Schizophrenia Research xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Cognitive functioning in first-episode schizophrenia: MATRICS Consensus Cognitive Battery (MCCB) Profile of Impairment

A. McCleery [a,*], J. Ventura [a], R.S. Kern [a,b], K.L. Subotnik [a], D. Gretchen-Doorly [a], M.F. Green [a,b], G.S. Hellemann [a], K.H. Nuechterlein [a,c]

[a] Semel Institute for Neuroscience and Human Behavior, Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine, UCLA, Los Angeles, CA, United States
[b] VISN 22 Mental Illness Research, Education, and Clinical Center (MIRECC), Greater Los Angeles VA Healthcare System, Los Angeles, CA, United States
[c] Department of Psychology, UCLA, Los Angeles, CA, United States

ARTICLE INFO

Article history:
Received 29 January 2014
Received in revised form 22 April 2014
Accepted 26 April 2014
Available online xxxx

Keywords:
MCCB
First-episode schizophrenia
Cognition
Profile analysis
First episode schizophrenia

ABSTRACT

Background: Although many studies have assessed cognitive functioning in first-episode schizophrenia (FESz), the pattern and severity of impairment across cognitive domains remain unclear. Moreover, few studies have directly compared the pattern of cognitive performance between FESz and chronic schizophrenia (CSz). In this study we examined the cognitive impairment profile in FESz using a standardized neurocognitive battery (MATRICS Consensus Cognitive Battery; MCCB).
Methods: MCCB data were compared from 105 FESz patients, 176 CSz patients and 300 non-psychiatric (NP) participants. Mixed model analysis evaluated group differences in MCCB profiles and relative strengths and weaknesses in the MCCB profiles of patients. Clinical implications of MCCB performance were also examined; we compared the proportion of participants from each group who exhibited clinically-significant global cognitive impairment based on the MCCB Overall Composite score.
Results: FESz and CSz showed impaired performance across all MCCB domains relative to NP. With the exception of relative preservation of working memory and social cognition in FESz, the MCCB domain scores were similar in FESz and CSz. The distribution of impairment on the Overall Composite score did not significantly differ between FESz and CSz; compared to NP, both patient groups were overrepresented in moderate and severe impairment categories.
Conclusion: The pattern, magnitude, and distribution of severity of impairment in FESz were similar to that observed in CSz. However, early in the illness, there may be relative sparing of working memory and social cognition.

1. Introduction

Marked cognitive impairment is a core, enduring feature of schizophrenia, prompting some researchers to posit that the illness can be conceptualized as primarily a disorder of cognition (Rund, 1998; Green and Nuechterlein, 1999). Among patients with chronic schizophrenia (CSz), cognitive impairment is diffuse and pervasive, with deficits typically 1 to 2 standard deviations below non-psychiatric control samples across various cognitive domains (Heinrichs and Zakzanis, 1998; Gold, 2004; Green, 2006). Cognitive impairment appears to be a relatively stable feature of schizophrenia (Hoff et al., 2005; Barder et al., 2013b), even across acute vs. remitted states (Nuechterlein et al., 1992), with limited response to antipsychotic treatment (Rund, 1998; Keefe et al., 2007). Cognitive impairment is present in first-episode schizophrenia (FESz; Gold et al., 1999; Hoff et al., 1999; Mohamed et al., 1999; Addington and Addington, 2002; Barder et al., 2013a), and likely precedes the onset of illness in an attenuated form (Cornblatt et al., 1999; Hawkins et al., 2004; Lencz et al., 2006; Simon et al., 2007; Seidman et al., 2010; Lewandowski et al., 2011). However, the findings have been mixed regarding the magnitude of cognitive impairment in FESz compared to CSz, with some studies reporting negligible differences between FESz and CSz (e.g., Hoff et al., 1992), and others reporting less impairment in FESz relative to CSz, at least on some cognitive tests (e.g., Saykin et al., 1994; Albus et al., 1996; Addington and Addington, 2002; Townsend and Norman, 2004; Braw et al., 2008). Hence, the pattern and severity of impairment in FESz across cognitive domains remain unclear.

A meta-analysis of 43 studies of cognition in FESz (Mesholam-Gately et al., 2009) provided strong evidence for notable impairment across all

* Corresponding author at: UCLA Semel Institute for Neuroscience and Human Behavior, Department of Psychiatry, David Geffen School of Medicine, 300 Medical Plaza, Room 2213, Los Angeles, CA 90095, United States. Tel.: +1 310 206 8979; fax: +1 310 206 3651.
E-mail address: amccleery@mednet.ucla.edu (A. McCleery).

http://dx.doi.org/10.1016/j.schres.2014.04.039
0920-9964/

cognitive domains, with medium to large mean effect sizes on par with those reported in CSz (Heinrichs and Zakzanis, 1998). Impairment was most pronounced in immediate verbal memory and processing speed, in addition to the global impairment observed in schizophrenia. Indeed, a selective deficit of verbal memory and processing speed has been reported elsewhere in the schizophrenia literature (e.g., Dickinson et al., 2008; Gonzalez-Blanch et al., 2010). The meta-analysis noted significant heterogeneity of effect sizes within cognitive domains and between studies, likely due to methodological variations across studies, such as differences in the operational definition of FESz, properties of the patient samples (e.g., diagnoses, demographic variables), medications, and possible cohort effects. Inconsistency in cognitive test batteries across studies provides an additional source of variability in that tests may differ substantially in reliability, which impacts estimates of effect size (Baugh, 2002). Moreover, given that the various tests were not normed on the same sample, it is difficult to directly compare differences in effect sizes across tests/domains (Russell et al., 2005).

The Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery (MCCB; Nuechterlein and Green, 2006) is a compilation of independently owned and published tests that initially had normative data from non-overlapping samples. The MCCB has the advantage of being *co-normed* (i.e., normative data for each test collected from the same sample) on the non-psychiatric (NP) community sample from the MATRICS Psychometric and Standardization Study (MATRICS PASS; Kern et al., 2008). The MCCB includes seven cognitive domains: speed of processing, attention/vigilance, working memory, verbal learning, visual learning, reasoning and problem solving, and social cognition. A brief description of the 10 tests comprising the MCCB can be found in Table 1. Five MCCB domains are assessed with one test each, thus the T-score and percentile for those domains are based on those individual tests. The speed of processing and working memory domains are assessed with multiple tests, and these domain scores are based on a composite of the included tests. In addition to the seven domain scores, the MCCB also provides an Overall Composite score, an index of cognitive functioning across domains. The Overall Composite score is derived through equal weighting of the seven MCCB domain scores (Nuechterlein and Green, 2006).

The profile of MCCB impairment for a CSz sample was previously reported (Kern et al., 2011). Compared to the NP sample, CSz patients were impaired across all MCCB domains, with greater relative impairment in speed of processing and working memory, and less relative impairment in reasoning and problem solving compared to their average performance across the remaining MCCB domains.

Adoption of the MCCB as a neuropsychological test battery in schizophrenia research is on the rise. At the time of this writing, *ClinicalTrials.gov*, an online registry of clinical trials across the globe maintained by the National Institutes of Health and National Library of Medicine, lists over 50 studies that employ the MCCB. The aim of this paper was to examine the overall magnitude and profile of cognitive impairment in FESz using the MCCB. Specifically, we compared MCCB domain scores for a FESz sample to data from CSz and NP participants in MATRICS PASS (Nuechterlein et al., 2008; Kern et al., 2011). Four hypotheses were tested: 1) that FESz patients would show significant impairment averaged across MCCB domains compared to NP; 2) that FESz patients would show similar magnitude of impairment as CSz patients; 3) consistent with the Mesholam-Gately meta-analysis (Mesholam-Gately et al., 2009), that FESz patients would exhibit particular weakness in speed of processing and verbal learning relative to performance in the remaining MCCB domains; and 4) finally, that the proportion of participants from each patient group who exhibit clinically-significant global cognitive impairment will not differ.

2. Methods

2.1. Participants

Three samples of participants provided data for these analyses. The FESz sample included 105 patients from the UCLA Aftercare Research Program, an outpatient research clinic for FESz. Inclusion criteria were: 1) onset of a first psychotic episode within 24 months of program entry, 2) fulfillment of DSM-IV (American Psychiatric Association, 1994) criteria for schizophrenia, schizoaffective disorder, depressed type, or schizophreniform disorder, 3) age of 18 to 45 years, and 4) sufficient fluency in English to allow for valid completion of the testing protocol. DSM-IV diagnoses were made using the Structured Clinical Interview for DSM-IV (SCID; First et al., 2001). These participants met criteria for schizophrenia ($n = 56$), schizoaffective disorder, depressed type ($n = 13$), or schizophreniform disorder ($n = 36$).

The other two samples were from the five academic sites (Duke University, Harvard University, University of Kansas, Maryland Psychiatric Research Center, and UCLA) in MATRICS PASS (Nuechterlein et al., 2008; Kern et al., 2011). The CSz sample included 176 patients with a DSM-IV diagnosis of schizophrenia ($n = 151$) or schizoaffective disorder, depressed type ($n = 25$). Inclusion criteria were: 1) a DSM-IV diagnosis of schizophrenia or schizoaffective disorder, depressed type, based on SCID interview, 2) age 18–65 years, and 3) clinical stability as indicated by stable outpatient or rehabilitation center status and no medication changes in month prior to testing. The NP sample included 300 community residents aged 20–59, representative of the 2000 U.S. Census with respect to gender, race, ethnicity, and level of education.

Patients with a diagnosis of schizoaffective disorder, depressed type were included in these analyses because previous research suggests that the cognitive impairments associated with that diagnosis are comparable with those observed in schizophrenia (Bora et al., 2009; Simonsen et al., 2011). Exclusion criteria for all participants were: 1) history of neurological disorder or head injury, 2) IQ less than 70 or evidence of pervasive developmental disorder, 3) alcohol or substance abuse (1 month prior to testing) or dependence (6 months prior to testing) and/or excessive lifetime use of alcohol or substances, and 4) use of any medications that could interfere with test performance. In addition, for NP participants, history of schizophrenia or any other psychotic-

Table 1
Description of MATRICS Consensus Cognitive Battery tests.

Domain	Test	Variable of interest
Speed of processing	BACS Symbol Coding Test (BACS SC)	Total number correct
	Category Fluency Test, animal naming (fluency)	Total number of animals named in 60 s
	Trail Making Test, part A (TMTA)	Time to completion
Attention/vigilance	Continuous Performance Test, Identical Pairs (CPT-IP)	Overall d'
Working memory	WMS 3rd ed., Spatial Span (WMS-III SS)	Sum of raw scores on forward and backward conditions
	Letter-Number Span Test (LNS)	Number of correct trials
Verbal learning	Hopkins Verbal Learning Test — Revised (HVLT-R)	Total number of words recalled correctly over three learning trials
Visual learning	Brief Visual Memory Test — Revised (BVMT-R)	Total recall score over three learning trials
Reasoning & problem solving	NAB Mazes Subtest (NAB Mazes)	Total raw score
Social cognition	MSCEIT Managing Emotions Branch (MSCEIT-ME)	Branch score using general consensus scoring

Note: BACS: Brief Assessment of Cognition in Schizophrenia, WMS-III: Wechsler Memory Scale —3rd Ed., NAB: Neuropsychological Assessment Battery, MSCEIT: Mayer-Salovey-Caruso Emotional Intelligence Test.

Please cite this article as: McCleery, A., et al., Cognitive functioning in first-episode schizophrenia: MATRICS Consensus Cognitive Battery (MCCB) Profile of Impairment, Schizophr. Res. (2014), http://dx.doi.org/10.1016/j.schres.2014.04.039