To the editors of *Nature Neuroscience*,

Please consider our article entitled: “Neural reinstatement reveals divided organization of fear and extinction memories in the human brain” for review at *Nature Neuroscience*.

Recent neurobiological research in rodent models has made great progress in identifying the exact neural substrates of fear and extinction memories. This research leverages chemogenetic tools in order to tag neurons which are active during learning and observe their subsequent activity during memory retrieval. The lack of such a technique in humans has posed a major hurdle in translating recent findings on the organization of emotional memories from rodent models. In this report, we present a novel approach to the study of emotional memory organization in humans, and successfully replicate key findings from rodent work in humans using fMRI.

Our approach combines an encoding-retrieval similarity analysis popular in the study of human episodic memory with a Pavlovian conditioning paradigm to isolate the reinstatement of associative memories based on the timepoint in which they were encoded (fear or extinction). We show that in healthy adults, fear memories are preferentially reinstated in the dACC and posterior hippocampus, while extinction memories are preferentially reinstated in the vmPFC and anterior hippocampus. Additionally, we report a misallocation of extinction memories in individuals with PTSD symptoms. That is, while these symptomatic individuals show reinstatement of fear memories in the dACC, they also display show reinstatement of extinction memories in this region, suggesting aberrant storage for experiences of safety.

Altogether, we feel that this report is a fitting candidate for review at *Nature Neuroscience.* These findings provide a conceptual replication of key neuroscientific findings form model organisms, as well as a new experimental paradigm for the study of emotional memory organization in humans.

**Abstract**

Neurobiological research in rodents has revealed that competing experiences of fear and extinction are stored as distinct memory traces in the brain. This divided organization is adaptive for mitigating overgeneralization of fear to related stimuli that are learned to be safe, while also maintaining threat associations for unsafe stimuli. Whether a similar division exists in the human brain remains unclear. Here, we used a hybrid form of Pavlovian conditioning with an episodic memory component to identify overlapping multivariate patterns of fMRI activity associated with the formation and retrieval of fear versus extinction. In healthy adults, distinct regions of the medial PFC and hippocampus showed selective neural coding for fear and extinction memories. This dissociation was absent in participants with PTSD symptoms. The divided neural organization of fear and extinction may support flexible retrieval of context-appropriate emotional memories, while their disorganization may promote overgeneralization and increased fear relapse in affective disorders.