

## The Cognitive Assessment Interview (CAI): Reliability and Validity of a Brief Interview-Based Measure of Cognition

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**Objective:** To obtain Food and Drug Administration approval for the treatment of cognitive impairments associated with schizophrenia, a drug will need to demonstrate benefits beyond those that may be documented on objective cognitive tests. Interview-based measures of cognition such as the Cognitive Assessment Interview (CAI) are candidate coprimary outcome measures. **Methods:** Psychiatrically stable schizophrenia outpatients ( $n = 150$ ) were studied using the CAI to obtain information about cognitive functioning from both the patient and an informant. Patients also received objective assessments of neurocognition, functional capacity, functional outcome, and symptoms, at baseline and 1 month later. **Results:** The CAI had good internal consistency (Cronbach's  $\alpha = .92$ ) and good test-retest reliability ( $r = .83$ ). The CAI was moderately correlated with objective neurocognitive test scores ( $r$ 's =  $-.39$  to  $-.41$ ) and moderately correlated with social functioning ( $r = -.38$ ), work functioning ( $r = -.48$ ), and overall functional outcome ( $r = -.49$ ). The correlations of CAI scores with external validity indicators did not differ significantly by source of information (patient alone ratings were valid). Overall functional outcome correlated more strongly with patient CAI scores ( $r = -.50$ ) than with objective neurocognitive test scores ( $r = .29$ ) or functional capacity ( $r = .29$ ). **Conclusions:** Field testing of the CAI produced reliable ratings of cognitive functioning that were correlated with functional outcome. Patient ratings alone yielded scores with reliability and validity values appropriate for use in clinical trials. The CAI appears to provide useful complementary information and possesses practical advantages for rating cognitive functioning including an interview-based method of administration, brief assessment time (15 min for the patient assessment), little or no practice effects, and ease of scoring.

**Key words:** schizophrenia/functional outcome/functional capacity/symptoms/informant ratings/neurocognition

### Introduction

Evidence continues to accrue indicating that cognitive deficits are pronounced in schizophrenia and that those deficits impinge on a patient's quality of life and ability to function on a daily basis. Traditionally, objective tests have been used to assess cognition. But the assessment of cognitive functioning might benefit from nonperformance-based person-oriented assessments. Assessing cognitive functioning through interview-based methods is practical and might enable the examination of the impact of cognition on daily functioning. Interview-based measures of cognitive functioning are already in the second generation of development, following Food and Drug Administration (FDA) guidance on the development of methods for assessing patient reported outcomes.<sup>1–3</sup> The assessment protocol for the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) initiative included both of the first-generation instruments, the Schizophrenia Cognition Rating Scale (SCoRS)<sup>2</sup> and the Clinical Global Impression of Cognition in Schizophrenia (CGI-CogS).<sup>4,5</sup> This enabled determination of whether these 2 relatively new "parent" measures could be combined to produce a shorter version. Using MATRICS data, modern psychometric methods such as item response theory (IRT) were used to develop a new 10-item measure, the Cognitive Assessment Interview (CAI).<sup>3,6</sup> Information obtained from a patient and an informant is integrated into a final rating made by a trained CAI rater. So far, evaluation of the CAI's validity has been reported only as extracted from the parent measures in the MATRICS Initiative, where it showed moderate correlations with objective measures of cognition (MATRICS Consensus Cognitive Battery [MCCB];  $r = .32$ ) and with functional outcome (Birchwood Social Functioning Scale;  $r = .32$ ).<sup>3</sup> But the CAI still needed validation independent of the dataset from which the measure was created.

Representatives from the FDA have taken the position that for a cognitive-enhancing drug to be approved for the treatment of schizophrenia, improvement must be observed in both objective cognitive performance and another functionally meaningful endpoint referred to as a “coprimary” outcome.<sup>4,7</sup> The original intent of requiring a coprimary endpoint was to help protect the public from possible claims that testing of a new cognitive agent might result in statistically significant but clinically insignificant changes in the patient’s real-world functioning. In the MATRICS-Validation of Intermediate Measures (VIM)<sup>7</sup> study, the University of California, San Diego (UCSD) Performance-based Skills Assessment (UPSA)<sup>8</sup> and the Test of Adaptive Behavior in Schizophrenia (TABS)<sup>9</sup> were regarded as strong coprimary endpoints because they demonstrated robust correlations ( $r$ ’s = .67 and .61, respectively) with the MCCB.<sup>10</sup> However, like the MCCB, the UPSA and TABS are performance-based measures of cognition, but with the added feature of including some aspects of ‘real-world’ relevance, such as questions on how to read a bus map. Unsurprisingly, these measures behave psychometrically very much like any other cognitive tests. Interestingly, multivariate analyses found that neurocognitive performance added little to the prediction of real-world functioning when functional capacity measures were considered.<sup>11,12</sup> Also worth recognizing is that other studies have found that the UPSA and TABS do not consistently correlate more strongly with real-world outcomes or quality of life than do objective measures of cognition.<sup>4,7</sup> These varied findings regarding the relationship between objective neurocognitive assessments and functional capacity measures with outcome provides a rationale for considering whether interview-based measures of cognition might provide unique additional information as coprimary endpoints.

The relationship between interview-based measures of cognition and relevant constructs in schizophrenia, eg, neurocognition, has been examined. The correlation between the SCoRS and cognitive functioning varied from medium ( $r = -.26$ )<sup>13</sup> to high ( $r = -.54$ ).<sup>2</sup> Data from the MATRICS-Psychometrics and Standardization Study (PASS)<sup>4</sup> indicate that the correlation between the CAI and neurocognition was as strong as the correlation between neurocognition and the “parent” instruments (SCoRS and CGI-CogS).<sup>3</sup> In fact, multivariate results using the MATRICS-PASS data suggest that the prototype of the CAI had a stronger relationship with real-world functional outcomes than did an objective test of neurocognition (MCCB) or a functional capacity measure (UPSA).<sup>3</sup> This raises the possibility that the CAI, which like most measures of functional outcome uses an interview-based data collection format and has rating anchors explicitly linked to real world functioning, might be capturing more directly the relations between cognition and other aspects of daily functioning. Previous research has shown that a patient’s self-report alone of

cognitive functioning is not well correlated with objective measures of cognitive functioning, so a clinically trained assessor might be needed to make reliable ratings using interview-based measures.<sup>14–17</sup> Furthermore, the role played by insight into cognition for interview-based assessments has not been well examined, leaving open the question of whether interview-based methods require patient insight. Additionally, very little is known about what influence caregiver burden has on informant reports about the patient’s cognitive functioning. Each of these is an important issue to address if the field of interview-based assessments is to advance and potentially crucial for understanding the real-world impact of possible treatments for cognitive impairments.

The aim of the current study was to field test the CAI to further evaluate: (1) the psychometric characteristics (internal consistency, test-retest reliability, and utility as a repeated measure), (2) the validity of the CAI, ie, correlation with cognitive performance, functional capacity, functional outcome, and symptoms, and (3) practicality and tolerability (need for informants and time of administration).

## Methods

### Subjects

The sample was comprised 150 clinically stable schizophrenia outpatients who were recruited from 3 University of California, Los Angeles (UCLA)-affiliated psychiatric facilities: the UCLA Department of Psychiatry, the Department of Psychiatry at the West Los Angeles Veterans Affairs Hospital, and the Los Angeles County San Fernando Mental Health Center. Clinical and demographic characteristics were typical for a sample of outpatients with schizophrenia (table 1). Many of the patients were current participants in other UCLA-affiliated research projects that involved a thorough diagnostic assessment. For patients who were not currently participating in research, the Structured Clinical Interview for *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*<sup>18</sup> was administered by trained raters to establish a diagnosis.<sup>19</sup>

### Procedures

Diagnostic and psychiatric history data were collected during the first visit to determine study eligibility. Objective tests of neurocognition and functional capacity as well as interview-based assessments of cognition, symptoms, insight into cognition, caregiver burden, and functional outcome were administered at baseline and 1 month later. To ensure independence of the assessments, the study team included at least 2 assessors. One assessor determined study eligibility, collected demographic information, and administered the neurocognitive and functional capacity assessments. A separate

clinical assessor who was uninformed about the objective test results administered the CAI, symptom rating scales, and functional outcome measures. Institutional Review Board (IRB) approval was obtained prior to data collection for all subjects.

#### *Cognitive Assessment Interview*

The CAI was derived from 2 “parent” interview-based instruments, the CGI-CogS and the SCoRS (for a complete description, see Ventura et al<sup>3</sup> and Reise et al<sup>6</sup>). As determined by psychometric methods used in the development phase, the CAI includes 10 items that assess 6 of the 7 MATRICS cognitive domains: verbal learning, working memory, reasoning and problem solving, speed of processing, attention/vigilance, and social cognition. The CAI was administered to the patient as well as an informant, who was required to know the patient well enough to comment on cognitive functioning (for demographic information, see table 1). The ratings from those assessments were then integrated into a final CAI rater score. CAI items were rated on a 7-point scale with defined anchor points referenced to healthy people of a similar educational and sociocultural background. Higher scores reflect worse cognitive deficits that impact everyday functioning. The mean score for the 10 items was the dependent measure in this study.

#### *Training and Quality Assurance for the CAI*

Training on the CAI was provided to raters that had experience with semistructured psychiatric interviews or symptom rating scales. The training was conducted by the study Principal Investigator (J.V.) using didactic material about cognitive deficits, videotaped CAI assessments with accompanying “gold standard” ratings, and included the corating of “live” CAI assessments. Raters were required to meet a minimum standard of intraclass correlation coefficient (ICC) = .80 across all items and all assessments. Once certified, the raters were entered into a quality assurance program (for a description, see Ventura et al<sup>20</sup>).

#### *Objective Cognitive Performance Measures*

**MATRICES Consensus Cognitive Battery.** The MCCB,<sup>10</sup> which has now been well described,<sup>21</sup> includes 10 tests from 7 different cognitive domains: (1) Trail Making Test: Part A, (2) Brief Assessment of Cognition in Schizophrenia: Symbol-Coding, (3) Hopkins Verbal Learning Test—Revised, (4) Wechsler Memory Scale-III: Spatial Span (5) Letter-Number Span, (6) Neuropsychological Assessment Battery: Mazes, (7) Brief Visuospatial Memory Test—Revised, (8) Category Fluency (Animal Naming), (9) Mayer-Salovey-Caruso Emotional Intelligence Test: Managing Emotions, and (10) Continuous Performance Test—Identical Pairs. The age- and gender-corrected

**Table 1.** Sample Characteristics

Patients ( <i>n</i> = 150 <sup>a</sup> )	
Mean age (SD)	38.8 (13.5)
Mean education (SD)	12.8 (1.9)
Gender (%)	
Male	79
Marital status (%)	
Single	79
Married	6
Divorced	15
Race (%)	
Caucasian	32
African-American	32
Latino	21
Asian/Pacific Islander	6
Other	9
Diagnosis (%)	
Schizophrenia	76
Schizoaffective	22
Schizophreniform	2
Mean number of years since psychosis onset (SD)	15.0 (12.4)
Mean BPRS symptom ratings at baseline <sup>b</sup> (SD)	
Reality distortion	3.0 (1.7)
Disorganization	1.6 (0.8)
Negative symptoms	2.2 (1.1)
Depression	2.5 (1.3)
Informants ( <i>n</i> = 150)	
Mean age (SD)	47.0 (11.9)
Gender (%)	
Female	75
Relationship to patient (%)	
Mother	20
Father	6
Brother/sister	8
Son/daughter	1
Spouse/significant other	5
Friend	9
Professional (eg, case manager)	51

Note: BPRS, Brief Psychiatric Rating Scale.

<sup>a</sup>For study analyses that involved multiple variables, pairwise analyses were performed and so the number of subjects might be lower than *n* = 150.

<sup>b</sup>All symptom domains were in the mild range and typically below clinically significant levels, range: 1–7.

composite *t* score was the dependent variable. Higher scores indicate better performance.

#### *UCSD Performance-Based Skills Assessment-Version 2.*

The UPSA-2<sup>8</sup> is a functional capacity measure of 5 general skills that were previously identified as essential to functioning in the community: organization/planning,

finance, communication, transportation, and household management. Subjects were also administered the Medication Management Ability Assessment<sup>22</sup> as part of the UPSA-2 assessment. This assessment involves role-play tasks that are simulations of situations that the person may encounter in the community. The dependent variable was the total score. Higher scores indicate better performance.

#### *Symptom Assessment Ratings*

Symptom assessments which were conducted by trained raters included the Brief Psychiatric Rating Scale (BPRS)<sup>23</sup> and were clustered into 4 symptom domains<sup>24,25</sup>: Reality distortion (hallucinations and delusions), disorganization (conceptual disorganization, bizarre behavior, and mannerisms and posturing), negative symptoms (blunted affect, motor retardation, and emotional withdrawal), and depression-anxiety (anxiety, depression, and guilt). Higher ratings reflect a greater severity of symptoms.

#### *Measurement of Functional Outcome, Insight into Cognition, and Perceived Family Burden*

*UCLA Social Attainment Survey.* The UCLA Social Attainment Survey (SAS) is an interview-based measure containing seven 5-point anchored ratings on different components of social functioning, with higher scores reflecting better functioning.<sup>26</sup> The domains covered include number and closeness of same-sex peer relationships, emotional involvement in opposite-sex peer relationships, leadership in same-sex relationships, dating and sexual history, initiation of recreational and social activities, and participation in organizations or social clubs. A “Social Functioning” factor was created by factor analysis using the patient sample data and then taking the mean of the factor score which included the following items: Same-Sex Peer Relationships, Leadership in Same-Sex Peer Relationships, and Initiation of Recreational and Social Activities.

*Strauss-Carpenter Level of Functioning Scale.* The Level of Functioning Scale is an interview-based measure containing 9 items that measure psychosocial, occupational, and symptom adjustment in psychiatric populations.<sup>27,28</sup> The scale assesses the frequency and quality of social contacts, quantity and quality of useful work, independent living, symptom severity, fullness of life, extent of recent psychiatric hospitalizations, and overall level of functioning. The items are rated using 4-point anchored scale, with higher scores reflecting better functioning. A “Work Functioning” score was created by taking the mean of the quantity and quality of useful work items. An “Overall Functioning” score was created by taking the mean of all items except symptom severity.

*The Subjective Scale to Investigate Cognition in Schizophrenia.* The Subjective Scale to Investigate Cognition in Schizophrenia (SSTICS) is a 21-item self-report questionnaire aimed at exploring cognitive complaints and difficulties that patients could experience in everyday life.<sup>29</sup> The questions address cognitive dimensions that have been reported to be impaired in schizophrenia. The total score was the dependent variable. Higher scores reflect greater unawareness of cognitive deficits.

*Perceived Family Burden Scale.* The Perceived Family Burden Scale (PFBS) was designed to assess the impact of patient behaviors on relatives.<sup>30</sup> This interview-based scale was administered to informants only and consists of 24 items which are each rated for the presence or absence of a behavior associated with schizophrenia. These items are also rated for the extent to which the behavior is distressing to the relative. When the informant was a professional, the measure was completed based on interviews and clinical knowledge of constructs assessed by the PFBS. The total score was the dependent variable of interest in the current study. Higher scores reflect a greater degree of family burden.

## **Results**

### *Patient and Informant Sample Characteristics*

A total of 175 participants with schizophrenia completed a patient CAI assessment. Of those cases, 25 (14%) did not have an accompanying CAI informant assessment. Of the resulting 150 patients, a total of 4 (2.7%) participants were missing either an MCCB or a UPSA, leaving a total of 146 participants with a complete CAI, MCCB, and UPSA. There were no statistically significant differences in the mean CAI patient scores with or without an informant ( $M = 2.99$  and  $M = 2.77$ , respectively;  $P < .20$ ). Those 146 cases were subjected to pairwise correlational analyses. A total of 136 subjects returned for 4-week follow-up assessments. Subjects were comparable to other samples of schizophrenia patients in clinical trials in age and symptom severity<sup>4,31</sup> and were clinically stable over the course of the study; the mean BPRS score was 2.00 (SD = 0.56) at baseline and 1.99 (SD = 0.55) at 1 month ( $t = 0.45$ ,  $df = 123$ ,  $P = .65$ ). The mean MCCB composite score at baseline was 29.2 (SD = 12.5), indicating that the sample was very comparable to the MATRICS-VIM study sample ( $M = 27.9$ , SD = 11.4).<sup>7</sup> At baseline, the mean CAI administration time was 15.7 minutes for the patient assessment and 15.2 minutes for the informant assessment, for a total administration time of 30.9 minutes.

### *Reliability of the CAI*

The internal consistency and test-retest reliability of the CAI were good to excellent. The 10 individual CAI rater scores correlated highly with the total CAI score



**Table 2.** Correlations Between the Individual CAI Rater Items, Patient Total Score, Informant Total Score, and Rater Total Score With the Total CAI Score ( $N = 150$ )

CAI Rater Items	$r$
Working memory	
Difficulty maintaining newly learned information	.80
Difficulty performing on the spot mental manipulations	.66
Attention vigilance	
Difficulty sustaining concentration over time	.74
Difficulty focus on selected information (without distraction)	.80
Verbal learning and memory	
Trouble Learning and remembering verbal information	.81
Difficulty recalling recent events	.77
Reasoning and problem solving	
Lack of flexibility in generating alternative plans when needed	.74
Problems in situations requiring judgment	.73
Speed of processing	
Performs tasks slowly	.71
Social cognition	
Difficulty appreciating another person's intentions or point of view	.73
Patient total	.89
Informant total	.93
Rater total	.99

Note: CAI, Cognitive Assessment Interview.

( $r$ 's range from .66 to .81), as did the patient, informant, and rater total ratings (table 2). Good internal consistency was found for the baseline CAI patient, informant, and rater scores (Cronbach's  $\alpha$ 's range from .87 to .92; table 3). Test-retest reliability for the CAI using data collected at baseline and at the 1-month follow-up point was excellent (ICC's range from .79 to .84; table 3). The magnitude of the differences (Cohen's  $d$ ) from baseline to the 1-month assessment was very small, indicating little or no practice effects for the patient ( $d = -0.11$ ), informant ( $d = -0.07$ ), and CAI rater score ( $d = -0.07$ ; table 3).

**Table 3.** Baseline and 1-Month Reliability Data for the 10-item CAI

CAI Ratings	Cronbach's Alpha (At Baseline), $n = 150$	Reliability (ICC) (Test-Retest), $n = 93$	Cohen's $d$ (Test-Retest), $N = 93$
CAI patient	.87	.79	-0.11
CAI informant	.92	.84	-0.07
CAI rater	.92	.83	-0.07

Note: CAI, Cognitive Assessment Interview.

### Validity of the CAI

The correlations between the mean patient, informant, and CAI rater scores were very high and comparable to our previous studies (table 4). The correlations indicated that the mean patient score and mean rater score were highly correlated ( $r = .86$ ), as were the mean informant and mean rater score ( $r = .91$ ). Although the mean patient and mean informant ratings had a slightly lower correlation ( $r = .70$ ), the Rater score did not appear to gain a great deal of additional information from the availability of nonredundant informant input. Therefore, although the interviewer tended to be somewhat influenced by the informant, a CAI rater could conduct a valid assessment with the patient information alone (table 4).

An important consideration for evaluating the concurrent validity of coprimary measures is the degree to which they correlate with cognitive performance, functional capacity, and functional outcome but not with psychiatric symptoms. Correlations between the mean CAI scores and the composite MCCB score were in the expected direction and moderate (table 5). The CAI was modestly correlated with the UPSA total score (table 5). Interestingly, there were no differences between the CAI patient and CAI informant rating in relationship to the MCCB ( $z = 0.30$ ,  $P > .75$ ) or the UPSA ( $z = 0.83$ ,  $P > .40$ ). Consistent with previous studies, the MCCB composite score ( $M = 29.5$ ,  $SD = 12.9$ ) was found to be highly correlated with the UPSA total score ( $M = 84.3$ ,  $SD = 16.2$ ;  $r = .68$ ). In addition, the CAI was moderately to highly correlated with social functioning, work functioning, and overall functional outcome (table 5). The patient CAI ratings were more highly correlated with overall functional outcome than was the MCCB ( $z = 1.99$ ,  $P < .05$ ) and the UPSA ( $z = 1.99$ ,  $P < .05$ ). Regarding divergent validity, the correlations between the CAI and symptom ratings were comparable to the correlations between the CAI and the MCCB and UPSA, except for positive symptoms, which were somewhat higher (table 5).<sup>32,33</sup>

### Correlations Between the CAI, Patient Insight into Cognition, and Caregiver Burden

The CAI ratings were moderately correlated with the patient's insight into his or her cognitive deficits as measured by the SSTICS, with higher correlations found for the patient and rater as compared with the informant (table 5). Also, there were modest to moderate

**Table 4.** Relationships Among the Mean CAI Patient, Informant, and Rater Scores (*n* = 150)

	CAI patient	CAI informant	CAI rater
CAI patient	1.0	0.70**	0.86**
CAI informant		1.0	0.91**
CAI rater			1.0

Note: CAI, Cognitive Assessment Interview.  
\*\**P* < .01.

correlations between the CAI and caregiver burden as measured by the PFBS. These correlations were higher when considering the informant’s score (table 5).

**Discussion**

The CAI is a semi-structured interview-based measure of cognitive functioning derived using modern statistics, eg, IRT, from 2 instruments, the CGI-CogS and the SCoRS.<sup>3,6</sup> In this study, consistent with our previous findings,<sup>3</sup> the CAI had good psychometric properties including excellent internal consistency, high item-to-scale correlations, and excellent test-retest reliability, with little or no practice effects. CAI scores were moderately correlated with objective measures of neurocognition and with functional outcomes. Indeed, the CAI was statistically more strongly related to functional outcome than the MCCB or the UPSA even though the latter test was designed to measure functional capacity and thus was putatively more closely linked to functional outcomes. Consistent with our previous findings, the CAI patient-only ratings were as reliable and valid as ratings that included an informant. Using patient-only informa-

tion, raters can thus derive a valid and reliable score on the CAI in about 15 minutes. Given the CAI’s high reliability and low practice effects, the CAI seems ideally suited for repeated assessments in research settings including in clinical trials. The CAI is a brief measure but not at the expense of a weaker correlation with neurocognition or functional outcome. The CAI meets most criteria to be recommended for use as a coprimary measure in clinical trials that aim to evaluate cognition-enhancing drugs or procognitive interventions in schizophrenia patients.<sup>4,34</sup>

Several potential coprimary measures for the MCCB were evaluated in the MATIRCS–VIM study including the UPSA, TABS, and the CAI. Ultimately, the UPSA and the TABS met the criterion of being correlated well with objective neurocognition and were selected.<sup>7</sup> The Committee’s decision not to endorse the CAI was because of the low correlation with neurocognition (*r* = .23). However, the UPSA has been moderately to highly and consistently correlated with the MCCB in previous studies, eg, *r* = .67<sup>7,11,12,35,36</sup> as well as in the current study (*r* = .68). This calls into question whether the UPSA or the TABS really provides a separate coprimary end point because of the amount of overlap in these types of assessments with cognition. The VIM committee decided to recommend rather than require the UPSA and the TABS, leaving room to explore interview-based measures such as the CAI or the SCoRS as another option. In fact, the SCoRS was found more responsive to antipsychotic treatment than the MCCB, indicating the promise for sensitivity to intervention of interview-based measures.<sup>37</sup> Perhaps the development of nonperformance-based measures of cognitive functioning should include the relationship to functional outcome? Interestingly, in the VIM study, the CAI was just as strongly correlated with the functional outcome as was the UPSA and the

**Table 5.** Correlations Between the CAI, Neurocognition, and Functional Capacity With Patient Lack of Insight into Cognition, Caregiver Burden, and Functional Outcomes and Symptoms

	CAI Patient	CAI Informant	CAI Rater	Neurocognition (MCCB)	Functional Capacity (UPSA)
Neurocognition ( <i>n</i> = 146)	−0.39**	−0.41**	−0.40**	1.00	0.68**
Functional capacity ( <i>n</i> = 146)	−0.25**	−0.34**	−0.30**	0.68**	1.00
Social functioning ( <i>n</i> = 133)	−0.35**	−0.36**	−0.38**	0.19	0.23
Work functioning ( <i>n</i> = 133)	−0.46**	−0.49**	−0.48**	0.28	0.16
Overall functioning ( <i>n</i> = 133)	−0.50**	−0.48**	−0.49**	0.29	0.29
Reality distortion ( <i>n</i> = 139)	0.32**	0.33**	0.33**	−0.19*	−0.07
Disorganization ( <i>n</i> = 139)	0.31**	0.32**	0.35**	−0.20*	−0.19
Depression-anxiety ( <i>n</i> = 139)	0.16*	0.02*	0.08	−0.06	−0.07
Negative symptoms ( <i>n</i> = 139)	0.18**	0.23**	0.27**	−0.18**	−0.06
Patient’s lack of insight into cognition ( <i>n</i> = 111)	0.37**	0.19**	0.27**	−0.30**	−0.04
Caregiver burden ( <i>n</i> = 111)	0.25**	0.43**	0.37**	−0.23*	−0.20*

Note: CAI, Cognitive Assessment Interview; MCCB, MATRICS Consensus Cognitive Battery; UPSA, Performance-based Skills Assessment.

\*\**P* < .01, \**P* < .05.

TABS ( $r = .27$ ,  $r = .25$ , and  $r = .23$ , respectively). Compared with our previous study,<sup>3</sup> field testing shows stronger relationships between the current version of the CAI ( $r$ 's =  $-.38$  to  $-.49$ ) as compared with the CAI that was embedded in 2 original instruments ( $r$ 's =  $-.27$  to  $-.32$ ). Interview-based measures might measure valuable yet different information from neurocognitive testing and functional capacity assessments. However, as we have stated previously, despite the advantages of the CAI, this method of rating cognitive functioning is not meant to be a substitute for objective cognitive testing.

As a coprimary measure, the CAI has the potential for evaluating whether a cognitive-based intervention or a drug improves the daily lives of people with schizophrenia. The correlation with insight indicates that, most likely, patients who have some insight into their cognitive deficits are more likely to be able to report how cognitive deficits influence their functioning. This underscores a basic staple of interview-based measures, ie, the rater cannot rely on patient self-report only, but should instead use all available information. This includes observations of the patient's behavior and an expert judgment of the patient's report of cognitive functioning. The current study supports the notion that CAI ratings might be more valid when patients have insight into their cognitive deficits. Because not all patients have insight, raters might benefit from some clinical rater training in evaluating a patient's report of his or her cognitive functioning. We found that CAI informant ratings were correlated with the degree of caregiver burden as assessed by the PFBS. This suggests the CAI is capturing whether the patient's level of real-world functioning is burdensome to family members.

Although this study has several strengths, there are limitations, several of which have already been discussed.<sup>3</sup> The study was conducted by the team who developed the CAI. The results might differ in settings where the CAI is administered by outside research groups. The fact that the CAI correlates moderately with functional outcomes might to some extent be because both the CAI and measures of functional outcome use an interview-based approach to collect data, and functional domains are part of the CAI's anchors. However, both types of assessment require evaluation by the interviewer about the accuracy of the information collected from the patient. Patients whose poor functioning is not related to poor cognition were not rated as impaired on the CAI. Also, this sample might not be fully representative of the United States as a whole. Finally, a practical limitation is that the study was not a treatment trial and was not designed to assess the sensitivity of the CAI to change in the context of "actual" cognitive change or improvement.

For the future, we need to continue improving the method of interviewing patients about their cognitive functioning if we want to rely on patient-only assessments. Raters should be aware that informants might

have a perspective that is different from the patient's, even if an informant is ultimately not assessed when interviewing patients. Rating cognition on the CAI requires the use of "expert" judgment and should not rely on the patient's self-report alone because many patients lack insight into their cognitive deficits.<sup>38,39</sup> Future work should examine whether patient-reported functional outcome might show reduced reliability and validity in patients with very poor cognitive functioning. Also, more needs to be understood regarding how symptoms, cognition, and daily functioning overlap to clarify the underlying construct measured with interview-based assessments. A critical future direction for the CAI includes determining empirically whether this instrument is sensitive to clinically meaningful cognitive change in response to a pharmacologic or cognitively oriented nonpharmacological intervention.

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### References

1. Burke L, Stifano T, Dawish S. *Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims*. Rockville, MD: U.S. Department of Health and Human Services Food and Drug Administration; 2006.
2. Keefe RS, Poe M, Walker TM, Kang JW, Harvey PD. The Schizophrenia Cognition Rating Scale: an interview-based assessment and its relationship to cognition, real-world functioning, and functional capacity. *Am J Psychiatry*. 2006;163:426-432.
3. Ventura J, Reise SP, Keefe RSE, et al. The Cognitive Assessment Interview (CAI): development and validation of an empirically derived, brief interview-based measure of cognition. *Schizophr Res*. 2010;121:24-31.
4. Green MF, Nuechterlein KH, Kern RS, et al. Functional coprimary measures for clinical trials in schizophrenia: results

- from the MATRICS Psychometric and Standardization Study. *Am J Psychiatry*. 2008;165:221–228.
5. Ventura J, Cienfuegos A, Boxer O, Bilder R. Clinical global impression of cognition in schizophrenia (CGI-CogS): reliability and validity of a co-primary measure of cognition. *Schizophr Res*. 2008;106:59–69.
  6. Reise SP, Ventura J, Keefe RSE, et al. Bifactor and item response theory analyses of interviewer report scales of cognitive impairment in schizophrenia. *Psychol Assess*. 2011;23:245–261.
  7. Green MF, Schooler NR, Kern RS, et al. Evaluation of functionally meaningful measures for clinical trials of cognition enhancement in schizophrenia. *Am J Psychiatry*. 2011;168:400–407.
  8. Patterson TL, Goldman S, McKibbin CL, Hughs T, Jeste DV. UCSD Performance-Based Skills Assessment: development of a new measure of everyday functioning for severely mentally ill adults. *Schizophr Bull*. 2001;27:235–245.
  9. Velligan DI, Diamond P, Glahn DC, et al. The reliability and validity of the Test of Adaptive Behavior in Schizophrenia (TABS). *Psychiatry Res*. 2007;151:55–66.
  10. Nuechterlein KH, Green MF. *MATRICS Consensus Cognitive Battery*. Los Angeles, CA: MATRICS Assessment, Inc.; 2006.
  11. Bowie CR, Reichenberg A, Patterson TL, Heaton RK, Harvey PD. Determinants of real-world functional performance in schizophrenia subjects: correlations with cognition, functional capacity, and symptoms. *Am J Psychiatry*. 2006;163:418–425.
  12. Bowie CR, Leung WW, Reichenberg A, et al. Predicting schizophrenia patients' real-world behavior with specific neuropsychological and functional capacity measures. *Biol Psychiatry*. 2008;63:505–511.
  13. Chia MY, Chan WY, Chua KY, et al. The Schizophrenia Cognition Rating Scale: validation of an interview-based assessment of cognitive functioning in Asian patients with schizophrenia. *Psychiatry Res*. 2010;178:33–38.
  14. Jungwirth S, Fischer P, Weissgram S, Kirchmeyer W, Bauer P, Tragl KH. Subjective memory complaints and objective memory impairment in the Vienna Transdanube aging community. *J Am Geriatr Soc*. 2004;52:263–268.
  15. Moritz S, Ferahli S, Naber D. Memory and attention performance in psychiatric patients: lack of correspondence between clinician-rated and patient-rated functioning with neuropsychological test results. *J Int Neuropsychol Soc*. 2004;10:623–633.
  16. Prouteau A, Verdoux H, Briand C, et al. Self-assessed cognitive dysfunction and objective performance in outpatients with schizophrenia participating in a rehabilitation program. *Schizophr Res*. 2004;69:85–91.
  17. Farias ST, Mungas D, Jagust W. Degree of discrepancy between self and other reported everyday functioning by cognitive status: dementia, mild cognitive impairment, and healthy elders. *Int J Geriatr Psychiatry*. 2005;20:827–834.
  18. First MB, Gibbon M, Spitzer RL, Williams JBW. *Structured Clinical Interview for DSM-IV Axis I Disorders. Patient Edition*. New York, NY: Biometrics Research; 1996.
  19. Ventura J, Liberman RP, Green MF, Shaner A, Mintz J. Training and quality assurance with the Structured Clinical Interview for DSM-IV(SCID-I/P). *Psychiatry Res*. 1998;79:163–173.
  20. Ventura J, Green MF, Shaner A, Liberman RP. Training and quality assurance on the Brief Psychiatric Rating Scale: the “drift busters”. *Int J Methods Psychiatr Res*. 1993;3:221–226.
  21. Nuechterlein KH, Green MF, Kern RS, et al. The MATRICS Consensus Cognitive Battery, part 1: test selection, reliability, and validity. *Am J Psychiatry*. 2008;165:203–213.
  22. Patterson TL, Lacro J, McKibbin CL, Moscona S, Hughs T, Jeste DV. Medication management ability assessment: results from a performance-based measure in older outpatients with schizophrenia. *J Clin Psychopharmacol*. 2002;22:11–19.
  23. Ventura J, Lukoff D, Nuechterlein KH, Liberman RP, Green MF, Shaner A. Brief Psychiatric Rating Scale (BPRS) expanded version: scales, anchor points, and administration manual. *Int J Methods Psychiatr Res*. 1993;3:227–243.
  24. Ventura J, Nuechterlein KH, Subotnik KL, Gutkind D, Gilbert EA. Symptom dimensions in recent-onset schizophrenia and mania: a principal components analysis of the 24-item Brief Psychiatric Rating Scale. *Psychiatry Res*. 2000;97:129–135.
  25. Andreasen NC, Carpenter WT, Jr, Kane JM, Lasser RA, Marder SR, Weinberger DR. Remission in schizophrenia: proposed criteria and rationale for consensus. *Am J Psychiatry*. 2005;162:441.
  26. Goldstein MJ. Further data concerning the relation between premorbid adjustment and paranoid symptomatology. *Schizophr Bull*. 1978;4:236–241.
  27. Strauss JS, Carpenter WT. The prediction of outcome in schizophrenia, I: characteristics of outcome. *Arch Gen Psychiatry*. 1972;27:739–746.
  28. Strauss JS, Carpenter WT. Prediction of outcome in schizophrenia, III: five-year outcome and its predictors. *Arch Gen Psychiatry*. 1977;34:159–163.
  29. Stip E, Caron J, Renaud S, Pampoulova T, Lecomte Y. Exploring cognitive complaints in schizophrenia: the subjective scale to investigate cognition in schizophrenia. *Compr Psychiatry*. 2003;44:331–340.
  30. Levene JE, Lancee WJ, Seeman MV. The perceived family burden scale: measurement and validation. *Schizophr Res*. 1996;22:151–157.
  31. Lieberman JA, Stroup TS, McEvoy JP, et al. Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med*. 2005;353:1209–1223.
  32. Ventura J, Hellemann GS, Thames AD, Koellner V, Nuechterlein KH. Symptoms as mediators of the relationship between neurocognition and functional outcome in schizophrenia: a meta-analysis. *Schizophr Res*. 2009;113:189–199.
  33. Ventura J, Thames AD, Wood RC, Guzik LH, Hellemann GS. Disorganization and reality distortion in schizophrenia: a meta-analysis of the relationship between positive symptoms and neurocognitive deficits. *Schizophr Res*. 2010;121:1–14.
  34. Buchanan RW, Davis M, Goff D, et al. A summary of the FDA-NIMH-MATRICES workshop on clinical trial design for neurocognitive drugs for schizophrenia. *Schizophr Bull*. 2005;31:5–19.
  35. Harvey PD, Keefe RS, Patterson TL, Heaton RK, Bowie CR. Abbreviated neuropsychological assessment in schizophrenia: prediction of different aspects of outcome. *J Clin Exp Neuropsychol*. 2009;31:462–471.
  36. Keefe RSE, Fox KH, Harvey PD, Cucchiari J, Siu C, Loebel A. Characteristics of the MATRICS Consensus Cognitive Battery in a 29-site antipsychotic schizophrenia clinical trial. *Schizophr Res*. 2011;125:161–168.
  37. Harvey PD, Ogasa M, Cucchiari J, Loebel A, Keefe RSE. Performance and interview-based assessments of cognitive



- change in a randomized, double-blind comparison of lurasidone vs. ziprasidone. *Schizophr Res.* 2011;127:188–194.
38. Medalia A, Thysen J. Insight into neurocognitive dysfunction in schizophrenia. *Schizophr Bull.* 2008;34:1221–1230.
39. Medalia A, Thysen J, Freilich B. Do people with schizophrenia who have objective cognitive impairment identify cognitive deficits on a self report measure? *Schizophr Res.* 2008;105:156–164.