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Do people with schizophrenia have differential impairment in episodic memory and/or working memory relative to other cognitive abilities?

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ABSTRACT

Efforts to identify differential or core cognitive deficits in schizophrenia have been made for several decades, with limited success. Part of the difficulty in establishing a cognitive profile in schizophrenia is the considerable inter-patient heterogeneity in the level of cognitive impairment. Thus, it may be useful to examine the presence of relative cognitive weaknesses on an intra-person level. In the present study we examined the rates of significant intra-person differences between crystallized verbal ability versus five other cognitive abilities among 127 persons with schizophrenia or schizoaffective disorder and 127 demographically matched normal comparison (NC) subjects. We found that the rates of significant discrepancies above the NC group base-rates was significantly greater in reference to those discrepancies involving visual memory relative to those associated with auditory memory, working memory, processing speed, and perceptual organization. The findings conflict with prior suggestions that working memory or auditory episodic memory are differential or core deficits in schizophrenia, and highlight the importance of considering visual memory in characterizing the cognitive effects of this condition.

1. Introduction

Much neuropsychological research on schizophrenia over the last three decades has been motivated by the hope that discovery of specific neurocognitive profiles may elucidate the underlying neuropathology of the disorder or foster development of effective rehabilitation programs (Palmer et al., 2009). The answer to one basic question remains unclear: are there differential or "core" cognitive deficits in schizophrenia? A variety of cognitive domains have been proposed as the core deficit in schizophrenia: attention (Elvevag and Goldberg, 2000; Barr, 2001; Hilti et al., 2008), working memory (Goldman-Rakic, 1994; Elvevag and Goldberg, 2000; Silver et al., 2003; Mitropoulou et al., 2005; Lee and Park, 2005; Forbes et al., 2009), processing speed (Rodriguez-Sanchez et al., 2007), episodic memory (Saykin et al., 1991; Palmer et al., 1997; Aleman et al., 1999; Gur et al., 2000; Whyte et al., 2005), and executive function (Zec, 1995; Wobrock et al., 2008).

Meta-analyses indicate episodic memory tests have the largest or near largest effect sizes in schizophrenia patients versus normal comparison (NC) subjects (Heinrichs and Zakzanis, 1998; Fioravanti et al., 2005; Mesholam-Gately et al., 2009), supporting the century-long focus on temporal/hippocampal and frontal–subcortical regions as prime suspects in the neurogenesis of schizophrenia (Kraepelin, 1913; Goldstein, 1939). However, it is difficult to draw definitive conclusions due to heterogeneity in effect sizes between studies (Fioravanti et al., 2005). Part of the difficulty

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establishing differential cognitive impairment in schizophrenia rests in the marked inter-patient heterogeneity in level of cognitive impairment. On average, schizophrenia is associated with mild-to-moderate cognitive impairment, but 20–30% of patients have normal range neurocognition (Palmer et al., 2009). Thus, it may be useful to examine the presence of relative cognitive weaknesses on an intra-person level.

The present study examined within-person cognitive differences among 127 patients with schizophrenia and 127 NC subjects. Cognition was measured with the Index scores from the 6-factor model for Wechsler Adult Intelligence Scale—Third Edition (WAIS-III)/Wechsler Memory Scale—Third Edition (WMS-III) (The Psychological Corporation [TPC], 1997; Tulsky et al., 2003).

Crystallized knowledge is relatively unaffected by schizophrenia and many other neurocognitive disorders (Allen et al., 1998; Dickinson and Coursey, 2002; Iverson et al., 2006), and has the strongest correlation with Full Scale IQ (TPC, 1997), so the Verbal Comprehension Index (VCI) was used as a marker of general cognitive ability. We hypothesized that VCI scores would be higher than each of the other five cognitive abilities for a significantly larger proportion of people with schizophrenia relative to the proportion among NC subjects. Given the effect sizes for episodic memory in means comparisons (Heinrichs and Zakzanis, 1998), and long-held suspicion of the frontal and temporal regions in neurogenesis of schizophrenia (Palmer et al., 2009), as well as cogent models of working memory as a core deficit underlying many facets of schizophrenia (Goldman-Rakic, 1994), we hypothesized that discrepancies with VCI would be particularly common among schizophrenia patients when evaluated in reference to episodic memory and working memory.

2. Methods

2.1. Participants

Participants included 127 persons with schizophrenia or schizoaffective disorder and 127 NC subjects. Patient data were collected as part of baseline evaluations for a study of medication adherence among middle-aged and older patients. NC data were derived from the WAIS-III/WMS-III standardization sample.

Inclusion criteria for patients were: i) DSM-IV-TR diagnosis of schizophrenia or schizoaffective disorder determined with the Structured Clinical Interview for the DSM-IV-TR (First et al., 2002); ii) age >40 years; iii) outpatient status; iv) currently prescribed antipsychotic medication; and v) written consent for participation. Exclusion criteria were known diagnosis of dementia, or Mini Mental State Exam total ≤20 (Folstein et al., 1975). Recruitment sources included the University of California, San Diego, Veterans Affairs San Diego Healthcare System outpatient psychiatry services, and San Diego area assisted living facilities and physicians.

NC subjects were screened to exclude those with uncorrected sensory impairments and other conditions that might affect cognitive functioning or test performance (TPC, 1997). NC data were provided by the test publisher using one-to-one matching (as closely as possible) based on age, education, sex, and ethnicity.

2.2. Measures

2.2.1. Demographics

Age, education, sex, and ethnicity were determined by self-report.

2.2.2. Clinical characteristics

Patients' medications were determined via interview or record review (10% received conventional neuroleptics, 69% second generation antipsychotics, and 21% a combination; 51% were also on anticholinergic medication). Patients' severity of psychopathology was assessed with the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987).

2.2.3. Neurocognitive assessment

Cognitive functioning was evaluated with the WAIS-III/WMS-III battery 6-factor Index scores (Tulsky et al., 2003; Tulsky and Price, 2003), including:

(1) Verbal Comprehension (VCI): Vocabulary, Information, Similarities
(2) Perceptual Organization (POI): Block Design, Picture Completion, Matrix Reasoning
(3) Working Memory (WMI): Spatial Span, Letter Number Sequencing
(4) Processing Speed (PSI): Digit Symbol, Symbol Search
(5) Auditory Memory (AMI): Logical Memory I (immediate recall) and II (delayed recall), Verbal Paired Associates I (immediate recall) and II (delayed recall)
(6) Visual Memory (VMI): Family Pictures Recall I (immediate recall) and II (delayed recall), Visual Reproductions I (immediate recall) and II (delayed recall).

Raw scores were converted to Index scores (normative mean = 100, SD = 15; higher scores represent better performance) using the published norms (Wechsler, 1997a,b; Tulsky et al., 2003).

2.3. Analyses

Demographic and Index scores among patients versus NC subjects were compared with *t*-tests or Pearson Chi-square, as appropriate.

Cut-scores defining "significant" ($p<.05$) discrepancy between VCI and other Index scores were calculated with the "simple difference" method (Wechsler, 1997a):

$$\text{Cut} - \text{score} \;=\; z\sqrt{SE_{\text{Ma}}{}^2 + SE_{\text{Mb}}{}^2}$$

wherein $z = 1.96$; the Standard Error of Measurement (SE_M) for each Index score was determined from published norms for the overall standardization sample (TPC, 1997; Tulsky et al., 2003). We tallied the proportion of subjects for whom the VCI was better than, worse than, or not reliably different from the compared Index score.

We examined the degree of concordance in specific discrepancy score patterns within each patient-NC matched pair. For each of the five discrepancy scores, within each subject, we determined whether the comparator Index score was significantly lower than his/her VCI. If the result was the same in the patient and NC in a pair, that pair was assigned a