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Changes in brain structure and emotional arousal in studies of subjects with amygdala damage

This review is of three studies: two involving subjects with bilateral amygdala damage that focus on gray matter structural abnormalities and invoking fear and panic by exposure to carbon dioxide, respectively, and one measuring emotional arousal to erotic, neutral, and aversive images in 18 subjects with unilateral medial temporal lobe resection including the amygdala. Because bilateral amygdala damage is exceedingly rare, the former two studies only have two and three test subjects, respectively, who are all females with Urbach-Wiethe disease. Both studies include patient SM, and the CO_2 study includes a pair of monozygotic twins. The unilateral amygdala resection study includes 18 adults who have undergone surgical resection to treat medial temporal lobe epilepsy that would not respond to medication—13 with right medial temporal lobe resections and 5 with left resections (Edmiston et al., 2013).

Feinstein et al. (2013) found that patient SM and monozygotic twins AM and BG all experienced fear and panic attacks when inhaling a 35% CO_2 mixture, and their self-reported levels of fear and panic were significantly higher ($P < 0.05$) than those who did not panic in the comparison group. SM has been a highly studied subject, but the authors believe this was the first time she experienced fear in any setting since childhood. All three subjects were surprised at their reactions to the CO_2 mixture, found it completely novel, and felt multiple emotions in the fear domain with no overlapping emotions in the anger domain, according to self-reports. This study contradicts the conclusion that the amygdala is required for fear, and because the subjects exhibited more fear and panic than subjects with intact amygdalae (some of which did not panic), it may indicate the amygdala actually inhibit general or acute panic, at least with respect to CO_2 inhalation. Further, there may be other brain structures that contribute to the fear response. Finally, the comparison group exhibited anticipatory responses including increases in heart rate, respiration, and skin conductance prior to the CO_2 challenge, but these responses were absent in the test group, which may confirm the amygdala physiologically prepares an organism for encountering a threat.

Boes et al. (2012) hypothesized there would be gray matter morphometric abnormalities in various areas of the brain in subjects with developmental bilateral amygdala lesions. In comparing scans from their two test subjects, SM (female, 44 years old) and AP (female, 23 years old), to comparison groups matched for gender and age ranging from 16 to 57 subjects, there were clear differences. Cortical thickness was higher in the ventromedial prefrontal cortex (vmPFC) and anterior cingulate cortex (ACC), lower in the ventral visual stream, and there was a significant proportional increase of gray matter volume in the vmPFC. These analyses were based on MRI scans of SM at 33, 37, and 42 years of age, and of AP at 19 years of age. There were also various non-hypothesized regions of increased and decreased thickness that were unique to SM or AP as compared to the comparison groups. Boes et al. concede that drawing conclusions from only two subjects is dangerous, but propose they have produced the first evidence that human amygdala lesions have a morphological impact on nearby and functionally connected cortical regions. They believe their work will complement and be supported by studies of animals regarding these lesions, given that human subjects are so rare—there have been fewer than 300 reported cases of Urbach-Wiethe disease since its discovery in 1929.

Edmiston et al. (2013) studied 18 subjects who received unilateral amygdala resection as a treatment for epilepsy. They showed them emotionally salient scenes rather than faces, because they believed scenes engage more visual regions. Their goal was to investigate whether the amygdala plays a vital role in the enhanced processing of such stimuli, and they did so using functional magnetic resonance imaging (fMRI) to measure the visual cortical blood oxygenation level-dependent (BOLD) signal of the subjects in response to aversive, neutral, and erotic scenes.

They found similar BOLD signal activation between the control group and test group in the aversive and erotic conditions, even in the visual cortex ipsilateral to the lesion. Their findings suggest the amygdalae are not needed for enhanced responses to emotional stimuli, and that the brain region(s) that are needed for such signals are not presently known but should be the target of future research. This is in contrast to previous findings, which concluded the amygdala are needed for emotional modulation of visual processing, usually based only on responses to faces and facial expressions. Edmiston et al. believe the applicability of prior studies was limited and that showing an immersive scene provides a more accurate metric of emotional engagement.

Edmiston et al. (2013) and Feinstein et al. (2013) both found that the amygdala function differently than was previously believed, and may be less essential to emotion and cognition in respect to fear and emotionally salient imagery. Boes et al. (2012) found that there are marked differences in various brain structures and morphology in two subjects with bilateral amygdala damage, and that these differences were consistent over a 9-year period with one subject. While all three studies introduce as many questions as answers, they show us that amygdalae are more complex or mysterious than scientists thought, and that important emotions and emotional responses of high magnitude can still be evoked in subjects despite amygdala damage. This may present consolation to patients with severe epilepsy who are facing amygdala resection, as well as aid research of Urbach-Wiethe and other diseases in the future. Given these findings, there may be other areas of the human brain responsible for fear and BOLD signal responses, and experiments with the brains of rats and monkeys can help guide such research, according to Boes et al. (2012, pp. 594). Furthermore, Boes and Feinstein's studies are notable for producing new findings in a field and with subjects that have been repeatedly examined in the past, and show there are still many stones unturned when it comes to amygdala research.

References

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