

A. Specific Aims

The Specific Aims of the study have not been modified.

B. Studies and Recruitment

We have carried out two studies with the support of the award from the Woodcock Institute (and supplemented with other funding): a behavioral study that provided important foundational assessment of the awake Targeted Memory Reactivation methods proposed in association with this project, and a fully executed fMRI study addressing the central aims of the award.

First, we used the resources provided by the Woodcock Institute to support participant compensation in a behavioral targeted memory reactivation (TMR) study ($N=40$) investigating awake TMR effects on behavioral assessments of memory for emotionally neutral information. The findings are now published in the journal *Cognition and Memory*. The findings in this research suggested that awake TMR is not likely to be as reliable as a method to investigate memory representations as has been previously asserted in the extant scientific literature, and as reflected in our application for the Woodcock Institute research grant. Accordingly, to achieve the second aim of this project, which entailed investigating the neural representations of fear-related information, we opted to refine the study protocol. Specifically, we replaced the proposed task with a new one, wherein participants ($N = 47$, young adults) were invited to the scanner twice over the course of a week. On their first visits, participants watched six short movie clips (day-1, intact), which were extracted from either neutral or fear-inducing (scary) movies not already familiar to participants. Participants viewed three neutral and three aversive clips, in a counterbalanced and randomized order. One week later, they came back to the scanner and re-watched the original six clips, but this time, epochs within the movie clips were hidden from view, thus placing a heavier demand on memory retrieval (day-8, disrupted). The disruption manipulation involved having the video clip alternate with a black screen after every 10 seconds (see design figure below), while the audio was kept intact. This new task procedure allowed us to investigate long-term memory reinstatement for neutral and aversive experiences during the second movie watching experience on day-8. Additionally, participants completed subjective valence ratings after watching each movie clip on both days, allowing us to test for associations between the neural representations of aversive experiences and subjective feelings related to these experiences.

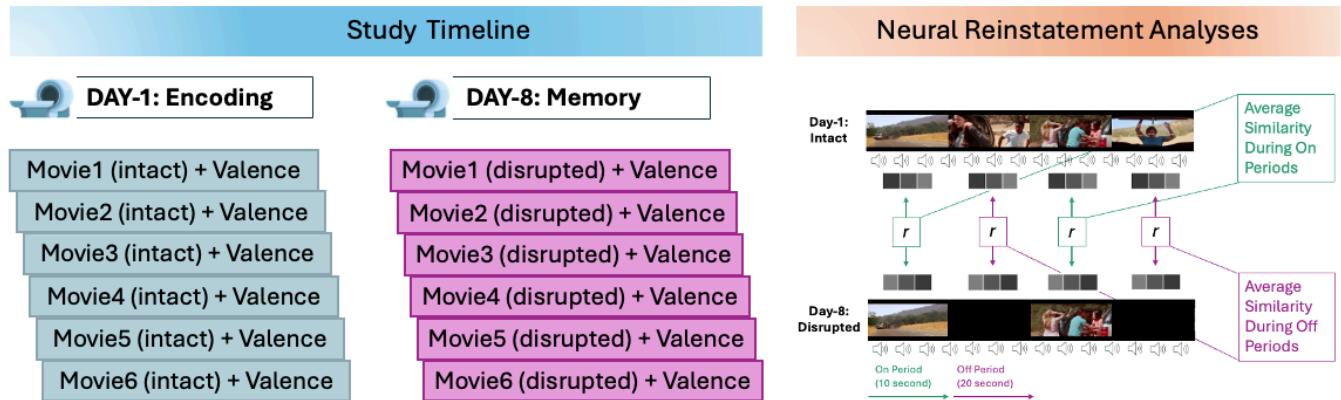


Figure 1: Study Timeline and Analysis Approach

Participant recruitment for the fMRI study was completed in December 2023. The scanning costs as well as the participant compensation for 20 of the 47 participants were funded through the remaining Woodcock Institute research award funds.

C. Results and Plans

Efforts to analyze the fMRI data have been ongoing since January 2024 and will continue throughout the Summer 2024. Our first analyses focus on the long-term reinstatement of movie events, for which we have conducted representational similarity analysis (RSA) to test neural similarity across the intact (day-1) and disrupted (day-8) movie watching experiences in the scanner. Here, we found that there was higher neural reinstatement in the right posterior hippocampus on day-8, but only for the movie clips that participants rated more positively (more favorable emotional experience) on day-8 compared to their initial ratings on day-1. This pattern of findings suggests that long-term memory reinstatement in the hippocampus is associated with a shift in valence towards more positive subjective experiences. Further, the fact that this pattern is only evident in the posterior hippocampus suggests that this effect is driven by highly detailed memory representations.

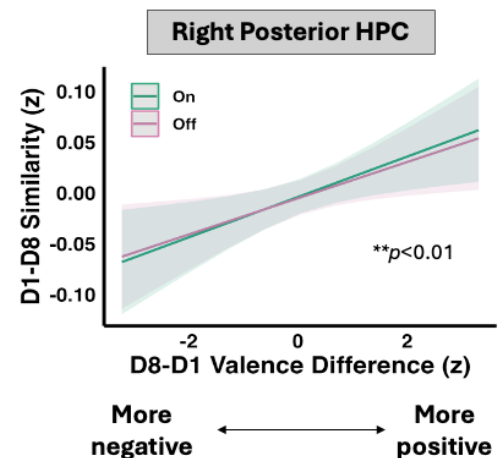


Figure 2: Higher day1-day8 neural similarity in right posterior hippocampus is associated with valence changes from day1 to day8.

Our ongoing analyses aim at testing whether this neural reinstatement is signaling the representation of specific events in each clip, or signaling the general representation of aversive events across clips. The outcome of this analysis will reveal if the aversive but unique events from a given clip are represented distinctly (neural differentiation) or the

aversive events from clips are represented more similarly (neural integration) in the long-term.

D. Distribution of Research Findings and Significance

As mentioned above, the results of our behavioral targeted memory reactivation (TMR) study are presented in a recently published article (Hoffman et al., 2024). Moreover, the results of the initial analysis we conducted on the fMRI study were presented at the annual meeting of Cognitive Neuroscience Society in April, 2024, in Toronto, CA, which was met with great enthusiasm by the larger scientific community. Additionally, the co-PI recently presented these findings as part of an invited talk at the Psychiatry Department at University of Pennsylvania, in May, 2024. Data analysis for ongoing analyses will continue throughout Summer 2024, and we anticipate that a manuscript detailing the findings will be submitted for publication by the end of Fall 2024.