The Simons Center for the Social Brain Newsletter

Fall 2022

SIMONS CENTER FOR THE SOCIAL BRAIN

Inside this issue

Publications Spotlight

Mylonas D., Machado S., Larson O., Patel R., Cox R., Vangel M., Maski K., Stickgold R., **Manoach D. S.** (2022) Dyscoordination of Non-Rapid Eye Movement Sleep Oscillations in Autism Spectrum Disorder. Sleep 45: 1-15. [https://doi.org/10.1093/sleep/zsac010]

Kamps F.S., Richardson H., Ratan Murty N.A., **Kanwisher N., Saxe R.** (2022) Using child-friendly movie stimuli to study the development of face, place, and object regions from age 3 to 12 years. Human Brain Mapping 43: 2782-2800. [https://doi.org/10.1002/hbm.25815]

Yildirim M., Delepine C., Feldman D., Pham V.A., Chou S., Ip J., Nott A., Tsai L., Ming G., So P.T.C., **Sur M.** (2022) Label-free three-photon imaging of intact human cerebral organoids for tracking early events in brain development and deficits in Rett syndrome. eLife, 11: e78079. [https://doi.org/10.7554/eLife.78079]

Ghosh S., Li N., Schwalm M., Bartelle B.B., Xie T., Daher J.I., Singh U.D., Xie K., DiNapoli N., Evans N.B., Chung K., **Jasanoff A.** (2022) Functional dissection of neural circuitry using a genetic reporter for fMRI. Nature Neuroscience 25: 390-398. [https://doi.org/10.1038/s41593-022-01014-8]

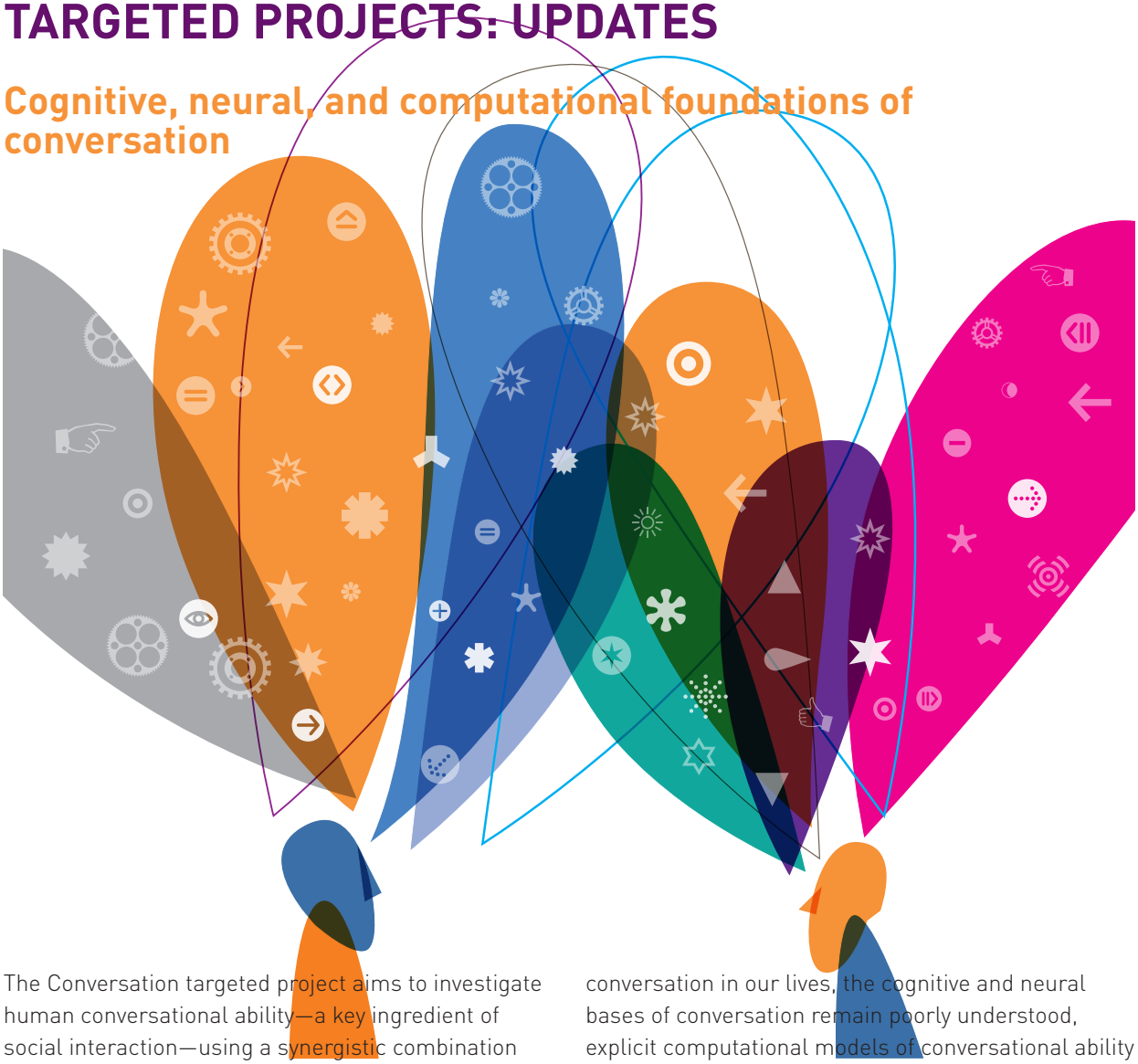
Grand G.*, Blank I.*, Pereira F., **Fedorenko, E.** (2022). Semantic projection recovers rich human knowledge of multiple object features from word embeddings. Nature Human Behavior 6: 975-987. [https://doi.org/10.1038/s41562-022-01316-8]
**Contributed equally*

Bloem B., Huda R., Amemori K., Abate A., Krishna G., Wilson A., Carter C.W., **Sur M., Graybiel A.M.** (2022) Multiplexed action-outcome encoding by striatal striosome-matrix compartments detected with a novel mouse cost-benefit foraging task. Nature Communications, 13: 1541. [https://doi.org/10.1038/s41467-022-28983-5]

Tomasello D.L., Kim J., Khodour Y., McCammon J.M., Mitalipova M., **Jaenisch R.,** Futerman A.H., **Sive H.** (2022) 16pdel lipid changes in iPSC-derived neurons and function of FAM57B in lipid metabolism and synaptogenesis. iScience 25:10355. [https://doi.org/10.1016/j.isci.2021.103551]

TARGETED PROJECTS: UPDATES

Cognitive, neural, and computational foundations of conversation



The Conversation targeted project aims to investigate human conversational ability—a key ingredient of social interaction—using a synergistic combination of behavioral, neural, and computational approaches with neurotypical adults and children and those with autism. This project is a collaborative effort among seven labs: the Fedorenko, Kanwisher, Gibson, Saxe, Levy, Tanenbaum labs at MIT, and the Robertson lab at Dartmouth.

Talking to others is ubiquitous in everyday life, from a casual exchange at a grocery store, to a job interview, to building friendships and romantic relationships. Conversation is also critical for language learning: children's most critical exposure to linguistic input is through conversation. Finally, conversation is likely a locus of atypical function in autism, one that is abundantly evident in the real-world experience of children and adults with autism, and one that is perhaps at the core of developmental language difficulties in infants and toddlers eventually diagnosed with autism. In spite of the critical role of conversation in our lives, the cognitive and neural bases of conversation remain poorly understood, explicit computational models of conversational ability are lacking, and the precise nature and scope of challenges that arise in communicative disorders, like autism, are still debated. To remedy the situation, we will use a synergistic combination of highly innovative approaches to illuminate the cognitive, neural, and computational bases of human conversational ability.

Ev Fedorenko, Associate Professor of Cognitive Neuroscience, and **Nancy Kanwisher**, Professor of Cognitive Neuroscience, will probe the organization of the socially-responsive cortex with the goal of discovering key components of the brain's 'conversation network'—a set of brain areas that process and integrate different informational components during conversational exchanges. They will draw on the data-driven fMRI voxel decomposition approach, intracranial recordings, and artificial neural networks.

Edward Gibson, Professor of Language and Cognitive Science, and **Caroline Robertson**, Assistant Professor of Cognitive Science and Neuroscience, will focus on core components of conversational ability, including the ability to time conversational turns and to maintain eye contact. They will draw on large-scale conversation corpora and cutting-edge psycholinguistic methods, including eye-tracking and naturalistic virtual reality paradigms.

Rebecca Saxe, Professor of Cognitive Neuroscience, will develop a novel highly engaging fMRI paradigm that would allow probing the brains of children during the time period when much of linguistic and social learning is taking place, and the period when challenges start to arise for children later diagnosed with autism. This paradigm could open a new frontier in investigations of typical and atypical brain development.

Finally, **Roger Levy**, Professor of Language and Cognitive Science, and **Josh Tenenbaum**, Professor of Computational Cognitive Science, will combine symbolic and deep learning modeling approaches to improve existing models of language processing and conversation. They will target several facets of conversational exchanges, like integrating utterances with contextual information and making inferences about the intended meanings, and includes model development and model evaluation against behavioral data from novel paradigms.

Understanding the cognitive and neural foundations of conversational ability would tell us a great deal about what it means to be human and how human social cognition is implemented in the mind and brain. Further, a deeper understanding of the nature, scope, and neural basis of difficulties that arise in autism during conversational exchanges may help develop more effective diagnostics and therapeutics.

Predictive Processing in Autism

The Predictive Processes targeted project aims to characterize multiple domains of prediction in autism. Uncertainty can pose challenges for individuals with autism. This may have consequences for navigating daily activities that may be unpredictable or rely on rapid updating of changing contingencies. Social interaction in particular, require adapting to rapidly

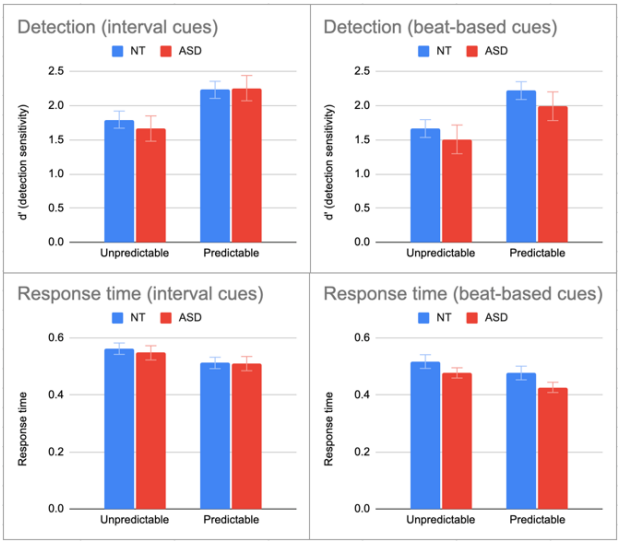


Figure 1. Predictability of auditory target timing due to reliable beat-based and interval-based cueing improves performance relative to unpredictable conditions in both NT and ASD groups, as measured by detection sensitivity and response time. The ASD group is showing less detection sensitivity and faster responses than the NT group in the beat-based condition, but no significant difference from the NT group in the effect of predictability.

changing perceptual, social, and linguistic demands. Recent theoretical and empirical work suggest that individuals with autism may show differences in prediction, but empirical findings are mixed across paradigms and participant samples. The Sinha, Gabrieli, and Snedeker labs continue to study autism in three domains: temporal auditory prediction, neural adaptation, and language. Each lab responded differently to COVID-19, and in 2022, the projects ramped up data collection under the pandemic's ongoing constraints. A systematic review published by Sinha's group in *Autism Research*, summarizes the literature on prediction in autism across domains and proposes new directions for research.

Pawan Sinha, Professor of Vision and Computational Neuroscience, partnered with the Simons Foundation's SPARK initiative, a nationwide registry of autistic individuals, which enabled the Sinha lab team to conduct several online experiments that participants completed from home. An auditory detection task required participants to detect beeps in background noise, with temporal cues that may aid performance. Results showed that non-autistic adults' performance improves with predictable interval- and beat-based cues, relative to randomly presented cues

(Figure 1) . Contrary to their hypothesis, they observe similar improvement across groups, indicating that the capacity to deploy attention to optimize detection using predictive timing does not appear systematically affected in autism, and suggesting that prediction differences in autism may be domain-specific, rather than generalized across all domains.

Additional experiments tested linguistic prediction and perception of volatility in probabilistic sequences, for which data analysis is now underway. The lab is currently implementing similar experiments using electroencephalography to probe neural responses to predictable and unpredictable auditory stimuli in person. Figure 2 shows an example ramping response from a neurotypical EEG participant.

John Gabrieli, Professor of Health Sciences and Technology and Cognitive Neuroscience, and his team continue to investigate how neural adaptation results in rapid brain plasticity in response to higher-level percepts (faces, speech, objects, and written words). Prior to COVID, his team scanned neurotypical and autistic adults using fMRI. Participants passively viewed blocks of repeating and non-repeating stimuli. Repeating stimuli are quickly recognized and therefore result in reduced brain activation, whereas non-repeating stimuli are more actively processed.

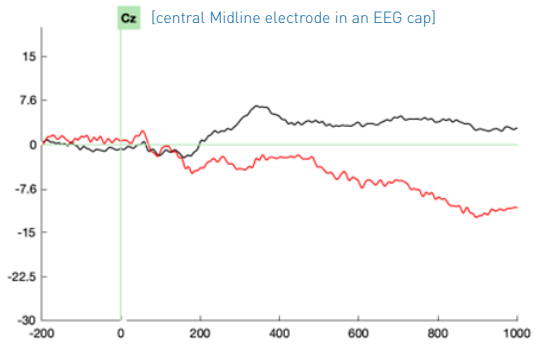


Figure 2. Ramping response to predictive (red) and nonpredictive (black) auditory tones.

Neural adaptation is the difference in activation between non-repeating and repeating stimuli. Neural adaptation may support prediction by measuring how well the brain distinguishes repeating from non-repeating events. New analyses of these neuroimaging data have revealed that individuals with ASD showed reduced neural adaptation to faces, but not to other domains tested. This reduced adaptation to faces was associated with specific challenges in social communication. Having returned to in-person data collection in Spring 2022, Gabrieli's group is actively collecting a second phase of neuroimaging data to test whether differences in top-down expectations, rather than simple bottom-up brain plasticity, may explain group differences in brain adaptation to faces.

Jesse Snedeker, Professor of Psychology at Harvard University, is examining predictions that people make about words as they listen to stories. Prior to COVID-19, her group was pursuing studies using electrophysiological measures to track complex linguistic predictions in children, and adapting some of the Sinha and Gabrieli lab paradigms for younger participants. The Snedeker lab plans to continue EEG testing with children as soon as it becomes safe to do so. Meanwhile, the Snedeker lab has shifted to implementing online behavioral experiments examining linguistic prediction in adults.

For example, in one such experiment her group is examining how the ability to predict an upcoming word may affect how it is heard. Participants listen to a story where occasionally parts of certain words are replaced with noise. This can lead to an illusion that the word was correctly pronounced, known as the "phoneme restoration effect." Comparing how often a listener experiences this illusion in predictable and unpredictable words given their context can provide insight into how prediction can affect our perception of speech. Consistent with prior work, early data from typically developing adults suggests that phoneme restoration occurs more often in words that are predictable. Confirming the expected pattern in typical adults is the final step before beginning studies in the next month with adults from the SPARK database.

Additional studies will investigate explicit predictions about upcoming words and when such predictions may affect language comprehension. Finally, by including a non-linguistic prediction task and characterizing participants based on their language ability, the group plans to examine whether linguistic prediction may differ with general predictive ability, language skill, or autism diagnosis.

As the results of these studies begin to emerge, the teams hope they will not only illuminate possible differences in prediction abilities between autistic and typically-developing individuals, but will also inform future versions of neuroimaging experiments in the lab setting when scientists return to campus.

Postdoctoral Fellows

Welcome to new 2022 SCSB Fellows!

Tomoe Ishikawa, Ph.D.

Project: Neural circuits for immune modulation during social contact with sick individuals

Laboratories: Gloria Choi, Ph.D. and Jun Huh, Ph.D.

PhD from: University of Tokyo

Hobbies: traveling and playing the piano

Chhavi Sood, Ph.D.

Project: Role of FMRP interactions with presynaptic ion channels in Fragile X Syndrome

Laboratories: Troy Littleton, Ph.D.

PhD from: University of Virginia

Hobbies: cooking, reading books, playing video games

Yugang Zhang, Ph.D.

Project: Conditional expression of therapeutic cargo in neurons of autism spectrum disorders

Laboratories: Feng Zhang, Ph.D., Guoping Feng, Ph.D.

PhD from: Cornell University

Hobbies: fishing and traveling

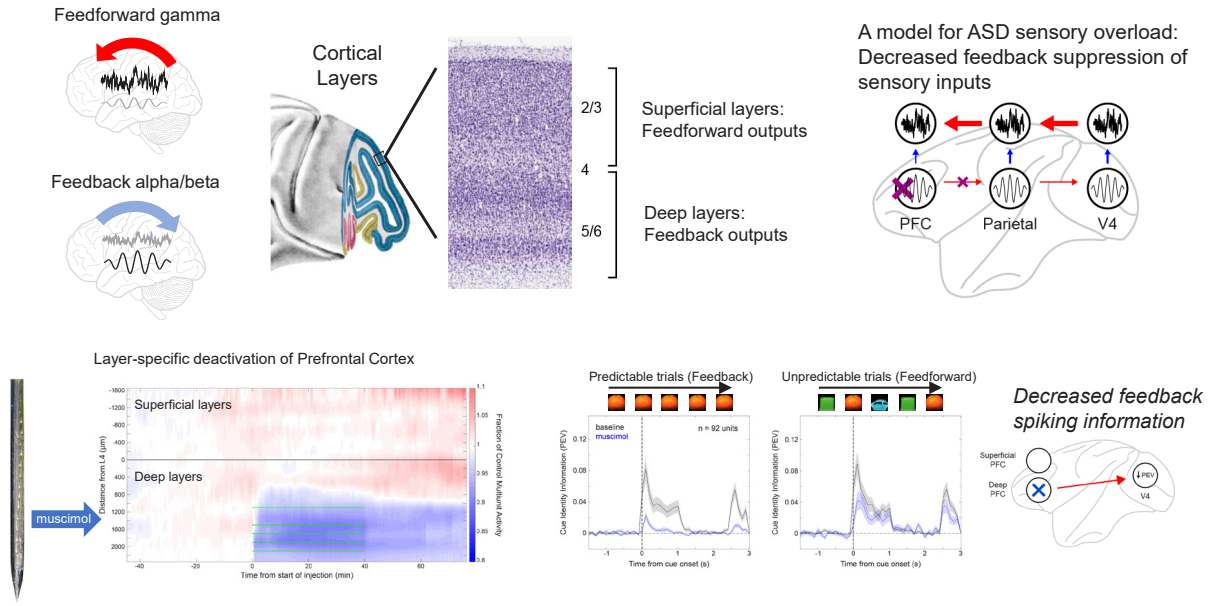
Simons Postdoctoral Fellows: Profile

Alex Major, Ph.D. | Miller Lab, Picower Institute for Learning and Memory, MIT

Project Title: Probing the cortical circuits that prevent sensory overload

Sensory overload, an exaggerated response to sensory stimulation, is common in autism spectrum disorder (ASD), causing distress and damaging social interactions and functional independence. In the neurotypical brain, predictable ambient sensory inputs are suppressed – the "volume is turned down". In ASD, over-responsivity to stimuli is caused by over-excitation of sensory cortices. This may result from a lack of feedback suppression from higher cortical regions.

My Simons fellowship project aims to test the physiological mechanisms of feedback suppression of sensory inputs. In the Predictive Coding model, feedback signals are sent from the deeper cortical layers and alpha/beta frequencies (~10–30 Hz), to suppress sensory cortex. In contrast, feedforward sensory input flows up the cortical hierarchy via gamma rhythms (> 30 Hz) in the superficial cortical layers. Using layer-specific pharmacology, this



Upper left: Sensory information (e.g., visual information) enters the brain through sensory cortex and feeds forward throughout the brain via gamma rhythms (> 35 Hz) in the local field potential (LFP). The brain's internal model (top-down prediction information) originates in associative cortex such as prefrontal cortex and feeds back through the brain via alpha/beta LFP rhythms (10–30 Hz). **Upper middle:** Superficial and deep cortical layers are shown in an example Nissl-stained histological slice of visual cortex. **Upper right:** A model for autism spectrum disorder (ASD) sensory overload: layer-specific pharmacological deactivation of deep layers of prefrontal cortex (PFC) will reduce feedback alpha/beta rhythms. This removal of feedback suppression will induce greater spiking and gamma activity in visual area V4. This is proposed to emulate reduced alpha/beta-mediated feedback suppression during ASD sensory overload, wherein there is over-activation of sensory cortices. **Lower left:** Population multiunit activity across different cortical layers during deep-layer-specific deactivation of PFC with GABAA receptor agonist muscimol. Decreased activity represented in blue. Drug spread is contained within layers below layer 4 (L4). **Lower middle:** Deep layer deactivation of PFC reduced spike-related information (proportion of explained variance, PEV) related to visual identity of stimuli, especially during predictable trial blocks when there are stronger feedback prediction signals. **Lower left:** Schematic representation of the effect of removing feedback prediction signals to visual area V4. Deep layer PFC deactivation results in reduced spike-related information.

project tests this model by deactivating the deep layers of prefrontal cortex and examines the effects on visual cortex. Preliminary results show that deep layer deactivation decreases the spiking information in visual area V4, especially during the presentation of predictable stimuli. The goal of this work is to identify a circuit that contributes to sensory overload in ASD and perhaps inform future treatment strategies.

Awards and Recognitions

Lei Jin
New position:
Principal Investigator (PI) at Lingang Laboratory, Shanghai, China

Elizabeth Norton
Tenure and promotion to Associate Professor of Communication Sciences and Disorders, Northwestern University

Seng Bum Michael Yoo
New position:
Tenure-track Assistant Professor at the Institution of Basic Science (IBS), Department of biomedical engineering, Sungkyunkwan University

Anila D'Mello
New position:
Assistant Professor and Jon Heighten Scholar in Autism Research, Department of Psychiatry and O'Donnell Brain Institute, UT Southwestern

Danielle Tomasello
New award:
the Rett Syndrome Foundation Fellowship

Upcoming Events: Fall 2022

Colloquium Series

SEPTEMBER

14 - Meng-Chuan Lai, M.D., Ph.D.
University of Toronto

OCTOBER

12 - Kate O'Connor-Giles, Ph.D.
Brown University

26 - Anne E. West, M.D., Ph.D.
Duke University

NOVEMBER

30 - Juan Carlos Izpisua Belmonte, Ph.D.
Salk Institute

DECEMBER

7 - Michael Long, Ph.D.
New York University

General Info:
Time: 4PM–5PM, *reception to follow*
Hybrid Location: Singleton Auditorium, 46-3002 + YouTube Stream, *registration required*

Lunch Series

September 23, 2022 – **Sajal Sen, Ph.D.**
Simons Postdoctoral Fellow, Alan Jasanoff Laboratory, MIT

October 21, 2022 – **Seng Bum Michael Yoo, Ph.D.**
Past Simons Postdoctoral Fellow, Mehrdad Jazayeri Laboratory. Current position: Assistant Professor, Sungkyunkwan University

November 18, 2022 – **Sophie Bridgers, Ph.D.**
Simons Postdoctoral Fellow, Laura Schulz Laboratory, MIT

December 2, 2022 – **Pawan Sinha, Ph.D.**
Professor, Department of Brain and Cognitive Sciences, MIT

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

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, as well as events that reach a wide audience.

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

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