



Spinal Cord Injury and Traumatic Brain Injury Research Grant Program Report

January 15, 2020

Author**Alaina DeSalvo**

Competitive Grants Administrator
Tel: 651-259-3988
Alaina.DeSalvo@state.mn.us

About the Minnesota Office of Higher Education

The Minnesota Office of Higher Education is a cabinet-level state agency providing students with financial aid programs and information to help them gain access to postsecondary education. The agency also serves as the state's clearinghouse for data, research and analysis on postsecondary enrollment, financial aid, finance and trends.

The Minnesota State Grant Program is the largest financial aid program administered by the Office of Higher Education, awarding up to \$207 million in need-based grants to Minnesota residents attending eligible colleges, universities and career schools in Minnesota. The agency oversees other state scholarship programs, tuition reciprocity programs, a student loan program, Minnesota's 529 College Savings Plan, licensing and early college awareness programs for youth.

Minnesota Office of Higher Education

1450 Energy Park Drive, Suite 350
Saint Paul, MN 55108-5227
Tel: 651.642.0567 or 800.657.3866
TTY Relay: 800.627.3529
Fax: 651.642.0675
Email: info.ohe@state.mn.us

Table of Contents

Introduction	1
Spinal Cord Injury and Traumatic Brain Injury Advisory Council	1
FY 2020 Proposal Solicitation Schedule and Proposals Received	3
Fiscal Year 2020 Annual Research Grant Proposal Solicitation Schedule	3
Fiscal Year 2020 Spinal Cord Injury and Traumatic Brain Injury Research Grant Proposals Received	3
Grant Selection Process	5
FY 2020 Spinal Cord Injury and Traumatic Brain Injury Research Projects	6
Spinal Cord Injury Research	6
Traumatic Brain Injury Research	9
FY 2020 Timeline and Anticipated Outcomes	14
APPENDIX A: Copy of Statute	15
APPENDIX B: 2020 Spinal Cord Injury and Traumatic Brain Injury Research Grant Program Applicants	18
Proposals Submitted – Spinal Cord Injury	19
Proposals Submitted – Traumatic Brain Injury	21
APPENDIX C: Annual Research Grant Proposal Review Form	23
APPENDIX D: Completed Projects: Accomplishments and Dissemination	26
Spinal Cord Injury and Traumatic Brain Injury Research Projects	27

Introduction

The State of Minnesota established the Spinal Cord Injury and Traumatic Brain Injury (SCI-TBI) Research Grant Program effective July 1, 2015. Minnesota 2015 Session Law, Chapter 69 directed the Commissioner of the Minnesota Office of Higher Education to establish a grant program for institutions in Minnesota to conduct research that would lead to new and innovative treatments and rehabilitative efforts for the functional improvement of people with spinal cord injuries and traumatic brain injuries. Research areas include, but are not limited to, pharmaceutical, medical devices, brain stimulus, and rehabilitative approaches and techniques.

Appendix A provides a copy of the grant program’s founding statute.

For the 2020-2021 biennium, \$3,000,000 was made available for each year from the 2019 Omnibus Higher Education Bill (Minnesota 2017 Session Law, Chapter 69) to support the SCI-TBI Grant Program, with a 3 percent administrative fee. As directed by the program’s statute, the Commissioner of the Office of Higher Education, in consultation with the program’s Spinal Cord Injury and Traumatic Brain Injury Advisory Council (Advisory Council), will allocate 50 percent of the grant funds to research involving spinal cord injuries and 50 percent to research involving traumatic brain injuries throughout the biennium. A total of \$459,313 was carried forward from funds unused in fiscal year (FY) 2019, for a grand total of \$3,459,313 available to be granted out to support this initiative in FY 2020.

In FY 2020, the Commissioner of the Office of Higher Education and the Advisory Council awarded a total of \$3,137,829 to support spinal cord injury and traumatic brain injury research and innovation. Sixteen new research projects were funded—seven spinal cord injury research projects and nine traumatic brain injury research projects.

In July 2018, the Spinal Cord Injury and Traumatic Brain Injury Grant Program was given a Special Revenue Account in order to extend project periods from a one to two years to a two-to-five-year timeline. Beginning with the FY 2020 competition, grantees are given 2-5 years to complete their research projects, with a possibility for an extension based on their progress and the complexity of the research. The timeline extension is crucial for the completion of projects based on lengthy Institutional Review Board (IRB) review processes and unexpected challenges that occur naturally with complex research and experimentation.

Spinal Cord Injury and Traumatic Brain Injury Advisory Council

The 2015 statute language that established the grant program also established the Spinal Cord and Traumatic Brain Injury Advisory Council. The Commissioner, in consultation with the Advisory Council, has the responsibility of awarding the SCI-TBI grants and developing the program. In 2015, an initial 12-member Advisory Council was set up using the Open Appointments process of the Minnesota Secretary of State’s office. In 2017, the statute language was updated to include two new seats: 1) Veteran with a Traumatic Brain Injury, and 2) Physician Specializing in the Treatment of Spinal Cord Injury. Both seats were filled in 2018, though the Veteran with a Traumatic Brain Injury representative resigned at the end of 2018 due to personal reasons.

One persistent challenge in maintaining continuity within the Advisory Council is securing veterans with a spinal cord injury or traumatic brain injury to fill those corresponding roles. Many veterans who have joined the council do not persist through their first year for personal reasons, mainly related to health and wellness. A future consideration is to reconfigure those council seats so that veterans with these injuries may send a representative from Veterans Affairs in their place.

In 2019, Mr. Robert Wudlick, advocate and community member with a spinal cord injury, was chosen to serve as the Advisory Council chair. Several of the 2017 appointments were also up for renewal. The Commissioner of the Office of Higher Education selected the four-member Advisory Council through the Minnesota Secretary of State’s Open Appointments process. The full membership of the Advisory Council is shown below (new members are in bold):

Table 1: Advisory Council Roster

Member	Representing
Dr. Uzma Samadani	Physician specializing in the treatment of traumatic brain injury
Dr. Maxim C-J Cheeran	University of Minnesota Medical School (replacing Dr. Walter Low)
Dr. Peter Grahn	Mayo Clinic
Ms. Nancy Ann Flinn	Courage Kenny Rehabilitation Center (replacing Dr. Mary Radomski)
Dr. Nova McNally	Hennepin County Medical Center (replacing Dr. Sarah Rockswold)
Dr. Andrew W. Grande	Neurosurgeon
Mr. Robert Wudlick, Chair	Person with a spinal cord injury
Mr. Matthew Rodreick	Family member of a person with a spinal cord injury
Ms. Christy Marie Caez Claudio	Person with a traumatic brain injury
Mr. Brian Morrissey	Veteran who has a spinal cord injury
OPEN	Veteran who has a traumatic brain injury
Dr. Mark Gormley	Gillette Children’s Specialty Healthcare
Mr. Bruce Richard Everling	Family member of a person who has a traumatic brain injury
Dr. Ann Parr	Physician specializing in the treatment of spinal cord injury (replacing Dr. Steven Jackson)

FY 2020 Proposal Solicitation Schedule and Proposals Received

Fiscal Year 2020 Annual Research Grant Proposal Solicitation Schedule

To support research projects with FY 2020 program funding, the following timeline was used to solicit proposals and award grant funds:

December 1, 2018	Request for Proposals (RFP) available to applicants
March 8, 2019	Deadline for receipt of intent to submit forms
4:30 p.m., April 5, 2019	Deadline for receipt of proposals
May 20, 2019	Proposal Review Meeting
June 10, 2019	Notification of recommendation for grant award
July 1, 2019	Project funding begins with grant contract encumbrance

Fiscal Year 2020 Spinal Cord Injury and Traumatic Brain Injury Research Grant Proposals Received

The Spinal Cord Injury and Traumatic Brain Injury Advisory Council received a total of 29 proposals for FY 2020 funding; 15 proposals with a focus on spinal cord injury research, and 14 with a focus on traumatic brain injury research. A combined total of \$7,272,224 was requested. A full list of proposals and applicants can be found in **Appendix B**.

A new funding mechanism was created by the Advisory Council for the FY 2019 RFP to categorize/organize proposal submissions and set appropriate parameters around funded projects. This worked well for the purpose of appropriately funding projects based on their level of complexity, prior established research, and resources necessary to complete proposed projects. Therefore, the Minnesota Office of Higher Education (OHE) used the same three-tier funding mechanism in FY 2020, and will continue to use this going forward.

The three distinct funding options were created by the Advisory Council. Each tier, with maximum allowable requests and project requirements, are listed below:

Tier 1: Pilot Project Grant

- Max Request: \$125,000.
- Project Time: two years + one-year no cost extension.
- Project Details: Reflects early investment as the researcher prepares to seek a larger grant award from a federal program or nonprofit organization. Preliminary data is not required.

Tier 2: Standard Research Grant

- Max Request: \$250,000.
- Project Time: two years + one-year no cost extension.
- Project Details: Primarily for research with supporting/preliminary data. If the budget is justifiable, the Standard Research Grant may also fund pilot projects. Applicants are encouraged to attach papers—in press and accepted/cited papers may be submitted separately as an appendix.

Tier 3: Clinical/Translational Research Grant

- Max request: \$500,000.
- Project Time: three years + two-year no cost extension.
- Project Details: Projects must have concurrent application or funding from federal or industry sources. Preliminary data must be published or in press in a scientific journal and cited or submitted separately as an appendix.

Grant Selection Process

At the May 20, 2019 meeting, the Advisory Council was split into two groups: one specializing in spinal cord injury proposal assessment and one specializing in traumatic brain injury proposal assessment. For the first time, the Council invited all applicants to give a brief, five-minute presentation of their proposed project, with an additional five minutes for questions. This allows applicants to describe their project in their own words, which helps mitigate conflict of interest and gives community members outside of the science community the opportunity to receive the information in laymen's terms that does not center medical/scientific jargon. It also allows all Advisory Council members to ask clarifying questions, the responses of which may have a big impact on proposal scores. Applicants were given the option to present in person or via WebEx. This new process received overwhelming positive feedback from both presenters and the Advisory Council.

The presentation process supplemented the proposal evaluation process that the Advisory Council is asked to complete annually. Each proposal was reviewed and scored by members of the specialty-area review panel reflective of the proposal's research focus. For the review, Advisory Council members with a scientific background gave particular attention to the scientific and technical merit of the proposals, while members with patient or community perspectives gave particular attention to the importance of the proposed research for patients. Proposals were scored individually and discussed during the May meeting, after each presentation. Advisory Council members were required to disclose any conflict of interest with any submitted proposals. If direct conflict of interest was present, the Advisory Council member did not review the proposal and was excused from the room when the proposal was discussed.

Through this process, the Advisory Council completed their reviews of the 29 research proposals submitted to OHE. Of the 29 proposals, 16 were recommended for funding. A total of \$3,139,350 was awarded.

FY 2020 Spinal Cord Injury and Traumatic Brain Injury Research Projects

Pursuant to the language of the statute establishing the research grant program, members of the Spinal Cord and Traumatic Brain Injury Advisory Council reviewed research proposals and recommended proposals for funding to the Commissioner. The Proposal Review Form used by the Advisory Council members is found in **Appendix C**. The 16 FY 2020 projects recommended for funding were:

Spinal Cord Injury Research

ESTAND 2.0 – Bridge to Clinical Approval of eSCS for SCI, Hennepin Healthcare – HCMC/Hennepin Healthcare Research Institute, University of Minnesota, receives \$351,000

Over the past several years, epidural spinal cord stimulation (eSCS) has arrived as a potential clinical therapy to restore function following spinal cord injury (SCI). Through the initial ESTAND study, investigators contributed to the growing body of literature demonstrating that eSCS has the capability to partially restore volitional movement, autonomic, and cognitive function after chronic SCI. However, evidence is mounting that cognitive dysfunction may be a widespread problem for chronic SCI patients that is often overlooked without specific testing and treatment. Direct attention is required to better characterize this phenomenon and investigate the utility of eSCS as a treatment. In this project, investigators will seek to study a generalizable chronic SCI population to test efficacy under a single protocol, and to test the presence and treatment of cognitive dysfunction and brain function with eSCS. They will be the first to quantitatively investigate this by enrolling 10 patients under the current ESTAND baseline protocol to determine the generalizable effectiveness for eSCS for chronic SCI. Investigators will measure cognitive function and brain function through EEG during a cognitive task, and extend the current optimization platform to discover optimal parameters for stimulation to restore cognitive, linked to integrated measures of cardiovascular, function. This project is designed to extend current efforts to understand the key effects of eSCS and how the effects interact across a sufficiently large patient population, which is the next critical step towards obtaining FDA approval for eSCS.

Principal Investigator(s): Dr. David Darrow; Dr. Ann Par; Dr. Thomas Bergman, 214-564-0623, darro015@umn.edu

Spinal Cord Regeneration by Cell Reprogramming in Chronic Spinal Cord Injury, University of Minnesota, receives \$151,000

The Holy Grail for spinal cord injury research is the regeneration of the spinal cord for complete repair after chronic injury. At the present time, this regenerative process is not possible in the spinal cord of humans and other mammals. However, certain animals such as amphibians are capable of complete spinal cord regeneration and restoration of movement after the spinal cord is completely severed. This regeneration process in amphibians replicates the process of development so that all of the damaged cells and nerve fibers are reinstated. The goal of this project is to re-activate the regenerative process in the mammalian spinal cord after

injury. The central hypothesis of this research is whether the reprogramming of certain types of cells in the spinal cord called “astrocytic glia” to become neuronal cells can re-engage the developmental process and result in the regeneration of the spinal cord after injury. This will be investigated in this project by re-programming the astrocytic glial cells into neurons in the spinal cord by introducing the gene, NEUROD1, into astrocytes following spinal cord injury in the acute and chronic setting. This method has previously been shown to regenerate the neocortex of rats that have suffered ischemic stroke; therefore, it should also work for the spinal cord.

Principal Investigator: Dr. Walter C. Low, 612-626-9203, lowwalt@umn.edu

Non-invasive Transcutaneous Spinal Cord Stimulation for Recovery of Hand Function after Spinal Cord Injury, Hennepin Healthcare – HCMC/Hennepin Healthcare Research Institute, receives \$201,000

Spinal cord injury (SCI) is a devastating neurologic condition resulting in significant deficits in sensory, motor, and autonomic functions, and multiple secondary medical complications such as neurogenic bowel/bladder, sexual dysfunction, spasticity, and neuropathic pain. Currently there are no effective treatment options for this condition. However, recent research has demonstrated that spinal cord stimulation (SCS) can improve standing, ambulation, and hand grip strength/function in individuals with chronic SCI. In this project, the investigators hypothesize that the non-invasive transcutaneous SCS (tSCS) may improve hand/arm function in individuals with SCI. This study is a single-arm study to evaluate the effectiveness of the tSCS with occupational therapy on improvement in hand and arm function after 12 weeks of in-clinic occupational therapy with and without stimulation. The study will enroll a maximum of 15 subjects; outcome measures include International Standards for Neurological Classification of Spinal Cord Injury score, pinch/grip force measurement, Graded Redefined Assessment of Strength Sensibility and Prehension, the Action Research Arm Test, the Capability of Upper Extremity Questionnaires/Test, and other quality of life questionnaires conducted before, during, and after therapy sessions. The goal is to investigate the effectiveness of non-invasive tSCS on improvement of hand and arm strength and function as a part of a pivotal trial with the goal of FDA approval of the tSCS in 3 years. Once the study shows effectiveness of tSCS in hand/arm function improvement, further research will be continued to investigate the effectiveness of tSCS on standing, core strength, balance, ambulation, and autonomic functions.

Principal Investigator(s): Dr. David Darrow; Dr. Thomas Bergman, 214-564-0623, darro015@umn.edu

3D Bioprinted spinal Neuro Progenitor Cell (sNPC) Scaffolds Accelerate Functional Neuronal Network Formation in both in vitro and in vivo after Spinal Cord Injury, University of Minnesota, receives \$151,000

Recent studies show that it is possible to transplant regionally specific human spinal neural progenitor cells (sNPCs) into rat SCI and that the transplanted sNPCs will display long term survival, mature in the cavity area, extend axons long distances, and even functionally integrate into the hosts’ neural circuitry. Regionally specific sNPC transplantation is thus a promising therapeutic option for restoring function to damaged pathways after traumatic SCI. This is especially exciting because these cells could potentially bridge gaps in the spinal cord that exist in chronic injuries in humans. Thus, this study proposes a completely different mechanism of action than that of other cell types that act in the subacute setting to prevent secondary injury. The hypothesis that drives this project is that the functional neural networks contained within our 3D bioprinted scaffolds can be optimized based on the location of the bioprinted cells, and that this will lead to enhanced functional outcomes in an acute

transected SCI rat model. The study hopes to further investigate network dynamics of sNPCs and scaffolds *in vitro* via optogenetics and calcium imaging. The investigators will then transplant the scaffolds into acutely transected rat SCI and examine integration, functional recovery, and electrophysiological outcomes.

Principal Investigator(s): Dr. Ann M. Parr; Dr. Michael McAlpine, 612-625-4102, amparr@umn.edu

Multi-Dose Safety and Feasibility Study of Autologous Culture Expanded Adipose Derived Mesenchymal Stem Cells (AD-MSCs) in the Treatment of Traumatic Spinal Cord Injury, Mayo Clinic, receives \$351,000

Due to the limited capacity for regeneration of the nerve cells in our body following traumatic damage, any injury to the spinal cord has the potential to result in permanent damage that may include paralysis, sensory impairment, and/or bowel/bladder/sexual dysfunctions. Currently, investigators are trying to address this condition using various treatment approaches. The use of stem cells as one of these treatment modalities has gained increasing popularity due to their systemic effects and regenerative potential. Therefore, the aim of this study is to investigate the safety and feasibility of multiple injections of AD-MSCs in the context of patients suffering from spinal cord injury. This study will include 10 patients with traumatic spinal cord injury. Fat tissue will be harvested in the baseline visit, and stem cells will be cultured using the cells obtained from fat harvest. After the expansion of stem cells to approximately a 100 million cell dose, cells will be injected into the spinal fluid of patients in the same way a spinal tap is performed. This process will be repeated every 3 months and patients will be monitored for any adverse events at each visit following the injection of stem cells. The investigator hypothesizes that multiple injections of AD-MSCs will have a cumulative effect on functional improvements and may evolve as a potential standard of care treatment for neurological recovery in the future.

Principal Investigator: Dr. Mohamad Bydon, 507-284-2511, Bydon.mohamad@mayo.edu

Therapeutic Targeting of Cellular Senescence to Promote Repair of the Chronically Injured Spinal Cord, Mayo Clinic, receives \$151,000

A recent discovery indicates that the chronically injured spinal cord expresses key markers of cellular senescence. Senescent cells are in a state of irreversible cell cycle arrest, have a distinctive secretory phenotype that limits innate tissue repair and drives age-related tissue deterioration. Although the pathophysiological role of cellular senescence in SCI has not been previously addressed, documented contributions to pathogenesis occur in atherosclerosis, osteoarthritis, pulmonary fibrosis, and neurodegenerative conditions. Moreover, clearing senescent cells using FDA-approved drugs, or with genetic approaches, substantially improves tissue repair, including enhancing neurogenesis as well as inter-vertebral glycosaminoglycan deposition, and functional outcomes in many of these pathologies. The overarching hypothesis to be tested in this project is that cellular senescence in chronic SCI limits the capacity for repair and can be targeted therapeutically to improve function. In addition, the investigator will test the hypothesis that locomotor training will augment the pro-reparative effects of senescent cell targeting. If these integrated hypotheses are correct, the proposed studies will serve to identify an important but understudied pathogenic mechanism relevant to chronic SCI that can be targeted pharmacologically alone, or in conjunction with rehabilitation, to improve outcomes.

Principal Investigator: Dr. Isobel Scarisbrick, 507-284-0124, scarisbrick.isobel@mayo.edu

Optimization of iPSC-derived Oligodendrocyte Progenitor Cell (OPC) Manufacture- a Key Step Toward Patient Treatment, Regents of the University of Minnesota, receives \$141,000

Oligodendrocytes are the glial cells of the central nervous system that wrap myelin around nerve axons to protect them and allow proper signal conduction. Nerve damage and secondary inflammation after spinal cord injury causes loss of oligodendrocytes and contributes to loss of function. Restoration of oligodendrocytes after injury by transplantation of their immediate precursor cell, the oligodendrocyte progenitor cell or POC, has been shown to be beneficial to restoring functional recovery in animal models and was the basis of the first human pluripotent stem cell derived clinical trial for spinal cord injury. The hypothesis of this project is that an accelerated method to induce and pattern neural progenitors from human pluripotent stem cells generates the spinal floorplate glial precursor cells that give rise to OPCs. This will be achieved by rapid differentiating hiPSCs in culture to generate the spinal cord precursor cells that give rise to OPCs. Two different approaches will then be compared to refine the optimal way to capture the OPC cell product that would be used in clinical translation. Spinal cord organoids will be cultured to validate the transition of the POC product into myelinating oligodendrocytes. Cell culture automation will be employed to demonstrate commercial scalability.

Principal Investigator: Dr. James R. Dutton, 612-626-2762, dutto015@umn.edu

Traumatic Brain Injury Research

Identification of Brainwide Network Activity Changes in Post-traumatic Epilepsy to Optimize the Therapeutic Effect of Vagus Nerve Stimulation on Post-traumatic Epilepsy, Mayo Clinic, receives \$125,000

Traumatic brain injury (TBI) accounts for 30% of all injury-related deaths in the U.S. Developing epilepsy after severe TBI is severely common, with rates as high as 40%-50%. Even so, treatment for TBI-related epilepsy is suboptimal due to a lack of understanding of the mechanisms involved in post-traumatic epilepsy (PTE). This study identifies neural network activity changes in animal models of PTE and develops a treatment method using vagus nerve stimulation (VNS). The central hypothesis is that TBI may induce brainwide neural activity changes and these changes may highly be involved in the development of PTE. Vagus nerve stimulation has been evaluated to control epilepsy – here the investigators will optimize stimulation parameters of VNS to reduce PTE. The evaluation of VNS will improve its efficacy for PTE suppression.

Principal Investigator(s): Dr. Su-Youne Chang; Dr. Azra Alizad, 507-293-0511, chang.suyoune@mayo.edu

Switching Off the Thrombin Receptor to Enhance Recovery after Traumatic Brain Injury, Mayo Clinic, receives \$250,000

Neurotrauma unleashes a cascade of cellular and molecular events that worsen the outcome of the initial injury. Recent findings show that increases in degradative proteases are a key part of inflammatory astrogliosis and play pivotal roles in the exacerbation of neural injury. Importantly, many of these proteases exert their effects by activating a G-protein coupled receptor referred to as a Protease Activated Receptor 1 (PAR1), also known as a thrombin receptor. When this receptor is switched on, it promotes injury – however, new findings indicate that switching off PAR1 decreases secondary pathogenesis and improves the repair and recovery of function. The identification of PAR1 as a key regulator of TBI pathogenesis is highly significant since FDA approved inhibitor, Vorapaxar, is already available and can be readily repurposed to improve recovery after TBI if the results of this pre-clinical study continue to suggest it is warranted. In this study, the investigator will pursue

both a pharmacologic and a genetic approach for switching off PAR1 to improve outcomes in a well-studied murine model of repetitive-mild TBI. In Aim 1, the investigator will determine whether administration of an FDA-approved small molecule inhibitor of PAR1 after repetitive-mild TBI improves outcomes. In Aim 2, the investigator will determine whether switching off the PAR1 gene using conditional targeting approaches also improves neural repair and recovery of function.

Principal Investigator: Dr. Isobel Scarisbrick, 507-284-0124, scarisbrick.isobel@mayo.edu

Multilineage 3-Dimensional Brain Organoids to Model Intracranial Pressure Linked to Chronic Traumatic Encephalopathy, University of Minnesota, receives \$81,443

Chronic traumatic encephalopathy (CTE) is a progressive neurodegenerative disorder uniquely characterized by depositions of phosphorylated tau (pTau) within the brain. It is generally assumed that CTE is the result of repeated mild traumatic brain injury and has been diagnosed in athletes in a wide range of contact sports, in active and veteran military personnel exposed to blast injuries, and also in individuals where compulsive head-banging was frequent. The underlying mechanisms behind CTE are beginning to be understood, yet much remains to be known due to the fact that a definitive diagnosis of CTE can only occur during post-mortem tissue evaluation. Furthermore, a lack of CTE-relevant disease models which recapitulate the progressive nature of the disease has also hindered progress. The hypothesis of this project is that a multilineage three-dimensional brain organoid, comprised of neurons, astrocytes, oligodendrocytes, and microglia is best suited to model CTE as these diverse cell types play important roles in the pathogenesis of CTE. Within a controlled cell culture environment, the organoids can be exposed to repeated transient increases in hydrostatic pressure, simulating repeated injuries. This system can be adapted for high-throughput drug screening of FDA-approved drugs that have already been well-characterized for safety and bioavailability in a clinical setting.

Commercially available FDA drug-screen libraries will then be used in a high-throughput setting to identify drugs that ameliorate accumulation of pTau, as indicated by a decrease in organoid fluorescence, relative to untreated, stressed organoids.

Principal Investigator: Dr. Andrew T. Crane, 612-626-9212, atcrane@umn.edu

Characterizing the Neuroinflammation Associated with Sequential TBI in a Rodent Model, University of Minnesota, receives \$125,000

Concussion is the most common type of traumatic brain injury (TBI) and most patients recover without significant CNS pathology. But these patients are susceptible to development of neurodegenerative and neuropsychiatric complications after repetitive TBI, which is common among soldiers and athletes. In addition to mechanical injury to the brain that occurs at the time of trauma, persistent inflammation in the brain is the dominant secondary injury mechanism associated with development of neurodegenerative disorders. The central hypothesis of this research is that a second injury after a mild TBI will result in an enhanced neuro-inflammatory response, which persists longer and results in greater behavioral deficits. This study proposes to use a well-established controlled cortical impact (CCI) mouse model of TBI. Neuro-inflammation after second sequential TBI will be assessed by three different approaches: (i) flow cytometry to assess changes in immune cell phenotypes, (ii) immunohistochemistry to determine the extent of neuronal damage and localization of infiltrated cells, and (iii) RT-PCR to determine altered gene expression levels of inflammatory cytokine in the brain. In addition, behavioral tests will be performed which will evaluate both the sensory motor and cognitive function of the patient.

Principal Investigator: Dr. Maxim C. Cheeran, 612-626-9930, cheeran@umn.edu

Validation of Cardiovascular Exercise Tests for Individuals with Traumatic Brain Injury, ExercisAbilities and Winona State University, receives \$123,984

The current cardiovascular exercise tests designed for wheel-chair bound individuals are often too difficult for individuals with traumatic brain injuries and are largely focused on use of an arm crank ergometer. The challenges associated with the existing cardiovascular testing protocols create difficulties in properly assessing a patient's baseline abilities and progress over time. Additionally, the arm crank ergometer does not help promote progress toward regaining a standing or walking form of exercise, which is a critical aspect of rehabilitation for individuals with traumatic brain injury. The central hypothesis of the proposed study is: Modified cardiovascular testing protocols using the arm crank ergometer and the Madonna Intelligently Controlled Assistive Rehabilitation Elliptical (ICARE) are both valid and reliable methods for predicting maximal exercise capacity in wheelchair-bound individuals with traumatic brain injury. In this project, researchers will compare the results of the currently utilized and validated tests with the results of the cardiovascular tests they have developed. Additionally, each test will be performed multiple times on the participant population to observe test-retest reliability. Statistical analyses will be used to determine the validity and test-retest reliability. This study will be the first to validate a sub-maximal cardiovascular exercise protocol using the Madonna ICARE.

Principal Investigator(s): Melanie Brennan, PT, DPT; Dr. Justin R. Geijer, 507-259-7570, melanie@exercisabilities.org

Acupuncture Treatment for Chronic Post-traumatic Headache in Individuals with Mild Traumatic Brain Injury, HealthPartners Institute, receives \$81,443

Chronic post-traumatic headache (CPTH) is the most common type of pain after mild traumatic brain injury (mTBI) which is extremely painful and makes it very difficult for people to do their daily activities. CPTH is when headaches last for more than 3 months after a mTBI. People with CPTH normally have headaches for about 26 days each month and are more likely to have other problems. A promising treatment option for CPTH is acupuncture, because it has provided pain relief to people who suffer from long-term pain, headaches, and migraines. The principal investigator will test the hypothesis that people suffering from CPTH will feel headache relief from acupuncture and that a high dose will help more than a low dose. This will be achieved by recruiting a total of 36 people with mTBI suffering from CPTH. The participants will be split into two groups: 1) low acupuncture group (5 treatments), and 2) high acupuncture group (10 treatments). The participants will be monitored and asked to report on their headache symptoms and duration. If successful, acupuncture could be a natural alternative to pain medication for those suffering from CPTH.

Principal Investigator: Dr. Amanda A. Herrmann, 651-495-6356, amanda.a.herrmann@healthpartners.com

Improving Communication about Sexual Health for Persons Undergoing Acute Inpatient Rehabilitation for Traumatic Brain Injury (TBI), Center for Veterans Research and Education (CVRE), receives \$124,961

Sexual dysfunction is one of the top five comorbid conditions experienced by persons with traumatic brain injury (TBI). Individuals surviving TBI report a lack of satisfaction with treatment of sexual health concerns during rehabilitation, desiring more openness from their providers to discuss these concerns. Little research has been

done on interdisciplinary rehabilitation staff training that could improve communication in this crucial realm. The goal of this project is to develop and implement a cutting-edge staff training that will help rehabilitation staff to better address sexual health concerns after TBI in the inpatient setting. The central hypothesis is that an interdisciplinary staff training focused on communication around sexual health concerns will lead to 1) increased staff sexual health knowledge, 2) increased staff comfort with sexual health topics, 3) increased frequency of addressing sexual health during rehabilitation, and 4) improved patient satisfaction with care. This will be achieved by developing an interdisciplinary rehabilitation team training aimed at improving communication about sexual health in the inpatient rehabilitation setting. Data will be collected regarding staff knowledge and comfort pertaining to sexual health topics prior to and upon completion of the training, and comparisons will be made to evaluate the impact of the training on staff knowledge and comfort. Data will also be collected from patients during inpatient rehabilitation regarding frequency in which sexual health problems are addressed and satisfaction with care.

Principal Investigator: Dr. Melanie Blahnik, 612-467-1792, melanie.blahnik@va.gov

Improving Functional Outcomes through Optimization of Surgical Subdural Hematoma Evacuation Technique, CentraCare Health-St. Cloud Hospital, receives \$479,081

The leading cause of traumatic brain injury (TBI) in adults living in Minnesota is falling, and the risk of injury only increases with age. For those elderly patients with a TBI requiring surgical treatment, the most common underlying pathology is subdural hematoma (SDH). This is often the result of what we would consider trivial head trauma, such as a light head bump without any loss of consciousness or other concerning features. Despite their insignificant cause, SDH can persist, begin to clot, and become chronic. Currently, the standard of care for SDH is surgical evacuation via craniotomy or burr hole, both of which have about a 10% recurrence risk. A newer minimally invasive approach to evacuation is with a Twist-drill Craniostomy (TDC) that, when executed optimally, has been shown to decrease the length of hospital stay by an average of four days. However, imperfect drill placement has contributed to a high failure rate. This project aims to optimize placement by using machine learning and hologram 3D visualization in surgical planning. The investigator proposes that using machine learning algorithms to mathematically determine TDC drill site placement leads to less residual hematoma and a higher success rate than those evacuations arbitrarily drilled at the middle of the hematoma. If proven, this innovation will significantly improve the success rate of minimally invasive TDC. It will directly improve length and quality of life in patients with SDH, the most common cranial neurosurgical problem in Minnesota elderly, because patients with less residual hematoma have shorter recovery time, better functional outcomes, and significantly decreased medical costs.

Principal Investigator: Dr. Uzma Samadani, 917-388-5740, uzma@samadani.com

Theta Burst Stimulation for Headaches after Traumatic Brain Injury, Center for Veterans Research and Education (CVRE), receives \$249,980

Chronic headache is the most debilitating clinical symptom in individuals who have suffered a mild traumatic brain injury (mTBI). Unfortunately, the debilitation caused by headaches is often accompanied by dysfunction in mood, attention, and memory which results in a profound negative impact on these individuals' quality of life. Conventional pharmacological treatments have been shown to be ineffective in alleviating headaches in the post-traumatic injury population. This project proposes an innovative, non-invasive intervention to treat post-

traumatic headaches and alleviate the suffering associated with this clinical syndrome. The primary objective of this study is to investigate the safety and efficacy of theta-burst stimulation (TBS) for the management of posttraumatic headache, thereby improving outcomes and quality of life for those who have suffered a TBI. Individuals will receive three doses of TBS on alternate days of the week. The design will allow for assessment of efficacy while leveraging an accelerated treatment course (9 stimulation sessions per week). The investigator hypothesizes that accelerated TBS will 1) be safe and well tolerated, 2) reduce the number of headache days and improve function and quality of life outcomes, 3) produce greater and faster improvement in headache symptoms than that reported in the literature for standard rTMS protocols, and 4) produce durable improvements in all outcome measures.

Twenty participants will be enrolled in this open-label pilot study, which will be the first study to examine TBS, as well as an accelerated course of TBS in individuals with post-traumatic headache.

Principal Investigator: Dr. C. Sophia Albott, 612-787-5146, albot002@umn.edu

FY 2020 Timeline and Anticipated Outcomes

The time period of FY 2020 projects depends on the research tier of each project-- two years with a one-year no cost extension for Tier 1 and Tier 2 grantees and three years with a two-year no cost extension for Tier 3 grantees. All grantees will send progress reports annually until the completion of their project, at which time they will submit a final report and total project expenditure to close out their contract.

Updated progress and/or outcomes of the projects listed in this report will be disseminated to the public during the Minnesota Spinal Cord Injury and Traumatic Brain Injury Research Symposium. The date of the event is tentatively scheduled for February 2021; an invitation will be extended to legislators once it is confirmed. Discoveries and innovations will also be shared with the scientific community through national presentations, journal articles and publications, and future collaborations. For a list of preliminary accomplishments from completed projects, see **Appendix D**.

One future collaboration is with the Ohio Department of Education (ODE), which recently acquired funding for spinal cord injury research from the state of Ohio. OHE has been partnering with ODE to assist in the set up and development of their competitive grant program. Through information/knowledge sharing, OHE and ODE will continue to work together in hopes of furthering and deeping spinal cord injury research and getting closer to a cure for paralysis.

The Spinal Cord Injury and Traumatic Brain Injury Advisory Council anticipates that through the innovations cited in the recommended research projects, and collaboration with other nationally-reknowned researchers, the novel outcomes from the funded projects should lead to advances in the fields of spinal cord injury and traumatic brain injury.

APPENDIX A: Copy of Statute

LAWS OF MINNESOTA 2019

136A.901 SPINAL CORD INJURY AND TRAUMATIC BRAIN INJURY RESEARCH GRANT PROGRAM.

Subd 1. Grant program

The commissioner shall establish a grant program to award grants to institutions in Minnesota for research into spinal cord injuries and traumatic brain injuries. Grants shall be awarded to conduct research into new and innovative treatments and rehabilitative efforts for the functional improvement of people with spinal cord and traumatic brain injuries. Research topics may include, but are not limited to, pharmaceutical, medical device, brain stimulus, and rehabilitative approaches and techniques. The commissioner, in consultation with the advisory council established under section [136A.902](#), shall award 50 percent of the grant funds for research involving spinal cord injuries and 50 percent to research involving traumatic brain injuries. In addition to the amounts appropriated by law, the commissioner may accept additional funds from private and public sources. Amounts received from these sources are appropriated to the commissioner for the purposes of issuing grants under this section.

Subd. 2. Report

By January 15, 2016, and each January 15 thereafter, the commissioner shall submit a report to the chairs and ranking minority members of the senate and house of representatives committees having jurisdiction over the Office of Higher Education, specifying the institutions receiving grants under this section and the purposes for which the grant funds were used.

136A.902 SPINAL CORD AND TRAUMATIC BRAIN INJURY ADVISORY COUNCIL.

Subd 1. Membership

The commissioner shall appoint a 14-member advisory council consisting of:

- (1) one member representing the University of Minnesota Medical School;
- (2) one member representing the Mayo Medical School;
- (3) one member representing the Courage Kenny Rehabilitation Center;
- (4) one member representing Hennepin County Medical Center;
- (5) one member who is a neurosurgeon;
- (6) one member who has a spinal cord injury;
- (7) one member who is a family member of a person with a spinal cord injury;
- (8) one member who has a traumatic brain injury;
- (9) one member who is a veteran who has a spinal cord injury;
- (10) one member who is a veteran who has a traumatic brain injury;
- (11) one member who is a family member of a person with a traumatic brain injury;
- (12) one member who is a physician specializing in the treatment of spinal cord injury;
- (13) one member who is a physician specializing in the treatment of traumatic brain injury; and
- (14) one member representing Gillette Children's Specialty Healthcare.

Subd. 2. Organization

The advisory council shall be organized and administered under section [15.059](#), except that subdivision 2 shall not apply. Except as provided in subdivision 4, the commissioner shall appoint council members to two-year terms and appoint one member as chair. The advisory council does not expire.

Subd. 3. First appointments and first meeting

The commissioner shall appoint the first members of the council by September 1, 2015. The chair shall convene the first meeting by November 1, 2015.

Subd. 4. Terms of initial council members

The commissioner shall designate six of the initial council members to serve one-year terms and six to serve two-year terms.

Subd. 5. Conflict of interest

Council members must disclose in a written statement any financial interest in any organization that the council recommends to receive a grant. The written statement must accompany the grant recommendations and must explain the nature of the conflict. The council is not subject to policies developed by the commissioner of administration under section [16B.98](#).

Subd. 6. Duties.

The advisory council shall:

- (1) develop criteria for evaluating and awarding the research grants under section [136A.901](#);
- (2) review research proposals and make recommendations by January 15 of each year to the commissioner for purposes of awarding grants under section [136A.901](#); and
- (3) perform other duties as authorized by the commissioner.

**APPENDIX B: 2020 Spinal Cord Injury and Traumatic
Brain Injury Research Grant Program Applicants**

Proposals Submitted – Spinal Cord Injury

Proposal #	Title and Applicant	Amount Requested
SCI-01	Mayo Clinic Dr. Mohamad Bydon Tier 1 <i>Efficacy of Intrathecal Serum-Derived Purified Exosomes in a Rat Model of Blunt Thoracic Spinal Cord Injury: A Pilot Study</i>	\$125,000
SCI-02	Mayo Clinic Dr. Mohamad Bydon Tier 3 <i>Multi-Dose Safety and Feasibility Study of Autologous Culture Expanded Adipose Derived Mesenchymal Stem Cells (AD-MSCs) in the Treatment of Traumatic Spinal Cord Injury</i>	\$500,000
SCI-03	Mayo Clinic Dr. Mohamad Bydon Tier 2 <i>Investigating the Therapeutic Potential of Multiple Intravenous Injections of Human Umbilical Cord Blood Mesenchymal Stem Cell (hUCMSCs) on Multiple Organs Following Spinal Cord Injury in Rats</i>	\$250,000
SCI-04	Mayo Clinic Dr. Isobel A. Scarisbrick Tier 2 <i>Therapeutic Targeting of Cellular Senescence to Promote Repair of the Chronically Injured Spinal Cord</i>	\$250,000
SCI-05	Hennepin Healthcare – HCMC/Hennepin Healthcare Research Institute, University of Minnesota Dr. David Darrow, Dr. Ann Parr, and Dr. Thomas Bergman Tier 3 <i>ESTAND 2.0 – Bridge to Clinical Approval of eSCS for SCI</i>	\$499,983
SCI-06	Hennepin Healthcare – HCMC/Hennepin Healthcare Research Institute Dr. David Darrow Tier 3 <i>Non-invasive Transcutaneous Spinal Cord Stimulation for Recovery of Hand Function After Spinal Cord Injury</i>	\$491,534
SCI-07	Regents of the University of Minnesota Dr. James R. Dutton Tier 2 <i>Optimization of iPSC-derived Oligodendrocyte Progenitor Cell (OPC) Manufacture – A Key Step Toward Patient Treatment</i>	\$240,312
SCI-08	Mayo Clinic Dr. Kristin Zhao Tier 3	\$499,783

Proposal #	Title and Applicant	Amount Requested
	<i>Characterization of Supraspinal Control Over Transcutaneous and Epidural Electrical Stimulation-Enabled Motor Function in Humans with Spinal Cord Injury</i>	
SCI-09	Mayo Clinic Dr. Kristin Zhao Tier 1 <i>Development and Validation of a Multifactorial Wellness Program to Improve Quality of Life After Neurologic Impairment</i>	\$125,000
SCI-10	Mayo Clinic Dr. Igor Lavrov Tier 2 <i>Identification of Neurophysiologic Mechanisms of Neuropathic Pain After SCI as Therapeutic Targets for Pain Prevention via Epidural Electrical Stimulation and Locomotor Training</i>	\$250,000
SCI-11	Center for Veterans Research and Education/Minneapolis VA Health Care System and University of Minnesota Dr. Gary Goldish and Dr. Christine Olney Tier 2 <i>Refining and Testing the Upper Body Dynamic Positioning System for Persons with SCI</i>	\$249,118
SCI-12	Regents of the University of Minnesota Dr. Ann M. Parr and Dr. Michael McAlpine Tier 2 <i>3D Bioprinted Spinal Neural Progenitor Cell (sNPC) Scaffolds Accelerate Functional Neuronal Network Formation both in vitro and in vivo after Spinal Cord Injury</i>	\$249,876
SCI-13	Regents of the University of Minnesota Dr. Ann M. Parr Tier 2 <i>Training Transplanted Spinal Neural Progenitor Cells (sNPCs) to Function after Chronic Spinal Cord Injury</i>	\$228,356
SCI-14	Regents of the University of Minnesota Dr. Walter C. Low Tier 2 <i>Spinal Cord Regeneration by Cell Reprogramming in Chronic Spinal Cord Injury</i>	\$250,000
SCI-15	BlueSky Design, Inc. Dianne Goodwin Tier 2 <i>Voice and Eye/Face Gesture Control of a Robotic Mounting and Positioning Arm</i>	\$250,000
TOTAL AMOUNT REQUESTED		\$4,458,962

Proposals Submitted – Traumatic Brain Injury

Proposal #	Title and Applicant	Amount Requested
TBI-01	Mayo Clinic Dr. Su-Youne Chang Tier 1 <i>Identification of Brainwide Network Activity Changes in Post-Traumatic Epilepsy to Optimize the Therapeutic Effect of Vagus Nerve Stimulation on Post-Traumatic Epilepsy</i>	\$125,000
TBI-02	Mayo Clinic Dr. Isobel A. Scarisbrick Tier 2 <i>Switching off the Thrombin Receptor to Enhance Recovery after Traumatic Brain Injury</i>	\$250,000
TBI-03	Regents of the University of Minnesota Dr. Andrew T. Crane Tier 1 <i>Multilineage 3-Dimensional Brain Organoids to Model Intracranial Pressure Linked to Chronic Traumatic Encephalopathy</i>	\$100,000
TBI-04	Regents of the University of Minnesota Dr. Maxim C. Cheeran Tier 2 <i>Characterizing the Neuroinflammation Associated with Sequential TBI in a Rodent Model</i>	\$243,903
TBI-05	Gillette Children’s Specialty Healthcare Dr. Angela Sinner Tier 1 <i>Ketogenic Diet Following Moderate to Severe Pediatric Traumatic Brain Injury: A Pilot Study</i>	\$122,707
TBI-06	Regents of the University of Minnesota Dr. Silvia Mangia Tier 2 <i>Orientation Selective Deep Brain Stimulation for Functional Recovery in TBI-Induced Vegetative State and Minimally Conscious State</i>	\$249,292
TBI-07	Regents of the University of Minnesota Dr. Maxim C-J. Cheeran Tier 2 <i>Modulating the Macrophage Response to Enhance Neurogenesis and Mitigate Memory Deficits Consequent to Traumatic Brain Injury</i>	\$250,000
TBI-08	ExercisAbilities; Winona State University Melanie Brennan and Dr. Justin R. Geijer Tier 1 <i>Validation of Cardiovascular Exercise Tests for Individuals with Traumatic Brain Injury</i>	\$123,984

Proposal #	Title and Applicant	Amount Requested
TBI-09	CentraCare Health – St. Cloud Hospital Dr. Uzma Samadani Tier 2 <i>Reductive Ventricular OsmoTherapy (RVOT) for Traumatic Brain Injury (TBI)</i>	\$247,943
TBI-10	HealthPartners Institute Dr. Bhavani Kashyap Tier 1 <i>Safety of a Low-Level Light Therapy Device for Traumatic Brain Injury in an Animal Model</i>	\$121,599
TBI-11	HealthPartners Institute Dr. Amanda A. Herrmann Tier 1 <i>Acupuncture Treatment for Chronic Post-Traumatic Headache in Individuals with Mild Traumatic Brain Injury</i>	\$124,812
TBI-12	Center for Veterans Research and Education/Minneapolis VA Health Care System Dr. Melanie Blahnik Tier 1 Improving Communication About Sexual Health for Persons Undergoing Acute Inpatient Rehabilitation for Traumatic Brain Injury (TBI)	\$124,961
TBI-13	CentraCare Health– St. Cloud Hospital Dr. Uzma Samadani Tier 3 Improving Functional Outcomes Through Optimization of Surgical Subdural Hematoma Evacuation Technique	\$479,081
TBI-14	Center for Veterans Research and Education/Minneapolis VA Health Care System Dr. C. Sophia Albott Tier 2 Theta Burst Stimulation for Headaches after Traumatic Brain Injury	\$249,980
TOTAL AMOUNT REQUESTED		\$2,813,262

**APPENDIX C: Annual Research
Grant Proposal Review Form**

**MINNESOTA SPINAL CORD INJURY AND TRAUMATIC BRAIN INJURY
RESEARCH GRANT PROGRAM
MINNESOTA OFFICE OF HIGHER EDUCATION
PROPOSAL REVIEW FORM FOR FISCAL YEAR 2020**

Application No. _____ Reviewer No. _____ Funding Requested: _____ Tier: _____

Principal Investigator(s) _____

OVERALL IMPACT

Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following five scored review criteria, and additional review criteria. An application does not need to be strong in all categories to be judged likely to have major scientific impact. **Please reference the FY2019 Reviewer's Handbook for instructions and tips on how to accurately score proposals.**

Overall impact: Provide a paragraph summarizing the factors that informed your Overall Impact score. (Score: 1-9) Score _____

SCORED REVIEW CRITERIA

Reviewers will consider each of the five review criteria below in the determination of scientific and technical merit, and give a separate score for each.

1. Significance (Score: 1-9) Score _____

Strengths

Weaknesses

2. Investigator(s) (Score: 1-9) Score _____

Strengths

Weaknesses

3. Innovation (Score: 1-9)

Score _____

Strengths

Weaknesses

4. Approach (Score: 1-9)

Score _____

Strengths

Weaknesses

5. Environment (Score: 1-9)

Score _____

Strengths

Weaknesses

**APPENDIX D: Completed Projects:
Accomplishments and Dissemination**

Spinal Cord Injury and Traumatic Brain Injury Research Projects¹

Institution	Principal Investigator	Project Title	Grant Cycle	Accomplishments	Dissemination
AbiliTech Medical, Inc.	Robert Wudlick	<i>Development of a Powered Hand Grip System for Quadriplegia</i>	FY18	During the project phase, several prototypes were developed for a powered hand grip device. This includes power systems, glove systems, and electronic configuration.	Results of this project are patented and future iterations of the concept design will be presented at conferences.
				Testing for performance of the glove systems was accomplished.	The product will eventually become commercially available.
				A provisional patent was filed with the technology. Consumer and clinician focus groups, interviews, and design reviews were conducted.	
Mayo Clinic	Kristin Zhao, PhD	<i>Safety and Feasibility of Low Level Epidural Electrical Stimulation for Individuals with SCI</i>	FY18	Results showed obvious trends over the year. These results support the notion that the usage of EES at low intensity for long durations may have a positive impact on activities of daily living on a self-perceived rating scale.	The research team continues to process data from the study.
				Patients were able to generate stepping movements on a treadmill consistently over a 12-month period of time.	Dissemination plan includes peer-reviewed publications as well as presentations/posters at national/international SCI conferences.

¹ Not an exhaustive list

Institution	Principal Investigator	Project Title	Grant Cycle	Accomplishments	Dissemination
Hennepin Healthcare/Minneapolis Medical Research Foundation	Chad Richardson, MD	<i>Traumatic Brain Injury Classification and Outcome Assessment</i>	FY17	Project resulted in a completed manuscript submitted for peer-review and demonstrated that there is a sufficient sensitivity and specificity for biomarkers to predict a patient's head CT scan and outcome after acute injury.	Findings were disseminated to communities of interest through poster presentations at national conferences and submitted manuscripts to relevant academic journals.
Minneapolis Medical Research Foundation	David Darrow, MD MPH; Uzma Samadani, MD, PhD	<i>Epidural Stimulation for Spinal Cord Injury</i>	FY18	Volitional movement in the lower extremity muscles was restored with epidural stimulation present.	The study website, ESTAND.org, was the primary outreach tool during the project; study milestones and achievements were communicated using the website's blog. This was also the tool used to recruit subjects during the study.
				Cardiovascular function was restored in participants. Stimulation was shown to prevent hypotension and presyncope symptoms during the tilt table assessments and fully return hypotensive subjects to normotensive in most cases.	Dr. Darrow and Dr. Theoden Netoff have given multiple presentations of the study findings to increase awareness at community groups and research conferences.
				Increased bowel control with prolonged stimulation use.	
Sexual function improvements in subject with stimulation compared to without stimulation.					

Institution	Principal Investigator	Project Title	Grant Cycle	Accomplishments	Dissemination
University of Minnesota	Ann Parr, PhD	<i>Non-invasive Glial Scar Ablation and Transplantation of Clinically Relevant, Human Induced Pluripotent Stem Cell (iPSC)-Derived Oligodendrocyte Progenitor Cells (OPCs) in a Rat Model of Chronic Moderate Contusion Injury</i>	FY17	Research suggests OPCs derived from human iPSCs survive after transplantation into a chronically injured rat spinal cord.	Manuscript submitted for publication.
				Preliminary results confirm the presence of transplanted cells, suggesting successful transplantation; transplanted cells tend to differentiate into the oligodendrocytes lineage in vivo.	
Center for Veterans Research and Educaiton	Gary Goldish, MD; Andew Hansen, PhD	<i>Upper Body Dynamic Positioning System for Persons with SCI</i>	FY18	Created a prototype of a trunk control device based on focus group feedback on various designs.	Manuscript submitted for publication.
				Protoype was tested; showed improved bilateral reach.	In process of procuring funding for the refinement of the trunk control device.
				A summary of likes and concerns was created based on feedback given by subjects.	Presented work on the protoype at the University of Minnesota's DMD conference in 2019.

Institution	Principal Investigator	Project Title	Grant Cycle	Accomplishments	Dissemination
Mayo Clinic	Igor Lavrov, MD, PhD	<i>Modulating the Spinal Cord Microenvironment and Sublesional Circuitry using Epidural Stimulation with Electrically Conductive Hydrogel Scaffolds Seeded with Schwann Cells</i>	FY18	As early as 2 weeks after SCI, rats implanted with the scaffolds showed improvement in stepping compared to those without scaffolds when they were electrically stimulated.	Results were presented at several international and local meetings and were disseminated to communities of interest.
				Rats with scaffolds showed improvements in angular displacement of the knee, ankle, and MTP s well as step length, step height, toe fluctuation, and drag phase.	Currently working on submission of RO1 grant using the results of this study as preliminary data.
				Overall, current results indicate that there is sub-functional reconnection through the scaffold and that this connection influences organization of spinal circuitry and stepping induced by EES.	
Mayo Clinic	Isobel A. Scarisbrick, PhD	<i>Metabolic Risk Factors as Targets to Improve Rehabilitation Outcomes after Spinal Cord Injury</i>	FY18	Completed studies to understand how systemic metabolic dysfunction in mice, triggered by consumption of a high fat diet with sedentary lifestyle, affects recovery after spinal cord injury. Findings demonstrate that even without SCI, consumption of a high fat diet reduced insulin-like growth factor 1 and its receptor in the spinal cord. After SCI, mice consuming a high fat diet experienced impaired sensorimotor recovery compared to those consuming a healthy diet.	Results have been presented across 10 published abstracts, including presentations at the Society for Neuroscience Meeting, the Minnesota SCI/TBI Research Symposium, and the American Society for Biochemistry and Molecular Biology among others.
				The presence of two risk factors of the Metabolic Syndrome do not affect FIM efficiency over the acute rehabilitation stay in individuals with AIS A thoracic SCI. Follow up studies are needed.	

Institution	Principal Investigator	Project Title	Grant Cycle	Accomplishments	Dissemination
Hennepin Healthcare	Sarah B. Rockswold, MD	<i>Eyetracking and Neurovision Rehabilitation of Oculomotor Dysfunction in Mild Traumatic Brain Injury</i>	FY18	<p>Findings suggest there is no correlation statistically between the optometrist's objective measurements/oculomotor dysfunction diagnoses and the eye tracker's measurements and ability to predict oculomotor dysfunction.</p> <p>A conclusion was drawn that the eyetracker is unable to accurately predict the presence or absence of oculomotor dysfunction as compared to the gold standard optometrist examination and diagnosis.</p>	Results have not been disseminated as this was a negative study.
Allina Health - Courage Kenny Research Center	Margaret M. Weightman, PT, PhD	<i>Exploring the Role of Combined Cognitive and Motor Dual-task Assessment and Rehabilitation for Individuals with Residual Symptoms after mTBI</i>	FY18	No within-group differences were found in ST versus DT conditions for cognitive or inertial sensor measures. Group differences in DT postural sway and head and trunk turning velocities were consistent with findings in acutely concussed athletes and those with chronic mTBI.	<p>Poster and platform presentations on both the preliminary and final findings of this protocol have been presented at state and national level conferences.</p> <p>Manuscripts for peer-reviewed journals are in progress to be submitted in early 2020.</p>
Center for Veterans Research and Education	Tasha Nienow, PhD	<i>TDCS as an Intervention for Patients with Traumatic Brain Injury</i>	FY18	<p>The resting state EEG analysis indicated that there was increased power across multiple frequencies after exposure to tDCS, indicating that the stimulation was effective in modulating brain activity as hypothesized.</p> <p>Veterans reported that the intervention caused mild itching and tingling in response to the neuromodulation procedures, but no significant adverse reactions; veterans are open to this type of intervention and it was well tolerated</p>	<p>Treatment results will be presented at national conferences attended by neuropsychologists and rehabilitation specialists. Findings will also be used to support applications for additional grant funding.</p> <p>Findings were presented at local and national conferences.</p>

Institution	Principal Investigator	Project Title	Grant Cycle	Accomplishments	Dissemination
University of Minnesota	William K. Durfee, Professor	<i>Muscle Powered Exoskeleton for Standing and Walking by People with Spinal Cord Injury</i>	FY18	Working prototype was created. Exoskeleton was a full ankle-knee-hip orthosis with fixed ankle and lockable joints at the hip and knee.	Dissemination was through conference presentations. Details of design methods, the engineering tests and the user tests are in the 118-page thesis publication of the graduate research assistant.
				A custom two-channel muscle stimulator was designed, fabricated, and tested.	
				A dynamic mathematical model of the complete system was simulated on the computer to determine design parameters for exoskeleton components. Further engineering testing was done with the system worn by a nonimpaired participant.	
				The complete device was tested by users with spinal cord injury and was successful, but feedback given requires a revision to the design that was not completeable in the time of the grant cycle.	



OFFICE OF
HIGHER EDUCATION

2020