Introduction. Individuals are motivated to exert agency such that they feel their choices and actions allow them to control their external environment. Studies on causal learning show that as early as infancy, humans learn the relations between actions and their outcomes[1] and are able to use this knowledge to act as successful agents in their environment. Most existing literature on agency emphasizes comparing the outcome of one's own actions with their internal predictions of those actions[2-5]. However, these processes have been limited to sensory perception and stimulus-response learning, precluding the ability to explore the effects of agency on episodic memory[6] and how sequences of information which unfold due to causal actions drive brain regions to support memory.

Background. Exercising agency over learning environments has been shown to improve memory[7,8], even when the choices do not relate to the content of the to-be-learned items. Previous work from our lab gave participants a simple choice between two 'cards' which would reveal an unrelated item. Participants better remembered items that appeared as a result of their choice[9,10]. Further, this memory enhancement was driven by an interaction between anticipatory activation within the striatum, a region associated with causal actions and motivation, and hippocampal (HPC) engagement during encoding. While this shows how agency over a choice can positively affect memory for the outcome of a choice, it does not shed much light onto memory for the overall decision sequence.

To explore how agency over a series of events affects associative memory for the components of the sequence, I developed a task where participant's agency was manipulated via a choice. In the "game show" task, participants assisted contestants in choosing one of three doors which reveal a hidden prize. On each trial, participants saw a trial-unique contestant and either freely chose between the doors ("agency" trials) or selected a highlighted door ("forced-choice" trials). Unbeknownst to the participants, the prize image presented was predetermined. After completion of the task, participants completed a surprise retrieval task which tested memory for the contestants presented in the encoding task, which door they selected, and the outcome hidden behind the door in three separate, consecutive memory tasks.

Across two studies (study 1 n = 28; study 2 n = 131), which serve as the foundation for this proposal, participants showed enhanced memory for the contestants (p<0.001), constant-prize pairs (p<0.05), contestant-door pairs (p<0.01), and prize-door pairs (p<0.01). These results show that by manipulating participant's agency to select which door to open, we are able to enhance memory for cues as well as associative memory between cues and outcomes. However, these results do not discriminate whether agency enhances memory separately for each individual pair, or whether agency facilitates the binding of all associations into one integrated sequence. Follow-up analysis explored whether agency facilitates memory integration by examining whether there was an inter-dependence upon memory measures such that memory for one pair was dependent on memory for the other pairs. Indeed, we found memory for the contestant-prize pair was modulated by memory for recalling both the contestant-door and door-prize pairs (p<0.01). Further, this effect was significantly higher for pairs that occurred in agency trials vs the forced-choice trials.

Intellectual Merit. While I have established a paradigm that modulates associative memory via agency, it is still unclear how mesolimbic-hippocampal engagement supports this learning. Understanding the timescale of how these systems interact will inform us on how agency modulates encoding and connect human and animal research. Much of the existing human literature exploring mesolimbic contributions to memory focus on how phasic dopamine drives learning in response to reward feedback[11]. However, rodent research has shown hippocampal engagement during exploration prompts sustained ventral tegmental area (VTA) engagement leading to greater response feedback to the hippocampus[12]. I propose exploring these temporal dynamics within the same paradigm to address the gaps in these two lines of research and contribute to the translation of rodent-to-human research. Using neuroimaging techniques, the current research seeks to: 1) examine sustained mesolimbic during encoding, 2) examine event-evoked VTA and hippocampal activation during encoding and its effects on memory, 3) explore the interactions between engagement at these different timescales. I hypothesize sustained mesolimbic activity during learning when an individual has agency increases cue and outcome based mesolimbic-hippocampal interactions. The relationship with the sustained and event-evoked activity will bias encoding to promote associative learning across and within decision sequences.

Methodology. Eighty healthy participants will be recruited to participate in a study at the Temple University Brain Research and Imaging Center, which houses a Siemens Prisma 3T MRI scanner. Participants will complete a modified version of the game show task. On each trial, they will see a trial-unique contestant (2s), and then will see and select one of the three doors (2-4s). Upon selection, the door will be highlighted, then removed to present a trial-unique prize image (2s). Again, participants will either get to freely choose one of the three doors (agency trials) or be forced to select a highlighted door (forced-choice trials). Participants will complete three runs of each condition, each run containing 20 trials. Runs will be pseudo-randomized across participants so no more than 2 runs of the same condition appear consecutively. Temporal jitters will be placed between cues and outcomes and between trials to improve both temporal and spatial resolution. Following encoding, participants will complete the three retrieval phases described earlier: contestant recognition, and contestant-prize, contestant-door, and door-prize associative memory.

Analyses. *Behavior:* In brief, item memory will be calculated for contestants using corrected recognition, which accounts for false alarm rates. Associative memory metrics will be calculated as hit rates (percent correct in selecting the old item). I will compare memory across agency and forced-choice conditions using paired t-tests. In line with my previous findings, I expect memory for items and item pairs to be enhanced for those that appear in agency compared to forced-choice trials.

Neuroimaging: 1) In order to examine sustained mesolimbic activation, I will compare sustained baseline VTA engagement using paired t-tests on parameter estimates from anatomical ROIs. I predict the sustained activation to be higher for agency compared to forced-choice runs and trials. 2) To explore how the event-evoked VTA-HPC coupling may drive memory, I will use a 2x2 within-subjects ANOVA with condition (agency, forced-choice) and memory (sequence intact, sequence disrupted) on parameter estimates from anatomical ROIs during cues and outcomes. I expect this coupling to predict memory for agency but not forced-choice trials. 3) To examine the interaction between engagement of these different time scales, I will relate measures of sustained VTA and VTA-HPC activations on the event-evoked memory signals across runs for both conditions, separately, using multi-level GLM models with a random effect of participant. Post-hoc analysis will make direct comparisons across conditions. I expect sustained VTA activation and VTA-HPC coupling during agency runs to be associated with event-evoked memory effects in the VTA and the hippocampus on agency trials, across runs.

Broader Impacts. Much of the literature exploring motivated learning comes from work that is particularly interested in response to reward feedback. However, motivated learning in the absence of reward may contribute to risk for development of substance abuse. Such learning may potentiate cues and contextual factors that strengthen drug associations independent of the anticipation or experience of the reward. I will use agency as a model to elucidate the neural underpinnings of motivated learning in the absence of rewards. This model will allow for the isolation of the core mechanisms that underlie substance abuse, which may depend on VTA-HPC interactions. The proposed research will dissect how VTA-HPC interactions contribute to the complexity of behaviors associated with substance abuse by elucidating how both state-dependent and event-evoked interactions drive memory encoding.

Additionally, the results of the proposed research may provide valuable contributions to improving pedagogical techniques. Understanding how agency might enhance learning at different timescales could support new teaching methods which incorporate agentic choices over both short and long term goals. Even in my anecdotal experience employing active techniques to engage mentees, I have found that giving individuals' agency over minor choices, such as choosing what topic to read and discuss, and more substantial choices, such as choosing a research topic, leads to significantly more engagement and long-term retention. The proposed research will directly test how agency can affect motivation and learning at various timescales, which will contribute both to our understanding of how it can support learning and how we may utilize it to broadly enhance teaching methods.

References. [1]Kuhn, 2012 [2]Haggard et al., 2002 [3]Haggard, 2009 [4]Wolpert et al., 1995 [5]Chambon et al, 2014 [6]Hon, 2017 [7]Gureckis & Markant, 2012 [8]Markant et al., 2016 [9]Murty et al., 2015 [10]Murty et al., 2019 [11]Shohamy & Adcock, 2010 [12]Lisman & Grace, 2005