This Week in The Journal

Orbitofrontal Cortex Receives Direct and Indirect Input from Amygdala

Clare Timbie and Helen Barbas

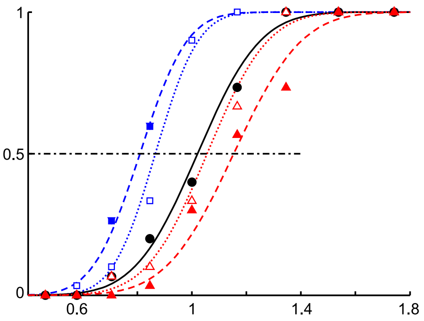
(see pages 11976–11987)

The amygdala is a cluster of nuclei best known for its roles in fear perception and conditioning, but it in fact contributes to many subjective experiences. The amygdala is important not only for generating appropriate emotional responses, but also for recognizing emotional expressions in others. Thus, the amygdala is essential in social interactions. It also promotes attention to and memory of emotion-laden stimuli and events. Many of these functions depend on direct projections from the amygdala to the posterior orbitofrontal cortex (pOFC), and lesions of these areas produce similar effects on emotional processing and expression. But the ability of past experiences to influence emotional reactions may be mediated by projections to pOFC from the magnocellular mediodorsal thalamic nucleus (MDmc), a nucleus involved in long-term memory. Interestingly, the MDmc also receives input from the amygdala, raising the possibility that the amygdala influences pOFC both directly and indirectly, via the MDmc.

To investigate this possibility, Timbie and Barbas injected anterograde tracers into monkey amygdala and retrograde tracers into monkey pOFC and examined the overlap of these tracers in MDmc. The region of overlap was substantial and many amygdalar axonal terminals were closely apposed to the somata and proximal dendrites of MDmc neurons that projected to the pOFC, supporting the hypothesis that the amygdala influences pOFC via MDmc.

To further investigate these pathways, Timbie and Barbas injected retrograde tracers into pOFC and MDmc. The tracers labeled intermingled but wholly nonoverlapping sets of amygdalar neurons. Notably, the MDmc-projecting neurons were larger than the pOFC-projecting neurons. Furthermore, whereas more amygdalar terminals in pOFC were labeled with antibodies against vesicular glutamate transporter 1 (VGLUT1) than VGLUT2, more terminals in MDmc were labeled with antibodies against VGLUT2 than VGLUT1. Finally, electron microscopic studies revealed that most amygdala axons (68%) formed synapses with calbindin-expressing MDmc neurons, which project primarily to upper cortical layers, but the remaining axons formed synapses with parvalbumin-expressing neurons, which project to middle cortical layers.

These results suggest that at least two distinct populations of amygdalar neurons influence the pOFC: one through direct projections, and one indirectly, through MDmc. Determining the functional differences between these populations will be an important future endeavor.



The perceived size of test disks relative to a reference disk was influenced by binocular disparity such that when the test disk appeared farther away (blue traces), it was perceived as bigger than it actually was, and when it appeared closer (red traces), it was perceived as smaller. See Tanaka and Fujita for details.

V4 Neurons Show Preference for Object Size

Shingo Tanaka and Ichiro Fujita

(see pages 12033–12046)

As one approaches an object, the image of the object on the retina grows larger. Nevertheless, the perceived size of the object does not change. This is because binocular disparity (the difference in the position of various features in the image on each retina), the overlap between the object and other objects in the visual scene, and other visual cues allow the observer to estimate the distance of the object, and this estimate is combined with the retinal image size to shape perception of the object's size.

The neural mechanisms underlying size constancy are poorly understood, but some of the required calculations are likely to take place in visual cortical area V4. This complex area contains different functional domains selective for color, orientation, shape, and binocular disparity, and it is thought to be important for object recognition. To examine the role of V4 in size constancy, Tanaka and Fujita examined the responses of monkey V4 neurons to random-dot stereograms containing disks of binocularly correlated dots that varied in size and binocular disparity. Initial tests revealed that humans' judgments of the size of such disks depended on the disparity; for example, people judged a disk that appeared closer to be smaller than it actually was.

The responses of many monkey V4 neurons varied with disk size, with different neurons tuned to different sizes. In most neurons, the preferred size depended on the binocular disparity. Specifically, neurons' peak responsiveness shifted to smaller disks when disparity was uncrossed (i.e., when the disks appeared farther away) and shifted to larger disks when the disparity was crossed (i.e., disks appeared closer). Further experiments suggested that individual neurons were able to accurately calculate object size at limited fixation distances, but that the optimal fixation distance of neurons varied across the population.

These results suggest that V4 neurons encode the actual size of objects, not just the size of the retinal image they produce. They further suggest that different neurons are best suited to calculate object size at different distances. Therefore, this population of V4 neurons may contribute to the perception of size constancy.

This Week in The Journal is written by Teresa Esch, Ph.D.