Mission Connect®
a program of TIRR Foundation

Powering Research Through Collaboration

Mission Connect

2023 Report on Research and Activities

- Spinal Cord Injury
- Traumatic Brain Injury
- Stroke

TIRR® FOUNDATION

The Institute for Rehabilitation and Research Foundation

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Mission Connect®
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Answering a Monumental Challenge

Defined by its collaborative structure, funding strategy, and policies, Mission Connect is our region's only neurotrauma research program where scientists from multiple institutions work side-by-side to benefit patients.

Mission Connect is a traumatic brain injury (TBI) and spinal cord injury (SCI) research program founded, managed, and sustained by TIRR Foundation. Twenty-six years ago, a few visionary individuals and Foundation leadership recognized the need for a broad range of partners and collaboration to accelerate the stagnating rate of discovery in SCI and TBI research. The ideal place to launch such a program was in the Texas Medical Center, home of the world's most extensive clinical and research facilities and concentration of the brightest minds in medicine. Their vision was to create a program serving as the center point where this valuable density of talent and institutional assets could intersect and join forces.

With a handful of members and three institutions agreeing to work collaboratively, Mission Connect launched in 1997 as our region's only multi-institutional research program. As word spread, Mission Connect quickly grew and today has more than 100 members from 19 premier regional, national, and international academic and medical institutions.

Mirroring this growth is a construct of knowledge revealing how the central nervous system responds to trauma and how to protect and restore function after injury. Mission Connect's proficient and diverse membership provides the physical and intellectual resources needed to form research teams performing at the highest level.

While a bank of data is growing faster than ever before, we must sustain this momentum and ensure these hard-earned discoveries are translated into clinical treatments. The best and possibly only way to achieve this is through cooperation, collaboration, open communication, and freely sharing assets. Mission Connect has mastered all of these approaches. Defined by its collaborative structure, funding strategy, and policies, Mission Connect is our region's only neurotrauma research program where scientists from multiple institutions work side-by-side to benefit patients.

Key Contributors to Success

100% Rule—*Always*

One hundred percent of every dollar of donor support designated to Mission Connect goes to research. Neither TIRR Foundation nor the recipient scientist's institution use Mission Connect funding for overhead expenses or the standard deduction levied by academic institutions for 'indirect costs' (current average rate of 56% of donated dollars.)

Transparency

Sharing research outcomes, progress, and discoveries within the consortium allows scientists to build rapidly on game-changing discoveries, avoid duplication of effort, and learn from the unexpected yet valuable results failing to prove a hypothesis.

Collaboration

Mission Connect breaks down research silos by providing a collaborative platform that eliminates institutional barriers to collaboration.

Evaluation

One of the reasons Mission Connect is at the forefront of neurotrauma research and discovery is its 15-member External Review Committee. TIRR Foundation relies upon this national panel of experts to identify research that is scientifically robust, innovative, seeks to answer critical questions, and represents value for the funds our donors provide.

Leveraging of Funding

Mission Connect scientists use the data they gather with our grants to apply for and receive follow-on funding from prominent, large-scale research institutes and foundations. Between 2015 and 2020, the total amount Mission Connect invested in research was $6.4 million. The recipient scientists used the data they gathered with Mission Connect funding to receive more than $63 million follow on funding.

External Review Committee

- An External Review Committee was established in 2002 by the founders of Mission Connect. This national panel of neurotrauma experts play a pivotal role in the evaluation and selection of newly funded research, and the review of ongoing investigations.
- The first onsite review of Mission Connect funded investigations was held in February 2003. For more than 20 years, their expert and unencumbered guidance has ensured that Mission Connect is funding the most robust, well-designed, and promising research.
- Mission Connect's 2023 Review of Science took place on April 13-15 in Houston.

Aileen Anderson, Ph.D., University of California Irvine (member since 2017)

Larry Benowitz, Ph.D., Harvard Medical School (member since 2018)

W. Dalton Dietrich, Ph.D., The Miami Project to Cure Paralysis (member since 2007)

Susan G. Dorsey, Ph.D., University of Maryland School of Nursing (member since 2017)

C. Edward Dixon, Ph.D., University of Pittsburgh (member since 2005)

Itzhak Fischer, Ph.D., Drexel University College of Medicine (member since 2001)

Candace L. Floyd, Ph.D., The University of Alabama at Birmingham (member since 2017)

John D. Houle, Ph.D., Drexel University College of Medicine (member since 2011)

Michelle C. LaPlaca, Ph.D., Georgia Institute of Technology (member since 2017)

Phil G. Popovich, Ph.D., The Ohio State University College of Medicine (member since 2010)

Shelly Sakiyama –Elbert, Ph.D. The University of Texas at Austin (member since 2021)

Yang (Ted) D. Teng, Ph.D., M.D., VA Boston Healthcare System (member since 2015)

Pamela VandeVord, M.D., Ph.D., Virginia Tech – Wake Forest University (member since 2018)

Stephen G. Waxman, M.D., Ph.D., Yale Univ. School of Medicine and VA Connecticut (member since 2007)

Alison Willing, Ph.D., University of South Florida (member since 2009)

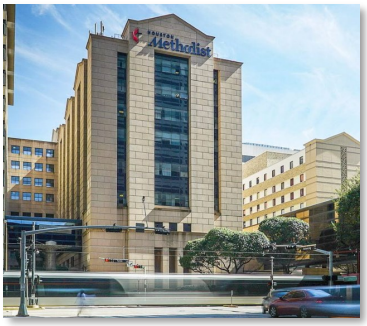
Mission Connect Member Institutions

Academic and Medical Institutions

University of Arizona
Baylor College of Medicine *
Emory University School of Medicine
Houston Methodist Research Institute
Michael E. DeBakey VA Medical Center
Rice University
Seton Brain and Spine Institute
Southern Illinois University
Texas A&M University at College Station
Texas Southern University
The University of California San Francisco
The University of Texas at Austin
The University of Texas Health Science Center at Houston *
The University of Texas Health Science Center at San Antonio
The University of Texas Medical Branch at Galveston *
The University of Maryland School of Nursing
Trinity University
University of Guadalajara
University of Houston
University of Texas Southwestern
Washington University School of Medicine in St. Louis
** Founding Institutions*

Member Clinical Affiliations

Ben Taub General Hospital
Children's Memorial Hermann
Houston Methodist
Michael E. DeBakey Medical VA Center
TIRR memorial Hermann
Memorial Hermann
Texas Children's Hospital



Houston Methodist


Rice University


Texas A&M University in College Station


Baylor College of Medicine


The University of Texas Health Science Center at Galveston

University of Houston

The Dr. Robert G. Grossman Annual Mission Connect Scientific Symposium—2022 and 2023

The 2023 Dr. Robert G. Grossman Mission Connect Annual Scientific Symposium will take place at the Cooley Life Center in Houston's Texas Medical Center on November 17, 2023. The keynote speaker will be Roman Giger, PhD. Dr. Giger is a Professor in Cell and Developmental Biology at the University of Michigan School of Medicine.

In 2022, the keynote speaker was David L. Brody, MD, PhD. Dr. Brody is the Director of the Center for Neuroscience and Regenerative Medicine (CNRM) and a professor of Neurology within the Uniformed Services University of the Health Sciences in Bethesda, Maryland. .

In addition to the keynote speaker, the Mission Connect Symposium features a poster presentation and competition. The competition allows graduate students and early postdocs to present their work before leaders in neuroscience research and medicine. They perfect their presentation skills and receive critical feedback from senior researchers from multiple institutions.

In 2022, 49 posters were on display representing nine regional institutions. Those presenting a poster at the symposium have the option to enter the judging. Senior members of Mission Connect serve as judges for the poster competition. Winners are announced at the end of the daylong event, and TIRR Foundation distributes cash awards.

In 2022, the cash awards given to the poster competition winners increased. This decision was based on a review of current award amounts at other competitions. In 2022, awards began at $250 and move to $500, and then $1,000 for the best overall score in SCI and TBI.

The 2023 Dr. Robert G. Grossman Annual Scientific Symposium is scheduled for November 17 and will be Mission Connect 's 17th annual symposium since the program launched in 2007.

Dr. Roman Giger's lab members at the Michigan School of Medicine

2023 Request for Proposals

On February 10, 2023, TIRR Foundation announced its *Request for Proposals* giving members of Mission Connect an opportunity to compete for the **Founders Award in Neurotrauma Research** and the **Robert Allan Shivers, Jr. Integrating Perspectives in Neurotrauma Research Award**. Our goal for 2023 is to fund approximately eight outstanding investigations. The 21 proposals submitted by our researchers are currently under review by Mission Connect's External Review Committee. Awards will be announced in July 2023 following approval from TIRR Foundation's Board of Directors.

Founders Award—$100,000

The basic science investigations funded under this award are fundamental to developing a complete understanding of how our central nervous system responds to injury. Knowing how and when to intervene to protect, repair, and restore function requires that we deeply understand the immediate and long-term processes taking place after injury. Discoveries made through basic science are the driving force behind the development of all drug therapies, targeted treatments, and rehabilitation strategies.

The Robert Allan Shivers, Jr. Integrating Perspectives in Neurotrauma Research Award—$187,500 (IP Award)

The IP Award transforms how we seek to solve some of the most complex medical problems diminishing the quality of life for persons living with brain and spinal cord injuries. The IP Award funds research teams with training and expertise from within and outside of the field of neurotrauma science and medicine. The goal is to bring in new investigator perspectives to help identify and understand the biological processes impeding the development of new treatments and therapies. The objective is to integrate research teams with specialists in urology, immunology, endocrinology, gynecology, gastroenterology, osteopaths, and other areas highly translatable to disorders caused by an SCI and TBI. Projects supported by this award must be highly innovative and focus on areas identified as most critical by those who are injured.

Spinal Cord Injury Research

Few injuries affecting humankind are more devastating than those associated with the spinal cord. More than 300,000 individuals in the United States live with SCI paralysis and more than two million worldwide. Those who are injured are three to five times more likely to die prematurely compared to those who are not.

Why Studying Spinal Cord Injury Matters

Researchers estimate that, as of 2019, 17,730 new SCI cases occur each year in the US and between 249,000 and 363,000 people are currently living with an SCI. Worldwide, 250,000 to 500,000 new spinal cord injuries occur annually.

Recent data on SCI indicate cases are 78% male, 22% female

Highest per capita rate of injury occurs between ages 16-30

Average age at injury – 43

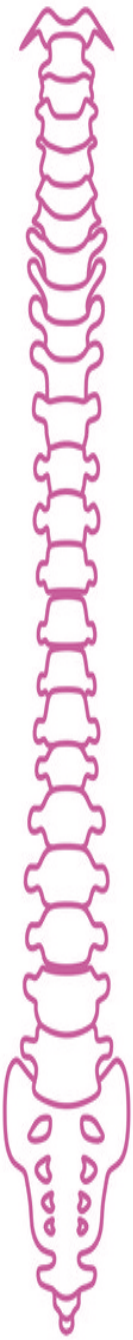
Median age at injury – 35.4

Mode (most frequent) age at injury-19

Individuals with a spinal cord injury are up to five times more likely to suffer a premature death. The average remaining years of life for persons with SCI have not improved since the 1980s and remain significantly below life expectancies of persons without an SCI.

About 30% of persons with SCI are re-hospitalized one or more times during any given year following injury. Among those re-hospitalized, the length of hospital stay averages about 19 days.

Only 12.5% of spinal cord injured persons are employed one year following their injury.



Spinal cord injury is associated with the development of deep vein thrombosis, urinary tract infections, muscle spasms, osteoporosis, pressure ulcers, chronic pain, and respiratory and metabolic complications.

First year expenses for paraplegics: $550,381. Annually thereafter, $69,800.

Average lifetime costs for paraplegics is between $1,636,959 and $2,494,338.

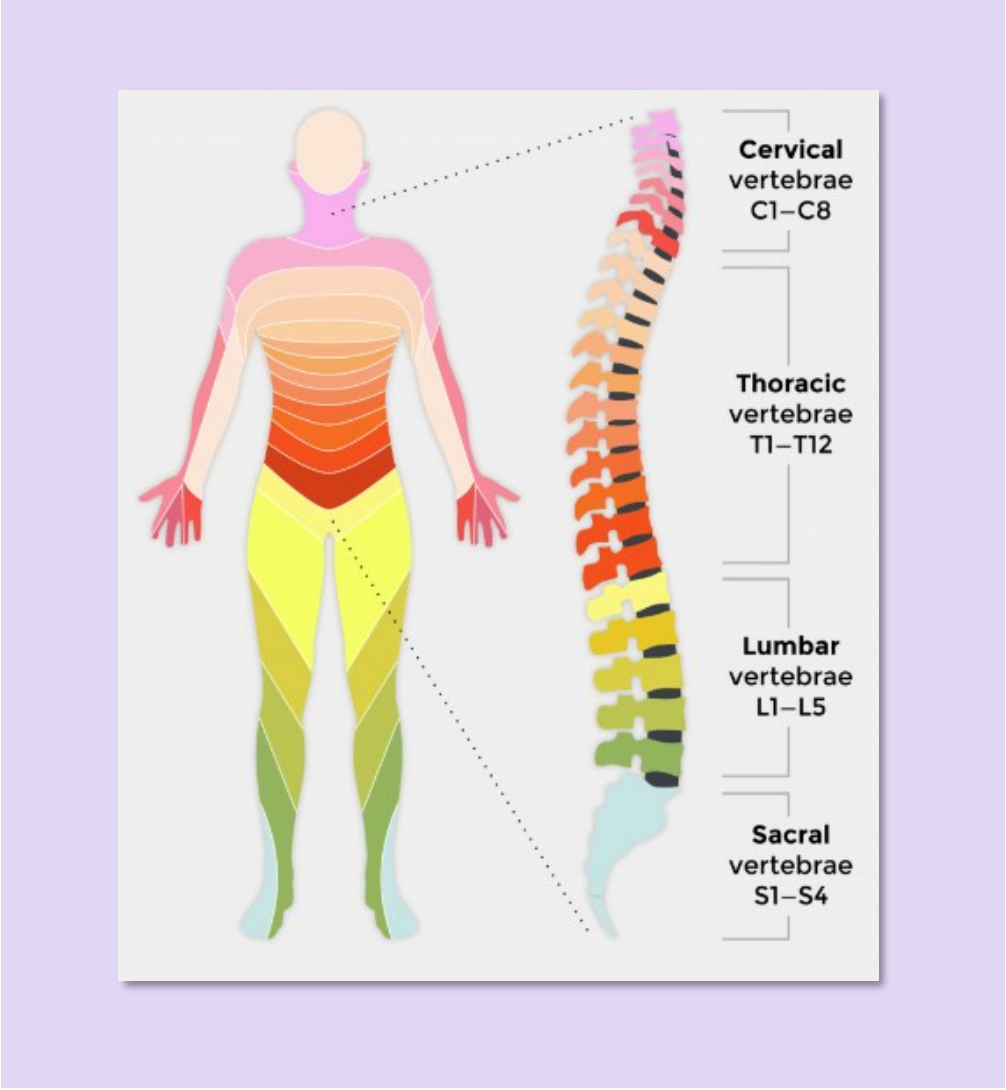
First year expenses for quadriplegics is $1,129,302. Annually thereafter, $190,000.

Average lifetime costs for quadriplegics: between $2,803,391 and $5,100,194.

"Unfortunately, there are at present no known ways to reverse damage to the spinal cord. However, researchers are continually working on new treatments, including prostheses and medications, which may promote regeneration of nerve cells or improve the function of the nerves that remain after an SCI."

Retrieved from "What are the Treatments for Spinal Cord Injury", US Department of Health and Human Services, National Institutes of Health https://www.nichd.nih.gov/health/topics/spinalinjury/conditioninfo/treatments

Spinal Cord Injury Levels of Paralysis



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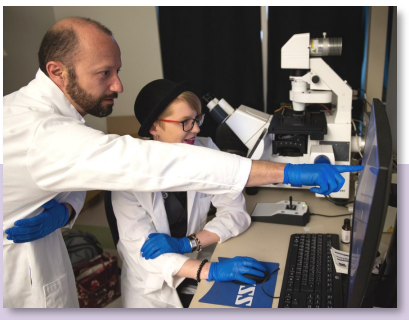
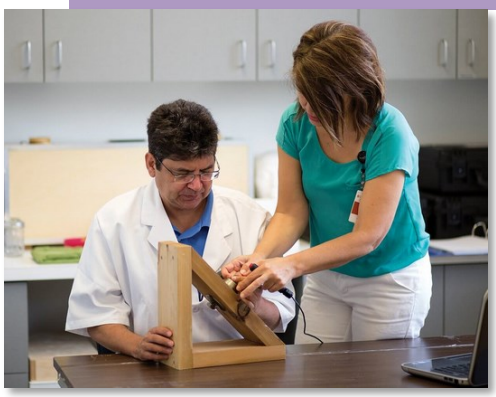
Portfolio of Active Spinal Cord Injury Research





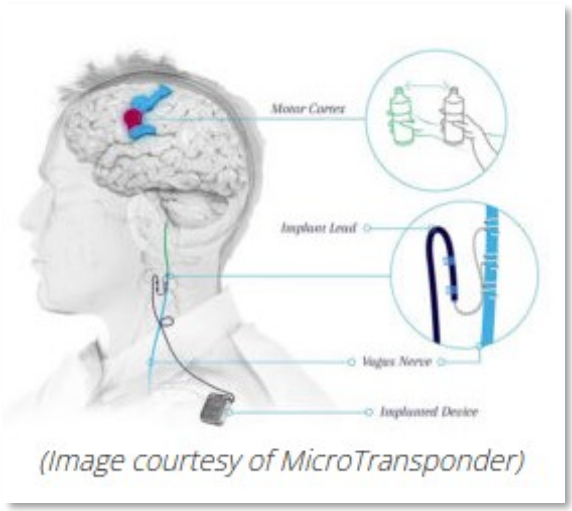





Safety and Feasibility of Paired Vagus Nerve Stimulation with Rehabilitation for Improving upper Extremity Function in People with Cervical Spinal Cord Injury; A Pilot Randomized Control Trial

Radha Korupolu, MD, MS, The University of Texas Health Science Center Houston

2022 IP Award (022-108) **Amount: $200,000** **Term: 2-Years**

Spinal cord injury (SCI) is a devastating event resulting in complications that lead to significant medical problems and physical dependency. Cervical SCI results in weakness of all four extremities, limiting patient independence and participation in activities of daily living such as feeding, bathing, grooming, dressing, toileting, and bladder and bowel management. Regaining upper extremity motor function is the number one priority for people with cervical SCI. In this investigation, Dr. Korupolu and her six-member team will perform a randomized control trial (RCT) utilizing an FDA-approved vagal nerve stimulator in combination with an advanced, task-specific exercise program previously tested in stroke patients. The goal is to maximize the return of arm and hand function. The proposed study will establish the safety and feasibility of paired vagal nerve stimulation (VNS) in people with SCI. This study will also provide insight into the efficacy of this intervention for improving upper extremity motor function and for influencing various comorbidities, including depression, anxiety, and heart rate variability. Successful completion of this study will lay the groundwork for a future multi-site RCT to study the effectiveness of paired VNS with rehabilitation in people with SCI.



(Image courtesy of MicroTransponder)

ERC Comments

The randomized, double-blind study will be carried out by a well-trained team of investigators with experience in all aspects of the proposed research and the conduction of clinical trials.

The study is of high significance and is likely to yield novel, impactful data that would help advance the translation of VNS for use as an intervention for SCI patients.

This is a strong team with extensive experience in conducting human-subject, interventional research trials.

The study design is excellent. Successful completion of this study will lay the groundwork for a future multi-site clinical trial.

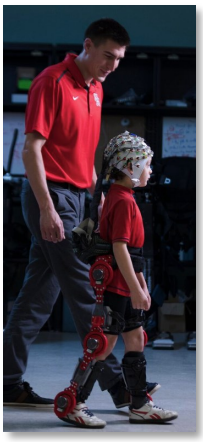
Promoting Access and Inclusivity of Pediatric Lower Extremity Gate System Exoskeleton

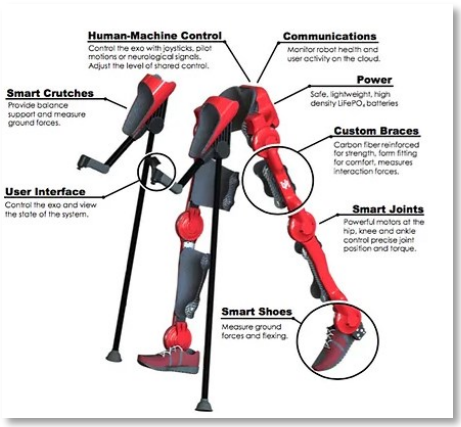
Jose Contreras-Vidal, PhD, University of Houston

2022 Founders Award (022-103) **Amount: $100,000** **Term: 2-Years**

Dr. Contreras-Vidal and his research group of engineers, physiatrists, and rehabilitation specialists have developed P-LEGS, a child-centered, lower-cost, personalized, powered pediatric exoskeleton. This innovative extremity gait system uses an open -access troll architecture to support and enable the development of interactive and adaptive gait assistance and training for children with lower body paralysis.

The goal of this study is to clinically validate and deploy this pediatric exoskeleton for assisted mobility for children with lower limb paralysis. The specific aims of this project are to initiate P-LEGS exoskeleton training and familiarization in this patient population. Then, demonstrate the feasibility of longitudinal testing of P-LEGS in children ages 4-12 with either SCI, Spina Bifida, brain injury, Cerebral Palsy, or hereditary Spastic Paraplegia. The overall hypothesis is that training with P-LEGS will lead to significant changes in the degree of motility, device usability, and health and quality of life of the participants.





ERC Comments

During the last decade, there has been an increase in the number of exoskeleton devices and research efforts to investigate the benefits of robotic-assisted gait therapy. This current system has many advantages over existing exoskeletons.

A key innovative element is an ability to grow with the child by simply replacing a few parts rather than the whole system. In addition, the "assist as needed" concept is highly innovative.

This proposal is of high clinical significance, and the successful completion would provide feasibility and proof-of-concept data needed for a larger study.

This is a highly collaborative study with experts in the area of Biomedical Engineering and PM&R (Physical Medicine and Rehabilitation), which is extremely appropriate for this study.

Targeting Phagocytic-Neuroimmune Pathways to Enhance Recovery After Spinal Cord Injury

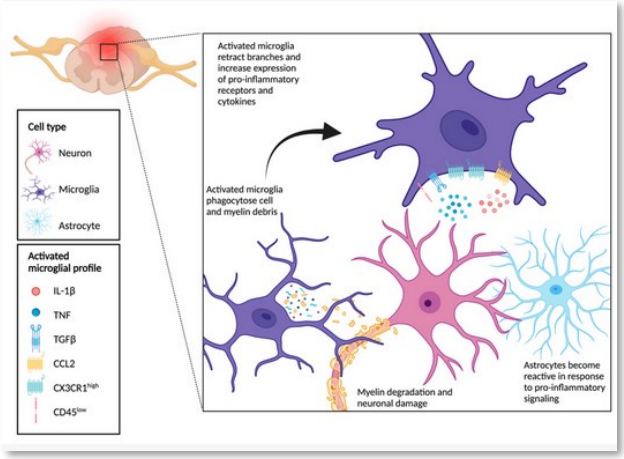
Andrew Gaudet, PhD, BSc, The University of Texas at Austin

2022 Founders Award (022-101) **Amount: $100,000** **Term: 2-Years**

Spinal cord injury (SCI) newly afflicts 18,000 Americans per year and has devastating effects on body function. Initial SCI trauma elicits a delayed cascade of damage ("secondary damage") driven by a harmful inflammatory response. This delayed damage creates a window for early intervention, yet there are no effective neuroprotective SCI therapies.

This investigation is focused on this secondary damage related to the inflammatory response following SCI. This study is examining the failure of microglia and macrophages to remove harmful debris and prevent the inflammatory response triggered by the injury. Immune activation is amplified by dying cells and debris, which accumulate after SCI. Immune cells called microglia and macrophages can engulf this debris—a process that also engages protective anti-inflammatory pathways.

This project's central hypothesis is that activating the phagocytic receptor MerTK, which removes harmful debris and dampens inflammation, there will be improved neuroprotection and neurological function after SCI.



ERC Comments

The proposed research is innovative. Although the role of neuroinflammation in exacerbating the consequences of SCI is well known, there are few, if any, available therapies aimed at suppressing inflammation to improve outcomes.

This work could have a major impact on the treatment of SCI.

An important concept, well worth pursuing. Could have a substantial impact on treatment after SCI.

The preliminary data are strong; the experimental design is clear, and the analysis includes both the inflammatory state and locomotor function, and neuropathic pain.

Promoting Functional Locomotor Recovery after Spinal Cord Injury Using Compounds Identified with a New Adult Neural Cell Screening Platform

Cedric Geoffroy, PhD, Texas A&M University, College Station

2022 IP Award (022-102) **Amount: $200,000** **Term: 2-Years**

More than 1.4 million people are living with a spinal cord injury (SCI) in the United States, costing our economy more than $40 billion annually. To date, there are no FDA-approved therapeutics for SCI, demonstrating a need for identifying new drugs that promote functional recovery.

Current drug screening projects are not using adult stem cells matching the population of those who have sustained an SCI (SCI occurs preferentially in adults ages 20 to 60). Dr. Geoffroy will be the first to use age-specific cortical neural cells in a high throughput fashion and the first using robotic and automated imaging/analysis systems, reducing human errors.

The long-term goal of this project is to develop novel therapeutic options that enhance recovery for patients with SCI.

High Throughput Screening

High throughput screening (HTS) is the use of automated equipment to rapidly test thousands to millions of samples for biological activity at the model organism, cellular, pathway, or molecular level.

As the name indicates, HTS is a drug discovery process that enables a biochemical or cellular event to be reproducibly and rapidly tested against chemical entities many hundreds of thousands of times. HTS utilizes robotics, liquid handlers, data processing, considerable software, and sensitive detection systems. The objective of HTS is to rapidly identify active compounds that modulate a particular target, pathway, or biochemical/cellular event. The output from an HTS campaign provides the basis upon which drug design and elaboration are used to generate lead compounds with appropriate physicochemical properties for therapeutic indications.

ERC Comments

This is a very innovative proposal that makes a strong argument, supported by bio-archives manuscripts (bioRxiv is for the distribution of preprints, which are complete but unpublished manuscripts).

This is a very interesting proposal that addresses a critical gap in screening for compounds that can promote recovery after SCI by focusing on adult neurons in a high throughput paradigm.

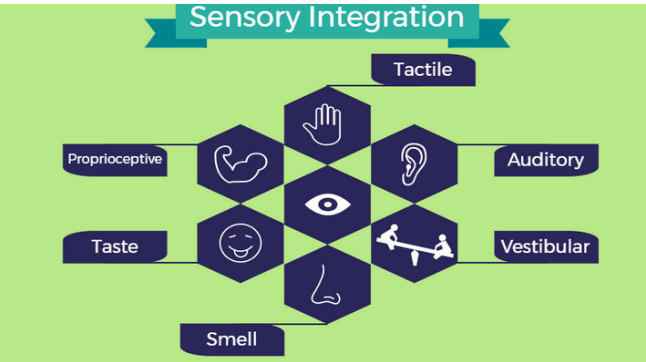
There are currently no drugs or treatments that promote the functional recovery of injured neurons. If drugs could be identified, it would be a tremendous benefit to the patients who suffer these traumatic injuries.

Putting the "Somatosensory" into Spinal Cord Injury Rehabilitation

Yuming Lei, PhD, Texas A&M University , College Station

2022 Founders Award (022-104) **Amount: $100,000** **Term: 2-Years**

A gently touch of the shoulder or a soft stroke on the hand matter more than words of affirmation.



Persons with spinal cord injury (SCI) sustain damage to ascending sensory pathways, which results in severe impairments in touch sensation and proprioception. Tactile and proprioceptive processing is central to life and involved in many functions, such as motor actions, body perception, social interaction, and affective touch.

Proprioception allows us to sense that our body parts belong to us and distinguish the physical self from the external world. Importantly, tactile, and proprioceptive signals play an important role in guiding motor actions. The absence of these play signals profoundly diminishes SCI survivors' ability to move and interact with their surroundings.

There are two aims in this study: Aim 1, focuses on determining the neurophysical alterations that underlie tactile and proprioceptive dysfunction using a novel pneumatic tactile stimulator and using a robotic exoskeleton to access proprioception; Aim 2 is to restore the sense of touch and proprioception through novel subcortical and cortical brain stimulation therapies.

The long-term goal of this research is to develop mechanistic-driven therapeutic strategies aimed at improving sensory function after SCI.

ERC Comments

This proposal addresses an understudied aspect of spinal cord injury (SCI), the effect of loss of tactile proprioceptive input on cortical and subcortical activity.

Good preliminary data and clever technical approaches.

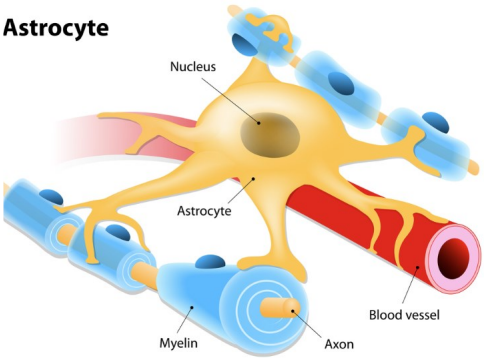
The importance of the work and its novelty are strengths of the proposal.

This proposal presents clear objectives incorporating state-of-the-art technologies and sophisticated analytics and, if realized, will be a major contributor to the field.

AstroCapsules: A Novel Tool to Detect and Modulate the Neurotrauma Microenvironment

Robert Krencik, PhD, Houston Methodist

2022 Founders Award (022-105) **Amount: $100,000** **Term: 2-Years**



Astrocytes constitute 20-40% of the cells in the brain and serve numerous essential functions. In injury, they establish barriers that limit damage and suppress infiltration of immune cells that cause cascades of secondary damage and inflammation.

This investigation tests a novel therapeutic approach to encourage astrocytes to maximize their beneficial effects upon human network repair while minimizing potential detrimental reactions to the neurotrauma microenvironment.

The Houston Methodist and Rice University team of researchers have combined organoid technology (using human pluripotent stem cells) with genetic engineering (cellular encapsulation) to create AstroCapsules. AstroCapsules will be implanted as a tool to detect signaling molecules in the neurotrauma microenvironment and provide therapeutic proteins to promote neuro repair.

or·ga·noid

Organoids are tiny, self-organized three-dimensional tissue cultures that are artificially grown from stem cells. Such cultures can be crafted to replicate much of the complexity of an organ, or to express selected aspects of it like producing only certain types of cells.

ERC Comments

This concept (implanting genetically engineering astrocytes in encapsulated in hydrogel polymers) could prove to be quite valuable in improving outcome after stroke, TBI, SCI, or other disruptive events in the CNS.

Good translational potential and preliminary data. Strong investigator prior experience and concern for experimental rigor.

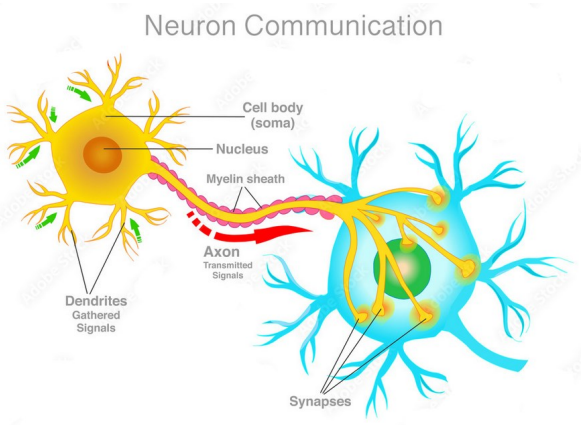
Excellent concept and rigorous experimental plan.

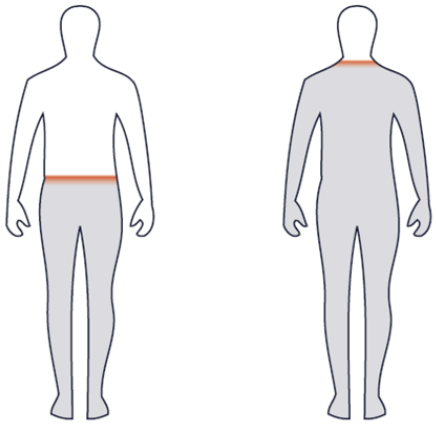
The level of innovation is high.

Synaptic Inputs to Motor Neurons in Human with Tetraplegia

Yuming Lei, PhD, Texas A&M University in College Station

2021 Founders Award (021-104) **Amount: $60,000** **Term: 2-Years**





Paraplegia **Tetraplegia** *(Quadriplegia)*

One of the most common impairments after cervical SCI is the loss of muscle function. In persons with tetraplegia, this loss of function reduces an individual's independence in activities of daily living, such as feeding, grooming, bathing, dressing, and toileting. Rehabilitation of deficits involving arm and hand control is a primary treatment goal. Recovery of muscle function after SCI largely depends on the reorganization of neural drives to paralyzed muscles. The goal of this project is better to understand the synaptic inputs to motor neurons after SCI. Understanding the physiological changes after SCI will assist with designing improved interventions to enhance rehabilitation. Secondly, the investigation will test the hypothesis that functionality significantly increases in these synaptic inputs when combined with noninvasive stimulation.

STDP

Spike-timing-dependent plasticity is a biological process that adjusts the strength of connections between neurons in the brain. The process adjusts the connection strengths based on the relative timing of a particular neuron's output and input action potentials.

ERC Comments

The work, if successful, would be both significant and impactful.

The PI is well-qualified for this work and has an excellent dissemination record.

The collaborative inclusion of Dr. David Wright as an independent data monitor adds rigor to the study.

The studies taken as a whole, carried out in humans, and the attempt to assess STDP, is novel, and, if successful, could directly impact the clinical practice paradigms aimed at the restoration of function.

Can Urine Biomarkers Characterize Developing Neurogenic Bladder in Acute SCI? - a Pilot Study

Argyrios Stampas, MD, UT Health Houston and TIRR Memorial Hermann

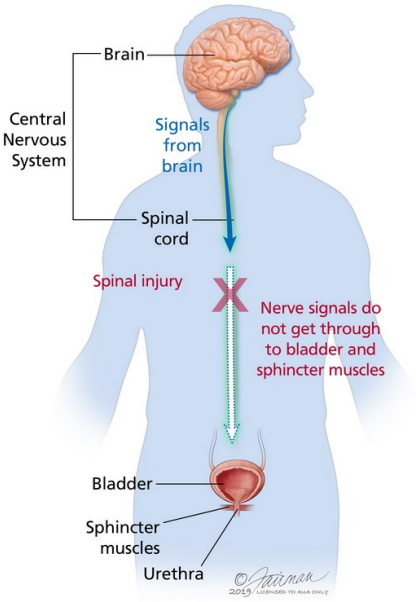
2021 Founders Award (021-109) **Amount: $60,000** **Term: 2-Years**

There are more than one million people living with spinal cord injury (SCI), affecting their movements, sensations, and their bladder. Improving bladder function is consistently identified as a high priority among people living with an SCI.

After SCI, the bladder slowly becomes hyperactive, causing significant health-related problems and a dramatic decline in quality of life. Unfortunately, little is known about the onset and progression of dysfunction within the bladder after SCI. This lack of knowledge impedes physicians from proactively preventing and effectively managing the onset of neurogenic bladder and secondary complications.

This study seeks to produce data that helps us better understand the progression of bladder damage and dysfunction and identify noninvasive predictive and diagnostic measures. There are two arms to this urodynamic study. An investigation looking at electrical stimulation of the tibial nerve to improve bladder function and prevent secondary complications is ongoing.

To further our knowledge, Dr. Stampas and his team are now collecting and analyzing urine biomarkers to learn if specific proteins (biomarkers) correlate to the progression of damage within the bladder. The goal is to develop interventions to prevent or reduce bladder problems from developing and use biomarkers as a noninvasive diagnostic tool to select treatment options.



Neurogenic bladder is a nerve-related disorder which affects the function of the urinary bladder and urethral sphincters. It causes severe inconvenience to the patient and affects the quality of life.

ERC Comments

This is an unmet problem in the field of SCI, and if the authors can utilize this biomarker approach to successfully diagnose early signs of neurogenic bladder, this could lead to better prognostic and treatment responses.

The research is highly innovative and fills a gap in clinical knowledge in the assessment of neurogenic bladder outcomes.

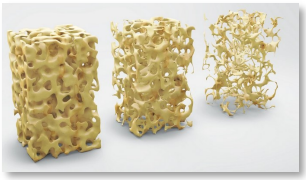
The study team is strong and includes Dr. Stampas, who is a physiatrist with expertise in the SCI populations and who is the PI of the collaborating random controlled trial. The co-investigator, Dr. Forster, has expertise in the urine proteome of neurogenic bladder. The team is supported by additional experts in neurogenic lower urinary tract function.

Does Loss of Sympathetic Nerve Signaling Underlie Acute Rapid Bone Loss after SCI

Michelle Hook, PhD, Texas A&M University, College Station

2021 IP Award (021-110) **Amount: $150,000** **Term: 2-Years**

People with a spinal cord injury (SCI) lose up to 50% of Bone in the lower limbs in the first 2 years post-injury. This loss of bone makes them 104 times more likely than an able-bodied person to have a fracture by the age of 50. After an injury, most fractures occur without a known trauma; patients notice swelling that is later clinically diagnosed as a fracture. Fractures in persons with an SCI increase morbidity, mortality, and healthcare costs.



Current treatments for bone loss are not effective after SCI. The reduced efficacy of treatments is likely due, in part, to the multi-factorial causes of SCI-induced bone loss. Dr. Hook's previous experiments have ruled out factors that cause bone loss in the general, uninjured, population. Interestingly, bone loss appears only in bones below the level of injury.

Dr. Hook hypothesizes that reduced neural signaling to the bone in the acute phase of SCI leads to changes in the activity and production of the cells responsible for bone formation. In this study, Dr. Hook and her research team seek to determine how the loss of neural signaling drives bone deterioration and whether replacing neural signals immediately after SCI can protect the homeostasis of the bone marrow.

Fractures in persons with an SCI increase morbidity, mortality, and healthcare costs.

ERC Comments

If this project is a success, it would identify new treatment targets for bone loss after SCI and ultimately benefit SCI patients.

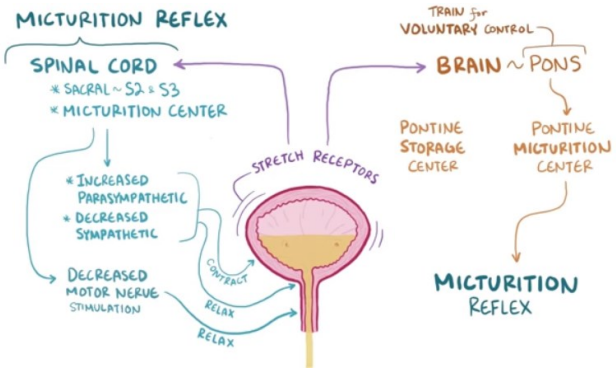
There are numerous strengths to this project, including the novelty of the project, the investigative team, the innovation, and the rigorous approach.

Dr. Allen at Indiana University is not a neurotrauma expert, but a bone expert. His involvement enriches the field of SCI.

Recovering Urological Function in SCI Through Multi-Target Neuromodulation

Mario Romero-Ortega, PhD, The University of Houston

2021 IP Award (021-111) **Amount: $150,000** **Term: 2-Years**



DSD is a consequence of a neurological pathology such as spinal injury or multiple sclerosis which disrupts central nervous system regulation of the micturition (urination) reflex resulting in dyscoordination of the detrusor muscles of the bladder and the male or female external urethral sphincter muscles. In normal lower urinary tract function, these two separate muscle structures act in synergistic coordination. But in this neurogenic disorder, the urethral sphincter muscle, instead of relaxing completely during voiding, dyssynergically contracts causing the flow to be interrupted and the bladder pressure to rise.

Many, or even most, patients with a spinal cord injury describe the restoration of bowel and bladder control as a priority that outranks even the restoration of ambulation. Urological dysfunction after spinal cord injury (SCI) is characterized by a neurogenic bladder with a loss of conscious control of voiding. Botulinum toxin is suggested as a treatment however has limited efficacy. A potential strategy and effective alternative to Botulinum toxin therapy is activating the muscles of the lower urinary tract using a current from electrodes. Previous investigations using electrodes have failed due to their size (large) and the large amount of activation current they emit. Dr. Romero Ortega has developed a highly sensitive, flexible, suture-like electrode with unmatched mechanical and electrochemical characteristics. This device will allow the team of researchers to evaluate simultaneous but differential control of three separate targets to improve voiding efficacy. The goal is to provide feasibility data on multi-target neuromodulation for the control of voiding and the prevention of detrusor-sphincter dyssynergia (muscular incoordination caused by a brain disorder.)

ERC Comments

This appears to be an excellent team to conduct the proposed studies involving a biomedical engineer and a clinician that specializes in urological problems. The approach is well-planned and appropriately rigorous.

This is an innovative approach targeting an important quality of life issue in many people living with the consequences of an SCI.

This proposal applies several technical innovations to improve the efficacy of electrical stimulation to help SCI patients manage lower urinary tract function.

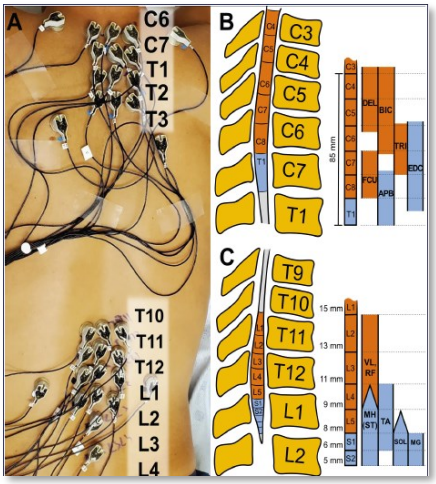
Decoding the Language of Spinal Sensorimotor Networks Using Non-Invasive Electrospinography

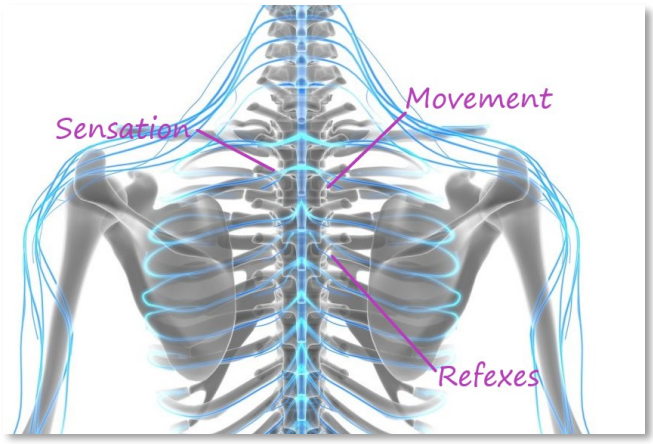
Jose Contreras-Vidal, The University of Houston

2021 IP Award (021-112) **Amount: $150,000** **Term: 2-Years**

This cross-disciplinary and multi-institutional research project proposes an innovative and quantitative model-based approach to investigate the "neural language" of the spinal cord, thereby offering new modalities for assessment, prognosis, and rehabilitation following spinal cord damage.

Specifically, Dr. Contreras-Vidal is assessing the viability of motor pathways and the state of the spinal sensorimotor networks using non-invasive, sensitive, and quantifiable Electrospinography (ESG). This study will provide clinically relevant information on the effects of SCI on spinal signaling and changes in the spinal networks due to an SCI. This information will be leveraged for the development of a non-invasive spinal cord computer interface to be used in rehabilitative treatments to restore sensorimotor function at the spinal cord level.





When the spinal cord is damaged, it prevents signals from being sent correctly. That is why a spinal cord injury causes loss of **movement, sensation,** and **reflexes.**

ERC Comments

Excellent collaboration between the University of Houston and Houston Methodist Hospital. The PI has vast experience, and a leadership record, and has teamed up with a neurosurgeon who has experience in neuromodulation and physiology.

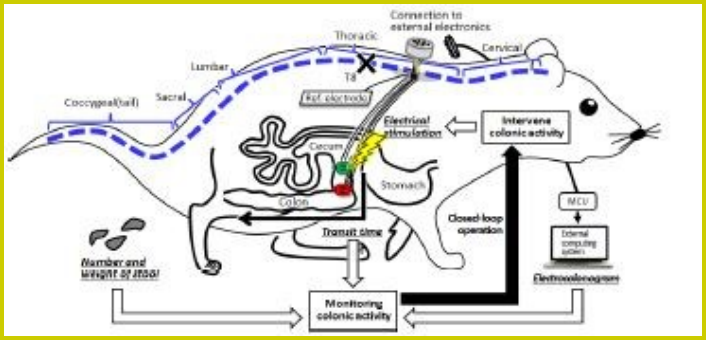
This proposal is highly innovative.

This project is a step towards a personalized rehabilitative approach for SCI and other neurological disorders.

Promoting Colonic Peristalsis after SCI with Closed-Loop Electrical Stimulation

Cedric Geoffroy, PhD, Texas A&M University, College Station

2020 IP Award (020-101) ***No Cost Extension*** **Amount: $200,000** **Term: 2-Years**



Peristalsis, involuntary movements of the longitudinal and circular muscles, primarily in the digestive tract but occasionally in other hollow tubes of the body, that occur in progressive wavelike contractions. **Peristaltic** waves occur in the esophagus, stomach, and intestines.

Among the devastating losses of normal central nervous system function caused by SCI is neurogenic bowel. Neurogenic bowel is a slow transit colonic dysfunction marked by constipation, rectal evacuation difficulties, decreased anorectal sensation, fecal incontinence or some combination thereof.

Neurogenic bowel is one of the most prevalent comorbidities of SCI and is recognized by afflicted individuals and caregivers as a lifelong physical and psychological challenge that profoundly affects quality of life.

Neurogenic bowel dysfunction (NBD) is an important area in SCI research. Breakthroughs are needed not only to improve quality of life, but also reduce the risk of life-threatening autonomic dysreflexia. Electrical stimulation has been shown to exert a positive effect on NBD; however, the results are inconsistent.

Dr. Geoffrey and his team seek to develop a closed-loop control for bowel function control and provide a detailed physiological and anatomical analysis of the colon dysfunction in a pre-clinical model of NBD after SCI. In addition, this study seeks to determine the long-term durability and effectiveness of the neural recording and stimulation system, and demonstrate the translational potential of closed-loop electrical stimulation.

ERC Comments

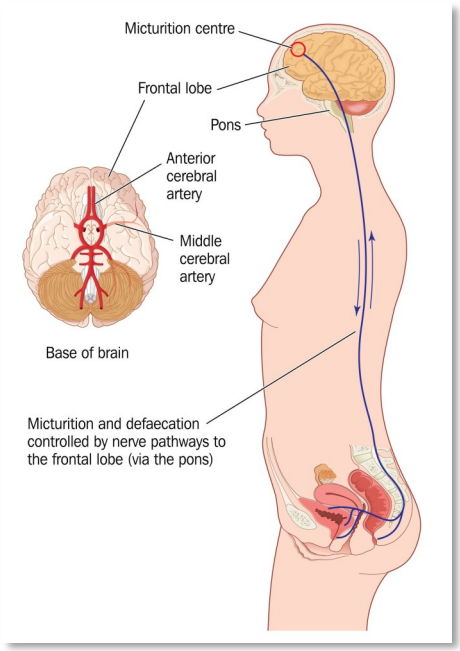
If this project is successful and able to be translated to the clinic, it will have an extremely positive impact for SCI patients.

This is an outstanding proposal that meets all the priorities of Mission Connect. It addresses and understudied problem that SCI patients are facing with an innovative approach that brings together a new perspective and excellent outside collaborators.

Sildenafil for Treatment of Urinary Incontinence

Kathleen Vincent, MD, The University of Texas Medical Branch at Galveston

2020 IP Award (020-103) *No Cost Extension* **Amount: $200,000** **Term: 2-Years**



More than half of all patients with spinal cord injury (SCI) also suffer from urinary incontinence (UI), resulting in a significantly reduced quality of life. UI mechanisms vary by differences in severity and location of the spinal injury, gender, and individual characteristics. UI is often caused by increased pressure in the bladder from bladder spasms (Urge UI) or Valsalva (cough or sneeze induced Stress UI), which overwhelms the ability of the urethral sphincter to seal the bladder and provide continence of urine.

This randomized, placebo-controlled, cross-over study examines the efficacy of sildenafil (a safe and effective FDA-approved drug), in reducing symptoms of stress and mixed-type urinary incontinence (UI) in SCI patients and explores reduced bladder spasms and increased urethral closing pressures.

The overall hypothesis is that sildenafil will help restore the balance between bladder contraction and sphincter relaxation by relaxing the smooth muscle of the bladder and improving blood flow and muscle function in the urethral sphincter.

ERC Comments

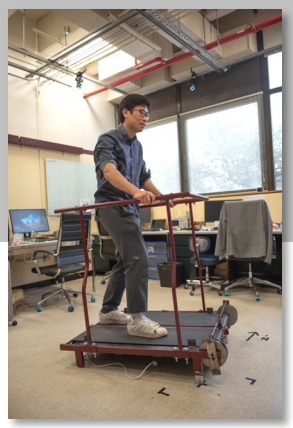
The pairing of an obstetrician/gynecologist and an expert in chronic disease research creates a unique perspective from which to approach the problem of UI in SCI patients.

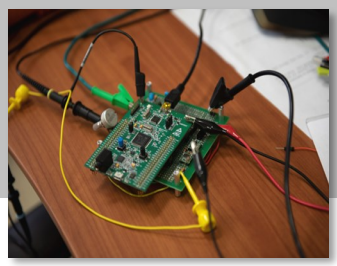
People living with an SCI have ranked urinary problems as the most important health problem after SCI. Thus, developing new approaches to overcome UI would significantly improve the quality of life for SCI individuals.

Closed-loop Peripheral Sensory-Driven Motor Augmentation to Promote Gait Rehabilitation after Spinal Cord Injury

Michelle Hook, PhD, Texas A&M University, College Station

2020 Founders Award (020-117) *No Cost Extension* **Amount: $60,000** **Term: 2-Years**





Recovering basic locomotor ability is critical to people who have sustained an SCI. The premise of Dr. Hook's study is to use a sensory-driven augmentation approach to improve gait rehabilitation. Specifically, Dr. Hook is looking at stimulation to the foot to learn if it can assist in correcting gait, then when used in conjunction with other therapies, have a significant impact. This novel study focuses on a new area of potential benefit; stimulating the peripheral nerve instead of the transitional interneurons. If successful, the development of a fully wearable/implantable peripheral neural recording and stimulation device will increase accessibility to gait rehabilitation and training, and transition therapy from a clinical-based burdensome procedure to a home-based procedure.

ERC Comments

If successful in rodent models, the potential for translation is high.

This work is highly significant as it will utilize a controlled animal model of incomplete SCI and augment cutaneous feedback from the foot, timed with gait phase to improve gait.

Excellent team with complementary expertise.

Strong preliminary data demonstrates feasibility and rationale for the proposed experiments.

Excellent team with complementary expertise.

Feasibility and Effectiveness of Home-Based Tele-Rehabilitation Program for Recovery of Upper Limb Functions in Incomplete SCI

Nuray Yozbatiran, PhD, UT Health Science Center Houston

2020 Founders Award (020-118) *No Cost Extension* **Amount: $60,000** **Term: 2-Years**

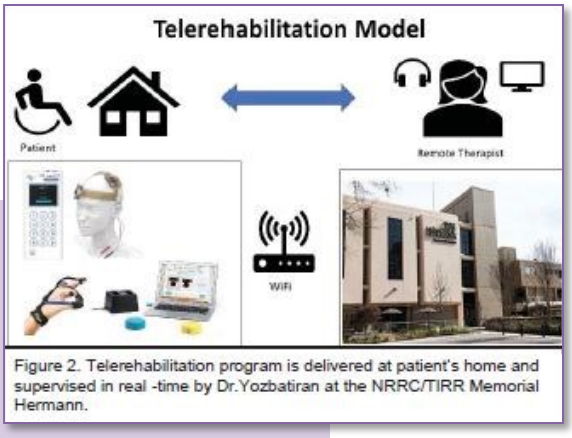


Figure 2. Telerehabilitation program is delivered at patient's home and supervised in real -time by Dr.Yozbatiran at the NRRC/TIRR Memorial Hermann.

Despite compelling evidence that the intensity of physical rehabilitation has a profound effect on motor recovery, only a small fraction of the SCI population are able to receive intensive in-clinic treatment. The purpose of this project is to investigate the safety, feasibility, and efficacy of a remotely-supervised home-based novel therapy program. This home-based therapeutic program focuses on the recovery of upper limb motor function in persons with tetraplegia due to an SCI. Transcranial direct stimulation is incorporated into this therapy program.

ERC Comments

Combining transcranial direct current stimulation with repetitive arm training at home is unique and could expand the potential for rehabilitation training to increase function after SCI.

Moving rehab into the home has multiple advantages for patients and family/care-givers.

Preliminary data suggest there is a high probability of success.

The study is well-designed and a biostatistician is involved with the project's planning.

Knowledge gained from this project could be used to expand tele-rehab on a larger scale with the potential to benefit persons (and families) living with SCI.

Synaptic Plasticity Mechanisms Underlying Chronic Pain –Induced Depression

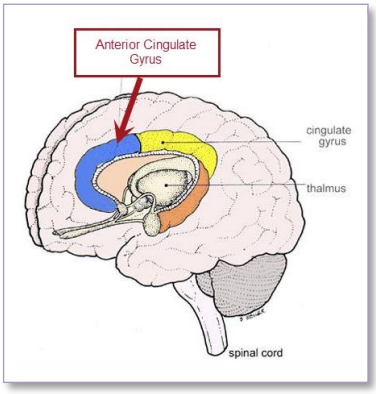
Lingyong Li, PhD, Baylor College of Medicine

2020 Founders Award (020-122) *No Cost Extension* **Amount: $60,000** **Term: 2-Years**

For persons with a spinal cord injury (SCI), chronic pain is a critical problem. The reported prevalence of chronic pain averages 65%, and approximately one-third of these people rate their pain as severe. According to a recent study, 18.7% to 26.3% of persons with an SCI are also diagnosed with a depressive disorder (a percentage far exceeding that of the general population.) When pain and depression are comorbid, a person's suffering is significantly intensified.

The underlying mechanisms of chronic pain and depression remain unclear; however, recent evidence suggests that common neuroplasticity changes and brain regions may be involved. Dr. Li and his team are investigating a region of the brain that processes both mood and pain (anterior cingulate cortex (ACC). A causal link between ACC hyperactivity and emotional aspects of pain has been shown. However, the molecular mechanisms underlying ACC hyperactivity in chronic pain-induced depression are unknown.

Dr. Li seeks to determine the role of a genetic protein (TIAM1) in ACC neurons in promoting depressive-like behaviors. Secondly, the team seeks to elucidate the mechanisms by which TIRAM1 mediates synaptic plasticity in the ACC that underlies pain's emotional impact.



ERC Comments

The concepts behind this work, approach, and investigators are excellent and the clinical problem is very important.

Identifying the mechanisms associated with chronic pain-induced depression will help in finding effective treatments with important clinical benefits.

The science is excellent.

Traumatic Brain Injury

A traumatic brain injury (TBI) is an injury to the brain that occurs as a result of a bump or blow to the head or from blunt or penetrating trauma. During the impact, the brain crashes back and forth within the skull resulting in bruising, bleeding, and the shearing of nerve fibers known as axons.

After the initial trauma, the brain will typically swell in response. This causes the brain tissue to push up against the inside of the skull, which can lead to further bleeding and reduced blood circulation.

If the swelling is not treated, parts of the brain can become starved of oxygen and other nutrients, leading to brain cell death. It is this cell death that typically causes the most common TBI symptoms.

TRAUMATIC BRAIN INJURY

Every nine seconds, someone in the United States sustains a brain injury.

Every day in the US, 137 people die due to a TBI-related injury.

Each year about 2.5 million individuals sustain TBIs of which approximately 50,000 result in death, and more than 80,000 suffer permanent disability.

The costs to society for care and lost productivity due to brain trauma are enormous and estimated at $76.5 billion annually.

TBI is the leading cause of death and disability in children and adults ages 1 to 44.

The most underreported, under diagnosed, and underestimated brain trauma by far is concussion.

Globally, 69 million people sustain a TBI each year.

Concussion accounts for 90% of TBI with millions of trauma cases every year.

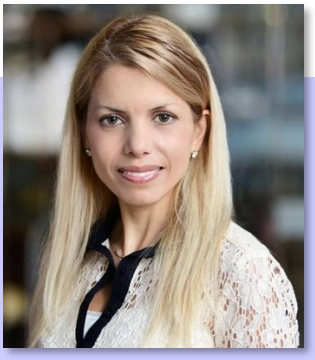
Causes of TBI:

Falls	(28%)
Vehicle crashes	(20%)
Struck by an object	(19%)
Assaults	(11%)
Others	(12%)

19.5% of high school athletes have sustained a concussion, 5% have sustained more than one. 99% of deceased NFL players in the brain donation program are diagnosed with concussion related brain damage.

Mission Connect®
a program of TIRR Foundation

Portfolio of Active Traumatic Brain Injury and Stroke Investigations

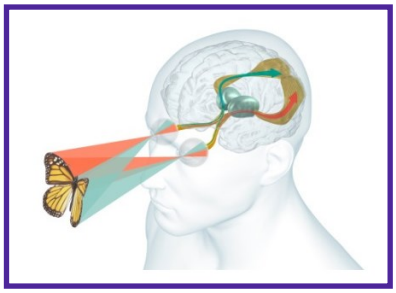


Elucidating Causal Mechanisms of Visual Motion Perception and Exploring AI-Assisted Linear and Nonlinear Decoders to Provide Sensitive and Specific MRI-Brain Computer Interface Neurofeedback to Cortically Blind Patients

T. Dorina Papageorgiou, Baylor College of Medicine

2022 IP Award (022-109) **Amount: $200,000** **Term: 2-Years**

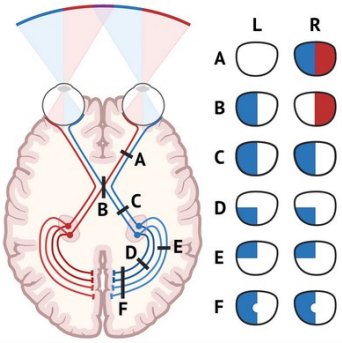
The overall goal of this project is to develop strategies that could promote the reorganization of visual pathways after brain injury downstream of the optic chiasm to improve visual motion perception and performance in cortically blind patients.



Currently, there are no successful MRI brain-computer interface applications for neural rehabilitation of visual deficits following cortical lesions. This innovative study is based on a neurofeedback delivery approach that will be patient-specific and reinforce new network involvement bypassing direct pathways that have sustained damage.

This highly collaborative study brings together researchers with expertise in the areas of neural imaging, brain-computer interface strategies, MRI brain-computer interface methodologies, neurofeedback, and innovative machine-learning approaches.

At present, there is no efficacious management to reliably evoke cortical visual plasticity in individuals with cortical blindness.



Cortical blindness can occur for small or large portions of the visual field, depending on the size and location of the brain lesion. Often there is cortical blindness for half of the visual field, to the left or right of both eyes, but it is also possible that only one quadrant or an even smaller area is affected.

With cortical blindness in both halves of the visual field, a person is essentially completely blind; he/she cannot consciously process visual input any longer, cannot identify or describe objects, cannot recognize faces, cannot read a text or reach for an item.

ERC Comments

This study should provide scientific knowledge and technical expertise for improving visual function in patients with traumatic brain injury, stroke, and other neurological conditions.

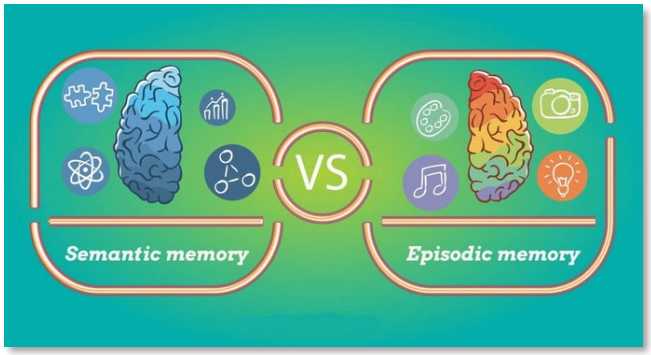
The authors are experts in functional MRI and brain-computer interface neurofeedback to induce cortical plasticity in this patient population.

This proposal targets an important clinical disability related to TBI with exhibited valuable. The study is felt to be highly innovative since, currently, there are no successful MRI brain-computer interface applications for neural rehabilitation of visual deficits following cortical lesions.

Mild-TBI Effects on Episodic Memory-Role of the PFC

John Broussard, PhD., UT Health Science Center Houston

2022 Founders Award (022-106) **Amount: $100,000** **Term: 2-Years**



Episodic memory is the memory of everyday events that can be explicitly stated or conjured. It is the collection of past personal experiences that occurred at particular times and places; for example, the party on one's 7th birthday.

Approximately 2 million mild TBI (mTBI) cases occur annually in the United States. People who suffer from mTBI often exhibit cognitive and behavioral dysfunction. While these impairments commonly normalize within a year, they persist in approximately 10-15% of mild TBI victims. One of the cognitive deficits often seen in TBI patients is impairments of episodic memory, or the ability to use navigational cues to direct memory. Even subtle alterations in prefrontal function caused by mild TBI produce profound deficits in memory. Impairments may stem from altered neuronal function and activity. This novel project will utilize probes to record electrical signals generated by individual neurons in the hippocampus and prefrontal cortex, two regions that are often damaged in human TBI. This study builds on previous work by Dr. Broussard that demonstrates that excess inhibition of the prefrontal cortex (PFC) may contribute to episodic memory dysfunction. In this study, the team will target excitatory neurons in the PFC in a rat model in an attempt to enhance memory and simultaneously test the response of prefrontal activity.

ERC Comments

This collaborative grant proposal shows important scientific and translational value.

Some anticipated findings will likely provide new leads about how to further advance neuroscience research on abnormalities of episodic memory (AEM) and devise therapeutic development approaches to managing AEM.

There will be a valuable collaboration between an in-vivo electrophysiologist and a TBI investigator.

The proposal is well-written and clear and is supported by preliminary data using innovative techniques.

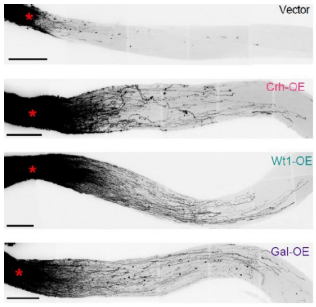
Molecular Function of Three Novel Regeneration Promoting Genes (022-107)

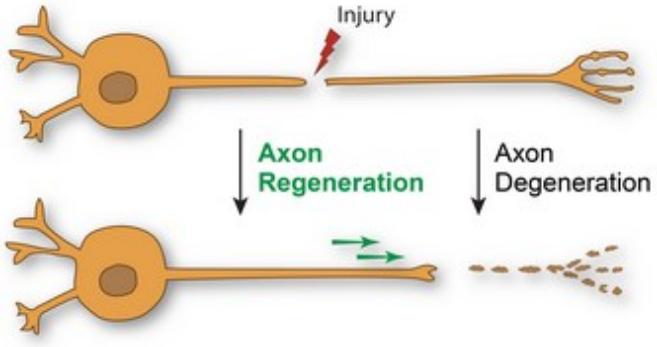
Nicholas Tran, PhD, Baylor College of Medicine

2022 Founders Award (022-107) **Amount: $100,000** **Term: 2-Years**

When the axons of neurons in the central nervous system are damaged, they generally fail to regrow and reform connections, resulting in functional loss and often leading to neurodegeneration. Thus finding treatments that can protect neurons, stimulate axon regeneration, and reform synaptic connections would be of great clinical value.

The investigators leading this research project recently discovered three genes, Crh, Gal, and Wt1, whose overexpression increases neuronal survival and promotes axon regeneration. These genes represent exciting new potential targets for regenerative therapies. The goal of this investigation is to better understand how these genes function with neurons. To achieve this, the research team will examine how each treatment affects the molecular profile of their target neuron and how different neuronal populations respond. The findings from this study will improve understanding of the pathways supporting regeneration and have the potential to lead to new treatment strategies for acute nerve injuries.





ERC Comments

Excellent investigator; a well-conceived project that may lead to improved axon regeneration in the optic nerve and other CNC pathways.

Finding effective strategies to promote axon regeneration of CNS neurons following injury has been and remains an unfulfilled challenge and an important therapeutic target.

This is a pilot study of a junior and talented investigator, who comes with outstanding training and good productivity.

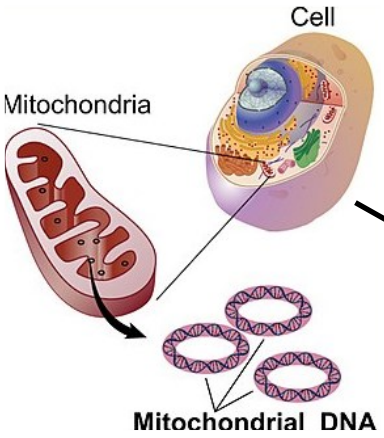
This project scores highly on all axes. The overall strategy is sound, well-reasoned, and appropriate.

Mitochondrial DNA as a Critical Active Signaling Molecule in Development of Neuroinflammation Post Mild-TBI

Bartosz Szczesky, PhD, The University of Texas Medical Branch at Galveston

2021 Founders Award (021-105) **Amount: $60,000** **Term: 2-Years**

Traumatic brain injury (TBI) is an important healthcare problem without effective therapies. Mild TBI (mTBI) accounts for nearly 75% of all TBI cases and induces detrimental neuroinflammatory responses that contribute to long-term cognitive and emotional deficits without identifiable tissue lesions or cavities in the cerebral cortex. Neuroinflammation, mitochondrial dysfunction, and oxidative stress are hallmarks of TBI. Neuroinflammation is considered a major secondary mechanism of neural injury.



Although TBI-induced neuroinflammation has been studied for many years, the molecular mechanisms underlying the activation of microglia are not well understood. In this project, Dr. Szczesky and his team seek to establish mtDNA as a critical signaling molecule in the neuroinflammatory response post-mTBI via mechanisms that are not linked to cell death.

Mitochondrial DNA is the DNA located in mitochondria, cellular organelles within eukaryotic cells that convert chemical energy from food into a form that cells can use, such as adenosine triphosphate.

ERC Comments

A strong team, and novel ideas, could provide a breakthrough in understanding mTBI.

Excellent analyses of the correlation between the functional defects and focus of damage, as assessed by multiple means.

Highly accomplished, well-trained investigators, overall an exciting proposal with a unique approach. Since there are no current treatments for TBI, this could have a significant impact.

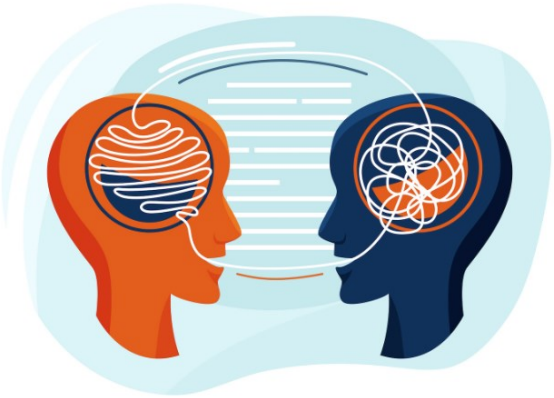
Good experimental design and sophisticated methodology to study cross-talk between neurons/astrocytes and microglia.

Language and Theory of Mind After Stroke

Tatiana Schnur, PhD, Baylor College of Medicine

2021 Founders Award (021-106) **Amount: $60,000** **Term: 2-Years**

Stroke is a common brain injury affecting at least 795,000 Americans every year. Left and right hemisphere strokes occur at similar frequencies, and both are associated with life-altering communication deficits. However, patients with right hemisphere (RH) stroke rarely receive speech-language intervention. This is likely because they do not present with obvious signs of aphasia. Instead, they have difficulties engaging in typical conversations, which require understanding what a speaker means, especially in contrast to what was actually said. This is a specific deficit in the ability to understand others' perspectives and intended meanings, known as the theory of mind. For those living with RH stroke, communication deficits have profoundly damaging effects on quality of life.



The central hypothesis of Dr. Schnur is that RH stroke causes discourse-level language deficits due to damage to brain areas critical to the human ability to understand others' perspectives, an essential component of social communication. To test this hypothesis, Dr. Schnur and her team seek to answer fundamental questions concerning the necessity of the theory of mind for production and comprehension and the brain regions associated with the theory of mind and language deficits.

ERC Comments

To my knowledge, understanding communication defects in patients with right hemisphere damage (RHD) is novel and interesting.

The experimental design is driven by clear hypotheses and predictions as well as rigorous analysis.

Outstanding collaboration with Dr. Margaret Blake, who will provide additional research and clinical expertise to help with scoring the behavioral data and the clinical implications of the behavioral outcomes.

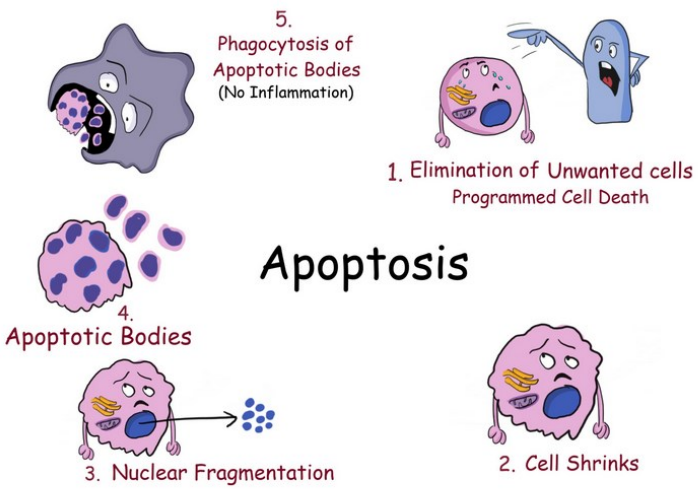
Transcription Factor Crosstalk in the Control of Neurodegeneration after CNS Axonal

Trent Watkins, PhD, The University of California San Francisco

2021 Founders Award (021-107) **Amount: $60,000** **Term: 2-Years**

This study focuses on neurodegeneration, an important consequence of central nervous system (CNS) axon injury, and how modulating the injury process may improve the functional consequence of TBI. Traumatic injuries to the CNS can be devastating not only from the damage caused by the initial insult but also by stimulating neurodegenerative processes. These processes triggered by the injury involve widespread changes in the nucleus of a neuron, some of which can be helpful and others that result in cell death.

Dr. Watkins and his team are investigating the mechanisms associated with the activation of the pro-apoptotic transcriptional programs to find targets to block apoptosis while maintaining beneficial aspects of stress signaling. How the transcription factors influence which cells live or die may reveal therapeutic targets to promote neuroprotection while preserving the potential for recovery.



Apoptosis is **the process of programmed cell death**. Apoptosis is mainly active during embryonic development, when deletion of redundant cellular material is required for the correct morphogenesis of tissues and organs; moreover, it is essential for the maintenance of tissue homeostasis during cell life. Cells also activate apoptosis when they suffer from various insults.

ERC Comments

Neurodegeneration is an important consequence of CNS axon injury, and modulating this process may improve the functional consequence of traumatic brain injury where neurons die not only from the primary trauma but also the subsequent inflammation and as secondary degeneration.

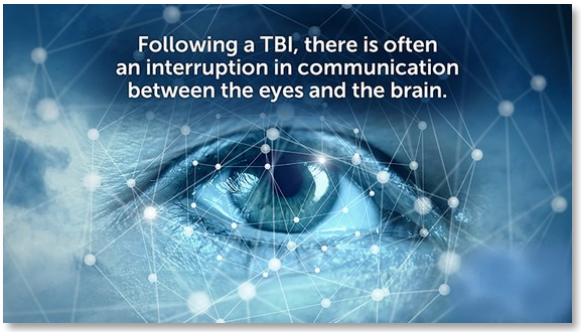
The proposal is well-designed and uses an innovative approach.

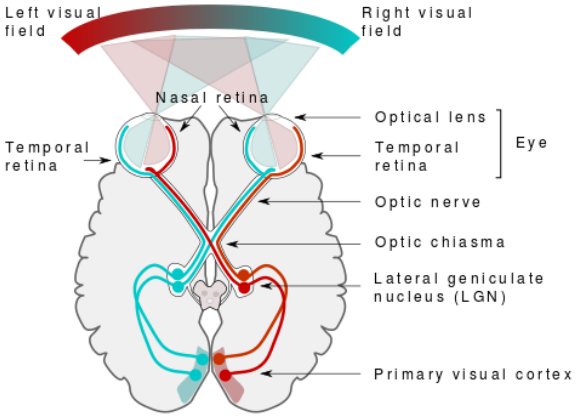
These experiments will produce preliminary data on the mechanism by which ATF_4 modulates transcription.

Decoding Causal Mechanisms of Visual Motion Perception Under the Induced Learning via an Individualized MRI-Compatible Brain Computer Interface

Dorina T. Papageorgiou, PhD, Baylor College of Medicine

2021 Founders Award (021-108) **Amount: $60,000** **Term: 2-Years**





According to the Brain Injury Awareness Association, a person in the U.S. sustains a brain injury every nine seconds, culminating in more than 3.5 million injuries each year. The most common type of TBI-induced injury affects the areas of the brain that control vision. TBI-induced visual dysfunction severely impacts a patient's quality of life. An inability to drive, read, and navigate one's environment leads to a loss of independence, isolation, and even depression. Standard visual rehabilitation relies on compensatory eye movements to scan the environment and has proven ineffective in these injuries. This investigation focuses on regaining vision by inducing neural plasticity in the brain. At the center of this study is a brain-computer interface system within an MRI developed by Dr. Papageorgiou. The goal of this noninvasive technology is to bypass damaged visual pathways and target and strengthen alternate intact areas, thus rerouting and reorganizing visual pathways.

Neural plasticity can be defined as the ability of the nervous system to change its activity in response to intrinsic or extrinsic stimuli by reorganizing its structure, functions, or connections.

ERC Comments

This project addresses an important problem related to TBI and Stroke, where some patients are left with severe visual field deficits and cortical blindness that has devastating consequences on their quality of life.

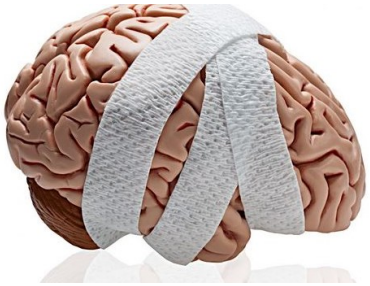
The technology utilized in this project to enhance visual motion is very innovative. The project is supported by promising preliminary data.

The excellent collaborative team Dr. Papageorgiou has assembled is complementary and will facilitate success in this project and future studies with TBI patients.

The Role of CART Peptide in TBI

Nobuhide Kobori, PhD , UT Health Science Center Houston

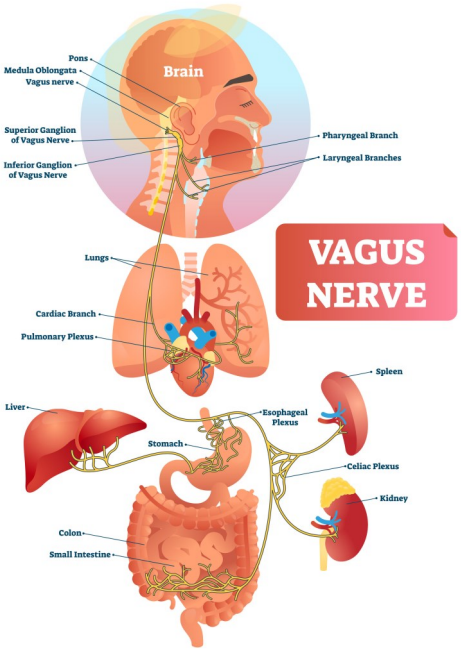
2020 Founders Award (020-119) ***No Cost Extension*** **Amount: $60,000** **Term: 2-Years**



Inflammation is associated with most brain diseases and is thought to contribute to secondary brain damage and neurodegeneration following traumatic brain injury (TBI). While the majority of research has focused on the role of central inflammation, the role of parts of the peripheral nervous system are poorly understood.

This innovative study led by Dr. Kobori, seeks to identify signaling molecules associated with the vagus nerve that block damaging inflammation. Of primary focus in this study is the role of Cocaine- and amphetamine-regulated **transcript peptides** (**CARTp,** neuropeptides that act as neurotransmitters in the brain of vertebrates.) This study proposes that CARTp acts to regulate peripheral inflammation and can be used to improve TBI outcome.

Dr. Kobori and his team are investigating the administration of synthetic CARTp in a rodent TBI model to explore its therapeutic utility in reducing inflammation and its effect on learning and memory.



Peripheral nervous system refers to parts of the nervous system outside the brain and spinal cord.

ERC Comments

A better understanding of post-TBI immune responses may illuminate new potential therapeutic targets.

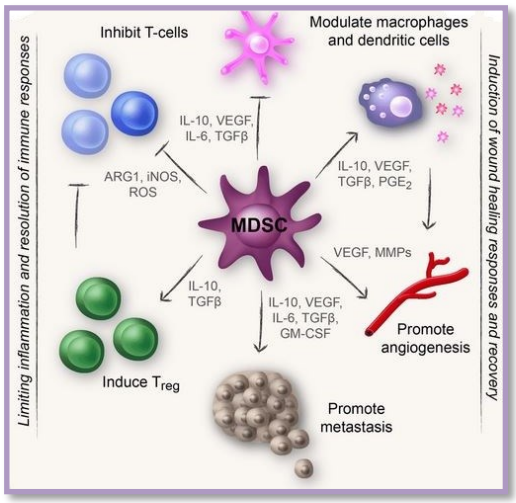
This research addresses a significant problem and the role of vagus nerve and peripheral inflammation following TBI is not fully understood.

The planned work holds excellent research and translational values.

Myeloid Derived Suppressor Cells in Traumatic Brain Injury

Scott D. Olson, PhD, UT Health Science Center Houston

2021 Founders Award (020-121) **Amount: $60,000** **Term: 2-Years**



MDSC

MDSC are a heterogeneous group of immune cells from the myeloid lineage. MDSCs strongly expand in pathological situations such as chronic infections and cancer, as a result of an altered hematopoiesis.

Traumatic brain injury (TBI) affects millions of people worldwide and is estimated to become the third leading cause of death in the Unites States in the near future. TBI patients suffer long-lasting immune dysfunction that results in opportunistic infections. One of the significant post-TBI sequelae that contribute to increased mortality/morbidity is development of opportunistic infections such as pneumonia. Studies in cancer and other chronic inflammatory diseases have found that a particular specialized immune cell type, called a Myeloid Derived Suppressor Cell (MDSC) is capable of paralyzing the immune system. Dr. Olson and his team are studying how MDSC are affected by TBI, and how this may, in turn, contribute to long-term injuries associated with TBI.

"We hypothesize that MDSC participate in a dysfunctional feedback-loop between the central nervous system and the systemic immune system to contribute to sub-acute and chronic immune dysfunction.", Scott Olson, PhD

ERC Comments

Enriching the field's knowledge and therapeutic capacity to prevent systemic complications and augment life quality is an essential goal of neurotrauma research.

This is a strong collaborative investigator team possessing needed expertise.

Very little is known about MDSCs in CNS injury. The proposed studies will add to our knowledge of their role in brain injury and post-injury immune suppression.

Special Funding Awards

Jerry Johnston Andrew Spinal Cord Injury Research Award

The Gene Alford Spinal Cord Injury Research Award in Robotics

Private and Donor Directed Funding

Jerry Johnston Andrew Spinal Cord Injury Research Award

The Jerry Johnston Andrew Spinal Cord Injury Research Award was created in 2011; the year she was honored at TIRR Foundation's dinner event aptly called "The Heroes Among Us." For more than 30 years, TIRR Foundation was fortunate to have Jerry and her constant optimism, passion for life, and immense kindness as part of our organization. As a long-time member of our board, she supported our efforts at every turn.

Following an automobile accident, Jerry sustained a spinal cord injury and lived the greater part of her life dependent upon a wheelchair. With immense drive and optimism, she was committed to improving the recovery, health, and quality of life of those who have sustained these life-altering injuries. Each year, a Mission Connect scientist working in the arena of spinal cord injury is selected to receive this award. It is our hope that the discoveries made through this $10,000 award will fulfill Jerry's aspiration to improve the lives of those with spinal cord injuries within our own community and throughout the world.
Jerry Johnston Andrew, 1938-2014

The 2022 recipient of the Jerry Johnston Andrew Spinal Cord Injury Research Award is Dylan McCreedy, PhD. Dr. McCreedy' s lab at Texas A&M University of focused on the roles of early inflammation in tissue damage and wound healing following spinal cord injury.

The 2023 recipients for these two named awards will be announced on September 28, 2023 at TIRR Foundation's annual fundraising dinner event.

The Dr. Eugene Alford Spinal Cord injury Research Award in Robotics

In 2013, TIRR Foundation honored board member Dr. Gene Alford by establishing the Dr. Eugene Alford Spinal Cord Injury Research Award in Robotics. Dr. Alford is an outstanding husband, father, and physician with an unrelenting desire to help others. Following a spinal cord injury in 2007 that left him paralyzed from the waist down, it was Dr. Alford's perseverance, support system, and passion that allowed him to continue helping others through his incredible surgical abilities.

With the use of a specialized electronic wheelchair, Dr. Alford continues to perform surgery and has become a key member of research teams that bring engineers and physicians together so that people with spinal cord injuries will one day walk again.

The 2022 recipient of the Dr. Eugene Alford Spinal Cord injury Research Award in Robotics is Mario Romero-Ortega, PhD from the University of Houston. Dr. Romero-Ortega's research interests are in nerve regeneration, peripheral neurointerfacing, spinal cord injury and bioelectronic medicines .

Private and Donor Directed Funding

SCI Research Lab Funding—$25,000 (021-103)
Dylan McCreedy, PhD, Texas A&M University in College Station
Donor: Anne and Tom Conner, and Emily Conner Hempel

Preservation of Time for Research - TIRR Memorial Hermann —$150,000 annually (020-114, yr. *1 of 3*), (021-114, yr. *2 of 3*), (022-114 yr., *3 of 3*)
Gerard Francisco MD, TIRR Memorial Hermann Hospital
Donor: Mission Connect/TIRR Foundation

Spinal Cord Injury Research Hiring Initiative (019-118)
Cedric Geoffroy, PhD , University of California San Francisco
Donor: Mission Connect/TIRR Foundation

Spinal Cord Injury Research Hiring Initiative (017-104)
Bo Chen, PhD, University of Texas medical Branch at Galveston
Donor: Mission Connect/TIRR Foundation

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