



Clinical neuroanatomy

Insular networks for emotional processing and social cognition: Comparison of two case reports with either cortical or subcortical involvement

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ABSTRACT

Introduction: The processing of the emotion of disgust is attributed to the insular cortex (IC), which is also responsible for social emotions and higher-cognitive functions. We distinguish the role of the IC from its connections in regard to these functions through the assessment of emotions and social cognition in a double case report. These subjects were very rare cases that included a focal IC lesion and a subcortical focal stroke affecting the connections of the IC with frontotemporal areas.

Materials & methods: Both patients and a sample of 10 matched controls underwent neuropsychological and affective screening questionnaires, a battery of multimodal basic emotion recognition tests, an emotional inference disambiguation task using social contextual clues, an empathy task and a theory of mind task.

Results: The insular lesion (IL) patient showed no impairments in emotion recognition and social emotions and presented with a pattern of delayed reaction times (RTs) in a subset of both groups of tasks. The subcortical lesion (SL) patient was impaired in multimodal aversive emotion recognition, including disgust, and exhibited delayed RTs and a heterogeneous pattern of impairments in subtasks of empathy and in the contextual inference of emotions.

Conclusions: Our results suggest that IC related networks, and not the IC itself, are related to negative emotional processing and social emotions. We discuss these results with respect to theoretical approaches of insular involvement in emotional and social processing and propose that IC connectivity with frontotemporal and subcortical regions might be relevant for contextual emotional processing and social cognition.

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1. Introduction

The insular cortex (IC) is localized deep in the lateral sulcus and is a brain region considered crucial for body representation and emotional experience. Specifically, the IC is involved in the recognition, experience and imagination of basic emotions (Jabbi et al., 2008; Sprengelmeyer et al., 2010), as well as in social emotions like empathy and moral judgment (Caruana et al., 2011; Decety et al., 2011). The right anterior IC (r-aIC) seems to play an integrative role in coordinating the awareness of body feelings (Craig, 2002), integrating contextual social clues (Amoruso et al., 2011; Ibanez and Manes, 2012), and representing uncertainty (Singer et al., 2009). The functional role of the insula in coordinating emotional and social cognition is supported by the wide array of structural connections of the IC with the orbitofrontal (OFC), dorsolateral prefrontal cortices (DLPFC), anterior cingulate cortex (ACC), medial and lateral temporal lobe structures, ventral striatum and amygdala (Mufson and Mesulam, 1982; Viskontas et al., 2007). In addition, functional connectivity measures during the resting state have identified the aIC as the main functional node related to cognitive, homeostatic and emotional cortico-subcortical networks (Deshpande et al., 2011). Together, these studies highlight the insula as a core region in a broad network integrating emotion and cognition.

The specific function of the IC in negative emotions remains a matter of debate, and there are a number of conflicting studies that still need to be reconciled. Functional magnetic resonance imaging (fMRI) studies in normal subjects show the role of the insula in the perception of aversive emotions (Jabbi et al., 2007; Murphy et al., 2003; Straube and Miltner, 2011), particularly disgust (Brown et al., 2011; Jabbi et al., 2008; Phillips et al., 1997; Reker et al., 2010; Wicker et al., 2003). These results seem compatible with studies in patients with left (Calder et al., 2000) and bilateral (Adolphs et al., 2003) insular damage, who show a deficit in the recognition and experience of disgust. However, in apparent contradiction with these findings, Straube et al. (2010) reported no impairment in disgust recognition and experience in a patient with a right IC stroke. These results have led to the current discussion regarding the specificity of the IC for disgust processing.

This debate among lesion studies has been difficult to resolve mainly because exclusive focal damage to the IC is extremely infrequent in everyday clinical practice because of its anatomical positioning and vascular supply from the middle cerebral artery (MCA) (Cereda et al., 2002). In fact, in all previous studies of IC lesions (Adolphs et al., 2003; Calder et al., 2000; Ibanez et al., 2010b; Manes et al., 1999a, 1999b, 1999c; Straube et al., 2010), the injuries were not fully constrained to the IC. Notably, these injuries included extra-insular damage, mainly to the basal ganglia, connecting white matter and structures like the amygdala, the ventral striatum and the claustrum, which also play a role in affective processing networks (Adolphs, 2002; Fernandez-Miranda et al., 2008). Therefore, previous lesion studies cannot rule out the participation of other adjacent areas in negative emotion processing.

On another level, the IC seems to be involved in social emotions and social cognition through interoceptive information and body awareness (Straube and Miltner, 2011). Interoceptive representation has been suggested to modulate motivational behavior (Craig, 2002; Wiens, 2005), empathy (Lamm et al., 2011; Lamm and Singer, 2010), risky decision making (Dunn et al., 2010), and social skills such as the theory of mind (Bird et al., 2010; Keysers and Gazzola, 2007) and intentional action understanding (Brass and Haggard, 2010). Importantly, these are complex social cognition processes that are supported by emotional and body feedback information (Lamm and Singer, 2010). Additionally, several functional connectivity analyses of fMRI data indicate that there is engagement of the IC and cingulate regions in both the dorsal network, which is involved in cognitive control, and the ventral network, which is mostly related to emotional experiences (Cauda et al., 2011; Dosenbach et al., 2007; Kober et al., 2008; Taylor et al., 2009; Touroutoglou et al., 2012). This aIC-ACC network, also known as the *saliency network*, is suggested to switch between attentional and resting state modes (Sridharan et al., 2008) and to integrate cognitive, homeostatic and emotional saliency information (Deshpande et al., 2011; Medford and Critchley, 2010). Furthermore, a combination of diffusion tensor imaging (DTI) and dissection techniques has revealed that through the external capsule, the IC structurally connects with the adjacent frontal, parietal, and temporal operculae and with the inferior occipitofrontal fascicle running from the PFC to the posterior temporal and occipital cortices (Cerliani et al., 2011; Fernandez-Miranda et al., 2008). Thus, it is intriguing to think that the external capsule and the thin gray matter sheet within it, the claustrum, might be crucial areas connecting IC with a frontotemporal network involved in the integration of basic emotional processing and higher-order social cognition processes (Ibanez and Manes, 2012; Viskontas et al., 2007).

Despite these converging lines evidence suggesting a role of the IC *and related connections* in social emotion and social cognition, the functional significance of this area had yet not been directly tested by means of lesion studies.

The objective of this work is to thoroughly examine the functional role of the IC through the study of two rare focal lesion cases. Our aims are to investigate multimodal emotion recognition (including aversive emotions such as fear and disgust) and social cognition processes such as empathy, contextual social-emotional inference and theory of mind. A key aspect of this investigation is the peculiarity of the lesions studied, which allows us to go beyond previous studies and distinguish the role of the IC *per se* from that of its connections within the frontotemporal cortical-subcortical network. The first case involves a focal, pure right IC ischemic lesion and the second case involves a right putaminal-white matter hemorrhagic injury, which disrupt the posterior insular connections from the frontotemporal network.

Our unexpected results show that processing of both negative (disgust included) and social emotions is not impaired in focal IC but is affected in the case of a subcortical lesion (SL) disrupting the connection between the insula and frontotemporal regions.

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