The Role of the Amygdala in Emotion-Attention Interactions

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The amygdala is a subcortical medial temporal lobe structure that is widely thought to be involved in processing emotional information[1]. Amygdala dysfunction and abnormal attention to affective events have been commonly observed in anxiety disorders[2]. Characterizing how the amygdala interacts with other brain regions to influence attention in healthy adults could prove useful in developing a better understanding of the mechanisms underlying these illnesses. This paper will primarily review evidence from human neuroimaging studies that have examined a potential role for the amygdala in emotion-attention interactions.

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Imagine that while watching the latest episode of your favorite television show, you suddenly hear glass breaking at your kitchen door. Although you're in the middle of an important scene, you freeze and strain your ears to try and listen for other sounds. Is someone trying to break in or has your cat knocked over a glass? Attention allows us to process important stimuli, like the sound of a possible intruder, at the expense of other items present in our environment (e.g. the television)[3]. As noted by the authors of a recent model of the neural systems of attention, reorienting attention toward "novel, potentially threatening" stimuli is of great importance[4, 5]. Fear conditioning studies in rodents and humans have shown that the amygdala is important for the acquisition and expression of conditioned fear and mediates a variety of behavioral and autonomic responses to threat-related cues[6-8]. Using positron emission tomography (PET) and functional magnetic resonance imaging (FMRI), investigators have found that the amygdala also responds preferentially to emotional faces[9, 10] and scenes[11]. For scenes, this response may depend on the arousal level of a stimulus rather than its valence[12-14]. Arousal refers to the energy or intensity level of a stimulus and can range from calm to excited, whereas valence indicates how pleasant or unpleasant a stimulus might be[15]. Early lesion studies in animals suggested that the amygdala might play a role in orienting to novel events[16] and low level amygdala stimulation can lead to "attention"-like orienting responses[17] and increased cortical arousal[18]. Behavioral data show that emotionally salient stimuli can be better identified than neutral items[19-21], may lead to facilitated detection of subsequent stimuli[22, 23] and can impair detection of other important events[24-27], possibly by "capturing" attention. The anatomical projections of the amygdala may enable it to influence attention via modulation of sensory areas[28], cortical regions implicated in attentional orienting and control[29], and subcortical structures involved in modulating arousal and attention[30]. This review will focus on evidence for the amygdala's role in modulating attention based on these three patterns of connectivity.

SENSORY MODULATION

According to the biased competition model of attention[31], stimuli in the environment compete for processing resources based on a combination of sensory salience and relevance to current goals. Top-down attention that biases sensory processing based on behavioral relevance is thought to be allocated by a frontoparietal network that includes the frontal eye fields (FEF) and areas along the intraparietal sulcus (IPS)[4]. These regions modulate activity in sensory areas in response to cues in order to direct covert attention[32-35] by increasing gain at attended locations[36] or by altering feature tuning[37]. Anatomical tracing studies in non-human primates have demonstrated that the amygdala sends topographically organized feedback projections to higher order visual areas (e.g. areas TE and TEO in the macaque) and sparser projections to earlier levels of the visual pathway including primary and secondary visual cortices[28, 38, 39]. These feedback connections from the amygdala to visual cortex may act in parallel to top-down attention by transiently boosting perceptual processing of emotional stimuli, allowing them to "out-compete" non-emotional items for available resources[28, 40].

Increased activity in primary and secondary visual cortices and the fusiform gyrus has been observed while participants view emotional relative to neutral faces[41-43] and scenes,[12, 44, 45] with a greater response to scenes than faces[11, 46]. The level of activity in the face responsive region of the fusiform gyrus varies as a function of the amygdala response to fearful compared to neutral faces[42] even when the faces appear outside the current focus of attention,[43] as long as attentional or perceptual resources are available[47, 48]. Vuilleumier and colleagues[49] performed a novel FMRI study using patients with damage to the amygdala and/or hippocampus due to medial temporal lobe epilepsy and healthy adult controls in order to examine the necessity of the amygdala for affective perceptual enhancement. Healthy adults and patients with damage limited to the hippocampus showed the expected increase in fusiform activity in response to fearful compared to neutral faces. Critically, this differential fusiform response to emotion was attenuated in patients who had amygdala damage and the level of right or left fusiform activity decreased as the level of ipsilateral amygdala sclerosis increased.

If emotional stimuli processed by the amygdala are more strongly represented in sensory areas, two potential predictions follow: when these stimuli appear at task relevant locations, they should be more readily detected and when they are task-irrelevant (*i.e.* distractors) they should interfere with detection of concurrent stimuli. Anderson and Phelps have proposed that the amygdala enhances sensory processing to facilitate attention for emotional stimuli based on a manipulation of the attentional blink (AB) paradigm[50]. In the AB task, detection of a target during a rapid serial visual presentation display temporarily impairs processing of a subsequent target[51, 52]. If an arousing, aversive word appears as a target at a short interval following the first target, it is more accurately identified than a neutral word even when emotion is irrelevant for the task[20]. Unlike healthy adults, patients with left or bilateral amygdala damage do not exhibit increased identification of aversive second targets[50]. However, there is no direct evidence that this results from sensory enhancement. Several studies have looked at how fearful faces impact performance on visual search tasks. One behavioral study found that task-irrelevant fearful faces may facilitate subsequent search for neutral items appearing in the same spatial location[23]. Greater amygdala activation in response to masked fearful faces correlates with faster detection of positive or negative schematic faces during a subsequent behavioral task[53]. In contrast to these findings, Williams and colleagues[54] observed that participants were worse at detecting fearful compared to happy faces in the presence of neutral face distractors even though the amygdala was more active when fearful faces were present in a search display. However, perceptual differences between the face stimuli may have led to the results of this study.

Lavie's model of selective attention under load indicates that processing of distractors decreases if the perceptual load of a task is high[55]. This suggests that emotional distractors present outside the current focus of attention may not always be processed by the amygdala and would therefore be incapable of influencing behavior. Consistent with this model, Hsu and Pessoa found that activity for fearful and neutral face distractors in the amygdala and fusiform gyrus decreased when the number of distinct items in a search display increased (reflecting greater perceptual load). When the sensory salience of the search display was degraded to reach the same level of difficulty as the perceptual load condition, face related activity increased relative to a baseline condition[56]. Reaction times on the search task were slower when faces were present, as compared to absent, during the salience condition, supporting the idea of increased distractor interference. Although activity in the amygdala and fusiform gyrus was greater for fearful faces relative to neutral faces during this condition, reaction times did not differ by expression. In summary, although much data strongly suggests that the amygdala can modulate sensory areas, there is little evidence that this modulation has a behavioral correlate.

ATTENTIONAL MODULATION

The effect of emotion on spatial attention has been extensively studied using a modified spatial cueing paradigm called the dot probe task[57, 58]. In this task, subjects typically view a pair of words, faces, or scenes in which one item is threat-related and the other neutral. A brief target stimulus is then presented in the same or opposite location as the emotional item. The affective cue is thought to attract attention in a stimulus-driven manner because it is not predictive of the upcoming target location. Several neuroimaging studies have used this task to examine the possibility that the amygdala facilitates spatial attention by interacting with regions involved in attentional allocation rather than by sensory enhancement alone. Armony and Dolan[59] used a version of this task combined with differential classical conditioning in an FMRI experiment to examine whether aversively conditioned cues could direct spatial attention. During trials in which an angry face that had previously been paired with an unpleasant noise (CS+) was presented with a different angry face unpaired with noise (CS-), participants were faster to detect a target when it appeared in the same location as the CS+ (cued trials) and slower when the target followed the CS- (uncued trials). The amygdala and fusiform gyrus were more active during presentations of the CS+ than the CS-. Crucially, the putative FEF, IPS, and lateral orbitofrontal cortex were more active during cued and uncued trials compared to when only the CS+ or CS- was presented on both sides of fixation. The behavioral and imaging data thus support the hypothesis that attention was modulated by the conditioned stimulus. Pourtois and colleagues found that following the appearance of a fearful face cue, the response in IPS contralateral to the fearful face was decreased for uncued targets, an effect that was not observed during cue-only trials[60]. The authors interpreted this to mean that allocating attention to emotional stimuli may produce a "processing cost" when subjects must subsequently reorient attention. However, the consequence of a potential processing cost in IPS is unclear, since there was no behavioral difference associated with fearful face cues and no amygdala activation was observed during this experiment. In typical spatial cueing studies, differences in reaction time between cued and uncued trials are not always found when the cue-target stimulus onset asynchrony (SOA) is approximately 200-500 msec[61], the interval used in the Pourtois study. The two experiments using a short cue-target SOA (<150 msec) in the dot probe task have found amygdala activation to fearful or angry face cues as well as cue validity effects, consistent with a role for the amygdala in orienting attention to potential threat[59, 62, 63].

Novel, unexpected environmental stimuli attract attention and elicit an orienting response that habituates rapidly in the absence of a significant associated outcome[64, 65]. The human amygdala responds to unfamiliar neutral faces[66, 67] and unusual scenes[12], but this response decreases quickly. Lesion studies in rats have shown that the amygdala is necessary for the acquisition of conditioned orientation to visual or auditory cues that cue food delivery, but does not participate in unconditioned orienting[65, 68, 69]. Several investigators have proposed that the amygdala acts as a detector for emotionally or biologically salient information[67, 70] and may provide an interrupt signal to reorient attention to highly important events[7, 63]. In contrast, an influential model of attention suggests that a ventral frontoparietal network, including the temporoparietal junction (TPJ), anterior insula and regions of the middle and inferior frontal gyri, is responsible for reorienting attention to behaviorally relevant events[4, 5]. A recent study found that the inferior frontal component of this network was specifically engaged during infrequent, presumably unexpected attentional shifts[71]. The inferior frontal gyrus makes up a significant portion of the ventrolateral prefrontal cortex[72] (VLPFC). Although the amygdala has few connections to lateral prefrontal and posterior parietal cortices, it has moderate reciprocal connections to the ventral-most portion of the inferior frontal gyrus, corresponding to area 47/12 of the VLPFC[29, 39, 73]. The potential functional similarities and anatomical connections of the VLPFC and amygdala suggest a possible mechanism by which the amygdala could influence cortical attentional networks in response to emotionally salient events, particularly if they are unanticipated. Brain regions involved in detecting unexpected or infrequent environmental changes have often been studied using oddball paradigms in which subjects detect a rare discrepant target among a series of standard stimuli[4]. The amygdala and VLPFC respond more to rare targets in auditory oddball tasks[74, 75] when they elicit an arousal response[76] and to aversive words presented among neutral words, but not to neutral oddballs differing in semantic or perceptual features[77]. Fichtenholtz and colleagues presented two groups of subjects with infrequent squares and aversive or neutral scenes among standard circle stimuli to examine whether attentional networks responded differently depending on whether the emotional items were relevant to current goals[78, 79]. The VLPFC was engaged by infrequently presented scenes regardless of task relevance but the response was greater for aversive than for neutral items. Reaction times were slowest for aversive scenes regardless of target status and fastest for square targets. These data support the idea that the VLPFC is involved in redirecting attention to novel events and suggest that it can be modulated by stimulus valence and/or arousal possibly due to input from the amygdala[78, 79]. In contrast, the IPS and TPJ did not appear to respond to infrequent aversive stimuli unless they were targets.[79] However, several complications arise when interpreting these results because the emotional stimuli used were negative and arousing. The right VLPFC has been linked to emotion regulation[80, 81] and response inhibition[82], and it is possible that the response to aversive items reflects greater cognitive control rather than attentional capture. Additionally, several studies have suggested that arousal itself may be particularly important for engaging the VLPFC[76, 83], and different parts of the inferior frontal gyrus may be sensitive to valence and arousal[84]. Two recent studies suggest that the amygdala and VLPFC may interact to evaluate emotional stimuli[85, 86]. Future studies could vary stimulus valence and arousal and more rigorously manipulate task-relevance and attentional focus to investigate the specific conditions under which the VLPFC and amygdala are employed.

When an affectively salient stimulus is irrelevant to ongoing goal-directed behavior and is not sufficiently important, attention is not fully redirected and is instead maintained on the current task. For example, distracting emotional information can cause subjects to respond more slowly[78], but performance failure occurs only when processing capacity is nearly exhausted[25]. The rostral, pregenual cingulate region corresponding to areas 24 and caudal 32 (rACC) is thought to have a role in detecting or resolving emotional distraction[87, 88] and has direct reciprocal projections with the amygdala[29]. The rACC is more active when participants must ignore negative compared to neutral word content during emotional Stroop tasks[87, 89], when fearful faces appear at unattended locations[43] and when aversive scene or fearful face distractors appear unexpectedly[78, 90]. Although these studies suggest a role for the rACC in detecting or resolving emotional distraction, most failed to show a behavioral correlate reflecting interference. In a modified attentional blink paradigm, task-irrelevant emotional items presented shortly before a target decrease target detection accuracy compared to neutral distractors[25]. Interestingly, this effect occurs for aversive, erotic, and conditioned complex scenes[25-27] but not fearful faces[91], possibly indicating the importance of arousal in capturing attention. Using FMRI, Most and colleagues[92] found that aversive scene distractors interfered with target detection and were associated with increased amygdala activation when compared to neutral scenes. Greater rACC activation in this study appeared to be driven by individual differences in subjects' ability to ignore emotional scenes, as evidenced by decreased amygdala activity. Conversely, a recent FMRI study found that more accurate detection of fearful relative to neutral face second targets in the AB task was related to greater rACC response in the absence of amygdala activation[21]. In this case, the fearful expression was unimportant for reporting facial identity and greater rACC activity could have reflected increased attention when participants were aware of the emotional stimulus. From these studies, it is unclear whether the rACC detects and/or resolves affective interference. Control of attention over distracting information is typically studied using Stroop-type paradigms in which conflict must be monitored or resolved[93] and none of these studies examined rACC function in conflict situations *per se*[94]. Etkin and colleagues[94, 95] developed a task in which participants had to report whether faces were fearful or happy while ignoring a congruent or incongruent word label, thereby providing response conflict. Conflict resolution was defined based on trials in which an incongruent trial followed a previous incongruent trial whereas conflict detection was thought to occur when an incongruent trial followed a congruent trial. In support of this dichotomy, amygdala activation increased during the conflict detection condition and subjects were slower to respond compared to the conflict resolution condition, which was associated with increased rACC activity and a concurrent decrease in amygdala response[94].

LINKS TO NEUROMODULATORY SYSTEMS

The amygdala may also influence sensory processing and attention through its connections with subcortical neuromodulatory systems[39]. Numerous studies have examined the importance of the amygdala and locus coeruleus noradrenergic system for emotional memory[96], but little work has been done to determine whether norepinephrine modulates attention to affective stimuli. A behavioral study in humans showed that increasing the availability of norepinephrine through a reuptake inhibitor improved the ability of subjects to detect emotional compared to neutral targets in an attentional blink task[97]. Tentative support for amygdala involvement in this process comes from a recent FMRI experiment showing increased amygdala activity to fearful faces in participants who had taken the same reuptake inhibitor[98]. The amygdala is also reciprocally connected with the nucleus basalis[39], which provides cholinergic input throughout cortex and is thought to be important for a variety of attentional functions such as normal attentional shifting to unattended targets[99-101]. Classical conditioning studies in animals have shown that amygdala-mediated release of acetylcholine is important to return auditory cortex neuron receptive fields to prefer a conditioned stimulus[102]. In humans, frequency specific changes in auditory cortex during differential classical conditioning are correlated with increased amygdala and basal forebrain[103] activity, which appears to be dependent on acetylcholine[104]. The amygdala also contributes to acetylcholine-dependent EEG desynchronization, which is thought to reflect increased cortical arousal or attention[105, 106]. When the relationship between a cue and its conditioned outcome changes unexpectedly, the amygdala interacts with a network that includes the nucleus basalis, substantia nigra and posterior parietal cortex to increase attention to the cue[65, 107-109]. Participants who had taken a cholinesterase inhibitor initially showed impaired performance during a house-matching task in the presence of unattended fearful faces compared to those who received a placebo, suggesting greater attentional capture by the fearful faces with increased acetylcholine levels[110]. The subjects who had taken the drug also showed greater activity to unattended fearful faces in the dorsal anterior cingulate, intraparietal sulcus and a region of the lateral orbitofrontal cortex similar to that observed during attentional shifts to conditioned stimuli[59]. The amygdala-mediated release of acetylcholine may therefore facilitate attention to emotional stimuli[99].

CONCLUSION

Current data suggest that the amygdala modulates sensory cortices to bias activity for emotional stimuli such that they compete more effectively than non-emotional items for attention. Enhanced attention to affective events may be bolstered by amygdala-VLPFC or neuromodulatory interactions and weakened by rACC influence. Future studies should more rigorously manipulate attentional demands and address the relative importance of arousal versus valence, specific emotions and possible differences resulting from stimulus type (e.g. faces versus scenes) in these processes.

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FURTHER INFORMATION

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