Title: Dissociable neural reinstatement of emotional memories in human PFC

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Neurophysiological research in rodents using activity-dependent neural tagging shows separate neural ensembles in the hippocampus, amygdala, and medial PFC activate at encoding and retrieval of threat memories and extinction memories (Frankland et al., 2019). Detailing this level of neuronal organization is not currently possible using human neuroimaging, but multivariate analysis of fMRI data can quantify reinstatement of encoding-related activity patterns during memory retrieval (Ritchey et al., 2013). Here, we developed a hybrid threat conditioning-episodic memory paradigm that allowed us to localize distinct patterns of threat versus safety memories using multivariate representational similarity analysis in healthy adults (N=24) and patients with PTSD (N = 24). Subjects first learned to associate non-repeating exemplars from a semantic category with a shock (CS+) or no shock (CS-), immediately followed by extinction. Then 24 hours later participants completed a surprise recognition memory test for all CS stimuli previously encoded during both conditioning and extinction. Encoding-retrieval overlap was analyzed by stimulus type (CS+/-), encoding phase (baseline, acquisition, extinction), and group (healthy, PTSD). Healthy controls showed dissociable reinstatement patterns for CS+ items relative to CS- items in the dACC for items encountered during conditioning, and in the vmPFC for items encoded during extinction. PTSD displayed significant reinstatement for both threat and safety memories in the dACC, but no reinstatement in the vmPFC, consistent with an extinction deficit associated with the disorder. These results provide evidence for the neural reinstatement of emotional memories in human PFC, and show dysregulation of extinction memory processing in PTSD.