BIOGRAPHICAL SKETCH

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NAME: Keller, Corey, M.D., Ph.D.

eRA COMMONS USER NAME (credential, e.g., agency login): COREYKELLER

POSITION TITLE: Assistant Professor, Stanford University

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Tufts University	B.S.	2003-2007	Electrical Engineering
Tufts University	M.S.	2007-2009	Biomedical Engineering
Albert Einstein College of Medicine	Ph.D.	2009-2015	Neuroscience
Albert Einstein College of Medicine	M.D.	2009-2015	Medicine
Stanford University	Residency	2015-2019	Psychiatry
Stanford University	Postdoctoral	2018-2019	Neuroscience

A. Personal Statement

My work maps the interaction between brain networks, stimulation-induced brain changes, and neuropsychiatric symptoms. I combine my backgrounds in electrophysiology, bioengineering, and neuroscience to perform translational research while practicing as an interventional psychiatrist, with a focus on mood disorders and treatment-resistant depression. During my PhD, I developed novel intracranial brain mapping tools and applied these to demonstrate the neural basis of resting functional MRI in humans. During residency and my postdoctoral fellowship, I co-developed fully automated non-invasive brain mapping techniques, now used across industry and academia. My laboratory combines techniques from computer science, neuroscience, and engineering coupled with a clinical understanding of psychiatry to focus on three central aims: 1) to better understand the mechanisms underlying human brain plasticity; 2) to develop novel methods to probe the human brain; and 3) to personalize brain stimulation by developing trans-diagnostic platforms for rapid biomarker development, evaluation, and integration into brain stimulation treatments. This approach has the expected outcome of producing novel stimulation treatments with enhanced specificity, plasticity, and efficacy. By increasing our mechanistic understanding and ability to monitor brain changes during stimulation, we will markedly increase the utility of these powerful techniques. Together, this work will help transform interventional psychiatry from a one-size-fits-all treatment approach to one that focuses on targeting objective biomarkers for the individual, pushing the field towards personalized neurotherapeutics.

I have the expertise, leadership, training (both in medical and scientific fields) and motivation necessary to successfully carry out the proposed research project. I have published 30 journal articles (13 first-author), mentored 20 students, been awarded the F31, K23, DP5, SBIR, R01, generated two patents, and overseen three clinical trials across 10 clinical centers, generating over 1500 collected subjects. I have 14 years of experience working with intracranial EEG data from epilepsy patients and six years of experience utilizing and researching TMS as a treatment for mood disorders.

The current application builds logically on my prior work. The approach is supported by rigorous and carefully designed experiments, with clear goals and expectations. Through my multi-modal approach to depression brain stimulation research, I have laid the groundwork for my role in the proposed research project by developing a strong background in clinical research methodology, invasive and non-invasive electrophysiology, and brain stimulation.

Highlighted ongoing and recently completed projects:

NIH (NIMH) R01MH126639-02   Keller (PI)   2020-2025
Closing the loop: development of real-time, personalized brain stimulation
The major goal of this grant is to develop a non-invasive personalized brain stimulation platform for neuropsychiatric disorders

Role: PI

NIH (NIMH) R01MH129018-01   Keller (PI)   2021-2026
CRCNS US-France Research Proposal: Probing the Dorsolateral Prefrontal Cortex and Central Executive Network for Improving Neuromodulation in Depression
The major goal of this grant is to optimize TMS procedures for depression by analyzing brain responses from TMS/EEG experiments and direct cortical stimulations in intracranial EEG.
Role: MPI

BWF Career Award for Medical Scientists   Keller (PI)   2021-2026
The major goal of this grant is to create a real-time monitoring system for brain changes and develop and test an adaptive stimulation paradigm to maximally drive individual brain changes and improve clinical outcome.
Role: PI

B. Positions, Scientific Appointments, and Honors

Positions and Employment:

2019-	Assistant Professor, Psychiatry and Behavioral Sciences, Stanford University
2019-2020	Chief Medical Officer, Alto Neuroscience, Inc
2019	Instructor, Clinical & Translational Neuroscience, Stanford University
2018-2019	NIMH T32 Postdoctoral Fellowship, Stanford University School of Medicine
2015-2019	Psychiatry Resident, Research Track, Stanford University
2009-2015	Research Scientist, Multimodal Human Brain Mapping, NS LIJ Hospital, Manhasset, NY
2007-2009	Research Scientist, Martinos Center for Biomedical Engineering, Harvard, Boston, MA
2007-2009	Research Scientist, Department of Neurology, Massachusetts General Hospital, Boston, MA

Honors:

2019	NIH DP5 Early Independence Award
2019	NIH K23 Mentored Patient-Oriented Research Career Development Award
2019	BWF Career Award for Medical Scientists (CAMS)
2018	NIMH Outstanding Resident Award
2018	Career Development Institute for Psychiatry
2018	NIMH T32 Postdoctoral Fellowship
2018	Alpha Omega Alpha Medical Honor Society
2017	Society of Biological Psychiatry Early Career Investigator Travel Award
2017	Winter Conference on Brain Research Travel Fellowship
2017	ASCP New Investigator Award
2016	Alpha Omega Alpha Postgraduate Research Award
2016	BrainBox Neuroscience Initiative Young Investigator Award
2015	Stanford Society of Physician Scholars Collaborative Research Fellowship
2015	American Society of Clinical Psychopharmacology Fellowship for Clinical Trials
2014	NINDS Combining Clinical and Research Careers in Neuroscience Travel Award
2014	Society of Biological Psychiatry Medical School Scholar
2013	Neural Systems and Behavior Course Endowed Scholarship
2011-2015	Ruth L. Kirschstein National Research Service Award Medical Scientist Training Program Pre-Doctoral Fellowship
2010-2011	Epilepsy Foundation Pre-Doctoral Research Training Fellowship
2009	Albert Einstein College of Medicine Senior Research Fellowship
2009	Eta Kappa Nu – Electrical Engineering Honors Society
2007	Magna Cum Laude and Senior Thesis Highest Honors
2007	Master's Thesis Highest Honors
2004-2007	Dean's List Honors, Tufts University

Other Experience and Professional Memberships

2020-	Clinical TMS Society, Research Committee Member
2019	International Neuromodulation Society, Research and Scientific Oversight
2019-	Member, StartX Entrepreneurial Incubator
2018	AOA, Research and Grants Chair
2018	Member, Alpha Omega Alpha Medical Honors Society
2015-	Member, American Medical Association
2015-	Member, International Neuromodulation Society
2015-	Member, Human Brain Mapping
2013-	Member, Society of Biological Psychiatry
2009-	Member, American Epilepsy Society
2009-	Member, Society for Neuroscience
2009-	Alumnus, Woods Hole MBL Neural Systems and Behavior Course

C. Contribution to Science

1. **Intracranial microelectrode development.** My early work with Sydney Cash focused on the mechanisms underlying inter-ictal spikes, which define epileptic cortex. We recorded simultaneous local field potentials and single neuron action potentials during inter-ictal discharges (IID) using high density microelectrode arrays implanted in patients with medically-resistant epilepsy to characterize the firing pattern that underlies IIDs. We determined that only ½ of neurons in epileptic areas modulate their firing rate during IIDs. Furthermore, as expected ¼ of neurons increased their firing rate during the IID. In direct contrast to predictive models of the IID, however, we identified a subset of population of neurons that modulate their firing rate *prior* to the IID. This subset of neurons were only observed in epileptic regions, suggesting they may play a role in the generation of the IID. During this time, we also developed a microelectrode that records simultaneous electrophysiology and hemodynamics and an algorithm for accurately localizing intracranial electrodes implanted in patients during epilepsy surgery.

   a. **Keller CJ**, Cash SS, Narayanan S, Wang C, Kuzniecky R, Carlson C, Devinsky O, Thesen T, Doyle W, Sassaroli A, Boas AD, Ulbert I, Halgren E. *Intracranial microprobe for evaluating neuro-hemodynamic coupling in unanesthetized human neocortex.* **Journal of Neuroscience** Methods 179 (2009) 208–218. PMC2680793.

   b. Dykstra A, Chan AM, Quinn BT, Zepeda R, **Keller CJ**, Cormier JE, Madsen JR, Eskandar EN, Cash SS. *Individualized localization and cortical surface-based registration of intracranial electrodes.* **NeuroImage** 59 (2012): 3563-70. PMC3288767.

   c. **Keller CJ**, Truccolo W, Gale JT, Eskandar E, Thesen T, Carlson C, Devinsky O, Kuzniecky R, Doyle WK, Madsen JR, Schomer DL, Mehta AD, Brown EN, Hochbert LR, Ulbert I, Halgren E, Cash SS. *Distinct Neuronal Firing Types During Interictal Epileptiform Discharges in the Human Cortex.* **Brain** 133 (2010) 1668-81. PMC2877906.

2. **Intracranial stimulation methods development.** functional MRI is now a mainstream neuroscientific tool, but the neurophysiology of positive and negatively correlated BOLD fluctuations – which consistently identify large scale networks implicated in cognitive, sensory, and motor functions, and which differentiate patients from healthy subjects in many neuropsychiatric diseases – is largely unknown and confounded by multiple artifacts that exist in these recordings. With a team of interdisciplinary collaborators, I documented the relationship between fMRI and underlying physiology directly demonstrated that the spatial distribution and magnitude of temporally correlated low-frequency BOLD fluctuations ('resting fMRI') predict the pattern and magnitude of evoked potentials measured intracranially following focal electrical stimulation. These findings were replicated across patients and functional subsystems and strengthened the notion that resting fMRI signals are grounded in neurophysiology. We furthermore demonstrated that positively and negatively correlated fluctuations of high gamma activity underlie positive and negative BOLD correlations, respectively, suggesting that both resting BOLD interactions have neurophysiological origins in slow power modulations of fast frequency activity. This work has driven >30 groups across the world to begin collecting cortico-cortical evoked potentials (CCEPs), where a causal electrical disturbance in the brain elicits brief changes in neuronal excitability that can be measured in the local field potential.

a. **Keller CJ**, Bickel S, Entz L, Ulbert I, Kelly C, Milham M, Mehta AD. *Intrinsic functional architecture predicts electrically-evoked responses in the human brain*. **Proceedings of the National Academy of Sciences** 108 (2011): 10308-13. PMC3121855.
b. **Keller CJ**, Bickel S, Honey CJ, Groppe DM, Craddock CR, Kelley C, Lado FA, Milham M, Mehta AD. *Neurophysiological investigation of spontaneous correlated and anticorrelated fluctuations of the BOLD signal.* **Journal of Neuroscience**. 33 (2013): 6333-42. PMC3652257.
c. **Keller CJ**, Honey CJ, Entz L, Bickel S, Groppe DM, Toth E, Lado FA, Ulbert I, Mehta AD. *Probing the human connectome: cortico-cortical evoked potentials reveal projectors and integrators within human brain networks.* **Journal of Neuroscience**. 34 (2014): 9152-63.
d. **Keller CJ**, Honey CJ, Megevand P, Entz L, Ulbert I, Mehta AD. *Mapping complex brain networks with cortico-cortical evoked potentials.* **Philosophical Transactions of the Royal Society B: Biological Sciences**. 1 (2014): 369 (1653).

3. **<u>Non-invasive TMS-EEG biomarker development.</u>** TMS paired with EEG recordings represents a powerful causal tool to probe human brain networks, but separating signal from noise is tedious and often manualized. Furthermore, biomarkers that predict treatment outcome are lacking in the field. To address these needs, I co-developed a fully automated analytic pipeline for analysis of concurrent transcranial magnetic stimulation (TMS) coupled with EEG, currently used across academia and industry. I also performed a randomized, double-blind, placebo-controlled clinical trial to investigate the electrophysiological underpinnings of clinical effects of daily repetitive TMS (rTMS) treatment for depression. I utilized the toolbox developed to show that rTMS treatment modulates TMS-evoked potentials and the strength of modulation predicts clinical outcome. This work suggests that specific TMS-EEG brain-based biomarkers may be used to predict non-responders, monitor brain networks during intervention, and be used to propose novel targets and treatment paradigms.

a. **Keller CJ***, Wu W*, Rogasch NC, Longwell P, Spigel E, Rolle CE, Etkin A. *ARTIST: A Fully Automated Artifact Rejection Algorithm for Single-Pulse TMS-EEG Data.* **Human Brain Mapping**. 00 (2018): 1-19. *These authors contributed equally. PMC6866546.
b. **Keller CJ***, Kerwin L***,** Wu W, Etkin A. *Test-Retest Reliability of Transcranial Magnetic Stimulation EEG Evoked Potentials.* **Brain Stimulation:** 3 (2018): 536-44. *These authors contributed equally.
c. **Keller CJ,** Huang D, Honey CJ, Du V, Fini M, Lado FA, Mehta AD. *Induction and quantification of excitability changes in human cortical networks.* *Journal of Neuroscience:* 23 (2018): 5384-98. PMC5990984.
d. Huang D, Herrero J, Entz L, Fabo D, Hajnal B, Mehta A, **Keller CJ**. *Intracortical dynamics underlying repetitive stimulation predicts changes in network connectivity. **Journal of Neuroscience:** 31 (2019): 6122-6135. PMC6668210.

Complete list of publications in MyBibliography:
http://www.ncbi.nlm.nih.gov/pubmed/?term=Corey+Keller