NeuroImage 78 (2013) 159–175

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Lateralization of affective processing in the insula

Emma G. Duerden [a,b,*], Marie Arsalidou [a,b], Minha Lee [a], Margot J. Taylor [a,b,c]

[a] Diagnostic Imaging and Neurology, Research Institute, The Hospital for Sick Children, Canada
[b] Neuroscience & Mental Health, Research Institute, The Hospital for Sick Children, Canada
[c] Department of Psychology, University of Toronto, Toronto, Canada

ARTICLE INFO

Article history:
Accepted 5 April 2013
Available online 13 April 2013

Keywords:
Insula
ALE
Emotion
Interoception
fMRI
Humans

ABSTRACT

Evidence from electrophysiological and functional neuroimaging studies has suggested strong lateralization of affective processing within the insular cortices; however, little is known about the spatial location of these processes in these regions. Using quantitative meta-analytic methods the laterality of: (1) emotional processing; (2) stimulus valence (positive vs. negative); (3) perception vs. experience of emotion; and (4) sex-differences were assessed using the data from 143 functional magnetic resonance imaging studies. Activation in response to all emotional stimuli occurred in bilateral anterior and mid-insula, and the left posterior insula. Positive emotional stimuli were associated with activation in the left anterior and mid-insula, while negative emotional stimuli activated bilateral anterior and mid-insula. Activation in response to the perception and experience of emotions was highest in bilateral anterior insula, and within the mid and posterior insula it was left lateralized. In males, emotional stimuli predominantly activated the left anterior/mid-insula and right posterior insula, whereas females activated bilateral anterior insula and the left mid and posterior insula. Spatial distinctions observed in emotional processing and its subcategories can provide a comprehensive account of the role of the insular cortices in affect processing, which could aid in understanding deficits seen in psychiatric or developmental disorders.

Introduction

The insula is an essential brain region for the integration of interoceptive information (sense of the physiological state of the body) and emotional experience (Craig, 2002, 2009). These properties are afforded to the insula through extensive viscerosensory input from the periphery and reciprocal connections with limbic, somatosensory, prefrontal and temporal cortices (Augustine, 1996; Mesulam and Mufson, 1982a, 1982b). The insula processes appetitive and aversive physiological sensations (i.e. thirst, hunger, pain) and the associated emotional arousal that results in the conscious perception of one's affective state (James, 1884; Lange, 1885; Russell, 2003; Schachter and Singer, 1962).

Evidence from electrophysiological studies and hemispheric inactivation procedures has indicated strong lateralization of affective processing within the insula based on autonomic input to this region (Hilz et al., 2001; Oppenheimer et al., 1992). However, inconsistent results have come from lesion studies in patients and findings from functional neuroimaging studies. Meta-analyses of functional imaging data permit the collation of findings across studies and can provide precise spatial localization of affective processing to develop a topographical model of emotional functions within the insula.

Historically, emotional processes were believed to be mediated by the right hemisphere (for review see (Harrington, 1995)). More recent reports with patients and functional neuroimaging studies have indicated that emotional processing is left- or right-lateralized based on stimulus valence (positive/negative emotions) (Davidson et al., 1979; Hellige, 1993; Silberman, 1986), behavior (approach/withdrawal) (Davidson et al., 1990) and/or phenomenal state (perception/experience) (Garrett and Maddock, 2006; Peelen et al., 2010; Zaki and Ochsner, 2011).

Lateralization of emotional processing in the insula has been supported by evidence suggesting differential autonomic inputs (parasympathetic/sympathetic) to this region (Craig, 2005). For example, direct stimulation of the left insula results in changes in parasympathetic functions (Oppenheimer et al., 1992) involving nourishment, safety, positive affect and approach behavior (Craig, 2005), whereas the right insula has been implicated in top-down control of sympathetic-nervous system functioning, which is involved in hunger, survival, negative affect and avoidance behavior.

Support for this stimulus-valence processing scheme has come from functional neuroimaging, but with some discrepancy among the findings (Caria et al., 2010; Phillips et al., 1997; Simmons et al., 2004, 2012; Sprengelmeyer et al., 1998; Wager et al., 2003). For example, functional imaging studies of passionate, maternal and unconditional love showed that these positive stimuli activated the left more than

Abbreviations: ALE, activation likelihood estimate; fMRI, functional magnetic resonance imaging; T, Tesla; AC, accessory gyrus; AS, anterior short insular gyrus; MS, middle short insular gyrus; PS, posterior short insular gyrus; AI, anterior long insular gyrus; PL, posterior long insular gyrus.

* Corresponding author at: Department of Neurology, The Hospital for Sick Children, Toronto, Ontario, M5G 1X8, Canada. Fax: +1 416 813 7362.
E-mail address: emma.duerden@sickkids.ca (E.G. Duerden).

1053-8119/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.neuroimage.2013.04.014

the right insula (for review, see (Ortigue et al., 2010)); however, these results may be influenced by sex as 83% of the studies reviewed tested female participants. In line with the valence hypothesis, the right anterior and mid-insula were activated during negative experiences including motion-induced nausea (Napadow et al., 2012) and viewing intense facial expressions of disgust (Phillips et al., 1997). In contrast, other imaging studies have indicated that the left anterior insula mediates negative stimuli, such as viewing unpleasant visual stimuli (Caria et al., 2010). To determine the effect of valence (positive and negative stimuli) on insular activation was one of the main aims of the current work, with a focus on the hemispheric contributions of anterior, middle and posterior regions.

Previous reports concerning the lateralization of emotional processing in the insula were based largely on results obtained from participants viewing emotional stimuli. Further distinctions can be made in the viewing of emotional stimuli in terms of perceiving or actually experiencing an emotion (Garrett and Maddock, 2006; Kober et al., 2008; Lindquist et al., 2012; Peelen et al., 2010; Zaki and Ochsner, 2011). Individual neuroimaging studies have tested this hypothesis and have suggested some lateralization of processing (Modinos et al., 2011; Wicker et al., 2003). For example, bilateral insular cortex was activated in individuals who smelled disgusting odors (experience), but only the left side was activated when viewing others performing the same act (perception) (Wicker et al., 2003). Few individual neuroimaging studies have contrasted self versus another's emotional experience within the same experimental protocol and therefore the laterality of these processes remains uncertain. In the present work, hemispheric and region-specific (anterior/middle/posterior insula) preferential emotional processing related to self and others was assessed.

Subtle differentiations in self/other emotional processing could have strong clinical relevance. For example, in individuals with autism spectrum disorder (ASD) atypical activity in the insula may underlie deficits in understanding the thoughts and emotions of others (Allman et al., 2005; Silani et al., 2008). Children with ASD were found to activate the right insula when viewing neutral images of themselves as seen in typically-developing children, but they did not activate the right insula when viewing images of others (Uddin et al., 2008). Improved understanding of the localizations of these subtleties of functions in a normative population will greatly facilitate the understanding of findings in clinical populations.

Lastly, further distinctions in emotional processing in the insular cortices may be influenced by the sex of the participants. This line of reasoning comes from several sources such as behavioral evidence suggesting that females are better than males at understanding the emotions of themselves and others (Baron-Cohen and Wheelwright, 2004; Eisenberg and Lennon, 1983). Females demonstrate increased affective arousal or expression of emotion during social interactions (Brody and Hall, 2000), although this may depend on contextual factors (Barrett et al., 1998). Key to emotional competence is the ability to recognize facial expressions; females compared to males have a greater ability to recognize facially expressed emotions, even in instances where stimuli are presented for brief periods (Donges et al., 2012; Hall, 1978; Hall and Matsumoto, 2004; Hoffmann et al., 2010). Several brain-imaging studies have demonstrated differential neural processing in females and males during emotional processing tasks (Cahill, 2006; Derntl et al., 2009; Hofer et al., 2006, 2007). For example, in an fMRI experiment that tested both sexes, only females recruited bilateral insular cortices in conjunction with the amygdalae during the perception of humorous stimuli (Kohn et al., 2011), a finding that the authors attributed to potentially greater emotional-regulation abilities in females. Some evidence also suggests sex-differences in the lateralization of stimulus-valence processing within the insula. An fMRI study examining cognitive modulation of emotion reported activation in the left insula only in females during the perception of aversive stimuli (Koch et al., 2007). Additionally, a recent meta-analysis of 88 studies examining brain activation associated with emotional stimuli reported that females activated the left insula in response to negative emotional stimuli whereas males showed bilateral activation in this region (Stevens and Hamann, 2012). Given these previous findings, we investigated activation in the insula in response to emotional stimuli in males and females separately.

Lateralization of emotional processing in the insular cortices is a fundamental aspect of interpreting the functions of this region; however, no clear consensus on the roles of the left and right insula in emotional processing has been established. Here, using affect-related data from fMRI studies, we explored topographical distinctions of the various aspects of emotional processing (i.e., positive, negative, perception, experience) within the insula and provide normative atlases for these processes in stereotaxic space. The meta-analyses tested: (1) right-insular cortex dominance for global emotional processing, (2) lateralization of stimulus valence (positive vs. negative), (3) perceiving vs. experiencing emotional stimuli and (4) sex differences.

Methods

Article selection and literature search

An initial broad search of the literature was conducted to determine the range of affective-, cognitive-, motor- and sensory-evoked activation in the insula measured using fMRI. The Web of Science (http://www.isiknowledge.com) was searched for articles published between January 1990 and October 2010 using the keywords fMRI and insula. The initial search yielded a total of 1263 articles. The studies were screened for the following inclusion criteria: (1) written in English; (2) fMRI experiment; (3) stereotaxic coordinates; (4) healthy human participant data; and (5) general linear model analyses. Exclusion criteria were: review articles, patient data, connectivity analyses, meta-analyses, case studies, special populations (e.g. savants, psychics), deactivation and pharmacological fMRI. The initial screening resulted in the exclusion of 545 articles (Reviews: 35; Meta-analyses: 14; Case studies: 8; Patients: 86; Special populations: 26; No healthy within-subject analysis: 88; Pharmacological fMRI: 19; Functional connectivity: 10; No coordinates: 191; Not fMRI: 22; Animal studies: 4; Other: 34; Not retrievable: 7; Duplicate study: 1).

A total of 718 studies meeting our criteria underwent full review and the following information was entered into a database: author names, year of publication, number of participants, mean age, Tesla (T) strength of scanner, task description, affect (positive/negative) and contrast(s). Of the 718 studies reporting activation in the insula, the largest single grouping, $n = 143$, used emotional stimuli. The remaining studies reported cognitive-related activation (e.g. language, executive functioning, working memory, reasoning, gambling, time perception, self viewing, reward, mentalizing), or activation in response to somatosensory stimuli (e.g. noxious, tactile) and other perceptual stimuli (e.g. auditory, olfactory, gustatory). Additionally, many studies reported motor-related activity. In the current work, the data from the 143 fMRI studies of emotion were analyzed.

These emotion studies were further categorized according to stimulus valence (positive or negative stimuli) and into perception and experience categories (Table 1 for details). Examples of positive stimuli included images of loved partners and friends or happy faces, whereas negative stimuli/protocols included the induction of feelings of regret, shock avoidance and images of others in pain. Studies were classified as perception or expression using similar criteria as outlined by Wager et al. (2008). The key distinction between the perception and experience categories was the intention of inducing a subjective emotion in the participants in the latter category. The perception category included studies that examined participants who viewed the emotion of others, whereas the experience category included studies with participants who viewed emotional stimuli that elicited