DIRECTORY OF GRANT AWARDS
2017 GRANT CYCLE

NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH

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MAY 2017

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 2017 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.

2017 MEMBERSHIP INFORMATION

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NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH

GRANT AWARDS

INDIVIDUAL RESEARCH GRANT RECIPIENT:

CBIR17IRG006
Bonnie L. Firestein, Ph.D.
Rutgers University
Dept. Cell Biology & Neuroscience
$502,500

Project Title: *Identification of Biomarkers of TBI in Brain-Derived Exosomes*

We will develop a new method for the detection of biomarkers for the diagnosis and potential treatment of TBI.

Traumatic brain injury (TBI) is the leading cause of death in people under 45 years of age in the United States and continues to have an enormous impact on public health. Although some progress has been made in reducing the annual incidence of TBI through brain injury prevention, there remains a tremendous need to develop biomarkers for the diagnosis of TBI to improve treatment for those who have suffered a TBI.

In this proposal, we use a novel method to identify potential biomarkers in vesicles released from the brain into the circulating blood for the diagnosis of TBI. We will determine whether proteins, RNA, and DNA in these vesicles, called exosomes, are present in different amounts in the blood of animals that have experienced a TBI than in control animals. In addition, we will determine whether these exosome components change in response to treatment with rapamycin, which we have shown promotes recovery after TBI.

Our ultimate goal in the future is to use the identified biomarkers to diagnose those in New Jersey who have suffered a TBI and use the biomarkers to develop individual therapies.

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INDIVIDUAL RESEARCH GRANT RECIPIENT:

CBIR17IRG019
Steven Levison, Ph.D.
Rutgers University BHS
$539,988

Project Title: *Protecting Subcortical White Matter and Promoting Remyelination After TBI*

We will test the hypothesis that subacute LIF administration after an adolescent concussive injury will reduce damage and increase the production of new myelinating glia to restore axonal conduction.

Concussions are prevalent among adolescents due to sports-related injuries and car accidents and until recently, the consequences of concussion were under-appreciated problem. In New Jersey, the financial burden of pediatric and adolescent TBI is ~$20 million/year in hospital costs alone (NJCBIR Annual Report). Given this enormous financial burden, the emotional burden placed on caregivers and the fact that injuries evolve differently in youths than adults, there is strong rationale to study the consequences and treatment of concussions in healthy adolescents.

Over the past 2 years we have developed a new model of adolescent concussive brain injury in mice and we have established that a naturally produced injury signal known as leukemia inhibitory factor (aka LIF) dampens the degree of secondary brain injury. But, the increase in LIF after injury is short-lived, therefore, we have hypothesized that extending the time when LIF is present will be beneficial. We have shown that LIF can be delivered in nose drops and that these nose drops containing the LIF deliver it far into the brain where it reduces the extent of damage and improves performance on behavioral tasks. But LIF is not only a neuroprotective molecule, it also promotes repair; therefore, an important goal of our future studies will be to not only study the neuroprotective benefits of LIF administration, but also to establish its regenerative potential in our adolescent model of adolescent concussive brain injury.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR17PIL007
Barry D. Waterhouse, Ph.D.
Rowan University
$172,874

Project Title: *Impact of Repetitive Mild Traumatic Brain Injury on Attention and Catecholamine Efflux in Prefrontal Cortex*

This study will evaluate the effects of repetitive concussion on attention in rats, and on the therapeutic actions of Ritalin® to reduce attention deficits following repetitive concussion.

The proposed pilot project will focus on the effect of repeated concussive events on specific dimensions of cognitive function; sustained and flexible attention. The ability to engage and alternate between these two modes of attention is critical to management of everyday tasks and workflow. Under normal conditions the catecholamine transmitter systems in the brain regulate 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 concussion.

The proposed work will characterize the effects of repetitive mild TBI on well-established rat models of sustained and flexible attention. Additional experiments will measure neurotransmitter release in brain regions responsible for regulating attention and examine the ability of methylphenidate (Ritalin®), a drug that elevates transmitter levels, to attenuate or reverse the effects of repetitive mild TBI on attention. As such, the project will seek to validate animal models of repetitive brain injury and attention for future study, investigate mechanisms of repetitive TBI, and evaluate methylphenidate as candidate drug for treating the consequences of repetitive head injury. This work is particularly relevant for treatment of New Jersey residents who experience multiple concussions as a result of participation in contact sports or military combat.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR17PIL021
Peii Chen, Ph.D.
Kessler Foundation
$177,593

Project Title: *Home-based Arm and Hand Exercise (HAHE) to Improve Upper Limb Function after Traumatic Brain Injury*

This pilot study will evaluate the feasibility of the HAHE protocol and generate pilot data needed to develop a programmatic area of research that can be supported by funding from federal agencies.

Arm and hand dysfunction, although not widely recognized, is a common and devastating consequence of TBI. Recommendations have been published that encourage clinicians to include upper extremity retraining within the TBI population; however, very little research exists that will help inform treatments for this population. In order to address this important knowledge gap, there is urgency to broaden the scientific evidence critical to informing upper limb rehabilitation for TBI survivors.

The proposed study will do just that by using a task-specific visuomotor exercise protocol that emphasizes upper limb movements which can be practiced by patients in their homes. This new home-based arm and hand exercise (HAHE) protocol is expected to improve functional recovery and quality of life among individuals with chronic upper limb impairment after moderate-to-severe TBI.

The proposed project is innovative in 1) that the exercise protocol integrates treatment elements established in stroke rehabilitation into a single treatment modality for TBI survivors, 2) the utilization of an alarm timer to achieve high treatment intensity by reminding patients of repetitive practices at home, and 3) the treatment aims to improve not only visuomotor coordination, but also patient-centered outcomes.

The success of the proposed 2-year pilot project will evaluate the feasibility of the treatment protocol and home setting, and will generate pilot information needed to develop a programmatic area of research that can be supported by additional funding from federal agencies.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR17PIL020
Namas Chandra, Ph.D.
New Jersey Institute of Technology
$152,747

Project Title: *Divergent Mechanisms of Early Cellular Injury in High-Rate Blast and Slow Impact TBI Determine Long-Term Neurological Outcomes*

This multidisciplinary study will determine the nature of early neuropathology after high-rate blast brain injury and their contribution to development of epilepsy and memory deficits.

Blast-related traumatic brain injury (TBI) is the most common brain injury sustained by combat troops in recent wars and is considered a signature injury of ongoing wars. In addition to wars, industrial explosions and current asymmetric warfare expose civilian populations to blast brain injuries as well. Impact brain injury, typically from falls, hits or being thrown against hard objects is known to increase the risk for epilepsy and lead to long-term and cognitive deficits. However, the specific risk for development of epilepsy after an isolated exposure to blast pressures is completely unknown. The limited data on blast brain injury indicates that the nature and evolution of cellular damage to brain tissue is different in blast and impact brain injuries. Therefore, characterizing the cellular consequence of blast and impact injury under comparable experimental conditions can lead to insights into specific disease processes and possible behavioral markets for blast injury. Thus, identifying the risk for development of epilepsy after blast brain injury and the underlying cellular and network mechanisms is essential to identify differences in disease progression after different forms of TBI and if evaluation and management strategies need to consider the nature of the injurious event.

Here, we will use a shock-tube blast injury model that has been validated by direct comparison to field data and combined long-term behavioral and electrophysiological monitoring to determine the development of epileptic seizures after blast brain injury and impact brain injuries at similar pressures. Multidisciplinary approaches will be used to determine how these physically different blast and impact injury affects brain tissue and subsequent neurobehavioral, cellular and network functional outcomes. Our studies will eliminate the existing knowledge gap concerning epileptogenesis after primary blast injury.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR17PIL012
Xiaobo Li, Ph.D.
New Jersey Institute of Technology
$180,000

Project Title: *Discovering the Neurobiological Substrate of Inattention in Children Post-Traumatic Brain Injury*

This project focuses on understanding the neurobiological underpinnings of attention deficits in children post traumatic brain injury (TBI).

TBI is a major public health concern, and the leading cause of disability and death in children in the U.S. Clinicians and families report that a variety of attention deficits occur in children post TBI, and significantly contribute to poor academic and social performances, and negatively impact quality of life. However, little is known about the brain mechanism of the attention deficits in children post TBI.

Based on our long-term research experiences in attention deficits in children, we hypothesize that injury induced anatomical and functional alterations in prefronto-parietal network play the central role in inattention in children post TBI. We propose to investigate both microstructural-level anatomical and functional mechanisms of TBI induced inattention in children, by 1) utilizing DTI to study the white matter alterations; 2) utilizing neurite orientation dispersion and density imaging (NODDI, a multi-shell diffusion MRI technique for estimating the microstructural complexity of dendrites and axons) to study the neuronal level gray matter alterations; and 3) task-based (attention network test (rANT)) to assess the functional brain networks for alerting, orienting, and executive control steps of attention processing, in children who have TBI induced persistent symptoms of inattention.

This study will have a significant impact on effective interventions and cures for children post TBI, by shedding light on the neural mechanisms of inattention in children post TBI, and suggesting the neurobiological target for treatment of this severe and common condition. It will further provide the neural foundation for us to investigate the biological correlate of treatment efficacy in children post TBI.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR17PIL025
Nancy Chiaravalloti, Ph.D.
Kessler Foundation
$177,260

Project Title: *Modification and Pilot Testing of the mSMT for Improving Learning and Memory in School-Aged Children with TBI*

This project entails both a modification of the mSMT for children with TBI and pilot testing of the pediatric mSMT to begin to establish efficacy.

Cognitive deficits following TBI often lead to the inability to functional optimally at school, maintain employment, engage in social activities, participate in the community fully and experience optimal quality of life. Deficits in new learning and memory are common and the effective treatment of this deficit should serve to significantly improve multiple aspects of daily living including the ability to function effectively in social, educational and occupational situations and overall quality of life.

The currently proposed study addresses a critical need in the clinical care of school-aged children with TBI through the modification of an existing, documented effective treatment protocol for learning and memory deficits in persons with moderate to severe TBI, the modified Story Memory Technique (mSMT). We will also conduct a small study to begin to examine post-treatment improvements in school-aged children with moderate to severe TBI. The documentation of the efficacy of the mSMT in children with TBI has the potential to greatly improve the everyday functioning and overall quality of life of this important population. The results of this study therefore have the potential to change clinical practice, inform policy, and improve the lives of children and adolescents living with TBI.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR17PIL022
Ekaterina Dobryakova, Ph.D.
Kessler Foundation
$177,214

Project Title: *Investigation of Neural Mechanisms during Feedback Learning in Individuals with Traumatic Brain Injury*

The goal of the current study is to examine neural mechanisms associated with learning through immediate and delayed feedback in individuals with traumatic brain injury. Traumatic brain injuries (TBIs) affect nearly 15,000 New Jersey residents every year and over 175,000 residents are already living with a disability due to a TBI. Many individuals with TBI also endure countless hours of rehabilitation, much of which involves learning and relearning tasks necessary to live a happy and normal life. This study will push the boundaries of medical research by taking a step forward at truly understanding the functional basis for learning. This knowledge will lead to better, more effective treatments for car accident victims, veterans, and various other TBI patients in our State of New Jersey.

In order to learn successfully, a person needs clear feedback to correct errors they may make and to improve their performance on a specific task. With effective feedback, a patient could apply the skills they learn during rehabilitation to their day-to-day lives. However, we have yet to explore how the brain functions during learning in individuals with TBI.

The proposed study focuses on the feedback aspect of learning, which can be presented either immediately or after a delay following the completion of a task. Previous studies suggest that individuals with TBI have issues with a specific brain region responsible for learning through immediate feedback, known as the striatum. But delayed feedback involves a different brain region. Thus, even though individuals with TBI may have difficulty learning through immediate feedback, they may still learn at a normal rate using delayed feedback.

The proposed study utilizes functional magnetic imaging (fMRI) to examine this hypothesis, as well as brain regions involved in learning through immediate and delayed feedback in individuals with TBI. The results of this investigation will provide a basis for modifying feedback that rehabilitation clinicians provide during their time with patients to achieve the best possible outcome following treatment.

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PILOT RESEARCH GRANT RECIPIENT:

CBIR17PIL024
Soha Saleh, Ph.D.
Kessler Foundation
$179,240

Project Title: *Combining Physical and Mental Practice for the Rehabilitation of Upper Extremity Movement Impairments secondary to Traumatic Brain Injury*

This proposal investigates the therapeutic benefit of combining mental practice with physical training for the recovery of hand function and its related effect on brain connectivity in TBI patients.

Many individuals with sustained moderate to severe traumatic brain injury suffer from impairment in hand movement and coordination, which often can prevent them from returning to work or resuming a fully active life. Effective treatments require long repeated intensive physical therapy training. Unfortunately, the amount and therefore the benefit of the therapy is often limited by attention deficits, fatigue and physical weakness.

This project proposes to combine physical and mental practice to achieve intensive training without inducing fatigue while maintaining high engagement during training sessions. The study will investigate the therapeutic benefit of combining physical and mental practice compared to physical practice alone for recovery of hand movement and coordination. The project will also assess how the intervention is effective at re-normalizing brain activity and the interaction between different regions associated with hand movement and control that were affected by the injury. Ultimately this study will provide valuable information on the benefit of combining mental and physical practice to help guide the design and development of more effective rehabilitation therapy.

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