Research Program Summary Cory Inman, Ph.D.

Emotion and memory for the important moments of life serve as the foundation for our sense of self in the moment and through time. People are stripped of their identity when control of these abilities is lost due to neural disease. To fully understand and control the neural systems underlying emotion and memory, we must study these behaviors in humans in complex, real-world settings. However, traditional methods of studying the human brain, like functional magnetic resonance imaging (MRI) and electroencephalogram (EEG), are limited in their ability to assess and manipulate the precise temporal and spatial patterns of neural activity in deep brain structures, like the amygdala and hippocampus, which mediate these fundamentally human behaviors. A more holistic approach to the study of emotion and memory in humans is needed. My laboratory aims to dissect the emotion and memory functions of the human brain with three complementary lines of research aimed at: 1) *understanding* the dynamic organization of neural circuits from single neurons to whole brain networks during emotion and memory processes using human intracranial electrophysiology and functional neuroimaging, 2) *modulating* the activity and organization of these networks to gain control of emotional experience or enhance memory using direct brain stimulation in humans, and 3) *translating* these laboratory-based discoveries to neuromodulation therapies that can restore functional behavior in real-world settings to help those suffering with neural disorders. My research draws upon theoretical perspectives and experimental techniques from multiple fields, including network neuroscience, cognitive science, neuroengineering, human neurophysiology, computer science, and neuromodulation. My research program is constructed upon studies using behavioral, neuroimaging, and neuromodulation approaches to study how the brain operates in traditional laboratory experiments with the explicit objective of gradually working toward neuroscience studies of real-world cognitive behaviors that extend from laboratory-based discoveries. With the promise shown by my neuromodulation studies aimed at understanding and treating a variety of memory and mood disorders (e.g., Inman, Manns, et al., 2018, *PNAS*; Riva-Posse, Inman et al., 2019, *Brain Stimulation;* Stangl, Topalovic, Inman et al., 2021*, Nature*), working towards neuroscientific studies of real-world cognition is the key translational step needed to push our neuroscientific insights from the laboratory to restoring real-life cognitive function in those suffering from devastating disorders of emotion and memory.

In the sections below, I describe my past and current contributions to the field and look ahead to specific studies my laboratory will perform to accomplish my goals to *understand* neural networks underlying emotion and memory functions, *modulate* these networks, and *translate* our discoveries to explore and treat real-world cognitive disorders. This work will ask fundamental questions such as: How do we study the neural formation of episodic memories in rich, complex real-world settings? How does the human brain prioritize specific experiences for long-term memory storage? What is the role of the human amygdala and emotion in this process? How do we modulate these systems with direct brain stimulation to treat debilitating disorders? Can we enhance memory for real-world experiences through direct stimulation of the human brain?

Past, Current, and Future Research

Modulating emotion and memory networks with deep brain stimulation (DBS). My work in DBS for depression (Riva-Posse, Inman, et al., 2019, *Brain Stimulation*) led to pursuing an opportunity to perform large-scale electrophysiology and DBS studies in patients with drug-resistant epilepsy undergoing intracranial monitoring to identify brain regions that caused their seizures. For my primary postdoctoral project, I developed a series of experiments examining the cognitive, emotional, and physiological effects of direct brain stimulation to the human amygdala. In our first studies, we examined the effects of changes in measures of autonomic reactivity (e.g., skin conductance and heart rate) and the safety of human amygdala stimulation. This work demonstrated that amygdala stimulation in humans was safe and effective for modulating autonomic reactivity in a dose-dependent manner (Inman et al., 2018b, *Neuropsychologia)*. Pairing these insights with the known functions of the amygdala in enhancing memory for emotional experiences, I developed a study with Dr. Joseph Manns to test whether direct amygdala stimulation could enhance declarative memory for neutral stimuli without inducing any changes in emotion physiology or experience. In this study, we found that brief electrical stimulation to the human amygdala reliably improved long-term recognition memory for images of neutral objects without eliciting an emotional response. This memory enhancement was accompanied by neuronal oscillations during retrieval that reflected increased interactions between the amygdala, hippocampus, and perirhinal cortex (Inman, Manns, et al., 2018, *PNAS*). This finding demonstrates that the human amygdala plays a *causal* role in the prioritization of specific declarative memories for long-term consolidation. This study also suggests that amygdala-mediated memory enhancement (AMME) is a unique neuromodulation technique to enhance declarative memory, unlocking new approaches to dissecting human emotion and memory.

After the success of our amygdala stimulation studies, I led the writing and construction of an NIH R01 grant application to further examine the “Mechanisms of amygdala-mediated memory enhancement in humans” that was funded in late 2020 (R01MH120194; $750,347 at Utah). Since receiving this grant, we have collected amygdala stimulation data on over 50 intracranial EEG recording patients across both the Utah and Washington University sites. Throughout the five completed years of this grant, I have led all project meetings and research efforts. My postdoctoral fellow is directly responsible for the day-to-day operation of this project and my graduate students have directly contributed to building experiments in service of the aims of this grant. In this grant, we have leveraged amygdala stimulation to interrogate connections to regions of the MTL network to manipulate neural network activity and enhance memory using intracranial electrodes in awake neurosurgery patients to isolate the contribution of the human amygdala to neural dynamics of memory. My lab and I have led the research efforts both at Utah and across all 3 study sites. This includes the mentorship of a postdoctoral fellow and 3 graduate students. In analyses of one specific aim, we’ve found that direct stimulation to the

human amygdala preferentially enhances memory for images of objects versus scenes (Wahlstrom et al., Under Review, Communications Biology). Martina Hollearn has contributed to this project by analyzing and publishing on individual differences in memory modulation (Hollearn et al., 2024). As part of his dissertation, Justin Campbell has published two papers related to the effects of direct brain stimulation to the amygdala on evoked potentials and single unit activity throughout the human brain (Campbell et al., 2025, Journal of Neuroscience; Campbell et al., 2025, eLife). My lab published a review of human amygdala function in Neuron in the Summer of 2023 (Inman et al., 2023) and our grant team will submit a renewal of this grant to understand the mechanisms of amygdala-mediated memory enhancement this coming year. Our collaborators at Washington University have also published two papers using data collected in my lab on the amygdala's role in fear processing (Xie et al., 2025, Molecular Psychiatry) and a neural code for object representation (Wang et al., 2025, Nature Communications). Finally, I was honored to present this work in an invited symposium at the Organization for Human Brain Mapping Meeting in Brisbane, Australia.

Translating laboratory discoveries to understand and treat real-world cognitive disorders. In a second postdoctoral fellowship, I developed a neural recording and stimulation platform to perform real-world navigation and memory experiments using a suite of wearable and wireless 1st person experience sensors. The overall goal of this work is to establish techniques for *translating* DBS-based memory enhancement approaches to real-world environments and experiences. My lab's current research project based on these developments uses mobile recording of deep brain activity to examine how the brain parses our continuous, large-scale, real-world experiences into memorable episodes and will demonstrate a brand-new method for investigating the neuronal mechanisms underlying real-world human cognition and behavior (i.e., navigating a ¾ mile route around a college campus). The advantage of a wireless chronic implant in humans is that freely moving behaviors can be explored unlike in traditional neuroimaging and neuromodulation methods.

My lab was awarded an NSF Foundations grant from the Integrative Strategies for Understanding Neural and Cognitive Systems program to continue making this vision a reality in 2021 (NSF 2124252; $1,000,000). The goal of this project is to build and evaluate a system for exploring how the human brain processes information about the real-world environments we navigate every day. To accomplish this goal, we have directly recorded from the brain while participants navigate the real world, synchronously capturing information about their first-person experience through a set of sensors that encompass various human senses, including cameras, microphones, eye-tracking, movement-tracking, and physiological recordings. Neurosurgical participants with epilepsy who have an implanted neural recording and stimulation system used to control their seizures, mentioned earlier, have volunteered for our experiments and provided rare direct recordings from the human brain while they navigate a complex, real-world environment. We are analyzing rich sensor data from participants' first-person experiences using interpretable deep learning, in relation to neural data, to infer how changes in neural oscillations relate to changes in one's experience. We have completed all the aims of this project by synchronizing the human experience with neuronal events and estimating changes in brain dynamics around salient experiences, such as a participant getting lost. This involved developing a robust, portable framework to record and synchronize neuronal activity along with data from wearable sensors that represent a broad subset of human sensory channels. Working towards aims 2 and 3, we have collected in-depth hippocampal oscillatory data with 5 participants as they navigate the real world with our collaborators at UCLA. Analyses of this incredibly rich and valuable dataset have revealed important changes in deep brain activity that occur during real-world behavior. I have fortunately been invited to present our findings at prestigious meetings around the world, including the NIH BRAIN Initiative Meeting and the Interdisciplinary Navigation Conference. We are preparing to start collecting real-world brain data in Utah this Fall, but have been delayed by data-sharing agreement negotiations between the University and our industry collaborator (Neuropace). As part of aim 2, primarily undergraduate RAs in my lab have collected and analyzed over 300 participants' worth of behavioral event segmentation data on the first-person videos generated from this study using the psychology participant pool. My student, Wyatt Wilson, was awarded the Psychology Department's Outstanding Honors Thesis in Psychology in Spring 2023 for his Honors Thesis on this project and Sydney Josifek is continuing his work on these questions from new perspectives as an honors student. The platform developed and proven as part of this NSF grant that allows for neural recording, direct brain stimulation, and synchronization with external, wearable devices will open an entirely new area of research at the intersection of computer science, neuroengineering, cognition, and clinical neuroscience. These studies will launch and accelerate an emerging and pivotal area of research that will provide therapeutic interventions, *proven in the real world*, for participants afflicted with debilitating cognitive disorders. In service of this medium and long-term goal for my lab, I received a large, multisite (3 sites) NIH BRAIN initiative grant (R61MH135109) in 2024 to continue this work and create a novel, lightweight system for recording a person's first-person experiences in truly real-world settings (museums, gardens, hikes, etc.) in sync with direct brain recordings. Across all sites, we will receive $5,044,157 in total funding over 5 years, and I will lead this project as Principal Investigator. Since receiving the grant in March 2024, our progress has included initial development of the CAPTURE smartphone application with integration of eye-tracking and psychophysiological measures (EDA, PPG) with data collected on a smartphone. This platform is in Beta testing by my new Postdoctoral Fellow, Alireza Kazemi. Overall, we are well on our way toward realizing the INMAN lab's research program. These initial grants are encouraging endorsements of the potential of our lab's research program in the near- and long-term. I plan to submit an NSF CAREER Award this year to build on our initial research success. My students and trainees have made key contributions to these research aims and have developed their own research projects for publication. Through the tenure processes, I'm excited to continue working with my lab and collaborators to answer cognition and neuroscience questions that will now be possible to explore due to our innovations.