The Simons Center for the Social Brain Newsletter

Fall 2023

SCSB
Simons Center
for the Social Brain

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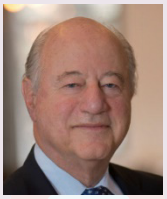
Upcoming Events: Fall 2023

Colloquium Series

September 13
R. Todd Constable, Ph.D.
Yale University
Host: Ev Fedorenko



October 4
Gerald Fischbach, M.D.
Simons Foundation
Host: Mriganka Sur

October 25
Stefano Anzellotti, Ph.D.
Boston College
Host: Rebecca Saxe

November 8
Sundari Chetty, Ph.D.
MGH, Harvard Medical School
Host: Dara Manoach

December 6
Moriel Zelikowsky, Ph.D.
University of Utah
Host: Steven Flavell

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

Lunch Series

September 8
Ruidong Chen, Ph.D.
SCSB Postdoctoral Fellow,
Mehrdad Jazayeri Laboratory

September 29
Chenjie Shen, Ph.D.
SCSB Postdoctoral Fellow,
Guoping Feng Laboratory

October 20
Sajal Sen, Ph.D.
SCSB Postdoctoral Fellow,
Alan Jasanoff Laboratory

November 17
Tamar Regev, Ph.D.
Postdoctoral Fellow,
Ev Fedorenko Laboratory

December 15
Alex Major, Ph.D.
SCSB Postdoctoral Fellow,
Earl Miller Laboratory

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

Targeted Project:

Mitigating sensory overload with closed-loop stimulation

by Earl Miller

The human brain is continually predicting what will happen next. This is to avoid being overwhelmed. It filters out expected information, which isn't informative. However, when unexpected events occur, our brain needs to adjust its predictions. When this prediction system doesn't work correctly, it could explain some aspects of autism, where individuals can become overwhelmed by sensory input, making it challenging to understand social cues, learn, or communicate.

Recent evidence emphasizes the crucial role of neural oscillations, or brain waves, in this process. Alpha/beta waves seem to assist in providing feedback for predictions, while gamma waves control the transmission of prediction errors. Sensory overload results from an imbalance in these waves, where excessive forward-propagating gamma waves dominate over the feedback-driven alpha/beta waves. Individuals with autism exhibit changes in both alpha/beta and gamma bands, affecting how they process prediction errors.

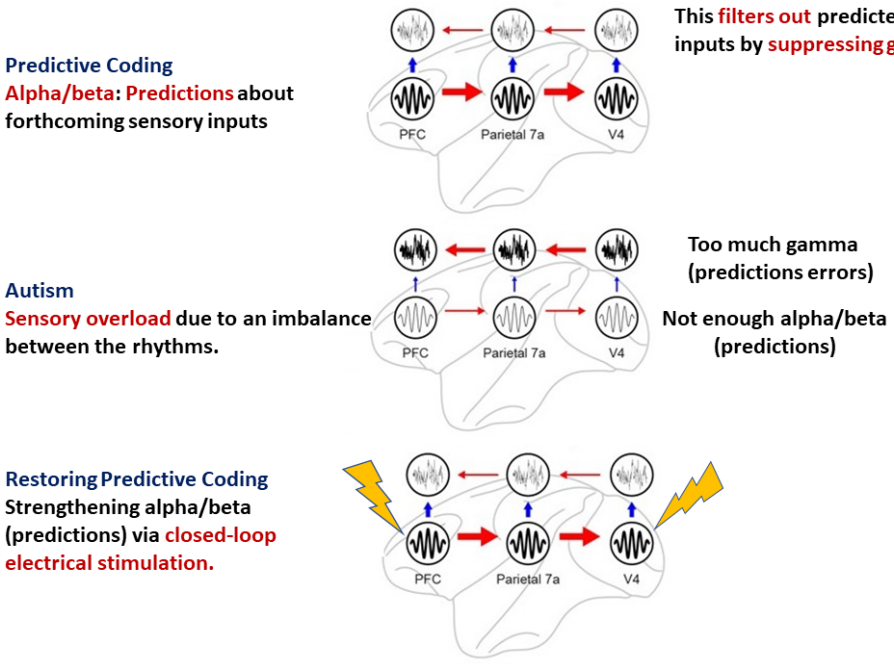


Figure 1. Neural correlates of predictive coding and its manipulation. In Predictive Routing, predictions carried by alpha/beta signals target posterior representations of the predicted stimulus (top). There are weak alpha/beta prediction signals to representations of unpredicted stimuli (violations, middle). By strengthening alpha/beta signals (bottom), we can strengthen predictions and mitigate sensory overload.

We're conducting research with macaque monkeys and marmosets that have a shank3 genetic deletion, a genetic model linked to Phelan McDermid Syndrome and autism. We are studying and directly manipulating their brain waves. Concurrently, we are also studying children with autism to assess whether their brain waves differ. Our ultimate goal is to develop a non-invasive closed-loop stimulation approach, combined with training, to enhance predictive coding and alleviate sensory overload in humans for therapeutic purposes.

Our research team comprises **Robert Desimone** (Director of the McGovern Institute and Professor in the Department of Brain and Cognitive Sciences at MIT), **Earl K. Miller** (Picower Professor of Neuroscience in the Picower Institute for Learning and Memory and the Department of Brain and Cognitive Sciences at MIT), and **Charles Nelson** (Richard David Scott Chair in Pediatric Developmental Medicine Research at Boston Children's Hospital).

Postdoctoral Fellows

Welcome to new 2023 SCSB Fellows!

Amrita Lamba, Ph.D.

Project: Social Learning and Inference Mechanisms in Asymmetric Social Exchanges

Laboratory: Rebecca Saxe, Ph.D.

Ph.D. from: Brown University

Hobbies: Piano, scrabble, and baking

Lace Riggs, Ph.D.

Project: Circuit mechanisms underlying autism-related anxiogenesis

Laboratories: Guoping Feng, Ph.D. and Fan Wang, Ph.D.

Ph.D. from: University of Maryland School of Medicine

Hobbies: Organizing, graphic design, plant keeping, and music

Gabriel Stine, Ph.D.

Project: Prediction and learning in the cerebello-thalamo-cortical pathway

Laboratories: Mehrdad Jazayeri, Ph.D. and Pawan Sinha, Ph.D.

PhD from: Columbia University

Hobbies: Tennis, snowboarding, and guitar

Simons Postdoctoral Fellows: Profile

Sophie Bridgers, Ph.D. | Past Simons Fellow, Laura Schulz Lab | Research Scientist at Google DeepMind

Project Title: Intentional Misunderstandings: How goal ambiguity and trade-offs between needs inform social compliance across development and neurodiversity

Finding and exploiting loopholes, a possible but unintended interpretation of a rule or request, is a familiar facet of fable, law, and everyday life. A child may respond to their parent who says "It's time to put the tablet down" by continuing to play with the tablet after physically putting it down on the floor. Engaging with loopholes requires a nuanced understanding of goals, social ambiguity, and value alignment. Loophole behavior might be of particular relevance for autistic individuals, who due to higher pragmatic and social uncertainty, may more often find themselves in situations where others perceive them as exploiting a loophole, when, in reality, they happened to parse the under-specification of a directive or request differently than what was expected. Greater uncertainty about others' goals may also lead autistic individuals to have difficulties understanding the loophole behavior of others.

Though loophole behavior appears to be common and consequential, the cognitive foundations of these creative workarounds, how humans learn to find them, and their function in social interaction is not well understood. In my fellowship work, we thus first set out to establish loopholes as an ecological phenomenon by asking parents about their

children's loophole behavior (N = 425 non-autistic children), and non-autistic adults about their own experience with loopholes (N = 501). We found that loophole behavior is indeed prevalent, emerging around five to six years of age, is rich and spans domains, and that people often exploit loopholes in situations of goal conflict (Study 1). In two experiments, we found that non-autistic adults (N = 360) also believe that loophole behavior will cause the recipient to be less upset and more amused than non-compliance (Study 2; Figure 1), and they predict others will exploit loopholes when people's goals are in conflict and the person giving the directive has the authority to exact punishment (Study 3). Children (N = 108 4- to 10-year-olds) also think loopholes will lead to less trouble with their parents than non-compliance (Study 4; Figure 2), and from five to ten years of age (N = 60) are increasingly able to generate loopholes on the spot given a request (Study 5; Figure 2). In our ongoing work, we are exploring the development of loophole behavior in autistic populations. Preliminary results suggest that high-functioning autistic adults may reason about loopholes similarly to non-autistic adults and that the development of loophole behavior in children may be protracted (emerging around 8 years in autistic populations vs. 5 years in non-autistic populations). Future research with larger samples and more rigorous diagnosis information is needed to verify these preliminary results.

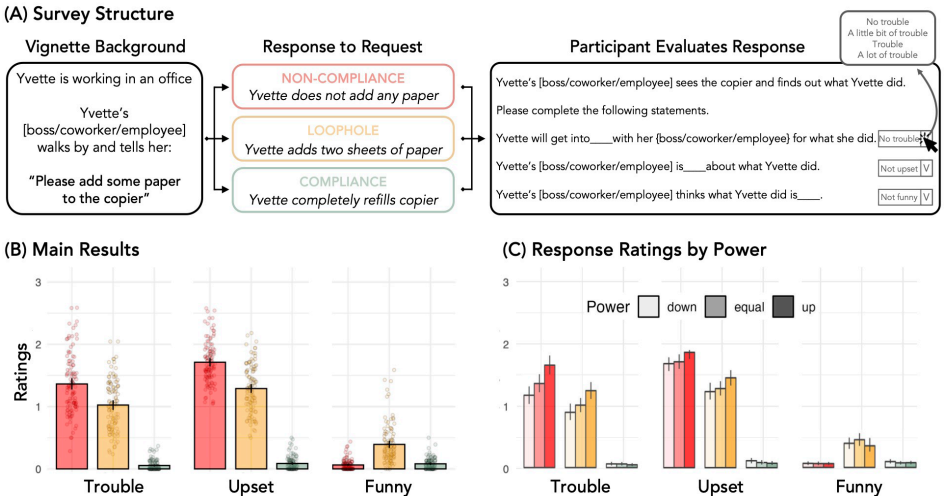


Figure 1. (A) Adults read vignettes where a person (the producer) complied, exploited a loophole, or did not comply in response to a directive. Adults rated the degree to which (1) the producer would get into trouble, (2) the recipient was upset, and (3) the recipient found the behavior funny. The relationship between producer and recipient varied, with the recipient in a lower (Down), equal (Equal), or higher (Up) position of power. (B) Mean ratings of Trouble, Upset, and Humor (Funny) for non-compliance (red), loophole (yellow), and compliance (green). (C) Mean ratings of Trouble, Upset, and Humor for each behavior at each level of power (Down (light), Equal (medium), Up (dark)).

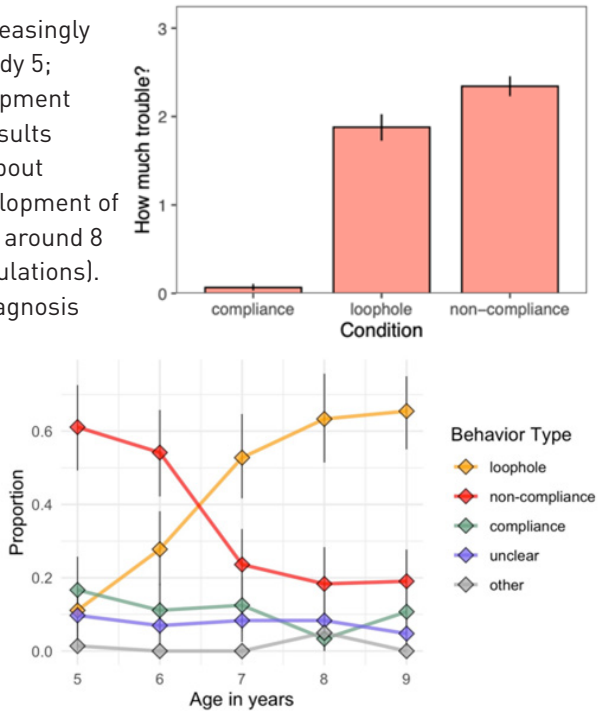


Figure 2. Top: Children's (4 to 10 yrs) ratings of Trouble for compliance, loophole, and non-compliance on a 4-point scale from "no trouble" (0) to "a lot of trouble" (3). Bottom: Proportion of children (5 to 10 yrs) who generated a loophole (yellow), non-compliant (red), compliant (green), unclear (purple), or other (grey) response given a parent's request.

In the same way that visual illusions shed light on the implicit assumptions and computations of the visual system, loopholes offer a different lens for the typical workings of communication and cooperation, making them a useful case study to better understand neurotypical development, as well as development in neurodiverse populations. Loopholes integrate language understanding, rational planning, and value alignment in a goal-directed context with real social stakes. Variance across development and neurodiverse populations could be due to differences in any one of the basic ingredients for loophole behavior, and in how they are combined. In collaboration with Dr. Peng Qian, we have implemented a computational model that formalizes and makes precise these ingredients, which will help us get a better handle on their various contributions to behavior and provide testable hypotheses for loci of change in development and of potential difference in autism.

Simons Center MSRP Summer students

Tsehai Boucaud | Senior, University of Central Florida

Laboratory: Nancy Kanwisher, McGovern Institute for Brain Research, MIT

Project: Using deep neural network (DNN)-based encoding models to reveal functional dissociations with the human visual scene processing network

Keywords: fMRI, Machine Learning, Cognitive Neuroscience, Vision, data analysis, DNN-encoding models

As a student in the Kanwisher Laboratory, my research focused on understanding the functional roles of two brain regions involved in visual processing, namely the parahippocampal place area (PPA) and the occipital place area (OPA). These regions are known to respond selectively to visual scenes as compared to other stimuli, but their specific functions have not been fully explored.

Tsehai and Nancy Kanwisher.
Photo courtesy of Mandana Sassanfar

To investigate this, I adopted a data-driven approach and trained deep neural network-based encoding models to understand the unique characteristics of the PPA and OPA. Using functional magnetic resonance imaging (fMRI), I found that these models accurately predicted responses to new stimuli held-out from the training data in both the PPA and OPA.

The findings were highly specific to each brain region, as the model-PPA performed better in predicting PPA data than OPA data, and vice versa for the model-OPA. This demonstrated the predictive power and specificity of the encoding models for each region.

Tsehai presenting at the MSRP Poster Session.
Photo courtesy of Mandana Sassanfar

I used the encoding models to generate hypotheses further to explore the functional differences between the PPA and OPA. By analyzing predictions on a large dataset of 1.5 million images, I found that scenes strongly drove both the PPA and OPA, providing strong validation for their scene selectivity.

Additionally, the models helped identify specific image features that differentiated the activation patterns of the PPA and OPA. Images with clear rectangular spatial layouts strongly activated the PPA, while images depicting the inside of airplanes or buses with ordered, repeating objects and a clear navigational path activated the OPA.

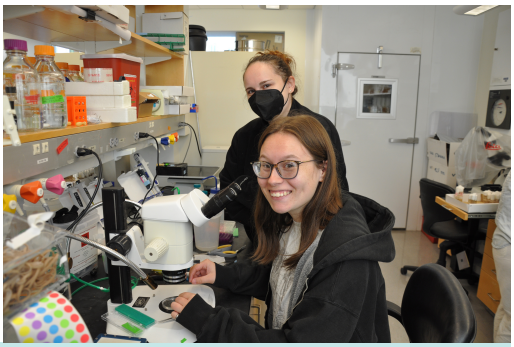
Moving forward, I plan to test these model-predicted images in the brain with fMRI to validate and further explore the findings. This research has provided computationally-precise models of the PPA and OPA, shedding new light on the functional distinctions between these brain regions involved in visual scene processing.

Payton Dupuis | Post-baccalaureate, MIT

Laboratory: Troy Littleton, Picower Institute for Learning and Memory, MIT

Project: Comparing synaptic development and maintenance pathways in larvae versus those in older adult Drosophila neuromuscular junctions.

Keywords: Drosophila Melanogaster, aging, neuromuscular junction, active zones, adult versus larvae



Payton with her mentor, Jessica Sidisky.
Photo courtesy of Mandana Sassanfar

This summer, I was a MSRP student in the Littleton lab where I worked under the supervision of Postdoctoral researcher Jessica Sidisky. I conducted an adult GAL4 motor neuron driver screen using known larval drivers to see if the same driver could be used in the adult ventral abdominal muscles. To do this, known larval drivers that are known to target type one and type two motor neurons were used and aged into adulthood. Common dissection techniques were used to be able to isolate the abdominal muscles. The preps were then fixed in paraformaldehyde and subjected to immunostaining for the muscle tissue and the neuronal membrane. The staining of the muscle tissue allows for verification of location while looking at the prep under confocal microscopy. As the driver has an RFP tag attached to the specific gene of interest, when using a blue light, the tag is excited and RFP can be seen. Using the RFP and the staining of the neuronal membrane, it was possible to determine if the driver was effective in the ventral abdominal muscles if the two overlapped in imaging. I found two drivers were successful in this region of the adult fly, (GMR65E07)-GAL4 and (GMR57F07)-GAL4. (GMR57F07)-GAL4 was a driver created for the DH31 gene, diuretic hormone 31 involved in courtship of the fly, and was thought to light up in type two boutons. (GMR65E07)-GAL4 was a driver created for the DH44 gene, involved in several processes, and was thought to light up in glia. Specific antibodies for type two boutons and glia will be used to stain the drivers to test if the hypothesized locations of expression were correct.

Payton presenting at the MSRP Poster Session.
Photo courtesy of David Orenstein

MSRP Poster Session, August 2023.
Photo courtesy of Nina Thirakoune

News & Announcements

Simons Postdoctoral Fellowship opportunities

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

Fall 2023 deadline: Friday, September 29, 2023
Spring 2024 deadline: Thursday, February 29, 2024

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. *We strongly encourage applications from under-represented and under-served backgrounds.*

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 to Diversity, Equity, Inclusion & Justice (DEIJ), visit here: https://bcs.mit.edu/diversity-equity-and-inclusion-bcs-and-building-46/outreach. To learn more about our postdoctoral resources that support personal, family, and community life here at MIT, visit here: 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, 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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