Facing the role of the amygdala in emotional information processing

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The neurobiology of social information processing provides a fascinating window into human nature and how primate brains evolved to deal with challenges of living in large social groups. Faces and facial expressions of emotion are critical for social identification and for modulation of appropriate responding in social situations. The decoding of emotional information, and the subsequent integration of this information into choices about behavior appropriate to particular contexts, is an integral part of everyday human behavior. Although, for most humans, these systems may be primarily taxed now by reading emotional cues to avoid embarrassing faux pas in social situations, evolutionary pressure to develop these systems likely emphasized rapid and reliable detection of threats. Hadj-Bouziane et al. (1), in PNAS, make remarkable strides in understanding these neural mechanisms, by using an unusual and powerful combination of methodologies in a study of rhesus monkeys.

Specialized regions in the temporal cortex are specifically engaged by visual processing of faces (2, 3). The amygdala is commonly thought to form the core of a neural system for processing fearful and threatening stimuli (4), including detection of threat and activation of appropriate fear-related behaviors in response to threatening or dangerous stimuli. Thus, it is a natural candidate for a neural structure that could modulate the emotional responsiveness of face processing areas in the brain. Indeed, humans with amygdala damage tend to be impaired in recognizing emotional facial expressions, especially fearful ones (5).

The mechanisms by which brain structures may interact in processing facial identity and emotion have been difficult to elucidate. Neuroimaging with functional MRI (fMRI) provides a means by which neural activity, inferred by changes in relative levels of blood oxygenation, can be mapped across large regions of the brain in awake, behaving monkeys and humans. An initial study in monkeys by Hadj-Bouziane et al. (6) identified face-specific cortical areas in the anterior and posterior inferior temporal (IT) cortex of macaque monkeys, as well as regions within IT whose activity was modulated by the emotional valence of faces. Some of the emotion-responsive areas did not overlap with the face-selective areas, potentially pointing toward independent cortical processing streams for face identity and emotion. Signal in the amygdala was also modulated by faces and by emotional valence. The anatomical connections of the amygdala and IT cortex would allow the amygdala to modulate activity of the cortex in response to the emotional valence of faces, but it is equally possible that information about facial identity and emotion is independently extracted within IT cortex, passed to the amygdala through feed-forward connections, and, from there on, modulates behavior.

Hadj-Bouziane et al. provide an as-yet rare opportunity to investigate the causal role between damage specific to the amygdala and its behavioral consequences.

These different possibilities become important when considering how to design artificial systems to recognize human facial stimuli, for example, computer facial-recognition algorithms to rapidly and automatically decode the information content of facial expressions. They are also germane to understanding how neurodevelopmental differences that are associated with changes in social behavior produce their effects. However, how to test the hypothesis that the amygdala specifically is necessary for the modulation of face processing within IT cortex?

Hadj-Bouziane et al. (1) address this question by analyzing fMRI activity associated with different emotional faces in the IT cortex of monkeys, either neurologically intact or with neurotoxic lesions of the amygdala. By examining the effects of selective amygdala damage on decoding of emotional information within IT cortex of monkeys, it is possible to test whether amygdala projections to IT are necessary for this computation, or whether IT can carry out the analysis of facial expressions of emotion on its own. This study provides intriguing insights into the neurobiology of social and emotional information processing that would be impossible to obtain through any other experimental modality.

Amygdala Damage Changes the Way the Social Brain Perceives Emotion

Most control monkeys in the study by Hadj-Bouziane et al. (1) showed greater activation, in both anterior and posterior face-selective regions of IT, to different emotional expressions (threat, fear grin, or lip smack, an affiliative expression) relative to a neutral face that showed no particular emotional expression. Similar modulations of face-selective activity were seen in the amygdala itself in these monkeys. In the three monkeys with amygdala damage, the pattern of modulation within IT was altered. There was practically no response to threat or lip smack expressions, even though responses to fear grins were largely preserved in the same cortical areas. These responses appeared to be driven by small amounts of preserved amygdala tissue that retained selectivity for fear grins; in hemispheres where the anterior or posterior amygdala was completely eliminated, there was no response even to fear grins in the corresponding region of IT cortex (anterior or posterior). Thus, selective damage to the amygdala extensively alters the neural processing of emotion within IT cortex, supporting the view that the amygdala is the engine that drives neural coding of emotional identity in this part of the brain.

It is notable that processing of fear grins appeared to be particularly resilient to amygdala damage, relative to other emotional expressions. It is tempting to speculate that this may represent some differential involvement of the amygdala in processing certain types of social and emotional stimuli. Fear grins may represent a particularly ambiguous type of emotional stimulus because they can represent the submissive gesture of a social inferior or a fearful response to an external stimulus. This is congruent with other analyses of amygdala function that have placed an emphasis on

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its role in processing of ambiguity or uncertainty rather than negative emotion per se (7) or in directing attention to stimuli whose consequences have become uncertain (8). The lateral extended amygdala, which is more responsive to averted gaze than directed gaze, has been implicated in the perception of ambiguous stimuli (9). The amygdala has also been implicated in encoding the relevance of the expression to the self, responding more when an expression is perceived as more intense, rather than gaze direction per se (10). This and other evidence suggests that the amygdala may play multiple roles in processing emotional faces: it may rapidly decode emotional content and then "reflectively" decode ambiguity in facial expressions (11).

These circuits may be key for processing of emotional information involved in maintaining social relationships in primates. The more posterior of the regions identified by Hadj-Bouziane et al. (1), located in area TEO within IT cortex, is extremely close to, if not overlapping with, the region that showed a positive correlation between gray matter density and social network size in monkeys (12). In addition, a proximal region of IT cortex showed a positive correlation between gray matter density and increasing social rank. Future studies with stimuli of monkeys at different places in the social hierarchy may be able to inform us whether the amygdala also influences the perception of socially important stimuli, or if this region of TEO is modulated by the monkey's place in the social hierarchy.

Functional MRI Provides an Important Method for Examining Common Mechanisms for Social Interaction Across Species

The use of fMRI in nonhuman primates is becoming more widespread because of improvements in technology and analysis techniques. Difficulty remains in obtaining these data from behaving monkeys as a result of the high-resolution images required, the need for specialist adaptations to MRI equipment, and the difficulty of training monkeys to perform a task in the MRI environment (13). There is a serious need for such studies, however, from evolutionary and psychological perspectives. The use of parallel techniques in humans and nonhumans is essential for forming hypotheses about the possible homologies between the two. fMRI is in an unrivaled position to facilitate the investigation of similarities of social processing across humans and monkeys as it allows the use of the same method, and even the same stimuli, in both species.

One way of overcoming the difficulty of performing awake MRI on monkeys performing a task is to exploit the existence of resting-state networks in the nonhuman primate brain. fMRI studies of resting-state networks have been of particular value in investigation of possible similarities between the human and nonhuman social brain. By using resting-state functional connectivity in a very large study of humans and monkeys, Oler et al. (14) showed strong evolutionary conservation between areas of the human and monkey extended amygdaloid complex. Mars et al. (15) used similarities in resting-state functional connectivity between monkeys and humans to draw conclusions about the locus of a region important for social cognition: the temporoparietal junction.

In addition to its value in the examination of evolution and social structure in the human and nonhuman brain, the work of Hadj-Bouziane et al. (1) highlights a second unique property of fMRI studies in monkeys: the possibility for evaluating the effect of brain lesions (specifically targeted and mapped to a particular area) at the whole-brain level. Many human studies of patients with brain lesions suffer the disadvantage that the lesions often span several brain areas, which complicated the interpretation of a similar study in humans (16). In contrast, lesion studies in monkeys such as that of Hadj-Bouziane et al. (1) provide an as-yet rare opportunity to investigate the causal role between damage specific to the amygdala and its behavioral consequences. Another example of this exceptional combination of approaches also illustrates its power: Schmid et al. (17) were able to causally investigate the role of the lateral geniculate nucleus in blindsight, and show unequivocally that, without it, the phenomenon, and the fMRI blood oxygen level-dependent activity that accompanies it, are abolished.

The powerful technique of combining interventions with fMRI in monkeys could, in the near future, be combined with behavioral paradigms to elucidate the role of the interaction between brain regions in guiding behavior. The advantage of an explicit behavioral task is that the monkey is making use of the information contained in the stimuli, which may guide its perception of a stimulus as fearful or threatening. For example, an interaction between gaze direction and stimulus identity could affect reaction times to part of space that was modulated by amygdala damage, which would elucidate whether the amygdala was providing critical feedback about social or fear-based stimuli. The findings of Hadj-Bouziane et al. (1) highlight how this relatively new field can be used to investigate the neural mechanisms underlying social cognition and how they can be altered in disease and developmental disorders. These intriguing results illustrate the potential for many more remarkable findings about the brain and cognition.

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