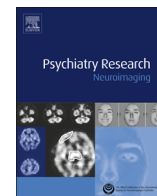




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Brief report

Brain structure in narcissistic personality disorder: A VBM and DTI pilot study

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ABSTRACT

We analysed T1-weighted MRI scans using voxel-based morphometry (VBM) and tract-based spatial statistics (TBBS) on diffusion tensor images (DTI) in narcissistic personality disorder (NaPD) patients and healthy controls. Grey matter deficits include right prefrontal and bilateral medial prefrontal/anterior cingulate cortices, and decreased fractional anisotropy in right frontal lobe white matter.

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Diffusion tensor imaging (DTI)

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1. Introduction

Narcissistic personality disorder (NaPD) is an established diagnosis in DSM-IV as well as in DSM-5. However, little is known about the neurobiology of this disorder, despite its clinical significance and potentially underestimated prevalence (Ronningstam, 2013). One recent study using voxel-based morphometry (VBM) indicated grey matter deficits in NaPD patients relative to healthy controls in the left anterior insula in a region-focused analysis, as well as bilateral superior and middle frontal gyri, cingulate cortices, and pre-/post-central gyri in a whole brain analysis (Schulze et al., 2013). A neurobiological model might therefore be based on the link between insular areas and empathy (Decety et al., 2012a; Decety and Moriguchi, 2007), as well as prefrontal areas and emotion regulation, but there is (to our best knowledge) a paucity of any other neuroimaging data in NaPD to further support this.

Here, we present pilot data from a study on male NaPD patients and matched healthy controls on both grey matter (using T1-weighted MRI and voxel-based morphometry), as well as white matter using diffusion tensor imaging (DTI). We aimed to replicate the insular and prefrontal findings of the previous VBM study (Schulze et al., 2013), as well as to provide an exploratory analysis

of brain structure in this disorder to guide subsequent research to areas of interest. In addition, we also included DTI analysis hypothesising alterations of fractional anisotropy of underlying/connecting white matter tracts.

2. Materials and methods

We studied six male patients with narcissistic personality disorder (mean age 27.5 years, S.D. 7.8), diagnosed by a board certified psychiatrist, based on DSM-IV criteria and SCID-II screening and interviews, as well as chart reviews, with subsequent confirmation of DSM-5 criteria on re-evaluation. Patients had minimal psychiatric co-morbidity, including a previous major depressive episode in two patients, but no current depressive episode. These two patients, along with another patient, were on antidepressant medication, but patients were else unmedicated. The control cohort included 48 healthy males (mean age 29.7 years, S.D. 9.3) matched for age (*t*-Test, two-tailed: $t=0.540$, $p=0.592$), gender (all male) and handedness (all being right-handed; laterality quotient based on Edinburgh Handedness Inventory; *t*-Test, two-tailed: $t=-0.437$, $p=0.664$). All controls were screened by a psychologist or psychiatrist to confirm that they had no history of psychiatric conditions or psychotherapy treatment (using a personal semi-structured interview). All participants provided written informed consent to a study protocol approved by the local Ethics Committee. None of the participants had a neurological or major medical condition, traumatic brain injury, learning disability, or substance abuse/dependence.

We used a 3 T Siemens Tim Trio scanner (Siemens, Erlangen, Germany) to acquire a high-resolution T1-weighted whole-brain scan with an MPRAGE sequence ($1 \times 1 \times 1 \text{ mm}^3$ voxel resolution; TR 2300 ms, TE 3.03 ms; flip angle 9° ; sagittal acquisition of 192 contiguous slices; field-of-view 256 mm), and a diffusion tensor imaging (DTI) data set (82 directions, 5 b_0 volumes, 60 axial 2-mm-slices, TR 8100 ms, TE 98 ms), all of which passed artefact checks and quality assurance protocols.

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Voxel-based morphometry (VBM) applying the VBM8 software package (<http://www.dbm.neuro.uni-jena.de/vbm/vbm8/>) including normalisation with the DARTEL algorithm, segmentation with an internal 0.2 grey matter threshold, and smoothing with a 12 mm FWHM kernel. For statistics, we used a $p < 0.005$ threshold (mirroring the whole-brain analysis threshold in Schulze et al. (2013), and given the small number of the patient sample we used threshold free cluster enhancement (TFCE) as a non-parametric approach to SPM statistics (Smith and Nichols, 2009).

DTI data were reconstructed using MRtrix software (Tournier et al., 2012) and spatial normalisation was performed using DTI-TK (Zhang et al., 2007) prior to TBSS analysis. Spatial normalisation with DTI-TK was based on tensor information instead of FA intensity values. Voxel-wise statistical analysis of the FA data was carried out using TBSS (Tract-based spatial statistics (Smith et al., 2006)), part of FSL software, and also using TFCE. TBSS projects all subjects' FA data onto corresponding positions on a mean FA tract skeleton, before applying voxel-wise cross-subject statistics.

3. Results

VBM analysis using TFCE identified grey matter deficits in NaPD patients in two prefrontal clusters ($p < 0.005$, uncorrected): right middle frontal gyrus (maximum voxel co-ordinates: (x,y,z) (36,20,36); $k=26$ voxels) and a cluster comprising left medial prefrontal cortex/ anterior cingulate cortex (maximum (2,53,7); $k=12$), as well as left middle occipital cortex (maximum $(-33,91,9)$; $k=466$), left fusiform/ inferior temporal cortex (maximum $(-38,-52,-6)$; $k=100$), right superior temporal cortex (maximum (62, $-1,-9$); $k=42$), left lingual gyrus (maximum $(-14,-81,-8)$; $k=120$).

DTI analysis showed lower fractional anisotropy ($p < 0.001$, uncorrected) in patients in the right frontal lobe (under the superior/middle prefrontal gyrus), the right anterior thalamic radiation, right anterior temporal lobe, left anterior/lateral temporal lobe, and right brain stem. Results are shown in Fig. 1.

4. Discussion

In this study, we provide pilot data in a sample of patients with narcissistic personality disorder. We replicate and extend findings of the only previous VBM study in NaPD (Schulze et al., 2013), while our DTI data give a first account of potential white matter alterations in this condition. Given the paucity of research into NaPD, the present data serve as a starting point in the development of a neurobiological model of the disorder, which would take into account its multiple facets.

The VBM grey matter findings point to right prefrontal and bilateral medial prefrontal pathology, in line with earlier findings (Schulze et al., 2013). Within the complex psychopathology of NaPD

(Ronningstam, 2010), fluctuations of internal control and lack of control over emotional and inter-personal interactions constitute a core pathology. It is therefore conceivable that prefrontal structural deficits could contribute to or aggravate a liability to emotional dysregulation or cognitive deficits in attribution or coping. However, prefrontal pathologies are also relevant to depression and possibly diathesis to depressive episodes. One of the clusters is located in the medial prefrontal cortex, an area where we recently identified a strong correlation with narcissistic traits in a non-clinical sample of healthy controls (Nenadic et al., unpublished data). However, our study fails to find changes in the insular cortex, an area highlighted in the study by Schulze et al. (2013) and linked to empathy (Decety and Moriguchi, 2007; Decety et al., 2012b), a function in which many NaPD patients are deficient. While lack of insular findings might be related to small sample size, variability in clinical symptoms might strongly influence effect sizes of regional findings.

Our DTI study provides the first analysis of white matter in NaPD. The findings in the frontal lobe are of interest as they provide a basis for disturbed structural connectivity of prefrontal areas. This includes the cluster beneath the right lateral prefrontal cortex, as well as the right anterior thalamic peduncle, a major frontothalamic tract linking mediodorsal thalamic nuclei with the medial and lateral prefrontal cortex. This suggests that white matter pathology might contribute to the structural cortical deficits. Obviously, these findings are in need of replication, but they meaningfully complement the grey matter findings in giving a systems neurobiological perspective of a potential breakdown in frontothalamic or frontolimbic systems relevant to NaPD pathology, which has similarly been reported in other cluster B personality disorders (Carrasco et al., 2012; Grant et al., 2007).

Support for right lateral prefrontal pathology in narcissism also comes from a recent functional MRI study using an affective picture paradigm revealing high narcissistic traits in a non-clinical sample of healthy subjects associated with diminished activation in the right anterior insula, but also right dorsolateral prefrontal cortex and lateral premotor cortex (Fan et al., 2011).

The main limitations of our study are the small patient sample and the issue of co-morbidity. Small sample size is certainly a limiting factor in identifying changes with small or moderate effect size, and it makes our analysis prone to false positive findings. Given, however, the paucity of imaging study in NaPD at all, our findings can provide a useful exploratory analysis, which can be followed up in subsequent confirmatory studies. The small sample size also limits the potential application of analysis of subgroups or correlation with symptoms. Secondly, co-morbidity is a limitation, as liability to depression might have contributed to effects in some of the patients. However, co-morbidity is not only most common in NaPD, but in fact depressive

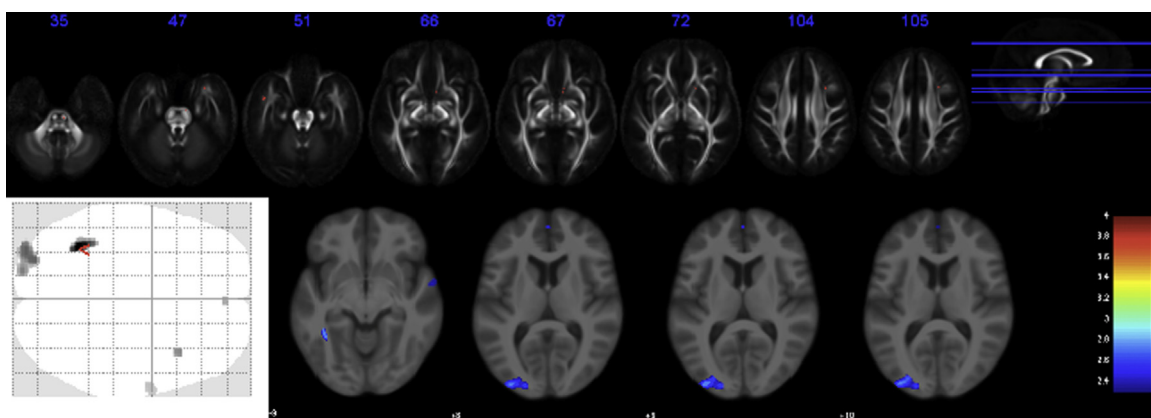


Fig. 1. Comparison of narcissistic personality disorder patients and healthy controls: upper panel shows TBSS analysis of diffusion tensor imaging (DTI) of reduced fractional anisotropy ($p < 0.001$) in patients; lower panel shows voxel-based morphometry (VBM) comparison of grey matter with red/yellow clusters indicating grey matter reduction in patients, blue relative grey matter reduction in controls ($p < 0.005$, uncorrected); all analyses apply threshold free cluster enhancement (TFCE). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

symptoms or substance abuse constitute the most common reasons for NaPD patients seeking psychiatric evaluation or treatment. Hence, restricting oneself to the study of patients with NaPD without comorbidity would not reflect typical clinical samples. All our temporal lobe findings are in need of further replication, as they do not fit in the current models of areas potentially involved in NaPD. Finally, lack of urine toxicology screening is a limitation when excluding substance-related disorders.

In conclusion, our VBM findings replicate prefrontal (although not insular) grey matter deficits in NaPD (Schulze et al., 2013), and provide a first account of potential prefrontal white matter alterations. Right lateral prefrontal pathology might be relevant to narcissistic personality disorder.

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