OFFICE OF HIGHER EDUCATION

Spinal Cord Injury and Traumatic Brain Injury Research Grant Program 2024 Report

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About the 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 more than $224 million annually 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.

About This Report

This is a legislative-mandated report. As requested by Minnesota Statutes, section 3.197, this report cost approximately $610.75 to prepare, including staff time.

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Table of Contents

Executive Summary

The Spinal Cord Injury and Traumatic Brain Injury (SCI-TBI) Research Grant, established in 2015 by the State of Minnesota, received 33 proposals for fiscal year 2024. Following a competitive review, the SCI-TBI Advisory Council awarded 19 projects totaling $3,000,000.

Introduction

The State of Minnesota established the Spinal Cord Injury and Traumatic Brain Injury (SCI-TBI) Research Grant Program on July 1, 2015, in accordance with Minnesota 2015 Session Law, Chapter 69. This statute directed the Minnesota Office of Higher Education (OHE) Commissioner 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.

In July 2018, the Spinal Cord Injury and Traumatic Brain Injury Grant Program was given a Special Revenue Account by Minnesota Management and Budget in order to extend project periods from one to two years to a two-to-five-year timeline. Beginning in FY 2020, new grantees were given two to five 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 the lengthy institutional review board (IRB) review processes. It also accounts for any unexpected challenges that occur naturally with complex research and experimentation. The Special Revenue Account continues to support the program and its grant recipients, as these projects have proven to take several years to complete.

For the 2023-2024 biennium, $3,000,000 was made available for each year from the 2023 Omnibus Higher Education Bill (Minnesota 2021 Session Law, 1st Special Session, Chapter 2[1]) to support the SCI-TBI Grant Program, with a three 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), allocated 50 percent of the grant funds to research involving spinal cord injuries and 50 percent to research involving traumatic brain injuries throughout the biennium.

Spinal Cord Injury and Traumatic Brain Injury Advisory Council

The 2015 statute language establishing the grant program also required creation of 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.

[1] https://www.revisor.mn.gov/laws/2021/1/Session+Law/Chapter/2/

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, although the Veteran with a Traumatic Brain Injury representative resigned at the end of 2018 due to personal reasons.

Veteran representation is a persistent challenge for maintaining continuity within the Advisory Council. Since the resignation the veteran representative living with a Traumatic Brain Injury in 2018, this seat has remained open despite many attempts to recruit eligible community members. Many veterans who have joined the council do not persist through their first year for personal reasons, mainly related to their health and wellness. A future consideration is to reconfigure those council seats so that veterans with these injuries may send a representative from the Minnesota Department of Veterans Affairs or another an organization representing Veterans in their place, or find other meaningful ways to participate on the council without holding a permanent seat.

In 2022, Matthew Rodereick, a family member of someone with a spinal cord injury, was chosen to serve as the Advisory Council chair through the 2024 biennium. Several of the 2021 appointments were also up for renewal. The Commissioner of the Office of Higher Education selected the Advisory Council through the Minnesota Secretary of State's Open Appointments process. The full membership of the Advisory Council at the time of the grant review is shown below:

Table 1: Advisory Council Roster

Member	Representing
Dr. Uzma Samadani	Physician specializing in the treatment of traumatic brain injury
Dr. David Titus	University of Minnesota Medical School
Dr. Peter J. Grahn	Mayo Clinic
Dr. Margaret M. Weightman	Courage Kenny Rehabilitation Center
Dr. Matthew Puderbaugh	Hennepin County Medical Center
Dr. Andrew W. Grande	Neurosurgeon
Mr. Robert Wudlick	Community member living with a spinal cord injury
Mr. Matthew Rodreick, Chair	Family member of a person with a spinal cord injury
Dr. Aleta Steevens	Community member living with a traumatic brain injury
Mr. David Sullivan-Nightengale	Veteran living with a spinal cord injury
OPEN	Veteran who has a traumatic brain injury
Dr. Mark Gormley	Gillette Children's Specialty Healthcare
OPEN	Family member of a person who has a traumatic brain injury
Dr. Ann Parr	Physician specializing in the treatment of spinal cord injury

Fiscal Year 2023 Annual Research Grant

In fiscal year 2023, $3,000,000 was available to award to research projects through the SCI-TBI Annual Research Grant.

Timeline

The timeline for the annual research grant opportunity was as follows:

- February 8, 2023: Request for Proposals available to applicants
- March 10, 2023: Deadline for receipt of intent to submit forms
- April 14, 2023: Deadline for receipt of proposals
- May 23, 2023: Proposal Review Meeting/Project Presentations
- June 1, 2023: Notification of recommendation for grant award
- July 1, 2023: Project funding begins with grant contract encumbrance

On April 14, 2023 OHE received a total of 29 proposals (13 TBI and 16 SCI) totaling just over $7,000,000 in requests. The total request for TBI research projects was $3,179,840.00 and the Advisory Council selected nine projects to receive awards, totaling $1,498,023.50. Of the $4,016,152.00 in total requests for SCI research, the Advisory Council selected seven projects totaling $1,505,000. The extra funds allocated for Spinal Cord Injury projects was from unspent funds in the Special Revenue Account allocated for Spinal Cord Injury grants.

Fiscal Year 2023 Awarded Research Grant Summaries

Spinal Cord Injury Research Grants

Development of Translatable Cell Transplantation Therapies to Promote Sensory Recovery After Spinal Cord Injury
University of Minnesota, Receives $125,000

Grantee's central hypothesis is that hiPSC-derived dsNPCs are able to receive connections from primary afferent neurons and that such connectivity may promote functional sensory recovery following SCI. In this study, they aim to address the hypothesis that hiPSC-derived, regionally specific dsNPCs receive connections from primary afferent neurons both in vitro and in vivo. For in vitro experiments, they will develop a co-culture system between their dsNPCs and an hiPSC-derived primary afferent neuron population commercially available from Anatomic Incorporated, a local biotech firm. Following long term co-culture, neuromodulatory techniques and histology will be used to measure communication between these two populations, thus indicating the presence of specific functional circuits that may be targeted for further study. For in vivo experiments, dsNPCs will be transplanted into a rodent SCI model, and animals will be monitored for signs of sensorimotor recovery. Subsequent histological analysis will be used to determine the extent to which host primary afferent neurons integrate with transplanted cells, providing further evidence that restoration of connectivity between these cell types may serve as a mechanism to promote sensory recovery after injury.

Principal Investigator: Ann Parr, amparr@umn.edu, 612-625-4102

Restoration of sexual function in spinal cord injury patients with electrical spinal cord stimulation
University of Minnesota, Receives $287,498

The central hypothesis of this study is that eSCS can restore some sexual function in people after loss of function after SCI. This grant aims to expand the scope of the ESTAND study by incorporating quantitative metrics of sexual function and further exploring the potential of eSCS in addressing sexual dysfunction in SCI patients. In Aim 1, Grantee will investigate sexual function and autonomic response in individuals with SCI and age-matched controls during exposure to erotic-stimuli (ES), compared to neutral nature videos. This objective will help elucidate normal sexual function in able- bodied individuals and identify the extent of functional loss after SCI.

In Aim 2, they will assess changes in sexual function in individuals with SCI during spinal cord stimulation. They anticipate significant improvements in genital blood flow and cardiac measures among responders, providing valuable evidence for the therapeutic potential of eSCS in addressing sexual dysfunction in this population. In Aim 3, they will enhance the ESTAND app, which is currently used for at-home assessment of stimulation settings, by incorporating validated measures of sexual function.

Principal Investigator: Theoden I Netoff, tnetoff@umn.edu, 952-451-5207

Searching for Hope: Optimization of Configuration and Therapy to Maximize Motor Outcomes in Individuals with SCI Implanted with EES for Non-Somatic Outcomes
University of Minnesota, Receives $331,310

Grantee will assess the effect on motor function using the NRS (NeuroRecovery Scale) obtained before therapy and after every 10 therapy visits and voluntary movement power assessments with Electromyography (EMG) before therapy and after the 40 therapy visits. Participants will have the opportunity to prioritize a functional task(s) to be addressed during therapy. They will also assess change in motor function and health outcomes prioritized by the participant without therapy over the course of 1.5 years with follow up assessments every 3 months using specifically the COPM (Canadian Occupational Performance Measure). Stimulation programs are assessed and optimized every three months and as needed. In addition, they will learn and evaluate challenges with long term use and the frequency that optimization of stimulation is needed. This is a single arm longitudinal interventional clinical trial focused on clinical outpatient therapy paired with spinal cord scES, and long term follow up.

Principal Investigator: Amanda DiRasmi, mill9724@umn.edu, 503-260-5649

Autologous Gene-Modified Leucoconcentrate with Translesional Spinal Cord Stimulation For Restoration After Spinal Cord Injury
Mayo Clinic, Receives $250,000

Grantee asks if the effect of novel GML therapy provides a better functional restoration than mesenchymal stem cell (MSC) therapy in the porcine SCI model. Their overall hypothesis is that GML will significantly improve recovery after SCI compared to MSC and that both GML and MSC will facilitate the immediate effect of EES to

enable motor functions after SCI. The effect of GML and MSC therapies will be tested after spinal contusion in mini pigs. Integrated behavioral and electrophysiological approach15 will be applied for advanced system-level analysis and compared weekly post-injury with the following histological evaluation.

Principal Investigator: Igor Lavrov, lavrov.igor@mayo.edu, 310-980-4457

Spinal Windowing to Allow for Ongoing In Vivo Visualization after Rat Spinal Cord Injury
University of Minnesota, Receives $125,000

The central hypothesis of Grantee's research is that the development of a spinal window model for rats will enable continuous, in vivo visualization of the spinal cord after injury, providing researchers with valuable insights into the dynamic processes involved in SCI. They hypothesize that this innovative approach will significantly enhance their understanding of the cellular events and mechanisms underlying SCI progression and recovery, facilitating the evaluation of potential therapies in real-time, and ultimately, accelerating the development of effective treatments for SCI patients.

To develop the spinal window model for rats, they will first design and fabricate a biocompatible, transparent window using a 3D printed polymer frame and a PET window. The window will then be implanted onto the spinal cord of rats, in both SCI and non-SCI models, to test its viability and durability. They will monitor the integrity of the window and assess the rats for any signs of infection, with the goal of maintaining functionality over a period of at least 12 weeks. Once the spinal window model has been optimized, they will conduct initial studies using calcium imaging to evaluate its effectiveness for in vivo spinal cord visualization. Additionally, they will transplant eGFP-labeled spinal neural progenitor cells (sNPCs) into the spinal cord to optimize the observation of cell integration and assess the potential of the spinal window model for evaluating cellular therapies. This methodology will provide the foundation for future studies, enabling researchers to continuously monitor the spinal cord's response to injury and treatment.

Principal Investigator: Ann Parr, amparr@umn.edu, 612-625-4102

Epidural Stimulation to Improve Corticospinal Tract Function
Minneapolis VA Healthcare System, Receives $287,498

Grantee's central hypothesis is that eSCS intervention will lead to the activation of arm and hand motoneurons and the improvement of strength and kinematic movements for patients experiencing upper limb paresis due to corticospinal tract injury. Their primary objective is to determine the safety and feasibility of eSCS in the dorsolateral epidural space for patients with corticospinal tract injury above C4. Secondary outcomes will assess 1) the capacity of eSCS to facilitate better restoration of strength and volitional movement in the upper limb in conjunction with standard-of-care rehabilitation and 2) the extent to which improvements in upper limb movements can be retained with stimulators turned off.

This study will recruit six new patients who will undergo a surgical procedure to implant a system that delivers electrical stimulation to the dorsolateral epidural space targeting spinal roots C5–C6 to T1. The overall goal of this study is to explore the safety and feasibility of epidural stimulation intervention by recruiting six patients with a motor-complete or near-complete corticospinal tract injury. Functional improvements of volitional movement in the upper limb will be assessed by using clinical outcome measures and kinematic analyses.

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

Blocking the Thrombin Receptor to Improve Neural Stem Cell-Mediated CNS Regeneration
Mayo Clinic, Receives $98,694

The overarching hypothesis to be tested is that neural stem cell "seeds" genetically engineered to remove the PAR1 protein will show improvements in engraftment and re-establishment of neural connectivity at sites of chronic spinal cord injury to significantly improve recovery of function. Grantee further hypothesizes that the beneficial effects of removing PAR1 from neural stem cells will be reflected in increases in the expression of regeneration associated genes and that this will occur in neural stem cells derived from either murine or human sources.

In the first Aim of this proposal, they will test the hypothesis that blocking the PAR1 protein will improve the capacity of neural stem cells to establish new neural connections after transplantation into an experimental murine model of chronic spinal cord injury. The neural stem cell seeds that are transplanted will have PAR1 switched off or left on and will be easily identified long after engraftment since they will be labeled with a green fluorescent protein. They will determine the cellular and molecular outcome of transplanted neural stem cells, how they contribute to replacing neurons and rebuilding synaptic connections, and the ultimate impact this has on restoration of function at early and late time points. In the second Aim of this proposal, they will grow both murine and human neural stem cells in cell culture and subject these cells to powerful gene sequencing analysis that will uncover how switching off the PAR1 protein improves regeneration associated gene programs. This project will leverage key expertise between researchers Dr. Scarisbrick (Mayo Clinic) and Dr. Dutton (University of Minnesota) and resources that are not available at either Institution alone. Dr. Scarisbrick will combine her team's expertise in the study of models of chronic spinal cord injury and the PAR1 protein with Dr. Dutton's expertise in gene editing technologies and making transplant ready skin-derived human spinal cord neural stem cells. Completion of the proposed Aims will provide the preliminary data and joint publications needed to make highly competitive grant submissions to the NIH enabling larger sources of funding to move their new discoveries to clinical translation.

Principal Investigator: Isobel Ann Scarisbrick, Scarisbrick.Isobel@mayo.edu, 507-398-8251

Traumatic Brain Injury Research Grants

Use of an Electronic Eye Tracking Device to Predict Concussion in the Pediatric Emergency and Specialty Clinic Setting after Traumatic Brain Injury
Children's Minnesota, Receives $125,000

Grantee hypothesizes that incorporating a brief eye tracking test into their clinical practice, both in the emergency setting and the outpatient clinical setting, will prove to be a feasible, acceptable, and clinically effective tool for identifying children who have sustained a concussion and who are at risk for prolonged vision-related symptoms, and for monitoring their recovery process. To test their hypotheses, they aim to enroll 200 patients aged 5-18 years with new head injuries in the pediatric Emergency Department (ED) and ask them to complete a brief eye tracking test, along with standard concussion symptom questionnaires. They will record whether or not they are diagnosed with a concussion. They will then follow the subset of these patients who go

on to receive care in the pediatric Concussion Clinic. They will also enroll additional patients initially presenting to the Concussion Clinic such that 80 patients are followed through Concussion Clinic discharge. These patients will be asked to complete the eye tracking test and standard concussion symptom questionnaires at each clinic visit.

Principal Investigator: Amy Linabery, amy.linabery@childrensmn.org, 651-276-7515

Direct Nose to Brain Delivery of Deferoxamine for Treatment of TBI
HealthPartners Institute, Receives $249,983

Grantee will determine whether IN DFO improves recovery after TBI in rats and begin to elucidate the mechanism by which this occurs. They hypothesize that administration of IN DFO will improve both functional recovery and brain tissue measures of TBI in rats, paving the way for translation to clinical trials in humans. Surgery will be performed in rats under anesthesia to induce a controlled cortical impact model of TBI.

Saline (placebo) or DFO will be administered intranasally starting four hours after injury and then daily. Behavior testing for memory and motor function will be performed to determine whether the treatment was effective. Brain tissue will be collected after 2 or 19 days, and post-mortem measures including lesion size, iron levels, and other measures of TBI will be compared among treatment groups.

Principal Investigator: Jared M Fine, jared.m.fine@healthpartners.com, 651-495-6359

Beyond Performance: Characterizing Changes in Cognitive Effort after TBI
University of Minnesota, Receives $124,009

A TBI can change how much mental effort it takes to complete a task. Grantee wants to understand how effort changes over the course of a day in adults with TBI compared to uninjured adults. They also know that in healthy adults, mental effort can be "aimed" with incredible precision, allowing for efficient use of mental resources. They hypothesize that a brain injury can disrupt this ability to use mental effort efficiently. They can use a scientific method called pupillometry to measure a person's effort *while* they are doing a task, and see how well they can "aim" their effort to complete goal-directed tasks. Their hypothesis is that pupillometry will show, in an objective way, that TBI disrupts the moment-by-moment use and efficiency of mental effort.

They want to understand how effort changes in daily life and also to understand how effort changes moment-to-moment, on a timescale that would be too fast to report with words. To understand how effort changes in daily life, they will ask people with and without a history of brain injury to complete short surveys multiple times per day over the course of a week. This method is called Ecological Momentary Assessment, and it will allow them to get a rich picture of how mental effort changes after a TBI. They also want to understand how the ability to efficiently use mental effort changes after a TBI. To do this, they will use a method called pupillometry. Pupillometry measures changes in the diameter of the pupil (the black part) of the eye. When they use more effort, their pupils get bigger (they dilate), and measuring that change can be used to track the effort involved in various activities. Pupillometry is useful because they are able to measure pupil size *at the same time* that a person is completing a task. It will let them measure effort objectively and in-the-moment. Pupillometry lets

them track effort on a millisecond-by-millisecond timescale, which means they can capture differences in mental effort that would be hard to show with less precise methods.

Principal Investigator: Natalie Covington, nvcoving@umn.edu, 402-321-6679

Generating Exogenic Microglia for Repair in Traumatic Brain Injury
University of Minnesota, Receives $250,000

The generation of authentic microglia with gene editing and stem cell blastocyst complementation requires the knockout of genes that are critical to the development of the microglia to create a niche for the development of the desired type of cells. Grantee hypothesizes that specific genes that they have identified will create niches for the generation of microglia. They will test this hypothesis characterizing authentic microglia as well as testing their function after transplantation. Mice will be used to isolate and characterize this distribution of authentic microglia in within the brains of chimeras. Mice will also be used to induce traumatic brain injury followed by transplantation with authentic microglia. Transplanted mice will be tested for cognitive function by spatial navigation in a maze.

Principal Investigator: Walter Low, lowwalt@umn.edu, 612-791-9124, 612-467-2264

Examining the Efficacy and Safety of Subanesthetic Ketamine on Depression and Post-traumatic Stress Disorder among Veterans with Mild and Moderate Traumatic Brain Injury
Minneapolis VA/UMN, Receives $162,235.45

While the use of ketamine to treat depression and PTSD among patients with TBI is an exciting possibility, there are no clinical studies to formally test it. The underlying brain pathology in TBI could make ketamine ineffective or even unsafe. The logical next step is to conduct a rigorous clinical trial to examine the efficacy and safety of repeated ketamine as an intervention to treat depression and PTSD in TBI.

Grantee proposes to conduct a 2-year, one-site, clinical study among Veterans with mild to moderate TBI and concurrent depressive and/or PTSD symptoms. Eligible subjects will be randomized to one of two treatment arms (midazolam 0.045 mg/kg vs ketamine 0.5 mg/kg). Participants will receive the study drug or placebo via intravenous infusion twice per week for 3 weeks and followed for 4 weeks after the last infusion.

Principal Investigator: Paulo Shiroma, paulo.shiroma@va.gov

A novel neuroendocrine system controlling left-right neural connectivity: implication for traumatic brain injury
Mayo Clinic, Receives $162,500

Grantee here asks if TBI in clinically relevant animal model impairs the left-right neurohormonal system and if the induced perturbations contribute to protracted asymmetric neurological deficits, e.g. hemiparesis and hemiplegia. Their overall hypothesis is that the left-right side-specific neuroendocrine system operates in the intact CNS where it coordinates and integrates the left and right sided processes between different levels of the neuraxis, e.g., between the left-right hypothalamus (HT) and left-right SpC. TBI, lateral SCI and stroke may impair

the balance between the "left" and "right" side-specific neurohormones and thus produce pathological neuroplasticity in the neuroendocrine system.

The role of endocrine signaling will be evaluated in Sprague Dawley rats whose descending neural tracts will be disabled by complete spinal transection that will be followed by the controlled cortical impact (CCI), the clinically relevant TBI model. The unique, integrated behavioral and electrophysiological approach will be applied for advanced system-level analysis. Gene expression and gene-gene co-expression patterns will be analyzed in the hypothalamus, pituitary, and lumbar spinal cord to identify and characterize coordination and integration of the left-right sided processes across these areas using bioinformatics.

Principal Investigator: Igor Lavrov, lavrov.igor@mayo.edu, 310-980-4457

Reading after Traumatic Brain Injury: Development of a Guiding Model for Assessment and Treatment
Courage Kenny Rehabilitation Institute, Receives $162,482.45

Grantee's central question is: *What factors are associated with better reading experiences for people with TBI?* They will address this question in three aims. First, they have developed a questionnaire about reading and confidence in reading abilities. Using this tool, they found that people judge their own reading based on how hard it is to read (*Effort*), how much they enjoy reading (*Enjoyment*), and how well they can stay focused or remember what they are reading (*Processing*). They then found that young adults with mild TBI don't enjoy reading as much after their injury. Now they will see if this tool is also useful for understanding reading in adults who experienced more severe brain injuries. Secondly, they will interview adults with TBI to learn more about how much they read, how they feel about reading, what they like to read or don't like to read, and if they use any strategies to help their reading. Lastly, some participants will complete some tests of reading and other tests of thinking and seeing so they can start figuring out how much cognitive, language, vision, and socioemotional factors influence reading after TBI.

Their study will include two phases. In the first phase, they will ask a large sample of adults with and without TBI to complete an online survey. They will ask each person questions about: 1) their reading habits, 2) their ability to see, 3) how easily they are able to complete other activities in their daily lives, 4) how they view their thinking and talking, and 5) how they feel about their reading. In the second phase, they will collect more in-depth data from some of the participants. These testing sessions will include cognitive tests, to understand how TBI has impacted each person's thinking skills related to reading, vision tests to see how their eyes move when they read, and in-depth interviews, to understand each person's unique perspective about how TBI has influenced their reading. They will analyze data from these surveys and tests together to learn what factors are most related to reading success after TBI. Overall, this analysis will allow them to better understand the reading needs, strengths, and strategies of adults with TBI.

Principal Investigator: Katy Parper O'Brien, katy.obrien@allina.com, 612-636-1621

Neurodynamics of Disorder of Consciousness Related to Traumatic Brain Injury
Minneapolis VA Healthcare System, Receives $161,813.60

Given the issues mentioned above, finding biomarkers that would assist practitioners in determining the presence of willful brain activity even when patients are not able to demonstrate a willful response, and that can add prognostic value for families and caretakers is critically needed. Electroencephalography (EEG) provides an easy-to-use method of collecting brain activity. EEG can be recorded at bedside, and it offers an optimal time-resolution, on the order of milliseconds, for capturing brain activity, which makes it a method of choice for evaluating the brain neural dynamics of these patients. Grantee aims to develop an EEG-based method for evaluating the neural dynamics of DOC patients, monitor changes of these neural dynamics across time, and assess their prognostic value. Their preliminary results suggest that there is a temporary increase of beta waves (12-25 Hz) and gamma waves (>30 Hz) close to the time of emergence to consciousness. In contrast, patients who do not emerge to consciousness do not show this increase in beta and gamma activity. In addition, they found the appearance of EEG signs of recognition of auditory stimuli even in patients who did not show behavioral improvement. These preliminary results indicate that an EEG-based methodology can provide invaluable objective information in regards to the assessment and prognosis of DOC patients.

They will record brain activity of DOC patients at rest as well as in response to auditory stimuli. EEG data of DOC patients will be recorded weekly during their stay in the Emerging Consciousness Program (ECP) to track potential changes in state of consciousness across time. In addition, they will perform the behavioral assessment of the level of consciousness of DOC patients using the CRS-r. They will examine EEG-based biomarkers of levels of consciousness, monitor potential changes of these biomarkers across time, and assess their prognostic value. They will determine whether the resting state EEG activity can be used as a biomarker of the level of consciousness and for prognosis (Specific Aim 1). In particular, based on their preliminary data, they hypothesize that the occurrence of strong beta and gamma waves of neural activity is a favorable prognostic biomarker of improvement of the level of consciousness. In addition, they will determine whether the EEG activity of DOC patients can detect the processing of peripheral stimuli even in the absence of a motor response (Specific Aim 2). They hypothesize that evidence of processing of peripheral stimuli in DOC patients can be determined from the difference in brain potentials of uncommon auditory stimuli relative to common auditory stimuli (auditory oddball task). Finally, the EEG data will be compared to control subjects, both neurologically healthy and brain-lesioned patients who have emerged from their DOC. At the end of the stay in the ECP, CRS-r score and Functional Independence Measure (FIM) will serve as outcome measures. They will assess the prognostic value of EEG measures of neural dynamics to these outcome measures.

Principal Investigator: Michelle D Peterson, Michelle.Peterson@va.gov, 612-467-1369

Predicting The Consequences of Chronic Effects Of Neurotrauma In The VA Population Using Image Processing, Machine Learning, And MRI Analytics
Center for Veterans Research and Education, Receives $100,000

Grantee proposes that distinctive objective biomarkers for the chronic effects of neurotrauma as caused by traumatic brain injury (TBI) can be distinguished when compared to other degenerative conditions, such as Alzheimer's dementia (AD), frontotemporal dementia (FTD), vascular dementia (VaD), normal pressure hydrocephalus (NPH), Lewy Body Dementia (LBD), microvascular ischemic disease, etc. using advanced radiographic analysis techniques on head MRI scans of veteran patients. From this comparative analysis, they

aim to develop a statistical model to better distinguish and predict the chronic outcomes of neurotrauma, in hopes to develop early intervention care strategies.

They will query the national VA database (VINCI) for head MRIs of veterans with at least 1 scan in the 2000-2012 period and at least 1 scan in a 10-year follow-up for analysis. MRI head image files (DICOM) will then be downloaded and analyzed. Radiographic features will be extracted from them using image processing and machine (deep) learning algorithms. In addition, all available demographic, physiologic, genetically predisposing, clinical, and comorbidity features will be included in the analysis. Machine learning will be used to classify chronic effects of neurotrauma as caused by TBI versus other neurodegenerative pathologies. MRI indications and impressions extracted from pertinent electronic medical records (EMR) will be used to validate the distinction by the learned objective markers. A predictive model for the chronic effects of neurotrauma will then be developed which can be applied to the initial head MRI.

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

Appendix A: Copy of Statute

Laws of Minnesota 2021

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[2], 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;

[2] https://www.revisor.mn.gov/statutes/?id=136A.902

(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[3], 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.

[3] https://www.revisor.mn.gov/statutes/?id=15.059

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.

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