Neural Mechanisms for Extinction, Generalization and Emotional Modulation of Learning and Memory

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Main body text

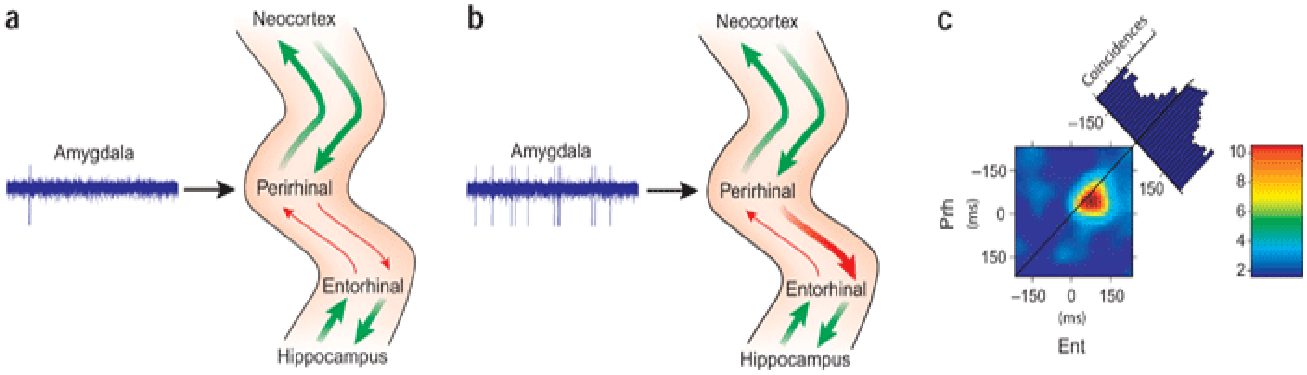
Our main aims and goals are: a. understanding of brain mechanisms that underlie generalization and specificity of learning; b. understanding of brain mechanisms that underlie extinction of learning; c. understanding the contribution of these two components (generalization and extinction) to a family of psychiatric disorders - disorders of anxiety in general and PTSD (post-traumatic-stress-disorder) in particular.

We focus on neural networks in the amygdala and the prefrontal cortex and their contribution to these questions. Earlier studies have shown the involvement of the amygdala and the prefrontal cortex in acquisition and extinction of fear memories and reward-based learning. The amygdala plays an important role in signifying emotional and motivational content and participates in formation of emotional memories. The prefrontal cortex (PFC), with its massive projections to and from the amygdala, regulates emotion expression and modulates emotional memories, and supports the complex interaction between rationale decisions and the motivational aspect.

Recent studies have focused on classical conditioning paradigms where a sensory stimulus is paired with a fearful event. These studies have showed that the amygdala is required for the acquisition, consolidation, and expression of the associations. However, we know little on how these associations can be generalized and/or extinguished.

Generalization: Living organisms take information acquired in one circumstance and use it in others. This capability to generalize from few encounters is the foundation of learning and what distinguishes it from memory. Central to learning is the ability to generalize correctly: when and how to use the newly acquired information (generalization), but also when not to use it (specificity). Whereas all animals show this capability to some degree, it has especially well evolved in primates and is a main evolutionary advantage of human intelligence. Accordingly, in modern mathematics and statistics (e.g. artificial intelligence), it is a key challenge to create theory and practice for learning algorithms that can generalize beyond specific examples.

From an evolutionary perspective, the ability to generalize has evolved for survival purposes. The most primitive use of learning is when experiencing an appetitive or aversive outcome. Importantly, the animal should generalize correctly following exposure to only few examples. Some popular examples can be remembering the location of food, but not the exact location – rather some tell-signs that suggest the possibility of it; or the possible encounter with a predator.



Sensory input flows from the neocortex to the hippocampus via the rhinal cortices (descending arrows). The hippocampus in turn assists in consolidating and storing this information through projections back to neocortex (ascending arrows). (a) During spontaneous activity, with low amygdala firing rates (blue traces on left), transfer of information from perirhinal cortex (Prh) to entorhinal cortex (Ent) is minimal (thin red arrows). (b) Following reward, the amygdala increases its firing rate and synchrony. This enables the transfer of sensory information through the rhinal cortices into the hippocampus (large red arrow). (c) The dependence of transfer through the rhinal cortices on amygdala activity is evidenced by peaks in the spike-triggered joint histogram (STJH, colored square). The STJH calculates the cross-correlation between perirhinal and entorhinal spike trains with reference to a third event, in this case a BLA spike. In the color plots, the x- and y-axes represent the latencies of entorhinal and perirhinal spikes relative to the occurrence of a BLA spike, respectively. Each cell of the grid represents the number of spike pairs that occurred with the corresponding latencies relative to a BLA spike. The red peak in the STJH indicates that shortly after a BLA spike, entorhinal cortex fires after perirhinal cortex, consistent with facilitated transmission in the perirhinal-entorhinal direction. The plot on the upper right corner of the STJH is a crosscorrelogram resulting from summing the leftward diagonal rows of the STJH along the rightward diagonal (indicated in black). This represents the number of pairs of entorhinal and perirhinal spikes that occur in the vicinity of a BLA spike. The effect of amygdala activity on rhinal throughput is a plausible mechanism for facilitation of emotional memory by the amygdala.

Indeed, paradigms that use highly aversive outcomes, as conditioned-taste-aversion or fear-conditioning, have demonstrated that learning can be a one-trial process. The complement of generalization – specificity, is equally important for survival: over- or inappropriate generalization is not only cost-expensive, but results in a wrong response and dangers the animal.

Extinction: Extinguishing memories does not erase them, but forms a new type of memory that competes and inhibits the original memory, and the medial PFC is important for this process. An emerging model suggests that the mPFC inhibits the amygdala and prevents the fear-response. Behavioral and imaging studies in patients with anxiety-disorders and PTSD have suggested the amygdala-mPFC circuit as a main site of dysfunction.

In our lab, we extend the current model of extinction to more complex forms of learning and memory, and test their validity for the primate brain, where the amygdala, the prefrontal cortex and the pathway that connects them have evolved extensively.

We use behavioral methods combined with multi-site physiological recordings in the amygdala-prefrontal pathway and a variety of computational methods for analysis and modeling of brain activity.

Selected publications

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