Neuropsychologia 84 (2016) 29–35

Contents lists available at ScienceDirect

Neuropsychologia

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

Specific disgust processing in the left insula: New evidence from direct electrical stimulation

Costanza Papagno [a,b,*], Alberto Pisoni [a,b], Giulia Mattavelli [a,b], Alessandra Casarotti [c], Alessandro Comi [c], Francesca Fumagalli [a], Mirta Vernice [a], Enrica Fava [c,d], Marco Riva [d], Lorenzo Bello [c,d]

[a] Dipartimento di Psicologia, Università di Milano-Bicocca, Piazza dell'Ateneo Nuovo 1, 20126 Milano, Italy
[b] Centro di Neuroscienze NeuroMi, Università di Milano-Bicocca, Piazza dell'Ateneo Nuovo 1, 20126 Milano, Italy
[c] Unit of Surgical Neurooncology, Humanitas Research Hospital, via Manzoni 56, Rozzano, 20089 (MI), Italy
[d] Department of Medical Biotechnology and Translational Medicine, Università degli Studi di Milano, via Manzoni 56, Rozzano, 20089 (MI), ITALY

ARTICLE INFO

Article history:
Received 20 October 2015
Received in revised form
26 December 2015
Accepted 29 January 2016
Available online 1 February 2016

Key words:
insular cortex
emotions
disgust
awake surgery
glioma

ABSTRACT

Neuropsychological and neuroimaging studies yielded controversial results concerning the specific role of the insula in recognizing the facial expression of disgust. To verify whether the insula has a selective role in facial disgust processing, emotion recognition was studied in thirteen patients during intraoperative stimulation of the insula in awake surgery performed for removal of a glioma close to this structure. Direct electrical stimulation of the left insula produced a general decrease in emotion recognition but only in the case of disgust there was a statistically significant detrimental effect ($p=0.004$). Happiness and anger were the best and the worst recognized emotion, respectively. The worst baseline performance with anger and, partly, fear could be explained with the involvement of the left temporal regions, striatum, and the connection between the striatum and the frontal lobe, as suggested in previous studies. Therefore, upon these intra-operative evidences, we argue for a selective role of the left insula in disgust recognition, although a (non significant) decrease in the recognition of other negative emotions was found. However, additional networks can develop, as demonstrated by the fact that disgust recognition was not impaired after surgery even in patients with insular resection in the current as in previous studies.

1. Introduction

Neuropsychological (Calder et al. 2000) and functional neuroimaging studies (Calder et al. 2001) have demonstrated that facial expressions of disgust consistently engage distinct brain areas (insula and putamen) compared to other facial expressions (Sprengelmeyer et al. 1998). Most evidence concerning the recognition of disgust comes from brain-damaged patients with vascular lesions or Huntington's disease (HD) (Kipps et al., 2007; Sprengelmeyer et al. 1998) and from neuroimaging studies.

Concerning stroke patients with a deficit for disgust recognition, a bilateral or left-sided involvement of the insula has been found (Adolphs et al. 2003, and Calder et al. 2000, respectively), with no impairment when the *right* insula is damaged (Straube et al. 2010).

Functional MRI (fMRI) studies on pre-symptomatic HD patients support a selective role of the left antero-ventral insula in disgust recognition: indeed, this structure and the left putamen are significantly activated in healthy subjects but not in pre-symptomatic HD (Hennenlotter et al. 2004). Similarly, voxel-based morphometry unveiled a positive correlation between the left antero-ventral insula volume and disgust recognition (Kipps et al. 2007), the ventro-anterior region being also involved in chemosensory processing (Pritchard et al. 1999), which suggests that the neural response to facial expressions of disgust is related to the region involved in the appreciation of unpleasant tastes (Phillips et al. 1997).

Contrasting evidence about the side of activation comes from a meta-analysis on 105 studies (using different tasks to assess emotion recognition) performed by Fusar-Poli et al. (2009) on voxel-based analysis of fMRI data: disgust and anger proved to activate the right insula with a higher intensity for disgust than for the other expressions. Additional support for the role of the insula is provided from studies on monkeys, in which stimulation of the insula elicits disgust (Caruana et al. 2011).

* Correspondence to: Costanza Papagno, Dipartimento di Psicologia, Università di Milano-Bicocca, Piazza dell'Ateneo Nuovo 1- Edificio U6, 20126 Milano, Italy., Tel.: +39 0264483738; fax: +39 0264483706.
E-mail address: costanza.papagno@unimib.it (C. Papagno).

http://dx.doi.org/10.1016/j.neuropsychologia.2016.01.036
0028-3932/

Despite the evidence of a selective insular activation in disgust processing (see also Wicker et al. 2003), Schienle et al. (2002) suggested a less specific role, based on an apparently similar activation for fear. More recently, no specific deficit in disgust recognition was found in 15 consecutive cases of patients with selective resection of the insular cortex (Boucher et al. 2015).

Therefore, at least two issues are still controversial, namely whether the insula processes disgust only or it is part of a more central circuit involved in monitoring motivationally salient stimuli (Damasio et al. 2000; Phan et al., 2002; Schienle et al. 2002; Campanella et al. 2014), and whether a left (Sprengelmeyer et al. 1998, Calder et al. 2000; Kipps et al. 2007), right (Fusar-Poli et al. 2009), or bilateral (Schienle et al. 2002; Adolphs et al. 2003) involvement is required.

A direct test of the role of the insula in emotion processing would be to assess errors during direct electrical stimulation (DES) in awake surgery. This technique allows mapping extremely small ($< 1\ cm^2$) brain areas (Ojemann et al. 1989) with an excellent spatial accuracy and temporal resolution. During brain surgery for tumor resection it is a common and recommended clinical practice to awaken patients in order to assess the functional role of selected brain regions, to maximize the extent of the resection while sparing the eloquent functions, generally with a particular attention to language and the motor-sensory system. Since emotional deficits are evident after surgery (Campanella et al. 2014) and are often reported by relatives or caregivers, we assessed emotion recognition when a potentially crucial region had to be (partially) removed. In the current study, patients were asked to perform a modified version of the Ekman Test while DES was temporarily applied to inactivate circumscribed regions around the tumor. By cumulating the performances over the investigated areas and across participants, a map of the functional role of different brain regions can thus be built.

2. Materials and methods

2.1. Participants.

Thirteen patients (seven women and six men, mean age 42.75, SD 15.26, range 29-69, mean education 13.5 years, DS 3.94, range 8-20) were enrolled in the study. Two patients were left-handed but the fMRI revealed a left lateralization of language. The protocol was carried out according to the ethical standards of the Declaration of Helsinki (BMJ 1991; 302: 1194), in compliance of a protocol approved by the local Ethical Committee.

Participants were selected when the following two criteria were concurrently met: (i) the site of the lesion allowed the stimulation of the insula and (ii) the performance on the modified Ekman test (see below) in the pre-surgery evaluation was at least 80% correct. All patients but one harboured a left hemisphere tumor. Patients' clinical and demographical data are reported in Table 1. All patients underwent a detailed neuropsychological evaluation (Papagno et al. 2012) and a volumetric 3 T MRI, as described later, the day before surgery (see Table 2). The lesions were not histologically homogeneous, as in the majority of studies with brain tumor patients (see for example Campanella et al. 2014; Giussani et al. 2008). However, a deficit observed in both low-grade (where re-organization can be expected) and high-grade gliomas/metastasis (in which this is not likely to occur) makes the observation more robust. Further support to the data obtained with lesions in evolution comes from focal (non-evolving) lesions, such as cortical dysplasia (patient N. 1). Moreover, the neuropsychological performance did not differ between low- and high-grade lesions (see Appendix A). No patients suffered language deficits before surgery, except in one case (mild decrease in semantic fluency for N. 5, see also Table 2 for adjusted scores in verbal tasks). Neuropsychological testing was repeated in the week after surgery (see Table 3).

2.2. Emotion test.

Emotion recognition was assessed before, during and after surgery. Stimuli were randomly presented each time to avoid learning effects. Twenty-five stimuli were selected from the FEEST set (Young et al. 2002) to create a modified version of the Ekman test. Five models (three women and two men) were chosen on the basis of the recognition rate for each expression, the similarity of the posed expression across models and the similarity of the muscle groups used to pose the expressions (Mattavelli et al. 2014). For each of these faces, we selected the emotions of anger, fear, happiness, disgust (excluding sadness and surprise) and a mildly neutral expression, which was obtained by using happiness at the 25% of its intensity. The mildly happy face was preferred because fully neutral faces can appear slightly cold and hostile (Ekman and Rosenberg, 1997); thus, as done in some previous studies (Mattavelli et al., 2014; Phillips et al., 1998, 1999), a 25% morph along a neutral to happy continuum was included as a more socially acceptable looking variant of a relatively unemotional face. Stimuli were displayed randomly on a laptop monitor. The patient replied orally, while being recorded by a microphone, reading the name of the correct emotion among the five alternatives written below the picture and, concurrently or alternatively, pointing to it. In the intraoperative session, before starting this task the patient was asked to read the five words denoting the emotions. Stimulation occurred during face presentation, with the patient being unaware of it. The

Table 1 –
Patients submitted to awake stimulation of the insula. In all patients (except n 13) the tumor was located in the left hemisphere.

N	Sex	age	education	handedness	symptom	Histology	Lesion site	Tumour volume	Residual volume
1	M	30	8	R	G	Focal cortical dysplasia IIa	Frontal 2	1.92	0
2	F	29	13	R	G	Oligodendroglioma II	Orbital, insular	82.706	10.3
3	F	37	13	R	G	Oligodendroglioma II	T anterior-inferior	14.99	
4	M	40	18	R	paresthesias	Anaplastic oligoastrocitoma III	Frontal 3, insula ant, T anterior-mesial	27.81	0
5	F	47	16	R	Visual deficits	Anaplastic oligoastrocitoma III	Insula, T pole	68.117	4.8
6	M	21	16	R	G	Anaplastic astrocitoma III	precentral	3.05	0
7	F	69	8	R	G	Anaplastic astrocitoma III	Frontal 1,2,3 ant	65.13	8.752
8	M	26	13	R	hypoesthesia	Anaplastic astrocitoma III	Frontal 1	7.614	0
9	F	58	17	R	G	Glioblastoma IV	T-O	11.8	0
10	M	47	13	L	language	Glioblastoma IV	Frontal anterior, T1,2	31.03	0
11	F	64	10	R	none	Metastasis	Frontal anterior	28.35	0
12	F	42	13	R	G	Oligoastrocitoma II	T insular	20.5	0
13	M	43	17	L	cacosmia	Anaplastic oligoastrocitoma III	Orbito-mesial frontal (right)	31.5	0

M=male, F= female, R= right, L= left, G=general seizure, T=temporal, T1= superior temporal gyrus, T2=middle temporal gyrus, Frontal 1=superior frontal gyrus, Frontal 2= middle frontal gyrus, Frontal 3= inferior frontal gyrus.