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Dimensional personality impairment is associated with disruptions in intrinsic intralimbic functional connectivity

Jenna M. Traynor[1,*], Johannes S. Wrege[2,*], Marc Walter[2] and Anthony C. Ruocco[1]

[1]Department of Psychology, University of Toronto Scarborough, Toronto, Ontario, Canada and [2]Department of Psychiatry (UPK), University of Basel, Basel, Switzerland

Original Article

*Indicates shared first author.

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Author for correspondence:
Anthony C. Ruocco,
E-mail: anthony.ruocco@utoronto.ca

Abstract

Background. Recently proposed alternative dimensional models of personality disorder (PD) place the severity of impairments in self and interpersonal functioning at the core of personality pathology. However, associations of these impairments with disturbances in social, cognitive, and affective brain networks remain uninvestigated.

Methods. The present study examined patterns of resting-state functional connectivity (rsFC) in a sample of 74 age- and sex-matched participants (45 inpatients with PD and 29 healthy controls). At a minimum, PD patients carried a diagnosis of borderline PD, although the majority of the sample had one or more additional PDs. rsFC patterns in the following networks were compared between groups and in association with dimensional personality impairments: default mode network (DMN)/core mentalization, frontolimbic, salience, and central executive. Further, the extent to which variation in rsFC was explained by levels of personality impairment as compared to typology-specific borderline PD symptom severity was explored.

Results. Relative to controls, the PD group showed disruptions in rsFC within the DMN/core mentalization and frontolimbic networks. Among PD patients, greater severity of dimensional self-interpersonal impairment was associated with stronger intralimbic rsFC. In contrast, severity of borderline PD-specific typology was not associated with any rsFC patterns.

Conclusions. Disruptions in core mentalization and affective networks are present in PD. Higher intralimbic functional connectivity may underlie self-interpersonal personality impairment in PD regardless of diagnostic typology-specific PD symptoms, providing initial neurobiological evidence supporting alternative dimensional conceptualizations of personality pathology.

Introduction

In recently proposed alternative dimensional models of personality disorder (PD), such as the alternative model of personality disorders (AMPD) in the Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition (DSM-5; Skodol et al., 2011) and the proposed International Classification of Diseases-11th Revision (ICD-11; World Health Organization, 2018), impairments in self and interpersonal functioning define the presence and severity of a PD. A primary goal of this reformulation is to address the long-standing problem of high comorbidity across traditional PD diagnostic types (e.g. borderline PD; Cacciola, Rutherford, Alterman, McKay, & Mulvaney, 1998; Chmielewski, Clark, Bagby, & Watson, 2015; Markon, Chmielewski, & Miller, 2011; Regier et al. 2013), which reflects the substantial interrelatedness among variants of personality pathology (Widiger & Rogers, 1989; Wright et al., 2012).

A reformulation of PD is supported by research showing that most pathological personality features can be grouped together under one general factor (Sharp et al., 2015; Wright, Hopwood, Skodol, & Morey, 2016) and that the severity of personality impairment—reflected in self-interpersonal functioning—rather than the presence of typology is a better prognostic predictor (Hopwood, 2011; Parker et al., 2002). By placing self-interpersonal impairment at the core of personality pathology, novel dimensional models offer a transformative paradigmatic shift in the conceptualization of PD. However, the neurobiology of self-interpersonal impairment in PD remains largely uninvestigated. As PDs have historically been considered difficult disorders to treat due to their complex clinical presentation (Ekselius, 2018), delineating the neural correlates of self-interpersonal impairment will contribute to the uncovering of biomarkers that cut across traditional boundaries of PD diagnoses and may be used prospectively to improve treatment outcomes (Marceau, Meuldijk, Townsend, Solowij, & Grenyer, 2018). Additionally, such an investigation is in line with the National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC) initiative, which proposes a dimensional neuroscience-based research framework for the study of psychopathology (Insel et al., 2010).

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Similar to the rationale underlying the DSM-5 Alternative Model and proposed ICD-11 dimensional reformulations of PD, the RDoC initiative acknowledges the limitations associated with categorical psychiatric taxonomy with respect to a failure to capture pertinent underlying neurobiological mechanisms. The RDoC serves as a research framework to study the underlying neural mechanisms of dysfunction associated with multiple systems and processes, including social processes relevant to the perception and understanding of the self and others, which intersect with the DSM-5 Alternative Model and proposed ICD-11 model for PD. Neurobiological research on self and interpersonal dysfunction as conceptualized in these alternative models could help to bring advancements in PD nosology in line with the RDoC framework and increase understanding of RDoC constructs pertinent to social processes.

Resting-state functional magnetic resonance imaging (rs-fMRI) is a powerful method used to investigate neuroimaging biomarkers of psychiatric illness. Rs-fMRI quantifies intrinsic, low-frequency oscillations in the blood-oxygen level-dependent (BOLD) signal, and offers an advantage over task-based fMRI, the latter of which produces results that are dependent on task selection and have historically been inconsistent (van Zutphen, Siep, Jacob, Goebel, & Arntz, 2015). In PD research, rs-fMRI has been most used to explore the default mode network (DMN), which is comprised of a set of functionally integrated structures that cross the brain's midline and lateral regions (Uddin, 2015). The DMN is strongly implicated in self-referential processing, including introspection (Buckner, Andrews-Hanna, & Schacter, 2008), reflection on one's own thoughts and feelings (Whitfield-Gabrieli & Ford, 2012) and social cognitive interaction (Li, Mai, & Liu, 2014). Two regions within the DMN—the MPFC and temporal–parietal junction (TPJ; comprised of the superior temporal sulcus (STS), supramarginal gyrus, and angular gyrus)—are strongly implicated in theory of mind (Saxe & Kanwisher, 2003) and mentalization (Bateman & Fonagy, 2004). As such, the MPFC and TPJ are collectively referred to as the core mentalization network (Van Overwalle & Vandekerckhove, 2013), which is a prime candidate for the investigation of self-interpersonal impairment in PD.

Rs-fMRI research on PD has frequently focused on borderline personality disorder (BPD), which is the most well understood PD from a neurobiological perspective (Ruocco & Carcone, 2016). BPD is associated with core impairment in self-interpersonal functioning, also referred to as disturbed relatedness (Sanislow et al., 2002). Meta-analyses of rs-fMRI in BPD converge on hyperactivation in the medial prefrontal cortex (MPFC)/ACC, (Amad, Radua, Vaiva, Williams, & Fovet, 2019; Visintin et al., 2016), but patterns of activation in the posterior DMN are more divergent (Amad et al., 2019; Visintin et al., 2016; Wolf et al., 2011). Laterally, patterns of hypoactivation in temporal regions of the DMN have emerged (Visintin et al., 2016), as well as lower mean overall connectivity (Quattrini et al., 2019). Task-based fMRI findings in BPD of higher MPFC activation during social exclusion (Wrege et al., 2019), and lower TPJ connectivity during theory of mind processing (ONeil et al., 2015) are consistent with the core mentalization deficits observed among individuals with BPD (Fonagy & Luyten, 2009). Outside of the DMN, rs-fMRI and task-based fMRI studies have identified substantial disruptions in the frontolimbic circuit in BPD (Ruocco & Carcone, 2016), converging on the orbitofrontal cortex, dorsolateral prefrontal cortex (DLPFC), and amygdala (Díaz-Marsá et al., 2011; Dudas et al., 2017; New et al., 2007; Silbersweig et al., 2007; Visintin et al., 2016). Indeed, BPD is often conceptualized as a disorder of emotion dysregulation, and limbic system abnormalities have been proposed as candidate endophenotypes of BPD (Ruocco, Amirthavasagam, & Zakzanis, 2012). Moreover, central executive network (CEN) and salience network (SAL) abnormalities have been identified (Doll et al., 2013; Quattrini et al., 2019) and correlated with self-interpersonal traits such as metacognitive ability and interpersonal aggression in BPD (Quattrini et al., 2019).

Although rs-fMRI PD research has predominantly been carried out on BPD, the results of studies on other PDs and PD traits point to common abnormalities across four networks: DMN, frontolimbic, SAL, and CEN. Indeed, rs-fMRI studies on antisocial personality disorder (ASPD; Jiang et al., 2017), obsessive–compulsive personality disorder (OCPD; Coutinho, Goncalves, Soares, Marques, & Sampaio, 2016; Lei et al., 2020), and narcissistic (Feng et al. 2018) and avoidant PD traits (Bauml et al. 2019), have observed disturbances in functional connectivity (FC) within these four networks. This apparent overlap in neural network dysfunction may be explained by common underlying symptom dimensions that cut across PD diagnoses. Self-interpersonal impairment across PD diagnoses may contribute to a significant degree of shared variance in FC in these four networks, a hypothesis that has yet to be explored in a PD sample using a cross-cutting measure of personality impairment. In fact, there is a clear paucity of research that explores the dimensional neurobiology of PD, as fMRI has almost exclusively been used to characterize the neural underpinnings of specific PD diagnoses, despite the potential of dimensional, neuroscience-based research to illuminate the neurobiology of PD (Koudys, Traynor, Rodrigo, Carcone, & Ruocco, 2019).

In the present study, we investigated interconnections within the DMN, frontolimbic, SAL, and CEN using resting-state functional connectivity (rsFC), which estimates the degree of functional coupling between neural regions by quantifying the temporal correlation in BOLD signal and permitting the visualization of connectivity between nodes of a network, which is consistent with the notion that psychiatric illness involves a disruption of network neurocircuitry (Morris & Cuthbert, 2012). We studied a sample of patients with a PD, at minimum carrying a diagnosis of BPD, but also other comorbid PDs, and a healthy control group. First, we compared the PD and healthy control groups in the strength of connectivity within these networks to examine potential disruptions in rsFC. Second, we used a dimensional measure of personality functioning to investigate associations of rsFC with Criterion A self and interpersonal impairments, and examined potential differential associations across the DMN, frontolimbic, SAL, and CEN. In an exploratory manner, we investigated the extent to which variation in rsFC in the PD group is explained by dimensional personality impairment as compared to the Borderline Symptom List – 23 Item (BSL-23; Bohus et al., 2009), a measure of BPD symptom severity, which is based on the DSM conceptualization of BPD and other BPD-specific symptoms (Kleindienst, Jungkunz, & Bohus, 2020). First, we hypothesized that patients with PD would show rsFC differences from healthy controls within the DMN/core mentalization, frontolimbic, SAL, and CEN networks. Second, we hypothesized that self-interpersonal impairment would be associated with patterns of rsFC within the DMN/core mentalization network, given the self-other processes that this more narrowly delineated network supports.

Materials and methods

Participants

Data from 74 participants were used (45 PD, 29 HC; Table 1). To determine eligibility, all participants completed a clinical interview with a licensed psychiatrist or psychology trainee under the

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Table 1. Demographic and diagnostic data

	PD group ($n = 45$)		Control group ($n = 29$)	PD *v.* Control Fisher's exact p value/ $T(df) = t$ value, p value	
Sex: f/m	35/10		25/4	Fisher's exact p value = 0.54	
Age: Mean (s.d.)	27.5 (7.9)		25.6 (5.9)	T (70) = 1.18, $p = 0.24$	
Full scale IQ: Mean (s.d.)	96.59 (11.1)		106.44 (17.6)	T (42) = - 2.68, $p = 0.01$*	
Psychotropic medication status (n, %)	Positive (26, 57.7) Negative (19, 42.2)		Positive (0, 0) Negative (29, 100)	Fisher's exact p value = 0.00*	
Symptom scores mean (s.d.)	PD group ($n = 45$)	Ratio f:m	Control group ($n = 29$)	$T(df) = t$ value, p value	
LPFS total	11 (2.0)	11(2):11(4)	Na	–	
LPFS self subscale	6 (1.0)	6(1):6(1)	Na	–	
LPFS interpersonal subscale	5 (1.0)	5(1):6(1)	Na	–	
BSL-23 Item	41 (20.0)		4.25 (4.3)	$T(50) = 11.9$, p value = 0.00*	
SCID-II (PD Group) list of axis II diagnoses	PD subjects who met full diagnostic criteria (n, %)		PD subjects 1 PD (BPD) (n, %)	PD subjects 2 PDs (BPD + 1 addit.) (n, %)	PD subjects 3^+ PDs (BPD + n addit.) (n, %)
Avoidant PD	11 (24.4)		(17, 37.7)	(19, 42.2)	(9, 20)
Dependent PD	9 (20)				
Obsessive compulsive PD	8 (17.7)				
Paranoid PD	7 (15.5)				
Schizotypal PD	3 (6.6)				
Schizoid PD	2 (4.4)				
Histrionic PD	2 (4.4)				
Narcissistic PD	6 (13.3)				
Antisocial PD	4 (8.8)				
Borderline PD	45 (100)				

supervision of a licensed psychiatrist. The interview consisted of a semi-structured psychodiagnostic assessment, and sociodemographic and symptom measures. Patients with PD were recruited from a 12-week inpatient treatment program at the Psychiatric University Hospital of Basel in Switzerland. All patients met criteria at minimum for BPD according to the *Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition – Text Revision* (DSM-IV-TR; American Psychiatric Association, 2000), as well as a number of other PDs. HC participants were recruited via community advertisements, and were not permitted to have a current or lifetime DSM-IV-TR psychiatric disorder, which was assessed during the interview. Patients and controls were assessed using the Structured Clinical Interview for DSM-IV-TR Axis II Personality Disorders (SCID-II) – German Version (Wittchen, Zaudig, & Fydrich, 1997) and the Structured Clinical Interview for DSM-IV (SCID-1) – German Version (Wittchen et al., 1997). Diagnoses were assigned after clinical information was reviewed at a consensus meeting. Additional exclusion criteria for all participants included the presence of acute psychotic symptoms or intoxication, dementia, neurological disorders, and standard MRI safety contraindications. All participants were capable and provided informed consent to participate. Additional details on procedures are available elsewhere (Wrege et al., 2019).

Measures

DSM-5 alternative model of personality disorders (AMPD), levels of personality functioning scale (LPFS)

The levels of personality functioning scale (LPFS; Bender, Morey, & Skodol, 2011) is a dimensional, clinician rated tool that operationalizes Criterion A of the DSM-5 AMPD, which is comprised of impairments in self (identity and self-direction) and interpersonal (empathy and intimacy) functioning, with initial research suggesting good reliability and validity (Morey, 2017; Zimmermann et al., 2014, 2015), and a high degree of intercorrelation between the self and interpersonal functioning scales, which is consistent with the notion that personality functioning is best represented as a single dimension (Bender et al., 2011; Morey, 2017). Using a five-point scale ranging from 0 (*no impairment*) to 4 (*extreme impairment*), participants received a clinician-rated dimensional score on each of the four LPFS scales: identity, self-direction, empathy, and intimacy (Bender et al., 2011). Identity and self-direction scores were summed to create a score representing 'self impairment', and empathy and intimacy scores were summed to create a separate score for 'interpersonal impairment'. Total raw scores represented the sum of self and interpersonal impairment. Ratings used in the present analysis were made by

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a licensed psychiatrist and were compared against a group of three independent raters. Kappa values indicated excellent inter-rater reliability for the self, interpersonal, and total scores, as demonstrated by 84.9, 82.6, and 79.6% agreement, respectively.

Borderline symptom list-23 (BSL-23)

All participants completed the Borderline Symptom List-23 (BSL-23; Bohus et al., 2009), a self-report consisting of items representative of typical BPD symptoms, and which are rated on a scale of 0 (*not at all*) to 4 (*very strong*). The BSL-23 has demonstrated good psychometric properties as observed by high internal consistency (Chronbach's alpha = 0.935–0.969), and discriminant validity (mean effect size = 1.13 when discriminating BPD from Axis I disorders; Bohus et al., 2009). Cronbach's alpha for scores in the present study was 0.94 indicating excellent internal consistency.

fMRI data acquisition

Participants were not permitted to consume alcohol or drugs for three days prior to the scan (excluding nicotine) and completed a breathalyzer test and urine toxicology screen prior to scanning. Some participants in the PD group were taking psychotropic medications (see online Supplementary Table S1). MR data were obtained using a 3 T MRI scanner (Siemens Magnetom Prisma, Erlangen, Germany) and a 20-channel phased array radiofrequency head coil. All participants underwent a 5:08 min resting-state MRI scan using an axial echo planar imaging sequence, TR/TE = 1800/28 ms; 35 interleaved slices; slice thickness = 3.5 mm; 0.5 mm interslice gap; flip angle = 82°; FoV = 224 × 224 mm^2; inplane image matrix = 64 × 64 resulting in a 3,5 × 3,5 × 3,5 mm^3 resolution; 168 measurements; bandwidth 2442 Hz/Px. A high-resolution structural T1 scan was acquired using a sagittal three-dimensional magnetization-prepared rapid acquisition gradient echo (3D-MPRAGE). Participants were instructed to relax, close their eyes, and to not fall asleep for the duration of the scan.

fMRI data preprocessing

Data were preprocessed using CONN Functional Connectivity Toolbox (Whitfield-Gabrieli & Nieto-Castanon, 2012). The first three functional volumes from each scan were discarded to account for T2 equilibration effects. Preprocessing included participant motion estimation and correction via realignment of the time series using a six rigid-body parameter, unwarping of the time series to reduce susceptibility-distortion-by-movement interaction (Andersson, Hutton, Ashburner, Turner, & Friston, 2001), co-registration of functional and structural images using a rigid-body transformation (Ashburner et al., 2013), gray matter/white matter/CSF segmentation, normalization of images to Montreal Neurologic Institute (MNI) space, resampling into 2 mm^3 isotropic voxels, functional outlier detection of movement greater than 0.9 mm or global mean intensity change of more than 5 S.D., and smoothing with a 6 mm full-width at half-maximum kernel. Participant-specific connectivity maps were produced in the first-level analysis after denoising was applied using the principle component-based noise correction method 'CompCor' (Behzadi, Restom, Liau, & Liu, 2007). Motion scrubbing was used to remove outlier scans identified during preprocessing (Power, Barnes, Snyder, Schlaggar, & Petersen, 2012). A linear detrending term was applied. All preprocessed scans were band pass filtered at 0.008–0.09 Hz. *t* tests revealed no significant differences between the PD and HC group in either mean t [72] = 0.89, $p_{two-sided}$ = 0.37, or maximum head motion t [72] = 1.45, $p_{two-sided}$ = 0.15.

Region of interest definition

Evidence-based *a priori* regions of interest (ROIs) were selected to examine within-network rsFC in the DMN/core mentalization, frontolimbic, SAL, and CEN (online Supplementary Table S2). DMN/core mentalization ROIs were selected with a focus on dividing the MPFC into dorsal and ventral regions with functional specialization in mentalizing (Amodio & Frith, 2006). The anterior parahippocampal gyrus was selected due its association with affective-related processing, as opposed to the visual-related posterior region (Aminoff, Kveraga, & Bar, 2013).

Functional connectivity analysis

Between-group differences in rsFC within the networks of interest were identified in the second-level ROI-to-ROI analyses in the CONN Toolbox. Effects represent the bivariate temporal correlation of each source ROI with every other target ROI within the network of interest (Whitfield-Gabrieli & Nieto-Castanon, 2012). The between-group analyses statistically controlled for significant differences in IQ and medication status between the PD and HC groups.

Within-group analyses explored relationships between rsFC in the PD group and (a) LPFS scores, and (b) BSL-23 scores, while controlling for medication status and sex. Then, more specific associations between frontolimbic rsFC and the LPFS self and interpersonal subscale scores were explored using a multivariate F test to first identify any effects among the self and interpersonal subscales on rsFC. Post hoc tests were used to explore simple main effects.

All results were considered significant if they survived correction for multiple comparisons at a threshold of $p < 0.05$ after applying a false discovery rate correction (FDR) (Benjamini & Hochberg, 1995). A Bonferroni correction was applied to post hoc tests by dividing alpha = 0.05 by six, for each of the pairwise comparisons examined (i.e. each of the two separate LPFS subscores across each of the three bivariate connectivity patterns that resulted from the omnibus F test), resulting in a significance threshold of $p = 0.008$.

Results

Descriptive data

Table 1 contains demographic and diagnostic information. Significant differences in IQ and medication status were found between the PD and HC group. The two groups did not significantly differ in age or sex ratio. Among PD participants, a relatively equivalent representation of Clusters A and C diagnoses was observed, with Cluster B being the most common (i.e. all participants met criteria for BPD).

Correlations between LPFS and BSL-23 scores

Correlations between the LPFS total and subscale scores, and the BSL-23 scores were explored via a correlation matrix using R statistical software (R Core Team, 2013). Pearson's correlation coefficients and significance values (alpha = 0.05) were calculated (see Table 2).

Between group differences in rsFC

Between-subject ROI-to-ROI effects are displayed in Table 3 (Section A) and Fig. 1*left* and *right*. Within the DMN, underconnectivity of the left anterior parahippocampal gyrus with the

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Table 2. Pearson's R correlation matrix: BSL-23 self-report and LPFS self, interpersonal, and total scores

	LPFS interpersonal	LPFS total	BSL-23
LPFS_Self	$r = 0.70$ $p = 0.0000$*	$r = 0.91$ $p = 0.0000$*	$r = 0.20$ $p = 0.12$
LPFS_Interpersonal	–	$r = 0.93$ $p = 0.0000$*	$r = 0.31$ $p = 0.03$*
LPFS Total	–	–	$r = 0.28$ $p = 0.06$

LPFS - Levels of Personality Functioning Scale; BSL-23 – Borderline Symptom List – 23.
* indicates statistical significance at $p < 0.05$.

precuneus/PCC was observed in PD participants compared to controls. In contrast, within the core mentalization network, overconnectivity within the TPJ (i.e. the left STS with the bilateral angular gyrus), and of the left STS with the dmPFC and vmPFC, was observed. Within the frontolimbic network, relative to controls, PD participants displayed right lateralized overconnectivity of the DLPFC with three closely interconnected limbic areas: anterior parahippocampal gyrus, amygdala, and hippocampus. There were no significant between-group differences in SAL or CEN rsFC. Statistically controlling for sex did not change the results.

ROI-to-ROI functional connectivity and the LPFS total score

Table 3 (Section B) and Fig. 2*a* display the effect of LPFS total score on rsFC within the PD group. LPFS total scores were associated exclusively with intralimbic connectivity. Specifically, positive associations between LPFS total score and rsFC were observed between (a) left amygdala and bilateral anterior parahippocampal gyri, (b) right amygdala and bilateral anterior parahippocampal gyri, and (c) right anterior parahippocampal gyrus and right hippocampus. When sex was not controlled for, the association between LPFS total score and right amygdala–right parahippocampal gyrus connectivity was no longer significant [$T(42) = 2.41$, $p_{FDR} = 0.114$]. LPFS total score was not associated with connectivity in the DMN, SAL, or CEN.

LPFS self and interpersonal scores and intralimbic rsFC in PD

The results are displayed in Table 3 (Section C) and Fig. 2*b*. After correcting for multiple comparisons, positive associations were observed between the LPFS interpersonal subscale and connectivity of the right hippocampus with the bilateral anterior parahippocampal gyri and between the right hippocampus and left amygdala.

Exploratory pairwise comparisons of the empathy and intimacy interpersonal components, revealed that empathy, but not intimacy scores, were associated with right hippocampus–bilateral anterior parahippocampal gyrus connectivity [right hippocampus–right parahippocampal gyrus: $T[41] = 3.82$, beta = 0.13, $R^2 = 0.26$, $p = 0.0004$; right hippocampus–left parahippocampal gyrus: $T[41] = 3.39$, beta = 0.12, $R^2 = 0.25$, $p = 0.001$]. The self subscale was not associated with any connectivity patterns when controlling for sex.

Notably, when sex was not controlled for, one additional effect on connectivity between the medial frontal cortex and right hippocampus [$F(2,41) = 4.62$, $p_{FDR} = 0.0426$] was observed, which was associated with the LPFS self subscore ($T[42] = -2.33$, beta = −0.058, $R^2 = 0.12$, $p = 0.025$) as opposed to the interpersonal subscore ($T[42] = -0.31$, beta = −0.007, $R^2 = 0.00$, $p = 0.76$), and was present in male ($T[7] = -3.34$, beta = −0.11, $R^2 = 0.62$, $p = 0.01$) but not in female PD participants ($T[32] = -1.09$, beta = −0.035, $R^2 = 0.04$, $p = 0.28$).

BSL-23 scores and rsFC in PD

No significant associations between BSL-23 scores and rsFC within any of the four networks investigated were identified in PD subjects (online Supplementary Table S3).

Discussion

DMN and frontolimbic circuitry alterations in PD v. controls

Partially consistent with our first hypothesis, disruptions in rsFC in the DMN/core mentalization, and frontolimbic networks in PD subjects, compared to controls, but not in the SAL and CEN, were found. Regarding the disruptions in DMN connectivity in PD subjects, DMN underconnectivity of the precuneus/PCC with the left parahippocampal gyrus was found, and parallels other work showing that the precuneus is a salient hub across PD categories (Coutinho et al., 2016; Kunisato et al., 2011; Lei et al., 2017; Tang, Jiang, Liao, Wang, & Luo, 2013; Yang et al., 2015; Zhu et al., 2017). Further, we found that within the DMN, core mentalization hyperconnectivity in PD participants converged on STS connectivity with the angular gyrus (i.e. TPJ connectivity), and with the dorsal and ventral MPFC. These findings are also consistent with our hypothesis of altered mentalization neurocircuitry in PD, and consistent with prior reports of mentalization deficits across PDs (Bateman & Fonagy, 2004; Drozek & Unruh, 2020; Newbury-Helps, Feigenbaum, & Fonagy, 2017) and the functional specialization of the left STS in theory of mind processing (Beauchamp, 2015). Moreover, previous work has demonstrated a social-cognitive-related functional subdivision of the medial frontal cortex, whereby more superior regions are associated with action monitoring, self-knowledge, person perception, and mentalizing, and ventral regions with outcome monitoring (Amodio & Frith, 2006). Our findings of disruptions in both dmPFC and vmPFC connectivity therefore suggest a possible neural correlate of broad social-cognitive deficits in PD pertaining to a number of these mentalization abilities.

Further, and also in line with our hypothesis, our findings of frontolimbic hyperconnectivity are consistent with previous studies that have found resting-state (Baczkowski et al., 2017) and task-based fronto-amygdala disruptions (Schulze & Roepke, 2014) in BPD and Cluster C PDs, and in trait narcissism (Feng et al., 2018), although the direction of findings across studies has varied, possibly as a result of the use of different statistical approaches. The current findings are specific to the DLPFC, and are therefore rooted in disruptions within the cognitive, model-based emotion control system in PD, rather than more implicit medial frontal-based control system (Etkin, Büchel, & Gross, 2015); hyperconnectivity of the DPLFC with the amygdala suggests an abnormal association between the explicit emotional control system and amygdala-based emotional reactivity (Etkin et al., 2015), and may be reflective of the chronic state of hyperarousal observed across PDs (Ruocco & Carcone, 2016), which may require more frequent or prolonged frontal executive regulation. In all, these findings mirror a recently published study on the

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Table 3. ROI-to-ROI analyses

A. Between-group ROI-to-ROI analysis (PD > HC)					
Network Name	Within network ROI-to-ROI connection	Direction of connectivity	*T*(69)	*p(unc.)*	*p(FDR)*
Contrast = PD > HC, controlling for medication status and IQ					
Central executive	Ns	–	–	–	–
Salience network	Ns	–	–	–	–
DMN	Anterior parahipp (L) - precuneus	Negative	−3.18	0.0022	0.0240
	Anterior parahipp (L)-PCC	Negative	−2.75	0.0075	0.0414
DMN (Core Mentalization)	STS(L) – vmPFC	Positive	3.00	0.0038	0.0212
	STS(L) –angular gyrus (R)	Positive	2.99	0.0039	0.0212
	STS(L) –angular gyrus (L)	Positive	2.65	0.0100	0.0274
	STS(L) – dmPFC	Positive	2.73	0.0080	0.0274
Frontolimbic	DLPFC(R) – Anterior parahipp (R)	Positive	3.08	0.0030	0.0332
	DLPFC(R) –amygdala (R)	Positive	2.64	0.0103	0.0414
	DLPFC(R) –hippocampus (R)	Positive	2.60	0.0113	0.0414
B. Within-group ROI-to-ROI analysis: significant effects of LPFS total score on patterns of connectivity strength in PD group					
Network name	Within network ROI-to-ROI connection	Direction of connectivity	*T*(41)	*p(unc.)*	*p(FDR)*
Within-group PD Effect of LPFS, controlling for medication status and sex					
Central executive	Ns	–	–	–	–
Salience network	Ns	–	–	–	–
DMN	Ns	–	–	–	–
Frontolimbic	Amygdala (L)- anterior parahipp (L)	Positive	3.17	0.0029	0.0289
	Amygdala (L)- anterior parahipp (R)	Positive	2.86	0.0067	0.0368
	Anterior parahipp (R)- amygdala (R)	Positive	2.61	0.0125	0.0459
	Anterior parahipp (R)- hippo (R)	Positive	3.05	0.0040	0.0368
	Anterior parahipp (L) amygdala(R)	Positive	2.95	0.0053	0.0289

C. Multivariate *F* Test for any effect among LPFS Self or Interpersonal Subscales within Frontolimbic Network *Within group PD, controlling for medication status and sex*				Post Hoc Test of Simple Main Effects of LPFS Subscores on Connectivity Strength				
Seed	Brain Region	*F* (2,40)	*p* < 0.05 FDR	LPFS Subscore	R^2	beta (effect size)	*T* (41)	*p* < 0.0083 (Bonferroni correction)
1. Hippo (R) -	aPaHC(R)	7.19	0.0236	1. Self	0.08	0.049	1.85	0.07160
2. Hippo (R) -	aPaHC(L)	5.73	0.0356	2. Self	0.09	0.038	1.44	0.15708
3. Hippo (R) -	Amygdala (L)	5.01	0.0421	3. Self	0.03	0.02	0.76	0.45206
				1. Interpersonal	0.25	0.08	3.73	0.00057*
				2. Interpersonal	0.24	0.07	3.25	0.00232*
				3. Interpersonal	0.17	0.06	2.73	0.00940

aPaHC, anterior parahippocampal gyrus; DLPFC, dorsolateral prefrontal cortex; dmPFC, dorsomedial prefrontal cortex; DMN, default mode network; Hippo, hippocampus; LPFS, Levels of Personality Functioning Scale; Parahipp, parahippocampal gyrus; PCC, posterior cingulate cortex; STS, superior temporal sulcus; vmPFC, ventromedial prefrontal cortex.

NIMH RDoC, which demonstrated substantial transdiagnostic overlap of DSM-5 PD symptoms onto two RDoC domains -*Social Processes* and *Arousal and Regulatory Systems* (Koudys et al., 2019), both of which are rooted in mentalization and frontolimbic circuitry.

Criterion A self-interpersonal impairment and intralimbic connectivity

To our knowledge, this is the first study to examine biomarkers of dimensional, Criterion A self-interpersonal impairment in PD, which is a strength of the study. In light of this investigation,

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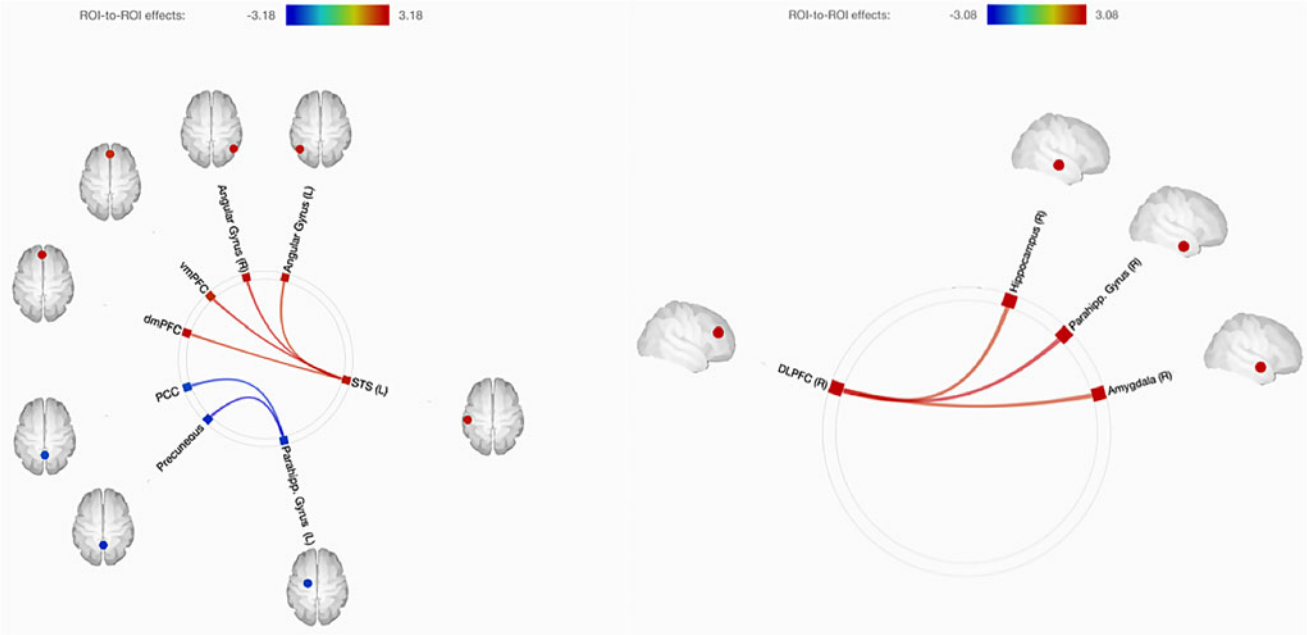

Fig. 1. Significant between-group differences in ROI-to-ROI connectivity within the DMN (left) and frontolimbic network (right). DMN – default mode network; dmPFC – dorsomedial prefrontal cortex; dlPFC – dorsolateral prefrontal cortex; vmPFC – ventromedial prefrontal cortex; STS – superior temporal sulcus; PCC – posterior cingulate cortex; parahipp – parahippocampal.

we show that instead of being associated with DMN connectivity as originally hypothesized, impairment across self and interpersonal functioning in PD is correlated solely with greater intralimbic connectivity strength of the parahippocampal gyrus with the hippocampus and amygdala. These findings are supported by previous work showing abnormal FC of the hippocampal/parahippocampal gyrus with the amygdala in BPD (Cullen et al., 2011; Krause-Utz et al., 2017; Salvador et al., 2016). Further, amygdala–hippocampal connectivity has been associated with childhood trauma (Fan et al., 2015), fear conditioning (Kruse, León, Stalder, Stark, & Klucken, 2018), and with personality traits observed across PDs, including impulsivity (Westlund Schreiner et al., 2019), and sensitivity to punishment during the anticipation of an aversive event (Hahn et al., 2010), which highlights the emotion-related function of these structures.

Moreover, within the two specific interpersonal domains of empathy and intimacy, we show that only deficits in empathy are associated with rsFC, and more specifically with connectivity of the right hippocampus and bilateral parahippocampal gyrii. Relatedly, another study found that compared to controls, BPD participants who were classified as having unresolved attachment trauma showed less activation of the parahippocampal gyrus while providing narrative reports of attachment-activating interpersonal scenes (Buchheim et al., 2008), which speaks to the involvement of the parahippocampal gyrus in interpersonal processing. In a similar regard, in individuals with schizotypal PD, reduced parahippocampal–precuneus rsFC has been found, and associated with levels of suspiciousness (Zhu et al., 2017), again suggesting an interpersonal functional specialization of the parahippocampal gyrus.

The hippocampus and parahippocampal gyrus maintain dense anatomical connections with each other and the neocortex, and support problem-solving by allowing one to make flexible associative inferences based on previously stored declarative memories (Eichenbaum, 2000), as well as to imagine personally relevant future events (Schacter, Addis, & Szpunar, 2017). In the presence of interference, which may be cognitive or emotional, the parahippocampal gyrus is implicated in the maintenance of information about stimulus familiarity (Eichenbaum, 2000). Taken together, the hippocampal structures appear to play a substantial role in emotional decision-making via flexible updating based on prior experience. Indeed, in controls, the parahippocampal gyrus activates during trial-by-trial suspicion about another person's trustworthiness, and is therefore involved in rational interpersonal updating (Bhatt, Lohrenz, Camerer, & Montague, 2012). We hypothesize that the ability to engage in flexible, rational interpersonal updating may be impaired or require more reserve in individuals with PD, who often experience emotional interference via a chronic state of hyperarousal (Ruocco & Carcone, 2016; Sharp, 2016). As a result, individuals with PD may display increasing connectivity of the interference-mediating parahippocampal gyrus with other limbic structures, which may be compensatory (i.e. adaptive) or pathological (i.e. leading to greater interpersonal impairment). Given our correlational analysis, the present results suggest an association between parahippocampal over connectivity and the broad limitations in empathy that are frequently observed across PD diagnoses. In future, a causative analysis approach could investigate whether parahippocampal disruptions are a correlate, a cause, or a consequence of the empathy deficits observed in PD.

Personality impairment v. BPD symptom severity and connectivity

The present study failed to find a significant association between the BSL-23 and rsFC in any of the four networks investigated, suggesting that a dimensional formulation of personality disorder based on self-interpersonal impairment may capture more

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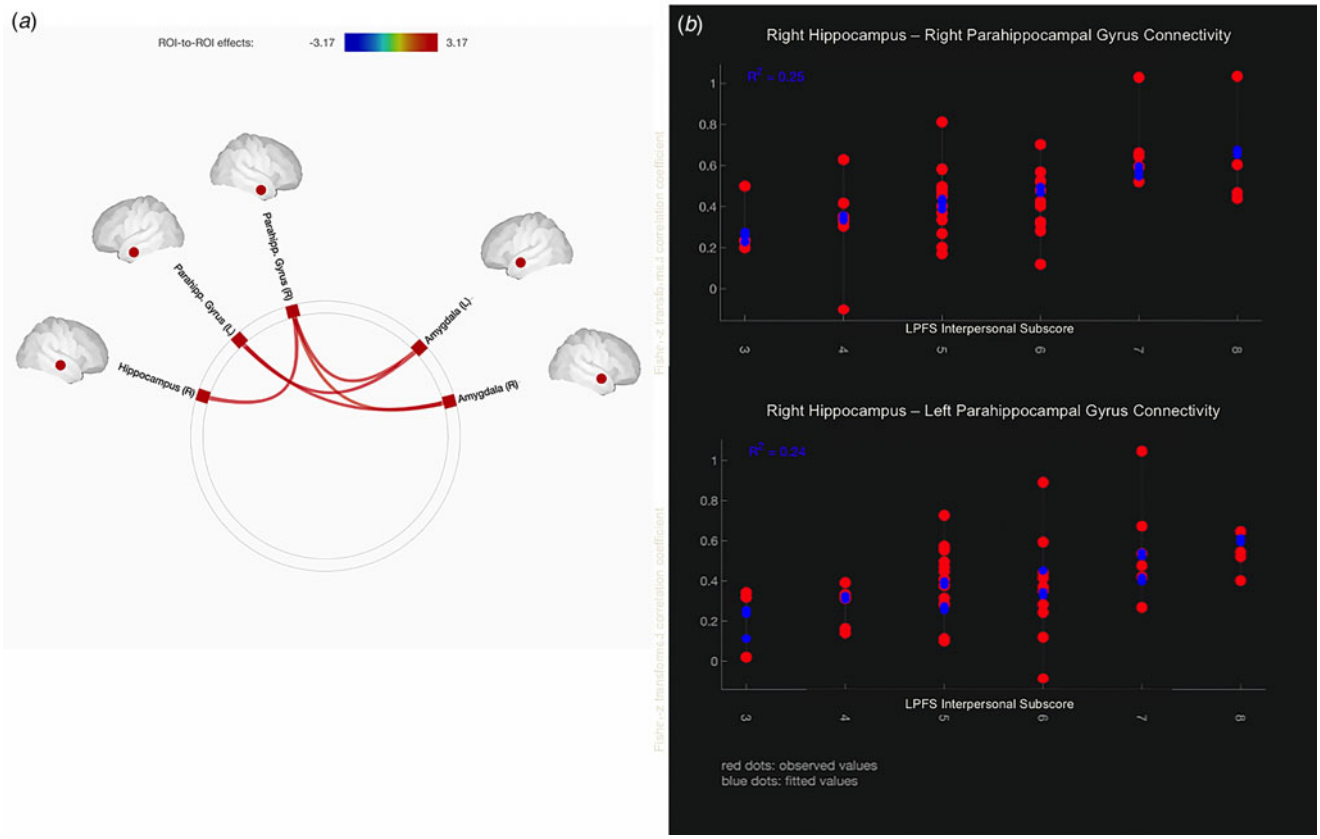

Fig. 2. A: Significant effect of LPFS total score on ROI-to-ROI connectivity within the PD group. B: post hoc test demonstrating significant effect of LPFS Interpersonal subscale score on hippocampal–parahippocampal connectivity strength. parahipp – parahippocampal; LPFS- Levels of Personality Functioning Scale.

variance in rsFC than a severity measure based on typology-specific symptoms.

Limitations

Although the largest percentage of participants in the present study had two categorical PD diagnoses (42.2%), all participants had a diagnosis of BPD and were recruited as part of a study in which BPD was an eligibility criterion (see Wrege et al., 2019). As such, these results should be replicated in more diverse diagnostic PD samples so as to further interrogate the suggestion that the neural correlates of self-interpersonal dysfunction cut across DSM-5 PD categories. Although our analysis failed to find any associations between rsFC and BPD-specific symptoms, and instead, found that rsFC is associated with typology-independent self-other impairment, replicating this analysis in a large sample comprised of a more balanced representation of Cluster A, B, and C diagnoses will further support the proposition that the current findings are not specific to BPD. Additionally, a more balanced sample in this respect would facilitate explorations of these associations both within and across diagnostic categories.

Further, to extend the current findings and contribute to the development of RDoC-based research on personality disorder, future research could recruit participants with a range of personality psychopathology, from subthreshold to severe levels of personality dysfunction, consistent with the RDoC initiative's aim to elucidate the neurobiology of social processes across a spectrum of functioning (Insel et al., 2010). The findings of the present study are most pertinent to the RDoC matrix's *Perception and Understanding of the Self and Others* constructs, which is subsumed under the *Social Processes* domain. Pending future interrogation across a fulsome range of personality functioning, the interconnections of the parahippocampal gyrus may be further considered for their potential relevance to these RDoC constructs.

Second, our sample consisted of mostly female participants, and future work with a more sex-representative sample is needed to generalize and follow up on our preliminary finding of a relationship between the LPFS *self* subscore and right hippocampal–medial prefrontal connectivity in male participants. Despite the preliminary nature of this finding, previous studies have found sex-differentiated structure (e.g. Persson et al., 2014; van Eijk et al., 2020) and right-lateralized function of the hippocampus in males (Frings et al., 2006; Persson et al., 2013). Further, a recent animal study demonstrated that social memory is regulated by hippocampal–medial prefrontal connectivity (Phillips, Robinson, & Pozzo-Miller, 2019), and in humans, sex differences in social cognition have been demonstrated when transcranial direct current stimulation is applied to the medial PFC (Adenzato et al., 2017). Indeed, it is plausible that personality self-functioning may be supported by a sexually dimorphic neurobiological architecture.

Finally, although a strength of the present study was that our PD sample was comprised of an inpatient population, presumptively maximizing any existing between-group differences, in contrast to other work (Doll et al., 2013; Quattrini et al., 2019), we did not find disruptions in the SAL or CEN, which may have been due to our substantially larger sample size reflecting a true lack

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of differences. Alternatively, this inconsistency may be due to the differing statistical approaches used across studies.

Conclusions

We identified differences in intrinsic rsFC in PD patients compared to controls in the DMN/core mentalization and frontolimbic networks. Further, in our PD sample, we revealed that connectivity between limbic structures is associated with self-interpersonal impairment, suggesting that disturbances in intralimbic connectivity may contribute to personality impairment regardless of diagnostic typology. In particular, connectivity of the parahippocampal gyrus emerged as a preliminary biomarker of interpersonal but not self-impairment, despite the strong correlation between these scales and prior suggestions that they form a single dimension of impairment. The pattern of findings could be interpreted as individuals with PD being prone to recall negative emotional memories in the context of a chronic state of hyperarousal, interfering with the ability to make rational interpersonal updates. Future work may begin to explore the prognostic utility of these findings. Importantly, these findings contribute to the integration of novel reformulations of PD with the NIMH RDoC initiative.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291721002865.

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Conflict of interest. None of the authors have any conflicts of interest.

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

References

Adenzato, M., Brambilla, M., Manenti, R., De Lucia, L., Trojano, L., Garofalo, S., … Cotelli, M. (2017). Gender differences in cognitive theory of mind revealed by transcranial direct current stimulation on medial prefrontal cortex. *Scientific Reports*, *7*, 41219. doi:10.1038/srep41219

Amad, A., Radua, J., Vaiva, G., Williams, S. C. R., & Fovet, T. (2019). Similarities and differences between borderline personality disorder and post traumatic stress disorder: Evidence from resting-state meta-analysis. *Neuroscience and Biobehavioral Reviews*, *105*, 52–59. doi: 10.1016/j.neubiorev.2019.07.018

American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., Text Revision). Washington, DC: American Psychiatric Publishing.

Aminoff, E. M., Kveraga, K., & Bar, M. (2013). The role of the parahippocampal cortex in cognition. *Trends in Cognitive Sciences*, *17*(8), 379–390. doi: 10.1016/j.tics.2013.06.009

Amodio, D. M., & Frith, C. D. (2006). Meeting of minds: The medial frontal cortex and social cognition. *Nature Reviews Neuroscience*, *7*(4), 268–277. doi: 10.1038/nrn1884

Andersson, J. L., Hutton, C., Ashburner, J., Turner, R., & Friston, K. (2001). Modeling geometric deformations in EPI time series. *Neuroimage*, *13*(5), 903–919. doi: 10.1006/nimg.2001.0746

Ashburner, J., Barnes, G., Chen, C., Daunizeau, J., Flandin, G., Friston, K., … Phillips, C. (2013). SPM8 Manual, Trust Centre for Neuroimaging, London, UK. Retrieved from: http://www.fil.ion.ucl.ac.uk/spm/.

Baczkowski, B. M., van Zutphen, L., Siep, N., Jacob, G. A., Domes, G., Maier, S., & van de Ven, V. (2017). Deficient amygdala-prefrontal intrinsic connectivity after effortful emotion regulation in borderline personality disorder. *European Archives of Psychiatry and Clinical Neuroscience*, *267*(6), 551–565. doi: 10.1007/s00406-016-0760-z

Bateman, A. W., & Fonagy, P. (2004). Mentalization-based treatment of BPD. *Journal of Personality Disorders*, *18*(1), 36–51. doi: 10.1002/j.2051-5545.2010.tb00255.x

Bauml, J. G., Baumann, N., Avram, M., Bratec, S. M., Breeman, L., Berndt, M., … Sorg, C. (2019). The default mode network mediates the impact of infant regulatory problems on adult avoidant personality traits. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *4*, 333–342. doi: 10.1016/j.bpsc.2018.11.005

Beauchamp, M. S. (2015). The social mysteries of the superior temporal sulcus. *Trends in Cognitive Sciences*, *19*(9), 489–490. doi: 10.1016/j.tics.2015.07.002

Behzadi, Y., Restom, K., Liau, J., & Liu, T. T. (2007). A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. *Neuroimage*, *37*(1), 90–101. doi: 10.1016/j.neuroimage.2007.04.042

Bender, D. S., Morey, L. C., & Skodol, A. E. (2011). Toward a model for assessing level of personality functioning in DSM–5, part I: A review of theory and methods. *Journal of Personality Assessment*, *93*, 332–346. doi: 10.1080/00223891.2011.583808

Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate—a practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society Series B Statistical Methodology*, *57*, 289–300. Retrieved from: https://www.jstor.org/stable/2346101?seq=1.

Bhatt, M. A., Lohrenz, T., Camerer, C. F., & Montague, P. R. (2012). Distinct contributions of the amygdala and parahippocampal gyrus to suspicion in a repeated bargaining game. *Proceedings of the National Academy of Sciences USA*, *109*, 8728–8733. doi: 10.1073/pnas.1200738109

Bohus, M., Kleindienst, N., Limberger, M. F., Stieglitz, R. D., Domsalla, M., Chapman, A. L., … Wolf, M. (2009). The short version of the borderline symptom list (BSL-23): Development and initial data on psychometric properties. *Psychopathology*, *42*(1), 32–39. doi: 10.1159/000173701

Buchheim, A., Erk, S., George, C., Kachele, H., Kircher, T., Martius, P., … Walter, H. (2008). Neural correlates of attachment trauma in borderline personality disorder: A functional magnetic resonance imaging study. *Neuroimaging*, *163*(3), 223–235. doi: 10.1016/j.pscychresns.2007.07.001

Buckner, R. L., Andrews-Hanna, J. R., & Schacter, D. L. (2008). The brain's default network: Anatomy, function, and relevance to disease. *Annals of the New York Academy of Sciences*, *1124*, 1–38. doi: 10.1196/annals.1440.011

Cacciola, J. S., Rutherford, M. J., Alterman, A. I., McKay, J. R., & Mulvaney, F. D. (1998). Long-term test-retest reliability of personality disorder diagnoses in opiate dependent patients. *Journal of Personality Disorders*, *12*(4), 332–337. doi: 10.1521/pedi.1998.12.4.332

Chmielewski, M., Clark, L. A., Bagby, R. M., & Watson, D. (2015). Method matters: Understanding diagnostic reliability in DSM-IV and DSM-5. *Journal of Abnormal Psychology*, *124*, 764–769. doi: 10.1037/abn0000069

Coutinho, J., Goncalves, O. F., Soares, J. M., Marques, P., & Sampaio, A. (2016). Alterations of the default mode network connectivity in obsessive-compulsive personality disorder: A pilot study. *Psychiatry Research: Neuroimaging*, *256*, 1–7. doi: 10.1016/j.pscychresns.2016.08.007

Cullen, K. R., Vizueta, N., Thomas, K. M., Han, G. J., Lim, K. O., Camchong, J., … Schulz, S. C. (2011). Amygdala functional connectivity in young women with borderline personality disorder. *Brain Connectivity*, *1*, 61–71. doi: 10.1089/brain.2010.0001

Díaz-Marsá, M., Carrasco, J. L., López-Ibor, M., Moratti, S., Montes, A., Ortiz, T., & Lopez-Ibor, J. J. (2011). Orbitofrontal dysfunction related to depressive symptomatology in subjects with borderline personality disorder. *Journal of Affective Disorders*, *134*, 410–415. doi: 10.1016/j.jad.2011.04.034

Doll, A., Sorg, C., Manoliu, A., Wöller, A., Meng, C., Förstl, H., … Riedl, V. (2013). Shifted intrinsic connectivity of central executive and salience network in borderline personality disorder. *Frontiers in Human Neuroscience*, *7*, 727. doi: 10.3389/fnhum.2013.00727

Drozek, R. P., & Unruh, B. T. (2020). Mentalization-based treatment of pathological narcissism. *Journal of Personality Disorders*, *34*, 177–203. doi: 10.1521/pedi.2020.34.supp.177

Dudas, R. B., Mole, T. B., Morris, L. S., Denman, C., Hill, E., Szalma, B., … Voon, V. (2017). Amygdala and dlPFC abnormalities, with aberrant connectivity and habituation in response to emotional stimuli in females with BPD. *Journal of Affective Disorders*, *208*, 460–466. doi: 10.1016/j.jad.2016.10.043

Eichenbaum, H. (2000). A cortical-hippocampal system for declarative memory. *Nature Reviews Neuroscience*, *1*, 41–50. doi: 10.1038/35036213

Ekselius, L. (2018). Personality disorder: A disease in disguise. *Upsala Journal of Medical Sciences*, *123*(4), 194–204. doi: 10.1080/03009734.2018.1526235

Etkin, A., Büchel, C., & Gross, J. J. (2015). The neural bases of emotion regulation. *Nature Reviews Neuroscience*, *16*(11), 693–700. doi: 10.1038/nrn4044

Fan, Y., Pestke, K., Feeser, M., Aust, S., Pruessner, J. C., Böker, H., … Grimm, S. (2015). Amygdala-hippocampal connectivity changes during acute psychosocial stress: Joint effect of early life stress and oxytocin. *Neuropsychopharmacology*, *40*, 2736–2744. doi: 10.1038/npp.2015.123

Feng, C., Yuan, J., Geng, H., Gu, R., Zhou, H., Wu, X., & Luo, Y. (2018). Individualized prediction of trait narcissism from whole-brain resting-state functional connectivity. *Human Brain Mapping*, *39*(9), 3701–3712. doi: DOI: 10.1002/hbm.24205

Fonagy, P., & Luyten, P. (2009). A developmental, mentalization-based approach to the understanding and treatment of borderline personality disorder. *Developmental Psychopathology*, *21*(4), 1355–1381. doi: 10.1017/S0954579409990198

Frings, L., Wagner, J., Unterrainer, J., Spreer, J., Halsband, U., & Schulze-Bonhage, A. (2006). Gender-related differences in lateralization of hippocampal activation and cognitive strategy. *Neuroreport*, *17*, 417–421. doi: 10.1097/01.wnr.0000203623.02082.e3

Hahn, T., Dresler, T., Plichta, M. M., Ehlis, A. C., Ernst, L. H., Markulin, F., … Fallgatter, A. J. (2010). Functional amygdala-hippocampus connectivity during anticipation of aversive events is associated with gray's trait "sensitivity to punishment.". *Biological Psychiatry*, *68*, 459–464. doi: 10.1016/j.biopsych.2010.04.033

Hopwood, C. J. (2011). Personality traits in the DSM–5. *Journal of Personality Assessment*, *93*, 398–405. doi: 10.1080/00223891.2011.577472

Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D. S., Quinn, K., … Wang, P. (2010). Research Domain Criteria (RDoC): Toward a new classification framework for research on mental disorders. *American Journal of Psychiatry*, *167*(7), 748–751. doi: 10.1176/appi.ajp.2010.09091379

Jiang, W., Shi, F., Liao, J., Liu, H., Wang, T., Shen, C., … Shen, D. (2017). Disrupted functional connectome in antisocial personality disorder. *Brain Imaging and Behaviour*, *11*(4), 1071–1084. doi: 10.1007/s11682-016-9572-z

Kleindienst, N., Jungkunz, M., & Bohus, M. A. (2020). Proposed severity classification of borderline symptoms using the borderline symptom list (BSL-23). *Borderline Personality Disorder and Emotion Dysregulation*, *7*, 11. doi: 10.1186/s40479-020-00126-6

Koudys, J. W., Traynor, J. M., Rodrigo, A. H., Carcone, D., & Ruocco, A. C. (2019). The NIMH Research Domain Criteria (RDoC) initiative and its implications for research on personality disorder. *Current Psychiatry Reports*, *21*(6), 37. doi: 10.1007/s11920-019-1023-2

Krause-Utz, A., Winter, D., Schriner, F., Chiu, C. D., Lis, S., Spinhoven, P., … Elzinga, B. M. (2017). Reduced amygdala reactivity and impaired working memory during dissociation in borderline personality disorder. *European Archives of Psychiatry and Clinical Neuroscience*, *268*, 401–415. doi: 10.1007/s00406-017-0806-x

Kruse, O., León, I. T., Stalder, T., Stark, R., & Klucken, T. (2018). Altered reward learning and hippocampal connectivity following psychosocial stress. *NeuroImage*, *171*, 15–25. doi: 10.1016/j.neuroimage.2017.12.076

Kunisato, Y., Okamoto, Y., Okada, G., Aoyama, S., Nishiyama, Y., Onoda, K., & Yamawaki, S. (2011). Personality traits and the amplitude of spontaneous low-frequency oscillations during resting state. *Neuroscience Letters*, *492*, 109–113. doi: 10.1016/j.neulet.2011.01.067

Lei, H., Huang, L., Li, J., Liu, W., Fan, J., Zhang, X., … Rao, H. (2020). Altered spontaneous brain activity in obsessive compulsive personality disorder. *Comprehensive Psychiatry*, *96*, 152144. doi: 10.1016/j.comppsych.2019.152144

Lei, X., Zhong, M., Liu, Y., Jin, X., Zhou, Q., Xi, C., … Yi, J. (2017). A resting-state fMRI study in borderline personality disorder combining amplitude of low frequency fluctuation, regional homogeneity and seed based functional connectivity. *Journal of Affective Disorders*, *218*, 299–305. doi: 10.1016/j.jad.2017.04.067

Li, W., Mai, X., & Liu, C. (2014). The default mode network and social understanding of others: What do brain connectivity studies tell us. *Frontiers in Human Neuroscience*, *8*, 74. doi: 10.3389/fnhum.2014.00074

Marceau, E. M., Meuldijk, D., Townsend, M. L., Solowij, N., & Grenyer, B. F. S. (2018). Biomarker correlates of psychotherapy outcomes in borderline personality disorder: A systematic review. *Neuroscience and Biobehavioral Reviews*, *94*, 166–178. doi: 10.1016/j.neubiorev.2018.09.001

Markon, K. E., Chmielewski, M., & Miller, C. J. (2011). The reliability and validity of discrete and continuous measures of psychopathology: A quantitative review. *Psychology Bulletin*, *137*, 856–879. doi: 10.1037/a0023678

Morey, L. C. (2017). Development and initial evaluation of a self-report form of the DSM-5 level of personality functioning scale. *Psychological Assessment*, *29*(10), 1302–1308. doi: 10.1037/pas0000450

Morris, S. E., & Cuthbert, B. N. (2012). Research domain criteria: Cognitive systems, neural circuits, and dimensions of behavior. *Dialogues in Clinical Neuroscience*, *14*, 29–37. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3341647/.

New, A. S., Hazlett, E. A., Buchsbaum, M. S., Goodman, M., Mitelman, S. A., Newmark, R., … Siever, L. J. (2007). Amygdala-prefrontal disconnection in borderline personality disorder. *Neuropsychopharmacology*, *32*(7), 1629–1640. doi: 10.1038/sj.npp.1301283

Newbury-Helps, J., Feigenbaum, J., & Fonagy, P. (2017). Offenders with antisocial personality disorder display more impairments in mentalizing. *Journal of Personality Disorders*, *31*(2), 232–255. doi: 10.1521/pedi_2016_30_246

ONeil, A., D'Souza, A., Samson, A. C., Carballedo, A., Kerskens, C., & Frodl, T. (2015). Dysregulation between emotion and theory of mind networks in borderline personality disorder. *Psychiatry Research: Neuroimaging*, *231*, 25–32. doi: 10.1016/j.pscychresns.2014.11.002

Parker, G., Both, L., Olley, A., Hadzi-Pavlovic, D., Irvine, P., & Jacobs, G. (2002). Defining disordered personality functioning. *Journal of Personality Disorders*, *16*, 503–522. doi: 10.1521/pedi.16.6.503.22139

Persson, J., Herlitz, A., Engman, J., Morell, A., Sjolie, D., Wikstrom, J., & Soderlund, H. (2013). Remembering our origin: Gender differences in spatial memory are reflected in gender differences in hippocampal lateralization. *Behavioral Brain Research*, *256*, 219–228. doi: 10.1016/j.bbr.2013.07.050

Persson, J., Spreng, R. N., Turner, G., Herlitz, A., Morell, A., Stening, E., … Soderlund, H. (2014). Sex differences in volume and structural covariance of the anterior and posterior hippocampus. *NeuroImage*, *99*(1), 215–225. doi: 10.1016/j.neuroimage.2014.05.038

Phillips, M. L., Robinson, H. A., & Pozzo-Miller, L. (2019). Ventral hippocampal projections to the medial prefrontal cortex regulate social memory. *eLife*, *8*, e44182. doi: 10.7554/eLife.44182

Power, J. D., Barnes, K. A., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2012). Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *Neuroimage*, *59*, 2142–2154. doi: 10.1016/j.neuroimage.2011.10.018

Quattrini, G., Pini, L., Pievani, M., Magni, L. R., Lanfredi, M., Ferrari, C., … Rossi, R. (2019). Abnormalities in functional connectivity in borderline personality disorder: Correlations with metacognition and emotion dysregulation. *Psychiatry Research: Neuroimaging*, *283*, 118–124. doi: 10.1016/j.pscychresns.2018.12.010

R Core Team (2013). *R: A language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing. Retrieved from: www.R-project.org/.

Regier, D. A., Narrow, W. E., Clarke, D. E., Kraemer, H. C., Kuramoto, S. J., Kuhl, E. A., & Kupfer, D. J. (2013). DSM-5 field trials in the United States and Canada: II. Test-retest reliability of selected categorical diagnoses. *American Journal of Psychiatry*, *170*, 59–70. doi: 10.1176/appi.ajp.2012.12070999

Ruocco, A. C., Amirthavasagam, S., & Zakzanis, K. K. (2012). Amygdala and hippocampal volume reductions as candidate endophenotypes for borderline personality disorder: A meta-analysis of magnetic resonance imaging studies. *Psychiatry Research: Neuroimaging*, *201*(3), 245–252. doi: 10.1016/j.pscychresns.2012.02.012

Ruocco, A. C., & Carcone, D. (2016). A neurobiological model of borderline personality disorder: Systematic and integrative review. *Harvard Review of Psychiatry*, *24*, 311–329. doi: 10.1097/HRP.0000000000000123

Salvador, R., Vega, D., Pascual, J. C., Marco, J., Canales-Rodríguez, E. J., Aguilar, S., … Pomarol-Clotet, E. (2016). Converging medial frontal resting state and diffusion-based abnormalities in borderline personality disorder. *Biological Psychiatry*, *79*, 107–116. doi: 10.1016/j.biopsych.2014.08.026

Sanislow, C. A., Grilo, C. M., Morey, L. C., Bender, D. S., Skodol, A. E., Gunderson, J. G., … McGlashan, T. H. (2002). Confirmatory factor analysis of DSM-IV criteria for borderline personality disorder: Findings from the collaborative longitudinal personality disorders study. *American Journal of Psychiatry*, *159*(2), 284–290. doi: 10.1176/appi.ajp.159.2.284

Saxe, R., & Kanwisher, N. (2003). People thinking about thinking people. The role of the temporo-parietal junction in "theory of mind". *Neuroimage*, *19*, 1835–1842. doi: 10.1016/s1053-8119(03)00230-1

Schacter, D. L., Addis, D. R., & Szpunar, K. K. (2017). Escaping the past: Contributions of the hippocampus to future thinking and imagination. In D. E. Hannula, M. C. Duff (Eds.), *The hippocampus from cells to systems* (pp. 439–466). Basel, Switzerland: Springer International Publishing AG. doi: 10.1007/978-3-319-50406-3_14.

Schulze, L., & Roepke, S. (2014). Structural and functional brain imaging in borderline, antisocial, and narcissistic personality disorder. In C. Mulert & M. E. Shenton (Eds.), *MRI In Psychiatry* (pp. 313–340). Berlin, Heidelberg: Springer. doi: 10.1007/978-3-642-54542-9_17.

Sharp, C. (2016). Current trends in BPD research as indicative of a broader sea-change in psychiatric nosology. *Personality Disorders*, *7*(4), 334–343. doi: 10.1037/per0000199

Sharp, C., Wright, A. G. C., Fowler, J. C., Frueh, B. C., Allen, J. G., Oldham, J., & Clark, L. A. (2015). The structure of personality pathology: Both general ("g") and specific ("s") factors? *Journal of Abnormal Psychology*, *124*, 387–398. doi: 10.1037/abn0000033

Silbersweig, D., Clarkin, J. F., Goldstein, M., Kernberg, O. F., Tuescher, O., Levy, K. N., … Stern, E. (2007). Failure of frontolimbic inhibitory function in the context of negative emotion in borderline personality disorder. *American Journal of Psychiatry*, *164*(12), 1832–1841. doi: 10.1176/appi.ajp.2007.06010126

Skodol, A. E., Clark, L. A., Bender, D. S., Kruegar, R. F., Morey, L. C., Verheul, R., … Oldham, J. M. (2011). Proposed changes in personality and personality disorder assessment and diagnosis for DSM-5 part I: Description and rationale. *Personality Disorders: Theory, Research, and Treatment*, *2*(1), 4–22. doi: 10.1037/a0021891

Tang, Y., Jiang, W., Liao, J., Wang, W., & Luo, A. (2013). Identifying individuals with antisocial personality disorder using resting-state fMRI. *PLoS One*, *8*(4), e:60652. doi: 10.1371/journal.pone.0060652

Uddin, L. Q. (2015). Salience processing and insular cortical function and dysfunction. *Nature Reviews Neuroscience*, *16*, 55–61. doi: 10.1038/nrn3857

van Eijk, L., Hansell, N. K., Strike, L. T., Couvy-Duchesne, B., de Zubicaray, G. I., Thompson, P. M., … Wright, M. J. (2020). Region-specific sex differences in the hippocampus. *NeuroImage*, *215*, 116781. doi: 10.1016/j.neuroimage.2020.116781

Van Overwalle, F., & Vandekerckhove, M. (2013). Implicit and explicit social mentalizing: Dual processes driven by a shared neural network. *Frontiers in Human Neuroscience*, *7*, 560. doi: 10.3389/fnhum.2013.00560

van Zutphen, L., Siep, N., Jacob, G. A., Goebel, R., & Arntz, A. (2015). Emotional sensitivity, emotion regulation and impulsivity in borderline personality disorder: A critical review of fMRI studies. *Neuroscience and Biobehavioral Reviews*, *51*, 64–76. doi: 10.1016/j.neubiorev.2015.01.001

Visintin, E., De Panfilis, C., Amore, M., Balestrieri, M., Wolf, R. C., & Sambataro, F. (2016). Mapping the brain correlates of borderline personality disorder: A functional neuroimaging meta-analysis of resting state studies. *Journal of Affective Disorders*, *204*, 262–269. doi: 10.1016/j.jad.2016.07.025

Westlund Schreiner, M., Klimes-Dougan, B., Mueller, B. A., Nelson, K. J., Lim, K. O., & Cullen, K. R. (2019). Neurocircuitry associated with symptom dimensions at baseline and with change in borderline personality disorder. *Psychiatry Research: Neuroimaging*, *290*, 58–65. doi: 10.1016/j.pscychresns.2019.07.001

Whitfield-Gabrieli, S., & Ford, J. M. (2012). Default mode network activity and connectivity in psychopathology. *Annual Review of Clinical Psychology*, *8*, 49–76. doi: 10.1146/annurev-clinpsy-032511-143049

Whitfield-Gabrieli, S., & Nieto-Castanon, A. (2012). Conn: A functional connectivity toolbox for correlated and anticorrelated brain networks. *Brain Connectivity*, *2*(3), 125–141. doi: 10.1089/brain.2012.0073

Widiger, T. A., & Rogers, J. H. (1989). Prevalence and comorbidity of personality disorders. *Psychiatric Annals*, *19*(3), 132–136. doi: 10.3928/0048-5713-19890301-07

Wittchen, H. U., Zaudig, M., & Fydrich, T. (1997). *SKID Strukturiertes klinisches interview für DSM-IV. Achse I und II*. Göttingen: Hogrefe, DM. 158.

Wolf, R. C., Sambataro, F., Vasic, N., Schmid, M., Thomann, P. A., Bienentreu, S. D., & Wolf, N. D. (2011). Aberrant connectivity of resting-state networks in borderline personality disorder. *Journal of Psychiatry and Neuroscience*, *36*(6), 402–411. doi: 10.1503/jpn.100150

World Health Organization (2018). International Classification of Diseases for mortality and morbidity statistics (11th revision)- Clinical Descriptions and Diagnostic Guidelines for Mental and Behavioural Disorders. Retrieved from https://gcp.network/en/private/icd-11-guidelines/disorders.

Wrege, J., Ruocco, A. C., Euler, S., Preller, K., Busmann, M., Meya, L., … Walter, M. (2019). Negative affect moderates the effect of social rejection on frontal and anterior cingulate cortex activation in borderline personality disorder. *Cognitive, Affective, & Behavioral Neuroscience*, *19*, 1273–1285. doi: 10.3758/s13415-019-00716-0

Wright, A. G., Hopwood, C. J., Skodol, A. E., & Morey, L. C. (2016). Longitudinal validation of general and specific structural features of personality pathology. *Journal of Abnormal Psychology*, *125*(8), 1120–1134. doi: 10.1037/abn0000165

Wright, A. G., Thomas, K. M., Hopwood, C. J., Markon, K. E., Pincus, A. L., & Krueger, R. F. (2012). The hierarchical structure of DSM-5 pathological personality traits. *Journal of Abnormal Psychology*, *121*(4), 951–957. doi: 10.1037/a0027669

Yang, W., Cun, L., Du, X., Yang, J., Wang, Y., Wie, D., … Qiu, J. (2015). Gender differences in brain structure and resting-state connectivity related to narcissistic personality. *Scientific Reports*, *5*, 10924. Retrieved from: https://www.nature.com/articles/srep10924.

Zhu, Y., Tang, Y., Zhang, T., Li, H., Tang, Y., Li, C., … Wang, J. (2017). Reduced functional connectivity between bilateral precuneus and contralateral parahippocampus in schizotypal personality disorder. *BMC Psychiatry*, *17*, 48. doi: 10.1186/s12888-016-1146-5

Zimmermann, J., Benecke, C., Bender, D. S., Skodol, A. E., Schauenburg, H., Cierpka, M., & Leising, D. (2014). Assessing DSM-5 level of personality functioning from videotaped clinical interviews: A pilot study with untrained and clinically inexperienced students. *Journal of Personality Assessment*, *96*(4), 397–409. doi: 10.1080/00223891.2013.852563

Zimmermann, J., Böhnke, J. R., Eschstruth, R., Mathews, A., Wenzel, K., & Leising, D. (2015). The latent structure of personality functioning: Investigating criterion a from the alternative model for personality disorders in DSM–5. *Journal of Abnormal Psychology*, *124*, 532–548. doi: 10.1037/abn0000059