

I've been thinking about the human brain for as long as I can remember.

As a young child growing up in the curiously-named town of Braintree, Massachusetts, I had a hypothesis – that people's minds grew among the branches of special "brain-trees," and that each person's brain was specially harvested just for them. Like many ideas that three-year-olds have, it was highly imaginative and not physically possible. But the flawed logic in my strange idea is remarkably akin to some of the current leading theories about how the brain works. The philosopher John Searle writes, "The philosophy of the mind is unique among contemporary philosophical subjects in that all of the most famous and influential theories are false." To date, no theory can fully explain the intricacies of human cognition. I believe that through the application of neuroimaging technologies, the scientific community is moving ever closer towards a concrete explanation of the mind's inner workings. During my undergraduate research, I've had the opportunity to explore the brain through both positron emission tomography (PET) and functional magnetic resonance imaging (fMRI). Through the Graduate Program for Neuroscience at Boston University (BU) and a career in research, I plan to find creative new uses for neuroimaging technologies, with the hope that someday we will fully understand how neural mechanisms give rise to memory, executive functioning, and consciousness.

Having the opportunity to run experiments solidified my passion for research.

As an undergraduate research assistant in Dr. Richard Chechile's Memory and Cognition Lab at Tufts University, I worked with a team of researchers to decipher the mechanisms by which memory is encoded. I specifically chose to work in this lab because Dr. Chechile shared my interdisciplinary interests in both psychology and mathematics. As a double major in Computer Science and Cognitive & Brain Science, I was eager to learn about the potential uses of STEM research methods for studying the human brain. As my introduction to hands on experiments, the research in Dr. Chechile's lab inspired me to think more deeply about how memory works. I left lab meetings pondering how mathematical models could be used as evidence in support of models of cognition and was inspired to spend my free time searching the web for related research. Still, I yearned for a link not only from behavior to mathematics, but also to the biochemical signals and neural underpinnings present in the human brain.

Through neuroimaging research, I built an interdisciplinary knowledge base.

In search of such a connection, I sought to gain research experience in human neuroimaging, and began working at the Martinos Center for Biomedical Imaging at Massachusetts General Hospital (MGH) in the lab of Dr. Jacob Hooker. There, I explored the brain through positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and simultaneous MR/PET imaging. My first few projects with Dr. Hooker's group involved improving existing software tools for kinetic modeling of PET radiotracers. Through these projects, I quickly learned new computer programming skills, built scientific connections in the neuroimaging community, and immersed myself in a new field of literature previously unknown to me. Additionally, I gained valuable experience sharing my work with colleagues during short lab-meeting presentations and published my first scientific journal article¹. Eager to share my work and newfound imaging-knowledge with colleagues in Psychology at Tufts, I presented at Tufts' Annual Undergraduate Research Symposium.

I am always searching for new technologies to utilize in brain research.

When tasked with completing a term-project in my Computational Biology course at Tufts University, I immediately turned to my prior research in Dr. Hooker's lab. Although the

Computational Biology course focused on genetics, I believed that similar computational methods could be applied to brain imaging research. After all, whether it is a genetic sequence or a brain image being analyzed, a computer only sees information stored as bits. Using machine-learning techniques from my Computational Biology class and image-processing skills I had developed in Dr. Hooker's lab, I created a computer program that could differentiate between the resting state fMRI scans of brains with schizophrenia and those of matched controls. By capitalizing on open-source data I found freely available online and the interdisciplinary connections I had made across institutions, I built this unique research opportunity, and explored new ways for Computer Science to be applied to brain imaging research.

After a year in Dr. Hooker's lab I was comfortable performing routine analyses and regularly assisted other lab members with their neuroimaging data analysis. One such side project in which I helped validate the efficacy of a new PET radiotracer led to my second peer-reviewed journal article². Eager to grow as an independent researcher, I decided to remain in the lab during my final year of undergrad to complete a Senior Honors Thesis. My thesis project capitalized on resources available through both MGH and Tufts, and made use of MGH's simultaneous MR/PET scanner. For the project, I was interested in further developing functional-PET imaging: a method of FDG-PET imaging meant to mimic the type of functional imaging done with fMRI. My project acted as a small pilot study and resulted in a short presentation at Tufts, a manuscript-style publication catalogued in the Tufts library, and a poster presented at Tufts' annual Cognitive and Brain Sciences student symposium. My project also earned Thesis Honors and was a factor considered when I was awarded the Joanne Mary Sullivan Prize from the Tufts Psychology department at graduation.

In graduate school I will continue to conduct interdisciplinary research.

After graduating from Tufts last spring, I began a PhD program in Computational Neuroscience at BU. Currently, I am completing laboratory rotations before I officially join the lab of Dr. Chantal Stern. I chose to attend BU because there is a strong community of both Neuroscientists and Computer Scientists working together to better understand the brain. Dr. Stern and her colleagues were recently awarded a major instrumentation grant from the National Science Foundation, which funded the installation of a new 3T MRI scanner at BU. The scanner is housed in an interdisciplinary facility where Dr. Stern's lab is located. The building is designed to catalyze collaborations across fields and is home to groups studying Computer Science, Biology, and Biomedical Engineering, whom I look forward to collaborating with. Dr. Stern's previous work in human neuroimaging has capitalized on hypotheses inspired by previous computational models. This work reminds me of the mathematical models of memory that first piqued my interest in brain science when I worked in Dr. Chechile's lab at Tufts. As a graduate student, I plan to develop new computational models and neuroimaging tasks to improve our understanding of memory and executive function. I am repeatedly fascinated by the ability of mathematics to predict how our minds work and I am excited that brain imaging technologies can both test and inform these hypotheses.

I am committed to the art of making science accessible.

In addition to contributing to the development of neuroscience through research, I am committed to helping this field grow on a societal level. One of my favorite things about conducting brain research is that it can be incredibly relatable to the general public. In Dr. Hooker's lab last summer, I volunteered to help with an open house event. In collaboration with the Alzheimer's Association, this event offered the general public the opportunity to hear from researchers first-hand and to see the research facilities up-close and personal. Paired with a blog

and Twitter account that lab members regularly contribute to, Dr. Hooker encourages all lab members to engage with their research outside of the lab and in the context of society as a whole. During my future research career, I plan to take the same “outside-in” approach to research. I believe that sharing science with the public and with people from other disciplines allows one to engage with research questions from new perspectives, and to ask more innovative questions.

To increase the number of people who can engage with science, I am an advocate for increased access to higher education. I believe that bringing diverse perspectives into science helps us consider empirical questions from different points of view. As a contributing author for *Enigma: Tufts Independent Data Journal*, I worked with a group of computer scientists, graphic designers, and journalists to conduct a study examining student attitudes surrounding financial aid. We found that financial aid status and socioeconomic status are both strongly associated with Tufts students’ employment status, involvement in clubs, and choice of academic major. We shared our findings in an online publication and at our club’s biannual symposium, inspiring follow-up articles in the school newspaper and a dialogue between students and administrators. This work inspired me to recently join Big Brothers Big Sisters of Massachusetts Bay as a mentor for a Boston public high school student who plans to apply to college.

By increasing diversity in STEM fields, we can ensure that STEM research has a greater positive societal impact. In some respects, brain science has suffered from a dark history – from the classification of homosexuality as a mental disorder in the DSM III to the performance of lobotomies on transgender individuals. I believe that increasing STEM diversity can help to avoid many of the negative impacts science can inadvertently have. Last year I was one of 100 LGBTQ individuals selected from an international pool of applicants to attend a conference at Stanford University. The meeting aimed to increase the diversity of individuals in STEM fields and to form a network of individuals committed to this cause. I had the opportunity to present some of my brain imaging research to attendees in the form of a TED-style talk and started some great conversations about LGBTQ representation in the field of neuroscience. I walked away from this event with a renewed passion for increasing diversity in and access to STEM education. Many of the conference organizers are graduate students in STEM fields, and I plan to become involved in planning next year’s conference now that I am a graduate student as well.

I am passionate about finding creative solutions for science’s most difficult problems.

In graduate school, I plan to dedicate the next phase of my career to pursuing answers to questions about the human mind and brain. With funding from the NSF GRFP, I will be able to ask novel neuroscience questions and to challenge standard ways of thinking. Throughout my career, I plan to bring my own unique perspective to the table and to share my research with people outside of my field as well as the general public. Eventually, I hope to become a professor in neuroscience with my own neuroimaging lab. Through a diverse team of researchers from various scientific fields and cultural backgrounds, I hope to produce sound scientific research with positive societal implications. By taking advantage of multiple imaging modalities and the latest computational methods, I hope to start answering questions about the mind that philosophers have posed for centuries. With luck, I will someday explain to my own child that although brains don’t grow on trees, we do know how they work.

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The Neural Computations of Reasoning Behavior: a Neuroimaging & Modeling Approach

Introduction: Complex reasoning behavior is uniquely human. One task that is used to investigate reasoning behavior is the Raven’s Progressive Matrices (RPM) task¹. Previous neuroimaging research using the RPM task suggests that successful reasoning ability in humans is associated with increased activity in the basal ganglia, prefrontal cortex (PFC), and parietal cortex²⁻⁵. Independently, computational researchers have created models of RPM task performance⁶⁻⁸. While these models have a strong basis in theory, future iterations could benefit from the biological information offered by neuroimaging. **I propose an fMRI study to investigate the neural correlates of rule learning and integration during reasoning (Aim 1). Imaging results from the task will inform the development of a biologically-based computational model of RPM task performance, bridging the gap between current computational models and studies of brain activity during reasoning (Aim 2).**

Background: During the RPM task, participants reason about elements in a 3x3 grid and identify the element that belongs in the bottom right field, which is intentionally left blank (see Figure 1). Successful completion of the task requires participants to integrate multiple rules that describe the relationship between items in both rows and columns of the grid. Neuroimaging work suggests that caudate activation may be related to the working-memory and updating demands of the task²⁻⁴. Activity in the parietal lobe is thought to be associated with the manipulation of spatial information or with visual attention in the task²⁻⁴. Studies have also reported activity in prefrontal regions including rostralateral, dorsolateral, and ventrolateral PFC, which are related to working memory, goal maintenance, and the retrieval of semantic relationships between task stimuli respectively²⁻⁴.

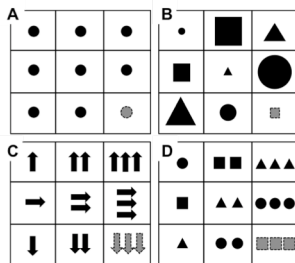


Fig. 1. RPM Rule Types. Solutions require no rule (A); one type of rule that is either a set rule (B) or a sequence rule (C); or both types (set & sequence) (D). Solutions in gray.

Across studies, activity patterns have been reported consistently in caudate and parietal regions, but inconsistently in prefrontal regions²⁻⁴. Because the frontal cortex is connected anatomically to the caudate through a series of ordered, parallel loops, it is unlikely that the observed inconsistencies in prefrontal activation are strictly due to noise^{2,9}. Models have proposed the existence of several computationally distinct *rule types* that can govern the relationship between elements in the RPM task^{6,7}. However, no imaging study of the RPM task has taken these different rule types into account. It is possible that conflicting reports of prefrontal activation patterns are due to variations in the rule types of stimuli designed for each study. I predict that through a carefully designed fMRI study, we can observe “ensembles” of prefrontal activation that are specific to each rule type. Through computational modeling, I will propose a mechanism by which the caudate preferentially “recruits” these ensembles depending on the computational task.

Specific Aim 1: Identify neural correlates of rule integration using fMRI. I propose a study using a modified version of the RPM task to investigate how individually learned rules are combined and represented in the human brain. Trials will require participants to either match a stimulus (Figure 1a), to implement a single rule (Figure 1b,c), or to implement two distinct rules simultaneously (Figure 1d). Rule types include *set* rules, which mandate that each row or column contain a specific collection of items (e.g. each row must contain a circle, a square, and a triangle) (Figure 1b) and *sequence* rules, which describe a consistent change between items from one field to the next (e.g. the number of arrows increases by one as you travel across a row) (Figure 1c). Participants will complete two visits to the lab. During the first visit, they will learn

the modified RPM task. During the second visit, they will undergo a one-hour fMRI scan while completing trials of the modified RPM task. The task is based on earlier work,² and will be piloted prior to imaging to ensure that each trial can be solved in a short amount of time and to control for trial-difficulty.

Using multivoxel pattern analysis, I will compare activation patterns for each of the four task conditions, and identify brain regions uniquely involved in each rule type, as well as regions necessary for integrating multiple rules. **I predict that activation patterns in the caudate and parietal cortex will be consistent across conditions, and that activation of unique prefrontal ensembles will vary with rule type. When multiple rule types are involved, I predict an activation pattern composed of the activation patterns observed in each subtype¹⁰.**

Specific Aim 2: *Develop a biologically-based computational model for the RPM task.* I propose an updated computational model of RPM task performance implemented using the Neural Engineering Framework (NEF) developed by Eliasmith¹¹. Using NEF, one can simulate computation in specific brain regions by altering neuron-types and cell counts^{7,11}. Based on the activation patterns observed in Aim 1, I will design a model to simulate the representation of single and multiple rules during the RPM task. To test the model, I will compare its performance on the modified RPM task to behavioral data collected in Aim 1. Because it is implemented using the NEF, “virtual lesions” can be created in this model simulating damage to certain brain regions. Perturbing the model in such a way would allow us to make predictions about the unique contributions of each brain region to the task.

Broader Impacts: This proposal seeks to bridge our understanding of human reasoning behavior across neuroimaging and computational modeling. The proposed imaging study will identify brain regions involved in reasoning behavior and the cortical system responsible for rule integration. Subsequent modeling will contribute to a better understanding of reasoning behavior, anchored in biologically based results from neuroimaging. Flexible application of the proposed model includes investigating how reasoning ability varies with development, age, or across learning. Moreover, this computational framework could be applied to artificial intelligence (AI). Currently, a major concern in the field is the creation of robots and other AI systems that can make informed decisions and apply learned-rules to situations in ways that are similar to humans. After the study has been published, all imaging data and code for computational models will be made freely available online. This study also provides valuable training in cognitive science and human neuroimaging, both to me and to the undergraduate students I will mentor in the lab. I will also be active in K-12 educational outreach events with the Stern Lab including Summer Pathways (BU high school STEM program) and Boston’s *Show me the Science* events.

Feasibility and Support: This work will be conducted in the lab of Dr. Chantal Stern at Boston University. Dr. Stern is the director of the Cognitive Neuroimaging Center (CNC), located in the Kilichand Center for Integrated Life Sciences and Engineering, a space specially designed to catalyze collaborations across fields. Scanning and behavioral piloting for this project will take place at the CNC, which houses a new NSF-funded 3T Siemens Prisma MRI scanner as well as cognitive testing rooms. Computational modeling will be done in collaboration with Dr. Mike Hasselmo, Dr. Marc Howard, and Dr. Chris Eliasmith.

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