The Insula and Evaluative Processes

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Abstract
The insula has been implicated as a component of central networks subserving evaluative and affective processes. This study examined evaluative valence and arousal ratings in response to picture stimuli in patients with lesions of the insula and two contrast groups: a control-lesion group (the primary contrast group) and an amygdala-lesion group. Patients rated the positivity and negativity of picture stimuli (from very unpleasant to very pleasant) and how emotionally arousing they found the pictures to be. Compared with patients in the control-lesion group, patients with insular lesions reported reduced arousal in response to both unpleasant and pleasant stimuli, as well as marked attenuation of valence ratings. In contrast, the arousal ratings of patients with amygdala lesions were selectively attenuated for unpleasant stimuli, and these patients’ positive and negative valence ratings did not differ from those of the control-lesion group. Results support the view that the insular cortex may play a broad role in integrating affective and cognitive processes, whereas the amygdala may have a more selective role in affective arousal, especially for negative stimuli.

Keywords
insula, amygdala, lesions, evaluative processes, valence, arousal, affect

Received 10/1/09; Revision accepted 7/29/10

The insular cortex is an important nodal point in forebrain circuits underlying autonomic regulation, emotion, and cognition. The insula has extensive reciprocal connections with limbic forebrain areas, such as the amygdala, medial prefrontal cortex, and anterior cingulate gyrus, which play an important role in emotion and affective regulation (Augustine, 1996). It is also reciprocally interconnected with frontal, parietal, and temporal cortical areas that have been implicated in attention, memory, and cognition (Augustine, 1996) and is thus anatomically positioned to broadly interact with the neural circuitry underlying both affective and cognitive processes (Craig, 2009; Critchley, 2009).

Researchers have suggested that the insula, as a polysensory integrative system, may serve as a substrate for representation of the state of the body, including both visceral and somatic components (Craig, 2009; Saper, 2002). The perception of internal bodily states has been shown to correlate with insular activity (Critchley, 2009; Pollatos, Gramann, & Schandry, 2007). More than a century ago, William James (1884) proposed that emotions were the perceptual consequences of somatovisceral feedback from bodily responses. Although the construct of emotions as merely the perceptual consequences of somatovisceral feedback may no longer be tenable, it is increasingly recognized that visceral afference may modulate affective and cognitive processes in important ways (Bechara & Damasio, 2005; Craig, 2009; Critchley, 2009). Visceral afference, for example, has been reported to influence emotional memory and cortical reactivity, in part via ascending relays through an interconnected network of structures including the amygdala, the basal forebrain cholinergic system, and the insula (Berntson, Sarter, & Cacioppo, 2003).

The convergence of visceral and somatosensory information in the posterior insular cortex has been suggested to support interoceptive representations, and may constitute a fronto-insular junction linked to networks involved in affective processes, including the prefrontal cortex and the amygdala (Augustine, 1996; Craig, 2009; Critchley, 2009). Studies have demonstrated insula activation during diverse emotional states, such as disgust, pain, anxiety, and conditioned fear, as well as in response to depictions of emotional contexts or facial expressions of emotion in self or other people (Britton et al., 2006; Critchley, Mathias, & Dolan, 2002; Jabbi, Swart, & Keysers, 2007).

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These and other findings have led to the suggestion that the insular cortex plays a broad role in cognitive-emotional integration that contributes to the subjective guidance of cognition and behavior (Bechara, Damasio, & Damasio, 2003; Craig, 2009; Singer, Critchley, & Preuschoff, 2009). Research has shown activation of the anterior insula when people make risk-averse decisions (Kuhnen & Knutson, 2005). Moreover, the magnitude of insula activation predicts the extent of risky decisions (Xue, Lu, Levin, & Bechara, 2010), and insular lesions have been reported to impair sensitivity to aversive outcomes and the ability to adjust betting strategies according to probabilistic odds (Clark et al., 2008). Researchers have also reported activation of the insula during anticipation of risky gains or risky losses (Knutson & Greer, 2008). These findings suggest that the role of the insula is not limited to aversive contexts, but may extend to the integration of both positive and negative emotions in cognition and behavior. Consistent with this suggestion is the report that individual differences in interoceptive awareness are associated with insular activation and with arousal ratings in response to both positive and negative stimuli (Pollatos et al., 2007). Similarly, insular activation has been reported to be associated with appetitive motivation and with the perception of positive emotions in other people (Britton et al., 2006; Jabbi et al., 2007). Together, these findings suggest that the insula has a broad role in evaluative processing.

Another structure that has been implicated in evaluative processes is the amygdala. The amygdala has been a major focus of research and theory on affective processes since Kluver and Bucy's (1939) early report on affective blunting following amygdala/anterior temporal lobe lesions. The amygdala appears to play an important role in fear conditioning, preattentive processing of threat-related stimuli, emotional memories, and decision making based on punishment-reward contingencies (Bechara et al., 2003; LaBar, 2007; Öhman, Carlsson, Lundqvist, & Ingvar, 2007; Phelps, 2006).

Emotional stimuli and contexts have been shown to induce amygdala activation, as measured by functional brain imaging (Critchley, 2009; Norris, Chen, Zhu, Small, & Cacioppo, 2004; Sabatinelli, Bradley, Fitzsimmons, & Lang, 2005). The magnitude of this activation is related to affective intensity and is generally greater for negative than for positive emotional stimuli (Critchley, 2009; Norris et al., 2004; Sabatinelli et al., 2005). In contrast with insular lesions, lesions of the amygdala disrupt fear conditioning and the perception of potential danger (Bechara et al., 1995; LaBar, 2007; LeDoux, 2003; Phelps, 2006). These and other findings clearly implicate the amygdala in negative affect, but its precise role remains to be fully elucidated. Although the amygdala appears to have a predominant role in the generation of negative emotions, it may also play a role in appetitive conditioning and positive affect (Hamann, Ely, Hoffman, & Kilts, 2002) and may code emotional intensity as well as emotional valence (Adolphs, Russell, & Tranel, 1999).

To further clarify the role of the insula in evaluative processing, we examined the valence and arousal dimensions of evaluative judgments of lesion patients. We obtained separate valence (positivity and negativity) and arousal ratings in response to affective pictures in patients with insula lesions, patients with control lesions (the primary contrast group), and patients with amygdala lesions (who served as an additional contrast group).

Method

Participants

Seven patients with lesions of the insula (1 female, 6 male) constituted the primary focus of the study. The primary comparison group comprised 9 lesion patients (6 female, 3 male) with damage that spared the insula, the amygdala/temporal lobe area, and other areas implicated in affect (control-lesion patients). An additional comparison group consisted of 12 patients with lesions of the amygdala (6 female, 6 male).

All patients had undergone neuroanatomical characterization according to the standard protocols of the University of Iowa Laboratory of Neuroimaging and Human Neuroanatomy. The selection criteria were persistence of a stable and chronic lesion at least 3 months after onset and involvement of a brain region that included either the insula or the amygdala or (for the control-lesion patients) that excluded these structures and other areas thought to be critical for emotional processing (e.g., the ventromedial prefrontal cortex and orbitofrontal cortex). Patients were also evaluated for neuropsychological functioning using standard University of Iowa protocols (Tranel, 2009).

The etiology of the brain damage in all the insula-lesion and control-lesion patients was the same: an ischemic stroke. All the insula-lesion patients had unilateral damage that included more than 50% of the insula (anterior and posterior insula) and varying degrees of damage in surrounding areas within the middle cerebral artery blood-supply territories (see Fig. S1 in the Supplemental Material available online). Although there may be lateral differences in the effects of insula lesions, the small number of participants (4 with right-side lesions, 3 with left-side lesions) precluded meaningful analyses of such differences.

The control-lesion patients had either unilateral middle cerebral artery strokes that spared the insula or posterior cerebral artery strokes. The selection of these patients from the University of Iowa Patient Registry was random except for two exclusion criteria: Patients were excluded if their lesions involved the target areas or if they were under the age of 30 (because none of the target patients were younger than 30).

Two of the control-lesion patients had a lesion in the lateral frontal region, 2 had lesions in the superior temporal area and posterior parietal region that spared the insula and somatosensory cortex (1 with right-side lesions, 1 with left-side lesions), and 5 had damage in the inferior calcaine region extending inferiorly into the inferior occipitotemporal region (2 right-side lesions, 3 left-side lesions). On average, the size of the lesions was similar in the insula-lesion and the control-lesion groups.
The amygdala-lesion patients all had anterior temporal lobectomies for the control of seizure disorders. Because the etiology of the lesions differed between the amygdala and the insula patients, and because the amygdala patients were significantly younger than the insula patients, the amygdala group was included only for ancillary analysis. The primary focus was on comparing the insula group and the control-lesion group.

The patient groups did not differ appreciably on most demographic or neuropsychological characteristics (see Table S1 in the Supplemental Material). Amygdala patients were younger than patients in the other groups, so age was included as a covariate in all statistical analyses that included this group. The only neuropsychological test that revealed a difference between groups was the Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977), on which the amygdala group had a higher depression score than the other groups did. This difference was largely attributable to 1 subject who had a CES-D score 3 standard deviations above the mean of the group. All statistical results were equivalent whether or not this subject was included, so to be conservative, we report analyses including that subject.

### Apparatus
Response recording was implemented using E-prime (Psychology Software Tools, Pittsburgh, PA). Patients used a computer mouse to indicate valence and arousal ratings in response to the stimuli. For positivity and negativity ratings, participants positioned a cursor on a bivariate display (a 5 × 5 grid) in which the horizontal dimension indicated positivity and the vertical dimension indicated negativity. The arousal rating entailed a similar cursor placement on a single dimension (a 1 × 7 grid that represented a 7-point scale). The arousal grid was always presented after the valence grid to avoid potential bias from switching the order of presentation between the unidimensional arousal scale and the bivariate valence scale.

### Stimuli
Stimuli were pleasant, unpleasant, and neutral pictures from the International Affective Picture System database (Lang, Bradley, & Cuthbert, 2008). We included five picture categories that were defined by evaluative extremity and were matched on a range of normative arousal ratings within each picture category (10 very pleasant, 5 moderately pleasant, 10 neutral, 5 moderately unpleasant, and 10 very unpleasant). The stimuli were selected to sample a full range of affective ratings, distinct emotions, and social versus nonsocial contexts.

### Procedure
Participants rated the stimuli on positivity, negativity, and arousal after completing a standardized instruction and practice session (for the timeline, see Fig. S2 in the Supplemental Material). Pictures were presented in a random order on a computer monitor for 6 s each. Participants were instructed to focus on the emotional content of the pictures and then to rate each picture on a 5-point bivariate scale of positivity and negativity (ranging from not at all to extremely) and on a 7-point bipolar scale (ranging from not at all to extremely) indicating how aroused the picture made them feel. The bivariate response grid was presented on the screen immediately after the stimulus (Larsen, McGraw, Mellers, & Cacioppo, 2004). After subjects responded, a second screen displayed the univariate arousal continuum. The next stimulus was presented 3 s after subjects completed the arousal rating.

In addition to performing the experimental task, patients were evaluated on a range of neuropsychological tests, as detailed in Table S1 (see the Supplemental Material).

### Results

#### Evaluative valence ratings
Omnibus analyses of variance (ANOVAs) revealed the expected overall effects of picture category both on positivity ratings, $F(4, 100) = 18.58, p < .01, \eta^2 = .69$, and on negativity ratings, $F(4, 100) = 32.47, p < .01, \eta^2 = .84$. These effects were characterized by significant linear, quadratic, and cubic trends across the picture categories for positivity ratings, all $F$s(1, 25) > 15.55, $ps < .01$, and for negativity ratings, all $F$s(1, 25) > 26.35, $ps < .01$. These trends reflect the increasingly positive ratings for progressively pleasant stimuli and increasingly negative ratings for progressively unpleasant stimuli (see Fig. 1). Ratings by patients in the control-lesion group were highly similar to the published normative results for these stimuli.

As illustrated in Figure 1, patients in the insula group differed significantly from patients in the control-lesion group for both positivity ratings, $F(4, 56) = 12.59, p < .01, d = 1.92$, and negativity ratings, $F(4, 56) = 6.32, p < .05, d = 1.33$. Like patients in the control-lesion group, patients in the insula group provided low positivity ratings for unpleasant and neutral stimuli and low negativity ratings for pleasant and neutral stimuli. However, compared with the control-lesion patients, the insula patients showed smaller increases in positivity ratings as pleasant stimuli became more pleasant and smaller increases in negativity ratings as unpleasant stimuli became more unpleasant. This finding was reflected in significant group differences in the quadratic trend across picture categories for both positivity ratings, $F(1, 14) = 3.91, p > .05$, and negativity ratings, $F(1, 14) = 3.78, p = .05$.

#### Arousal ratings
An ANOVA revealed the expected main effect of picture category on arousal ratings, $F(4, 100) = 14.22, p < .01, \eta^2 = .44$ (see Fig. 1). In addition, the ratings of the insula and control-lesion groups had significantly different quadratic trends across the picture categories, $F(1, 14) = 9.64, p < .01$. These effects reflect...
the higher arousal ratings to increasingly pleasant or unpleasant stimuli. A main effect of lesion group further revealed that the arousal ratings of patients in the insula group were attenuated, compared with the arousal ratings of patients in the control-lesion group, and this pattern was most apparent for the very pleasant and very unpleasant pictures, $F(1, 14) = 6.99, p < .01, d = 0.91$.

**Comparisons with amygdala lesions**

**Amygdala versus control lesions.** An ANOVA revealed that the positivity and negativity ratings of the amygdala group were comparable to those of the lesion-control group, $F(4, 76) = 1.09$, $p > .05, d < 0.01$, and $F(4, 76) = 0.86, p > .05, d < 0.01$, respectively. The amygdala group, however, exhibited a selective attenuation of the arousal response to negative stimuli, as documented by a Lesion Group × Picture Category interaction: The ratings showed a significant group difference in quadratic trends across the picture categories, $F(1, 19) = 5.51, p < .05$. The control-lesion group exhibited a typical trend: Their arousal increased incrementally as pictures became less neutral (for both pleasant and unpleasant pictures). In contrast, the amygdala group exhibited a typical increment only for pleasant pictures, and the increment in their arousal ratings for

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![Graph](https://example.com/graph.png)

**Fig. 1.** Valence ratings (top panel) and arousal ratings (bottom panel) by three groups of lesion patients in response to five picture categories. The positivity and negativity scales were combined to display the results in this figure; the positivity scale is represented by positive values, and the negativity scale by negative values. Error bars represent standard errors of the mean.
increasingly unpleasant pictures was notably attenuated. This pattern of results is comparable to what we have reported previously (Berntson, Bechara, Damasio, Tranel, & Cacioppo, 2007).

**Amygdala versus insula lesions.** In comparison with patients in the amygdala group, the insula patients provided attenuated valence ratings in response to both pleasant and unpleasant stimuli. An ANOVA on positivity ratings revealed a main effect of lesion group, $F(1, 17) = 6.90, p < .05$, $d = 0.36$, and a Lesion Group × Picture Category interaction, $F(4, 68) = 3.19$, $p < .05$, which was characterized by differences in the linear and cubic trends in positivity ratings across the picture categories, $F(1, 17) > 7.22, ps < .05$. Both groups had low positivity ratings for neutral and unpleasant stimuli, but the trend differences reflect the insula patients’ attenuated increment in positivity ratings for increasingly pleasant stimuli. Similar results were obtained for negativity ratings, as revealed by a main effect of lesion group, $F(1, 17) = 5.67, p < .05$, $d = 0.29$, and a Lesion Group × Picture Category interaction, $F(4, 68) = 4.21, p < .05$, which was also characterized by differences in the linear and cubic trends across picture categories, $F(1, 17) > 5.00, ps < .05$. Paralleling the results for positivity ratings, the negativity ratings for neutral and pleasant stimuli were low for both groups, but patients in the insula group exhibited a smaller increment in negativity ratings for increasingly negative stimuli.

Like patients in the amygdala group, patients in the insula group displayed a significant attenuation of arousal ratings relative to patients in the control-lesion group. However, the arousal ratings of patients in the insula group were not attenuated selectively for unpleasant stimuli, but rather were attenuated for both pleasant and unpleasant pictures, as indicated by a significant main effect of lesion group (i.e., insula group vs. amygdala group), $F(1, 17) = 4.97, p < .05$, $d = 0.27$, and a significant difference in the cubic trend across picture categories, $F(1, 17) = 4.04, p < .05$. As illustrated in Figure 1, the insula group gave lower arousal ratings than the amygdala group, but this difference was most apparent for the pleasant pictures.

**Discussion**

Relative to patients in the control-lesion group, individuals with insula lesions exhibited progressively reduced arousal ratings for progressively more pleasant or unpleasant pictures. This pattern did not appear to reflect an overall bias in arousal ratings, as the insula groups’ ratings of neutral stimuli were similar to the ratings made by patients in the other groups. Rather, insula patients failed to show typical arousal increments in response to affective picture content, and this was the case for both pleasant and unpleasant stimuli. In contrast, the amygdala group exhibited a similar attenuation of arousal ratings in response to unpleasant stimuli, but displayed typical increments in arousal in response to pleasant stimuli.

One interpretive caveat is that the etiology in the amygdala group was distinct (i.e., temporal lobectomies for seizure disorders) relative to the insula and lesion-control groups (i.e., strokes). Thus, lesion locus is confounded with etiology and associated differences in variables such as chronicity and medication. The results of this study, however, are virtually identical to those of an earlier study in which we used the same paradigm (i.e., the same evaluative task) and included patients who had amygdala damage secondary to herpes simplex encephalitis (Berntson et al., 2007). Regardless of etiology, amygdala lesions yield a consistent pattern of selective deficit in arousal to unpleasant pictures in this paradigm.

Although the arousal ratings were given after the pictures were removed, the results are not likely attributable to a memory deficit, as the patients were not impaired in standard memory tasks (Wechsler Memory Scale, Wechsler, 1981, and the Benton Visual Retention Test, Benton, 1974; see Table S1). Another interpretive caveat is that valence and arousal were measured by self-report, so we cannot be certain that the intended psychological dimensions were directly measured. Our findings, however, are in accord with the literature.

Our results for arousal ratings are also consistent with the literature, which suggests that the insula may be involved broadly in emotion across both positive and negative contexts (Pollatos et al., 2007), and that the amygdala may play a more salient role in negative affect than in positive affect (Berntson et al., 2007; Critchley, 2009; Norris et al., 2004; Sabatinelli et al., 2005). The involvement of the insula in disgust reactions and aversive reactions has been recognized classically (Craig, 2009). In addition, activation of the insula has been shown to be associated with positive appetitive contexts (Britton et al., 2006), decisions about pleasantness and expected value of odors (Rolls, Grabenhorst, & Parris, 2009), the expected magnitude of reward (Smith et al., 2009), anticipation of gains as well as losses (Knutson & Greer, 2008; Xue et al., 2010), and empathy for both positive and negative emotions (Jabbi et al., 2007). Classic studies of the amygdala tended to focus on negative affect, especially fear, fear conditioning, and anger (Kluver & Bucy, 1939). Although it is now recognized that the role of the amygdala may be much broader than the processing of negative stimuli and contexts, the amygdala is nonetheless particularly sensitive to negative contexts (Adolphs et al., 1999; Phelps, 2006). This pattern is consistent with our finding of a selective attenuation of arousal ratings in response to negative stimuli among patients with amygdala lesions, although other studies suggest a more general involvement of the amygdala regardless of stimulus valence (Cunningham, Raye, & Johnson, 2004).

Damage to the insular cortex attenuated valence ratings for both pleasant and unpleasant stimuli. Like patients in the control-lesion group, the insula patients displayed low positivity ratings for neutral and unpleasant stimuli and low negativity ratings for neutral and pleasant stimuli. The insula group, however, showed an abbreviated increment in positivity ratings for increasingly pleasant stimuli and in negativity ratings...
for increasingly unpleasant stimuli. Thus, lesions of the insula appear to broadly affect evaluative processes, including both arousal and valence judgments for both pleasant and unpleasant stimuli. This finding does not appear to reflect a tendency of the insula patients to underrate on self-rating scales generally, as they displayed typical self-ratings on the UCLA Loneliness Scale (Russell, Peplau, & Cutrona, 1980) and the CES-D depression scale. Instead, the insula patients may have failed to recognize, attend to, or appropriately categorize the pleasant and unpleasant picture content.

In contrast, amygdala lesions may not disrupt the requisite perception, categorization, and labeling of affective picture content. Patients in the amygdala group provided valence ratings comparable to those provided by patients in the control-lesion group. Amygdala lesions appeared to selectively attenuate the arousal response to negative stimuli, even though the patients recognized and accurately categorized the negative picture content. The selectivity of the arousal deficit in the present study is not likely attributable to the fact that all the amygdala patients had unilateral lesions because the results are highly consistent with those of a prior study that included patients with bilateral lesions (Berntson et al., 2007). These findings are consistent with the report that the amygdala appears to preferentially process arousal rather than valence (Adolphs et al., 1999). The findings are also in general accord with reports that amygdala lesions may disrupt the development of conditioned autonomic arousal responses, even though patients with amygdala lesions can acquire explicit cognitive knowledge about stimuli and outcome contingencies (Bechara et al., 1995; LaBar, LeDoux, Spencer, & Phelps, 1995).

In summary, our results point to distinct roles for the insula and the amygdala in evaluative processes. The amygdala may not be necessary to determine whether and to what extent a stimulus is appetitive or aversive, hostile or hospitable; rather, it may be important for registering the arousal or emotional impact of stimuli (and especially of aversive stimuli). In contrast, the insular cortex appears to be more broadly involved in the recognition, processing, and assignment of evaluative valence, and may contribute to affective arousal. Although the amygdala and insula are discussed here as categorical entities for the convenience of exposition, these terms belie the underlying structural and functional complexities of these brain structures, as well as the rich interactions between these structures and other neural circuits. Further research may help clarify these complexities.

Declaration of Conflicting Interests

The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

Funding

This research was supported by a program project grant from the National Institute of Neurological Disorders and Stroke (Grant NS19632 to D.T. and A.B.), by the National Institute on Drug Abuse (Grant DA022549 to D.T. and Grant R01DA023051 to A.B.), and by grants from the National Institute of Mental Health and the Templeton Foundation to J.T.C.

Supplemental Material

Additional supporting information may be found at http://pss.sagepub.com/content/by/supplemental-data

References


