A structural MRI study of cortical thickness in depersonalisation disorder

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1. Introduction

Depersonalisation is a distressing impairment of self-awareness characterised by the following characteristics: a feeling of detachment from the body, subjective emotional numbing, and feelings of estrangement from personal memories and one’s surroundings (Sierra et al., 2005). Depersonalisation disorder (DPD) is included in the classification systems of the DSM-5 (American Psychiatric Association, 2013) and the ICD-10 (World Health Organization, 1992). Psychophysiological and neuroimaging research has revealed distinct abnormalities which support the idea that the condition is firmly grounded in neurobiological mechanisms.

An impaired sense of self is arguably a central symptom cluster in depersonalisation disorder (Mohr and Blanke, 2005). Closely related to this are out-of-body experiences (OBEs) sometimes experienced by neurological patients (Blanke et al., 2004) and often associated with lesions in the temporo-parietal junction (TPJ). Blanke et al. (2005) subsequently showed, using electroencephalography (EEG), that OBEs produce TPJ activation in healthy volunteers while they imagine looking on themselves from the outside, as typically reported by neurological patients with autoscopy. Stein and Simeon (2009) suggested that aberrant temporal lobe activity could be a contributing factor in producing DPD symptoms. A transcranial magnetic stimulation (TMS) study by Mantovani et al. (2011) substantiated this line of evidence by demonstrating a significant reduction in depersonalisation and dissociation scores in 6 out of 12 participants through stimulation of the TPJ. In sum, there is increasing evidence for a link between altered cortical functioning in temporo-parietal areas and dysfunctional perception of their own body in patients with DPD.

More broadly, a fronto-limbic ‘suppressive’ mechanism has been proposed for depersonalisation whose ecological function may be to preserve coping behaviour from potentially disorganising levels of anxiety at times of extreme threat. For instance, functional magnetic resonance imaging (fMRI) studies have revealed that in comparison to controls, patients with DPD show hyperactive prefrontal areas (i.e. an enhanced blood oxygenation level dependent [BOLD] response) relevant in the regulation of emotional responses, together with under-activation (i.e. reduced response relative to controls) of limbic-related areas, such as the amygdala, hypothalamus (Lemche et al., 2007), and anterior insula (Phillips et al., 2001), relevant for experiencing emotion. It has also been found that patients with DPD show attenuation of autonomic sympathetic responses to arousing visual stimuli (Sierra et al.,...
Finally, there has been longstanding interest in the notion of depersonalisation that is secondary to clear-cut brain disorders, particularly those affecting the temporal lobes (Sierra et al., 2002b) [e.g. temporal lobe epilepsy (TLE); Lambert et al., 2002]. Despite the increasing evidence for a neurobiological underpinning of DPD, there have been no structural imaging studies of (primary) DPD to date, and it remains unknown whether the previously reported differences at a functional level in DPD are mediated by atypical brain structure.

We therefore carried out a structural neuroimaging study on a well-characterised sample to test the primary hypothesis that individuals with DPD have abnormalities in brain anatomy that differentiate them from healthy controls. As this is the first structural neuroimaging study in this condition, we formulated predictions based on the growing functional neuroimaging literature in the disorder (see above), and related disorders (e.g. anxiety). That is, previous functional neuroimaging research in DPD suggests involvement of prefrontal areas known to play a role in emotion regulation (Ochsner and Gross, 2005), or regions regulated by them. These include the anterior insula (Phillips et al., 2001; Medford et al., 2006) and other lateral (Simeon et al., 2000; Phillips and Sierra, 2003) and medial temporal lobe structures (Lemche et al., 2007). Temporal lobe involvement may also link with DPD in patients with TLE (Lambert et al., 2002). Also of possible relevance are magnetic resonance imaging (MRI) studies using vertex-based morphometrics which have reported abnormal brain structural changes in patients with anxiety disorders, centred on a network regulating fear and arousal (Blackmon et al., 2011; Kühl et al., 2011; Syal et al., 2012; Frick et al., 2013) that predominantly includes the amygdala and orbitalfrontal cortex (OFC).

To test our hypothesis of atypical brain structure in DPD, we used a vertex-based approach, which allowed us to investigate brain anatomy at a high level of specificity based on different morphometric features, such as cortical thickness (CT) and regional cortical volume (CV).

2. Methods

2.1. Participants

A total of 42 participants consented to enter the study, which was part of a controlled trial of imaging-guided transcranial magnetic stimulation (Jay et al., 2014). Twenty-one patients referred to a Depersonalisation Disorders Clinic at the Maudsley Hospital, London were diagnosed with DPD according to ICD-10 criteria by an experienced psychiatrist (MS). All patients had established (≥ 2 years) depersonalisation as their primary condition and scored above the clinical cut-off of 70 on the Cambridge Depersonalisation Scale (CDS; Sierra and Berrios, 2000). None had a primary diagnosis of panic disorder or generalised anxiety disorder. Twenty-one right-handed healthy controls were recruited from the local community who answered advertisements calling for volunteers, and were screened to ensure that they had neither a history nor a current experience of psychiatric illness, no on-going neurological disorder, and were not taking any psychotropic or other medication. One of the patients was excluded from the analysis based on the previously reported differences at a functional level in DPD are mediated by atypical brain structure.

2.2. MRI data acquisition

MRI data were acquired on a GE 1.5-T HDx system (General Electric, Milwaukie, WI, USA) at the Institute of Psychiatry, London. Localiser and calibration scans were followed by 2D T2-weighted Fast Spin Echo and FLAIR (Fluid Attenuated Inversion Recovery) scans. A 3D T1-weighted Inversion Recovery prepared Spoiled Gradient Echo (IR-SPGR) scan was then collected with the following parameters: echo time (TE) = 5 ms; repetition time (TR) = 12 ms; inversion time (TI) = 300 ms; excitation flip angle = 18°; matrix size 320 × 224 × 220 over a 288 × 202 × 198 field of view, giving an isotropic 0.9-mm voxel size over the whole brain. The manufacturer’s eight k-channel head coil was used for signal reception, with the body coil being used for radio-frequency transmission.

2.3. Image processing

The FreeSurfer software provides measures of cortical thickness (CT), surface area (SA) and cortical volume (CV). Given explicit models for the white/grey and grey/ cerebrospinal fluid (CSF) surfaces, the measure of absolute CT at any given point on the white/grey matter surface was taken to be the closest distance from the grey/white matter boundary to the grey matter isocentre at each vertex on the tessellated surface (Fischl and Dale, 2000). Vertex-based estimates of SA were obtained as outlined by Winkler et al. (2012). Estimates of regional cortical volume were derived by multiplying CT and SA at each vertex on the cortical surface, or CV=CT×SA. Therefore, CT, SA, and CV for the left and right hemisphere grey matter was obtained by a vertex-based algorithm, and image segmentation using a connected components algorithm. Then, a surface tessellation was generated for each white matter volume by fitting a deformable template. The grey matter and cerebrospinal fluid surfaces were also modelled using a similar process.

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