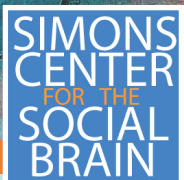


THE SIMONS CENTER FOR THE SOCIAL BRAIN (SCSB) NEWSLETTER | Fall 2019

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PUBLICATION SPOTLIGHT

Bo Qing, Elizabeth P. Canovic, Aleksandar S. Mijailovic, Anna Jagielska, Matthew J. Whitfield, Alexis L. Lowe, Elyza H. Kelly, Daria Turner, **Mustafa Sahin, Krystyn J. Van Vliet**. [Probing Mechanical Properties of Brain in a Tuberosous Sclerosis Model of Autism](#). *Journal of Biomechanical Engineering* 141: 1–10, 2019 [https://doi.org/10.1115/1.4040945]

Xin Tang, Jesse Drotar, Keji Li, Cullen D. Clairmont, Anna Sophie Brumm, Austin J. Sullins, Hao Wu, Xiaoxiao Shawn Liu, Jinhua Wang, Nathanael S. Gray, **Mriganka Sur, Rudolf Jaenisch**. [Pharmacological enhancement of *KCC2* gene expression exerts therapeutic effects on human Rett syndrome neurons and *Mecp2* mutant mice](#). *Science Translational Medicine* 11: 1–13, 2019 [https://doi.org/10.1126/scitranslmed.aau0164]

Boaz Barak, Zicong Zhang, Yuanyuan Liu, Ariel Nir, Sari S. Trangle, Michaela Ennis, Kirsten M. Levandowski, Dongqing Wang, Kathleen Quast, Gabriella L. Boulting, Yi Li, Dashzeveg Bayarsaihan, Zhigang He, **Guoping Feng**. [Neuronal deletion of *Gtf2i*, associated with Williams syndrome, causes behavioral and myelin alterations rescuable by a remyelinating drug](#). *Nature Neuroscience* 22: 700–708, 2019 [https://doi.org/10.1038/s41593-019-0380-9]

Hayley Smith, Alice S. Carter, Erik Blaser, **Zsuzsa Kaldy**. [Successful attentional set-shifting in 2-year-olds with and without Autism Spectrum Disorder](#). *PloS One* 14: 1–17, 2019 [https://doi.org/10.1371/journal.pone.0213903]

Olessia Jouravlev, David Zheng, Zuzanna Balewski, Alvince Le Arnz Pongos, Zena Levan, Susan Goldin-Meadow, **Evelina Fedorenko**. [Speech-accompanying gestures are not processed by the language-processing mechanisms](#). *Neuropsychologia* 132: 1–16, 2019 [https://doi.org/10.1016/j.neuropsychologia.2019.107132]

POSTDOCTORAL APPLICATIONS: FALL 2019

We are pleased to announce the 2019 Round 2 funding opportunities for Postdoctoral Fellowships.

Postdoctoral Fellowships are intended for outstanding candidates with very recent PhDs who wish to conduct autism-related research at MIT under the mentorship of MIT faculty researchers. Applicants currently completing their PhD outside MIT, who wish to carry out postdoctoral research at MIT, are strongly encouraged to apply.

Deadline: Friday, September 27, 2019.

For information on how to apply and eligibility, please visit our website at: <http://scsb.mit.edu/funding/postdoctoral-fellowship-funding/>

NEW TARGETED PROJECT:

PREDICTIVE PROCESSES IN AUTISTIC AND NEURO-TYPICAL INDIVIDUALS: A BEHAVIORAL, NEURAL AND DEVELOPMENTAL INVESTIGATION

The Predictive Processes targeted project aims to investigate how multiple aspects of prediction may differ in autism using behavioral and neuroimaging techniques, through collaborative efforts among the Sinha, Gabrieli, and Snedeker labs.

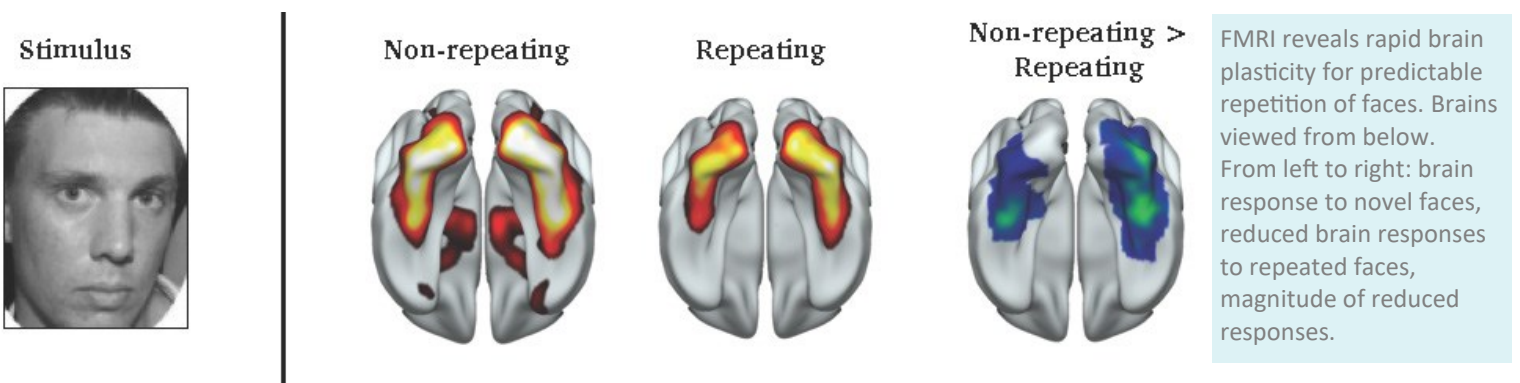
People use prior experiences to predict how present challenges should be best managed. Environmental uncertainty can present challenges for individuals with autism. This may have consequences for navigating daily activities that may be noisy or unpredictable and rely on rapid updating of changing contingencies. Social interaction and communication, in particular, require adapting to rapidly changing perceptual, social, and linguistic demands. Recent theoretical and empirical work suggest that individuals with autism may show differences in predictive skills, but empirical findings are mixed across a variety of paradigms and samples of people with autism. These prior studies each examined one paradigm assuming that the paradigm reflects a unitary process of prediction. The Predictive Processes targeted project will implement a set of interlocking studies at MIT and Harvard, adopting a more integrative approach.

Pawan Sinha, Professor of Vision and Computational Neuroscience, whose group proposed the “Magical World” theory of autism as a disorder of prediction, will undertake research to elucidate processing of probabilistic and metronomic auditory sequences and contingencies, using electrophysiological measures.

John Gabrieli, Professor of Cognitive Neuroscience, will investigate how neural adaptation results in rapid brain plasticity in response to simple higher-level percepts in adults using fMRI.

Jesse Snedeker, Professor of Psychology at Harvard University, will examine the predictions that we make about words as we listen to natural stories. These studies will use electrophysiological measures to track complex linguistic predictions in adults and children. Her group will also use a subset of the Sinha and Gabrieli lab paradigms in children.

This approach will provide a comprehensive, integrated, and rigorous study of predictive skills in autism, made possible by the new partnerships across these laboratories which have each studied separate aspects of predictive skills in autism but never in such a synergistic fashion. The study has implications for characterizing autism through a new lens, and a better understanding of predictive mechanisms could potentially contribute to improved support for individuals with autism spectrum disorders.



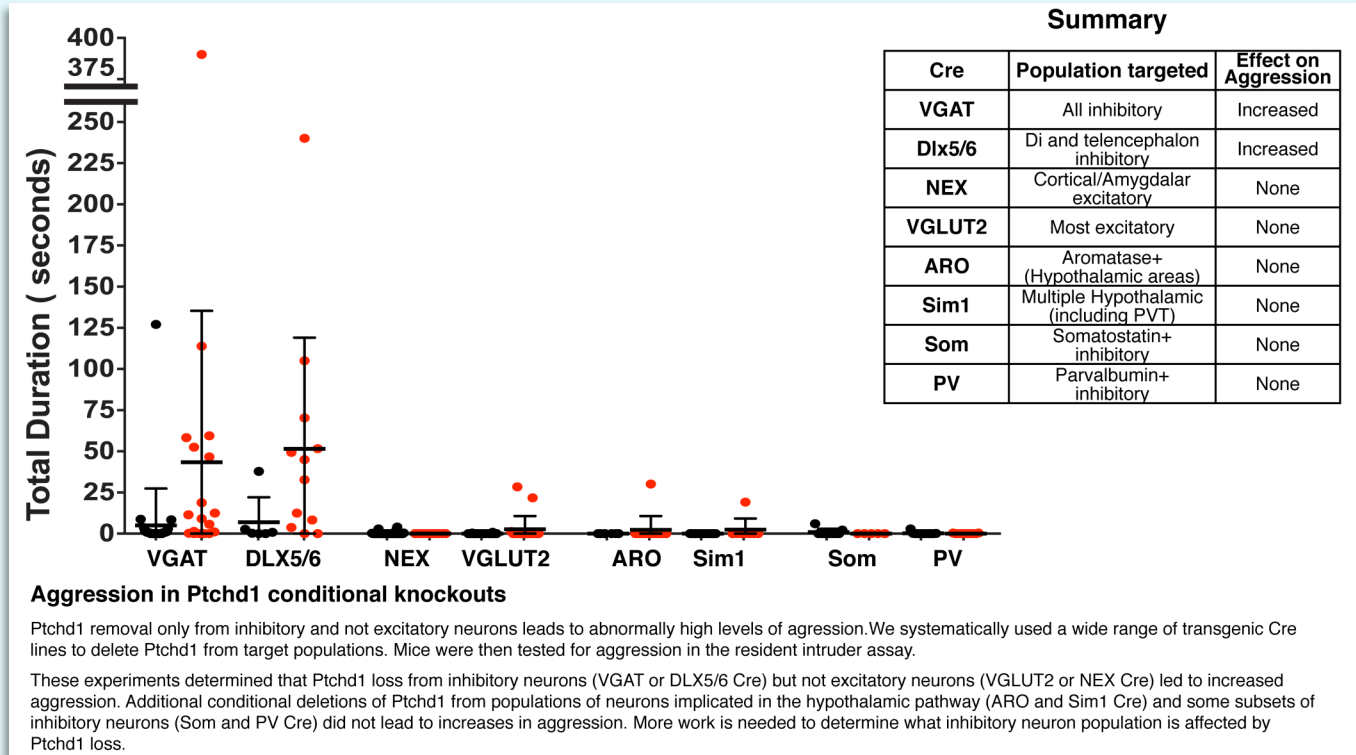
SIMONS POSTDOCTORAL FELLOWS:



Sasha Krol, Ph.D. | Feng lab, McGovern Institute, MIT

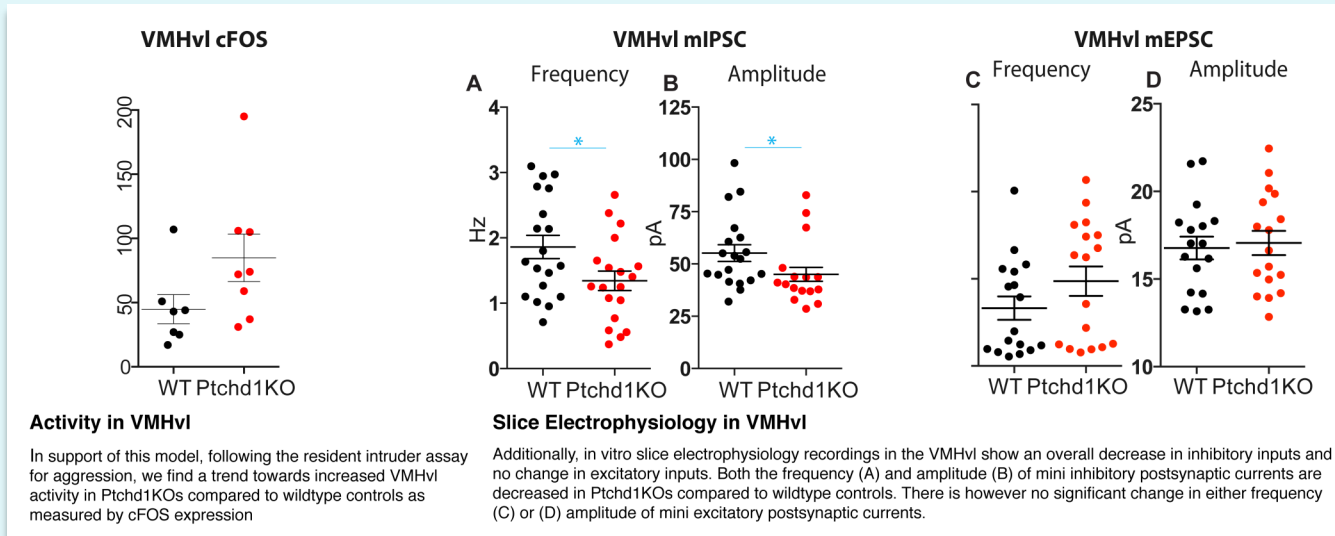
UNCOVERING THE DEVELOPMENTAL AND CIRCUIT ORIGIN OF ASD-ASSOCIATED AGGRESSION

In addition to core symptoms including social communication deficits, individuals with autism spectrum disorder (ASD) experience a wide range of other symptoms including aggression, an extremely challenging social disruption. Irritability or aggressive conduct affects 25-50% of children with ASD. Unfortunately aggression in the context of ASD is poorly understood due to a lack of good models. Deletions in *PTCHD1* contribute to ~1% of ASD cases with intellectual disability and can lead to hyper-aggression. Mouse *Ptchd1* Knockout (KO) animals have many behavioral deficits including hyper-aggression, making them a good model to study ASD-linked aggression. In wildtype animals, an extended limbic-hypothalamic network centering on the ventrolateral part of the ventromedial hypothalamus (VMHvl) has been shown to be critical in mediating aggressive behaviors. However, the origin of aggression in ASD in general or in *Ptchd1* KO mice specifically is unknown.



We are testing whether dysfunction of hypothalamic circuitry, and in particular the VMHvl is responsible for *Ptchd1*-mediated, ASD-related aggression. Further, we are dissecting the temporal requirement of *Ptchd1* in the development of aggressive behavior. Together our results will identify a target circuit and temporal window for designing and testing therapies for aggression in ASD and other disorders.

Using FISH for Ptchd1 in the mouse brain shows variable levels of Ptchd1 expression throughout the nervous system in both excitatory and inhibitory neurons. However when we remove Ptchd1 from different populations of neurons, using Cre lines, we find that removing Ptchd1 from inhibitory but not excitatory neurons leads to abnormal aggression. Given VMHvl itself is excitatory, our results suggests a model where increased aggression in Ptchd1KO mice is specifically due to Ptchd1 loss in inhibitory neurons, resulting in decreased inhibition of VMHvl, and, consequently, increased VMHvl activity.



PAST SIMONS POSTDOCTORAL FELLOWS: WHERE ARE THEY NOW?



Elizabeth Norton, Ph.D. | Assistant Professor, Northwestern University

EXAMINING THE DEVELOPING SOCIAL BRAIN IN NATURAL CONTEXT

My work as a Simons Fellow has propelled my career as a developmental cognitive neuroscientist, now as an Assistant Professor in the Department of Communication Sciences and Disorders at Northwestern University.

My research examines behavior and brain predictors and correlates of communication disorders including autism, dyslexia, and developmental language disorder.

One of the most formative things about the Simons Fellowship was seeing how other fellows and labs at MIT took completely new and creative approaches to questions about autism. In this spirit, I was curious about whether we could take a new, naturalistic and social approach to assessing the brain in autism, especially in children.

Continued on next page...



A mother and toddler participate in a social EEG study in Dr. Norton's lab

Data from a few studies suggested that adults with autism or subtle autism-related traits showed less neural similarity or synchrony with a communication partner. This method of observing natural behavior is more consistent with the face-to-face communication situations in which individuals are assessed for an autism diagnosis and the types of situations in which treatment occurs.

We developed techniques to overcome the movement artifacts of EEG and variety of engagement states during communication in order to examine this in toddlers. I applied for and received an exploratory/developmental R21 grant from NIH (National Institute of Deafness and Other Communication Disorders) to examine parent-toddler dyads, in which the child has autism or not, with EEG while the parent and child interact like they typically would. We call this approach "social EEG." We are analyzing the child's brain states and their neural synchrony with their parent. Partnering with researchers and our department clinic, we have recruited dozens of children and are in the process of analyzing these data. If early differences in neural synchrony are associated with autism, this tool could be used to assess children before traditional measures are feasible.



Boaz Barak, Ph.D. | Assistant Professor at Tel Aviv University, Israel

NEURON-GLIA INTERACTIONS: ROLES IN MYELINATION AND SOCIAL BEHAVIOR

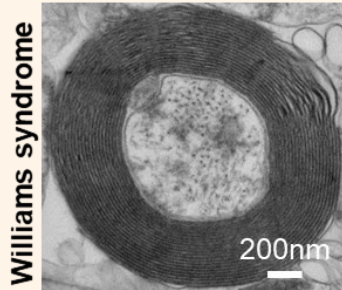
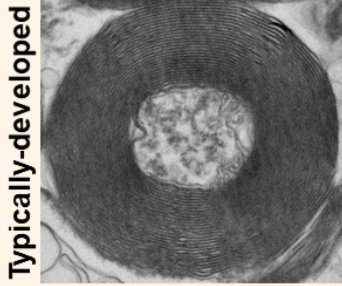
Social behavior abnormality is a complex and devastating characteristic of multiple neuropsychiatric disorders, whose prevalence may have sharply increased recently. Whereas many of the genetic causes for the disorders are known, a long-standing and fundamental question in the field of social behavior is which neural circuits and cell types are affected and are therefore contributing to the abnormal social behavior. One of these neuropsychiatric disorders,

Williams syndrome (WS), is a neurodevelopmental disorder caused by a heterozygous microdeletion of about 26 genes and characterized by hypersociability and unique neurocognitive abnormalities. Of these genes, general transcription factor II-i (Gtf2i), has been linked to hypersociability in WS, although the molecular and cellular mechanisms mediated by Gtf2i deletion are poorly understood.

We recently published an article in Nature Neuroscience, showing that selective deletion of Gtf2i in the excitatory neurons of the forebrain caused neuroanatomical defects, fine motor deficits, increased sociability and anxiety. Unexpectedly, 70% of the genes with significantly decreased messenger RNA levels in the mutant mouse cortex are involved in myelination, and mutant mice had reduced mature oligodendrocyte cell numbers, reduced myelin thickness and impaired axonal conductivity.

Restoring myelination properties with clemastine or increasing axonal conductivity rescued the behavioral deficits. The frontal cortex from patients with WS similarly showed reduced myelin thickness, mature oligodendrocyte cell numbers and mRNA levels of myelination-related genes. Our study provides molecular and cellular evidence for myelination deficits in WS linked to neuronal deletion of Gtf2i.

Nerve axons wrapped by myelin in the human brain



In my new lab at Tel Aviv University in Israel, our research is focused on understanding the neurobiological and etiological mechanisms of genetic neurodevelopmental disorders such as Williams syndrome and autism spectrum disorders. Specifically, 1) we study how genes, molecular processes and brain regions regulate social and anxiety-related behaviors in health and illness, 2) we focus our research on understanding how these factors are disrupted in genetic neurodevelopmental disorders such as autism and Williams syndrome, 3) we aspire to translate findings from our basic research to clinical aspects that will ultimately improve the diagnosis, understanding and treatment of neurological and psychiatric disorders.

As a postdoctoral fellow in SCSB I gained extensive experience in using mouse genetics, and molecular and cellular approaches to dissect neural circuitry mechanisms and the genetics behind social abnormalities in neuropsychiatric disorders. Along the years I had the privilege to attend and present my research in multiple international scientific conferences, establish a wide network and collaborations, and publish scientific articles which were supported by the SCSB.

Altered myelination properties in Williams syndrome was found to play a critical role in the etiology of hypersociability. Significantly decreased myelin thickness was measured in the frontal brain of Williams syndrome subjects compared to controls.

Past SCSB Postdoctoral Fellows Current Faculty Positions

Yang Zhou

PI, Montreal Neurological Institute & Hospital;
Asst. Prof., Department of Neurology & Neurosurgery,
McGill University, Canada

Neville Sanjana

Core Faculty, New York Genome Center;
Asst. Prof. of Biology, NYU; Asst. Prof. of
Neuroscience and Physiology, NYU Medical School

Ian Slaymaker

Asst. Prof., Icahn School of
Medicine, Mount Sinai

Bradley Carter

Asst. Prof., Biology, University of
Wisconsin-Eau Claire

Elizabeth Norton

Asst. Prof., Dept. of Communication Sciences and
Disorders, Northwestern University

Fernando Bustos

Asst. Prof., Universidad Andres Bello,
Santiago, Chile

Paul Muentener

Asst. Prof. of Psychology, Tufts University

Stefano Anzellotti

Asst. Prof., Department of Psychology,
Boston College

Boaz Barak

Asst. Prof., School of Psychological Sciences and
Sagol School of Neuroscience, Tel Aviv University

Limor Friefield

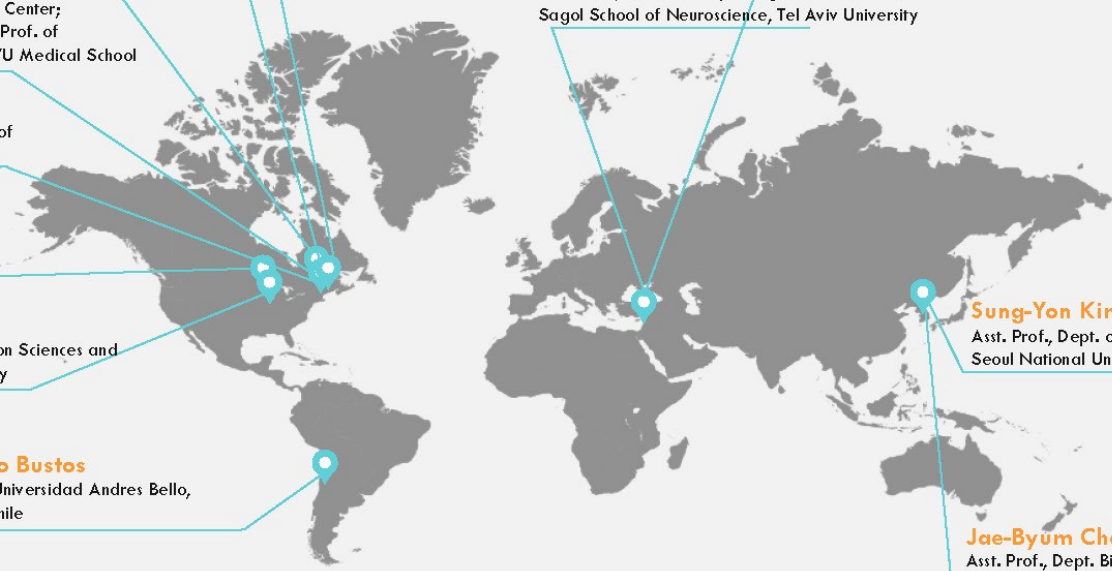
Asst. Prof., Department of Biomedical
Engineering, Tel Aviv University

Sung-Yon Kim

Asst. Prof., Dept. of Chemistry,
Seoul National University

Jae-Byum Chang

Asst. Prof., Dept. Biomedical Engg.,
Sungkyunkwan University, Seoul



COLLOQUIUM SERIES

SEPTEMBER

11 - Elizabeth Norton, Ph.D.
Northwestern University

18 - Alison Singer
Autism Science Foundation

OCTOBER

2 - Judith Burkart, Ph.D.
University of Zurich

9 - Sally Ozonoff, Ph.D.
MIND Institute,
UC Davis Medical Center

NOVEMBER

13 - Devanand Manoli, M.D., Ph.D.
University of California, San Francisco

DECEMBER

4 - Neville Sanjana, Ph.D.
New York University

General Info:

Time: 4PM - 5PM, reception to follow

Location: Singleton Auditorium,
Building 46, Room 3002
43 Vassar Street, Cambridge, MA 02139

All events are open to the public, registration is not required

LUNCH SERIES

- September 6, 2019 – **Matthew Wilson, Ph.D.**
Sherman Fairchild Professor of Neurobiology,
Picower Institute for Learning and Memory,
Department of Brain & Cognitive Sciences, MIT
- September 27, 2019 – **Sasha Krol, Ph.D.**
Simons Postdoctoral Fellow, Guoping Feng Laboratory,
McGovern Institute for Brain Research, MIT
- October 18, 2019 – **Jitendra Sharma, Ph.D.**
Research Scientist, Picower Institute for Learning and
Memory, MIT; Assistant Neuroscientist, Martinos Center
for Biomedical Imaging & Instructor in Radiology,
Massachusetts General Hospital, Harvard Medical School
- October 25, 2019 – **Oliver Wilder-Smith, Ph.D.**
Simons Postdoctoral Fellow, Media Laboratory, MIT
- November 8, 2019 – **Dara S. Manoach, Ph.D.**
Professor of Psychology, Department of Psychiatry,
Harvard Medical School

General Info:

Time: 12PM - 1PM

Location: SCSB Conference room, Building 46, Room 6011
43 Vassar Street, Cambridge, MA 02139



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