Gray matter abnormalities in patients with narcissistic personality disorder

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ABSTRACT

Background: Despite the relevance of narcissistic personality disorder (NPD) in clinical settings, there is currently no empirical data available regarding the neurobiological correlates of NPD. In the present study, we performed a voxel-based morphometric analysis to provide initial insight into local abnormalities of gray matter (GM) volume.
Methods: Structural brain images were obtained from patients with NPD ($n = 17$) and a sample of healthy controls ($n = 17$) matched regarding age, gender, handedness, and intelligence. Groups were compared with regard to global brain tissue volumes and local abnormalities of GM volume. Regions-of-interest analyses were calculated for the anterior insula.
Results: Relative to the control group, NPD patients had smaller GM volume in the left anterior insula. Independent of group, GM volume in the left anterior insula was positively related to self-reported emotional empathy. Complementary whole-brain analyses yielded smaller GM volume in fronto-paralimbic brain regions comprising the rostral and median cingulate cortex as well as dorsolateral and medial parts of the prefrontal cortex.
Conclusion: Here we provide the first empirical evidence for structural abnormalities in fronto-paralimbic brain regions of patients with NPD. The results are discussed in the context of NPD patients' restricted ability for emotional empathy.

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1. Introduction

As stated by the DSM-IV-TR, "a pervasive pattern of grandiosity, need for admiration, and lack of empathy" are defining features of narcissistic personality disorder (NPD; American Psychiatric Association, 2000), a serious mental disorder with a median lifetime prevalence of 1% in the general population (Pincus and Lukowitsky, 2010). Previous findings have highlighted the relevance of NPD for mental health services by showing that NPD is associated with severe impairments in psychosocial functioning (Miller et al., 2007), a high co-morbidity rate of affective as well as substance use disorders (Ritter et al., 2010; Stinson et al., 2008), and an increased

rate of suicidal behavior (Blasco-Fontecilla et al., 2009; Ronningstam et al., 2008). Nonetheless, up to now, there has been a severe lack of empirical research investigating psychological and neurobiological factors related to the clinical presentation of NPD (Miller and Campbell, 2010). In particular, neurobiological abnormalities in patients with NPD are, to the best of our knowledge, currently unknown, both at a structural and a functional level. In the present study, we aimed to provide initial insight into brain structural abnormalities in patients with NPD and compared local GM volume between patients with NPD and healthy controls using voxel-based morphometry (VBM). Given the lack of previous neurobiological investigations, our main hypothesis regarding group differences in GM volume focused on a highly characteristic and experimentally supported feature in patients with NPD: "lack of empathy".

Impaired empathy is unequivocally considered to be highly characteristic of patients with NPD and has a longstanding tradition in theoretical conceptualizations of this mental disorder (Akhtar

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and Thomson, 1982; Blais et al., 1997; Kernberg, 1970; Ronningstam, 2010). However, it was only recently that an experimental study explicitly investigated empathic abilities in patients with NPD (Ritter et al., 2011). In accordance with multidimensional models of empathy (Blair, 2005; Decety and Meyer, 2008; Singer, 2006), Ritter et al. examined the ability to infer mental states of another person (i.e., cognitive empathy; Baron-Cohen and Wheelwright, 2004) as well as emotional responses regarding the observed emotional state of another person (i.e., emotional empathy; Eisenberg and Miller, 1987; Mehrabian and Epstein, 1972). The experimental investigation indicated that NPD patients have impaired emotional empathy, whereas cognitive aspects of empathy were found to be unaffected (Ritter et al., 2011). In other words, patients with NPD are not characterized by a general impairment in empathy, but rather a specific deficit in their ability to emotionally respond to the observed emotional state of another person.

The neural representation of empathy has received considerable attention in recent years (for meta-analyses, see Fan et al., 2011a; Lamm et al., 2011). Meta-analytic evidence of functional neuro-imaging findings highlighted the bilateral anterior insula, anterior and median parts of the cingulate cortex, and the supplementary motor area to represent a core network activated during empathy related processes (Fan et al., 2011a). Complementary evidence regarding the neural representation of empathy was provided by volumetric studies in patients with neurodegenerative diseases (Rankin et al., 2006) and mental disorders such as schizophrenia and autism (Hadjikhani et al., 2006; Hooker et al., 2011). For example, smaller GM volume in the ventromedial prefrontal cortex of individuals with schizophrenia significantly contributed to deficits in theory-of-mind skills (i.e. cognitive empathy, Hooker et al., 2011). Impairments in emotional empathy, in contrast, were related to smaller GM volume of the bilateral insula in adolescents with conduct disorder (Sterzer et al., 2007).

The results of a recent study indicated neurofunctional abnormalities of empathy-related brain regions in healthy individuals with marked narcissistic personality traits (Fan et al., 2011b). More specifically, narcissistic participants were found to exhibit abnormal functioning of the anterior insula when asked to emotionally empathize with other individuals. Consequently, the results of this study stress again the importance of abnormalities in emotional empathy and highlight anterior parts of the insular cortex to represent a potential neurobiological correlate of these impairments in narcissism.

In light of the findings presented above, and due to a lack of available neurobiological studies investigating healthy and pathological narcissism, we specifically investigated gray matter abnormalities in the anterior insula of NPD patients. To more closely associate GM abnormalities of the anterior insula with impaired emotional empathy in NPD, we additionally assessed the correlation between GM volume of this brain region and self-reported emotional empathy, as measured by the Interpersonal Reactivity Index (IRI; Davis, 1983; Sterzer et al., 2007). Finally, exploratory whole-brain analyses were calculated to provide further indications of structural abnormalities in NPD.

2. Methods

2.1. Participants

Seventeen patients with a primary diagnosis of NPD (12 male, 5 female) and 17 healthy individuals (12 male, 5 female) were enrolled in the study. All participants were right-handed. Healthy controls were recruited via public advertising and NPD patients were recruited from in- and out-patient treatment facilities. All patients had a history of psychiatric inpatient treatment. However, at the time of study participation, just one NPD patient was in inpatient psychiatric care, whereas all other patients were in outpatient psychiatric or psychotherapeutic care. Both groups were matched on basic demographic parameters, such as age and intelligence (all $ps > .5$). Descriptive results are presented in Table 1.

All participants underwent diagnostic screening with the German versions of the Mini-International Neuropsychiatric Interview (M.I.N.I., Sheehan et al., 1998) for Axis-I Mental Disorders and the Structured Clinical Interview for Axis-II Personality Disorders (SCID-II, Fydrich et al., 1997). Diagnostic interviews were conducted by clinically experienced psychologists and psychiatrists. Diagnoses of NPD were verified with the patients' therapist (psychiatrists or psychologist) and the supervisor of this study (last author, senior psychiatrist). Inter-rater reliability of SCID-II personality diagnosis of NPD was previously assessed for a sample of eight patients by pairwise diagnostic interview. Three interviewers blind to the diagnosis were asked to rate these interviews. Kappa was acceptable, $\kappa = 0.797$ (Vater et al., 2013).

Healthy controls were only included if they did not take any psychotropic medication and had neither a current nor a lifetime diagnosis of mental or neurological disorders. Exclusion criteria for NPD patients were past or present diagnosis of a psychotic disorder, bipolar disorder, substance-associated disorders within three months prior to data acquisition, cognitive disorders (e.g., delirium, dementia), or neurological diseases (e.g., traumatic diseases of the central nervous system). The most frequent ($n > 1$) co-morbid Axis-I diagnoses of NPD patients were depression ($n = 5$ current, $n = 8$ lifetime diagnosis), polytoxicomania ($n = 5$ lifetime) and substance abuse ($n = 3$ lifetime). The most frequent co-morbid Axis-II disorders in our sample of NPD patients were borderline personality disorder ($n = 4$) and antisocial personality disorder ($n = 3$). Thirteen patients with NPD were free of psychotropic medication. One patient received citalopram once per day, another patient received fluoxetine once per day, one patient received quetiapine, and the final patient received paroxetine and methylphenidate.

Individual differences in cognitive and emotional empathy were assessed with the German version of the Interpersonal Reactivity Index (IRI: Davis, 1983; German Version: Paulus, 2006). The subscales "perspective taking" and "empathic concern" are commonly used to capture cognitive and emotional aspects of empathy (e.g., Rankin et al., 2006; Ritter et al., 2011). Questionnaire scores were not available for two patients with NPD. Descriptive results of both scales are presented in Table 1. In short, NPD patients describe motivational deficits for cognitive empathy ($t_{30} = 2.08$, $p = .046$), while impairments in emotional empathy failed to reach significance ($t_{30} = 1.43$, $p = .162$).

All participants provided written informed consent after the procedures had been fully explained and received financial

Table 1
Demographic and psychometric results of healthy controls (HC) and patients with narcissistic personality disorder (NPD). Group comparisons were conducted using t-tests.

	HC		NPD		T	P	d
	Mean	SD	Mean	SD			
Demography							
Gender (female/male)	5/12		5/12				
Handedness (left/right)	0/17		0/17				
Age	35.2	7.3	36.4	8.5	-0.43	.67	-0.15
Intelligence quotient	114.1	7.4	112.1	9.7	0.65	.52	0.23
Self-reported empathy							
Perspective taking	24.9	4.5	21.1	5.8	2.08	.05	0.73
Empathic concern	24.3	5.2	21.5	5.7	1.43	.16	0.51

Note. Intelligence was measured using the German Wortschatztest (Schmidt and Metzler, 1992).

compensation for their efforts. The procedures of the study were approved by the ethics committee of the Charité — Universitätsmedizin Berlin.

2.2. Image acquisition

Magnetic resonance imaging (MRI) data were obtained on a 1.5 T scanner (Siemens, Magnetom, Sonata, Erlangen, Germany) equipped with a standard head coil. Head movements were minimized using a vacuum pad. The structural scan consisted of 176 slices and was acquired in sagittal plane using a high-resolution T1-weighted magnetization-prepared rapid acquisition with gradient echo (MPRAGE) sequence (repetition time = 12.24 ms, echo time = 3.56 ms, flip angle = 23°, matrix = 256 × 256, voxel size: 1 × 1 × 1 mm).

2.3. Image pre-processing

Initially, all T1 scans were visually checked for gross anatomical abnormalities and scanner artifacts. For subsequent pre-processing of MRI data, we used the VBM toolbox (http://dbm.neuro.uni-jena.de/vbm/) with default settings as implemented in SPM (Wellcome Trust Center for Neuroimaging, London, United Kingdom). The VBM toolbox extends the unified segmentation approach provided by SPM (Ashburner and Friston, 2005) and integrates tissue classification, image registration as well as a bias correction for magnetic field inhomogeneities. Unified segmentation provides advantages in the detection of small brain abnormalities compared to the optimized VBM protocol (Good et al., 2001) and avoids the circularity problem related to the initial tissue segmentation (cf. Meisenzahl et al., 2008). Within the pre-processing procedure, Hidden Markov Random Fields (HMRF) were applied that provide spatial constraints on tissue segmentation based on the intensities of neighboring voxels (Zhang et al., 2001). HMRF increase the signal-to-noise ratio of the final tissue maps. For instance, isolated voxels unlikely to be associated with a certain tissue class are removed from the final tissue maps. All images were registered to a template provided by the International Consortium of Brain Mapping and high-dimensional DARTEL was used for spatially normalizing tissue maps into MNI space.

Finally, the modulated and normalized gray matter maps were smoothed with a standard 8 mm full-width-at-half-maximum (FWHM) isotropic Gaussian kernel (e.g., Bergouignan et al., 2009; Kosaka et al., 2010).

2.4. Statistical analysis

Initially, global volumes of GM, white matter (WM) and cerebrospinal fluid (CSF) as well as total intracranial volume (TIV) were calculated for each subject using native-space tissue maps. Group comparisons were calculated using SPSS (Statistical Package for the Social Sciences). The significance level was set at $p < .05$.

Subsequently, a two-sample t-test was used to assess group differences in local gray matter volume between patients with NPD and healthy controls. In addition, separate regression analyses comprising the factor group as well as the respective sum scores of "perspective taking" or "empathic concern" were calculated. These scales of the Interpersonal Reactivity Index measure cognitive and emotional aspects of empathy, respectively (e.g., Rankin et al., 2006; Ritter et al., 2011). In all analyses, total GM volume was included as a covariate and an absolute gray matter threshold of .25 was used to prevent edge effects located at the border regions of gray and white matter or cerebrospinal fluid (Reetz et al., 2008).

In light of our a-priori hypotheses, regions-of-interest analyses were performed for the bilateral anterior insula. For definition of

Table 2
Global tissue volumes of patients with narcissistic personality disorder (NPD) and healthy controls (HC).

	HC		NPD		T	P	d
	Mean	SD	Mean	SD			
Global brain volumes							
Gray matter	730.0	80.5	691.4	50.3	1.68	.10	.57
White matter	573.1	72.7	537.3	60.5	1.56	.13	.53
Cerebrospinal fluid	250.1	34.3	246.6	36.2	0.29	.78	.10
Total intracranial volume	1553.3	172.6	1475.3	122.9	1.52	.14	.52

the anterior insula, anatomical masks of the insula provided by the Harvard-Oxford cortical and subcortical structural atlases were split at $y = 0$ in anterior and posterior parts. Results were considered significant at $p < .05$, family-wise error (FWE)-corrected. Given the lack of neuroimaging findings in patients with NPD, additional whole-brain comparisons were calculated with the results threshold set at $p < .005$ (uncorrected) at the voxel level. To correct for multiple comparisons across the whole-brain, cluster extent correction procedures were used (e.g., Kluetsch et al., 2012; Nenadic et al., 2010). The extent threshold is defined by the number of expected voxels per cluster based on random field theory. Cluster sizes are known to vary with local roughness of the provided images and were thus adjusted using non-stationary random field theory procedures (Hayasaka et al., 2004). For the two-sample t-test minimum cluster size was determined to be 169 adjacent voxels. Effect sizes (Cohen's d and r) were calculated in SPSS for significant peak voxels in the anterior insula and for significant clusters at the whole-brain level by extracting individual GM estimates.

3. Results

Comparing global volumes of gray matter, white matter, cerebrospinal fluid, and total intracranial volume between healthy controls and patients with narcissistic personality disorder yielded no significant differences in global volumes of the respective tissue maps (all $ps > .10$). Results are presented in Table 2.

Relative to healthy controls, NPD patients presented significantly smaller GM volumes in the left anterior insula ([−41,6,−5], $T = 3.32$, $p < .05$ [FWE], $d = 1.09$; see also Fig. 1). A similar, albeit marginally significant, effect was found in the right anterior insula ([42,6,1], $T = 3.01$, $p < .10$ [FWE], $d = .98$).[1]

The complementary whole-brain analysis illustrated pathological narcissism to be characterized by smaller GM volume in a fronto-paralimbic network (Fig. 2). In particular, patients with NPD showed smaller GM volumes in the left anterior insular region, the bilateral superior frontal gyrus (including dorsolateral and medial areas) and the bilateral middle frontal gyrus. Furthermore, smaller GM volume in patients with NPD was found in the right rostral and left median cingulate cortex, as well as in parts of the pre- and post-central gyrus (see Table 3). The reverse contrast (indicating greater GM volume in NPD patients) revealed no significant clusters.

In order to test whether GM volume of the anterior insula is associated with self-reported empathy, regression analyses were calculated. Independent of the factor group, GM volume of the left

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[1] Smaller GM volume in the left anterior insula ([−35,23,−2], $T = 3.87$, $p < .05$ [FWE], $d = 1.47$) was also found when excluding 4 patients with co-morbid borderline personality disorder. A similar, albeit marginally significant, effect was again found in the right anterior insula ([42,6,0], $T = 3.15$, $p < .10$ [FWE], $d = 1.12$).
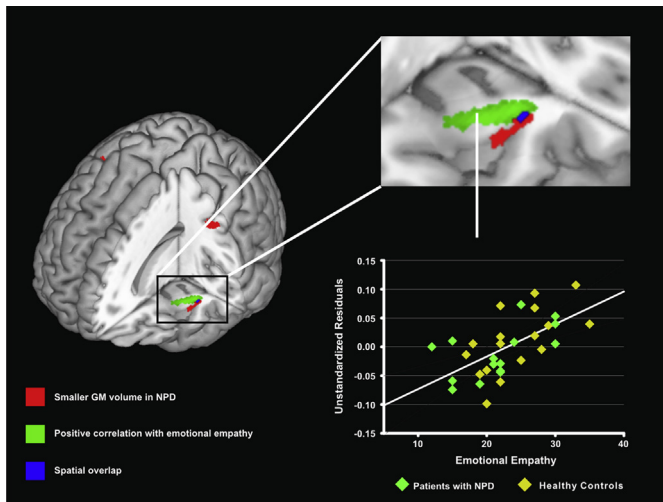
Fig. 1. Visualization of the reported group difference (red) and the positive association of emotional empathy with GM volume (green) as well as the overlap of both effects (blue) in the anterior insula. Results are overlaid on a template provided by MRIcron and the result threshold was set at $p < .005$ uncorrected for visualization purposes. The scatterplot illustrates the relation between lower levels of self-reported empathic concern and gray matter volume for the left anterior insula. The effects of global GM volume (covariate in the statistical analysis) on local estimates of gray matter volume in the anterior insula were regressed. Therefore, the scatterplots depicts the relation between unstandardized residuals and empathic concern. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

anterior insula was marginally, positively correlated with emotional empathy (left anterior insula: [−35,5,−14], $T = 3.01$, $p < .10$ [FWE], $r = .62$; right anterior insula [39,0,−15], $T = 2.25$, $p > .30$ [FWE]). For visualization see Fig. 1. Neither group specific effects nor relations of cognitive empathy with GM volume of the anterior insula were found.

4. Discussion

In the present study, we provide the first empirical evidence for differences in GM volume of the left anterior insula in patients with NPD relative to healthy controls. Complementary whole-brain analyses yielded abnormalities in a fronto-paralimbic network in pathological narcissism. More specifically, smaller GM volume was found in the left anterior insula, rostral and median cingulate cortex as well as dorsolateral and medial parts of the prefrontal cortex. Interestingly, and in addition to the left anterior insula, all these brain regions broadly overlap with the neural circuitry commonly implicated in the representation of empathy (for meta-analyses, see Fan et al., 2011a; Lamm et al., 2011). Smaller GM volume in these brain regions, and the left anterior insula in particular, might be consequently related to impairments in empathy, a hallmark
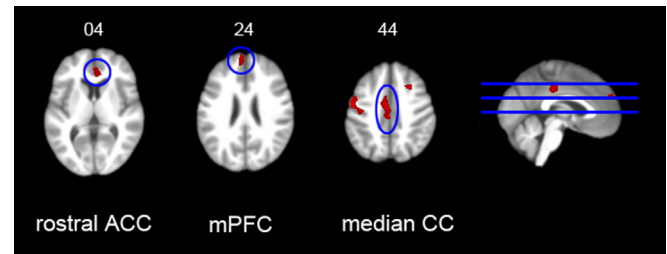

Fig. 2. Significantly smaller GM volume in patients with narcissistic personality disorder compared to healthy controls as determined using a cluster extent correction procedure (height threshold of $p < .005$ uncorr. and cluster extent threshold of $k > 169$ voxels). Significant voxels are overlaid on the mean anatomical image of all participants (see also Table 3). Smaller GM volume was found in rostral parts of the anterior cingulate cortex (ACC), medial parts of the prefrontal cortex (mPFC) and in the median cingulate cortex (CC).

feature of NPD patients (e.g., American Psychiatric Association, 2000; Kernberg, 1970; Ronningstam, 2010).

To more closely examine the association between local GM volume of the anterior insula and empathy, regression analyses comprising cognitive and emotional components of empathy were calculated, respectively. At a trend level, we found a positive correlation between emotional empathy and GM volume in the left anterior insula that was independent of diagnostic status (cf. Fig. 1). Previous findings by Sterzer et al. (2007) suggested a positive association between GM volume of the anterior insula and emotional empathy in adolescents with conduct disorder, underlining the potential role of this brain region in the representation of emotional empathy. In our study, impairments in self-reported emotional empathy failed to reach significance between healthy controls and NPD patients, which is in accordance with previous findings (Marissen et al., 2012; Ritter et al., 2011). Ritter et al. (2011), for instance, found impaired emotional empathy in pathological narcissism using ecologically valid experimental designs, whereas group differences failed significance using self-report instruments. Traditional self-report instruments, such as the IRI to measure cognitive and emotional aspects of empathy, require self-insight that is likely reduced in pathological narcissism (Gosling et al., 1998). Consequently, future studies might benefit from the use of a multi-method approach for the behavioral assessment of empathy in order to more closely link different aspects of empathy to GM volume (Hooker et al., 2011) and to highlight NPD patients' impaired ability for emotional empathy (Ritter et al., 2011).

Neurobiological abnormalities in the left anterior insula of NPD patients and the possible link to emotional empathy are in line with recent neuroimaging findings in healthy individuals indicating that narcissistic traits are also associated with abnormalities in the anterior insula (Fan et al., 2011b). Although group differences were also found in the dorsolateral prefrontal cortex and the posterior/

Table 3
Results of the whole-brain analysis comparing local gray matter volume between healthy controls and patients with narcissistic personality disorder. Whole-brain results were corrected using cluster-extent correction procedures. The reverse contrast yielded no significant results. Significant clusters are presented from anterior to posterior.

Healthy controls > patients with narcissistic personality disorder

Left hemisphere								Right hemisphere							
Region	BA	[X Y Z]			k	T	d	Region	BA	[X Y Z]			k	T	d
Sup. frontal g., medial	10	−3	59	25	236	3.61	1.25	Anterior cingulate g.	24	9	33	6	231	3.17	1.07
Middle frontal g.	10	−32	39	16	274	3.69	1.05	Middle frontal g.	8	29	17	42	639	4.10	1.47
Insula	13	−41	6	−5	300	3.32	1.23	Sup. frontal g., dl.	6	20	−4	57	222	3.54	1.10
Median cingulate g.	24	−5	−9	42	1259	3.84	1.51	Middle frontal g.	6	42	−4	60	440	3.43	1.18
Postcentral g.	4	−51	−10	49	647	4.56	1.34								

BA − Brodman Area, dl. − dorsolateral, g. − gyrus, k − cluster size in voxels, T − T-value of the peak voxel, d − Cohen's d of the significant cluster.

median cingulate cortex of highly narcissistic individuals (two regions characterized by smaller GM volume in patients with NPD in the present study), only functional abnormalities of the anterior insula were unequivocally attributable to emotional empathy (Fan et al., 2011b).

Nevertheless, alternative interpretations of the observed abnormalities in GM volume of NPD patients are plausible and will be discussed here. In doing so, we aim to highlight possible avenues for future research that more closely link local brain abnormalities to the psychopathology of NPD. Besides alterations in empathic processes, NPD patients' symptomatology includes grandiosity, self-esteem dysregulation, a hypersensitivity to perceived criticism, and self-referential processing biases (Pincus and Lukowitsky, 2010). Critically, neuroimaging studies have highlighted the involvement of the anterior insula, medial prefrontal cortex and anterior cingulate cortex during self-referential processing and decision-making (Enzi et al., 2009; Heatherton, 2011; Johnson et al., 2005; Modinos et al., 2009; for a meta-analysis, see Northoff et al., 2006). It could therefore be argued that the reported group differences in local GM volume are related to self-referential processing biases, which are closely related to the ego-centric perspective of NPD patients. Furthermore, dorsolateral prefrontal and anterior cingulate cortices are consistently implicated in emotion regulation processes (cf. Ochsner and Gross, 2005; Ochsner and Gross, 2007). Several studies in non-clinical (Domes et al., 2010; Kanske et al., 2011; Ochsner et al., 2004) and clinical populations (Erk et al., 2011; Johnstone et al., 2007; Schulze et al., 2011) have emphasized the importance of prefrontal structures in this regard. Smaller GM volume in the dorsolateral prefrontal and anterior cingulate cortex might be related to impaired emotion regulation processes in NPD (Fulford et al., 2008; Ronningstam, 2010), which are especially evident under conditions of threatened self-esteem (Baumeister et al., 1996).

Although the results of our study do provide a promising starting point for the investigation of neurobiological processes in NPD, the preceding paragraph illustrated the need for future research to more clearly disentangle the role of specific cognitive/emotional processes, behavior and local brain abnormalities in NPD. The combination of functional MRI with experimental paradigms investigating emotional empathy (e.g., Dziobek et al., 2008; Moriguchi et al., 2007), regulatory processes in the context of threatened self-esteem (e.g., Eisenberger et al., 2011; Gyurak et al., 2012), or self-referential processing and decision-making might represent a fruitful approach to fundamentally advance our current understanding of NPD.

Besides the need to assess brain-behavior relationships of NPD patients more closely in the future, the present study has some limitations that need to be considered in the interpretation of our results. First, while all patients had NPD as a primary diagnosis, the clinical sample was also characterized by additional co-morbid mental disorders. Although a high prevalence of co-morbid disorders (particularly of affective and substance use disorders) is inherent to the clinical presentation of NPD (Ritter et al., 2010; Stinson et al., 2008) and underlines the representative-ness of our sample, it might be questioned whether the reported group differences are exclusively attributable to NPD. Thus, post-hoc comparisons for the reported whole-brain findings between NPD patients without a history of co-morbid depression ($n = 9$) and healthy controls were calculated using SPSS. Except for the left middle frontal gyrus, all cluster remained significant or were significant at a trend level, despite a substantial loss of power ($d = .83–1.49$). Next, healthy controls and NPD patients without a lifetime history of substance-related disorders ($n = 8$) were compared with healthy controls. All clusters remained significant ($d = 1.04–1.79$). Given the considerable loss of power, these findings illustrate the stability of the reported whole-brain findings in NPD patients. Nevertheless, future research should include a psychopathological control group to further investigate the specificity of the reported findings for NPD (Brunner et al., 2010). Second, we acknowledge that four patients received antidepressant medication, which might have confounded our results. Although the results of recent meta-analyses in obsessive−compulsive disorder (Radua and Mataix-Cols, 2009) or depression (Sacher et al., 2013) suggest that antidepressants do not influence the direction of GM abnormalities, future research is needed to clarify this point. Third, the sample sizes of our groups were at the lower limit of VBM analyses. Thus, more subtle alterations in local GM volume of patients with NPD might have been falsely rejected as the reported findings were controlled for false positives using correction procedures at the voxel- or cluster level, respectively (for a discussion, see Friston, 2012). Similarly, future research is needed to determine the relationship between psychiatric treatment status and global tissue volumes. Although group comparisons were not significant possibly due to the small sample sizes, effect size estimates yielded medium-sized effects suggesting smaller gray matter, white matter, and total intracranial volume in NPD patients.

4.1. Summary/conclusions

To summarize, in the present study we provide initial evidence for neurobiological abnormalities in a sample of patients with NPD. In contrast to healthy controls, patients with NPD were characterized by smaller GM volume in fronto-paralimbic brain regions, such as the left anterior insula, the rostral part of the anterior cingulate cortex and the median cingulate cortex. In particular, the left anterior insula might be a promising neural correlate of impaired emotional empathy that seems central for diagnosis and treatment of NPD.

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None.

Contribution

I Dziobek, H Heekeren, and S Roepke designed the study. L Schulze and A Vater acquired the data, which were analyzed by S Roepke and L Schulze. H Heekeren, M Bajbouj, I Heuser, B Renneberg, S Roepke and L Schulze contributed to the interpretation of the data. S Roepke and L Schulze wrote the article. All authors reviewed the article. All authors approved its publication.

Conflicts of interest

None.

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