In healthy adults there is a functional separation of fear and extinction in the mPFC

This organization of emotional memories is most likely serves an adaptive function. Don’t want to overwrite experiences of fear given safety, as still might need them in the future. In the mPFC, this seems to be accomplished with a separation in the circuits that code memories with opposite valence. In subcortical structures, these experiences are encoded in overlapping neural circuits.

We also observed significant reinstatement in the hippocampus. Unlike in the mPFC, there was no difference in reinstatement between CS+/- items form the same encoding context. Rather, we found that different subfields along the long axis of the hippocampus preferentially reinstated all items of a specific context, based on valence. Reinstatement in the posterior hippocampus was specific for the fear conditioning context, and specific to the extinction context in the anterior hippocampus.

The expected functional divisions along the long-axis of the hippocampus in these processes is unclear. Previous work has found a role of the anterior hippocampus in both the retrieval of fear and extinction memories. However, the role

Work in tOur data strongly suggest that the posterior hippocampus is involved in the retrieval of fear memories. Not only was local reinstatement specific to items encoded in the fear conditioning context, but posterior hippocampal univariate activity and reinstatement both predicted a bias in mPFC reinstatement towards the dACC. The anterior hippocampus may be involved in both the retrieval of fear and extinction. While local univariate activity predicted a bias in mPFC reinstatement to the dACC, the amount of local reinstatement instead predicted a bias towards the vmPFC.

Surprisingly, we did not detect any significant CS or context specific reinstatement in the subfields of the amygdala. A possible explanation is that during the recognition memory test, participants are not actively perceiving possible threats, and thus not engaging the amygdala. Even though subfields of the amygdala did not engage in significant reinstatement, we were able to show that amygdala is still involved in the balance in reinstatement between the dACC and vmPFC. Overall univariate activity in both the BLA and CeM, and local reinstatement in the CeM, all predicted a bias in mPFC reinstatement towards the dACC, consistent with the role of these regions in maintaining representations of learned fear.

We used increased reinstatement of CS+ items compared to CS- as our proxy for emotional memory reinstatement. An interesting aspect of the experimental design is that the present task did not actually prompt retrieval of the associative memories. We measured elicited reinstatement elicited during the recognition memory test. This suggests that even when there are no task demands to evaluate the threat of a given stimulus that the mPFC still represents information about past emotional valence. The fact that reinstatement was measured during the recognition memory test and not during a test of associative memory retrieval could be one reason why there was no significant reinstatement in the amygdala.

In healthy adults, although there was a double dissociation across the mPFC, we also observed significant reinstatement of fear memories in the vmPFC. Why is information about threats being represented in a region that primarily codes for learned safety? A recent study of patients with focal vmPFC lesions found an impairment of fear learning in these individuals. The authors suggest that although extinction learning may be a main function of the vmPFC, it may also be necessary for the acquisition of learned fear in humans. This is supported in part both by the results presented in the present study and other work outlining a role for the vmPFC in learning.

We observed significant differences between healthy adults and individuals with PTSS specifically in regards to the reinstatement of extinction memories. In healthy adults, we observed extinction related reinstatement both in the vmPFC and the anterior hippocampus. These results reflect a similar circuit from rodent physiology, with the IL and ventral hippocampus In contrast, in individuals with PTSS we observed

These data describe a deficit in extinction memory retrieval, that is unlikely due to any differences in behavior. As discussed, we previously reported no difference in behavioral extinction between healthy adults and PTSS on day 1. Both groups demonstrated successful extinction of both autonomic arousal and explicit threat expectancy. However, as we previously report, PTSS display enhanced return of fear the following day during the renewal test (see Hennings et al., 2020). Together with the data presented here, these results suggest that while individuals with PTSD are able to learn extinction, they may do so through different neural mechanisms than healthy adults. This is supported by the observation that in PTSS, extinction memories were reinstated in the dACC and insula, both regions that are normally involved in the learning and retrieval of fear associations.