The Simons Center for the Social Brain Newsletter

Spring 2025

Simons Center for the Social Brain

Inside this issue

Massachusetts Institute of Technology

Upcoming Events: Spring 2025

Colloquium Series

February 5
Robert Froemke, Ph.D.
New York University

March 5
Haitham Amal, Ph.D.
Hebrew University of Jerusalem

March 19
Helen Tager-Flusberg, Ph.D.
Boston University

April 30
Oliver Rollins, Ph.D.
Massachusetts Institute of Technology

May 21
X. Shawn Liu, Ph.D.
Columbia University

General Info
Time: 4PM–5PM, *reception to follow*
Location: Singleton Auditorium, 46-3002
registration is not required

Lunch Series

February 14
Emalie McMahon, Ph.D.
Postdoctoral Associate,
Nancy Kanwisher Laboratory, MIBR

February 28
Yunjin Lee, Ph.D.
Postdoctoral Researcher,
Jun Huh Laboratory, Harvard Medical School

March 21
Amrita Lamba, Ph.D.
SCSB Postdoctoral Fellow,
Rebecca Saxe Laboratory, BCS

April 18
Lukas Vogelsang, Ph.D.
SCSB Postdoctoral Fellow,
Pawan Sinha Laboratory, BCS

May 16
Christopher Fell, Ph.D.
SCSB Postdoctoral Fellow,
Abudayyeh & Gootenberg Laboratory, MIRB

General Info
Time: 12PM–1PM
Hybrid Location: Simons Center Conference Room, 46-6011 + Zoom Meeting, *registration is not required*

All events are open to public, please visit our website for all upcoming events: scsb.mit.edu/events

Autism and Neurodevelopmental Disorders: Past, Present, and Future

New autism research projects represent a broad range of approaches to achieving a shared goal

Written by David Orenstein

A panel of faculty members listens to a question from an audience member: Ev Fedorenko, Gloria Choi, Charles Nelson, Earl K. Miller and moderator Mriganka Sur. Photo: David Orenstein

At a symposium last Fall of the Simons Center for the Social Brain, six speakers described a diversity of recently launched studies aimed at improving understanding of the autistic brain.

From studies of the connections between neurons, to interactions between the nervous and immune systems, to the complex ways in which people understand not just language but also the unspoken nuances of conversation, new research projects at MIT supported by the Simons Center for the Social Brain are bringing a rich diversity of perspectives to advancing the field's understanding of autism.

As six speakers lined up to describe their projects at a Simons Center symposium Nov. 15, MIT School of Science Dean Nergis Mavalvala articulated what they were all striving for: "Ultimately we want to seek understanding—not just the type that tells us how physiological differences in the inner workings of the brain produce differences in behavior and cognition, but also the kind of understanding that improves inclusion and quality of life for people living with autism spectrum disorders."

Simons Center director Mriganka Sur, Newton Professor of Neuroscience in The Picower Institute for Learning and Memory and Department of Brain and Cognitive Sciences (BCS), said that even though the field still lacks mechanism-based treatments or reliable biomarkers for autism spectrum disorders, he is optimistic about the discoveries and new research MIT has been able to contribute. MIT research has led to five clinical trials so far, and he praised the potential for future discovery, for instance in the projects showcased at the symposium.

"We are, I believe, at a frontier—at a moment where a lot of basic science is coming together with the vision that we could use that science for the betterment of people," Sur said.

The Simons Center funds that basic science research in two main ways that each encourage collaboration, Sur said: large-scale projects led by faculty members across several labs, and fellowships for postdocs who are mentored by two faculty members, thereby bringing together two labs. The symposium featured talks and panel discussions by faculty and fellows leading new research.

In her remarks, Associate Professor Gloria Choi of The Picower Institute and BCS department described her collaboration's efforts to explore the possibility of developing an autism therapy using the immune system. Previous research in mice by Choi and collaborator Jun Huh of Harvard Medical School has shown that injection of the immune system signaling molecule IL-17a into a particular region of the brain's cortex can reduce neural hyperactivity and resulting differences in social and repetitive behaviors seen in autism model

Gloria Choi describes her team's work to develop a potential immunotherapy for autism. Photo: Giro Studio

mice compared to non-autism models. Now Choi's team is working on various ways to induce the immune system to target the cytokine to the brain by less invasive means than direct injection. One way under investigation, for example, is increasing the population of immune cells that produce IL-17a in the meningeal membranes that surround the brain.

In a different vein, Associate Professor Ev Fedorenko of the McGovern Institute for Brain Research and BCS is leading a seven-lab collaboration aimed at understanding the cognitive and neural infrastructure that enables people to engage in conversation, which involves not only the language spoken but also facial expressions, tone of voice, and social context. Critical to this effort, she said, is going beyond previous work that studied each related brain area in isolation to understand the capability as a unified whole. A key insight, she said, is that they are all nearby each other in the lateral temporal cortex.

"Going beyond these individual components we can start asking big questions like, what are the broad organizing principles of this part of the brain?," Fedorenko said. "Why does it have this particular arrangement of areas and how do these work together to exchange information to create the unified percept of another individual we're interacting with?"

While Choi and Fedorenko are looking at factors that account for differences in social behavior in autism, Picower Professor Earl K. Miller of The Picower Institute and BCS is leading a project that focuses on another phenomenon: the feeling of sensory overload that many autistic people experience. Research in Miller's lab has shown that the brain's ability to make predictions about sensory stimuli, which is critical to filtering out mundane signals so attention can be focused on new ones, depends on a cortex-wide coordination of the activity of millions of neurons implemented by high frequency "gamma" brain waves and lower-frequency "beta" waves. Working with animal models and human volunteers at Boston Children's Hospital (BCH), Miller said his team is testing the idea that there may be a key difference in these brain wave dynamics in the autistic brain that could be addressed with closed-loop brain wave stimulation technology.

Panel discussion with SCSB Postdoctoral Fellows [from left to right: Lace Riggs, Chhavi Sood, Lukas Vogelsang], moderated by past SCSB fellow, now Assistant Professor at Harvard University, Michael Segel. Photo: Giro Studio

Simons Postdoctoral Fellow Lukas Vogelsang, who is based in BCS Professor Pawan Sinha's lab, is looking at potential differences in prediction between autistic and non-autistic individuals in a different way: through experiments with volunteers that aim to tease out how these differences are manifest in behavior. For instance, he's finding that in at least one prediction task that requires participants to discern the probability of an event from provided cues, autistic people exhibit lower performance levels and undervalue the predictive significance of the cues while non-autistic people slightly overvalue it. Vogelsang is co-advised by BCH researcher and Harvard Medical School Professor Charles Nelson.

Fundamentally, the broad scale behaviors that emerge from coordinated brainwide neural activity begins with the molecular details of how neurons connect with each other at circuit junctions called synapses. In her research based in The Picower Institute lab of Menicon Professor Troy Littleton, Simons Postdoctoral Fellow Chhavi Sood is using the genetically manipulable model of the fruit fly to investigate how mutations in the autism-associated protein FMRP may alter the expression of molecular gates regulating ion exchange at the synapse , which would in turn affect how

frequently and strongly a pre-synaptic neuron excites a post-synaptic one. The differences she is investigating may be a molecular mechanism underlying neural hyperexcitability in fragile X syndrome, a profound autism spectrum disorder.

SCSB Symposium reception, featuring the "UnrulyArt" gallery. Photo: Giro Studio

In her talk, Simons Postdoctoral Fellow Lace Riggs, based in the McGovern Institute lab of Poitras Professor of Neuroscience Guoping Feng, emphasized how many autism-associated mutations in synaptic proteins promote pathological anxiety. She described her research that is aimed at discerning where in the brain's neural circuitry that vulnerability might lie. In her ongoing work, Riggs is zeroing in on a novel thalamocortical circuit between the anteromedial nucleus of the thalamus and the cingulate cortex, which she found drives anxiogenic states. Riggs is co-supervised by Professor Fan Wang.

After the wide-ranging talks, supplemented by further discussion at the panels, the last word came via videoconference from Kelsey Martin, executive vice president of the Simons Foundation Autism Research Initiative. Martin emphasized that fundamental research like that done at the Simons Center, is the key to developing future therapies and other means of supporting members of the autism community.

"We believe so strongly that understanding the basic mechanisms of autism is critical to being able to develop translational and clinical approaches that are going to impact the lives of autistic individuals and their families," she said.

From studies of synapses to circuits to behavior, MIT researchers and their collaborators are striving for exactly that impact.

Scan for talk recordings and photo gallery

New SCSB Targeted project

Marmoset Circuits: Developing knowledge and tools to facilitate therapeutic development for ASD

Written by Chaoyi Zhang and Wenyu Tu

This new SCSB targeted project involves two labs: Guoping Feng (McGovern Institute) and Alan Jasanoff (McGovern Institute).

While advances in gene therapy offer promising treatments for severe forms of autism spectrum disorder (ASD), only a small fraction of patients with monogenic causes are likely to benefit. For the majority, ASD results from a complex interplay of polygenic risks, developmental disruptions, and environmental factors. To develop effective treatments for this broader population, we must first deepen our understanding of the neural circuit mechanisms underlying core ASD symptoms. Targeting these circuits could yield transformative therapies that significantly improve the quality of life for individuals with ASD.

Although mice have been invaluable for neuroscience research, their limited prefrontal cortex development and significant species differences in neuron types, connectivity, and gene expression restrict their ability to model higher brain functions implicated in psychiatric disorders. The common marmoset, a small New World

primate, offers a powerful alternative. With rich social structures, complex vocal communication, rapid breeding cycles, and lower housing costs, marmosets are uniquely suited for studying the neural underpinnings of social interaction and communication deficits relevant to ASD.

Our latest research using functional ultrasound imaging (fUSi) in Shank3 mutant mice has revealed striking findings: these mice exhibit greater hyperactivation than wild-type mice, particularly in the frontal cortex and striatum, during social interactions (Figure 1). This discovery of social-evoked hyperactivity in frontal-striatal circuits marks a novel insight into ASD models and opens new pathways for investigating the neurobiological basis of social deficits. Building on these findings, our next goal is to determine whether similar circuit abnormalities exist in Shank3 marmoset models of ASD and to test whether targeted circuit manipulation could mitigate or even rescue social deficits.

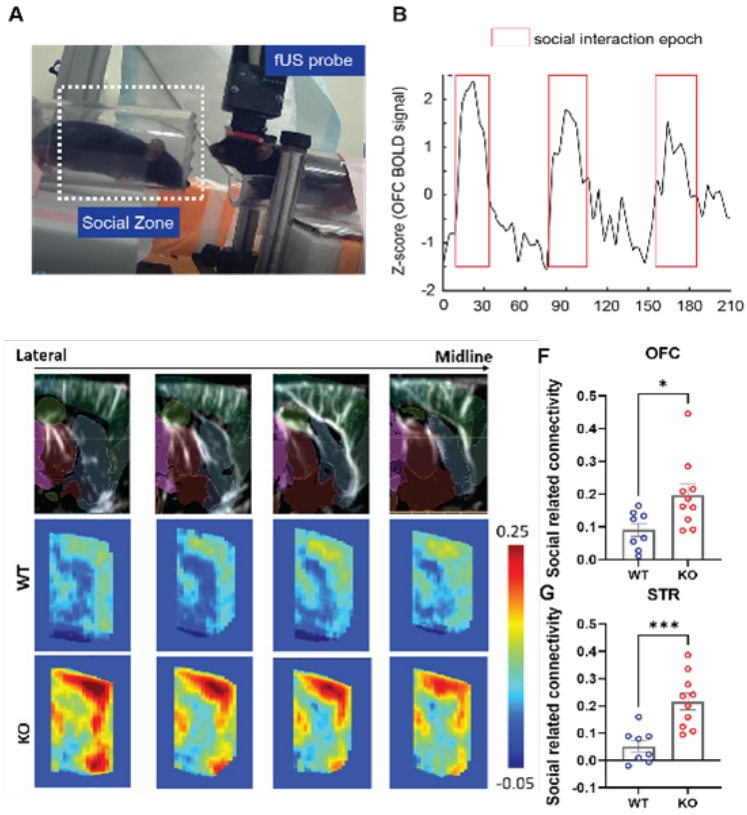

Fig. 1. Social related fUSI in awake WT and Shank3 mutant mice. **(A)** Experimental setup for awake imaging under social event stimulation. **(B)** Example of relative hemodynamic response in OFC under social event stimulation. Pink shadow boxes indicate social events. Social events trigger significant OFC activity changes. **(C)** Power doppler images depicting the sagittal field of view, from lateral to midline (left to right). **(D-E)** Average activity map images depicting the sagittal field of view from lateral to midline slices in WT (D) and mutant (KO) mice (E) during social event stimulation. Color bar: correlation coefficient indicating a time-specific increase of the signal during social stimulation in the related pixel. **(F, G)** Quantification of local functional connectivity in orbital frontal cortex (OFC; F) and Striatum (STR; G); Unpaired T test, WT=10 mice, KO=10 mice. *p<0.05;***p< 0.001.

Through this targeted project, we are leveraging the unique strengths of the MIT research community—combining advanced mouse and marmoset models with cutting-edge neuroimaging technologies (fUSi and fMRI). Our team, including Guoping Feng (Associate Director of the McGovern Institute and Professor in the Department of Brain and Cognitive Sciences at MIT) and Alan Jasanoff (Professor of Biological Engineering and Brain and Cognitive Sciences, and McGovern Institute), is working collaboratively to uncover the circuit mechanisms driving ASD-related symptoms. By integrating findings across species and methods, we aim to lay the foundation for developing next-generation circuit-based therapeutics for ASD.

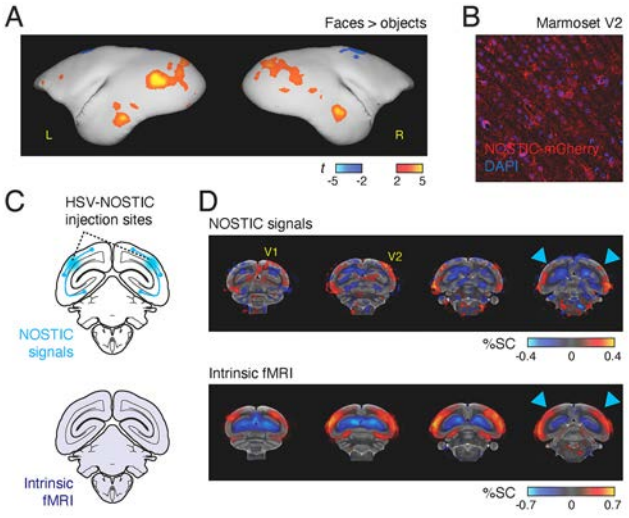

Fig. 2. Conventional and circuit-specific fMRI of visual responses in awake marmosets. (A) Face-responsive brain regions in wild-type marmosets serve as a basis for comparison with Shank3 animals and for targeting of the circuit-specific fMRI probe NOSTIC. **(B)** Visualization of NOSTIC expression in the visual cortex of a virally treated marmoset. **(C)** Schematic showing expected sources of circuit-specific signals (top) and nonspecific intrinsic fMRI signals (bottom) in animals injected with the retrograde vector HSV-NOSTIC. **(D)** Preliminary NOSTIC-specific functional imaging signals during visual stimulation are defined as the difference between fMRI data acquired following injection of saline and the NOSTIC inhibitor 1400W (top), whereas nonspecific visual response maps (bottom) are obtained using fMRI in the presence of 1400W alone.

Postdoctoral Fellows

Welcome to new SCSB Fellows!

Gwangsu Kim, Ph.D.

Project: Computational Modeling of Joint Encoding of Visual and Valence Cues in Amygdala

Laboratories: James DiCarlo; Rebecca Saxe

Ph.D. from: Korea Advanced Institute of Science and Technology

Hobbies: Playing the piano

Marvin Lavechin, Ph.D.

Project: Vocal analytics: novel automated tools for decoding infant babbling patterns

Laboratories: Roger Levy; Elika Bergelson

Ph.D. from: Meta AI & École Normale Supérieure (Paris, France)

Hobbies: I love discovering new coffee places and climbing!

Wenyu Tu, Ph.D.

Project: Brain-wide analysis of neural perturbations in a marmoset ASD model
Laboratories: Alan Jasanoff; Guoping Feng

Ph.D. from: The Pennsylvania State University

Hobbies: Hiking and cooking

Jen Yong, Ph.D.

Project: Identifying the role of mucus-associated bacteria and phages in modulation of autism spectrum disorder
Laboratories: Jun R. Huh; Gloria Choi

Ph.D. from: Yonsei University

Hobbies: Going for walks and finding cute cafes

News & Announcements

Simons Postdoctoral Fellowship opportunities

The Simons Center has two rounds of funding annually for postdoctoral fellowships.

Fall 2025 deadline: Tuesday, September 30, 2025
Spring 2026 deadline: Tuesday, March 31, 2026

Postdoctoral Fellowships are intended for outstanding candidates with recent PhDs (please see eligibility criteria on our website) who wish to conduct autism-related research at MIT under the mentorship of MIT faculty researchers. Applicants currently completing their PhD outside MIT (external candidates), who wish to carry out postdoctoral research at MIT, are strongly encouraged to apply.

As part of the Brain & Cognitive Sciences complex at MIT, the Center offers supportive mentorship to postdoctoral researchers, an exceptional environment for scientific inquiry, and a strong commitment to an inclusive, welcoming culture. To learn more about our commitment, visit here: https://scsb.mit.edu/our-values/. To learn more about postdoctoral resources that support personal, family, and community life here at MIT, visit: https://postdocs.mit.edu/.

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

Support Our Research

We urge you to support the Simons Center for the Social Brain (SCSB) at MIT. Your gift will fund groundbreaking research into causes, mechanisms and treatments of neurodevelopmental disorders including autism spectrum disorders (ASD). The center supports laboratories that study the brain at multiple levels spanning molecular, circuit and computational mechanisms of brain function and cognition. Our programs include funding for innovative, collaborative team projects and postdoctoral fellowships, and events that reach a wide audience, as well as outreach efforts within the larger community.

Please consider making a gift: Simons Center for the Social Brain - **Autism Research Fund 3836050**

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Editing and Design: Alexandra Sokhina
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Contributing Writers: Targeted Project PIs and their laboratories; David Orenstein

SCSB team:
Director: Mriganka Sur | msur@mit.edu
Senior Administrative Manager &
Director of Development: Eleana MacPhail | ericci@mit.edu
Program Coordinator: Alexandra Sokhina | asokhina@mit.edu