used to suppress neurogenesis. Thus, in the proposed study, we will be able to label and manipulate the neurons specifically born in response to injury using transgenic mice to better understand how these neurons may be directly contributing to hyperexcitability and memory dysfunction. The proposed study will challenge the previously perceived notion that TBI-induced neurogenesis is a beneficial recovery process and may reveal a potential therapeutic target for the development of future treatment options.

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FELLOWSHIP RESEARCH GRANT

CBIR19FEL020

Ms. Esmā Cetinkaya

New Jersey Institute of Technology - \$100,500

Electrophysiological Monitoring of Cerebellar Injury Using Spontaneous Signals D

Investigation of different level of biological changes due to cerebellar injury and the cerebellum`s role in movement for the purpose of using it to help patients with brain injury.

Brain injury is a major cause of morbidity worldwide. Based on New Jersey Commission on Brain Injury Research report, nearly 175,000 New Jersey residents suffer from traumatic brain injury. The cerebellum, which is also known as little brain, is most of the time not affected from the direct injury toward the cerebellum thanks to its well protected anatomical location.

However, studies highlight that indirect injury of the cerebellum due to traumatic brain injury is very common and occurs even in mild cases. In these cases, insult is towards the cerebral parts of the brain, but the event cascades in the long term, alter and damage the cerebellum.

Cerebellar injury triggers both motor and cognitive deficits.

In the last years, brain injury studies increased, but cerebellar injury is still underappreciated.

This study focuses on the cerebellar injury and the main significance of the study is to fulfill this gap in science. This study will investigate different level of biological changes due to cerebellar injury and the cerebellum`s role in movement for the purpose of using it to help patients with brain injury. This multimodal project combines different research areas together and benefits from both engineering and life science tools to help brain injury patients.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR19PIL014

Vikram Handiru, Ph.D.

Kessler Foundation - \$176,233

Targeted Noninvasive Brain Stimulation for Upper-limb Motor Rehabilitation in Traumatic Brain Injury Patients

This study aims to investigate the combined benefits of non-invasive brain stimulation and MusicGlove exercises for recovery of hand functions and its effects on the brain networks in TBI patients.

Traumatic Brain Injury (TBI) is a serious medical and health problem in the US. Moderate and severe Traumatic Brain Injury (TBI) commonly causes upper extremity physical impairments that persist even after years of injury; these deficits are attributed to damage in brain structure and changes in structural and functional connectivity. Considering the fact that almost 85% of the TBI patients suffer from upper limb motor deficits, it is crucial to address the issue with better rehabilitation techniques. Although the conventional rehabilitation approaches are helpful in assisting the motor recovery, nearly half of the TBI survivors do not regain their ability to use their arms for daily activities.

The current therapeutic approaches involve intensive physical therapy training involving repetitive tasks which causes fatigue and lack of engagement in the patients. To address this issue, our proposed study aims to combine individually targeted non-invasive brain stimulation and music-assisted hand exercises to reorganize in a desired manner to achieve functional recovery. Further, the project will also investigate how the intervention modulates the brain activity (recorded using EEG) in terms of brain connectivity before- and after-intervention. In the end, this study will allow us to understand the cortical dynamics of TBI rehabilitation upon brain stimulation. Extending further, this could pave a way to advance the knowledge of behavioral and neural aspects of motor control in patients with different types of neuromuscular disorders.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR19PIL021

Glenn Wylie, Ph.D.

Kessler Foundation - \$174,199

An Investigation of the Interaction of Physical and Mental Fatigue in TBI

We aim to investigate the interaction of physical and mental fatigue on both behavior and brain function in individuals who have sustained a moderate to severe TBI.

Fatigue, which can be both mental and physical, is one of the most troubling and prevalent symptoms in a variety of neurological disorders including the damage sustained by the brain following a Traumatic Brain Injury (TBI). Although disabling and prevalent, TBI-related fatigue is poorly understood because until now there has been no good way to study it. Recently, we have demonstrated success in measuring mental fatigue using fMRI, and have identified a network of brain regions that are sensitive to mental fatigue.

In the current project, we propose to leverage what we have learned about mental fatigue to better understand how physical fatigue and mental fatigue are related to one another. We will do this by 1) inducing mental fatigue and testing subjects' ability to perform a physical task, and 2) inducing physical fatigue and testing subjects' ability to perform a mental task. In addition to recording subjects' behavior, we will also record brain activation and physiological measures.

Physical and mental fatigue have a severe negative impact on the quality of life of individuals who have sustained a TBI, and often impede an individual's ability to maintain employment, social relationships, leisure activities and activities of daily living. By better understanding the interplay of mental and physical fatigue, we will be in a better position to develop strategies to alleviate fatigue, which will enable individuals with TBI to return to their lives, and to enjoy a better quality of life.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR19PIL007

Mark Zimering, M.D.

VA New Jersey Health Care System - \$176,000

Cognitive Dysfunction following Traumatic Brain Injury in Older Adults: Interaction with Diabetes

The goal is to determine whether diabetes increases the risk of accelerated cognitive decline following mild traumatic brain injury in older adults.

Traumatic brain injury contributes to global disability and has been associated with major depressive disorder through unknown mechanisms. Diabetes increases in older adults and is a risk factor for traumatic brain injury. A recent study found increased autoantibodies in the bloodstream of older patients with diabetes and depression. The autoantibodies targeted a receptor on vascular cells and brain cells highly expressed in brain regions involved in normal mood and thinking.

The proposed studies will test whether following traumatic brain injury, plasma serotonergic autoantibodies adversely affect mood and thinking in a genetic strain of diabetic fatty rats harboring serotonergic autoantibodies, and whether the effects can be prevented by administration of specific serotonin receptor antagonists. The proposed studies will also explore whether diabetes enhances the risk of depression and accelerated cognitive decline following traumatic brain injury. Aim 1 will investigate whether diabetic patients who experienced a prior mild traumatic brain injury suffer with accelerated cognitive dysfunction compared to age-matched adults without diabetes who experienced similar kinds of traumatic brain injury. Aim 2 will investigate whether the mechanism of cognitive decline following traumatic brain injury in diabetes involves autoantibodies which target specific brain neurons and vascular cells.

Understanding how diabetes contributes to worsening depression and cognitive dysfunction following traumatic brain injury is a key factor in preventing the late effects following TBI in all persons. The knowledge gained from the proposed studies could lead to the development of new techniques for identifying persons at high risk for depression and cognitive decline 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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PILOT RESEARCH GRANT RECIPIENT:

CBIR19PIL018

Erica Weber, Ph.D.

Kessler Foundation - \$179,035

Improving Time-Based Prospective Memory in Individuals with Traumatic Brain Injury using Computer-Based Cognitive Rehabilitation

This pilot study seeks to explore the ability of computer-based cognitive rehabilitation of strategic cognitive functions to improve time-based prospective memory in individuals with TBI.

Thousands of traumatic brain injuries (TBI) occur each year in New Jersey, resulting in approximately 9,000 hospitalizations and 900 deaths. Although it is becoming more common for those with TBI to survive their injuries due to advances in medicine, they must still rely on others for daily care due to significant brain damage and resulting cognitive difficulties. One specific cognitive problem is in the area of prospective memory, which is the ability to remember to do something in the future (or “remembering to remember.”) Individuals with poor prospective memory often have problems remembering to take their medications, have difficulty staying employed, rely more so on loved ones for daily assistance, and tend to report a lower quality of life. Although researchers have demonstrated the importance of prospective memory, they have been less successful in finding effective ways to rehabilitate it.

This proposed study will test a new rehabilitation strategy for prospective memory (computer-based cognitive training), using principles from a well-established theory of prospective memory as a guide. By completing this pilot study, we will be able to a) determine if the intervention may be successful in improving time-based prospective memory, and b) determine the amount of treatment necessary to get the desired effect. These two components will be essential for securing grant funding for a planned larger-scale study with 1) a greater and more diverse group of individuals with TBI, 2) more detailed assessments to demonstrate how this training may improve participants’ abilities to remember to perform tasks in their everyday lives (not just in the laboratory), and 3) longer follow-up, to see if study participants still benefit from training after they’ve completed the study. It is the goal of this line of research to improve everyday cognitive abilities so that New Jerseyans who have sustained a TBI may become more independent and experience greater quality of life.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR19PIL010

Mohammed Abdul Muneer Peringady, Ph.D.

John F. Kennedy Medical Center - \$180,000

Nrf2 Signaling as Therapeutic Target: A Novel Peptide Therapy for Traumatic Brain Injury

We will study the therapeutic significance of Nrf2 activator III TAT peptide, which can alleviate neurovascular impairments by the activation of Nrf2 transcription factor in mouse model of blunt TBI.

Traumatic brain injury (TBI) is characterized by physical brain injury that causes temporary or permanent disability or death. TBI causes approximately 1.7 million deaths and hospitalizations annually in the United States alone. Clinical and experimental reports have shown that TBI causes both short and long-term neuropathological changes, although the underlying biochemical mechanisms are not yet fully elucidated. Several clinical trials are being conducted for developing a better therapeutic strategy for TBI and for a variety of reasons, none of those found fully effective. Hence, newer vistas for developing therapeutic methods against TBI need to be explored. From the studies conducted by us and others it is evident that oxidative signaling is the central mechanism in TBI-associated neurovascular impairments and remediation of accumulating oxidative radicals is a straightforward approach when considering therapeutic approach against TBI.

This proposal will study a novel hypothesis that cerebral vascular injury and associated neuroinflammation and neurodegeneration caused by TBI-induced oxidative damage can be repaired by activating the anti-oxidant signaling Nrf2 (nuclear factor E2-related factor 2) pathway. The Nrf2 (nuclear factor E2-related factor 2) transcriptional system, an endogenous defense mechanism present within the cells, has the potential to develop a novel and clinically relevant therapeutic methods. We will treat the injured animals with Nrf2 Activator III TAT peptide (Nrf2 activating peptide, briefly called as Nrf2 peptide), a synthetic cell penetrating peptide and analyze its effect against TBI associated neurovascular complications. The effect of Nrf2 peptide on functional recovery from TBI-induced sensorimotor deficits and anxiety will be evaluated using behavioral tests including rotarod, grid walk, balance beam, and dark-light test.

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