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Social information processing following resection of the insular cortex

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ABSTRACT

The insula has been implicated in social cognition and empathy in several neuroimaging paradigms. Impairments in social information processing, including specific deficits in disgust recognition, have been described following isolated insular damage, although the evidence remains limited to a few case studies. The present study examines social cognition and empathy in a group of fifteen patients for whom the insula was removed as part of their epilepsy surgery. These patients were compared to a lesion-control group of 15 epileptic patients who had a surgery in the anterior temporal lobe that spared the insula, and to 20 healthy volunteers matched on age, sex, and education. Participants were assessed on an Emotion Recognition Task (ERT), the Reading the Mind in the Eyes test, and a self-administered empathy questionnaire. Patients who underwent insular resection showed poorer ability to recognize facial expressions of emotions and had lower scores of perspective taking on the empathy questionnaire than healthy controls. Using results from healthy controls as normative data, emotion recognition deficits were more frequent in insular patients than in both other groups. Specific emotion analyses revealed impairments in fear recognition in both groups of patients, whereas happiness and surprise recognition was only impaired in patients with insular resection. There was no evidence for a deficit in disgust recognition. The findings suggest that unilateral damage to the operculo-insular region may be associated with subtle impairments in emotion recognition, and provide further clinical evidence of a role of the insula in empathic processes. However, the description of 15 consecutive cases of insula-damaged patients with no specific deficit in disgust recognition seriously challenges the assumptions, based on previous case reports, that the insula is specifically involved in disgust processing.

1. Introduction

The insula is located deep in the Sylvian fissure, hidden behind the frontal, temporal, and parietal opercula, and is considered as the fifth lobe of the human brain. It has long been viewed roughly as part of the "visceral brain", which was supported by direct electro-cortical stimulation of the insular cortex eliciting visceral sensory and motor responses in patients undergoing brain surgery (Penfield and Faulk, 1955; Pool, 1954). These findings have been replicated on several occasions since then (Isnard et al., 2004; Nguyen et al., 2009; Stephani et al., 2011), and the role of the insular cortex in viscero-sensory processing is now well-established (e.g., Craig, 2002). However, with the advent of functional neuroimaging techniques, the insular cortex has been shown to be also involved in processing complex information, such as social and emotional stimuli (Damasio et al., 2000; Kurth et al., 2010; Phan et al., 2002). Although no global interpretation of insular function prevails, neuroimaging studies have contributed to the formulation of different hypotheses, including salience detection, subjective awareness, and neural representation of body states which are integrated in other cerebral structures for higher-order cognitive processes (Bechara and Damaio, 2005; Craig, 2002; 2009; Damasio, 1994; Menon and Uddin, 2010).

Despite converging evidence from neuroimaging studies that the insula is activated during social information processing (e.g., Kurth et al., 2010; Melloni et al., 2014; Singer et al., 2004), what essential role it actually plays remains unclear. This is mostly attributable to the very low incidence of lesions restricted to this area (Cereda et al., 2002). In a pioneering case study, Calder et al. (2000) described the case of a patient who presented with a specific impairment in the experience and recognition of the

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emotion of disgust following left hemisphere infarction that involved the insula and the basal ganglia. This, combined with data from neuroimaging studies (e.g., Phillips et al., 1997; Wicker et al., 2003), lead to the proposal that the insula plays a major role in disgust processing. Impaired recognition of facial expressions of disgust, along with emotional disturbance, has also been later reported in another rare patient with an ischemic lesion involving the left posterior insula (Borg et al., 2013). However, others have reported no such impairment following isolated insular injury (Straube et al., 2010). Furthermore, the specificity of the insula for processing disgust has been questioned by several studies which suggested an involvement in processing other emotions as well (e.g., Britton et al., 2006; Dal Monte et al., 2013; Schienle et al., 2002). A recent case study reported impaired perception of pain in others in three patients with isolated anterior insular lesions, providing further support for a more global role of the insula in empathic processes rather than a specific role in disgust processing (Gu et al., 2012). Still, clinical evidence for a role of the insular cortex in socio-emotional processing relies mostly on exceptional, anecdotal reports of single or a few patients with heterogeneous clinical presentations, and larger studies with systematic assessments of patients with isolated insular damage are still lacking.

The insula has been shown to be involved in the epileptogenic zone of a non-negligible proportion of drug-resistant epileptic patients (Isnard et al., 2004; Nguyen et al., 2009). With the recent advances in microsurgical techniques, an increasing number of insular resections have been reported for epilepsy control purposes (Kaido et al., 2006; Malak et al., 2009; von Lehe et al., 2009) which may, in the meantime, disrupt insular function by tissue removal or destruction. For instance, resection of the left insula may result in transient expressive language deficits (Boucher et al., 2015; Duffau et al., 2006; Sanai et al., 2010). However, whether insular resection for seizure control is associated with impairments in social processing remains undocumented. The assessment of social information processing and empathy in these patients may also uncover crucial information on the role of the insular cortex.

The present study examines social information processing in a group of patients who had partial or complete removal of the insular cortex as part of their epilepsy surgery. Patients were compared to a group of healthy controls, and to a lesion-control group of patients who had epilepsy surgery that spared the insula. The latter group was recruited to exclude the possibility that social information processing deficits in insular patients are solely attributable to the effects of intractable epilepsy, or to non-anatomically-specific effects of brain tissue resection and surgery. Given the higher prevalence of temporal lobe epilepsy and in order to create a homogeneous group, patients who underwent anterior temporal lobe (including the medial structures) epilepsy surgery were recruited as lesion-controls, although specific fear recognition or more global social cognition impairments have previously been documented in this population (Adolphs et al., 2001; Ammerlaan et al., 2008; Cohn et al., In press; Dellacherie et al., 2011; Gosselin et al., 2011). We hypothesized that insular surgery would be associated with a global impairment in the ability to recognize emotions and mental states in others, whereas temporal lobe surgery would be specifically associated with impaired recognition of fearful expressions.

2. Material and methods

2.1. Participants and procedure

All adult patients who underwent partial or complete insular resection for control of drug-resistant epilepsy in our epilepsy service, during the period extending from November 2004 to July 2013, were invited to participate to this study, with the exception of one patient with an epileptic focus which involved the frontal lobe and the insula who presented with notable behavioral problems prior to his surgery. None of these patients had a major sensory, motor, or language impairment that could have affected their performance in the present study, as revealed by standard neuropsychological assessment (Boucher et al., 2015). All seventeen patients accepted our invitation but two were excluded after data collection because they had undergone an additional resection involving a large portion of the prefrontal cortex, which may have affected their results.

The insular patients were matched with two control groups: a lesion-control group ($n=15$) of patients who had epilepsy surgery in the anterior temporal lobe that spared the insula, and a healthy control group ($n=20$). Participants from both control groups were selected in order to be comparable to the insular group on age, sex, education, and for the lesion-control group, hemisphere of resection and time since surgery. The healthy control group was recruited using ads published on the hospital's intranet page; criteria of selection were: age between 18 and 55 years, and no history of neurological problems.

The final sample of insular patients ($n=15$) along with information on their surgeries, are described in Table 1; Table 2 reports the same information for the lesion-control group. Fig. 1 depicts resection overlap among insular patients and representative cases of insular resections. Individual post-operative MRI scans from each patient from the insular group can also be found in Supplementary Fig. 1. The list of psychoactive drugs taken by each patient at time of assessment, including anticonvulsants, antidepressants, and anxiolytics, is reported in Supplemental Table S1.

Assessments were conducted by a licensed neuropsychologist (O.B.), after obtaining informed written consent from the study participant. Patients were assessed at least four months after neurosurgery. Three patients (two in the insular group, one in the temporal group) were assessed in English because they were native English speakers; all the other participants were tested in French. A 50$ financial compensation was given to each participant at the end of the assessment. The study protocol was approved by our institutional Ethics committee.

2.2. Social processing assessment

2.2.1. Emotion Recognition Task

We created an experimental task using the stimuli from the Directed Emotional Faces database (Goeleven et al., 2008; Lundqvist et al., 1998) to assess recognition of facial expressions of emotions. This Emotion Recognition Task (ERT) was implemented with E-Prime (Psychology Software Tools, Pittsburgh, PA). Stimuli were frontal pictures of 20 human faces (10 of each gender) each displaying the six basic emotions (anger, fear, disgust, happiness, surprise, and sadness). All pictures were gray-scaled, sized-adjusted, and cropped to exclude non-facial clues, and presented on a computer screen with black background. Stimuli were presented for 200 ms and were immediately followed by a white-noise mask lasting 250 ms. Then, the six-emotion response choice was presented on the screen, and remained until the participant gave his/her answer using the computer keyboard. The following stimulus was preceded by a fixation cross (1500–2500 ms) at the center of the screen. Each picture was presented once in one of two blocks of 60 trials, each of which contained an equal number of pictures of each emotion. The first block was preceded by a practice trial, which included one picture of each emotion. The number of correct responses and reaction times for correct responses were collected for the complete experiment as well as for each emotion separately.