BRAIN MODULATION LAB
MASS GENERAL NEUROSURGERY

Updates for research participants, colleagues, collaborators, and other friends…

2020 GRANT MILESTONES

BRAIN Initiative U01 Awarded

The 5-yr project ***Cortical-Basal Ganglia Speech Networks*** continues collaborative multidisciplinary studies initiated in 2016 (PI: Richardson) to study circuit-level electrophysiological correlates of speech production, by recording iEEG in patients undergoing DBS implantation, with new collaboration from the Gunther Lab at Boston University.

Collaborative Epilepsy R01

The 5-yr project ***Targeting Pathologic Spike-ripples to Isolate and Disrupt Epileptic Dynamics,*** conceived and submitted by Catherine Chu from MGH Epilepsy Neurology, (multi-PIs: Eden, Kramer, and Richardson) will ultimately inform brain stimulation protocols to disrupt mechanisms of spike-ripple generation in patients with epilepsy.

Pilot Study of Odor Perception

The 3-yr project ***Mapping the Human Intracranial Olfactory Perception Network*** will enable translational efforts to create an olfactory prosthesis for people who have lost their sense of smell following a neurological insult. This pilot work was initiated with Richard Costanzo and Dan Coelho from Virginia Commonwealth University, Eric Holbrook from Mass Eye & Ear, and funding partner Lawnboy Ventures.

BRAIN Initiative U01 Submitted

Computational Neuroscience of Language Processing in the Human Brain is a 5-yr project, conceived and submitted by Ev Fedorenko from MIT Brain and Cognitive Sciences (co-PI: Richardson), that will combine iEEG recordings with advances in artificial neural network models to shed light on how we construct complex meanings from word sequences.

Intracranial Atlas R01 Submitted

Vasily Kokkinos submitted his first R01 application ***An Atlas of Intracranial EEG for Distinguishing Normal from Epileptic Activity***, an international effort with commitments from ten leading centers worldwide (co-PI: Frauscher (MNI); co-Is: Gotman, Cash, Westover, Richardson).

COLLABORATION has been creed in the Brain Modulation Lab since our inception nearly ten years ago, but the past year uniquely highlighted the value of our collaborative efforts. Despite having to complete our MGH reboot during the pandemic, a combination of long-standing and new collaborations kept us busy and pushed the lab to become better at our work.

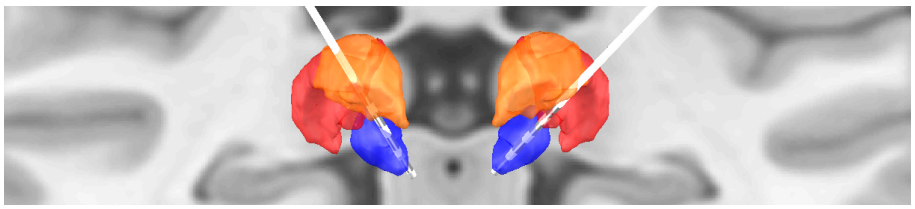
A recent milestone was the re-initiation of intra-operative intracranial human neuroscience research in patients undergoing DBS implantation surgery. After navigating the challenges of IRB creation and approval, new equipment acquisition, troubleshooting, and novel task design, Alan Bush and Sonika Agarwal successfully recorded from the lab's inaugural MGH DBS participant in December. These studies are the first intracranial exploration of the role of the basal ganglia in speech motor learning and volume control, and mark the culmination of planning by our new **Cortical Basal Ganglia Speech Networks U01** group, with collaborators from the University of Pittsburgh, Carnegie Mellon, Johns Hopkins and Boston University. At the same time, our team continues to analyze and publish findings from our first three years of speech production studies.

Simultaneous cortical-basal ganglia recording during speech production research in DBS surgery.

Another major DBS-related project, **CRCNS: Deep Neural Network Approaches for Closed-loop DBS**, is based on collaboration with the Movement Disorders group at Charité Hospital in Berlin. Thanks to the efforts of Julian Neuman, who leads the German side of the collaboration, and his student Timon Merk, along with our new machine learning expert Victoria Peterson, much progress was made and data were presented at the International Conference on DBS. We especially appreciated the remote efforts of Dr. Peterson, who finally arrived from Argentina in January, after many months of pandemic-induced delays.

In movement disorders clinical trial news, research manager Irene Lerman has coordinated efforts with our lab neighbor Todd Herrington, MGH Neurology Director of Deep Brain Stimulation, to launch two DBS clinical trials and prepare for upcoming gene therapy studies.

On the epilepsy side of the lab, Vasily Kokkinos didn't miss a beat in transitioning from Pittsburgh to Boston, co-editing a Neurosurgery Clinics issue on ***Epilepsy Surgery: the Network Approach*** with Dr. Richardson, submitting an R01, uniquely supporting presurgical evaluations, and driving several publications. Dr. Kokkinos's seminal work on ictal response biomarkers of Responsive Neurostimulation is a foundation of the lab's long-term goals for our RNS project **BRAINStim (Biophysically Rational Analysis for Individualized Neurostimulation).** We were very fortunate that a primary architect of the BRAINStim platform, Nathan Sisterson, continued his work in the lab over the past year, as an MGH neurosurgery resident! We also recruited Sid Simon, a Computer Engineering-Computer Science double major, to aid in software development for this project.



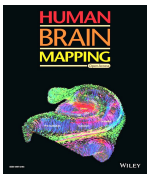
Reconstruction of thalamic RNS electrodes in a patient with idiopathic generalized epilepsy. .

2020 PUBLICATIONS

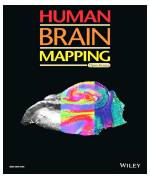
Movement-Related Coupling of Human Subthalamic Nucleus Spikes to Cortical Gamma. Fischer P, Lipski WJ, Neumann WJ, Turner RS, Fries P, Brown P, Richardson RM. *eLife*

Subthalamic Nucleus Activity Influences Sensory and Motor Cortex during Force Transduction. Alhourani A, Korzeniewska, Wozny TA, Lipski WJ, Kondylis ED, Ghuman AS, Crone NE, Crammond DJ, Turner RS, Richardson RM. *Cerebral Cortex*

Ictal Onset Signatures Predict Favorable Outcomes of Laser Thermal Ablation for Mesial Temporal Lobe Epilepsy. Zaher N, Urban A, Antony A, Plummer C, Bagic A, Richardson RM, Kokkinos V. *Frontiers in Neurology*



Ex Vivo Mesoscopic Diffusion MRI Correlates with Seizure Frequency in Patients with Uncontrolled Mesial Temporal Lobe Epilepsy. Ke J, Foley LM, Hitchens TK, Richardson RM, Modo M. *Human Brain Mapping*



Mesoscale Diffusion Magnetic Resonance Imagine of the Ex Vivo Human Hippocampus. Ly M, Foley L, Manivannan A, Hitchens TK, Richardson RM, Modo M. *Human Brain Mapping*

Interpretation of the Intracranial sEEG Signal. Kokkinos V. *Neurosurgery Clinics*

Neuromodulation of Epilepsy Networks. Sisterson ND, Kokkinos V. ***Neurosurgery Clinics***

Decision Making in Epilepsy Surgery. Richardson RM. ***Neurosurgery Clinics***

The Hippocampal Barque: An Epileptiform but Non-epileptic Hippocampal Entity. Kokkinos V, Richardson RM, Urban A. ***Frontiers in Human Neuroscience***

Responsive Neurostimulation of the Thalamus Improves Seizure Control in Idiopathic Generalized Epilepsy. Kokkinos V, Urban A, Sisterson N, Li N, Corson D, Richardson RM. ***Neurosurgery***

A Rational Approach to Understanding and Evaluating Responsive Neurostimulation. Sisterson ND, Wozny TA, Kokkinos V, Bagic A, Urban AP, Richardson RM. ***Neuroinformatics***

Anterior Sensorimotor Subthalamuc Nucleus Stimulation is Associated With Improved Voice Function. Jorge A, Dastolfo-Hromack C, Lipski WJ, Kratter IH, Smith LJ, Gartner-Schmidt JL, Richardson RM. ***Neurosurgery***

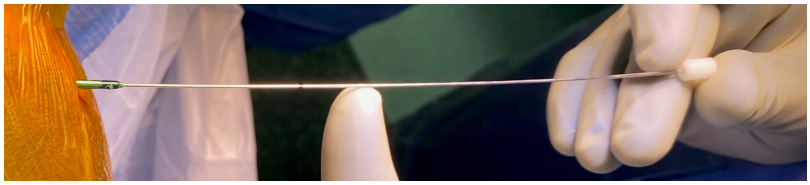
Robotic-Assisted Stereotaxy for Deep Brain Stimulation Lead Implantation in Awake Patients. Faraji AH, Kokkinos V, Sweat JC, Crammond DJ, Richardson RM. ***Operative Neurosurgery***

Endogenous Activity Modulates Stimulus and Circuit-Specific Neural Tuning and Predicts Perceptual Behavior. Li Y, Ward MJ, Richardson RM, G'Sell M, Ghuman AS. ***Nature Communications***

Working with Drs. Kokkinos and Sisterson, data scientist Varun Saravanan has continued to evolve the lab's significant focus on *rigor in data science*, building out our existing data infrastructure for these epilepsy projects, as well as working with Dr. Bush to build a robust system for cognitive neuroscience project data. In addition to fulfilling data sharing obligations for our BRAIN Initiative funded projects, Dr. Saravanan is creating the data sharing pipeline for **InBRAIN (Intracranial Brain Recording and Informed Neuromodulation)**, a new framework for collaboration between MGH Neurosurgery and MIT Brain and Cognitive Sciences.

In that regard, the lab has been working on initiating a number of projects with colleagues at MIT. In collaboration with Angelique Paulk and the Cash Lab (MGH Neurology), we have piloted new vision and language studies in patients undergoing intracranial monitoring for epilepsy, with Nancy Kanwisher and Ev Fedorenko, who are leading the MIT components of the InBRAIN collaboration. Preliminary work is underway also with other MIT faculty, including efforts to establish electrical stimulation-fMRI research in SEEG patients (Bob Desimone) and to model seizure networks in RNS patients (Emery Brown). Two MIT students also established projects in the lab: Isaac Treves developed an independent project to investigate heart rate-related electrophysiology in the insula, and Jasmine Zou is working with Dr. Bush on novel findings related to aperiodic components of basal ganglia and thalamic local field potentials in patients with movement disorders.

An important facet of our intracranial human neuroscience research at MGH is the development of a comprehensive **Patient Engagement** strategy, guided by principles of *pragmatic neuroethics,* in consultation with Eric Racine (Montreal). This effort is spearheaded by Drs. Bush and Saravanan, as well as by Ashley Walton. Dr. Walton, a postdoctoral fellow with Adina Roskies in the Cognitive Science Program at Dartmouth, also submitted the K99 proposal ***Neuroethical Approaches to the Development of Closed-loop Stimulation in Epilepsy*** (co-mentors: Jacobson, Richardson).



Insertion of stereo-electroencephalography (SEEG) electrode for seizure network mapping.

The Brain Modulation Lab was lucky again this past year to have had several other talented folks join projects, including Rhodes Scholar Tariq Parker and Harvard HSBT grad student Yanming Zhu, both of whom are working on aspects of our Cortical-Basal Ganglia Speech Networks project. Matteo Vissani, from the Computational Neuroengineering Lab of the Biorobotics Institute of Sant'Anna School of Advanced Studies, will join us in April as a postdoc on that project as well. Neurosurgery resident Athar Malik is analyzing single unit data from the thalamus recorded during speech, and neurosurgery resident Myron Rolle and medical students in the Harvard Global Health Program Deen Garba and Andre Boyk, have initiated an important project ***Disparities in Utilization of Treatments for Functional Neurological Disorders***.

Our entire team is indebted to PA Nora Daly, administrative coordinator Tatyana Pearson, our clinical partners, *and most importantly to our patient participants*, whose combined efforts make the lab's intracranial human neuroscience work possible.

A uniquely exciting addition to the lab family this year was Sebastian Bush, seen here having constructed his first snowman under the tutelage of his parents, Alan and Andrea. In the new year, we look forward to re-engaging with our friends - old and new!