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General intellectual ability does not explain the general deficit in schizophrenia

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ABSTRACT

Patients with schizophrenia demonstrate a generalized deficit across multiple cognitive domains. However, it is unknown whether this deficit is largely due to lower intelligence, or if there is an impact of schizophrenia which cannot be accounted for by measures of general intellectual ability (GIA). We created four IQ-matched strata of equal width between 89 healthy volunteers (HC) and 77 patients with schizophrenia (SZ) who had very similar IQ and reading scores within each stratum, then compared each stratum's performance on the MATRICS Consensus Cognitive Battery (MCCB). We hypothesized that any patient impairment on the MCCB after matching on IQ would be evidence that GIA does not fully explain the general deficit seen in schizophrenia. We found that patients showed evidence of greater neuropsychological impairment than what would be expected based solely on their IQ and reading ability scores. Further, this deficit was stronger in some cognitive domains than others, namely, processing speed and social cognition. These results suggest the presence of a distinction between GIA and generalized neuropsychological impairment that was consistent in magnitude across all patients, regardless of IQ.

1. Introduction

Meta-analyses provide overwhelming evidence that patients with schizophrenia demonstrate marked deficits across cognitive domains (Heinrichs and Zakzanis, 1998; Fioravanti et al., 2005; Dickinson et al., 2007; Reichenberg and Harvey, 2007; Reichenberg, 2010). While there is variability in the extent of impairment, evidence suggests that impairment is generalized across the cognitive operations assessed by widely used clinical neuropsychological measures. Further, it appears that the extent of impairment across these domains (i.e., attention, processing speed, working memory, etc.), is highly intercorrelated. Dickinson et al. (2008) used structural equation modeling to demonstrate that 64% of the between-group variance in neuropsychological performance between healthy controls and individuals with schizophrenia is shared on a common general deficit factor, with more specific deficits accounting for very little additional between-group variance (Dickinson et al., 2004, 2008).

With evidence of a generalized deficit across cognitive domains, the question arises whether the “general deficit” might simply be a reflection of a reduction in general intellectual ability (GIA), i.e., intelligence. Indeed, IQ measures are typically highly correlated with neuropsychological performance. For example, in a sample of 117 individuals with schizophrenia (SZ), WASI-estimated IQ scores correlated with the composite score from the MATRICS Consensus Cognitive Battery (MCCB, Kern et al., 2008; Nuechterlein et al., 2008), r = .733, $p < .001$ with a very similar correlation observed in a sample of 77 healthy controls (HCs), r = .695, $p < .001$ (August et al., 2012). These substantial correlations are noteworthy because the MCCB was deliberately composed of measures particularly impaired in schizophrenia and/or particularly important for functional outcome. Thus, one would expect to see a schizophrenia deficit “signal” in MCCB performance that extends beyond GIA. We speculate that across the WASI and MCCB there are two “pools” of variance: 1) a pool of variance associated with GIA reflected in the high correlation of the two measures, and 2) a pool of variance associated with the impact of schizophrenia on more discrete aspects of cognitive function that are captured on the MCCB which cannot be accounted for by GIA.

We took two approaches to this issue. First, we compared the MCCB performance of healthy volunteers and patients with schizophrenia who had very similar WASI IQ scores. If IQ accounts for neuropsychological performance across groups, the IQ-matched groups should show similar levels of performance on the MCCB. Alternatively, any patient impairment on the MCCB, after matching on IQ, would be evidence that the “general deficit” and GIA are not synonymous. In addition, we performed the same matched group approach using measures of single word reading which are thought to index “premorbid” ability (Spreen and Strauss, 1998; Lezak et al., 2004). With both the WASI and reading measures, this approach addresses the question of whether patients are more impaired than they “should” be for their level of reading and IQ performance, and allows for a quantitative estimate of how far patients deviate from the level that would be expected had they not become ill. We examined these questions by creating groups that ranged from low to high levels of GIA to provide additional information about whether patients who have higher levels of cognitive ability are spared the

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neuropsychological impairments that have most frequently been documented in samples with average–low average levels of GIA. Second, we used an ANCOVA approach that provides further information on whether patients show greater impairments in some domains than others after controlling for the role of GIA.

2. Methods

2.1. Participants

Participants in the full sample included 143 individuals with a DSM-IV diagnosis of schizophrenia or schizoaffective disorder (SZ) as confirmed by the Structured Clinical Interview for DSM-IV (SCID; First et al., 2002). SZs were recruited from the Maryland Psychiatric Research Center and other community clinics. SZs were found to be clinically stable by their clinicians and had been receiving stable psychotropic medication with no changes to type or dosage for four weeks prior to testing. Diagnosis was established at a best estimate diagnostic conference chaired by J.M.G. based on the review of a SCID interview, medical records, and informant reports, along with a direct patient interview in most cases. 110 healthy subjects (HC) were recruited to be used as a healthy comparison group. HCs were recruited through a combination of random digit dialing, newspaper and web advertising, and word of mouth among these participants. HCs were confirmed to not be taking any psychiatric medications and to be free of any past or current psychiatric diagnoses with the SCID, and denied a history of psychosis in first degree relatives. All participants were between the ages of 18 and 55, clinically stable, and screened for any medical conditions that may have influenced study results, such as a history of neurological injury or disorder and the presence of substance abuse or dependence.

2.2. Measures

2.2.1. MCCB and additional cognitive measures

Participants were given the Wide Range Achievement Test reading subtest (WRAT; Wilkinson and Robertson, 2006), Wechsler Test of Adult Reading (WTAR; Wechsler, 2001), the Wechsler Adult Scale of Intelligence (WASI; Wechsler, 1999) two-subtest estimate of IQ, and the MCCB. Note that the two-subtest WASI does not include measures of working memory or processing speed and therefore WASI-estimated IQ scores are likely to be higher than actual Wechsler Adult Intelligence Scale-III (WAIS-III; Wechsler, 1997) and WAIS-IV (Wechsler, 2008) scores. The MCCB was used to provide a test of key cognitive domains significantly impaired in schizophrenia, including processing speed, attentional vigilance, working memory, verbal learning, visual learning, reasoning, problem solving, and social cognition. Each test was administered as part of a behavioral research protocol at the Maryland Psychiatric Research Center, per the standard test administration protocol provided in the manuals.

2.2.2. Procedure

After providing written informed consent, participants provided medical history and were given the SCID to confirm diagnosis. Participants were then given the WRAT, WTAR, and WASI Vocabulary and Matrix Reasoning subtests, with breaks provided in between each as needed. Following these tasks, participants completed the MCCB. Testing took approximately 1.5 to 2 h.

2.2.3. Data analysis

In the original sample of 110 HCs and 143 SZs, there was a wide range of performance on the WASI IQ and average reading scores. Notably, the distributions of IQ and reading scores among SZs included a number of individuals with scores considerably lower than were seen among HCs. To examine how the magnitude of HC–SZ differences remained among participants with comparable WASI IQ and reading scores, we restricted our analysis to participants for whom the WASI IQ was between 90 and 130 and the average reading score was between 80 and 120 (see Table 1 for demographics). The lowest-performing 5% and highest-performing 15% of HCs were removed, along with the lowest-performing 42% and highest-performing 4% of SZs to achieve our new sample. Thus, the retained sample excludes the most impaired patients (see Supplementary materials). An initial analysis was conducted by dividing these participants into four strata of equal width on each measure, which resulted in groups of HC and SZ with closely comparable IQ or reading scores within the respective reading or IQ stratum. Table 2 provides a summary of the sample size, mean, and standard deviation of each stratum for both IQ and reading scores. The largest average HC–SZ difference in IQ or reading score within any stratum was 1.5 points, and most differences were smaller, suggesting adequate matching on IQ and reading. Further, we verified that age was not significantly different between HCs and SZs in any of the individual stratum. We then used two way ANOVA to examine what the average HC–SZ differences across IQ (or reading) strata on the MCCB composite and domain T-scores were, and whether the magnitude of these HC–SZ differences varied among the IQ (or reading) strata. We hypothesized that SZ MCCB scores would be lower than HC MCCB scores, even when participants were matched across groups by WASI or reading.

We were also interested in examining the extent to which GIA explained the degree of impairment observed across domains. To do this, ANCOVA was used to estimate HC–SZ differences on the seven MCCB cognitive domains, adjusting for WASI IQ and the average of

Table 1
Participant characteristics.

Characteristic	SZ	HC	Group comparisons
N	77	89	
Age	38.32 (10.95)	39.02 (10.67)	t = 0.42, p = .68
Education	13.29 (1.78)	14.58 (1.97)	t = 4.42, p < .001
Maternal education	13.71 (3.16)[a]	13.54 (2.29)[c]	t = −0.38, p = .71
Paternal education	14.56 (3.42)[b]	13.11 (2.97)[d]	t = −2.86, p < .01
Gender (% male)	82	64	χ^2 = 9.53, p < .05
Race (% Caucasian)	65	53	χ^2 = 2.45, p = .115
Cognitive performance			
WASI	104.52 (10.27)	112.11 (9.50)	t = 4.95, p < .001
WRAT	99.27 (9.45)	101.83 (10.11)	t = 1.68, p = .096
WTAR	103.58 (12.00)	106.69 (11.04)	t = 1.73, p = .085
MCCB	34.83 (10.94)	50.42 (10.35)	t = 9.42, p < .001

N.B. The values represent means (or frequencies where mean is not appropriate), with standard deviations in parentheses.
[a] Data unavailable for five subjects.
[b] Data unavailable for six subjects.
[c] Data unavailable for two subjects.
[d] Data unavailable for one subject.

Table 2
Stratum IQ and reading scores by group.

Stratum	HC (N = 89)			SZ (N = 76)		
	N	Mean	S.D.	N	Mean	S.D.
Mean WASI IQ by WASI stratum in healthy controls (HCs) and people with schizophrenia (SZ).						
90–100	10	96.1	3.8	34	95.1	3.6
101–110	31	105.8	2.7	21	106.0	3.0
111–120	28	116.0	2.5	15	114.5	2.8
121–130	20	124.5	2.6	7	124.1	2.2
Mean reading score by reading stratum in healthy controls (HC) and people with schizophrenia (SZ).						
80–80	11	87.1	2.5	13	85.5	2.6
91–100	20	94.8	2.6	22	95.9	2.8
101–110	25	106.0	2.8	24	105.3	3.0
111–120	33	114.4	2.9	18	114.5	2.8