Functional connectivity of consolidated memory circuits in rabbit after trace eyeblink conditioning

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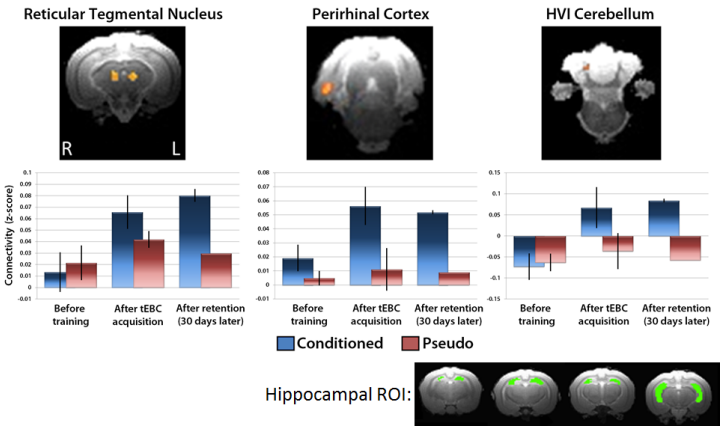
TARGET AUDIENCE: Those interested in functional connectivity and learning and memory-related plasticity

PURPOSE: The acquisition of memory is initially dependent on the hippocampus[1] but long-term storage likely resides in a distributed neural network[2]. Neurophysiological recordings are limited in spatial extent and may miss areas and interactions important for the establishment of long-term memory. Magnetic resonance imaging is well-suited to study the entire brain and examine the ensemble of regions involved in memory storage[3,4]. This study aimed to characterize the seed-based functional connectivity of sites mediating long-term memory in rabbits, namely the prefrontal cortex and hippocampus.

METHODS: Baseline functional connectivity was acquired in female rabbits (n=10; 5 conditioned, 5 pseudo-conditioned) in a 7T Bruker ClinScan MRI with a resting-state acquisition (200 volumes; TR=2.5s; TE=25ms; 0.5x0.5x2mm resolution). Trace eyeblink conditioning (250ms whisker stimulation (CS) followed by a corneal airpuff (US) after a 500ms trace period; pseudo-conditioning entailed random pairings of CS and US) was conducted for 10 days on the bench with MR resting-state sessions immediately after each training session. Thirty days after training, rabbits received three additional conditioning sessions. MR preprocessing steps included slice-timing and motion correction, volume registration, transformation into a common space, extraction of subject motion and average whole-brain signal, and bandpass filtering (0.005-0.1Hz). The timecourse from a prefrontal and hippocampal ROI was cross-correlated with the rest of the brain producing z-transformed connectivity maps. T-tests identified differences in connectivity patterns between the conditioned and pseudo-conditioned groups as well as effects of training (pre-training vs post-training) (p=.001, minimum cluster size=5mm^3).

RESULTS: Compared to pseudo-conditioned rabbits, conditioned rabbits demonstrated greater hippocampal connectivity with HVI of the cerebellum, the perirhinal cortex and thalamic regions near the right reticular nucleus and pulvinar. The pattern of network connectivity changed significantly when comparing pretraining to posttraining. The hippocampus was significantly correlated with the posterior somatosensory cortex before conditioning but less so after training. In addition, the prefrontal area was more correlated with the cholinergic basal forebrain after conditioning.



DISCUSSION/CONCLUSION:

Patterns of network connectivity gradually but significantly change as a result of learning a forebrain-dependent Pavlovian conditioning task. Given these promising preliminary results, future studies may identify additional regions showing connectivity changes as a result of learning.

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