The Penn
brainSTIM
Center

brainSTIM:

2021 Year in Review

Director's Welcome Letter

Dear brainSTIM family,

Despite our initial collective hope that 2021 would represent a dramatic improvement compared to the tumult of 2020, it's safe to say that last year offered its own formidable challenges. We continue to battle a global pandemic. Initially buoyed by the introduction of effective vaccines, the story of our return to normalcy has been complicated by setbacks in recent months. Yet, despite this and other hardships, I'm pleased to report that the Penn Brain Science, Translation, Innovation, and Modulation Center (brainSTIM) not only survived its second year, but thrived. Once again, I want to thank all of the faculty, staff, and supporters who have contributed to brainSTIM's ongoing success, and I'm excited to share our progress with you in this report.

BrainSTIM draws together the University of Pennsylvania's most well-established experts and rising pioneers in the science of neuromodulation. The work of brainSTIM faculty spans the fields of neurology, psychiatry, neurosurgery, neurorehabilitation, biomedical engineering, psychology, cognitive neuroscience, animal research, and others, to create an outstanding platform for multidisciplinary work in translational neuromodulation. As you will read in the pages that follow, brainSTIM faculty have continued to make tremendous scientific strides, employing neuromodulation 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.

Over the course of 2021, brainSTIM continued to enjoy growth as an organization, as we welcomed additional members of the Penn community into our ranks. We are very excited by the recent arrival of Dr. Casey Halpern, a neurosurgeon-scientist doing groundbreaking research that combines invasive and noninvasive neuromodulation techniques. Last year we were also delighted to welcome a number of outstanding cognitive neuroscientists and clinician-scientists as center affiliates. In addition to expanding its presence at Penn, brainSTIM has made itself known far beyond the walls of the University. During the 2021-2022 academic year, in partnership with the Mahoney Institute for Neurosciences (MINS), brainSTIM has been hosting the MINS/brainSTIM Year of Neuromodulation. This year-long celebration of the science of neuromodulation has featured invited lectures from national and international luminaries in the field, and has provided a platform both for promoting cutting-edge scientific innovations and for introducing the broader neuromodulation community to the wealth of talent and innovation here at Penn.

BrainSTIM has a lot to look forward to in 2022. We continue to develop outstanding research innovations, building on the initial support of the Perelman School of Medicine through numerous new grants and awards, and through recent, generous philanthropic gifts to brainSTIM investigators. We are developing a robust curriculum as we anticipate bringing on the next generation of neuromodulation-focused trainees in the coming academic year. There are several exciting clinical trials on the horizon, and we continue to work toward the development of truly multidisciplinary translational and clinical research operations involving neuromodulation at Penn. Additionally, the MINS/brainSTIM Year of Neuromodulation will culminate in the late spring with a symposium that will include some of world's most highly recognized experts in the field. This is an exciting time for brainSTIM!

In closing, I again want to thank all of those who committed their ideas, energy, time, and support to ensuring the success of brainSTIM. Please enjoy this annual review, and here's to a happy, healthy, and productive 2022!

Roy Hamilton, MD, MS
Director, Penn Center for Brain Science, Translation, Innovation, and Modulation (brainSTIM)

> " Through the ongoing commitment of its faculty, staff, and many supporters, brainSTIM has continued to thrive and deliver on its goal of fostering highly innovative, multidisciplinary neuromodulation research at the University of Pennsylvania. I want to thank the many brainSTIM members and partners who continue to make this possible. "

brainSTIM:
2021 Year in Review

Recent Changes to brainSTIM

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> " Drawing together and supporting eminent and aspiring faculty from a wide range of fields is the key to achieving brainSTIM's mission of advancing innovative, multidisciplinary scientific discoveries in the field of neuromodulation. "

Welcome to brainSTIM!

Now entering its second year, the brainSTIM Center is proud to have expanded its core group of exceptional faculty, who are engaged in groundbreaking research and clinical work involving neuromodulation. In 2021, we were particularly excited that Neurosurgery joined Neurology, Psychology, and Physical Medicine & Rehabilitation on the growing list of clinically-relevant neuroscientific fields represented within brainSTIM. BrainSTIM membership also includes investigators in the Penn School of Arts & Sciences, School of Engineering, and the Wharton School. Thus, our faculty comprises a cross-cutting network of neuromodulation scientists ideally situated to foster research collaboration across the University of

Pennsylvania and other institutions around the globe. Our core group of faculty continues to be joined by rising stars in neuromodulation research at Penn, as well as by outstanding collaborators who have partnered with us to make novel discoveries using neuromodulation. 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 new members of the Penn brainSTIM Center, and highlight some of the important work done this past year by our faculty and partner laboratories.

New Member of Faculty Steering Committee

Casey H. Halpern, MD

Casey H. Halpern, MD is an Associate Professor of Neurosurgery and Director of Stereotactic and Functional Neurosurgery at the University of Pennsylvania. Dr. Halpern's clinical focus is in the treatment of movement disorders such as Parkinson's, tremor, dystonia, and Tourette, as well as epilepsy and psychiatric disease. See Faculty Spotlight for more info on Dr. Halpern.

New Affiliated Center Scientists

Key collaborators with brainSTIM faculty

Russell Epstein, PhD

Russell Epstein, PhD, is a Professor of Psychology at the University of Pennsylvania. Dr. Epstein directs the University of Pennsylvania's Epstein Lab, where he leads a team in studying both perception, memory, and the neural mechanisms underlying visual scene perception, event perception, object recognition, and spatial navigation in humans.

Emily Falk, PhD

Emily Falk, PhD, is a Professor of Communication, Psychology, and Marketing at the University of Pennsylvania. Dr. Falk directs Penn's Communication Neuroscience Lab, and is a Distinguished Fellow of the Annenberg Public Policy Center. Dr. Falk's research interests include behavior change, persuasion, and how ideas and behaviors spread. She is an expert in the science of behavior change, and uses psychology, neuroscience, and communication to examine what makes messages persuasive, why and how ideas spread, and what makes people effective communicators.

Martha J. Farah, PhD

Martha J. Farah, PhD, is a Walter H. Annenberg Professor of Natural Sciences and Professor of Psychology at the University of Pennsylvania, with secondary appointments in Neurology and the Graduate School of Education. Dr. Farah also directs the Center for Cognitive Neuroscience (CCN), as well as the Center for Neuroscience & Society (CNS). Dr. Farah is a cognitive neuroscientist with interests in the problems at the interface between neuroscience and society, which includes the effects of childhood poverty on brain development, the expanding use of neuropsychiatric medications by healthy people for brain enhancement, novel uses of brain imaging, in e.g. legal, diagnostic and educational contexts, and the many ways in which neuroscience is changing the way we think of ourselves as physical, mental, moral and spiritual beings.

Taneeta Ganguly, MD

Taneeta Mindy Ganguly, MD, is an Assistant Professor of Neurology at the University of Pennsylvania. She is also board certified in neurology and epilepsy, and a practicing physician at the Penn Epilepsy Center. She is a collaborating clinician for the Center for Neuroengineering and Therapeutics and a clinical trials fellow at the Institute for Translational Medicine and Therapeutics.

Dr. Ganguly is interested in implementing clinical trials to expand the scope of diagnostic and therapeutic tools in the management of epilepsy. Her work primarily focuses on the use of devices in epilepsy, including transcranial electric stimulation, responsive neurostimulation, and continuous EEG monitoring.

Adrian Raine, PhD

Adrian Raine, PhD, is the Richard Perry University Professor of Criminology, Psychiatry, and Psychology at the University of Pennsylvania. His interdisciplinary research focuses on the etiology and prevention of antisocial, violent, and psychopathic behavior in children and adults, including biological interventions to reduce aggressive and antisocial behavior. His neuromodulation studies to date have focused on modulation of prefrontal cortical activity to reduce aggression and upregulate moral decision-making.

Internal Advisory Board
Leaders in neuroscience who guide brainSTIM

External Advisory Board
International luminaries in neuromodulation and technology who advise brainSTIM

Operations Team & Advisory Boards

Operations Team

Roy Hamilton, MD
Director

Desmond Oathes, PhD
Co-Director

Theresa Tritto, PhD
Associate Director

Olu Faseyitan, MS
Operations Manager

Lacinda Benjamin, MS
Executive Administrator

John Detre, MD
- Professor of Neurology and Radiology
- Director, Brain Science Center
- Director, Center for Functional Neuroimaging
- Co-Director, Center for Magnetic Resonance and Spectroscopy

Murray Grossman, MD, EdD
- Professor of Neurology
- Founding Director, Penn Frontotemporal Degeneration Center (FTDC)

Raquel Gur, MD, PhD
- Karl and Linda Ricks Professor of Psychiatry
- Vice Chair for Research Development
- Director, Neuropsychiatry Section
- Co-Director, Penn Medicine Translational Neuroscience Center

Frances Jensen, MD
- Arthur Knight Asbury, MD Professor of Neurology
- Chair of the Department of Neurology
- Co-Director, Penn Medicine Translational Neuroscience Center
- CPUP Board of Directors

Joseph Kable, PhD
- Baird Term Professor of Psychology
- Director, Center for Outreach, Research, and Education (mindCORE)

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

Sharon Thompson-Schill, PhD
- Christopher H. Browne Distinguished Professor of Psychology
- Founding Director, Center for Outreach, Research, and Education (mindCORE)

David Wolk, MD
- Professor of Neurology
- Chief of the Cognitive Neurology Division
- Co-Director, Penn Memory Center
- Director, Penn Alzheimer's Disease Research Center
- Co-Director, Institute of Aging

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 in 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
- Layton McCurdy Endowed Chair in Psychiatry

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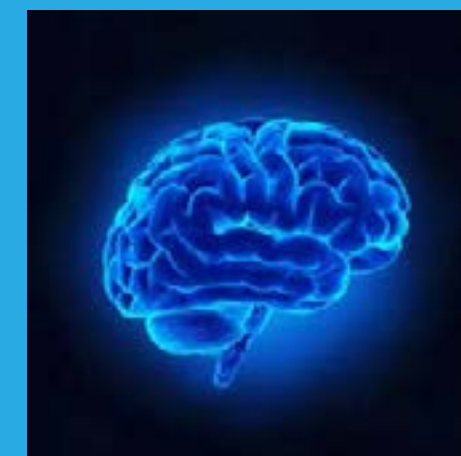- EU Prize for Women Innovators from the European Commission EC Recipient (2014)

Alvaro Pascual-Leone, MD, 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
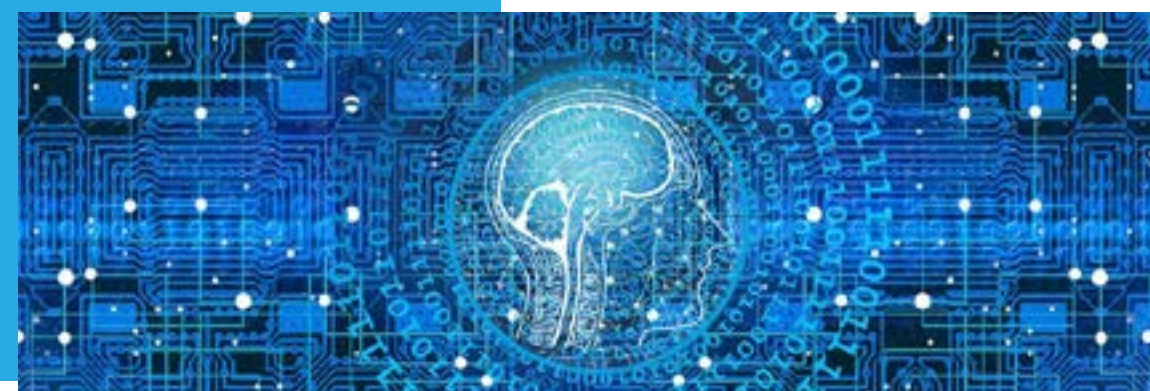
Center Highlights

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Recent Achievements for the brainSTIM Center

The brainSTIM Center and Faculty have had many accomplishments in 2021. The brainSTIM Center was involved with philanthropy, were organizers of the Year of Neuromodulation, and the development of a neuromodulation training course. The faculty showed many successes this year including new funding and grants, high profile publications, and media appearances. Here are just a few of the highlights from 2021.

2021 Center Highlights

Philanthropy

Creation of The Hart Fund in Cognitive Neuroscience

Allison & Jed Hart

Acceleration of Neuromodulation Innovation Through Generous Giving

One of the most exciting developments for the brainSTIM community in 2021 was the creation of *The Hart Fund in Cognitive Neuroscience,* which will serve to radically accelerate the scientific work of brainSTIM investigators, Desmond Oathes, PhD, and Roy Hamilton, MD, MS. Through the generous giving of Allison and Jed Hart, a total of $2.5M over the next six years will be used to accelerate innovations in noninvasive neuromodulation that will translate into improved treatments of psychiatric and neurologic patient populations.

As Co-Director of Penn's brainSTIM Center and Associate Director of Penn's Center for Neuromodulation in Depression and Stress (CNDS), Dr. Oathes is leveraging cutting edge neuroimaging methods to generate novel, individualized, brain-based treatments for psychiatric disorders such as depression, anxiety, and PTSD, as well as enhancing complex cognitive functions including working memory and decision making. With the support of the Hart Fund, using functional MRI (fMRI), Dr. Oathes and his team have proposed to use deep learning (a form of machine learning/artificial intelligence) to define individual brain stimulation targets that fit known anxiety/depression brain patterns ('decoding'). Those targets would then be carried into a combined transcranial magnetic stimulation (TMS) and fMRI session in which TMS frequency adjustments will be made for each patient in real time to determine an optimal stimulation protocol to mitigate patient negative thought patterns. These strategies would bring precision medicine to treatment for psychiatric disorders—bringing a level of individualized care that has never been achieved before.

As Director of the brainSTIM Center and the Laboratory for Cognition and Neural Stimulation (LCNS), Dr. Hamilton employs noninvasive brain stimulation to enhance a variety of human cognitive abilities in order to develop badly needed rehabilitative interventions for patients with cognitive deficits due to neurologic disease. Recently, Dr. Hamilton and his collaborators, including brainSTIM members John Medaglia, PhD, Denise Harvey, PhD, and Danielle Bassett, PhD, have demonstrated that it is possible to apply network neuroscience principles borrowed from neuroengineering to characterize individual differences in the structural connectivity of key language regions like Broca's area. These individual network differences influence how TMS applied to the language system influences language performance. They are currently exploring whether these same network features in the reorganized language networks of persons with post-stroke aphasia similarly determine the effects of TMS. Through the support of the Hart Fund, Dr. Hamilton's team aims to elucidate whether personal individual anatomical networks can be used to determine which brain area is the best TMS target for each individual living with stroke and post-stroke aphasia, allowing for the delivery of optimized, personalized neuromodulation in persons living with this common and often debilitating condition.

Taken together, support from the Hart Fund will enable these brainSTIM investigators to develop next-generation precision medicine approaches for determining where we should stimulate each patient and how we should stimulate those sites to achieve the best results. In addition to their individual projects, support from the Hart Fund will provide further opportunities for these brainSTIM investigators to collaborate and work synergistically to develop research projects along their many shared interests.

Year of Neuromodulation

In the 2021-2022 academic year, brainSTIM has been partnering with the Mahoney Institute for Neurosciences (MINS) to host the "MINS/brainSTIM 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. The Year of Neuromodulation kicked off in September 2021 with a student-led virtual symposium highlighting a diverse range of work being done by trainees in the Philadelphia area in this bourgeoning field. Another high point in the Year of Neuromodulation was the annual Flexner Lecture, one of Penn's three highly prestigious eponymous lectureships in neuroscience. This year's invited speaker, Sarah H. Lisanby, MD, Director, Division of Translational Research at the National Institutes of Menal Health (NIMH), provided an overview of her large, impactful body of research and shed light on what the future of neuromodulation holds from the perspective of key funding organizations and programs like NIMH and the BRAIN Initiative. Additionally, throughout the year, brainSTIM and MINS have teamed up to host other luminaries and emerging leaders in the field of neuromodulation as lecturers in two highly complementary seminar series.

The MINS/brainSTIM Year of Neuromodulation will culminate in April with our spring symposium, where we will host the invited speakers for Penn's two other major neuroscience lectureships: the Sprague Lecture, to be delivered by Warren M. Grill, PhD (Duke) and the Adler Lecture, to be delivered by Alvaro Pascual-Leone, MD, PhD (Harvard). At the symposium, we will also announce our "Rising Star Award" recipient. This exceptionally talented early career scientist will present their work at the symposium and will receive a $10,000 prize. The Year of Neuromodulation has been, and will continue to be, an outstanding way for brainSTIM scientists to connect with preeminent leaders in the field of brain stimulation, present their own innovative research, and elevate interest in neuromodulation within the Penn academic community and beyond.

Year of Neuromodulation Seminar Series

October 28, 2021
Wynn Legon, PhD
Virginia Tech

November 11, 2021
Mike Fox, MD, PhD
Harvard University

December 16, 2021
Marom Bikson, PhD
City College of New York

January 20, 2022
Katherine Scangos, MD, PhD
University of California, San Francisco

February 10, 2022
Azadeh Yazdan-Shahmorad, PhD
University of Washington

March 17, 2022
Kim Butts Pauly, PhD
Stanford University

March 23, 2022
Zafiris J. Daskalakis, MD, PhD
UC San Diego Health

May 18, 2022
Christoph Zrenner, MD
University of Toronto

Special Lectures

48th Annual Louis B. Flexner Lecture:
Sarah Hollinsworth Lisanby, MD
Director, Division of Translational Research
Director, Noninvasive Neuromodulation Unit
National Institute of Mental Health

"Adventures in Psychiatric Neuromodulation"

Lectures at our April 2022 Symposium

Sprague Lecture:
Warren M. Grill, PhD
Edmund T. Pratt, Jr. School Distinguished Professor of Biomedical Engineering
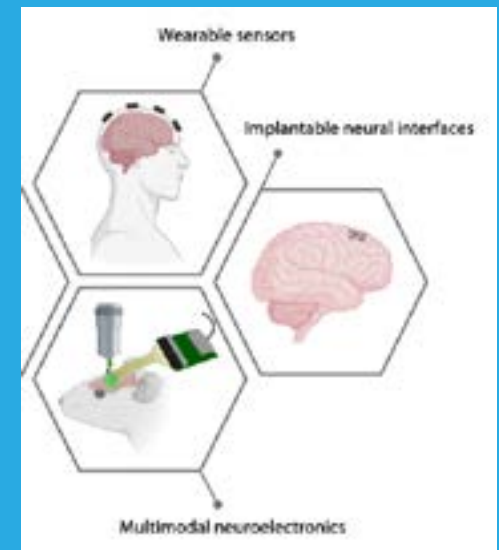Duke University

"Closed Loop Brain Stimulation"

Adler Lecture:
Alvaro Pascual-Leone, MD, PhD
Professor of Neurology and Director of the Berenson-Allen Center for Noninvasive Brain Stimulation
Hebrew Senior Life

"Promoting Brain Health and Addressing Brain-Related Disabilities"

Faculty Highlights

3

© Flavia Vitale, PhD

Chapter
3

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, we would like to highlight some of our brainSTIM Center faculty 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 2021 Highlights

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. Here are just a few of the highlights from our faculty members for 2021.

Nick Balderston, PhD is an experimental psychologist focusing on anxiety and a Research Assistant Professor of Psychiatry at the University of Pennsylvania. He received the 2021 Klerman Prize for Exceptional Clinical Research from the Brain, & Behavior Research Foundation: https://www.bbrfoundation.org/sites/default/files/pdfs/2021-kf-program.pdf. He was also awarded the 2021 NARSAD Young Investigator Award for his project entitled: Examining the Effect of FPN Stimulation on Anxiety-Related BOLD Activity using Simultaneous TMS/fMRI, Brain & Behavior Research Foundation.

Mario Cristancho, MD is the director of the Transcranial Magnetic Stimulation and Neuromodulation Program at Penn Psychiatry as well as the Medical Director of the Outpatient Psychiatry services. He was featured in Philly Voice in an article entitled "Lane Johnson shines a spotlight on anxiety disorders and the drugs used to treat them". The article was a discussion of the Eagles star experience with withdrawal symptoms after stopping an SSRI. https://www.phillyvoice.com/lane-johnson-eagles-anxiety-treatments-medications-ssri-prozac/

2021 was an eventful year for Roy Hamilton, MD, MS, Director of brainSTIM. His team published multiple papers (with more in the pipeline), examining the relationship between TMS measures of cortical excitability and different genotypes of brain-derived neurotrophic factor (BDNF) in healthy persons and in persons with stoke and aphasia. His team continues to explore the relationship between anatomical network properties of the language system and response to TMS, publishing its second paper demonstrating that individual differences in these networks predict different responses to TMS after stimulation of Broca's area. Excitingly, Dr. Hamilton's research efforts will be further bolstered through the generous support of the Hart Fund (see p. 11), made possible by a philanthropic pledge made in 2021. Dr Hamilton also assumed new leadership roles in 2021, serving as the new President of the Society for Behavioral and Cognitive Neurology (SBCN), a national organization for neurologists who focus on disorders of human cognition.

Denise Harvey, PhD, Research Assistant Professor of Neurology, did multiple conference presentations about her work in aphasia including at the Academy of Aphasia, American Neurological Association, and the Society for the Neurobiology of Language annual conferences. She is continuing her use of tACS to enhance language abilities in post-stroke aphasia. She is also furthering her training after being accepted and having completed in Jan 2022 a grant writing workshop (Training in Grantsmanship for Rehabilitation Research [TIGRR]).

Desmond Oathes, PhD, Co-Director of brainSTIM, became associate member at the American College of Neuropsychopharmacology. He is also receipient of the generous multi-year philathropic gift given by Allison and Jed Hart for establishment of the Hart Fund for Cognitive Neuroscience (see p.11).

Michael Platt, PhD, Penn Integrates Knowledge (PIK) Professor, has had a successful grant writing season with a renewed R01 and R37 NIH grant for the study of social cognition and social behavior, a new R21 to study prefrontal cortex in primates, and an NSF grant in collaboration with his startup company Cogwear LLC. Additionally, the Wharton Neuroscience Initiative brought on 2 new corporate partners: Mars Inc. and Slalom Inc., and renewed partnerships with Amplio Inc., SEB Bank, and AIIR Inc.

Ted Satterthwaite, MD, an Assistant Professor in the Department of Psychiatry and an attending physician at the Hospital of the University of Pennsylvania has two new NIH R01s for personalized networks. One entitled "Personalized Functional Network Modeling to Characterize Cognitive Functions of Youths" and the other "Precision Mapping of individualized Executive Networks in Youth". In addition, Dr. Satterthwaite is the recipient of a NIMH Merit Award and has published new scientific papers in the journals Neuron, Nature Methods, and Neuropsychopharmacology.

Yvette Sheline, MD, a Professor of Psychiatry, Radiology, and Neurology, and the Director of the Center for Neuromodulation in Depression and Stress (CNDS), has had another successfuly year. Among her successes are the awarding of two new grants. One from the Baszucki Brain Research Fund for research in TMS treatment for bipolar disorder entitled "Intensive TMS for Rapid Relief of Bipolar Depression Symptoms." The other is a NIH grant entitled "Reducing Neural Perseveration Through Closed Loop Real Time fMRI Neurofeedback to Alleviate Depressive Symptoms."

Kelly Sloane, MD is Assistant Professor of Neurology. Dr. Sloane recently launched a randomized controlled trial to evaluate the effectiveness of tDCS to augment cognitive therapy for subacute stroke patients called TRAINS (TDCS and Rehabiliation to Ameliorate Impairments in Neurocognition after Stroke). This study builds on prior work by LCNS to understand the effect of tDCS on cognitive performance. It is uniquely located within the acute inpatient neurorehabiliation service at PIRM, allowing us to provide opportunities for patients to be involved in innovative neurorecovery research during their inpatient stay. She was also awarded the CTSA KL2 Mentored Career Development Award and the McCabe Award, both from the University of Pennsylvania. See Faculty Spotlight for more information on Dr. Sloane.

Flavia Vitale, PhD is Assistant Professor of Neurology and Physical Medicine & Rehabilitation at the University of Pennsylvania where she works on engineering new technologies related to neurological and neuromuscular disorders such as epilepsy, Parkinson's, nerve injury, and chronic pain. Along with brainSTIM colleague John Medaglia, PhD, from Drexel, they were awarded a NIH R01 for the development of the next-generation of dry EEG using MXene electrodes (a two-dimensional transition metal carbide nanomaterial). Their work was also chosen to be the cover article for Science Translational Medicine's September 2021 issue.

Highlighted Publications

Media & Awards

MXene-Infused Bioelectronic Interfaces for Multiscale Electrophysiology and Stimulation

BrainSTIM faculty Drs. Flavia Vitale and John Medaglia published an article together in the journal Science Translational Medicine on the use of titanium carbide MXene to fabricate multichannel electrode arrays capable of both recording and stimulating intracranial brain activity in animal models. Moreover, the electrodes were also shown to be compatible with magnetic resonance imaging and computed tomography. Of note is the flexibility and utility in both sensing and neuromodulation.

Causal Role of the Right Temporoparietal Junction in Selfishness Depends on the Social Partner

BrainSTIM Co-Director Dr. Desmond Oathes and collaborators Drs. Joseph Kable and Kristin Brethel-Haurwiz recently published an article in the journal Social Cognitive and Affective Neuroscience examining the role of the right temporoparietal junction (rTPJ) in social decision making. Looking to clarify the causal role of the rTPJ. Dr. Oathes and colleagues conducted a TMS study using the Dictator Game. The results of this work suggest rTPJ plays a role in differentiating between others but does not reduce general selfishness when deciding how equitably to divide resource.

Local Accumbens In Vivo Imaging During Deep Brain Stimulation Reveals a Strategy-Dependent Amelioration of Hedonic Feeding

In an article published in the Proceedings of the National Academy of Sciences, Dr. Casey Halpern and colleagues report the results from work using deep brain stimulation (DBS) applied to the nucleus accumbens to attenuate binge eating. Comparing the efficacy of continuous DBS (cDBS) vs responsive DBS (rDBS) stimulation in a transgenic mouse model, the research team was able show changes in GCaMP signaling with both protocols led to a reduction in high-fat intake compared to controls but only rDBS had a more enduring effect. This work suggests the possible use of rDBS as a therapeutic intervention for overeating.

A Novel Physiological Vital Sign for Anxiety

Published in the Journal of Precision Medicine, Dr. Michael Platt and colleagues propose a novel method to identify symptoms of anxiety disorder using physiologic measurements like ones acquired by fitness trackers and wearables. By using consumer-grade mobile EEG sensors combined with machine learning, the authors were able to identify vital signs which were the strongest predictors of anxiety. The implications of this proof-of-concept study could one day enable precision personalized medicine in behavioral health space.

Deep Brain Stimulation of the Ventral Capsule/Ventral Striatum for Treatment-Resistant Depression: A Decade of Clinical Follow-Up

Dr. Mario Cristancho and colleagues recently published results from work investigating the variable efficacy of deep brain stimulation (DBS) as a therapy for treatment-resistant depression (TRD) in the Journal of Clinical Psychiatry. Following a cohort of 8 patients with ventral capsule/ventral striatum DBS enrolled in a trial for over a decade (2009 - 2020), the authors saw a 44.9% mean improvement in MADRS depression scale over the course of the trial. The results of this study demonstrate the potential for sustained improvement of depressive symptoms for TRD patients.

Proof of Concept Study to Develop a Novel Connectivity-Based Electric-Field Modelling Approach for Individualized Targeting of Transcranial Magnetic Stimulation Treatment

In the journal Neuropsychopharmacology, brainSTIM colleagues Drs. Balderston, Oathes and Sheline published a proof-of-concept study on the use of resting state functional connectivity, symptom scores and e-field modeling to predict symptom change following hypothetical neuromodulation treatment. The study predictively identified sites within BA9 and BA46 as optimal targets of stimulation for depression symptoms when compared to motor control targets. The results of this novel approach to TMS targeting proposes an effective way to identify optimal TMS treatment responders and help individualize target selection in therapeutic interventions using TMS.

MEDIA

Flavia Vitale on Developing New Technologies to Solve the Mysteries of the Brain

Flavia Vitale was featured in both Penn Medicine News and Penn Today where she discussed her work that interfaces three disciplines: neurology, bioengineering, and physical medicine and rehabilitation. Dr. Vitale discusses her path to Penn and two grants that were recently awarded. "My main goal is to create tools that can help solve mysteries of the brain, and address the needs of clinicians," she says.

https://www.pennmedicine.org/news/news-blog/2021/august/developing-new-technologies-to-solve-the-mysteries-of-the-brain
https://penntoday.upenn.edu/news/developing-new-technologies-solve-mysteries-brain-flavia-vitale

MEDIA

Michael Platt's book, The Leader's Brain, named one of Wharton Press's bestsellers

Michael Platt's book, The Leader's Brain: Enhance Your Leadership, Build Stronger Teams, Make Better Decisions, and Inspire Greater Innovation with Neuroscience, was named in Wharton School Press's Top 5 Bestsellers of 2021.

https://wsp.wharton.upenn.edu/blog_post/wharton-school-press-bestseller-list-2021/
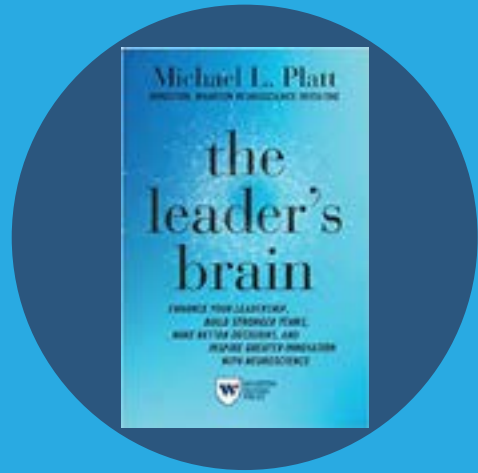
AWARD

Ted Satterthwaite Selected for NIMH Merit Award

Together with Damien Fair, Ted was selected for the NIH Merit award for their R01 submission "Precision mapping of individualized executive networks in youth." This project follows up on previous work from both PennLINC (e.g., Cui et al., Neuron 2020) and Damien's group at University of Minnesota. The MERIT award mechanism provides the opportunity to receive an additional 5 years of funding for this project with administrative (rather than peer) review.

AWARD

Nick Balderston is the 2021 KLERMAN PRIZE Winner for Exceptional Clinical Research

Nick Balderston, PhD, was recently awarded by the Brain & Behavior Research Foundation the the 2021 Klerman Prize for exceptional clinical research. "Winning the Klerman Prize is an incredible honor, and a reminder of the importance of the work to be done. More broadly, receiving support from BBRF has been instrumental in launching my career as an independent investigator and has facilitated my ability to push toward translating my basic scientific findings into potential new treatments for people with anxiety disorders."

https://www.bbrfoundation.org/sites/default/files/pdfs/2021-kf-program.pdf

MEDIA

Yvette Sheline featured in People Magazine

Dr. Yvette Sheline was featured in an article in People magazine that profiled writer Jenny Lawson and the discussion of her unusual cure for her depression. Lawson describes her experience with what she called "unrelenting depression" and turned to the use of transcranial magnetic stimulation, or TMS, in 2018. She describes it as "life changing".

Faculty Spotlights
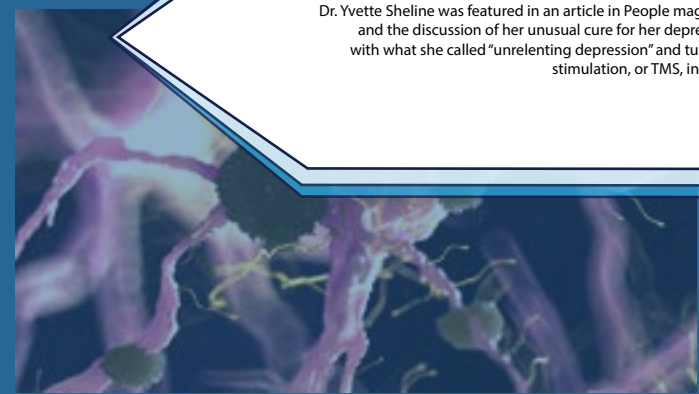

Chapter 4

Faculty Spotlights

The brainSTIM Center is made up of faculty that span departments, representing a variety of disciplines, all with interests in multiple types of neuromodulation. The next section highlights two brainSTIM scientists and gives an introduction to them as well as their research, both ongoing and upcoming.

First up is Casey Halpern, MD, a recent recruit to Penn and a new member of brainSTIM's faculty Steering Committee. You will read about Dr. Halpern's work trying to bridge the gap between invasive and non-invasive neuromodulation. Second is Kelly Sloane, MD, and one of brainSTIM's Center Scientists. You will read about her new clinical trials focusing on tDCS in stroke and cognitive impairment after TIAs. Both profiles give insight into the exciting work being done by just two of our clinician-scientists within the brainSTIM Center.

Faculty Spotlights
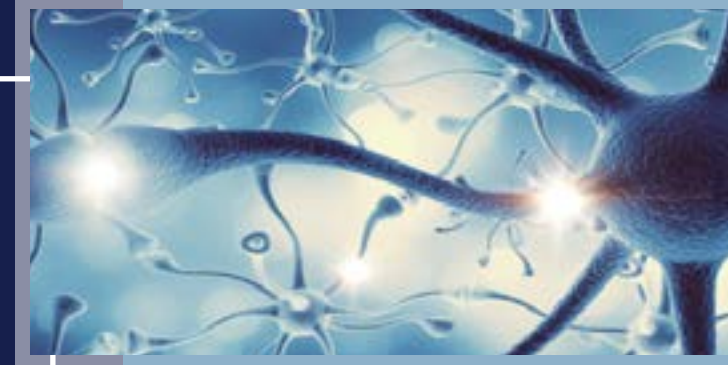
SPOTLIGHT ON CASEY HALPERN, MD: New arrival at Penn and new member of the brainSTIM Faculty Steering Committee

Casey H. Halpern, MD, is an Associate Professor of Neurosurgery and Chief of Stereotactic and Functional Neurosurgery at the University of Pennsylvania. Dr. Halpern's clinical focus is in the treatment of movement disorders such as Parkinson's, tremor, dystonia, and Tourette, as well as epilepsy and psychiatric disease. He has a particular research interest in preclinical studies and developing clinical trials to expand indications for deep brain stimulation and other novel neuromodulatory therapies. He is actively examining the role of targeting the reward circuitry of the brain with neuromodulation for obesity, obsessive-compulsive disorder and addiction, studies that could lead to possible novel treatments for these extremely common disorders.

While Dr. Halpern's clinical focus is deep brain stimulation and other exciting neuromodulatory techniques for movement disorders, he is collaborating with colleagues in Neurology and Psychiatry to expand the indications of these novel therapeutics to mental health.

The aim of his lab is to translate experimental findings from mouse models and advanced neuroimaging in humans to trials of deep brain stimulation and focused ultrasound for new indications.

What is your vision?

My vision is that invasive studies can substantially inform strategies of non-invasive brain stimulation that can scale to these broad populations of patients. Moreover, non-invasive studies can also inform invasive strategies by optimizing target selection and testing for disease reversibility.

What big projects are you working on here at Penn?

The Halpern Lab is currently conducting 3 clinical trials of deep brain stimulation given preclinical evidence of efficacy for binge eating disorder, obsessive-compulsive disorder, and even sleep disorders.

What is one of your future research endeavors?

Examining the ability of transcranial magnetic stimulation and other non-invasive therapeutics to predict effects of invasive neuromodulation.

What is it like collaborating with other brainSTIM researchers?

Given Dr. Hamilton's central research focus revolves around using noninvasive brain stimulation to explore the characteristics and limits of functional plasticity in the intact and injured human brain, I cannot imagine a better collaborator to carry out these studies.

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SPOTLIGHT ON KELLY SLOANE, MD: brainSTIM Center Scientist

Kelly Sloane received her BA in Classics at University of Pennsylvania. She received her MD from Johns Hopkins School of Medicine and went on to complete her residency in Neurology at Johns Hopkins Hospital. After residency, she earned fellowships in Vascular Neurology at Massachusetts General Hospital/Brigham and Women's Hospital as well as Neurorecovery at Mass General/Spaulding Rehabilitation Hospital.

Interview with Dr. Sloane:

I have always felt a strong affinity with the elderly and benefited from close relationships with my grandparents. I gravitated to volunteer opportunities that would allow me to work with the elderly. During college, I volunteered at the Penn Memory Center where I became interested in cognitive disorders. This experience — seeing the profound effect that neurological disorders, like dementia, can have not only on one's sense of self but also others' perception of oneself — motivated me to pursue a career in neurology.

During my neurology residency, I had the privilege of caring for stroke patients from the hyperacute stage (when they entered the emergency department) to their inpatient hospitalization and into their recovery. Many of these patients experienced cognitive impairments that affect their sense of self, relationships and quality of life, and just as in neurodegenerative diseases, there are few therapeutic options to improve cognition. Having been inspired from these clinical experiences, I sought to pursue subspecialty fellowship training in vascular neurology and brain injury medicine and to expand my knowledge of cognitive neuroscience.

What are some of the big projects you have going on at Penn?

- TRAINS (TDCS and Rehabilitation to Ameliorate Impairments in Neurocognition after Stroke): In the first few weeks after stroke and the acute brain injury, there is a period of heightened plasticity in which the fastest and most significant recovery occurs. We are using transcranial direct current stimulation, which is a form of non-invasive brain stimulation, to augment cognitive therapy and to optimize recovery during this critical period. This study is an exciting collaboration with the rehabilitation specialists at Pennsylvania Institute for Rehabilitation Medicine (PIRM) and is the first rehabilitation research study being performed on the inpatient rehabilitation unit at PIRM. We have received funding from Penn ITMAT and University Research Foundation. Clinical research in non-stroke patient populations has shown that tDCS directed over a cognitive hub, left dorsolateral prefrontal cortex, in the brain's extensive cognitive networks can improve cognitive performance. This project is a randomized controlled trial of tDCS vs sham intervention to determine if tDCS does improve cognition after stroke. We will also be conducting neuroimaging analyses to determine the role of cognitive network connectivity in responsiveness to neuromodulation.

- TACT (Tracking Assessments of Cognition after Transient Ischemic Attack): Transient Ischemic Attack (TIA) is commonly referred to as a mini-stroke or stroke warning. The definition of a TIA is that it causes transient symptoms and does not result in any injury to the brain. However, small observational studies have suggested that people who experience a TIA have resulting cognitive impairment. In collaboration with the Imperial College of London, we are studying the cognitive performance of patients who have suffered a recent TIA using a web-based platform called Cognitron. The goal of this study is to determine the prevalence of cognitive impairment after TIA and to use clinical and demographic information to predict who will develop cognitive impairment after TIA.

What are your future research endeavors?

My work as a clinician, witnessing the resiliency and perseverance of my patients who have experienced the life-changing effects of stroke or other brain injury, has inspired my research focus and passion. As a clinician-scientist, my goal is to leverage our understanding of neurophysiology and cognitive network connectivity to develop cognitive rehabilitation interventions that optimize natural post-injury neuroplastic processes. In addition to neuromodulatory techniques like tDCS or TMS, I am interested in other innovative, technology-based approaches to rehabilitation like web or mobile application based interventions that improve affordability and accessibility.

Thoughts on collaborating with brainSTIM?

The Penn brainSTIM Center is composed of experts from multiple disciplines who are committed to interdisciplinary conversation, collaboration, and translation to clinical research. All the collaborators at brainSTIM value teamwork and supportiveness, and it is evidenced by the fruitful partnerships that have emerged at the Center.

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Looking to 2022 & Beyond

> " Even though the future is notoriously difficult to predict, we know that brainSTIM has a lot to look forward to in 2022 and beyond. "

Chapter 5

What Does the Future Hold?

Looking back at 2021, it is hard to imagine that one could have predicted many of the events that came to pass, including but not limited to the rise (and hopefully the fall) of the omicron variant to COVID-19. However, even during an undoubtedly challenging year, brainSTIM managed to follow through on many of its goals and milestones for 2021. In 2022, we look forward to continued growth as an organization, greater innovation, and richer collaboration between brainSTIM investigators.

We are excited to continue our ongoing clinical trials for disorders like depression, attention deficit hyperactivity disorder (ADHD), chronic stroke, and dementia. We also anticipate new clinical trials that focus on diagnostic and therapeutic approaches in disorders such as acute stroke, epilepsy, and obsessive compulsive disorder (OCD). In the coming year, many brainSTIM researchers will focus on three specific scientific priorities. First, we will continue to develop individualized circuit- and network-guided neuromodulation interventions for neurologic and psychiatric disorders. Second, investigators will continue to develop real-time neuromodulation approaches that can lead to further personalization of neuromodulation approaches. Of note, our pursuit of research in these two specific areas will be greatly accelerated by generous support offered through the Hart Fund. Finally, brainSTIM will intensify its focus on the development of novel materials and tools that will propel the next generation of brain stimulation technologies.

We are particularly excited by the recent arrival of new brainSTIM core faculty member, Dr. Casey Halpern. As he establishes his lab and neurosurgical practice, we look forward to the development of collaborative interdisciplinary projects that use deep brain stimulation for conditions like OCD and obesity and which span the use of both invasive and noninvasive neuromodulation. Additionally, in July, brainSTIM will welcome its first neuromodulation-focused cognitive neurology fellow, Dr. Catherine Norise, who brings with her extensive prior experience on the use of tDCS in persons with post-stroke and neurodegenerative aphasias.

In addition to our excellent research and outstanding new investigators, we look forward to the culmination of our year-long MINS/brainSTIM Year of Neuromodulation in April, when we will host our much anticipated Spring Symposium. We also continue to work on the development of a excellent training course in transcranial magnetic stimulation (TMS), featuring lectures and workshops led by our multidisciplinary team of outstanding brainSTIM faculty.

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

Giving Opportunities

6

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

Chapter 6

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.
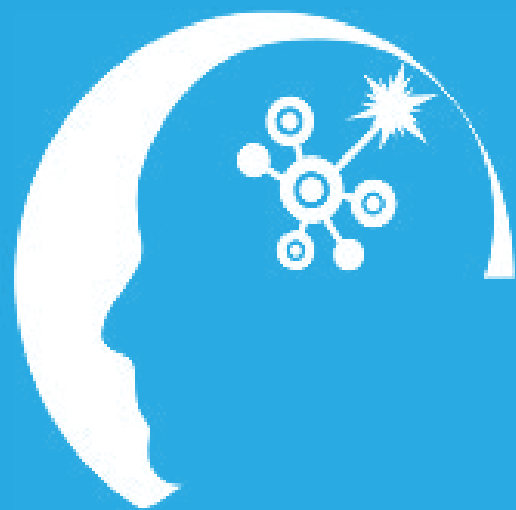
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