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Short communication

Short communication: Diffusion tensor anisotropy in the cingulate in borderline and schizotypal personality disorder

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ABSTRACT

Despite considerable phenomentological differences between borderline personality disorder (BPD) and schizotypal personality disorder (SPD), research increasingly provides evidence that some BPD symptoms overlap with SPD symptoms (e.g., disturbed cognitions). We examined the cingulate, a brain region implicated in the pathophysiology of both disorders, to determine similarities/differences between the groups, and similarities/differences from healthy controls (HC's). 3T structural and diffusion tensor magnetic resonance imaging scans were acquired in BPD ($n = 27$), SPD ($n = 32$), HC's ($n = 34$). Results revealed that BPD patients exhibited significantly lower FA in posterior cingulate white matter compared to HC's ($p = 0.04$), but SPD patients did not.

1. Introduction

Borderline personality disorder (BPD) is characterized by affective instability and impulsive behavior (Gunderson and Singer, 1975; Kernberg, 1977). Schizotypal personality disorder (SPD), on the other hand, is characterized by symptoms of odd behavior, magical thinking, social anxiety, and paranoid ideation. As such, emotion dysregulation is among the primary symptoms used to diagnose BPD, whereas disturbed cognition constitutes one of the primary criteria for diagnosing SPD. Despite these nosological differences between the two disorders, research increasingly provides evidence of BPD difficulty with symptoms that are typically associated with SPD (e.g., odd thinking, non-delusional paranoia) (Farsham et al., 2017; Rawlings et al., 2001; Zanarini et al., 2013), which may result, at least in part, from similar neurobiological underpinnings.

The current study aimed to investigate neurobiological factors contributing to the aforementioned aspects of BPD that may overlap with and/or diverge from aspects of SPD. It examined the integrity of the cingulate, a functionally heterogeneous brain region frequently implicated in the affective symptomatology of BPD and in the cognitive symptomatology of SPD. Specifically, it aimed to examine gray and white matter cingulate structural integrity among three groups: healthy controls (HC) vs. BPD individuals without comorbid SPD vs. SPD individuals without comorbid BPD.

The cingulate consists of several functionally distinct subdivisions that help modulate many of the functions with which both BPD and SPD individuals experience difficulty. Specifically, the anterior cingulate is divided into affect- and cognition-related sections; the ventral division plays a large role in emotion processing, and its dorsal division is thought to be involved in a number of cognitive functions, including modulation of attention/executive functions, motivation, and motor control (Bush et al., 2000). The posterior cingulate also has been implicated in areas of cognition, as well as in aspects of social functioning (Kennedy et al., 2006; Ochsner et al., 2005; Vogt et al., 1992). As such, given its involvement in these wide-ranging aspects of functioning, several of which constitute areas of weakness for BPD and/or SPD individuals—both shared and disorder-specific—the cingulate is thought to provide an ideal backdrop against which to compare these disorders. Specifically, the current study sought to investigate the integrity of these functionally distinct subdivisions of the cingulate to help clarify overlapping/differing neurobiological abnormalities across patient groups. Further, due to research reporting cingulate gray and white

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matter volumetric abnormalities in both of these groups and their potential relation to overlapping/diverging symptomatology (Hazlett et al., 2005), this study aimed to expand upon those findings by comparing other aspects of these cingulate subdivisions in these groups, namely diffusion-related measures of cingulate white and gray matter structure using diffusion tensor MRI (DTI).

DTI is one of the primary methodologies used to examine the orientation and microstructural integrity of brain tissue. DTI measures the motion of water molecules in tissues, which then is used to infer their microarchitecture (Taylor et al., 2004). Empirical studies have employed several different DTI quantitative measurements, including but not limited to fractional anisotropy (FA; measure of anisotropy of a diffusion process), axial diffusivity (AD; measure of parallel diffusivity), and radial diffusivity (RD; measure of perpendicular diffusivity).

To date, few DTI studies have been conducted in SPD and BPD. One of the first DTI studies reported lower fractional anisotropy (FA) in the uncinate fasciculus in SPD but found no SPD-HC group differences in the cingulate gyrus (Nakamura et al., 2005). Similarly, our group's more recent investigation of white matter integrity in the cingulum bundle in SPD patients did not find a group difference from HC's (Lener et al., 2015). Four prior DTI studies have examined the integrity of the cingulate in BPD (Lischke et al., 2015; Ninomiya et al., 2018; Rusch et al., 2010; Whalley et al., 2015). One of these studies examined FA in the anterior and posterior sections separately, reporting reduced FA in the anterior portion of the cingulum in BPD (Whalley et al., 2015). A separate investigation (Lischke et al., 2015) examined FA, axonal anisotropy, and radial diffusivity in the cingulum but did not find HC-BPD group differences.

Given the aforementioned findings, as well as increased studies reporting altered gray matter structural integrity using DTI in other populations (Li et al., 2018), the current study examined FA in both white and gray matter in the cingulate. It was hypothesized that altered FA would be detected in the affect-related ventral portion of the anterior cingulate in BPD patients because affective symptomatology has traditionally represented a core feature of the disorder. In SPD patients, it was hypothesized that altered FA would be detected in the cingulate subdivisions thought to subserve certain cognitive and social skills because both domains consistently have been highlighted as primary areas of SPD weakness.

2. Methods

2.1. Participants

Overall, 93 participants were included. Participants were recruited through local newspaper advertisements and clinical referral. Table 1 contains all demographic specifics. Also of note, we have previously published fMRI BOLD data in this sample (Hazlett et al., 2012). Group differences in age, education, and gender were assessed using Student *t*-tests and chi-square, and there were no significant differences.

Table 1
Demographics of study sample.

Variable	BPD(n = 27)	SPD(n = 32)	HC(n = 34)	Test statistic
Age (years):	31.5(9.4)	34.9(10.0)	31.8(9.1)	F(2,90) = 1.2, p = 0.3
Range:	18–51	20–55	22–56	
Education:	4.8(2.7)	4.4(1.9)	5.4(2.8)	F(2,78) = 1.1, p = 0.3
Gender:				
Men	12(44%)	20(63%)	18(53%)	χ2(2) = 1.9, p = 0.4
Women	16(56%)	12(37%)	16(47%)	

Note. BPD = Borderline Personality participants. SPD = Schizotypal. Personality Disorder participants. HC = Healthy Control participants. Education = Highest Degree Earned. 1 = No High School Diploma; 2 = GED;. 3 = High School Diploma; 4 = Technical Training; 5 = Some College, No Degree;.
6 = Associate Degree; 7 = Bachelor's Degree; 8 = Master's Degree;.
9 = MD/PhD/JD/PharmD. *p < 0.05 (2-tailed).

2.2. Materials and procedures

All eligible participants were administered the Structured Clinical Interview for DSM-IV Axis I disorders (SCID-IV) (First et al., 1996) and the Structured Interview for DSM-IV Personality Disorders (SIDP) (Pfohl et al., 1997). Two self-report ratings were administered to assess affective symptomatology, Affective Lability Scale (ALS) (Harvey et al., 1989) and Affective Intensity Measure (AIM) (Larsen and Diener, 1987). Given the study's objective to parse out differences between BPD and SPD patients, none of the BPD patients met criteria for a comorbid diagnosis of SPD and none of the SPD patients met criteria for a comorbid diagnosis of BPD, making it a unique sample. That is, all patients met DSM-IV criteria for either BPD or SPD, but none met full criteria for both. However, BPD patients were allowed to have a sub-threshold number of SPD traits, and BPD patients were permitted to have a sub-threshold number of SPD traits to maintain external validity. Specifically, in diagnosing patients, each of the DSM-IV criteria for each personality disorder was rated on a 4-point scale (0 = absent, 0.5 = somewhat present, 1.0 = definitely present/prototypic, 2.0 = severe, pervasive). As required for a DSM-IV diagnosis of SPD, these patients met at least five of the nine SPD criteria with a rating ≥ 1.0. SPD patients were allowed no more than three BPD criteria with two items rated as 1.0 and one item rated as 0.5 in order to control for comorbidity and/or co-occurring traits but still maintain external validity. As required for a DSM-IV diagnosis of BPD, these patients met at least five of the nine DSM-IV criteria. BPD patients were allowed no more than three SPD criteria with two items rated as 1.0 and one item rated as 0.5.

All participants were ummedicated at the time of their MRI scan (>6 weeks). Participants with a history of schizophrenia, psychotic disorder, bipolar (Type I) disorder, or current major depressive disorder (episode occurring within 2 months of the scan) were excluded. Exclusion criteria also included severe medical or neurological illness, head injury, or alcohol/substance dependence or alcohol/substance abuse during the prior six months. All participants had a negative urine toxicology screen for drugs of abuse during the study's screening visit and on the day of the MRI. Healthy control participants had no Axis I or II diagnosis and no Axis I disorder in any first-degree family member. All participants provided written informed consent in accordance with the Mount Sinai School of Medicine Institutional Review Board guidelines.

2.3. Image acquisition and processing

MRI acquisition for all participants occurred on a Siemens Allegra 3T-head-dedicated MRI system to acquire axial structural images and DTI using a pulsed-gradient spin-echo sequence with Echo Planar Imaging pulse sequence (EPI) acquisition (Segal et al., 2010). A *b*-factor of 1250 was chosen based on tests performed to find the optimal balance for SNR and diffusion weighting. Twelve gradient directions with $b = 1250$ x/mm^2 were used (TR = 4100 ms, TE = 80 ms, FOV = 21 cm, matrix = 128 × 128, 28 slices, thickness = 3 mm, skip = 1 mm). To solve the components of the diffusion tensor, 13 diffusion EPI images were obtained: 12 with different, non-colinear and non-coplanar gradient encoding directions and one with no diffusion gradient applied. Five acquisitions were averaged to improve the signal-to-noise ratio. The tool 'eddy' was used to correct the diffusion-weighted images for distortions and head movement. The diffusion tensor was obtained by solving the 13 simultaneous signal equations relating the measured signal intensity to the diffusion tensor (Basser et al., 1994; Papadakis et al., 1999). This resulted in a tensor for every voxel (1.6 × 1.6 × 3 mm^3) in a slice. The eigenvectors and eigenvalues were then computed for every tensor, forming the raw dataset for