Simons Center for the Social Brain

The Simons Center for the Social Brain (SCSB) at MIT was founded in January 2012. Its mission is to understand the neural mechanisms underlying social cognition and behavior and translate this knowledge into better diagnosis and treatment of autism spectrum disorders (ASDs).

The Simons Center studies mechanisms of autism spectrum disorders in both humans and relevant model organisms and systems, as neural correlates of social cognition and behavior exist in diverse species. Our approaches take advantage of MIT's strengths in genetics and genomics, molecular and cell biology, analyses of neural circuits and systems, cognitive psychology, computation, and engineering.

Our programs include funding for innovative, collaborative team projects and postdoctoral fellowships, as well as events that reach a wide audience, including a colloquium series and a lunchtime talk series.

SCSB is funded by a block grant from the Simons Foundation Autism Research Initiative (SFARI). In late 2016, SFARI confirmed the next phase of funding for SCSB (spanning the period 2017–2019).

Symposia and Events

A core mission of SCSB is to strengthen the community of researchers working on autism spectrum disorders and the social brain. Over 2016–2017, we continued to develop our colloquium series as the major Boston-area forum on the social brain and its disorders, along with other events that build the community. It was held roughly on alternate Wednesdays during the spring and fall terms. The SCSB lunch series was held approximately once a month. This event featured postdoctoral fellows and faculty seed grant principal investigators presenting their research to colleagues, students, and other researchers. SCSB hosted 14 external speakers as part of its colloquium series and 13 internal speakers as part of its lunch series. Additionally, SCSB co-hosted special seminars and book signing events with the Knight Science Journalism Program that were relevant to autism and developmental brain disorders.

Research

Seed Grants and Postdoctoral Fellowships

In 2016, we continued our outreach efforts with respect to announcing, receiving, reviewing, and awarding seed grants and postdoctoral fellowships. Announcements were widely advertised to various departments and centers at MIT as well as institutions throughout the Boston area. As in the past, the grant application and funding cycle occurred in two rounds (February and September). Applications were reviewed by peer committees that were set up for each round of applications and overseen by the SCSB steering committee, which met after each round of reviews. Seed grants were awarded through 2016; postdoctoral fellowships continue to be awarded in 2017, following renewal funding of SCSB.

Equipment Awards

In 2016, we continued calls for equipment grants to further expand our efforts and encourage collaborative research. Applicants included all funded and previously funded SCSB and SFARI investigators. Equipment awards were made through 2016.

Targeted Projects

The Simons Center for the Social Brain supports collaborative, focused projects undertaken by multiple laboratories to explore in depth specific aspects or mechanisms of autism. These targeted projects are structured to enable collaboration among researchers in order to quickly and flexibly address pressing questions in autism research. SCSB supported two targeted projects in 2016–2017.

The first project focused on the nature of the pragmatic impairment in autism spectrum disorders. This project, which received its second year of funding in 2016 and its third in 2017, involved three components:

- Characterizing the contributions of three neural systems—the core language system, the theory of mind system, and the cognitive control system—to pragmatic reasoning (Evelina Fedorenko and Rebecca Saxe)
- Investigating the nature of the pragmatic impairment among individuals with ASDs using a set of robust communicative paradigms (Edward Gibson)
- Conducting a computational and behavioral investigation of how developing and mature individuals with ASD and neurotypical participants reason about others' utility functions (Laura Schulz and Josh Tenenbaum)

The second project addressed the role of the thalamic reticular nucleus (TRN) in thalamocortical coordination, cognitive processing, and sleep among those with ASDs. This project, initiated in November 2016, also involved three components:

- The role of the TRN in spindle generation and hippocampal-neocortical coordination during wake/sleep (Matthew Wilson)
- Spindle activity and thalamocortical interactions (Dara Manoach)
- Molecular diversity and the role of ASD risk genes in the TRN (Guoping Feng)

In 2016, two previous targeted projects—one focusing on 16p11.2 deletion syndrome and the other on the Shank3 deletion—completed their three-year funding terms. Our targeted projects have been an instrumental part of the Simons Center's success. Going forward, we will continue to expand our targeted project program by identifying multi-level collaborative teams with specific benchmarks and endpoints.

Major Research Publications

Human chromosome 16p11.2 microdeletion is the most common gene copy number variation in autism, but the synaptic pathophysiology caused by this mutation is largely unknown. Using a mouse with the same genetic deficiency, targeted project investigator

Mark Bear and his team reported in *Nature Neuroscience* that mGluR5 (metabotropic glutamate receptor 5)-dependent synaptic plasticity and protein synthesis were altered in the hippocampus and that hippocampus-dependent memory was impaired. Notably, chronic treatment with a negative allosteric modulator of mGluR5 reversed the cognitive deficit.

Because autism spectrum disorders are neurodevelopmental disorders and patients typically display symptoms before the age of three, one of the key questions in autism research is whether the pathology is reversible in adults. Shank3 deletion is a prominent monogenic autism gene that is estimated to contribute to approximately 1% of all ASD cases, and targeted project investigator Guoping Feng and his team reported in *Nature* that they could reverse many effects of the deletion in mice. They generated a novel Shank3 conditional knock-in mouse model and showed that re-expression of the Shank3 gene in adult mice led to improvements in synaptic protein composition, spine density, and neural function in the striatum. They also provided behavioral evidence that certain abnormalities, including social interaction deficits and repetitive grooming behaviors, could be rescued. Together, these results reveal the profound effect of post-developmental activation of Shank3 expression on neural function.

Simons Fellow Yeong Shin Yim and the laboratories of seed grantees Gloria Choi (Department of Brain and Cognitive Sciences, McGovern Institute for Brain Research) and Jun Huh (Harvard Medical School, Brigham and Women's Hospital) reported in *Nature* that cortical and behavioral abnormalities appear in mice exposed to maternal inflammation and that maternal gut bacteria promote neurodevelopmental abnormalities in mouse offspring.

Language comprehension involves both language-specific mechanisms and domain-general mechanisms that are engaged in many cognitive processes. In the human cortex, language-selective mechanisms are implemented in the left-lateralized "core language network," whereas domain-general mechanisms are implemented in the bilateral "multiple demand" (MD) network. Targeted project investigator Evelina Fedorenko reported in the *Journal of Neuroscience* the first direct comparison of the respective contributions of these networks to naturalistic story comprehension. Using a novel combination of neuroimaging approaches, she found that MD regions track stories less closely than language regions. This finding constrains the possible contributions of the MD network to comprehension, contrasts with accounts positing that this network has continuous access to linguistic input, and suggests a new typology of comprehension processes based on their extent of input tracking.

Impact

The impact of SCSB on the community is manifest in many ways. Over 74 investigators across 18 departments, labs, and centers at MIT and 11 Boston-area institutions are engaged as investigators or as postdoctoral mentors. SCSB has supported 31 postdoctoral researchers as Simons Fellows.

As of 2017, SCSB researchers had published more than 200 original research papers and obtained over $43 million in external funding. A significant number of Simons Fellows have obtained faculty or independent research positions.

Administration and Governance

SCSB continues to be run by a small administrative core in which each individual performs a wide range of functions. In 2016–2017, the team included Mriganka Sur (director), Eleana Ricci (program administrator and facilities officer), Alexandra Sokhina (administrative assistant and events coordinator), and Leia Amarra (fiscal officer).

SCSB has two levels of governance, and both were actively engaged in 2016–2017:

- Review committees made up of six to eight reviewers across MIT met during each round of funding to evaluate applications for seed grants and postdoctoral fellowships.
- The steering committee (Richard Hynes, Robert Desimone, Douglas Lauffenburger, Mriganka Sur, and Louis Reichardt) met following each review committee meeting to offer advice on funding decisions, targeted projects, and the overall direction of the center.

Mriganka Sur
Director
Newton Professor of Neuroscience, Department of Brain and Cognitive Sciences