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Enhanced vulnerability to distraction does not account for working memory capacity reduction in people with schizophrenia

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ABSTRACT

Although working memory impairment has been well-documented among people with schizophrenia (PSZ), the underlying mechanism of this impairment remains unknown. The present study was conducted in a large sample of PSZ and healthy control subjects (HCS) to test the hypothesis that one putative mechanism – vulnerability to distraction from task-irrelevant stimuli – (1) can account for working memory impairment among PSZ, and (2) is associated with other neurocognitive and clinical variables that are highly predictive of functional outcome in schizophrenia. Participants (127 PSZ and 124 HCS) completed a visual change detection task in which a distractor stimulus (mask) was presented on half of the trials during the delay period between sample and test array. PSZ lost proportionately more information from working memory than did HCS, but this effect was small (Cohen's $d = 0.36–0.38$), and large differences between groups in working memory capacity remained when differences in distractibility were factored out. Furthermore, vulnerability to distraction was not strongly associated with any clinical or cognitive variables of interest. These results suggest that, although PSZ may be somewhat more susceptible to distraction than HCS, this impairment is unlikely to be a significant factor accounting for the robust capacity deficits observed in this population.

1. Introduction

Despite a large body of literature demonstrating that people with schizophrenia (PSZ) have reduced working memory (WM) capacity (Lee and Park, 2005), the underlying mechanism of this impairment remains unknown. Recently, the conception that an unusual vulnerability to distraction by task-irrelevant stimuli decreases retention of to-be-encoded items among PSZ has garnered attention (e.g., Anticevic et al., 2012; Mayer et al., 2012). Basic science research has documented a relationship between susceptibility to distraction and variation in working memory capacity among psychiatrically healthy individuals (Fukuda and Vogel, 2011). While a "distractibility hypothesis" of capacity limitations is an appealing framework in this respect, it is also noteworthy that decreased capacity in PSZ has been reported in the absence of any obvious distracting stimuli (Erickson et al., 2014; Gold et al., 2006). Such findings suggest that delineating the specific effects of distraction may be critical for understanding its impact on WM storage in PSZ.

There are two primary forms of distraction that are described in the literature: (1) distraction can take place at the encoding stage if selective attention mechanisms fail to prevent the encoding of task-irrelevant items thereby reducing capacity available for relevant items, or (2) distraction can occur following encoding by disrupting maintenance of the WM representation. PSZ appear to exhibit different levels of susceptibility to these two forms of distraction. For instance, we have previously reported that PSZ exhibit generally intact ability to suppress encoding of salient distractors in a spatial WM paradigm, despite overall reductions in capacity (Erickson et al., 2014). Similarly, Smith et al. (2011) found that PSZ were able to use color cues to guide target words into WM storage and exclude non-target words—again, despite overall reductions in capacity. These recent studies are consistent with earlier work from Gold et al. (2006) demonstrating that PSZ are able to select task-relevant items for WM storage while inhibiting the encoding of task-irrelevant items. One exception may be a failure to filter out extremely salient distractors (especially those that strongly activate the magnocellular pathway) during the encoding of low-salience target items (Hahn et al., 2010; Leonard et al., 2014). Taken together, these results suggest that failures of selective attention during encoding cannot explain the ubiquitous reduction in WM storage capacity in PSZ.

In contrast to findings of generally intact resilience to distractors at the encoding stage, PSZ appear to be vulnerable to distraction by stimuli that occur after the offset of the to-be-encoded stimuli, during either the consolidation phase or the maintenance phase. For instance, Fuller and colleagues (Fuller et al., 2005, 2009) reported evidence for slowed

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consolidation in PSZ by presenting masks at various latencies during the delay interval between encoding array and test. It was found that retention of items was impacted by the masks to a greater degree in PSZ compared to healthy control subjects (HCS), even when PSZ were given as long as 800 ms to consolidate the visual array (Fuller et al., 2009). Similarly, Anticevic et al. (2012) found that distractors presented during the maintenance period of a working memory task significantly impaired accuracy in PSZ relative to HCS, and that this vulnerability to distraction was associated with abnormal patterns of connectivity between the dorsolateral prefrontal cortex (DLPFC) and other cortical and subcortical regions.

A critical issue that remains unresolved is the degree to which vulnerability to distraction during maintenance can account for the WM impairment in PSZ. A second, but related issue concerns the extent to which disruption of working memory processes by distraction can account for broader cognitive disturbances. That is, if distraction is the primary mechanism by which working memory fails in PSZ, can it also explain impairment in other forms of cognition or functional outcome? Indeed, the notion that working memory impairment is central to many neurocognitive deficits motivates much of the present work on capacity limitations in PSZ (e.g., Green et al., 2000; Johnson et al., 2013; Lee and Park, 2005).

The present study was conducted to serve two primary purposes. First, we aimed to determine whether enhanced vulnerability to distraction can account for decreased storage capacity in PSZ. Second, we tested the hypothesis that vulnerability to distraction is associated with clinical and cognitive variables that are highly associated with functional outcome in schizophrenia. Two hundred fifty-one participants (127 PSZ and 124 HCS) completed a change detection WM task in which on half of the trials a mask was presented during the retention interval between the cue and test array. To determine the impact of distraction on working memory storage capacity, measured here as *K* (Cowan, 2001), distractibility was quantified in two ways: first, as the difference in number of items stored between mask- and no-mask trial types (K_{DIFF}), and second as the proportional change in number of items stored between mask- and no-mask trial types (K_{RATIO}). The former index indicates the absolute number of items lost to distractibility, while the latter index quantifies the proportion of WM capacity that is impacted by task-irrelevant stimuli. If PSZ are more vulnerable to distraction during the consolidation/maintenance phase of WM, PSZ should exhibit larger K_{DIFF} and K_{RATIO} compared to HCS. Furthermore, if vulnerability to distraction can account for reduced WM capacity in PSZ, group differences in capacity should be eliminated when distractibility is taken into account as a covariate. In addition to providing sufficient power to detect between-group differences in susceptibility to distraction as it relates to WM storage, the present study design and large sample permit evaluation of the relationship between distractibility and predictors of functional outcome.

2. Methods

2.1. Participants

One hundred twenty-seven individuals with a DSM-IV diagnosis of schizophrenia or schizoaffective disorder (83 male) and 124 psychiatrically healthy individuals (74 male) participated in the present experiment (see Table 1 for demographic information). The groups were statistically similar on gender ($\chi^2 = 0.86$; $p = 0.36$), age ($t = 0.37$; $p = 0.71$), race ($\chi^2 = 3.85$; $p = 0.57$), and parental education, a proxy measure of socioeconomic status ($t = 1.42$; $p = 0.16$). However, PSZ had significantly fewer years of education than did HCS ($t = 8.31$; $p < 0.001$), and had a significantly lower IQ ($t = 6.79$; $p < 0.001$). Diagnosis was confirmed using the Structured Clinical Interview for the DSM-IV (SCID-I/P; First et al., 2002), as well as a review of medical records and informant reports when appropriate. All PSZ were reported to be clinically stable by their mental health providers and had not received any changes in medication dosage for at least four weeks prior to testing. Haloperidol dose equivalents were calculated according to the formula recommended by Andreasen et al. (2010). All HCS were free from any current Axis I diagnosis or Schizotypal Personality Disorder (SPD), were not taking any psychiatric medications, and all denied a family history of psychosis. Participants in both groups were between the ages of 18 and 55, and reported no

Table 1
Demographic information from full sample (mean ± SD).

	Healthy Controls	Schizophrenia Patients	Effect Size (Cohen's d)
Gender (M: F)	74: 50	83: 44	–
Age	38.14 ± 10.45	38.64 ± 10.89	0.05
Race (AA: C: Other)	49: 68: 7	47: 70: 10	–
Education (years)	14.92 ± 2.00	12.65 ± 2.32*	1.05
Parental Education	13.90 ± 2.52	13.40 ± 2.96	0.18
Haloperidol dose equivalent (mg/day)	–	11.75 ± 7.97	–
BPRS Total Score	–	36.03 ± 7.02	–
BPRS Positive Symptoms (mean)	–	2.29 ± 1.08	–
BPRS Negative Symptoms (mean)	–	1.80 ± 0.67	–
BPRS Disorganized Symptoms (mean)	–	1.35 ± 0.36	–
SANS Total Score	–	25.88 ± 11.56	–
WASI	112.52 ± 21.02	93.36 ± 23.58*	0.86
WRAT-4	107.15 ± 14.04	95.21 ± 13.46*	0.87
WTAR	109.90 ± 13.02	98.31 ± 15.57*	0.81
MATRICS Total Score	52.24 ± 10.50	30.55 ± 13.15*	1.82
MATRICS Processing Speed	53.61 ± 10.40	34.48 ± 11.53*	1.74
MATRICS Attention/Vigilance	51.19 ± 8.79	38.90 ± 10.55*	1.27
MATRICS Working Memory	53.08 ± 9.51	38.30 ± 10.53*	1.47
MATRICS Verbal Learning	49.08 ± 15.24	37.43 ± 12.86*	0.83
MATRICS Visual Learning	44.98 ± 14.78	33.30 ± 15.08*	0.78
MATRICS Problem Solving	51.90 ± 10.17	41.57 ± 9.89*	1.03
MATRICS Social Cognition	52.42 ± 10.50	30.55 ± 13.15*	1.84
Level of Functioning Total Score	–	19.83 ± 7.19	–
Level of Functioning: Social	–	4.60 ± 2.45	–
Level of Functioning: Occupational	–	2.80 ± 2.63	–

MCCB = MATRICS Consensus Cognitive Battery; WASI = Wechsler Abbreviated Scale of Intelligence; WTAR = Wechsler Test of Adult Reading; WRAT = Wide Range Achievement Test; BPRS = Brief Psychiatric Rating Scale.
* p < 0.001.