The Penn
brainSTIM Center
2020

brainSTIM:
A Year in Review

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Director's Welcome Letter

Dear brainSTIM family,

Without a doubt, 2020 has been an eventful and trying year for all of us. Among other challenges, we have all dealt with the complete restructuring of our lives due to the COVID-19 pandemic. However, despite a year that has been full of obstacles, one accomplishment that I am excited to celebrate with all of you is the successful launch of the Penn Center for Brain Science, Translation, Innovation, and Modulation (brainSTIM). In a year in which almost every major event has been canceled, postponed, or virtualized, the brainSTIM team has managed to persevere. I want to offer my utmost gratitude to all of you - faculty, staff, and supporters - who have made this possible.

The idea behind brainSTIM is simple. There are many renowned experts in the field of neuromodulation in and around the University of Pennsylvania. Each of these well-established neuroscientists and clinicians has accomplished so much, just imagine what they could accomplish together through close collaboration and the sharing of ideas and expertise! Thus, the mission of brainSTIM is to draw together these eminent and emerging experts to accelerate technical innovation in the field of neuromodulation and to discover novel ways to revitalize and enhance the plasticity and performance of the human brain.

In its first year—thanks to the generous initial support of the Perelman School of Medicine—the brainSTIM center made excellent progress toward fulfilling its mission. We've assembled an outstanding core group of faculty whose expertise spans the fields of neurology, psychiatry, neurorehabilitation, biomedical engineering, psychology, cognitive neuroscience, and animal research. As you will read in the pages that follow, brainSTIM faculty have been making tremendous scientific strides, employing neuromodulation both as a tool for both characterizing the dynamic, complex nature of the brain and as a potential treatment for a range of psychiatric, neurologic and other medical conditions. We've also been excited to welcome to the center a number of junior scientists and investigators who are focused on developing careers in the field of neuromodulation, as well as collaborators in related fields who have partnered closely with brainSTIM faculty to use neuromodulation methods to advance their scientific work. Finally, we are fortunate to have guidance from luminaries in neuroscience and technology both at Penn and internationally in the form of our internal and external advisory boards. In creating this eclectic, dynamic team, brainSTIM is committed to drawing from the most diverse pools of talent and to creating an inclusive culture where all can thrive.

There is much to look forward to in the new year for brainSTIM. We are eagerly anticipating exciting new grants and clinical trials, the development of a new curriculum for neuromodulation trainees, a year-long international neuromodulation event hosted at Penn (the "Mahoney Institute for Neurosciences Year of Neuromodulation"), and more. Additionally, for those considering supporting the center through philanthropic giving, there are many opportunities to further advance the mission and goals of brainSTIM in the new year.

In closing, I want to reiterate my thanks to all of those who have committed their time, effort, and support to the success of brainSTIM. Have a happy and healthy new year! Enjoy this annual review and remember that the best days of brainSTIM are yet to come!

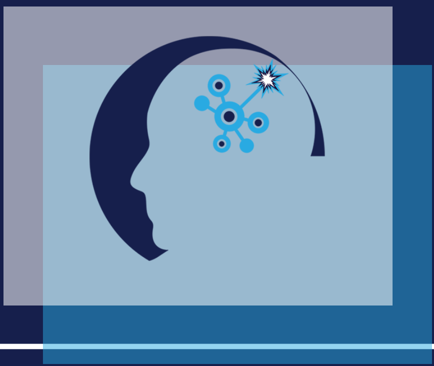
Sincerely,
Roy Hamilton MD, MS
Director, Penn Center for Brain Science, Translation, Innovation, and Modulation

In a year in which almost every major event has been canceled, postponed, or virtualized, the brainSTIM team has managed to persevere. I want to offer my utmost gratitude to all of you - faculty, staff, and supporters - who have made this possible."

Chapter 01

Meet the brainSTIM Team

01



“It’s all about advancing neuroscientific discoveries, and improving the delivery of neuroscience-informed treatments for patients.”

Welcome to brainSTIM

In its inaugural year, the brainSTIM Center is proud to have assembled a core group of truly exceptional faculty, who are engaged in groundbreaking research and clinical work involving neuromodulation. With laboratories housed in three clinical departments of Penn Medicine (Neurology, Psychology, and Physical Medicine & Rehabilitation), the Penn School of Arts & Sciences, School of Engineering, and the Wharton School, the brainSTIM faculty comprise a cross-cutting network ideally situated to foster research collaboration across the University of Pennsylvania and other institutions around the globe.

Our core group of faculty have been joined by a growing number of rising stars in neuromodulation research, as well as outstanding collaborators who have partnered with us to make novel discoveries.

Collectively, our work runs the gamut from theoretically-motivated investigations involving computational and animal models of brain function to clinically-focused trials that directly examine the efficacy of brain stimulation as a therapeutic intervention.

In the following section, we will introduce you to the members of the Penn brainSTIM Center, and highlight some of the important work done this past year by our faculty and partner laboratories.

Faculty Accomplishments

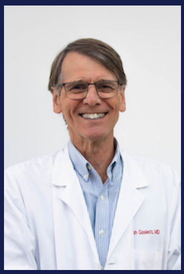
The Center for Brain Science, Translation, Innovation, and Modulation draws together an eminent team of investigators and clinicians who apply their diverse skills and expertise to better understand the organization of the human brain, and to develop neuromodulation-based interventions for common, debilitating disorders of the brain. We applaud our faculty whose outstanding research and clinical engagement worked to advance these goals in 2020.

Roy Hamilton, MD, MS, is an Associate Professor of Neurology with a secondary appointment in Physical Medicine & Rehabilitation. In addition to being the director of the brainSTIM Center, he also leads Penn's Laboratory for Cognition and Neural Stimulation (LCNS).

2020 was a busy year for Dr. Hamilton. In addition to leading brainSTIM, Dr. Hamilton's team at the LCNS has launched two clinical trials in employing transcranial direct current stimulation (tDCS) as a potential treatment for primary progressive aphasia. He has been working closely with Dr. H. Branch Coslett, MD, on a clinical trial involving the use of transcranial magnetic stimulation (TMS) in patients with aphasia after stroke. His team has continued to elucidate factors that directly influence the effectiveness of neuromodulation in modulating brain function, including the brain's network properties and biological factors such as BDNF genotype.

In addition to his research, Dr. Hamilton has continued to be a public-facing expert on the brain, cognition, and neuromodulation, speaking at numerous national and international scientific meetings, appearing on both local and national public radio, and serving as the keynote speaker at the Pennsylvania Department of Aging Forum on Alzheimer's Disease and Related Disorders.

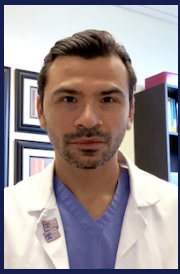
In a year that has witnessed a national reckoning with racial justice, Dr. Hamilton has been an outspoken institutional and national advocate for diversity, equality, and inclusion in science, academia, and patient care. In 2020, Cell Press identified Dr. Hamilton as one of its '1000 Inspiring Black Scientists'.



H. Branch Coslett, MD, is a William N. Kelley Professor of Neurology at the Center for Cognitive Neuroscience at the University of Pennsylvania, Research Neurologist at the Moss Rehabilitation Hospital, and is the Co-Director of Penn's Laboratory for Cognition and Neural Stimulation (LCNS), alongside Dr. Roy Hamilton. Dr. Coslett employs TMS as an experimental approach in neurology, and emphasizes its usefulness when used in conjunction with traditional methods in cognitive neuroscience investigations.

Dr. Coslett and the LCNS are currently conducting a five-year NIH-funded study of TMS in conjunction with speech therapy to treat chronic aphasia in participants with six or more months of aphasia due to stroke. Dr. Coslett hopes to use the results of this study to improve the care of aphasia, a debilitating chronic condition.

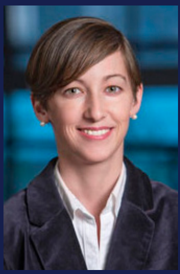
Dr. Coslett hopes to continue to innovate and elevate the field of neurology through his work with the brainSTIM Center, and in using brain stimulation for therapeutic and scientific purposes. By continuing his search for answers to outstanding questions in cognitive neuroscience, Dr. Coslett aims to create individualized and effective treatment approaches for patients with a variety of conditions. In collaboration with other investigators at the brainSTIM Center, Coslett hopes to advance the use of novel treatments to research, repair, and enhance human brain function. In addition to his work with the LCNS, Dr. Coslett has published multiple other research findings and studies in 2020.



In 2020, **Mario Cristancho PhD**, Assistant Professor of Clinical Psychiatry at the University of Pennsylvania, Director of Penn's Transcranial Magnetic Stimulation and Neuromodulation Program and Attending Physician at the Hospital of the University of Pennsylvania, did not expect that he would be seeing his patients through telehealth visits for the majority of the year. However, he took this sudden change in stride, and sees more patients than ever.

In addition to his continuing commitment to his patients, Dr. Cristancho has been collaborating this past year with brainSTIM members Desmond Oathes, PhD, and Yvette Sheline, MD, to improve TMS targeting, accuracy, and individualization of treatment. Dr. Cristancho hopes to continue his research into TMS targeting and DBS for the treatment of treatment resistant depression, in addition to continuing to treat and improve the quality of life his patients' experience.

Dr. Cristancho hopes to use research findings and subsequent trials to advance the widespread use of novel treatments, and to one day enable access to neuromodulation for every patient who needs it. He hopes that as a part of the brainSTIM community, the Center's faculty can work together to elevate patient care, treatment, and access to these life changing treatments.



Danielle Bassett PhD, Associate Professor of Bioengineering at the University of Pennsylvania and Director of the University of Pennsylvania's Complex Systems Laboratory, has had multiple studies and research efforts published in 2020.

Dr. Bassett and her team at Complex Systems Laboratory study biological, physical, and social systems by using and developing tools from network science and complex systems theory. Their broad goal is to isolate problems at the intersection of basic science, engineering, and clinical medicine that can be addressed using systems-level approaches. The group's current focus is on network neuroscience, where they seek to develop tools to probe communication patterns and pathway in the brain in order to identify, diagnose, and develop personalized therapeutics for the treatment and rehabilitation of brain injury, neurological disease, and psychiatric disorders.

In her most recent study, Dr. Bassett and her collaborator investigated "How humans learn and represent networks", where they sought to introduce and better understand the field of graph learning, which studies how humans learn and represent networks in the world around them. They reviewed progress toward understanding how people analyze and understand the complex web of relationships which underlie sequences of items and information received on a daily basis. Dr. Bassett hopes to continue to examine concepts in this field, as well as collaborate further with her brainSTIM affiliates in 2021.

brainSTIM faculty member **Sudha Kessler MD, MSCE**, is an Assistant Professor of Neurology at the Perelman School of Medicine at the University of Pennsylvania, in addition to being board-certified in Neurology, Pediatrics and Child Neurology. In 2020, she was hard at work in both her research and in her clinical practice as a Pediatric Neurologist at the Children's Hospital of Philadelphia, where she primarily examines children with epilepsy. Dr. Kessler is interested in the epileptic mechanisms of the human brain, specifically in children, and the effect that transcranial magnetic stimulation has on those neural processes.

In addition to her clinical work, Dr. Kessler contributed to many published research pieces over the last year, including "Analyzing 2,589 child neurology telehealth encounters necessitated by the COVID-19 pandemic", where she and other researchers reflected on their clinical work, and assessed in person and telehealth encounters for patient demographics and diagnoses. Researchers also analyzed follow-up care and technical challenges.

Prior to the onset of the COVID-19 pandemic, Dr. Kessler examined "Unplanned Readmissions of Children with Epilepsy in the United States", which investigated the burden and characteristics of childrens' unplanned readmission after an epilepsy-related discharge in the United States, and analyzed the characteristics of each initial hospitalization and the risk factors for readmission. Dr. Kessler and her collaborators found that the most common readmission diagnosis was epilepsy, and that establishing a benchmark readmission rate for pediatric epilepsy would be useful to health systems as they design quality improvement efforts.

John Medaglia PhD, is an Assistant Professor of Psychology and Neurology at Drexel University and Adjunct Professor of Neurology at the University of Pennsylvania. His primary research interests are how to improve cognitive control in health and disease using multimodal neuroimaging, neuromodulation, and network neuroscience. At Drexel University's Cognitive Neuroengineering and Wellbeing Laboratory, Dr. Medaglia and his team combine network neuroscience, brain stimulation, and behavioral assessment to achieve these goals.

Dr. Medaglia has contributed to multiple publications throughout 2020.Dr. Medaglia has made multiple appearances and presentations to showcase recent work by he and his team at Drexel University's Laboratory for Cognition and Neural Stimulation, including efforts to individualize neuromodulation treatments and how network anatomy varies across subjects.

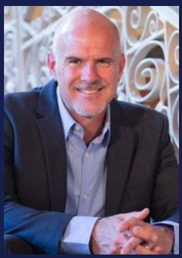
Dr. Medaglia has also collaborated this year with many of his faculty steering committee peers, including Dr. Roy Hamilton and Dr. Branch Coslett at the LCNS, as well as Dr. Flavia Vitale at the Vitale Lab. Dr. Medaglia's research attempts to reconcile the functions and operations of single, cognitively relevant regions of the brain with the properties of whole brain networks. In performing research with the Vitale Lab, Dr. Medaglia explored whether the use of micro-electrodes can be used in surface electroencephalography (EEG), and hence be used to better understand the physiologic effects of neuromodulation.

Dr. Medaglia expressed his excitement for the continuation of his research and work in 2021, and hopes to collaborate further with his fellow brainSTIM faculty members.

Desmond Oathes, PhD is an Assistant Professor of Psychiatry at the University of Pennsylvania and Associate Director of the Center for Neuromodulation in Depression and Stress (CNDS) at the University of Pennsylvania, as well as being a board-certified clinical psychologist (CA). Dr. Desmond Oathes leads the Oathes Laboratory within the Center for Neuromodulation in Depression and Stress aiming to understand casual communication between brain networks as well as develop noninvasive brain stimulation tools for optimally modulating brain activity, behavior, and neuropsychiatric symptoms.

Dr. Oathes and his team at the Oathes Lab have focused their recent work on the usage of TMS and fMRI into finding pathways to the subcortical brain in order to better treat patients with depression, anxiety and PTSD.

Dr. Oathes also collaborated with brainSTIM members Danielle Bassett PhD, and Ted Satterthwaite, MD, among others throughout the year. In a particular study, he and his collaborators investigated the right temporoparietal junction (rTPJ)'s role in social decision making, as its role in such is unclear, despite its critical role in strategic interactions. Through examining the effects of rTPJ TMS, researchers concluded that the causal role of the rTPJ in selfishness depends on the social context thereof. Dr. Oathes also frequently collaborates with CNDS Director and brainSTIM faculty member Dr. Yvette Sheline to further his research into depression, anxiety, PTSD, and ADHD. He hopes to continue his collaboration efforts with his fellow faculty members in 2021.



Michael Platt, PhD, a Professor of Marketing, Psychology, and Neuroscience at the University of Pennsylvania, the Director of the Wharton Neuroscience Initiative at the University of Pennsylvania, as well as the Director of PlattLabs, has spent his year working on an array of exciting projects and publications, including his own book, "The Leader's Brain: Enhance Your Leadership, Build Stronger Teams, Make Better Decisions, and Inspire Greater Innovation with Neuroscience", which came out in October.

Dr. Platt and his team have spent the past year working on developing high quality EEG devices that can be used to enhance patient care and achieve increased accuracy in readings. PlattLabs has also been working with optogenetics in human and non-human primates to confront neurobiological problems. His lab also recently contributed to the launch of a new centralized optogenetics database, "The Open Science Framework", which works to list all attempts of using optogenetics in the primate brain in order to make more informed evidence-based decisions in studies of optogenetics in primates. In collaboration with fellow brainSTIM faculty member Flavia Vitale, PhD, PlattLabs has explored the possibility of using nanomaterials to deliver highly focal, invasive modulation. This approach holds promise for preventing seizures in epilepsy as well as attenuating or aborting psychotic episodes in persons with schizophrenia.

In his new book, Dr. Platt translates his extensive research of the workings of the human brain into strategies that will help businesspeople get ahead in the workplace, and examines how brain science can transform one's approach to leadership, team building, and marketing.

Ted Satterthwaite, MD, is an Assistant Professor of Psychiatry at the University of Pennsylvania, attending physician at the Hospital of the University of Pennsylvania, Director of the University of Pennsylvania's Lifespan Informatics & Neuroimaging Center. Dr. Satterthwaite also leads a team of researchers in his lab at the University of Pennsylvania's Lifespan Informatics & Neuroimaging Center (LINC), who study brain development through a variety of techniques.

Dr. Satterthwaite's goal is to utilize multimodal neuroimaging to better understand both normal and abnormal brain development, as well as the origin of psychiatric symptoms in the context of brain development and reward system function. Additionally, Dr. Satterthwaite studies how functional brain networks evolve in relation to both health and disease, as well as how reward system function relates to a variety of symptoms associated with psychiatric diagnoses.

In addition to his clinical work, Dr. Satterthwaite has contributed to a number of publications over the past year, including collaborations with brainSTIM Faculty Steering Committee members Desmond Oathes PhD, and Danielle Bassett, PhD, as well as having conducted a session with his collaborators focusing on the examination of brain health across the life span, with respect to brain development and the development of psychiatric disorders.

In 2021, Dr. Satterthwaite hopes to continue his collaboration with members of the brainSTIM faculty, as well as continuing his work in his research interests and in treating his patients clinically.

Yvette Sheline, MD, a Professor of Psychiatry, Radiology, and Neurology, and the Director of the Center for Neuromodulation in Depression and Stress (CNDS), has contributed to multiple studies and publications over 2020, in addition to her clinical work. Her lab uses innovative neuroimaging methods to interrogate brain networks that are involved in affective illness and to develop individualized brain-based treatments targeting these networks using real time fMRI, cognitive behavioral therapy, novel pharmacotherapy, vagus nerve stimulation and TMS.

Dr. Sheline and her team at the CNDS are currently working to augment cognitive behavioral therapies (CBT) with computer exercises to produce changes in task-evoked fMRI brain activity. They are also working to use this and fMRI connectivity in order to examine individuals' relationship to treatment responses. Researchers are also examining the use of real time fMRI feedback in reducing depression and in examining symptoms across individuals. Dr. Sheline has also worked on a number of research publications this year, including those collaborating with brainSTIM center scientist Nick Balderston, PhD, and brainSTIM faculty member Desmond Oathes, PhD. She has also worked on a variety of aforementioned research efforts with brainSTIM faculty member Mario Cristancho, PhD.

Dr. Sheline hopes to continue her efforts in researching and pioneering treatments for anxiety, depression, and PTSD in the coming year, and expresses hope for increased collaboration amongst faculty members and disciplines within the brainSTIM Center.

Flavia Vitale, PhD, an Assistant Professor of Neurology, Bioengineering, and Physical Medicine and Rehabilitation at the University of Pennsylvania, as well as the Director of the Vitale Lab at the University of Pennsylvania, has spent her year performing extensive research into the use and engineering of nanomaterials and nanostructures for the use of monitoring and treating disorders of the nervous and neuromuscular systems. Dr. Vitale has also presented at multiple events this year, including brainSTIM's Mini Symposium on Neuromodulation, and has made media appearances on broadcasts such as the BBC's "Crowdscience" podcast.

This year, many exciting innovations emerged from the Vitale Lab. Researchers at Vitale's Lab have begun to use MXene electrodes to create bioelectronic, implantable, microelectrode arrays to collect high fidelity data. Dr. Vitale is also collaborating with brainSTIM faculty steering committee member John Medaglia, PhD, to explore whether MXene can be used to develop the next generation of electrodes for use in surface electroencephalography (EEG). This would allow investigators to better monitor brain activity, and in turn better understand the physiologic effects of neuromodulation and transcranial electric stimulation. In addition to her work with Dr. Medaglia, Dr. Vitale is also working with faculty steering committee member Michael Platt, PhD, to develop applications for nanomaterials. As mentioned before, Dr. Vitale and Dr. Platt have also found the possibility of illuminating different parts of the brain noninvasively and wirelessly in order to stop seizures in epilepsy, or shut off schizophrenic episodes by modulating activity in different areas of the human brain.

Dr. Vitale expresses her continued commitment to the translation of her findings and work to the development and use of technologies and devices that will directly translate into the enhancement of patient care and treatment outcomes. She looks forward to continuing her collaborations with brainSTIM faculty steering committee members in the coming year, and looks forward to future development and research opportunities.

Center Scientists

Our up-and-coming neuromodulation researchers and clinicians

Denise Harvey, PhD

Dr. Denise Harvey is a Research Associate of Neurology at the University of Pennsylvania, as well as an Adjunct Professor of Cognitive Psychology at Drexel University. Dr. Harvey is also a Research Associate at the University of Pennsylvania's Laboratory for Cognition and Neural Stimulation (LCNS). Her research focuses on the application of brain stimulation in persons with aphasia.

Nick Balderston, PhD

Dr. Nick Balderston is a Research Assistant Professor of Psychiatry at the University of Pennsylvania, and is a faculty member at the University of Pennsylvania's Center for Neuromodulation in Depression and Stress (CNDS). An experimental psychologist focusing on anxiety, his research uses an interdisciplinary approach to develop and test brain behavior hypotheses aimed at understanding the mechanisms that mediate clinical anxiety.

Kelly Sloane, MD

Dr. Kelly Sloane is an Assistant Professor in the Department of Neurology at the University of Pennsylvania, as well as an Investigator at the University of Pennsylvania's Laboratory for Cognition and Neural Stimulation (LCNS). Her clinical and research interests focus on recovery of cognitive function after stroke as well as healthcare technology. She has led studies on motor-cognitive recovery after stroke and technology-based cognitive assessment tools, and has authored numerous peer-reviewed research publications.

Brian Erickson, PhD

Dr. Brian Erickson is a Research Assistant Professor at Drexel University's Cognitive Neuroengineering and Wellbeing Research Lab (CogNeW). Dr. Erickson's main interests are in connecting technology to neurology in order to improve health outcomes, develop of cognitive enhancements for healthy people, and in discovering the principles of communication between the brain and machines, in addition to combining his background in engineering with his work in cognitive neuroscience.

Abby Ahearn

Social Media/Communications Specialist

Olu Faseyitan

Operations Manager

brainSTIM Center Staff

Affiliated Scientists

Key collaborators with brainSTIM faculty

Michelle J. Johnson, PhD

Dr. Michelle J. Johnson is an Associate Professor of Physical Medicine and Rehabilitation at the University of Pennsylvania. She also has a secondary appointment as an Associate Professor in Bioengineering at the University of Pennsylvania, and is a member of the Mechanical Engineering and Applied Mechanics graduate group at the University of Pennsylvania. Dr. Johnson directs the Rehabilitation Robotic Research and Design Laboratory at the Pennsylvania Institute of Rehabilitation Medicine at the University of Pennsylvania.

Timothy Markman, MD

Dr. Timothy Markman is a Cardiologist with a focus on Cardiac Electrophysiology. His research focuses on the use of autonomic neuromodulation for the treatment of abnormal heart rhythms and other cardiac conditions. Dr. Markman's goals are to characterize the complex network for cardiac autonomic innervation in order to improve treatment options for patients with arrhythmias, and to modulate this system using neural stimulation.

Lacinda Benjamin

Executive Administrator

Theresa Tritto, PhD

Associate Director

brainSTIM Center Staff

Internal Advisory Board

Leaders in neuroscience who guide brainSTIM

John Detre, MD

- Professor of Neurology and Radiology, University of Pennsylvania
- Director, Brain Science Center, University of Pennsylvania
- Director, Center for Functional Neuroimaging
- Co-Director, Center for Magnetic Resonance and Spectroscopy

Raquel Gur, MD, PhD

- Karl and Linda Ricks Professor of Psychiatry, University of Pennsylvania
- Vice Chair for Research Development
- Director, Neuropsychiatry Section
- Co-Director, Penn Medicine Translational Neuroscience Center

Murray Grossman, MD EdD

- Professor of Neurology, University of Pennsylvania
- Director, Penn Frontotemporal Degeneration Center (FTD)

Frances Jensen, MD

- Professor of Neurology, University of Pennsylvania
- Chair, Neurology Department, University of Pennsylvania
- Co-Director, Penn Medicine Translational Neuroscience Center
- CPUP Board of Directors, University of Pennsylvania

Joseph Kable, PhD

- Baird Term Professor of Psychology, University of Pennsylvania
- Director, Center for Outreach, Research, and Education (mindCORE)

Brian Litt, MD

- Professor of Neurology, Neurosurgery, and Bioengineering, University of Pennsylvania
- Director, University of Pennsylvania Epilepsy Center
- Director, Center for Neuroengineering and Therapeutics (CNT)

Sharon Thompson-Schill, PhD

- Christopher H. Browne Distinguished Professor of Psychology, University of Pennsylvania
- Founding Director, Center for Outreach, Research, and Education (mindCORE)

David Wolk, MD

- Professor of Neurology, University of Pennsylvania
- Co-Director, Penn Memory Center
- Associate Director, Alzheimer's Disease Core Center

External Advisory Board

International luminaries in neuromodulation and technology who advise brainSTIM

Marom Bikson, PhD

- Professor of Biomedical Engineering, The City College of New York
- Co-Director of Neural Engineering, The City College of New York
- Co-Director, New York Center for Biomedical Engineering

Mitchell J. Blutt, MD

- Clinical Assistant Professor of Medicine, Weill Cornell Medicine Graduate School of Medical Sciences
- CEO, Consonance Capital

Michael D. Fox, MD, PhD

- Associate Professor of Neurology, Harvard Medical School
- Raymond D. Adams Distinguished Chair of Neurology
- Director, Center for Brain Circuit Therapeutics, Brigham & Women's Hospital
- Kaye Family Research Director, Brain Stimulation Program
- Director, Laboratory for Brain Network Imaging and Modulation

Mark S. George, MD

- Distinguished Professor of Psychiatry, Radiology & Neuroscience, Medical University of South Carolina
- Founding Director, Center for Advanced Imaging Research
- Director, Brain Stimulation Laboratory, Psychiatry
- Endowed Chair, Layton McCurdy Endowed Chair in Psychiatry

Ana Maiques

- CEO, Neuroelectrics
- Co-Founder, StarLab
- EU Prize for Women Innovators from the European Commission EC Recipient (2014)

Alvaro Pascual-Leone, PhD

- Professor of Neurology, Harvard Medical School
- Medical Director, Deanna and Sidney Wolk Center for Memory Health
- Senior Scientist, Hinda and Arthur Marcus Institute for Aging Research at Hebrew SeniorLife
- Founder, Berenson-Allen Center for Noninvasive Brain Stimulation, Beth Israel Deaconess Medical Center

Chapter

02

Innovations & Advancements

02

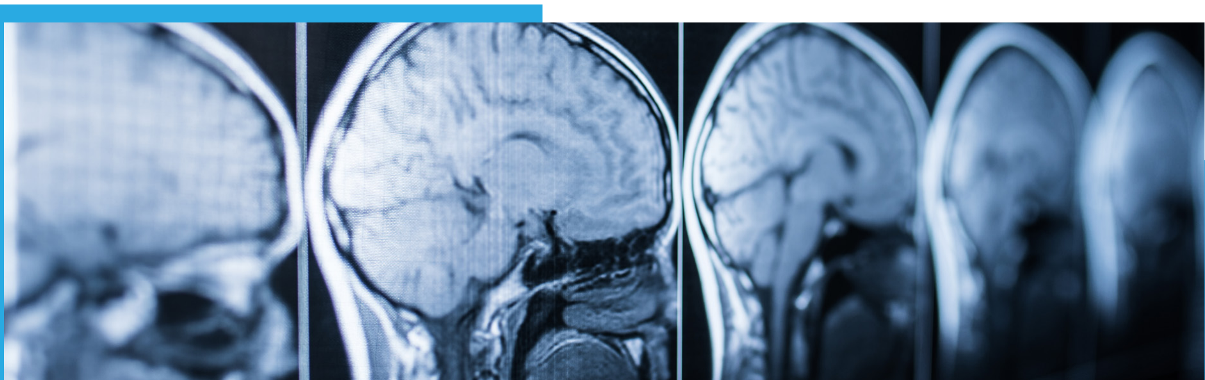
> ...person-centered network neuroscience can improve the prediction of neuromodulation outcomes and drive new neuromodulation practices.

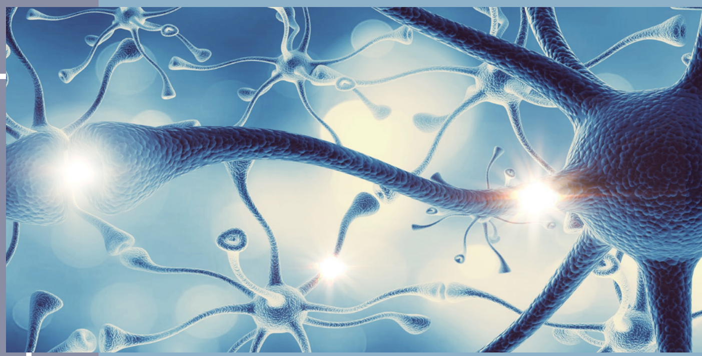
Our Faculty's Latest Advancements and Achievements

In recent years, researchers have made historic progress in the increase of understanding of the functional organization of the human brain.

The brainSTIM Center is honored to have many affiliated laboratories and institutions who continue to strive everyday to make novel innovations in a variety of fields, including neuromodulation, bioengineering, and psychology.

In the following section, the Center would like to highlight some of our faculty steering committee members who have made significant achievements in their fields and laboratories, as well as the published studies and research efforts put forth by various members of our faculty over the course of the past year.





Faculty Spotlights

Latest Research & Laboratory Developments

At the brainSTIM Center, we strive to bring together individuals from a variety of disciplines, in order to foster both a vision and collaboration within the Center which bridges departmental and university borders. The research interests of the following faculty members are varied and unique, and the brainSTIM Center seeks to provide them and our other members with support for their work. This past year, our faculty members made huge strides in the fields of neuromodulation and bioengineering, some of which were highlighted at the brainSTIM Center's Mini Symposium on Neuromodulation, as well as many other events throughout the year.

Advancing Network Neuroscience to Personalize Neuromodulation

Faculty Steering Committee member John Medaglia, PhD, applies models and methods developed in various disciplines to optimize human brain function. At Drexel University's Cognitive Neuroengineering and Wellbeing Laboratory (CogNeW), Dr. Medaglia and his team combine network neuroscience, brain stimulation, and behavioral assessment to achieve these goals.

Dr. Medaglia emphasizes how network anatomy varies across subjects, and how that can guide network function and cognition, in addition to how it can affect outcomes or differ in individuals. At the CogNeW lab, Dr. Medaglia and his team also focus on how person-centered network neuroscience can improve the prediction of neuromodulation outcomes and drive new neuromodulation practices. Individual outcomes of neuromodulation are a direct reflection on the interaction between the characteristics of the patient and the neuromodulation being applied.

Dr. Medaglia poses the question of how to take general network intuition and use that to ask behavioral questions to predict outcomes, and therefore enhance results to improve function. He also seeks to find mechanisms that can be used to mediate outcomes of neuromodulation treatment, which in the long run would aim to produce improved outcomes for patients. To approach this notion, Dr. Medaglia emphasizes the need for personalizing neuromodulation, whether through statistical fitting or mechanistic models.

In studies with both his lab and in partnership with Dr. Hamilton's Laboratory for Cognition and Neural Stimulation (LCNS), Dr. Medaglia researches the reconciliation of single regions of the brain and the processes thereof with whole brain network properties. Medaglia and his team have found a link between the role of the language control region of the brain and context-rich semantic demands, or finding the words to convey different concepts. Researchers used this concept to indicate how individuals may react to transcranial magnetic stimulation.

Dr. Medaglia poses the outstanding questions of how anatomy guides dynamics that predict language and cognitive control, as well as whether or not simple, reliable measures of a target's intermodule connectivity are linked to high-value clinical outcomes, followed by the question of whether or not researchers can assign subjects based on the network roles of the targets and

John Medaglia, PhD, performs TMS on a patient.

use that to predict neuromodulatory outcomes.

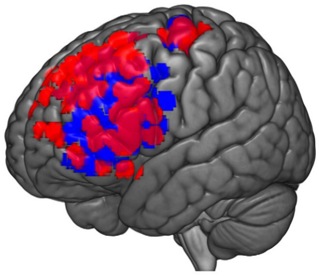
Dr. Medaglia presents a couple of options for personalized treatment approaches: statistical fitting and mechanistic models. Statistical fittings entail taking stock of genotypes, as well as social and demographic variables, before moving on to the examination of neural networks and responses to TMS. When using a mechanistic model, researchers examine a person as an expression of their genotype, and by their role in their environments, and then examine how that is reflected in their brain anatomy. After doing this, researchers would observe this through neural and cognitive models, before predicting responses to TMS treatments.

This year, CogNeW has extensively researched how mechanistic models relate to networks in every individual's brain. Each individual engages different networks for different things, which is a challenge for neuromodulation. Because of this, neuromodulation must navigate going from group inferences to individual ones, and examine how networks function in relation to everyone's anatomy. In the coming year, Dr. Medaglia hopes to continue his work in asking how neuromodulation outcomes could improve with person-centered network neuroscience that drives new neuromodulation practices.

TMS Applications for the Treatment of Anxiety & Depression

In the past year, Dr. Desmond Oathes and his team at the Oathes Lab continued their research into methods of improving rTMS clinical treatment of depression by further individualizing target selection.

Dr. Oathes presented recent studies relying on group functional images to select rTMS targets, and suggested that though this method is an important step toward more accurate treatments, such targets cannot be effective for every patient, and lack specificity. He emphasized the importance of garnering individualized data from each patient and using that information as a guide for applying stimulation.



A model illustrates that positive (shown in red) functional connectivity works better than negative (shown in blue) for modulating subcortical targets involved in depression, which aids in improving symptoms.

By overlaying individual functional maps over the structural brain image of his patients, Dr. Oathes stimulates cortical regions with high functional connectivity to the subgenual anterior cingulate cortex which have been shown to predict treatment response. Researchers at the Oathes Lab also use interleaved concurrent TMS/fMRI to observe and measure the induced brain effects resulting from the stimulation of these individualized targets. This allows researchers to assess not only the efficacy of their targeting method but also to better understand the factors influencing TMS effects on proximal and distal distributed brain regions.

Dr. Oathes also sought to find causal pathways to distant subcortical regions involved in anxiety and depression. By using their targeting method and interleaved TMS/fMRI, Dr. Oathes and his team aimed at selectively modulating the subgenual cingulate cortex and the amygdala, both important brain structures involved in affective dysregulation. Over the year, Dr. Oathes presented data showing their ability to selectively drive the activity of those two brain structures by stimulating the individualized functional connectivity based targets designed for that specific purpose. They found that the anatomical location of the prefrontal targets designed to modulate the subgenual anterior cingulate cortex did not influence their capability to drive the activity of this region, as long as the target displayed high functional connectivity. This is particularly important, as it could lead to new potential targets for the treatment of depression and PTSD.

Dr. Oathes recieves experimental treatment to demonstrate the application of TMS.

Dr. Oathes also plans to use individualized targeting to modulate brain structures associated with specific impaired behavioral processes such as fear conditioning extinction in PTSD.
In one study, his lab used interleaved TMS/fMRI to capture brain's response to TMS single pulses before and after a three-day iTBS mini-treatment in depressed patients. In doing so, they found that the evoked response induced in the subgenual anterior cingulate cortex following single-pulse TMS was associated with symptom changes, including changes in positive affect, general distress, anxiety, and depression. This outcome is very encouraging, and is being translated into treatment for people suffering from depression and PTSD. These findings indicate that moving and connecting the dots between symptoms and brain areas with neuropsychiatric relevance will bring innovations for brain-based treatments in the future, which Dr. Oathes and his team will continue to research in the coming year.

The Future of Nanomaterials and Brain Stimulation

Like her colleagues, brainSTIM Faculty Steering Committee member Flavia Vitale, PhD, has led her lab in conducting groundbreaking research and developing novel technology in 2020. Dr. Vitale's primary research interests revolve around using and developing flexible bioelectronic and nanostructured materials and devices for high resolution, minimally invasive recording and stimulation of neurological and neuromuscular activity. These interests have been particularly highlighted throughout the past year, where Dr. Vitale and her team of researchers at the Vitale Lab have been hard at work developing high resolution depth microelectrodes and dry, low-cost EEG for multimodal brain mapping, as well as translating these innovations for use in improving patient care.

Laying out the case for her lab's dry EEG method for brain mapping, Dr. Vitale put forth the drawbacks to traditional gel EEG methods, which can be irritating to patient's skin, leaves residue in hair, is very time consuming to prepare, drying out over time, before offering her alternative dry EEG. The Vitale Lab dry EEG is made with biocompatible carbon nanomaterials, and is safer, lower cost, presents comparable results to gel EEG's, and is compatible with clinical neuroimaging.

Dr. Vitale examines nanomaterials developed in her lab.

In collaboration with fellow brainSTIM faculty steering committee member Dr. John Medaglia, Dr. Vitale's lab recorded EEG using dry MXene electrodes on human subjects. Through this test, researchers concluded that conventional materials are inadequate to work with electrical and mechanical properties of human tissues, and thus critically hamper the spatial and temporal resolution of current EEG technologies. Dr. Vitale and Dr. Medaglia found that these nanomaterials can enable a novel class of neural interfaces that are cheaper, easier to make and prepare, and can record from hairy areas of scalp without conductive gels. In addition to these findings, Dr. Vitale and Dr. Medaglia are exploring whether Ti_3C_2 MXene can be used to develop the next generation of electrodes for use in surface electroencephalography (EEG). By creating better tools for monitoring brain activity, clinicians and neuroscientists can better understand the physiologic effects of neuromodulation. Moreover, the development of superior electrodes may be promising for investigators who employ transcranial electrical stimulation (tES) and related neuromodulation technologies that deliver brain stimulation via electrodes.

Highlighted Publications

Alterations in measures of neuroplasticity following sleep deprivation and recovery sleep in major depression

Yvette Sheline, MD, and fellow researchers examined if changes in neuroplasticity as BDNF correlated to the 50% of individuals with major depressive disorder (MDD) who show rapid mood improvement following sleep deprivation, but relapse once sleep occurs. Researchers' objective was to examine changes in neuroplasticity during sleep deprivation and recovery sleep using serum BDNF and behavioral measures of learning and memory.

Brain derived neurotrophic factor polymorphism influences response to singlepulse transcranial magnetic stimulation at rest

In a study led by Roy Hamilton, MD MS, multiple brainSTIM members collaborated to discern the ability of noninvasive brain stimulation to modulate corticospinal excitability and to find whether or not plasticity is influenced by genetic predilections such as the coding for brainderived neurotrophic factor (BDNF). They investigated whether BDNF polymorphism influences baseline excitability under TMS conditions that are not repetitive or plasticity inducing.

Case series of transcutaneous magnetic stimulation for ventricular tachycardia storm

Dr. Roy Hamilton and brainSTIM Affiliated Scientist Timothy Markman teamed up with Saman Nazarian to investigate the feasibility of applying transcutaneous magnetic stimulation (TCMS) to the left stellate ganglion as a treatment for ventricular tachycardia storm. Transcutaneous magnetic stimulation (TCMS) is a noninvasive procedure which utilizes magnetic fields to stimulate nerve cells in the brain, and can be used to treat neurological conditions. The study suggests that modulation of this autonomic center could safely suppress ventricular tachycardia storm, a potentially life-threatening type of cardiac arrhythmia.

Decomposing loss aversion from gaze allocation and pupil dilation

brainSTIM faculty member Michael Platt PhD and collaborators investigated the concept of loss aversion by synthesizing distinct views into an integrative framework and by probing underlying mechanisms associated with the behavior. The study revealed a double dissociation in physiology underlying the decision process, and provides a framework for the cognitive processes that drive loss-averse decisions and highlights the biological heterogeneity of loss aversion across individuals.

Dimensional connectomics of anxious misery, a human connectome study

In a four-year study, brainSTIM Faculty Steering Committee member Yvette I. Sheline MD, MS and her colleagues sought to define constructs within the Negative Valence System (NVS), which is primarily responsible for responses to situations such as fear, anxiety, or loss. To do so, researchers examined potential brain circuitry and behaviors associated with loss and responses to sustained threat. By examining these brain circuits together, Dr. Sheline and her team sought to separate these dimensions to more accurately target disabling symptoms.

Gene coexpression patterns predict opiate-induced brain-state transitions

brainSTIM core faculty steering committee member Danielle Bassett, PhD, and collaborators examine opioid addiction and its association with persistent changes in brain plasticity. As a result, individuals with chronic drug exposure may experience a higher abuse liability related to the reconfiguration of brain plasticity. Researchers compared FOS expression in mice that were unexposed to morphine, morphine-dependent, or had undergone 4 weeks of withdrawal from chronic morphine exposure, in order to construct and examine network models that revealed a persistent reduction in connectivity strength following opiate dependence, as well as the correlation between gene expression and the opiate-induced changes in network connectivity.

Media Highlights

Increased power by harmonizing structural MRI site differences with the ComBat batch adjustment method in ENIGMA

A team of researchers, including brainSTIM's Ted Satterthwaite, MD, tested whether the batch adjustment method, ComBat, can further reduce site-related heterogeneity and increase statistical power. Researchers compared the imaging data between individuals with schizophrenia and healthy controls, and found that the use of ComBat substantially increased the statistical significance of the findings as compared to random-effects meta-analyses.

Individual variation in functional topography of association networks in youth

Several brainSTIM members collaborated to examine the spatial distribution of large-scale functional networks on the cerebral cortex differs between individuals and how it is particularly variable in association networks that are responsible for higher-order cognition. They found that the functional topography of association networks is refined with age, allowing accurate prediction of unseen individuals' brain maturity. Results emphasized the importance of considering the plasticity and diversity of functional neuroanatomy during development and suggest advances in personalized therapeutics.

A preliminary study of fMRI-guided rTMS in the treatment of generalized anxiety disorder

Center Scientist Nick Balderston, PhD, and his team of researchers recently used rTMS, a noninvasive brain stimulation technique, to reduce fear and anxiety in a recent trial. The preliminary effort involved 19 healthy human subjects who were exposed to various stimuli designed to trigger their 'startle' response to a variety of possible threats. Based on their findings, researchers believe that low frequency rTMS is a potential treatment for anxiety disorders, which they hope to explore further in larger trials.

Unplanned readmissions of children with epilepsy in the United States

Dr. Sudha Kessler and her collaborators examine the burden and characteristics of unplanned readmission after epilepsy-related discharge in children in the United States, which is not known. Seizures are among the most frequent reasons for hospitalization in children. Researchers found that clinical factors were more strongly associated with readmission than demographic characteristics, and that interventions to reduce pediatric epilepsy readmissions may have the highest yield when targeting children with neurodevelopmental comorbidities.

Your Brain During a Pandemic

In this interview with WHYY's "The Pulse" podcast, brainSTIM Director Roy Hamilton discussed the concept of brain stimulation, what it does and whether at-home stimulation techniques are feasible or effective.

Combating Zoom Fatigue

Dr. John Medaglia spoke with local radio station 1060 KYW about the fatigue stemming from constant video chatting many are subject to as a result of the COVID 19 pandemic.

Can A Machine Read My Mind?

Dr. Flavia Vitale spoke with the BBC World Service's Crowscience podast regarding her lab's development and use of novel materials for neuro-electronic interfaces.

Chapter

03

Looking to 2021 & Beyond

03

> Even though the future is notoriously difficult to predict, we know that brainSTIM has a lot to look forward to in 2021 and beyond.

What Does the Future Hold?

To paraphrase a quote that has been attributed variously to Niels Bohr, Mark Twain, Yogi Berra, among others, "…it's hard to make predictions, especially about the future". After all, who could have predicted a year ago we would be spending most of our days at home, wearing masks on a daily basis, or waiting with bated breath for the distribution of vaccines? Even though the future is notoriously difficult to predict, we know that brainSTIM has a lot to look forward to in 2021 and beyond.

In the coming year brainSTIM will continue to focus on three major goals. First, we will continue to translate advances in neuromodulation research into clinical practice. We are excited by our ongoing clinical trials in neuromodulation for conditions like depression, attention deficit hyperactivity disorder (ADHD), chronic stroke, and dementia. The new year will also see the initiation of newly funded work that will employ noninvasive neuromodulation in other clinical contexts, for instance, as an intervention to recover cognitive functions in new stroke survivors (Dr. Sloane, PI). Secondly, we look forward to the ongoing development of innovative neuromodulation technologies and approaches, including work involving novel materials and analytic techniques. We are particularly excited about the exploration of nanomaterials (Dr. Vitale) as new tools for recording, and eventually stimulating, brain activity. With respect to analytic approaches, a number of brainSTIM investigators are pursuing work that we believe will culminate in the development of personalized neuromodulation informed by individual differences in brain network organization that our team members are working to elucidate. Finally, we are committed to developing outstanding training opportunities for the next generation of neuromodulation-focused clinical researchers and neuroscientists. We are currently developing a comprehensive, multidisciplinary curriculum for the use of TMS that will help prepare aspiring researchers and clinicians to employ this important neuromodulation tool safely and with sophistication.

As we focus on these objectives brainSTIM will remain in the public eye, both at Penn and beyond. In the 2021-22 academic year, brainSTIM will partner with the Mahoney Institute of Neuroscience (MINS) to host the "MINS Year of Neuromodulation." This year-long event provides an opportunity to engage global leaders in the field of neuromodulation as invited speakers, host symposia that highlight cutting-edge advances in brain stimulation, and to showcase the outstanding work being done at the University of Pennsylvania.

With its excellent team of scientists and clinicians, its impactful future projects, and its committed collaborators and intellectual stakeholders, the future of brainSTIM is bright. We look forward to working with all of you in the new year and what we hope will be many years to come.

Chapter

04

Giving Opportunities

04

> We all have a stake in preserving and optimizing our brains' remarkable abilities.

Thank You

We all have a stake in preserving and optimizing our brains' remarkable abilities. Thanks to your generous support, the Penn Brain Science, Translation, Innovation, and Modulation Center (Penn brainSTIM Center) is making great progress toward groundbreaking discoveries in neuroscience. These discoveries allow us to develop novel treatments for a wide range of neurologic and psychiatric disorders and to find new ways to revitalize and enhance the performance of the human brain throughout the lifespan.

Every day, our globally renowned experts and scientific pioneers are turning innovative discoveries involving neuromodulation into novel treatments for brain disorders. Scientists and clinicians at the Penn brainSTIM Center are focused on understanding the complex organization of the brain and harnessing its ability to reorganize in the setting of disease. Armed with this knowledge, we aim to stimulate the brain in order to undo the symptoms of some of the most common, debilitating disorders of the brain, including depression, anxiety, stroke, and dementia. With faculty whose work spans the fields of neurology, psychiatry, neurosurgery, neurorehabilitation, biomedical engineering, psychology, cognitive neuroscience, and animal research, the brainSTIM Center is a cross-cutting network ideally situated to foster research collaboration across Penn and other institutions around the globe. Your support will make a positive impact, both in the field of neuroscience and in the lives of patients and their families.

Donor support for the brainSTIM Center supports our core efforts in three ways: first, philanthropy is critical to recruiting and retaining the most qualified clinical and translational scientists at the brainSTIM Center. Second, generous giving also supports promising research projects, including seed funding for highly innovative, early stage research. Finally, philanthropic giving allows the brainSTIM Center to nurture the next generation of translational scientists (PhDs and MDs), who will advance scientific discoveries and develop novel treatments for brain disorders using neuromodulation. Donors like you help us make discoveries that will reverse the burden of degenerative disorders, and with your support today, we can keep that momentum going.

Your philanthropic dollars make a world of difference in advancing research and clinical innovations in neuromodulation, and we are extremely grateful for your partnership. For additional information, or to donate to the Center, please visit the brainSTIM Giving Page, or the 'Donate' section of the brainSTIM website.

brainstim@pennmedicine.upenn.edu

med.upenn.edu/brainstimcenter

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