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Short communication

Dorso- and ventro-lateral prefrontal volume and spatial working memory in schizotypal personality disorder

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ABSTRACT

Schizotypal personality disorder (SPD) individuals and borderline personality disorder (BPD) individuals have been reported to show neuropsychological impairments and abnormalities in brain structure. However, relationships between neuropsychological function and brain structure in these groups are not well understood. This study compared visual–spatial working memory (SWM) and its associations with dorsolateral prefrontal cortex (DLPFC) and ventrolateral prefrontal cortex (VLPFC) gray matter volume in 18 unmedicated SPD patients with no BPD traits, 18 unmedicated BPD patients with no SPD traits, and 16 healthy controls (HC). Results showed impaired SWM in SPD but not BPD, compared with HC. Moreover, among the HC group, but not SPD patients, better SWM performance was associated with larger VLPFC (BA44/45) gray matter volume (Fisher's Z p-values <0.05). Findings suggest spatial working memory impairments may be a core neuropsychological deficit specific to SPD patients and highlight the role of VLPFC subcomponents in normal and dysfunctional memory performance.

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Schizotypal personality disorder (SPD) is characterized by asocial tendencies, difficulties with language, paranoia, odd behavior, and magical thinking. Borderline personality disorder (BPD), on the other hand, is characterized by affective instability and impulsive behavior and was first included in DSM-III [1,2]. Many of the earlier SPD studies included symptoms related to conceptions of BPD, but diagnostic overlap was somewhat modified when the criterion of paranoid ideation under stress in BPD was introduced in DSM-III-R [3,4]. Nonetheless, co-morbidity of SPD and BPD is not uncommon [5], which may be due to overlapping areas of impairment [6] or to similar diagnostic nomenclature. Given the potentially overlapping and diverging neurobiological and phenotypic aspects of SPD and BPD, as well as the inherent complexity of both, this study worked to clarify commonalities and distinctions among SPD, BPD and HC individuals on one specific type of neuropsychological functioning, visual–spatial working memory, and the dorsolateral prefrontal cortex (DLPFC) and ventrolateral prefrontal cortex (VLPFC) morphometric correlates.

Previous studies reviewing neuropsychological impairments in individuals with SPD consistently document disruptions in working memory [7–12]. Neuropsychological investigations of individuals with BPD also reveal deficits in non-verbal domains of functioning [13–17], including visual–spatial working memory [18]. Nonetheless, although a meta-analysis of neuropsychological findings in BPD by Ruocco [16] revealed that BPD deficits seem to be primarily lateralized to the right hemisphere [19], it also included studies that failed to detect any neuropsychological difficulties in BPD. Ruocco [16] concluded that further examination of brain–behavior relationships is required to better characterize and elucidate neurocognitive functioning in BPD and personality disorders in general. In the current study, our aim was to investigate one aspect of this brain–behavior relationship, namely volume of DLPFC and VLPFC regions subserving visual–spatial working memory function in SPD and BPD—two personality disorder groups shown to exhibit cognitive deficits and frontal lobe dysfunction [20,21]—as compared

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Table 1
Clinical interview and self-report ratings in healthy control, borderline personality disorder, schizotypal personality disorder groups.

	Healthy controls			Borderline PD patients			Schizotypal PD patients		
	n	Mean	SD	n	Mean	SD	n	Mean	SD
Symptom severity[a]	16	–	–	18	7.53	0.98	18	7.14	1.22
State-Trait Anxiety Inventory for Adults-Trait (STAI-T)	13	30.46_a	7.47	18	51.22_a	11.75	17	41.53_a	11.69

	Healthy controls		Borderline PD patients		Schizotypal PD patients	
	n	%	n	%	n	%
Past MDD[b]	–	–	10_b	56%	4_b	22%

Means in same row that share subscripts differ at $p<0.05$. Given these group differences, we correlated STAI-Trait [65] as well as Past MDD with SWM performance, and they were not significant. Thus, STAI-T and Past MDD were not used as covariates.

[a] Symptom severity = total of individual symptom ratings for each DSM-IV diagnostic criterion.

[b] MDD = past major depressive disorder (MDD) was defined as prior episode occurring >2 months from time of fMRI scan.

with HC. Thus, our goal was to investigate the association between spatial working memory functioning and volume of frontal brain regions thought to subserve working memory function.

Given this aim to explore the potential association between nonverbal deficits and prefrontal cortex morphometric correlates, it is important to note previous studies implicating the DLPFC Brodmann areas (BA9/10/46) and VLPFC Brodmann areas (BA44/45) in working memory processes [22–26]. In addition to this work, functional neuroimaging studies examining SPD and BPD patients provide additional support for the idea that abnormalities in DLPFC and VLPFC may underlie neuropsychological impairments [27–31]. Evidence also exists for DLPFC and VLPFC volumetric abnormalities in BPD and SPD [32–35]. Further, research supports the notion that smaller prefrontal regions in SPD are associated with executive function deficits in a healthy control group with schizotypal personality features [36] and reduced volume of BA10 is related to increased impulsiveness in BPD [32].

To date, there is little work comparing neurocognitive function across different personality disorder groups and its relationship with prefrontal cortex volume. The current study sought to determine whether performance on measures of visual–spatial working memory differs for both patient groups, as compared with HC, and/or if deficits are specific to one personality disorder, and characterize the relationship between visual–spatial working memory and DLPFC/VLPFC volume. As such, this study works to advance our limited understanding of the phenotypic and endophenotypic aspects among and within SPD and BPD patients, respectively. We hypothesized that both groups would evidence visual–spatial working memory deficits but, given more consistent reporting of poor performance in SPD [10,31] patients, we predicted more impairment in this group. The second goal of this study was to explore the volumetric correlates of visual–spatial working memory function in these groups. Because both DLPFC and VLPFC have been shown to play a role in working memory in HC, and both regions have been shown to be dysfunctional in SPD and BPD patients, we hypothesized that, among HC, larger prefrontal cortex volume would be associated with better performance on measures of visual–spatial working memory, but these relationships would not be evidenced in SPD nor BPD patients.

All diagnoses were made through interviews by a psychologist using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) [37] and the Structured Interview for DSM-IV Personality Disorders (SIDP) [38] followed by a consensus meeting. Diagnostic methods have been reported previously [39]. Patients with a history of schizophrenia, a psychotic disorder, bipolar (type I) affective disorder, substance abuse within 6 months of study entry or current (in the last 6 months) major depressive disorder (MDD) were excluded. All patients were unmedicated at the time of the study (>2 weeks prior to testing sessions). Healthy volunteers diagnosed with an Axis I or II psychiatric illness or an Axis I diagnosis in a first-degree relative were excluded from this study. Exclusion criteria for all participants included: severe medical illness, neurological illness, head injury, past substance dependence, as well as substance abuse in the past 6 months, positive urine toxicology test on scan day, and females with a positive pregnancy test on scan day. Written informed consent approved by the Mount Sinai Institutional Review Board was provided by all participants.

A total of 52 adults participated in the study. We excluded one HC who was >2 SD from the healthy control mean on SWM performance. There were two additional HC participants who approached 2 SD on SWM so we conducted all analyses with and without these participants, and the results were essentially the same and significant either way. Therefore, we present analyses with these two HC subjects included in order to be more conservative. We studied 18 SPD patients with no BPD traits (11 M/7 F; mean age = 35.33 ± 11.0); 18 BPD patients with no SPD traits (7 M/11 F; mean age = 33.50 ± 9.52); and 16 HC (9 M/7 F; mean age = 30.63 ± 8.11). Participants in the three groups did not differ on age, sex, years of education (SPD mean = 14.94 ± 3.32; BPD mean = 14.0 ± 2.50; HC mean = 15.63 ± 3.28), or Wechsler Abbreviated Scale of Intelligence Full Scale (WASI FSIQ) [40] (SPD mean = 104.76 ± 9.91; BPD mean = 107.07 ± 17.62; HC mean = 108.19 ± 18.13), all p's > 0.11.

SWM performance errors were significantly correlated with WASI FSIQ ($r=-0.51$, $p<0.05$), years of education ($r=-0.29$, $p<0.05$), and age ($r=0.46$, $p<0.05$) across all participants regardless of group. Therefore, we used two covariates: age and years of education, instead of WASI FSIQ, because we had data for all participants on this variable, whereas five of the 52 participants were missing WASI data. See Table 1 for clinical symptom severity ratings and self-report ratings. To calculate the level of clinical symptom severity, we added up the individual symptom ratings for each DSM-IV diagnostic criterion. Ratings were on a 4-point scale (0 = absent, 0.5 = somewhat present, 1.0 = definitely present/prototypic, 2.0 = severe, pervasive).

Gray matter volume [39] in the Brodmann areas and diffusion tensor imaging (DTI) [41] has been reported previously for this sample. Neuropsychological measures were not a component of the study initially and thus were administered only to a subset of the original sample published previously [39].

All participants completed the Spatial Working Memory (SWM) subtest of the Cambridge Neuropsychological Test Automated Battery (CANTAB) [42], a standardized computer battery, as part of the full CANTAB battery. Findings from the remaining tests of the battery are reported elsewhere [43,44]. The CANTAB has demonstrated adequate reliability [45,46].

Spatial Working Memory (SWM). See Fig. 1A for details on the test. There are two outcome measures: a 'Between Search Error' involving the number of errors made (i.e. touching boxes that are empty or revisiting boxes that have already been checked) and