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Toward a more parsimonious assessment of neurocognition in schizophrenia: A 10-minute assessment tool

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ABSTRACT

Background: Many individuals with schizophrenia experience a profound deficit in global cognitive ability, which is related to poor functional outcomes. Historically, the standard of assessing neurocognitive impairments is one of extensive neuropsychological batteries that are labour-intensive. The present study examined whether a brief neurocognitive assessment (BNA) instrument could effectively estimate global neurocognition and further examined its clinical utility.

Methods: The validity and clinical utility of a BNA that takes approximately 10 min to administer was examined against a full neuropsychological battery that takes approximately 90 min to administer in a large and heterogeneous sample of 1303 patients with schizophrenia.

Results: The BNA explained 76% of the variance in global neurocognition in the total sample and remained consistent in subsamples stratified by clinical characteristics (e.g., severity of psychopathology) and in randomized re-sampling simulations. The two items that comprised the BNA were the letter-number sequencing test, a measure of working memory, and the digit-symbol test, a measure of processing speed. Next, perhaps more importantly, the BNA and full neuropsychological battery were related to symptoms and functional status to a similar degree in both univariate and multivariate regression models; moreover, both instruments were sensitive to longitudinal treatment related change to a similar degree.

Conclusions: The BNA is able to rapidly, easily, and validly assess global neurocognition in schizophrenia. The BNA was associated with important clinical outcomes to a similar degree as a full cognitive battery. This tool provides clinicians and researchers a means to assess global neurocognitive impairments without requiring extensive neuropsychological testing.

1. Introduction

Schizophrenia is a complex and debilitating disorder characterized by a constellation of symptoms including positive (e.g., hallucinations, delusions), negative (e.g., avolition, blunted affect) and cognitive symptoms (e.g., planning) (Freedman, 2003). Although current treatments have helped alleviate the burden of positive symptoms, they have had minimal impact on core negative and cognitive symptoms (Harvey and Keefe, 2001; Kirkpatrick et al., 2006). Moving beyond the treatment of psychotic symptoms, focus on the development of novel therapeutics has shifted to treatments of cognitive and negative symptoms as these have been related to the prominent psychosocial disability often associated with this illness (Green, 1996; Green et al., 2000; Milev et al., 2005; Mohamed et al., 2008; Perlick et al., 2008).

There are now several clinical trials with neurocognition as the primary treatment outcome (Keefe et al., 2013). Despite the recognized importance of cognitive symptoms (Green, 1996; Green et al., 2000), though, they are not routinely assessed clinically and are not always apart of psychopathology assessments in the context of research as are other symptom domains. This may, in part, be due to the lengthy assessment time required by most traditional neuropsychological batteries (Lezak, 2004). Such lengthy assessments not only limit applicability in clinical settings, but also increase participant burden in research studies wishing to assess this important domain. Here, a short and easy to administer neurocognitive instrument is proposed to overcome these shortcomings. At the outset, we emphasize that such abridged batteries cannot, by definition, capture the full pattern and degree of cognitive

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impairment afforded by a full battery, but suggest that such a tool provides a means of capturing the gist in a way that is clinically meaningful.

Other brief batteries exist that have been developed for similar purposes (e.g., decrease administration time). Some examples include the Brief Assessment of Cognition in Schizophrenia (BACS) which requires 35 min (Keefe et al., 2004), the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) which takes 25 min (Gold et al., 1999; Hobart et al., 1999), the Brief Cognitive Assessment (BCA) which takes about 15 min (Velligan et al., 2004), and the Brief Cognitive Assessment Tool for Schizophrenia (BCATS) which takes about 11 min (Hurford et al., 2011). However, the administration time for the BACS and RBANS may still be too long for practical use in clinic. The BCA and BCATS are, in our opinion, short enough for employment in clinic and provide an excellent means to quickly assess global neurocognition. However, the original development of these shortened instruments focused primarily on shared variance between the short and full batteries. Although this is an excellent start to indicating validity, to further suggest their use across clinical and research settings it should be demonstrated whether this shared variance predicts outcomes similarly. That is, after indicating that a brief instrument is valid in estimating global neurocognition, the utility of the instrument should be established. It may well be that although a shortened measure shares 70% of variance with the full battery, the two measures may relate to say functioning and symptoms to a differential degree, perhaps relating to the 30% of unexplained variance. In such a scenario, a brief instrument, regardless of being a valid predictor of global neurocognition, would have questionable clinical utility. Accordingly, we find it critical to demonstrate the usefulness of the brief instrument by showing similar relationships with outcome variables relevant to clinical research. Although some previous research has demonstrated that abbreviated cognitive assessments are related to important clinical outcomes such as functioning (Gold et al., 1999; Harvey et al., 2009; Keefe et al., 2006b; Velligan et al., 2004); unfortunately, this has not been established for existing abbreviated batteries with the same participants having completed both the shortened and full neurocognitive assessment batteries.

In the present study we demonstrate the validity and utility of a brief neurocognitive assessment (BNA) tool. For this, we use the large and rich dataset collected as a part of the NIMH sponsored Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study (Stroup et al., 2003). We first examined whether a few test scores can predict a sizeable amount of variance of a full neuropsychological assessment battery. Next, we extended clinically relevant findings in the field relating to cognition to test whether findings that emerge are similar between the BNA and full battery. This latter aim, in our opinion, is a critical test of applicability of a short instrument and serves as the primary goal for the present study.

2. Methods

2.1. Participants

Data were drawn from the CATIE study for chronic schizophrenia (n = 1460). Details of the study design and rationale (Stroup et al., 2003), as well as primary findings (Lieberman et al., 2005), have been presented elsewhere. The primary purpose of the CATIE study was to compare the effectiveness of atypical and conventional antipsychotics through a randomized controlled clinical trial conducted at 57 sites in the United States (16 university clinics, 10 state mental health agencies, 7 Veterans Affairs medical centres, 6 private nonprofit agencies, 4 private-practice sites, and 14 mixed-system sites). The study inclusion and exclusion criteria have been reported elsewhere (Stroup et al., 2003); notably, all participants had a diagnosis of schizophrenia confirmed using the Structured Clinical Interview for DSM-IV (First, 1997).

Here we report on those subjects who were missing three or less test scores, hence permitting a composite neurocognition score to be calculated (n = 1331) (Keefe et al., 2006a). Further, we excluded individuals who were missing scores on any test that was not computerized or required a specific apparatus (n = 28 excluded) (see below).

The study was approved by the institutional ethics review board at each site, and written informed consent was obtained from the patients or their legal guardians.

2.2. Measures

The neuropsychological tests that comprised the full CATIE cognitive battery (FCCB) have been described in detail in a previous report (Keefe et al., 2003). Briefly, these measures include the Wechsler Adult Intelligence Scale– Revised Digit Symbol Test (DST), Hopkins Verbal Learning Test (HVLT), Continuous Performance Test (CPT), a computerized version of the Wisconsin Card Sorting Test (WCST), Controlled Oral Word Association Test and category instances (COWAT), Grooved Pegboard, Wechsler Intelligence Scale for Children – Revised Mazes, Letter-Number sequencing test (LNS), and a computerized test of visuospatial working memory (WM). Scores on individual tests were converted to z-scores and combined to construct the following cognitive domain scores: Processing Speed, Working Memory, Verbal Memory, Vigilance and Reasoning. Of note, these are all domains assessed by the MATRICS Cognitive Consensus Battery (Green et al., 2004; Nuechterlein et al., 2008). The 5 domain scores were then averaged to create a neurocognitive composite score. This neurocognitive battery required approximately 90 min of administration time. Details on the baseline characteristics of neurocognition (Keefe et al., 2006a) and response to treatment (Keefe et al., 2007a) in the CATIE study have been published previously.

Other measures of interest included the Clinical Global Impression – Severity scale (CGI–S) to assess overall clinical severity (Guy, 1976), Positive and Negative Syndrome Scale (PANSS) to assess psychopathology (Kay et al., 1987), Calgary Depression Scale for Schizophrenia (CDSS) to assess depressive symptoms (Addington et al., 1990), and the Heinrichs–Carpenter Quality of Life Scale (QLS) to assess psychosocial and community functioning (Heinrichs et al., 1984).

2.3. Selection of tests for BNA

One goal of the present analyses was to determine whether a few short items could capture a significant portion of the total variance of a full neurocognitive test battery. Although previous work has demonstrated that this indeed possible (Keefe et al., 2006a), we repeated this analysis using the current subsample of participants in the CATIE study (n = 1303), as well as determined the robustness of this estimation using re-sampling techniques (see below). An emphasis was put on individual tests that were brief and did not require an apparatus beyond that of paper and pencil. These points were highlighted to ensure that the brief instrument could be translated into clinical use with ease. This precluded the inclusion of the WCST, WM, CPT and Grooved Pegboard tests as these are either computerized or require a specific apparatus. Next, we wanted to keep the brief instrument as short as possible, and opted for a maximum administration time of 10 min. As each of the individual tests takes approximately 3–6 min or more to administer, only 2 tests could be included in the BNA to keep within a 10 min time frame.