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Research paper

Does cognitive performance map to categorical diagnoses of schizophrenia, schizoaffective disorder and bipolar disorder? A discriminant functions analysis

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ABSTRACT

Objectives: Despite known overlaps in the pattern of cognitive impairments in individuals with bipolar disorder (BD), schizophrenia (SZ) and schizoaffective disorder (SZA), few studies have examined the extent to which cognitive performance validates traditional diagnostic boundaries in these groups.
Method: Individuals with SZ ($n=49$), schizoaffective disorder ($n=33$) and BD ($n=35$) completed a battery of cognitive tests measuring the domains of processing speed, immediate memory, semantic memory, learning, working memory, executive function and sustained attention.
Results: A discriminant functions analysis revealed a significant function comprising semantic memory, immediate memory and processing speed that maximally separated patients with SZ from those with BD. Initial classification scores on the basis of this function showed modest diagnostic accuracy, owing in part to the misclassification of SZA patients as having SZ. When SZA patients were removed from the model, a second cross-validated classifier yielded slightly improved diagnostic accuracy and a single function solution, of which semantic memory loaded most heavily.
Conclusions: A cluster of non-executive cognitive processes appears to have some validity in mapping onto traditional nosological boundaries. However, since semantic memory performance was the primary driver of the discrimination between BD and SZ, it is possible that performance differences between the disorders in this cognitive domain in particular, index separate underlying aetiologies.

Cognitive impairment is a hallmark symptom of psychotic disorders including schizophrenia (SZ) and schizoaffective disorder (SZA: Green et al., 2004). Accumulating evidence indicates that patients with bipolar disorder (BD) also have significant impairments in cognitive functioning that may be qualitatively, but not always quantitatively comparable to those seen in psychotic illnesses (Bora et al., 2010; Burdick et al., 2011, 2015; Harvey et al., 2014; Van Rheenen and Rossell, 2014b). Such impairments are known to impact the capacity for social cognition (Brekke et al., 2005; Van Rheenen et al., 2014; Van Rheenen and Rossell, 2013) and have significant implications for long-term functional outcomes in these disorders, independent of clinical symptomatology (Allen et al., 2014; Fervaha et al., 2014; Green et al., 2004; Van Rheenen and Rossell, 2014c). Indeed, cognitive impairments are likely to be core to the psychopathology of psychosis and BD given that they persist even during times of clinical symptom resolution (Bourne et al., 2013).

Although there are exceptions, on the whole patients with BD generally appear to have cognitive performance that is intermediate to that of SZ and controls (Harvey et al., 2014). Preliminary evidence also suggests that the factor structure of cognitive functioning across the clinical disorders presents in a relatively similar manner, with other research showing that patients with both disorders demonstrate the same *pattern* of impairments across a number of lower-order and higher-order cognitive domains (Barch and Sheffield, 2014; Gogos et al., 2010; Krabbendam

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et al., 2005; Pradhan et al., 2008; Schretlen et al., 2013).

In the context of current evidence, whether the cognitive impairments seen in SZ and BD represent the same underlying dysfunction remains a matter of debate. On the one hand, it is possible that commonly reported *magnitude* differences in performance between the two, indicate differences in disease-specific variables such as those related to neurodevelopment or clinical course. On the other hand, similarities in the qualitative *pattern* of current cognitive function between BD and SZ compared to controls, suggest that such impairments could represent biologically meaningful shared features that potentially map onto common underlying genetic mechanisms.

So far, studies assessing cognition across these disorders have generally tended to highlight overlaps or differences in SZ and BD on the basis of quantitative neuropsychological test performance. However such comparisons in and of themselves, provide only weak evidence around whether these disorders are neurocognitively distinguishable, since group-wise comparisons of separate cognitive domains do not assess whether differences in performance magnitude actually validate and reflect distinct diagnostic categories. Thus, the boundaries of nosology cannot be explicitly supported or rejected on the basis of statistical comparisons of such tests by themselves, because it is possible that variance could still overlap between groups on the basis of *a combination* of cognitive factors. Indeed, work by Heinrichs and colleagues (2008) shows that statistically significant magnitude differences in neuropsychological performance do not necessarily translate to diagnostic validation in psychosis spectrum disorders.

Given that recent evidence indicates that the assessment of cognitive performance may help to classify psychiatric illnesses into more clinically or biologically meaningful subtypes (Burdick et al., 2014; Geisler et al., 2015; Hallmayer et al., 2005; Heinrichs, 2005; Lewandowski et al., 2014; Weickert et al., 2000), we aimed to assess the extent to which cognitive vulnerabilities in BD and SZ respect nosological boundaries in individuals carrying these diagnoses. Specifically, we aimed to compare well-matched groups of patients with BD and SZ on a battery of cognitive tests that assess domains of known impairment in these disorders using discriminant functions analysis (DFA). Since it is possible that distinguishing neuropsychological factors for BD and SZ could index separate underlying biological substrates, we were primarily interested in assessing whether there were generalised or specific cognitive domains that could discriminate the disorders diagnostically.

A further research aim was to better understand cognitive functioning in patients with SZA, relative to those with SZ and BD. This relates to a tendency for many past studies to group together individuals with SZ and SZA (Green et al., 2004), despite SZA representing a diagnostic category in its own right. Although SZA does share phenotypic similarities with SZ in terms of persistent psychotic features, the disorder also shares similarities with BD in relation to its mood features (American Psychiatric Association, 2013). The grouping of SZ and SZA patients therefore has the potential to distort cognitive findings and may hamper progress toward elucidating if there are discriminating factors between the disorders. Therefore in this study, we included individuals with SZA in the analysis to determine whether cognitive performance could distinguish these patients as being part of a separate, albeit related, group.

1. Materials and method

A subset of participants was drawn from a database of individuals who had participated in studies examining cognition in severe psychiatric illness (e.g., see Neill and Rossell, 2013; Tan and Rossell, 2014; Van Rheenen and Rossell, 2014a). Each study was approved by relevant Hospital and University review boards and abided by the Declaration of Helsinki. Written informed consent was obtained from each participant before his or her respective studies began.

1.1. Participants

A total of 117 individuals with a DSM-IV-TR diagnosis of SZ ($n=49$), SZA ($n=33$) or BD I ($n=35$, history of psychosis $n=26$) were included in the analysis. All patients entered the their respective studies with a pre-existing diagnosis of BD, SZ or SZA and their psychiatric diagnoses were confirmed by the MINI International Neuropsychiatric Interview (Sheehan et al., 1998) or the Structured Clinical Interview for DSM-IV(First et al., 1996) depending on the study through which they were originally enrolled. Patients with significant visual or verbal impairments, a known neurological disorder, and/or a history of substance/alcohol abuse or dependence during the previous six months were excluded. Symptomatology was assessed with the Brief Psychiatric Rating Scale (Overall and Gorham, 1962) and the Montgomery Asberg Depression Rating Scale (Montgomery and Asberg, 1979). All participants were fluent in English, were between the ages of 18 and 65 years, and had an estimated pre-morbid IQ as scored by the

Table 1
Demographic and clinical characteristics of the sample.

	BD			SZA			SZ			Group comparisons			
	n/%	*M*	*SD*	*n*/%	*M*	*SD*	*n*/%	*M*	*SD*	*f* /χ^2	*df*	*p*	*Post-hoc comparisons*
N	35			33			49						–
Gender (M/F)	12/23			17/16			23/26			2.26	2	.32	–
Age	40.11	13.48		43.03	9.71			42.57	11.26	.65	2,114	.52	
Premorbid IQ (scaled)		109.26	12.15		103.47	11.10		104.92	9.86	2.64	2,113	.08	–
Age at diagnosis (years)		26.43	13.09		24.99	7.58		24.57	8.00	.92	2,114	.67	–
BPRS		22.66	4.37		35.76	10.53		34.25	8.61	27.12	2,113	.01	BD < SZA & BD < SZ
MADRS		10.86	10.97		9.28	8.89		8.90	7.69	.50	2,112	.61	
% on Antipsychotic	46			94			98			43.53	4	.01	BD < SZ & SZA
% typical	6			3			8			–	–	–	–
% atypical	40			85			86						
% on Antidepressant	46			24			14			14.23	4	.01	BD > SZ & SZA
% on Mood stabiliser/anticonvulsant	69			15			8			46.34	4	.01	BD > SZ & SZA
% on Benzodiazepine	17			6			6			6.23	4	.18	

Post-hoc group differences significant at $p < .001$; BPRS=Brief Psychiatric Rating Scale; MADRS=Montgomery Asberg Depression Rating Scale; premorbid IQ measured using the Wechsler Test of Adult Reading.