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Social cognition in patients following surgery to the prefrontal cortex

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ABSTRACT

Impaired social cognition, including emotion recognition, may explain dysfunctional emotional and social behaviour in patients with lesions to the ventromedial prefrontal cortex (VMPFC). However, the VMPFC is a large, poorly defined area that can be sub-divided into orbital and medial sectors. We sought to investigate social cognition in patients with discrete, surgically circumscribed prefrontal lesions. Twenty-seven patients between 1 and 12 months post-neurosurgery were divided into groups based on Brodmann areas resected, determined by post-surgical magnetic resonance imaging. We hypothesised that patients with lesions to the VMPFC ($n=5$), anterior cingulate cortex ($n=4$), orbitofrontal cortex ($n=7$) and dorsolateral prefrontal cortex (DLPFC, $n=11$) would perform worse than a control group of 26 extra-cerebral neurosurgery patients on measures of dynamic facial emotion recognition, theory of mind (ToM) and empathy. Results indicated the VMPFC-lesioned group performed significantly worse than the control group on the facial emotion recognition task overall, and for fear specifically, and performed worse on the ToM measure. The DLPFC group also performed worse on the ToM and empathy measures, but DLPFC lesion location was not a predictor of performance in hierarchical multiple regressions that accounted for other variables, including the reduced estimated verbal IQ in this group. It was concluded that isolated orbital or medial prefrontal lesions are not sufficient to produce impairments in social cognition. This is the first study to demonstrate that it is the combination of lesions to both areas that affect social cognition, irrespective of lesion volume. While group sizes were similar to other comparable studies that included patients with discrete, surgically circumscribed lesions to the prefrontal cortex, future large, multi-site studies are needed to collect larger samples and confirm these results.

1. Introduction

Patients with lesions to the ventromedial (VM) prefrontal cortex (PFC) display a specific syndrome of behavioural disturbances, including severe changes in emotional and social function that some researchers have suggested are related to poor recognition of emotion (Hornak et al., 2003; Mah et al., 2004). These patients often exhibit disinhibited behaviour, are socially inappropriate, are impulsive, have poor judgment and decision-making, have blunted emotional experience, have difficulty monitoring themselves, and lack awareness of their behaviour (Eslinger and Damasio, 1985; Barrash et al., 2000; Beer et al., 2006). Thus, patients with VMPFC lesions have been likened to sociopaths (Eslinger and Damasio, 1985; Blair and Cipolotti, 2000). Lesions to this area can lead to severely negative psychosocial consequences, including loss of employment, divorce and bankruptcy (Eslinger and Damasio, 1985).

A difficulty with research in these patients is that organic lesions are not selective, and those affecting the VMPFC are often large and involve parts of the orbital (OFC) and medial (MPFC) PFC, both of which have been separately implicated in emotion recognition and social cognition. For example, OFC lesions result in impairments in recognition of facial and vocal emotional expressions (Hornak et al., 2003), and other nonverbal social and emotional cues such as body language (Mah et al., 2004). Lesions

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to the MPFC also result in impaired recognition of facial and vocal emotion (Hornak et al., 2003; Baird et al., 2006). Neuroimaging studies have observed activation in a part of the MPFC known as the anterior cingulate cortex (ACC) in response to a range of emotional facial expressions (George et al., 1993; Dolan et al., 1996; Morris et al., 1998; Phillips et al., 1998; Blair et al., 1999; Wicker et al., 2003), particularly sadness (Phan et al., 2004). Another potential explanation for impaired social behaviour in patients with VMPFC lesions is that they have deficits in empathy, an ability to share the emotions of others (Singer, 2006), that is disrupted in patients with OFC lesions (Grattan et al., 1994; Eslinger, 1998; Shamay-Tsoory et al., 2003; Shamay-Tsoory et al., 2005; Hynes et al., 2006). Also a key factor for social interactions is the understanding of the thoughts and intentions of others, which includes theory of mind (ToM) (Premack and Woodruff, 1978) or mentalizing (Frith and Frith, 1999), functions that have been demonstrated in neuroimaging studies to involve the MPFC (Frith and Frith, 1999; Gallagher and Frith, 2003).

Thus, subcomponents of the VMPFC may offer distinct contributions to social cognition. While many studies poorly define the VMPFC, a noteworthy exception is the study by Hornak et al. (2003) which investigated recognition of emotion in patients with surgically circumscribed lesions to the PFC. Such an approach had the advantage of determining more precisely the role of subcomponents of the PFC in emotion recognition. The present study adopted this approach and furthered the earlier work in a number of ways, including by dynamically varying the intensity of expression in the facial emotion recognition task and by measuring social cognition in the form of ToM and empathy. The present study also included more precise radiological analysis of post-surgical magnetic resonance imaging (MRI) scans to allow a finer classification of patients into groups based on Brodmann areas (BAs) resected. To reduce the potential influence of compensatory recovery mechanisms, we used strict inclusion criteria of patients between 1 and 12 months post-surgery. Finally, an additional improvement was the inclusion of a non-cerebral neurosurgical control group.

Given that the OFC and MPFC have both been implicated in the recognition of facial emotion, it was hypothesised that these two groups and the VM group would be impaired on a test of dynamic facial emotion recognition compared with a control group of extra-cerebral neurosurgery patients. It was also hypothesised that patients with MFPC lesions would be impaired on a ToM measure, that patients with OFC lesions would be impaired on an empathy measure, and that patients with VMPFC lesions would be impaired on both measures. Finally, based on a study using a reward-related task (Hornak et al., 2004), it was hypothesised that any impairment in social cognition in a group with dorsolateral PFC (DLPFC) lesions would be related to impairments in attention.

2. Methods

2.1. Participants

Participants were 27 patients post-neurosurgery to the PFC, with a single surgical resection cavity confirmed by MRI. Of these, 25 were recruited from a neurosurgical inpatient ward and outpatient neurosurgery clinic at the Royal Melbourne Hospital. Two patients were recruited from an inpatient ward of St Vincent's Hospital, Melbourne. Control participants were 26 patients post-spinal surgery at the Royal Melbourne Hospital, who had undergone cervical and lumbar laminectomy, discectomy or rhizolysis. Thus, this group had also experienced a serious neurosurgical operation, without cerebral involvement.

All participants were aged over 18 years and within 1–12 months post-neurosurgery. Consent was obtained according to the declaration of Helsinki and the Human Research Ethics committees of The University of Melbourne, The Royal Melbourne Hospital and St Vincent's Hospital, Melbourne. Exclusion criteria were nerve sheath tumour, neurological disease other than reason for surgery (e.g., cerebrovascular accident, dementia), history of heart disease or heart failure, documented cerebral trauma, vision or hearing problems other than corrective lenses, and poor English comprehension and expression (score <13) on the Frenchay Aphasia Screening Test (Enderby et al., 1987).

2.2. MRI analysis

Lesion site and volume were ascertained from post-surgical structural MRI scans closest to the date of testing. The brain regions were segmented from these images using the Brain Extraction Tool (BET; Smith, 2002; Jenkinson et al., 2005) within the brain image analysis package FSL 4.1 (Smith et al., 2004; Woolrich et al., 2009). These brain-extracted images were then normalised by co-registration to the Montreal Neurological Institute (MNI) 2-mm standard brain using a 12-parameter affine algorithm (FLIRT; Jenkinson and Smith, 2001; Jenkinson et al., 2002) within FSL. The image analysis programme Analyse (version 9.0 Mayo Clinic Biomedical Imaging Resource, Rochester, MN) was used to manually correct for inaccuracies in this automatic segmentation and to segment the lesions. Regions of interest (ROIs) outlined the resection cavity on every slice. All ROIs were traced by the primary author (LMJ) and confirmed by a neuroradiologist (PP).

2.3. Group categorisation

Participants were divided into groups according to BAs resected. A volumetric BA map (Drury et al., 1998) from MRIcro (Rorden and Brett, 2000) was co-registered to MNI space using FSL, and masks created for each BA. The number of voxels in each area of interest was calculated by adding the number of voxels in each BA, i.e., ACC=BA24+BA25+BA32; OFC=medial BA10+BA11+BA47; DL=BA6+BA8+lateral BA9+BA44+BA45+BA46 (no other BAs were resected in any patients). The number of voxels in the overlap of each patient's ROI with each area of interest was calculated as a percentage. Participants were assigned to the group for which they had the largest percentage of resection.

Participants with more than 5% resection of the ACC plus more than 5% resection of the OFC were assigned to a VM group. Three of these VM patients also had more than 5% resection of the DL area, but no patients in the DL group had more than 5% resection of the ACC or orbital area. We chose 5% rather than 'at least some part' which was used by Hornak et al. (2003, p. 1693) due to potential registration or ROI-drawing error, and the relative inexactness of BA maps. Patients with BA25 lesions also had orbital lesions, so they were included in the VM group; therefore, the ACC group comprised patients with pregenual and dorsal ACC lesions. The lesion locations of individuals within each group are presented in Figs. 1–4.

2.4. Lesion characteristics

Most brain surgery patients had primary tumours. Table 1 shows the frequencies of World Health Organisation (WHO) tumour type and grade, by group. Although the VM group contained all the patients with the highest WHO grade (IV) lesions, a Fisher's exact test found no significant between-group difference in WHO grade.

A Kruskal–Wallis test found a significant difference between groups in lesion volume (cubic mm), $H(3)=12.26$, $p<0.01$ (ACC $M=1234.50$, S.D.= 253.58 cm^3; Orbital $M=881.14$, S.D.=861.48 cm^3; VM $M=5563.40$, S.D.=4828.69 cm^3; DL $M=914.45$, S.D.=736.73 cm^3). The VM group had the largest lesions compared with all other groups. That was expected given that the VM area is a combination of the ACC and OFC areas.

Point-biserial correlations between each group and lesion volume found a significant coefficient for the VM group, $r_{pb}=0.624$ ($p<0.001$), indicating that 38.93% of the variance in lesion volume was accounted for by VM location. Lesion volume therefore was a potential confounding factor. In order to determine whether group effects remained after controlling for lesion volume, hierarchical regression was favoured over a covariate approach due the sample size.

2.5. Demographic characteristics

Table 2 presents demographic results. Thirty participants identified themselves as Australian, three as English, two Italian, two Vietnamese and one each from the following countries: El Salvador, Cyprus, Uruguay, Poland, Iraq, Spain, USA, Hungary, Phillipines, South Africa, Finland, Turkey, Yugoslavia, Netherlands/China, Croatia and Papua New Guinea. Fisher's exact tests found no significant between-group differences ($p>.05$) in the proportion of participants who spoke English as a second language (ESL). There were also no significant between-group differences in proportion of males and females, age, days since surgery, or years of education.

2.6. Screening measures

Standard tests screened for language impairment, attention, estimated intelligence quotient (IQ), anxiety and depression. The Frenchay Aphasia Screening Test (FAST)- Comprehension and Expression subtests (Enderby et al., 1987) is a brief screening test for English comprehension and expression. The Test of Everyday