# NJCBIR 2016

# NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH

**Annual Report State Fiscal Year 2016** 







March 1, 2017

The Honorable Chris Christie, Governor Office of the Governor State House PO Box 001 Trenton, New Jersey 08625

Dear Governor Christie:

On behalf of the New Jersey Commission on Brain Injury Research, I am pleased to present the Annual Report for Fiscal Year 2016. Once again, the Commission has had an active and productive year. We recently completed the tenth competition for research projects directed at mechanisms of neural regeneration and repair, and are confident that these efforts will make significant contributions to our knowledge of recovery from traumatic brain injury, the development of effective interventions, and ultimately to the improvement of the quality of life for people who have sustained catastrophic brain injuries.

I would like to acknowledge the efforts and enthusiasm of all the Commissioners during the past year, as well as the New Jersey Department of Health for their valuable support and contributions.

Sincerely. Daniel Keating, Ph.D Chairman

# NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH



## **2016 ANNUAL REPORT**

January 30, 2017

### **New Jersey Commission on Brain Injury Research**

### **Members of the Commission**

Daniel Keating, Ph.D., Chairman Dennis Benigno Richard Boergers, Ph.D., ATC Meiling Chin, MBA Shonola Da-Silva, M.D., MBA John Giraud Nicholas Ponzio, Ph.D. Mark Evan Stanley, Ph.D. Dennie Todd Karen Tucker, M.A. Anthony Welch

### **Commission Personnel**

Christine Traynor, Administrator Mary Ray, Fiscal Administrator

### **ACKNOWLEDGEMENTS**

The New Jersey Commission on Brain Injury Research would like to express its sincere appreciation to all present and past Commission members, to Commission staff members Christine Traynor and Mary Ray for their support, and to the New Jersey Department of Health.

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# EXECUTIVE SUMMARY New JERSEY COMMISSION ON BRAIN INJURY RESEARCH

# The New Jersey Commission on Brain Injury Research was established in 2004 to fund brain injury research projects in New Jersey.



Since 2007, the New Jersey Commission on Brain Injury Research (NJCBIR) has awarded over \$35 million to individual scientists at various academic and research institutions, and approved 91 separate scientific research projects.

- o Since 2007, thirty-six scientific research projects have been completed.
- o Progress made by researchers has been presented in abstracts, scientific conferences, symposia, and meetings.
- o NJCBIR programs have facilitated scientific interaction and research collaborations, in New Jersey as well as out-of-state.
- o Success in achieving NJCBIR funding has resulted in academic and career advancement for New Jersey researchers.

### NJCBIR offered three grant programs in Fiscal Year 2016:

- o Individual Research Grants
- o Pilot Research Grants
- o Postdoctoral and Graduate Fellowship Grants

### NJCBIR 2016 Achievements:

- o Fifty-three applications requesting \$16.4 million were submitted.
- o Fourteen awards were made in 2016 totaling \$3,787,026.
- o Four Individual Research grants totaling \$2,136,275, seven Pilot Research grants totaling \$1,248,007, and three Fellowship grants totaling \$402,744 were approved.

### INTRODUCTION

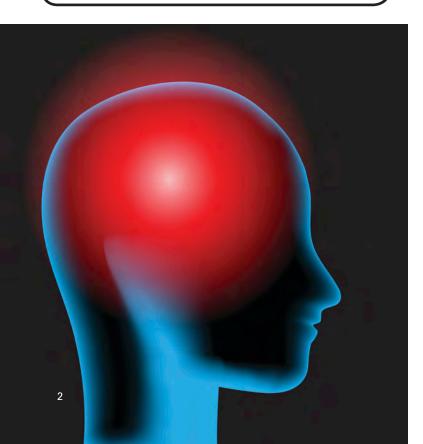
This report is written in accordance with P.L. 1968, c.410, (N.J.S.A. 52:9EE-1, et seq.) which stipulates, in part, (C.52:9EE-4) an annual report on status of the fund. The Brain Injury Research Act created the New Jersey Commission on Brain Injury Research and the New Jersey Brain Injury Research Fund to support its activities. It resulted from the collaborative efforts of people with brain injuries and their families, clinicians, scientists, public officials, and representatives of research, rehabilitation, and non-profit organizations.

# EXECUTIVE SUMMARY New JERSEY COMMISSION ON BRAIN INJURY RESEARCH

### Facts & Figures

- o Approximately 175,000 New Jersey residents suffer from traumatic injuries that damage the brain.
- o Approximately 12,000\* new injuries occur each year that require inpatient or outpatient treatment.
- o The total cost of Emergency Department visits, hospitalizations, and deaths related to traumatic brain injuries, either alone or in combination with other injuries, exceeds \$82 billion annually.
- o Motor vehicle traffic injury is the leading cause of traumatic brain injury related deaths in the nation.
- o Nationally, an estimated 1.7 million people sustain a traumatic brain injury annually. Of them:
  - ✤ 52,000 die,
  - ✤ 275,000 are hospitalized and
  - 1.365 million, nearly 80% are treated and released from the emergency department.

\*Based on 2015 estimates from the Centers for Disease Control and the New Jersey Department of Health Center for Health Statistics.



### NEW JERSEY'S COMMITMENT TO BRAIN IN-JURY RESEARCH

The Brain Injury Research Act anticipates that brain injury research will lead to effective treatments and cures for brain injuries and relieve other consequences of brain injury.

New Jersey is a leader in supporting research aimed at developing effective interventions and cures for disabilities associated with traumatic brain injury.

The NJCBIR provides research grant programs for both established scientists and young researchers committed to the goals of brain injury research. The Commission also supports the New Jersey Department of Health, which maintains a database of traumatic brain injuries in New Jersey.

Now in its twelfth year of operation, the NJCBIR has funded 91 scientific research projects and supported individual scientists at institutions around the state. Its impartial and scientifically rigorous application and review process has helped make the Commission vital to New Jersey's best scientists in their pursuit of brain injury research.

# NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH

Created as a semi-independent public body, the New Jersey Commission on Brain Injury Research is "...al-located in, but not of..." the New Jersey Department of Health. It is subject to all the administrative rules and procedures of the Department, but is not part of the budget.

The NJCBIR establishes and oversees the operations of the grants process and other activities that are implemented by its administrative staff. Eleven uncompensated commissioners are appointed by the Governor with the advice and consent of the Senate, and serve a three-year term. Two commission seats are designated by statute to represent the state's major academic research institutions and stakeholders. Public members provide a diversity of backgrounds and interests united by a shared commitment to the cause of brain injury research. The Commission will always have one or more individuals from each of the following institutions and categories:

> The Commissioner of the New Jersey Department of Health, or designee, Rutgers, The State University of New Jersey Eight Public Members – at least one licensed physician, an individual with a brain injury, a parent of an individual with a brain injury, one public member appointed by the President of the Senate and one public member appointed by the Speaker of the Assembly

All public members shall be residents of the state, or otherwise associated with the state, and shall be known for their knowledge, competence, experience or interest in brain injury medical research.

Any qualified person wishing to be considered for appointment may submit his or her name to the Governor's Office of Appointments. Information on how to apply can be found on the following website at: <u>http://www.state.nj.us/governor/admin/bca</u>.

Public meetings are held at least four times a year. Members are recused from discussing or voting on matters in which they may have a potential conflict. A Chair and Vice-Chairperson are elected annually and preside over all formal proceedings.

The NJCBIR also maintains standing committees that meet and provide an informal structure to discuss issues on an ad hoc basis prior to presenting them to the commission.

### **ADMINISTRATION**

The NJCBIR administrative office provides the vital linkages to implement its programs and ensure the integrity of its operations. The office staff manages the day-to-day operations, including program administration, interaction with applicants and grantees, contract administration, budgeting and financial matters, record-keeping and reporting.

The office staff schedule and facilitate all activities, manages the scientific merit review process, negotiates with outside vendors, and maintains the necessary relationships within state government.

### NEW JERSEY BRAIN INJURY RESEARCH FUND

The work of the NJBIR is supported entirely by a statutory one-dollar surcharge on all traffic and motor vehicle fines or penalties. Monies generated from these fines or penalties are collected by the State Treasurer for deposit into the New Jersey Brain Injury Research Fund. All grant programs and other activities are funded entirely from this dedicated source. No part of the operating budget is paid for out of New Jersey's general tax revenue.

### **MISSION AND GOALS**

The NJCBIR mission is to encourage and promote innovative brain injury research projects in New Jersey through the funding of approved research projects at qualifying research institutions in the State of New Jersey.

The NJCBIR supports meritorious research projects that advance the understanding of traumatic brain injuries, and is committed to accelerating research to develop effective interventions and treatment for the disabilities associated with traumatic brain injury. Simply stated, the commission's goals are:

- To advance and accelerate brain injury research,
- To promote collaboration among brain injury researchers in New Jersey,
- To promote the development of brain injury researchers and their research capabilities for obtaining federal and other external funding, and,
- ✤ To encourage innovative research.

Brain injury is often misdiagnosed, misunderstood and under-funded. Until there is a cure, people who sustain brain injuries must have timely and equal access to expert trauma care, specialized rehabilitation, lifelong disease management and individualized support services. This is critical for individuals to live healthy, independent and satisfying lives. The State of New Jersey benefits in savings on medical and support costs as well as research activities for treatments and cures for brain injuries and their effects.

### **OBJECTIVES**

The NJCBIR is committed to accelerating research to develop effective interventions and cures for the disabilities associated with traumatic brain injury. Its primary objectives are:

- To advance the field of brain cell repair and regeneration in the New Jersey research community by encouraging established scientists to apply their expertise to the brain injury.
- To foster collaborative, interdisciplinary approaches to brain injury research.
- To develop models of neural repair and regeneration that establishes a basis for additional scientific investigation.
- To develop models of neural repair and regeneration after brain injury that can lead to clinical interventions.

- To stimulate epidemiological analysis of the New Jersey Traumatic Brain Injury Registry data to improve injury prevention, develop treatment guidelines and enhance patient outcomes.
- To promote dissemination of the research findings generated by those scientists supported by the New Jersey Commission on Brain Injury Research.
- To develop and evaluate clinical interventions that lead to improved treatment and function after traumatic brain injury.

### **RESEARCH FUNDING PRIORITIES**

The NJCBIR guidelines set forth the Commission's scientific agenda, research criteria and areas of interest. They offer applicants detailed guidance and instruction on funding criteria and policies. The full text appears on the website at: <u>www.nj.gov/health/njcbir</u>.

An array of grant programs is offered including Individual Research Grants, Fellowships, Pilot Research Grants and Programmatic Multi-Investigator Research Grants. Each of these programs is designed to support and encourage brain injury research in New Jersey.

The NJCBIR funds research activities that hold the promise of developing effective treatments, interventions and cures for the disabilities associated with traumatic brain injury. The areas of research listed below highlight the focus of current emphasis and funding.

### **Basic Studies**

- Studying strategies to promote neuronal growth and survival, encourage the formation of synapses, enhance appropriate myelination, restore axonal conduction, replace or regenerate injured brain cells, or otherwise improve function after brain injury.
- Evaluating the efficacy of drugs and other interventions that prevent or reduce secondary neuronal injury or providing insight into the mechanisms causing progressive damage.

- Defining anatomical characteristics of brain injury in well-defined animal models and in the human brain, specifically documenting the cellular systems vulnerable to injury and the functional losses which occur.
- Translational research on the mechanism and interventions that promote recovery of function after brain injury.

### **Clinical Studies**

- Demonstrating the efficacy of innovative rehabilitation strategies based on basic research that offer promise to promote recovery of function (e.g., physiologic function, cognitive impairment, activity limitation, social participation, quality of life) through their clinical application.
- Demonstrating mechanisms of action and rehabilitation intervention based on changes in brain activity (e.g., functional imaging), neurocognitive function, or psychosocial factors (e.g., resilience).
- Comparative effectiveness research to evaluate the relative risks and benefits of alternative rehabilitation interventions intended to promote recovery of function.
- Epidemiological studies of the New Jersey Traumatic Brain Injury Registry data, to identify contributions of demographic and risk factors, patient transport, rehabilitation and physical therapy, and medical/surgical interventions to population treatment and outcomes.

# THE NJCBIR APPLICATION AND REVIEW PROCESS

The grants review process was designed to emulate the National Institutes of Health standards and procedures to provide an impartial and rigorous review. This effort has been largely successful and has earned respect from grantees and applicants.

The grant application process is now entirely electronic utilizing New Jersey's Grant Management system and is accessible through the website at: <u>http://nj.gov/health/grants/</u>. The on-line process ensures broad access, convenience, flexibility, and greatly reduces administrative workloads for applicants, the commission office, and the Scientific Merit Review Panel.

The grant review process consists of a three-step review. First, all grant applications are reviewed by the Commission's administrative staff to ensure compliance with New Jersey statutes and regulations and to ensure accuracy. Secondly, an independent relevance review is conducted by a three-person panel appointed by the office of the NJCBIR. The panel determines the relevance of all applications to the NJCBIR mission, priorities and Research Guidelines, and will assign scientific reviewers for each proposal that meets the relevancy requirements. In the event the panel determines that an application does not meet those requirements, the application will be triaged, and will not be forwarded for independent scientific merit review. Thirdly, members of the Independent Scientific Merit Review Panel convene to evaluate all grant applications forwarded by the Independent Relevance Review Panel, applying the criteria described below. This panel will assign scores to each application and make funding recommendations to the NJCBIR.

- If it is determined that an ad hoc expertise is needed, additional scientific referees may be used.
- The Independent Scientific Merit Review Panel will forward its recommendations to the NJCBIR for final review and action.

Grants triaged by either the Independent Relevance Review Panel and/or the Independent Scientific Merit Review Panel will not be forwarded to the NJCBIR, and will not be funded. Lastly, the authority to authorize or not authorize grants is fully vested in the NJCBIR according to New Jersey statute (N.J.S.A. 52:9EE-1).

### **CURRENT GRANT PROGRAMS**

Grant programs are designed to provide opportunities attractive to a wide range of researchers. Awards are intended to promote collaboration among brain injury researchers in New Jersey and encourage innovative research. The intent is not to provide long-term support for research. It is expected that this initial support will lead investigators to acquire necessary levels of preliminary data so they may compete successfully for federal grant support.

The Individual Research grant is designed to fund senior independent researchers, while the Fellowship grant offers encouragement to graduate students and post-doctoral researchers. The Multi-Investigator grant supports collaborative research from at least three investigators from different laboratories, and the Pilot Research grant enables researchers to pursue a new direction in brain injury research, or encourages new investigators who want to gather preliminary data for larger research projects. Newly offered this year, the Brain Injury Core Facilities grant was designed to make research more efficient and provides state-of-the-art equipment and highly skilled staffing to support researchers with centralized expertise.

Inter-institutional and/or inter-state collaboration is strongly encouraged. Complete details on all grant programs are available on-line.

### INDIVIDUAL RESEARCH GRANTS

- Individual Research Grants support senior scientists to explore meritorious novel scientific and clinical ideas.
- ♦ Up to \$540,000 for up to three years (\$180,000 per year).
- The key goal is to enable established researchers to test and develop pilot data needed for future funding.

### **FELLOWSHIP GRANTS**

- Postdoctoral and Graduate Student Fellowships engage promising young investigators in brain injury research.
- All fellowships include an annual stipend, research allowance and travel budget.
- Post-doctoral Fellowships are three year awards based on years of relevant research experience since obtaining a doctoral degree and range from \$64,550 to \$83,376 a year.
- ♦ Graduate Fellowships are three year awards with a total award of \$33,500 per year.

### **PILOT RESEARCH GRANTS**

- Enable independent investigators to pursue a new direction in brain injury research, or new investigators who want to gather preliminary data for larger research projects.
- ✤ Up to \$180,000 for a two year award (\$90,000 per year).

### **PROGRAMMATIC MULTI-INVESTIGATOR RESEARCH GRANTS**

- Support collaborative research from at least three investigators from different laboratories.
- Preference is given to proposals that demonstrate complementary approaches to addressing a research question through multi-disciplinary investigations.
- Collaborations are encouraged among independent laboratories within the same institution or among laboratories from different institutions.
- Up to \$720,000 per year for up to three years with a maximum of \$2.1 million.

### **BRAIN INJURY CORE FACILITIES GRANTS**

- Brain Injury Core Facilities Grants make research more efficient and productive by providing services and technologies that cannot be readily reproduced in individual laboratories in an efficient, cost-effective manner.
- Provides state-of-the-art equipment along with highly skilled staffing to support researchers.
- Makes use of sophisticated technologies and equipment to provide researchers with access to centralized expertise and service.
- Provides education and training opportunities for aspiring researchers.
- Up to \$1,500,000 is available to provide researchers with an opportunity to facilitate the establishment of new Brain Injury Core Facilities.



### 2007-2016 NJCBIR SUMMARY AND PERFORMANCE RECORD

Since 2007, the NJCBIR has funded 91 separate scientific research projects to scientists at New Jersey academic and research institutions. These awards represent an investment in brain injury research of over \$35 million.

Approximately 35 grant applications are received annually; approval of ten or more new grant awards totaling \$3-\$4 million are made.

Due to its continued investment in brain injury research, the number of New Jersey researchers interested in the field is growing.

### NEW JERSEY QUALIFIED RESEARCH INSTITUTIONS

Under the Brain Injury Research Act, funds may only go to researchers affiliated with "New Jersey Qualified Research Institutions." The following organizations have been designated by the New Jersey Commission on Brain Injury Research.

- o University of Medicine & Dentistry of NJ
- o Rutgers, State University of New Jersey
- o Kessler Foundation
- o Stevens Institute for Technology
- o Princeton University
- o Cooper University Hospital/Health System
- o Atlantic Health Systems Hospital Corporation
- o St. Barnabas Medical Center
- o Edge Therapeutics, Inc.
- The Center for Neurological & Neurodevelopment Health LLC, Clinical Research Center of NJ, & The Center for Neurological & Neurodevelopment Health II, Inc. – NeurAbilities
- o Centra State Medical Center
- o Montclair State University
- o Coriell Institute for Medical Research
- o New Jersey Institute of Technology
- o Hackensack University Medical Center
- o International Brain Research Foundation

- o Englewood Hospital Research
- JFK Neuroscience Institute, JFK Health System & Seton Hall University School Health Medical Science
- o Rowan University
- o Morristown Medical Hospital & Medical Center
- o VA NJ Health Care System & Veterans Biomedical Research Institute
- o The College of New Jersey
- o Visikol, Inc.

The Commission is committed to broadening its portfolio of institutional grantees and increasing the size and diversity of its funding activities. Through outreach activities, the Commission encourages participation by all research organizations with an interest in brain injury research.



### 2016 A YEAR IN REVIEW New JERSEY COMMISSION ON BRAIN INJURY RESEARCH

The NJCBIR developed policy guidelines to accommodate what promises to be an exciting research agenda for the New Jersey science community. The Commission is providing the opportunity for New Jersey to become a leader in traumatic brain injury research, as our program was the first of its kind in the nation.

As we move forward, it is our belief that the Commission will serve as a role model for other states to follow in search of medical research, treatments and interventions. It is our belief that the early recognition of unmet needs in traumatic brain injury research is paving the way to develop methods of regeneration and repair.

Grant programs are designed to provide opportunities attractive to a wide range of researchers. Awarded grantees and grantee institutions have capitalized on the opportunities afforded by the availability of Commission funding through advancement of individual careers, increased institutional investment, and applying for additional outside funding.

The Commission has been a major factor in fostering this interest and continued involvement in brain injury research within the State of New Jersey.

### 2016 Overview & Applications

The NJCBIR has been in existence for twelve years and is in its tenth cycle of grants. In 2016, three types of grant programs were offered and included: Individual Research grants, Fellowship grants, and Pilot Research grants. The NJCBIR allocated up to \$4.5 million for brain injury research projects, but it is not required to award any, or all that amount.

A total of 53 grant applications were received. Fourteen grants were awarded totaling \$3,787,026. The grant awards included four Individual Research grants, three Fellowship grants, and seven Pilot Research grants.

#### 2016 Outreach and Development Efforts

The Commission maintains an ongoing interest in expanding brain injury research in New Jersey. Direct contacts, attendance at events and meetings, plus website and publication resources are some of the ways used to publicize grant opportunities throughout the state.

### **Publication of Grant Programs**

Official Notices of Grant Availability advise interested parties of the NJCBIR grant programs. These notices are published annually on the Commission's website and in the New Jersey Department of Health's *Directory of Grant Programs*.

#### 2016 GRANT CYCLE INFORMATION

Grant Application Deadline: October 5, 2015 Award Notification Date: May 30, 2016 *Available Grant Programs:* 

- Individual Research Grants
- Fellowship Grants
- Pilot Research Grants

### **GRANTS PROGRAM FOR 2017**

For Fiscal Year 2017, the NJCBIR allocated up to \$2.5 million dollars for brain injury research projects. In 2017, two types of grant programs were offered. They included Individual Research grants, and Pilot Research grants. The NJCBIR allocated up to \$2.5 million for brain injury research projects, but it is not required to award any, or all of that amount.

### **2017 GRANT CYCLE INFORMATION**

Grant Application Deadline: October 5, 2016 Award Notification Date: May 30, 2017 *Available Grant Programs:* 

- Individual Research Grants
- Pilot Research Grants

# New Jersey Commission on Brain Injury Research

### NEW JERSEY BRAIN INJURY REGISTRY

The "Brain Injury Research Act" mandated the establishment of a central registry on people who sustain brain injuries throughout the state. This registry consists of a database that provides information on the incidence and prevalence of brain injuries and serves as a resource for research, evaluation, and information on traumatic brain injuries.

The Registry, collects brain injury data from New Jersey hospitals, and provides data analysis for health professionals.

New Jersey Traumatic Brain Injury Surveillance System

	Males	S	Female	S	Total	
Year	N	Rate	N	Rate	N	Rate
2000	4,934	126.7	3,070	65.3	8,004	94.8
2001	4,733	120.3	2,884	61.2	7,607	89.7
2002	4,783	120.9	2,904	60.7	7,687	89.5
2003	5,006	125.5	3,173	64.8	8,179	94.1
2004	4,986	124.8	3,219	64.9	8,205	93.8
2005	5,109	126.7	3,256	65.4	8,365	95.1
2006	5,510	135.4	3,524	70.2	9,034	102.0
2007	5,526	135.3	3,659	71.8	9,185	102.6
2008	5,556	135.0	3,786	73.3	9,342	103.3
2009	5,816	140.4	4,072	77.1	9,888	107.7
2010	5,765	137.3	3,942	74.2	9,707	104.7
2011	5,563	131.9	4,042	75.1	9,605	102.4
2012	5,893	137.7	3,963	72.6	9,856	103.8
2013	5,609	129.7	3,995	71.6	9,604	99.5
2014	5,442	124.1	4,041	71.3	9,483	96.6
2015	5,083	115.2	3,668	63.8	8,751	88.2

### Hospitalizations for TBI by gender, New Jersey, 2000-2015

Rates are age-adjusted using the 2000 US Standard Population, calculated per 100,000 population. Bridged-race estimates are used in calculations. Hospitalization data are from the New Jersey Central Nervous System Injury Surveillance, 2016.

# New Jersey Commission on Brain Injury Research

	Unde	r 15	15-	24	25-	44	45-	64	65	+	To	tal
Year	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	AARate
2000	1,010	57.4	1,236	122.4	1,932	73.7	1,345	69.8	2,481	222.6	8,004	94.8
2001	904	51.2	1,287	125.3	1,782	68.5	1,300	65.6	2,344	210.3	7,607	89.
2002	865	48.8	1,240	118.9	1,708	66.2	1,368	67.1	2,506	224.6	7,687	89.5
2003	925	52.2	1,209	113.9	1,727	67.6	1,469	70.1	2,849	254.7	8,179	94.1
2004	821	46.5	1,211	112.3	1,664	66.0	1,548	72.0	2,961	264.5	8,205	93.
2005	828	47.4	1,245	113.5	1,713	68.9	1,568	71.1	3,011	268.7	8,365	95.
2006	843	48.9	1,347	121.2	1,817	74.3	1,779	78.9	3,248	288.8	9,034	102.0
2007	804	47.1	1,318	117.6	1,652	68.4	1,862	81.0	3,549	312.5	9,185	102.0
2008	827	48.7	1,167	103.5	1,717	71.9	1,923	82.3	3,708	320.2	9,342	103.3
2009	812	47.9	1,139	100.4	1,609	68.1	2,074	86.9	4,254	362.5	9,888	107.
2010	805	47.6	1,125	98.6	1,580	67.3	2,117	87.0	4,080	342.7	9,707	104.
2011	695	41.3	999	87.3	1,527	65.3	2,081	84.4	4,303	356.1	9,605	102.4
2012	678	40.5	1,006	87.8	1,557	66.8	2,230	90.2	4,385	350.6	9,856	103.8
2013	626	37.6	822	71.5	1,431	61.5	2,176	87.6	4,549	354.3	9,604	99.
2014	553	33.4	763	66.2	1,292	55.6	2,108	84.5	4,767	362.9	9,483	96.
2015	444	27.0	614	53.5	1,190	51.3	1,842	73.6	4,661	346.9	8,751	88.3

### Hospitalizations for TBI by Age Group, New Jersey, 2000-2015

Except where noted, rates are CRUDE RATES directly calculated using the NJ age-specific population, calculated per 100,000. Bridgedrace estimates are used in calculations. Hospitalization data are from the New Jersey Central Nervous System Injury Surveillance, 2016.

### Discharge Disposition of the Major Causes of Traumatic Brain Injuries, 2015

	Home, ro	outine	Extend	1.0	Home, servic	2	LTC, nur hospi	3	Reha	ıb.	Left A	MA	Dischrg/ plann readmiss	ed	Die	d	Total
Gause of Injury	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N
Motor vehicle (traffic)	877	63.3	129	9.3	44	3.2	10	0.7	224	16.2	20	1.4	2	**	80	5.8	1,386
Falls	2,194	39.4	1,523	27.4	404	7.3	184	3.3	846	15.2	56	1.0	5	0.1	350	6.3	5,562
Assault	455	81.0	23	4.1	5	0.9	3	**	26	4.6	30	5.3	Ó		20	3.6	562
Self-inflicted	15	34.1	11	25.0	0		2	**	0		0	1	0		16	36.4	44
Other and Unknown	636	53.1	221	18.5	71	5.9	32	2.7	149	12.4	11	0.9	1"	**	76	6.3	1,197
Total	4,177	47.7	1,907	21.8	524	6.0	231	2.6	1,245	14.2	117	1.3	8	0.1	542	6.2	8,751

Hospitalization data are from the New Jersey Central Nervous System Injury Surveillance, 2016; percentages are based on New Jersey residents admitted to New Jersey hospitals, all outcomes. \*\* Percentages not calculated for under 5 observations.

Notes:

<sup>1</sup>Includes: Discharges/transfers to other short term general care hospitals, skilled nursing and intermediate care facilities, federal hospitals, psych units, and critical access hospitals <sup>2</sup>Includes: Discharges/transfers to home withi either a home health service provider or M therapy

<sup>3</sup>Includes: Discharges/transfers to long-term care facilities, Medicaid certified nursing facilities, and hospice

<sup>4</sup>Includes: Discharges/transfers to home/self care, short term general hospitals, skilled nursing and intermediate care facilities, custodial or supportive care facilities, cancer centers or children's hospitals, home with services, law enforcement, federal hospitals, Medicare swing-bed facilities, rehab facilities, long-term care, Medicaid-certified nursing facilities, psych hospitals, critical access hospitals, and others not elsewhere classified; with planned inpatient readmission to an acute care hospital. (New beginning in 2013)

# FINANCIAL STATEMENTS New JERSEY COMMISSION ON BRAIN INJURY RESEARCH

### FINANCIAL STATEMENTS

The activities and programs of the NJCBIR are supported by the New Jersey Brain Injury Research Fund as established by the Brain Injury Research Act.

Revenue obtained from the statutory one-dollar surcharge is collected and forwarded to the State Treasurer for deposit into the New Jersey Brain Injury Research Fund. Interest earned on the money collected, through the Division of Investments, New Jersey State Department of Treasury, is credited to the Fund.

The NJCBIR is committed to granting a substantial majority of the Fund each year to support as much meritorious research as possible, while retaining the ability to meet expenses.

	SFY 2016	SFY 2016	SFY 2017
	Projected	Actual	Projected
Opening Fund Balance: (July 1)	\$1,447,348	\$1,447,836	\$467,613
Revenues			
Assessments <sup>1</sup>	\$3,600,000	\$3,716,857	\$3,600,000
Investments Earnings - Interest <sup>2</sup>	<u>\$12,000</u>	<u>\$35,746</u>	<u>\$12,000</u>
Total Revenue:	\$3,612,000	\$3,752,603	\$3,612,000
Total Funds Available:	\$5,059,348	\$5,200,439	\$4,079,613
Disbursements and Expenses			
Spending Plan Reduction		\$1,540,000	
Disbursements to Grantees <sup>3</sup>	\$4,500,000	\$3,128,961	\$3,100,000
Total Disbursements:	\$4,500,000	\$4,668,961	\$3,100,000
Evenence			
Expenses Administrative & Office Expense	\$110,000	\$36,615	\$110,000
Professional Review Panel	\$50,000	\$27,250	\$50,000
NJCBIR Registry	\$00,000 \$0	\$0	\$00,000 \$0
Total Expenses:	\$160,000	\$63,865	<u>\$0</u> \$160,000
Total Disbursements and Expenses:	\$4,660,000	\$4,732,826	\$3,260,000
Closing Fund Balance: (June 30)	\$399,348	\$467,613	\$819,613

### **State Fiscal Year 2016 Fund Balance Statement:**

Below is a project summary of the individual research grant recipients:

#### CBIR16IRG017

Vijayalakshmi Santhakumar, M.D., Ph.D. Rutgers University Biomedical & Health Sciences \$534,800

### **Project Title: Does Enhanced Dentate Neurogenesis Promote Early and Long Term Circuit Dysfunction and Brain Injury?**

This multidisciplinary study will determine whether early abnormal increase in hippocampal neurogenesis after brain injury contribute to long-term neurocognitive decline and risk for epilepsy. Traumatic brain injury (TBI) is a major risk factor for several chronic disorders such as temporal lobe epilepsy and memory and cognitive dysfunction. The incidence of TBI from falls, traffic accidents, assault, combat injuries, and sports is constantly on the increase. Recent reports estimate over 1.7 million TBI cases in the US each year resulting in an annual economic burden beyond \$60 billion.

Neurogenesis in the adult hippocampus replaces degenerating neurons with new neurons which are essential for maintaining proper memory and cognitive functions. As we age there is a decline in hippocampal neurogenesis which results in age associated memory and cognitive deficits. Brain injury rapidly increases generation of new neurons which has been proposed to help recovery of memory function. However, it has been shown that new neurons born after seizures tend to be abnormal and contribute to excessive excitability and epilepsy.

The proposed study will determine what happens to the pool of neural stem cell precursors and newly born neurons from the point of injury at time points over the course of several months after injury to determine if injury-induced increase generation of new born neurons leads to long term accelerated cognitive decline observed after brain injury. Additionally, the study will determine if new neurons born after injury contribute to early deficits in memory and long term increased risk for seizures. Thus, the proposed study will provide novel insights into the role of neural stem cells in neuropathology and neurological recovery after traumatic brain.

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Below is a project summary of the individual research grant recipients:

CBIR16IRG032 David Margolis, Ph.D. Rutgers University Cell Biology & Neuroscience \$540,000

### Project Title: Role of Cortical Network Plasticity in Recovery from Traumatic Brain Injury

This project uses novel in vivo imaging methods in mice to investigate brain plasticity underlying recovery from traumatic brain injury, and to screen candidate drugs to improve recovery.

Traumatic brain injury is a significant public health problem that has devastating cognitive and behavioral consequences in those affected. There is a critical need to discover treatments that improve recovery of brain function after injury. We still know too little about how brain activity changes in response to the initial injury and how these changes cause lasting detrimental effects on mental function and behavior. Research has shown that large brain networks are affected by injury, even in cases of focal head trauma. This is because brain areas are highly interconnected. Indeed, connections between brain areas are key for proper brain function. Therefore, it is critically important to understand how brain networks change their function over time after injury, and how this goes hand in hand with behavioral recovery. Some individual's recovery is faster than others. If we can show how brain networks account for behavioral and cognitive recovery, it might be possible in the future to change the function of those networks through drugs or rehabilitation to improve behavior and cognitive performance.

Our work uses a mouse model and cutting-edge neuroscience methods to test how brain networks respond to and recover from traumatic brain injury. Our team uses imaging to visualize brain activity of specific types of neurons across the entire cerebral cortex, and quantitative methods to measure how connections between brain areas change over time. Using our novel approach, the experiments aim to identify the mechanisms and timing of the brain's recovery from injury and to relate brain changes in the same subjects to cognitive and behavioral recovery. We believe our system will enable rapid screening of drugs that have potential therapeutic value for treating traumatic brain injury, with clinical implications within New Jersey and beyond.

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Below is a project summary of the individual research grant recipients:

CBIR16IRG025 Michael F. La Fountaine, EdD, ATC Seton Hall University \$526,549

### Project Title: Evaluating the Role of Baroreceptor Sensitivity in the Post-Concussive Symptomatic Milieu

The project measures changes to baroreceptor sensitivity following a concussion; information useful in identifying those with reduced ability to accommodate situations where blood pressure increases.

As public awareness of concussion grows and evidence demonstrates that repeated head impacts contribute to long-term risk of neurological damage, a shift in focus to assist our understanding of what a concussion does to clinically accessible processes in the body is necessary. By gaining this insight, we may be able to better appreciate the breadth of the clinical consequences that an injury and its symptomatic limitations impose. Although numerous assessment scales are available for the immediate evaluation and diagnosis of injury, the fact remains that much is still to be learned about how concussions affect body systems and reduce functional capacity for a brief time, especially among those with optimal functional performance (i.e., athletes). In evaluating how a concussion affects the brain's ability to coordinate responses, it may be important to include assessments that involve physical challenges where responses are made in proportion to the magnitude of a challenge. Deficits that may exist as a result of an injury, and its severity, would be expected to resolve on repeat evaluation as the injury "heals." Therefore, an approach to evaluate the brain's ability to coordinate these responses is a logical progression to facilitate this understanding.

The current proposal tests this approach by exploring changes to the arterial baroreflex during rest and physical stress on repeated evaluations over the first week following a concussion injury. The arterial baroreflex is a mechanism in the cardiovascular system under nervous system control that monitors blood pressure changes (both increases and decreases) with compensations to heart rate on a beatto-beat basis. This reflex helps protect against large fluctuations in blood pressure which may contribute to syncope (i.e., fainting due to low blood flow to the brain) or pressure-related damage to end-organs (i.e., the brain) and in the context of the current proposal, exercise intolerance when the injury pervades.

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Below is a project summary of the individual research grant recipients:

CBIR16IRG041 A.M. Barrett, Ph.D. Kessler Foundation \$534,926

### **Project Title: Improving Medication Self-Administration and Health after Brain Injury**

We model an innovative care pathway, by combining medication self-administration assessment we developed under Commission pilot funding, with an evidence-based reminder protocol.

After a traumatic brain injury, self-administering medication is a daily activity that provides a foundation for recovery, health and function. Taking medications incorrectly (medication self-administration or MSA errors) affects competence and dignity, but also strongly predicts the skilled help a person with brain injury will need after hospital discharge.

In this project, our interdisciplinary research group will extend our research on methods to identify and predict MSA errors over three years of intervention. We will add video call reminders, which others demonstrated improves medication adherence in a different clinical population. Participants with TBI will receive these video call reminders at the actual time when medication doses are scheduled to be taken. We will compare this approach to usual and standard care (no reminders) and automated texts, which were recently shown to enhance cardiac medication compliance. Impact of the three interventions will be compared based on participant's percentage of MSA errors identified on computerized pill bottle monitoring. These "Fitbits for medication accuracy" allow us to follow how participants take each medication dose throughout the six months they are enrolled in the study. We will also follow on a monthly basis whether participants are re-hospitalized, how caregivers assess their functional status, and how they self-rated quality of life.

Most people who are undergoing neurorehabilitation are completely unaware when they cannot perform MSA. We hope the assessment and intervention care pathway outlined in this study would help support a complete process that is patient-oriented, but yet does not require patient initiation or self-advocacy. We further hope this project will launch a model for further evaluation and demonstration, which would become part of standard neurorehabilitation care and accelerate brain injury recovery.

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# 2016 RESEARCH GRANT AWARDS - FELLOWSHIP RESEARCH GRANTS

Below is a project summary of the fellowship research grant recipients:

CBIR16FEL013 Przemyslaw Swiatkowski Rutgers University Cell Biology & Molecular Biology \$100,500

**Project Title:** The Role of Cypin in Recovery of Electrophysiological and Cognitive Functions Following Traumatic Brain Injury

Elucidating therapeutic targets for manipulation of the molecular mechanisms guiding protein recycling vital for formation of longterm memories in the brain after traumatic brain injury.

Traumatic brain injury (TBI) is caused by head trauma and displacement of the brain within the skull. Neurons, which are the principal cells of the brain, are damaged due to physical impact against the skull and/or any foreign object. Often neurons die, leading to motor and cognitive deficits. Although the effect of TBI on learning and memory has been extensively characterized, there is no effective treatment to improve cognitive functions affected by TBI. It is critical, therefore, to identify a way of protecting neurons responsible for learning and formation of memories after TBI.

Cytosolic PSD-95 interactor (cypin) is a protein that has been extensively studied and described by our laboratory. Our animal studies show that decreasing amounts of cypin present in neurons improves learning and memory following TBI in mice. I predict that cypin plays an important role in learning and memory, and downregulating its expression, via genetic manipulation, will improve cognitive functions after TBI. This study will provide new insights into the molecular mechanisms of how TBI affects learning and memory and explore possible therapies.

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### 2016 RESEARCH GRANT AWARDS - FELLOWSHIP RESEARCH GRANTS

Below is a project summary of the fellowship research grant recipients:

CBIR16FEL009 Anna Giarratana Rutgers University Biomedical & Health Sciences Robert Wood Johnson Medical School \$100,500

### Project Title: Effect of Genetic Polymorphisms on Recovery and Treatment after Traumatic Brain Injury

This project will assess how genetic differences effect recovery after traumatic brain injury (TBI) and explore possible treatment methods. Traumatic brain injury is a serious and potentially life threatening clinical problem. An estimated 12,000 to 15,000 TBIs occur in New Jersey alone, 1,000 of which are fatal. In addition, TBI can cause severe lifelong disability. Currently, 175,000 New Jersey residents live with disability due to TBI, a number that grows every year. TBI begins with an initial primary injury caused by events such as falls, vehicle accidents, or sports collisions. The primary injury sets off a cascade of events that initiates a secondary injury which may be responsible for the long-term neurological disabilities associated with TBI. While safety precautions that limit the occurrence of TBI are certainly very important, once a primary insult has occurred, the goal of researchers should be to investigate the best method of preventing the secondary insult from occurring and thereby prevent the development of long-term disabilities that stem from TBI.

One promising way to better manage treatment of TBI would be to stratify patients into risk categories based on their own genetic makeup, and even tailor treatment to patients who have varying genotypes. Clinicians have long noticed that certain patients recover better than others after TBI, and determining what makes some patients more susceptible than others is a vital step in identifying high risk patients who are more likely to have a severe reaction and lifelong disability due to a TBI.

Genetic polymorphisms, or differences in DNA between people, are an important facet of what gives people genetic diversity. Two specific polymorphisms that have been suggested to confer higher risk for poor recovery following TBI according to preliminary clinical studies on humans are Apolipoprotein E4 (ApoE4) and Brain-derived neurotrophic factor (BDNF) Val66Val. However, the initial studies have not been in complete agreement because it is hard to be consistent in trials that use human subjects due to the heterogeneous nature of the injuries they have suffered and their complex genetic background. That is why it is vital for us to do experimental mouse studies where we can limit the confounding genetic factors and create a homogeneous and replicable injury.

Our study will investigate the effect of the ApoE4 and Val66Val polymorphisms in genetically engineered mice on recovery following a repeated, mild TBI, which mimics the pattern that is shown in human sports injuries. We will look at cellular and behavioral outcomes following the TBI in order to determine if the ApoE4 and Val66Val polymorphic mice show worse recovery than the ApoE3 and Val66Met polymorphic mice. If we find that these specific polymorphisms do confer greater risk, it will be very useful to know in populations such as student athletes. A simple blood test will be able to determine if someone is at a higher risk for suffering damage after injury, allowing parents and athletes to make informed decisions about their participation in sports, and reinforcing the importance of immediate treatment following concussions. We will also examine biomarkers in serum and cerebrospinal fluid as well as use magnetic resonance imaging to identify indicators of injury and repair that correlate with the cellular and behavioral changes we observe. The biomarkers we identify will allow physicians and patients to monitor the injury and recovery process in a quantifiable way to improve diagnosis and decisions about return to play.

Finally, we will look at possible treatments for TBI, to investigate if we can improve recovery in patients with these high-risk genetics. Specifically, we will investigate the use of human mesenchymal stem cells (hMSCs) which can be derived from adult bone marrow and have been shown to improve outcome in spinal cord injury. In summary, this study will explore the ways to best manage and treat patients who have TBI in an effort to reduce the burden that New Jersey and its citizens currently suffer due to TBI.

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## 2016 RESEARCH GRANT AWARDS - FELLOWSHIP GRANT RECIPIENTS

Below is a project summary of the fellowship research grant recipients:

CBIR16FEL010 Jessica Verpeut, Ph.D. Princeton University Neuroscience Institute \$201,744

**Project Title: Effects of Cerebellar Perturbation on Neocortical Adaptation to Post-Traumatic Brain Injury** 

This project will analyze neural circuitry of the cerebellum and forebrain to determine alterations in dendritic growth and morphology with possible interventions following traumatic brain injury.

Chronic effects of traumatic brain injury (TBI) result from disruptions in neural circuitry. The forebrain is the primary region of injury during blunt force trauma and has long-distance connections with distal brain regions. Interactions between brain regions are typically studied by focusing on acute effects, such as diaschisis of blood flow and neural activity. This project seeks to probe these long-distance interactions in vivo using a focal-injury model of TBI, two-photon microscopy, and pharmacogenetic perturbation of neural activity. The result will be to understand long-term effects of TBI on both the directly injured region, as well as interactions with distal regions that may be involved indirectly.

The work will be organized into: (1) Quantifying the remodeling of the forebrain post-injury to the contralateral hemisphere of the forebrain or to the cerebellum by observing changes in neural circuitry in vivo, (2) Perturbing inhibitory signals from the cerebellum and analyzing contralateral forebrain neural circuitry after TBI. These studies will test the hypothesis that inhibitory signals from the cerebellum may modulate critical periods of development and neural plasticity. These windows may be reopened by turning off inhibitory signals from the cerebellum or contralateral forebrain. These studies will provide an understanding into the long term effects of TBI on neural circuitry and identify sites distal from the site of injury as potential targets for TBI intervention and rehabilitation.

#### **Contact Information:**

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Below is a project summary of the pilot research grant recipients:

CBIR16PIL018 Bryan Pfister, Ph.D. New Jersey Institute of Technology \$180,000

**Project Title: In Vitro Platform for Medium Throughput Study of Injury to Human Glutamatergic Cortical Projection Neurons** 

Develop a multiwell in vitro platform to study mechanisms of traumatic brain injury in live human neurons and establish a technology to perform large-scale experimentation and drug screening.

Out of two million traumatic brain injuries (TBIs) a year only 500,000 are hospitalized; the remainder are those who do not seek medical attention or their unreported cases are managed with observation, rest and avoidance of repeated trauma. Identification of drugs to decrease the consequences of TBI or promote recovery is greatly needed. Currently, we are limited to investigating human TBI clinically in survivors, or pathologically using tissues available after a subject has died. Due to these constraints, the development of treatments presents formidable challenges and non-human models are required to explore mechanisms for treatment. Despite undeniable strengths, animal models are not practical for screening of biochemical libraries for their effects on trauma. The evaluation of new treatments could greatly benefit from an experimental system to study brain injury in live human neurons. The availability of such a platform on a high-throughput scale would allow the screening of compounds for their effects directly in human neurons.

Neuronal culture models have had significant impact by identifying important biological processes involved in TBI pathology. Currently these models are limited by experimentation of single samples, one-by-one, keeping productivity slow. The discovery of new treatments for many diseases, however, is accelerated with the use of high throughput tissue culture techniques. In this fashion, cell culture is more cost effective and rapid than animal models, providing an efficient method for screening for biomarkers and potential therapies. This proposal is to develop a neuronal culture platform to study the effects of potential treatments in differentiated human neurons and establish a technology to perform large-scale experimentation such as drug discovery. The unique characteristics of this model are its replication of injury and cell population that are directly relevant to human TBI that can be studied in a rapid fashion.

#### **Contact Information:**

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Below is a project summary of the pilot research grant recipients:

CBIR16PIL015 David Shreiber, Ph.D. Rutgers University Biomedical Engineering \$180,000

Project Title: Multi-Functional Biomaterials for Simultaneous Protection from Free Radicals and Targeting of Therapeutics after TBI

We will develop a biomaterial that protects neurons from damage from free radicals and polymerizes via these free radicals to localize delivery of neurotrophic factors.

TBI starts with physical trauma to the head, which is followed by a persistent multi-faceted secondary injury cascade that can continue to damage neurons long after the initial trauma. We believe that components of the secondary injury cascade can also be used to control the presentation of trophic factors that promote neuronal survival by reacting with a responsive carrier ma. Since the injury site has the largest concentration of these components, this would act to localize the delivery of therapeutic molecules at the injury site. In addition, the reaction of the responsive material with the different components may prevent the components from reacting with and damaging cells. Thus, if successful, our approach will improve neuronal survival in two ways: (1) protecting neurons from components at the injury site and (2) localizing and sustaining the presentation of trophic factors at the injury site. Both of these aspects of the biomaterial can potentially improve outcome following TBI. Together, we believe that this novel, multi-potent approach will significantly enhance neuronal survival following TBI. This Pilot Proposal describes a series of aims and objectives that are designed to generated proof of principle for the stimuli-responsive biomaterial. If successful, we will then move to establish efficacy in vivo and determine the best means of delivery.

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Below is a project summary of the pilot research grant recipients:

CBIR16PIL026 Joshua Berlin, Ph.D. Rutgers Biomedical & Health Sciences New Jersey Medical School \$180,000

Project Title: Cellular Events Precipitating Seizure-Like Neuronal Activity After Traumatic Stretch Injury to a Cortical Network Relevance for Therapeutics

This project seeks to investigate acute cortical neuron hyperexcitability following stretch injury as an experimental model for seizure activity following traumatic brain injury. Post-traumatic seizures is a serious morbidity for many people who experience traumatic brain injury. Current therapies are inadequate so new approaches are needed. To determine what novel therapeutic approaches might be successful, we would be greatly aided if we understood the processes that initiate the development of post-traumatic seizures. Unfortunately, current experimental systems miss many of the early events that set the injured brain onto the course to seizure activity.

Using a collaborative, interdisciplinary approach the principal investigators of this proposal have developed a novel in vitro model for seizure activity. We have developed data suggesting that this model system shares important properties with established traumatic brain injury models in which neuronal hyperexcitability is a common precursor to seizure development. Thus, we propose in this exploratory project to collect data that describe the changes in neuronal function occurring immediately following stretch injury. Towards this goal, we are asking specific questions about the behavior of the neurons in our model system to determine if and how they show hyperexcitable behavior, consistent with seizure activity.

The data derived from proposed experiments will allow us to define the basis for the early changes in neuronal function following injury, so that we can develop specific hypotheses to test in future experiments. In developing these data, we will necessarily employ experimental manipulations and pharmacological agents that target specific types of channels and receptors, thereby opening a window on potential approaches to minimize hyperexcitability after stretch injury and pointing the way towards future research to investigate therapeutic interventions to prevent seizures following traumatic brain injury.

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Below is a project summary of the pilot research grant recipients:

CBIR16PIL025 Helen Genova, Ph.D. Kessler Foundation \$173,762

### **Project Title: Examining Neural Changes** Following an Emotional Processing Intervention

This study will examine functional and structural changes following an intervention for emotional processing deficits in TBI using functional magnetic resonance imaging and diffusion tensor imaging.

Individuals with Traumatic Brain Injury (TBI) experience a number of physical and cognitive symptoms. Recent evidence suggests that in addition to these issues, a significant number of individuals with TBI have difficulty in emotional processing and social cognition. Specifically, some individuals with TBI have difficulty correctly identifying emotions from facial expressions. Deficits in emotional processing can have a significantly negative impact on social interactions, mood, and quality of life. Therefore, treatment of emotional processing deficits is critical to improving the lives of individuals with TBI.

The current study examines a treatment for emotional processing deficits in TBI. Specifically, this study examines the neural changes which occur as a result of an emotional processing intervention. Using functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI), the proposed study will examine both brain structure and function before and after the intervention. It is hypothesized that brain activity will increase following the intervention, especially in those brain regions involved in social cognition. Further, we expect that the integrity of white matter tracts connecting brain regions associated with social cognition will be improved following the intervention. The current proposal is an extension of a funded project which examines the efficacy of the emotional processing intervention on objective behavior.

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Below is a project summary of the pilot research grant recipients:

CBIR16PIL021

Mohammed Abdul Muneer Peringady, Ph.D. New Jersey Institute of Technology \$177,469

Project Title: A Therapeutic Approach to Alleviate Angiotensin II Induced Neurovascular Complications in Traumatic Brain Injury

This proposal is to undertake a therapeutic intervention to mitigate angiotensin II induced oxidative stress, hypertension, BBB impairment, neuroinflammation & neurodegeneration in blast induced TBI.

Traumatic brain injury (TBI) is characterized by physical brain injury that temporarily or permanently causes the disability by affecting cognitively, physically and emotionally. TBI causes approximately 1.7 million deaths and hospitalizations in the United States and about 20,000 people state wide annually.

Individuals exposed to explosive blast are at increased risk for TBI. Military casualties have enhanced the incidence and morbidity associated with TBI, particularly due to blast exposure. Blast TBI (bTBI) results in many neurobiological disorders, most of them lead to permanent disability. The recent clinical and experimental reports show that blast waves cause short and long term neuropathologies. While the biochemical mechanisms are still elusive, we have been trying to find out the mechanism of bTBI caused by primary blast waves. In several other biochemical mechanisms Angiotensin II (Ang II) has been reported as a mediator of oxidative stress generation via activation/induction free radical generating enzymes NADPH oxidase (NOX) and inducible nitric oxide synthase (iNOS).

In this proposal, we bring a novel hypothesis that Ang II could induce oxidative stress, which contributes the BBB disruption, neuroinflammation and neurodegeneration mediated via TBF-beta1 and MMPs signaling pathways in bTBI. This will be the first study to attempt a therapeutic approach by blocking the binding of Ang II to its receptor, Ang T1 receptor using Angiotensin receptor blocker, Losartan to prevent or reduce the neurovascular complications due to bTBI. The study will create an impact for treating BBB damage, which leads to BBB leakage, neuroinflammation and hemorrhagic stroke.

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Below is a project summary of the pilot research grant recipients:

CBIR16PIL035 Davide Comoletti, Ph.D. Rutgers University Biomedical & Health Sciences \$180,000

### Project Title: Neuronal Cell Surface Molecules that Stimulate Myelination

Preliminary data show that CASPR2 stimulates oligodendrocyte-neuron interactions. We will study the molecular details of how oligodendrocytes myelinate neurons in development and after brain injury. Traumatic brain injury is different from other types of bodily injury because it can affect all aspects of our lives including our physical and mental abilities, and personality. Brain injuries heal more slowly than other injuries and often incompletely. Mechanisms of recovery remain uncertain and the consequences of similar injuries may be very different. The brain of healthy humans undergoes constant turn-over of the white matter (rich in myelin) such that myelin can be added to new neuronal projections and restored after mild traumatic lesions. In TBL, damaged axons need to be remyelinated to protect neurons and facilitate recovery of neuronal function.

Oligodendrocytes are the cells in the brain that recognize the axons of the neurons and wrap around them producing the myelin sheets. At the molecular level, only a handful of molecules have been found to stimulate oligodendrocytes to myelinate neurons in the central nervous system. The question of which molecules allow the oligodendrocytes to recognize, adhere and envelop the appropriate neurons is central to understanding how myelination occurs and how to enhance it (or protect) it after traumatic episodes. Our data suggest that a protein called CASPR2 is important in these initial steps of oligodendrocyte-neuron recognition and it is sufficient to trigger myelination through their association with a specific partner on the oligodendrocyte surface.

In this project we plan to use various assays to understand the mechanistic details of how CASPR2 triggers myelination. Knowing more about CASPR2-mediated myelination has the potential to translate rapidly into better tools to improve remyelination after TBI as CASPR2 may become a target for therapeutic interventions to help a subset of patients to cope with the disease. In the future, a clear understanding of the molecular mechanisms of oligodendrocyte-neuron recognition will be important to find strategies to maximize and stimulate remyelination.

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Below is a project summary of the pilot research grant recipients:

CBIR16PIL021 Kathy Chiou, Ph.D. Kessler Foundation \$176,776

Project Title: Mindful Mending: Evaluating the Effects of Mindfulness Meditation on Metacognition in Moderate to Severe Traumatic Brain Injury

This study evaluates the efficacy of a mindfulness meditation program in improving metacognitive functioning after moderate to severe TBI and identifies the neural mechanisms underlying this practice.

Metacognition refers to in-the-moment awareness of performance while completing a cognitive task and is a cognitive domain that has been shown to influence community re-integration and quality of life after TBI. Problematically, adults with TBI experience metacognitive deficits after injury, but treatment options to improve metacognition are currently limited. Recently, research has emerged showing that healthy adults improve their metacognitive functioning after engaging in mindful meditation. While these study findings are promising, it remains unknown whether the efficacy of mindfulness meditation in treating metacognition also generalizes to adults with moderate to severe TBI.

This study is a randomized clinical trial designed to determine whether the practice of mindfulness meditation improves metacognitive functioning after moderate to severe TBI. Additionally, functional magnetic resonance imaging (fMRI) will be used to document the effect of mindfulness practices on neural activation after injury. Documented patterns of activation will serve as biomarkers that will be critical to advancing our understanding of neuroplastic responses to treatment after TBI.

The evaluation of meditation mindfulness as an effective approach to improving metacognition after TBI provides the first step towards the development of rehabilitative interventions for a cognitive domain that is being increasingly recognized for its important influence on functional capacities after injury. Improving metacognitive functioning in individuals with TBI will ultimately increase their ability to function independently and improve their overall quality of life.

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