The MATRICS consensus cognitive battery for the assessment of cognitive impairment in schizotypal personality disorder

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ABSTRACT

Cognitive deficits are a core impairment across the range of schizophrenia (SZ) spectrum disorders, including schizotypal personality disorder (SPD). The MATRICS Consensus Cognitive Battery (MCCB) was developed to be a robust, specific, and valid cognitive assessment battery to assess cognition in clinical trials for treating cognitive impairments in SZ. Despite the similarity of cognitive impairments shown in SPD and SZ and the clear relevance of uniform assessment across a diagnostic spectrum, the MCCB has yet to be validated in SPD. As such, this is the first study to evaluate the sensitivity of the MCCB for the assessment of cognitive function in individuals with SPD. Participants were 30 individuals with SPD and 54 healthy controls (HC) assessed with the MCCB and supplemental neurocognitive assessments (Trails B, DOT test, Paced Auditory Serial Addition Test (PASAT), AX Continuous Performance Task (AX-CPT), and N-back). Individuals with SPD performed worse than HC participants on all MCCB subtests, as well as on converging supplemental tasks including Trails B, DOT test, PASAT, AX-CPT, and N-back. These results indicate that the MCCB was sensitive to cognitive impairment in SPD compared to controls. SPD participants demonstrate impairments similar to data of SZ participants within the literature, although to a slightly lesser degree of severity. Taken together, these results highlight the generalizability of using the MCCB across SZ spectrum diagnostic groups to assess cognition. Such findings allow for further comparison across disorders, greater understanding of the cognitive characteristics in the spectrum, and use of uniform assessment within cognitive intervention research.

1. Introduction

Cognitive deficits are a core feature of schizophrenia (SZ; Fatouros-Bergman et al., 2014) and a robust predictor of functional impairment (Green, 2006; Green et al., 2000). Despite strong efforts towards improving the treatment of cognitive impairments in SZ, these symptoms persist with all current treatments (Goldberg et al., 2007; Harvey, 2009). The National Institute of Mental Health (NIMH) supported the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) initiative, with several different development steps, starting with an expert panel to develop a robust, specific, and valid cognitive assessment battery to uniformly assess cognition in SZ (Nuechterlein et al., 2008). The MATRICS Cognitive Consensus Battery (MCCB) contains ten neurocognitive assessments, measuring seven cognitive domains: speed of processing, attention/vigilance, working memory, verbal learning, visual learning, reasoning and problem-solving, and social cognition. The MCCB is now a widely used, gold-standard battery to assess cognitive functioning and cognitive changes in SZ. Several comprehensive studies have shown that the MCCB is sensitive to cognitive impairments in participants in treatment trials for

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schizophrenia (e.g., Georgiades et al., 2017).

Schizotypal personality disorder (SPD) falls within the SZ spectrum and has genetics, psychophysiology, neuroanatomy, cognitive functioning, and social/role functional characteristics similar to SZ (Siever and Davis, 2004; Hazlett et al., 2008; Hazlett et al., 2014; Dickey et al., 2005). Researchers have investigated SPD as a method to better understand the pathophysiology, neurobiology, and underlying characteristics of SZ (Rosen et al., 2014; Szekely et al., 2022; Velikonja et al., 2019). Moreover, the SPD population is unique in that they often do not have the impacts of chronic antipsychotic medication use, frequent hospitalizations, and repeated psychotic episodes commonly seen in SZ and other SZ spectrum disorders, such as individuals at clinical high risk for psychosis (CHR) or first episode psychosis. This allows for examination of the core correlates of schizophrenia spectrum disorders with less confounding by medication and life experience factors.

Individuals with SPD have impairments in similar cognitive domains to SZ patients including attention, learning and memory, working memory, reasoning and problem-solving, and executive functions (McClure et al., 2013; Siever and Davis, 2004; Mitropoulou et al., 2005). SPD groups tend to perform similarly to healthy control and SZ group comparisons on most cognitive tasks, although they perform similarly to SZ patients on measures of working memory (McClure et al., 2008; Mitropoulou et al., 2005). Furthermore, cognitive impairments are associated with more vocational and everyday functioning in SPD groups (McGurk et al., 2013; McClure et al., 2013), with everyday functioning reaching a similar degree of impairment as in SZ patients (McClure et al., 2013). These impairments appear to be unique to the SZ spectrum in that they are not seen in other personality disorders (Harvey et al., 2006; McClure et al., 2008; Mitropoulou et al., 2005). Considering the significant impact of cognitive impairments on functioning in SPD, researchers have been working towards identifying effective treatments for the cognitive symptoms, such as cognitive enhancement or remediation interventions. As such, it is important to have universal methods of assessing deviations in the presentation of cognitive functions across SZ spectrum disorders.

Despite the similarity of cognitive impairments seen in SPD and SZ and the clear significance of using uniform assessment across a spectrum of participants, the MCCB has yet to be evaluated in SPD. As such, the goal of the current paper is to present the results of a study evaluating whether the MCCB is sensitive to detect the cognitive impairments known in SPD compared to healthy control participants. It was hypothesized that SPD participants would perform significantly lower on all cognitive tasks of the MCCB and supplemental cognitive tasks compared to healthy control participants.

2. Material and methods

2.1. Participants

Participants were 30 individuals with schizotypal personality disorder (SPD) and 54 healthy controls (HC) recruited from the community in and around the Mount Sinai Medical Center. Table 1 includes participant demographic information. Participants were administered the Structured Clinical Interview for DSM-IV (SCID-I/P, First et al., 2002) and the Structured Interview for DSM Personality Disorders (SIDP-IV; Pihl et al., 1997) to determine group eligibility for the study (for a full description, please see McClure et al., 2019). All interviews were conducted by one or two doctoral-level clinical psychologists who were supervised by an expert in personality disorder pathology (MMM). SPD participants with current or past bipolar I disorder, schizophrenia or other psychotic disorders, or current Major Depressive Disorder were excluded. Additional exclusion criteria include: significant medical conditions, traumatic brain injury with loss of consciousness, current psychotropic medication use, current substance abuse (within the last 6 months), or past dependence on stimulants, opioids or other potentially neurotoxic drugs. HC participants with a current DSM-IV Axis I or II diagnosis were excluded, with the exception of past diagnoses of adjustment disorder, dysthymic disorder, depressive disorder not otherwise specified, specific phobia, and sleep disorders. HC participants were excluded if they endorsed significant medical conditions, traumatic brain injury with loss of consciousness, or a family history of psychotic disorder. All participants provided informed consent in accordance with institutional IRB regulations.

Participants in the SPD group included 23 males and 7 females, while the HC group included 25 males and 31 females. Further demographic data is included in Table 1. Group differences were shown for education (t(880) = 4.85, p = 0.001), with the SPD group having lower education than the HC group. Additionally, there was a statistically significant association between gender and group (φ2(1) = 9.04, p = 0.003), such that there were more men in the SPD group compared to the HC group, which is consistent with previous literature in SZ spectrum samples (McEly et al., 2014; Mitropoulou et al., 2005). There were no statistically significant group differences on any other demographic variable.

2.2. Procedure

Participants were recruited as part of a study investigating the efficacy of a D1 agonist drug for improving cognitive function in individuals with SPD. Participants completed the cognitive assessment battery following the diagnostic assessments. Data presented in the current paper include baseline cognitive assessment of SPD and HC participants that were done prior to randomization and participation in the drug intervention.

2.3. Cognitive assessment

Participants were administered a subset of tasks taken from the MATRICS Consensus Cognitive Battery (Nuechterlein et al., 2008), the Neuropsychological Assessment Battery (NAB) Mazes, Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT), and Continuous Performance Test-Identical Pairs (CPT-IP) subtests were not administered. Age and gender-corrected T-scores based on the MCCB norms for each subtest served as the dependent variable. In addition, participants were administered several additional cognitive assessments that have been shown to be particularly sensitive in SPD samples (McClure et al., 2013), including assessments of context processing (the Modified AX-CPT; Barch et al., 2004), auditory working memory (the Paced Auditory Serial Addition Test (PASAT); Stuss et al., 1988), visual-spatial working memory (the DOT test; Keefe et al., 1997), visual working memory (the N-back Test; Braver et al., 1997), and executive functioning (Trail-making Test Part B; Reitan and Wolfson, 1993) (for a full description of supplemental cognitive tasks, please see McClure et al., 2019). The Benton Judgment of Line Orientation Test (JLOT) was administered as a comparison control test. For the supplemental tests, raw scores were used as the dependent variables (See Table 2).

2.4. Statistical analyses

Analyses were conducted using SPSS version 28.0.1 (SPSS Inc., Armonk, NY). A series of t-tests for each cognitive outcome variable were performed. An ANCOVA was conducted to assess education as a co-
Considering the substantial impact of cognitive impairment on functional outcomes and functional capacity similar to SZ patients (McClure et al., 2013), converging support that cognitive impairments are present in this specific sample and can be detected by the MCCB. Altogether, these results highlight the generalizability of using the MCCB within SPD groups to assess cognition.

Expanding the use of the MCCB to SPD groups allows for a more direct comparison of the profile of impairments seen in SZ and SPD, especially in response to interventions targeting cognitive function. Considering the substantial impact of cognitive impairment on functional outcomes and functional capacity similar to SZ patients (McClure et al., 2013), cognitive enhancement and remediation interventions

### 4. Discussion

This is the first study to evaluate the sensitivity of the MCCB for the assessment of cognitive function in individuals with SPD. Results indicate that the MCCB was in fact sensitive enough to detect cognitive impairment in this population as individuals with SPD performed worse than HC participants on all MCCB subtests. In fact, SPD participants scored approximately one standard deviation below normative mean performance on each MCCB task, which is similar although to a slightly lesser degree of severity than SZ patients who score approximately 1–2 SDs below normative mean performance on MCCB domains (McGee et al., 2014; Kern et al., 2011; Keefe et al., 2011). Additionally, individuals with SPD performed worse than HC participants on important supplemental cognitive tasks including Trails B, DOT test, PASAT, AX-CPT, and N-back. These cognitive tasks are established measures routinely used in assessing cognition in SPD groups (McClure et al., 2008; Mitropoulou et al., 2005; McClure et al., 2013), providing converging support that cognitive impairments are present in this specific sample and can be detected by the MCCB. Altogether, these results highlight the generalizability of using the MCCB within SPD groups to assess cognition.

Overall, participants in the SPD group performed significantly worse compared to the HC group on all MCCB tasks, as well as on the additional neurocognitive tasks with the exception of the Benton Line Orientation task, which was administered as a comparison control test. Results are shown in Table 2 and Fig. 1.

As there were significant group differences for education, this was entered as a co-variate in statistical analyses and the results remained statistically significant, as such the t-test results are presented in Table 2. In addition, the significant group differences for gender were addressed by using age and gender-corrected T-scores for all MCCB subtests.

### 3. Results

#### Table 2

<table>
<thead>
<tr>
<th>Cognitive task performance.</th>
<th>HC</th>
<th>SPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>Mean(SD)</td>
<td>t-Statistic</td>
</tr>
<tr>
<td>MCB subtests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trails A</td>
<td>49.59</td>
<td>38.87</td>
</tr>
<tr>
<td>(11.05)</td>
<td>(12.21)</td>
<td></td>
</tr>
<tr>
<td>BACS: Symbol coding</td>
<td>50.26</td>
<td>36.7</td>
</tr>
<tr>
<td>(10.51)</td>
<td>(8.93)</td>
<td></td>
</tr>
<tr>
<td>HVLT-R</td>
<td>47.52</td>
<td>40.47</td>
</tr>
<tr>
<td>(9.2)</td>
<td>(8.38)</td>
<td></td>
</tr>
<tr>
<td>WMS-III: Spatial span</td>
<td>48</td>
<td>35.63</td>
</tr>
<tr>
<td>(11.07)</td>
<td>(10.91)</td>
<td></td>
</tr>
<tr>
<td>WMS-III: LNS</td>
<td>50.33</td>
<td>38.13</td>
</tr>
<tr>
<td>(7.82)</td>
<td>(9.98)</td>
<td></td>
</tr>
<tr>
<td>BVSAT-R</td>
<td>49.35</td>
<td>40.63</td>
</tr>
<tr>
<td>(12.40)</td>
<td>(10.31)</td>
<td></td>
</tr>
<tr>
<td>Category</td>
<td>52.85</td>
<td>42.8</td>
</tr>
<tr>
<td>FLUENCY</td>
<td>(10.0)</td>
<td>(9.36)</td>
</tr>
</tbody>
</table>

Note. SPD participants performed worse than HC participants on all neurocognitive tasks (p < 0.01), with the exception of the Benton Judgment of Line Orientation Test (JLOT) which was used as a comparison control task. MCCB subtest t-scores are reported. BACS = Brief Assessment of Cognition in Schizophrenia; HVLT-R = Hopkins Verbal Learning Test—Revised; WMS-III: LNS = Wechsler Memory Scale-III: Letter/Number Span; BVMT-R = Brief Visuospatial Memory Test- Revised; PASAT = Paced Auditory Serial Addition Test; AX-CPT = AX Continuous Performance Test. All significant p-values survived correction for multiple comparisons.

**Fig. 1.** MATRICS performance by group.

Caption. SPD participants performed worse than HC participants on all neuropsychological tasks (p < 0.01). BACS = Brief Assessment of Cognition in Schizophrenia; HVLT-R = Hopkins Verbal Learning Test—Revised; WMS-III: LNS = Wechsler Memory Scale-III: Letter/Number Span; BVMT-R = Brief Visuospatial Memory Test- Revised. The red dashed line signifies 1 standard deviation below mean performance, which is also where schizophrenia patients typically score on these neuropsychological assessments. The black dashed line signifies normative mean performance. T-scores are age and gender-corrected. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
could be multiple courses of intervention for individuals with SPD. As of now, multiple studies have shown encouraging results in SPD groups with improvements in cognitive function in response to specific medications such as guanfacine (alpha2A agonist; McClure et al., 2007) and pergolide (dopamine agonist; McClure et al., 2010). Recent work has also shown an enhanced effect of a paired cognitive and behavioral intervention (cognitive training with social skills training), in conjunction with guanfacine showing improvement in problem-solving, reasoning, social cognition, and everyday functioning to a greater degree than the cognitive and behavioral interventions alone (McClure et al., 2019). Future research can now utilize the MCCB to compare the effectiveness of interventions across the SZ spectrum, to better pinpoint differences and potential areas of risk and/or protective factors.

There are several limitations to the current study. There was not a SZ comparison group included, which limits the comparability of cognitive impairments across the SZ spectrum in this study. However, as described, studies have shown that SZ participants tend to reliably score 1–2.5 SDs below mean performance using the MCCB (McCleery et al., 2019). Future research can now utilize the MCCB to compare the effectiveness of interventions across the SZ spectrum, to better pinpoint differences and potential areas of risk and/or protective factors.

5. Conclusions
Altogether, this study provides foundational evidence for using the MCCB in assessing cognitive functioning in SPD groups. Establishing the generalizability of using the MCCB across the SZ spectrum allows for further comparison across disorders, greater understanding of the cognitive characteristics in this spectrum, and use of uniform assessment within cognitive intervention research.

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CRediT authorship contribution statement
Katelyn N. Challman: Formal analysis, Writing – original draft. Daniel R. Rosell: Investigation, Writing – review & editing. Deanna Barch: Conceptualization, Formal analysis, Funding acquisition, Writing – review & editing. Harold W. Koenigsberg: Writing – review & editing. Phillip D. Harvey: Conceptualization, Funding acquisition, Methodology, Writing – review & editing. Erin A. Hazlett: Writing – review & editing. M. Mercedes Perez-Rodriguez: Funding acquisition, Investigation, Writing – review & editing. Antonia S. New: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Writing – review & editing. Margaret McNamaara McClure: Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Supervision, Writing – review & editing.

Declaration of competing interest
Dr. Harvey has received consulting fees or travel reimbursements from Alkermes, Bio Excel, Boehringer Ingelheim, Karuna Pharma, Merck Pharma, Minerva Pharma, and Sunovion (DSP Pharma) in the past year. He receives royalties from the Brief Assessment of Cognition in Schizophrenia (Owned by WCG Endpoint Solutions, Inc. and contained in the MCCB). He is chief scientific officer of i-Function, Inc. and Scientific Consultant to EMA Wellness, Inc. Dr. Perez-Rodriguez has received consulting fees from Alkermes and Neurocine Biosciences.

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