Orbitofrontal pathways for learning and forgetting emotional events

The goal is to understand how primates learn to attach emotional value to an event, and how they can undo that process when their circumstances change. For example, soldiers on a battlefield learn to associate loud noises with danger, an association they must break when they return to civilian life. Some veterans adjust quickly, but some do not and suffer from post-traumatic stress disorder. How does the brain learn and then forget emotional associations?

At the NSF-funded CELEST Science of Learning Center, the research team consisting of Helen Barbas, Basilis Zikopoulos, Clare Timbie, and Daniel Bullock are investigating two parts of the brain: the orbitofrontal cortex, which has a role in attaching emotional value to events, and the amygdala, which has a key role in emotions. We have found that part of the orbitofrontal cortex communicates through a strong pathway with the parts of the amygdala which are composed entirely of inhibitory neurons – neurons that stop other neurons from firing. These neurons have a key role in how the amygdala communicates with parts of the brain that elicit emotional responses to danger, or return to a normal state when the threat of danger subsides. How do these pathways achieve these opposing functions? We have found that the inhibitory neurons in rhesus monkey amygdalas are made up of different types of neurons, as shown in Figure 1. Two classes of neurons differ markedly from each other, and are part of distinct biochemical pathways. This complex system requires study with experimental and mathematical modeling, a problem that can be uniquely addressed by experimentalists and modelers at CELEST. We will use combined approaches to determine if one of these systems has a role in learning and another in unlearning emotional associations, in functions that are essential for flexible behavior.

![Figure 1](image.png)

**Figure 1**: A. Cross section through the middle of the amygdala shows the terminations of a pathway (green) in the amygdala (red). B-E, Some inhibitory neurons stain for various enzymes and proteins. B, D, C, E. Bottom panels are magnified images showing close (connections) of orbitofrontal cortex terminals with amygdala neurons. F, Large terminals from the pathway (Lb, red) that target amygdala neurons. G, Sequential images through the connection (synapse) were reconstructed in three dimensions and show a spine from a dendrite (pink) forming a synapse with an axon terminal from the orbitofrontal cortex (blue).