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Neurocognitive insight and objective cognitive functioning in schizophrenia

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ABSTRACT

Neurocognitive impairment is a core component of schizophrenia affecting everyday functioning; the extent to which individuals with schizophrenia show awareness of neurocognitive impairment (neurocognitive insight) is unclear. This study investigated neurocognitive insight and examined the cross-sectional relationships between neurocognitive insight and objective neurocognition and functional capacity performance in a large outpatient sample.

214 participants with schizophrenia-spectrum disorders completed measures of neurocognition, functional capacity, and self-reported neurocognitive problems. Latent profile analysis classified participants with regard to neuropsychological performance and self-report of neurocognitive problems. The resulting classes were then compared on executive functioning performance, functional capacity performance, and psychiatric symptom severity.

More than three quarters of the sample demonstrated objective neurocognitive impairment (global deficit score ≥ 0.50). Among the participants with neurocognitive impairment, 54% were classified as having “impaired” neurocognitive insight (i.e., reporting few neurocognitive problems despite having objective neurocognitive impairment). Participants with impaired vs. intact neurocognitive insight did not differ on executive functioning measures or measures of functional capacity or negative symptom severity, but those with intact neurocognitive insight reported higher levels of positive and depressive symptoms.

A substantial portion of individuals with schizophrenia and objectively measured neurocognitive dysfunction appear unaware of their deficits. Patient self-report of neurocognitive problems, therefore, is not likely to reliably assess neurocognition. Difficulty self-identifying neurocognitive impairment appears to be unrelated to executive functioning, negative symptoms, and functional capacity. For those with intact neurocognitive insight, improving depressive and psychotic symptoms may be a valuable target to reduce illness burden.

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1. Introduction

Little doubt remains regarding the significance of cognitive dysfunction in schizophrenia. Empirical evidence has consistently demonstrated stable, enduring deficits in attention, processing speed, working memory, learning, and executive function (Heaton et al., 2001; Heinrichs and Zakzanis, 1998), and that domain-specific deficits are

relative and exist against a backdrop of generalized dysfunction (Heinrichs and Zakzanis, 1998). Furthermore, a critical link has been identified between cognitive impairment and functional outcome; that is, neuropsychological dysfunction affects performance of real-world everyday activities that are necessary to live independently in the community (Green et al., 2000).

Several types of insight, or awareness of dysfunction, have been described in schizophrenia. Clinical insight refers to awareness of psychotic illness (Amador et al., 1993). Metacognition is a broad term that generally refers to “thinking about thinking”; conceptually, it is related to but not synonymous with neurocognition (Lysaker et al., 2011a). Two subtypes of metacognition include cognitive insight, which refers to awareness of “mistakes in thinking” such as jumping to conclusions or catastrophizing (Beck et al., 2004), and neurocognitive insight,

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defined as awareness of neuropsychological dysfunction (e.g., impaired attention, memory, problem-solving) (Medalia and Thysen, 2008) expressed through subjective cognitive complaints (Stip et al., 2003).

The domains of clinical and cognitive insight in schizophrenia and their relationships with neurocognition have been extensively investigated (Nair et al., 2014). For example, several studies demonstrated that greater clinical and cognitive insight was associated with better executive functioning (Aleman et al., 2006; Burton et al., 2011; Larøi et al., 2000; Medalia and Thysen, 2010; Monteiro et al., 2008; Mysore et al., 2007; Orfei et al., 2010; Shad et al., 2004; Simon et al., 2009), lending support to the view that poor insight in schizophrenia may be a function of specific prefrontally-mediated neurocognitive deficits rather than a global deficit in neuropsychological functioning (Shad et al., 2004).

Clinical and cognitive insight have also been studied in relation to psychiatric symptomatology and functioning. Better clinical insight is modestly associated with less severe positive and negative symptoms but more severe depressive symptoms (Mintz et al., 2003; McEvoy et al., 2006; Sabbag et al., 2012; Wiffen et al., 2010). Some data suggest that good cognitive insight is related to less severe positive symptoms (Bora et al., 2007; but see also Greenberger and Serper, 2010). In terms of functioning, good clinical insight is associated with improved functional skills ratings (Schwartz et al., 1997).

There is less known about neurocognitive insight. Instruments to directly measure neurocognitive insight have been created to assess awareness of cognitive deficits in comparison to actual performance on cognitive tests, as well as to allow reliable measurement of patients' or caregivers' opinions about a patient's degree of neurocognitive deficit (Keefe et al., 2006; Medalia and Thysen, 2010; Stip et al., 2003). Although the literature on neurocognitive insight is limited, there is some evidence that individuals with schizophrenia have poorer insight into their neurocognitive symptoms than their clinical symptoms, prompting researchers to encourage that they be addressed separately in treatment (Medalia and Thysen, 2010). For example, a 2011 review indicated that 14 of 26 published studies found no correlation between objective cognitive performance and subjective cognitive complaints (Homayoun et al., 2011). Another study reported that 95% of participants were cognitively impaired, though more than half of the sample had no awareness of cognitive dysfunction (Medalia and Thysen, 2008). Still other researchers have concluded that even when patients express cognitive difficulties, their specific complaints do not align with the cognitive domains tested (Prouteau et al., 2004). To date, no consistent evidence has emerged to suggest that neurocognitive insight or self-reported cognitive functioning converges with objective global or composite cognitive performance (Durand et al., 2015; Gould et al., 2015; Johnson et al., 2011; Keefe et al., 2006, 2015; Medalia et al., 2008; Medalia and Lim, 2004; Moritz et al., 2004; Poletti et al., 2012; Saperstein et al., 2012). Surprisingly few studies have examined the link between neurocognitive insight and executive functioning specifically; those that did reported negative findings from relatively small samples using one subtest from the same cognitive battery (Brief Assessment of Cognition Scale) (Medalia and Thysen, 2008; Poletti et al., 2012).

Similarly, the relationship between neurocognitive insight and everyday functioning has not been extensively examined; in a previous analysis of this database, greater discrepancies between self-reported and clinician-rated cognitive functioning were associated with poorer everyday outcomes as rated by clinicians (Gould et al., 2015). Another published study determined that metacognitive mastery was associated with functional competence in comprehension/planning (Lysaker et al., 2011b).

Despite the apparent lack of association between neurocognitive insight and objective global cognitive performance, numerous studies have demonstrated that greater self-report of cognitive problems is significantly related to increased depression and anxiety (Durand et al., 2015; Medalia et al., 2008; Moritz et al., 2004; Sabbag et al., 2012; Saperstein et al., 2012). The relationship between neurocognitive

insight and negative symptoms has not been fully examined; one study suggested no significant relationship (Medalia and Thysen, 2010). Furthermore, a recent study showed that higher rates of self-reported cognitive complaints were associated with lower treatment utilization, suggesting that clinicians may need to target those at risk for drop out with more intensive follow-up care, compensatory strategies, and psychoeducation (Gooding et al., 2012).

In summary, despite the known cognitive dysfunction associated with schizophrenia, the extent to which affected individuals show awareness of such impairment is unclear as are its performance-based correlates. The aims of this study were to explore neurocognitive insight among a large, multi-site sample of individuals diagnosed with schizophrenia and demonstrating objective cognitive impairment, and to evaluate cross-sectional relationships between neurocognitive insight and objective cognitive and functional capacity performance. Given the equivocal evidence regarding the relationship between insight and executive functioning, the first hypothesis was that participants with impaired neurocognitive insight would demonstrate domain-specific impairment in executive functioning. We also hypothesized that participants with impaired neurocognitive insight would demonstrate poorer functional capacity, and that individuals with impaired neurocognitive insight would have more severe negative symptoms but less severe depressive symptoms (Sabbag et al., 2012).

2. Method

2.1. Participants

These analyses were conducted as part of the larger Validating Everyday Real-World Outcomes Study (VALERO) Phase II, which aimed to identify the determinants of impaired self-assessment in schizophrenia. Participants included 214 individuals diagnosed with schizophrenia or schizoaffective disorder receiving outpatient care at one of three sites: UCSD Outpatient Psychiatric Services ($n = 100$), the University of Miami Miller School of Medicine ($n = 79$), and Skyland Trail Rehabilitation Services in Atlanta ($n = 35$). Participants were enrolled in the VALERO II parent study that was approved by each site's institutional review board. On average, participants were 41 years old and had completed 12 years of education; the majority of the sample was male, Caucasian, diagnosed with schizophrenia, and prescribed antipsychotic medication (Table 1).

Table 1

Demographic and clinical features of the full sample and the neurocognitively impaired sample.

	Full sample ($n = 214$)	Neurocognitively impaired sample ($n = 168$)
	Mean (SD) or %	Mean (SD) or %
Age, years	41.2 (12.4)	42.7 (12.3)
Education, years	12.3 (2.2)	12.1 (2.1)
% male	65.4	67.3
% Caucasian	54.7	51.2
% Hispanic ethnicity	23.4	21.4
% African American	36.0	40.5
% schizophrenia (vs. schizoaffective)	58.2	63.0
% prescribed antipsychotic medication	98.1	98.2
% living independently	73.3	72.6
% employed	9.8	10.1
% never married	53.2	50.3
PANSS positive symptoms total	15.7 (5.5)	16.1 (5.7)
PANSS negative symptoms total	15.7 (6.1)	16.2 (6.3)
BDI-II total	15.3 (11.7)	15.0 (11.6)

Note. BDI-II = Beck Depression Inventory, second edition; PANSS = Positive and Negative Syndrome Scale.

2.2. Procedures

Potential participants were referred to the study by treating clinicians or self-response to recruitment flyers posted in psychiatric care centers; all participants provided written informed consent prior to any data collection. Participants' diagnoses were confirmed via structured diagnostic interview (Mini International Neuropsychiatric Interview) (Sheehan et al., 1998) administered by a trained research assistant. Inclusion criteria were: (a) age between 18 and 65, (b) DSM-IV diagnosis of schizophrenia or schizoaffective disorder, (c) English-speaking, and (d) minimum 8th grade reading level. Patients were excluded if they had (a) history of unconsciousness greater than 10 min, (b) a seizure disorder or other neurological condition affecting cognition, (c) current substance abuse or dependence, (d) for patients aged 55 or older, a score less than 27 on the Mini Mental State Exam (Folstein et al., 2001). Participants completed a one-time comprehensive neuropsychological, clinical, and functional battery.

2.3. Measures

Premorbid intellectual functioning was measured with the reading subtest of the Wide Range Achievement Test – Third Edition (Wilkinson, 1993). Psychiatric symptom severity was measured with the Positive and Negative Syndrome Scale (Kay et al., 1987) and the Beck Depression Inventory – II (Beck et al., 1996). Self-reported frequency of cognitive problems was measured with the Measure of Insight into Cognition – Self-Rated (MIC-SR) (Medalia et al., 2008). The MIC-SR consists of twelve statements about attention, executive functioning, and memory (e.g., “I have trouble listening and paying attention”; “I have difficulty thinking through possible solutions to problems”) rated by respondents in terms of frequency: never, once a week or less, twice a week, or almost daily. The maximum score is 36; higher scores indicate greater frequency of cognitive problems.

Current cognitive functioning was measured with a modified version of the MATRICS Consensus Cognitive Battery (MCCB) (Nuechterlein et al., 2008); the social cognition measure was excluded from the VALERO trial due to concern that social cognition measures would differ from neurocognitive measures in terms of their relationship to everyday functioning. The other nine subtests of the MCCB measured six neurocognitive domains, as follows:

1. Speed of processing (Trail Making Test, Part A; Brief Assessment of Cognition in Schizophrenia Symbol Coding subtest; Category Fluency Test, animal naming)
2. Attention/vigilance (Continuous Performance Test – Identical Pairs Version [CPT-IP])
3. Working memory (Wechsler Memory Scale, 3rd edition, Spatial Span subtest; Letter–Number Span test)
4. Verbal learning (Hopkins Verbal Learning Test – Revised, immediate recall)
5. Visual learning (Brief Visuospatial Memory Test – Revised, immediate recall)
6. Reasoning and problem solving (Neuropsychological Assessment Battery, Mazes subtest)

Because phase II of the VALERO trial explored impaired self-assessment in schizophrenia, a metacognitive version of the Wisconsin Card Sorting Test (WCST) was also included to measure executive functioning (Koren et al., 2004). In this task, the WCST is administered following the standardized instructions; however, prior to receiving feedback about the accuracy of the sort, participants are asked to (1) rate their confidence in the correctness of that sort on a “0” (guessing) to “100” (completely confident) scale, and (2) decide whether they do or do not want that sort to be “counted” toward their overall performance score on the test. Several key metacognitive variables can be derived; for example, the accuracy score is calculated as the number of correct sorts out of the total number of volunteered sorts.

Everyday functional skills were evaluated with the UCSD Performance-based Skills Assessment, Brief version (UPSA-B) (Mausbach et al., 2007), in which participants perform everyday tasks related to finance (e.g., write a check to pay a utility bill), and communication (e.g., call a doctor to reschedule an appointment). The UPSA-B takes 10–15 min to administer and yields raw subscale scores as well as raw scores that are converted into a total score ranging from 0 to 100, with higher scores indicating better functional capacity.

2.4. Analyses

All continuous variables were normally distributed. To first identify participants with objective neurocognitive impairment, a global deficit score (GDS) was calculated for each participant (Heaton et al., 2007). To accomplish this, each of the nine t-scores calculated by the MCCB scoring program was assigned a numerical degree of deficit on a scale of 0 (t-score ≥ 40 ; no deficit) to 5 (t-score ≤ 19 ; severe deficit) in five point decrements in the t-score. The GDS is the average deficit score across measures. In this sample, eight participants were missing at least one MCCB score (seven participants were missing one score, and one participant was missing three scores); for these participants, the GDS was calculated from all available data. The recommended cutoff for cognitive impairment is GDS ≥ 0.50 , which roughly corresponds to mild impairment on half of the component measures (Heaton et al., 2007). For the remaining analyses, only participants with objective cognitive impairment were included, both because the intent of the study was to evaluate awareness of existing neuropsychological dysfunction rather than knowledge of neuropsychological status in general, and due to the clinical relevance of identifying and engaging individuals with such neuropsychological dysfunction in cognitive remediation treatment.

To examine participants' level of neurocognitive insight, latent profile analysis (LPA) was used to group cases based on participants' similarities on two continuous observed variables: the GDS (objective neurocognition) and the MIC-SR total score (subjective report of neurocognitive problems). Conceptually similar to cluster analysis, LPA is a multivariate approach that groups individuals based on shared characteristics that distinguish members of one group from members of another group. LPA determines class assignment through fit statistics and tests of significance, and uses probabilities to take uncertainty of membership (error) into account (Herman et al., 2007). For the descriptive fit indices, lower values are considered indicative of better fit for the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and Adjusted BIC; higher values indicate better fit for Entropy. The Lo–Mendell–Rubin Test (LMRT) of Significance indicates whether the model under consideration is statistically a superior fit to the lower-order model (e.g., if a 3-class model fits better statistically than a 2-class model). A cutoff of $<.05$ is used for significance. Similar to other data reduction techniques like factor analysis, LPA statistically indicates the optimal number of groups, then the values of relevant variables are examined to descriptively label the groups.

The three hypotheses were tested using the resulting groups from the LPA. The groups were compared via t-tests for independent samples on the following variables: executive functioning (Koren WCST accuracy score; Mazes t-score), functional capacity (UPSA-B total score), positive and negative symptom severity (PANSS positive total and negative total scores), and depressive symptom severity (BDI-II total score). To correct for multiple comparisons, alpha for significance was set at 0.008 (0.05/6).

Exploratory analyses examined domain-specific neurocognitive awareness using Pearson correlations between: MIC-SR attention score and CPT-IP t-score, MIC-SR executive function score and Mazes t-score/Koren WCST accuracy score, and MIC-SR memory score and MCCB HVLT total recall t-score. Data were analyzed using Mplus (Version 7.11) and SPSS (Version 21).

Table 2
Descriptive and statistical fit indices.

Cognitively impaired (<i>n</i> = 168)	1 class	2 classes	3 classes
AIC	1680.06	1663.97	1663.02
BIC	1692.55	1685.83	1694.26
Adjusted BIC	1679.89	1663.67	1662.60
Entropy	N/A	0.705	0.611
LMRT	N/A	0.001	0.8773

Note. Favorable values are indicated in bold font. AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; LMRT = Lo–Mendell–Rubin Test of Significance.

3. Results

Among all 214 participants, 168 (78.5%) were classified as neurocognitively impaired ($GDS \geq 0.5$), whereas 46 (21.5%) were classified as neurocognitively intact. The remainder of the analyses included only the 168 cognitively impaired participants (Table 1).

The LPA demonstrated that on two of the four descriptive fit indices as well on the statistical test of model fit, a 2-class model was preferable to both a 1- and 3-class solution (Table 2). Because the LMRT for the 3-class model was not significant, further higher-order models were not analyzed. According to the class assignments yielded by this LPA, one group included 77 participants (46%) with a mean GDS score of 1.75 and mean MIC-SR of 27.89. This group was labeled “intact neurocognitive insight” owing to the high degree of cognitive impairment and high self-reported frequency of cognitive problems. The other group included 91 participants (54%) with a mean GDS of 1.61 and a mean MIC-SR of 9.49; this group was described as “impaired neurocognitive insight” due to high cognitive impairment but low self-reported frequency of cognitive problems. The groups did not statistically differ on any demographic variables (Table 3). The intact neurocognitive insight group were rated as having significantly more severe positive symptoms (mean PANSS positive total score 17.58 versus 14.89; $t = -3.09$; $df = 162$; $p = .002$) and reported more depressive symptoms (mean BDI-II total score 20.25 versus 10.39; $t = -5.87$; $df = 144.08$; $p < .001$). The groups did not differ significantly on Koren WCST accuracy score, Mazes t-score, UPSA-B, or PANSS negative symptom total score (Table 3). Follow-up item analysis of the PANSS positive symptoms subscale indicated that participants with intact neurocognitive insight were rated more highly on delusions, hallucinatory behavior, suspiciousness, and hostility (all $ps < .016$), though across items the mean ratings were “minimal” to “mild”.

Table 3
Demographic, clinical, and cognitive differences between participants with intact versus impaired neurocognitive insight (*n* = 168).

	Intact		Impaired		<i>t</i> or χ^2	<i>df</i>	<i>p</i>	Cohen's <i>d</i>
	<i>n</i>	Mean (SD) or %	<i>n</i>	Mean (SD) or %				
Age, years	77	43.6 (12.0)	91	41.9 (12.5)	−0.91	166	0.364	
Education, years	77	11.9 (1.9)	90	12.3 (2.2)	1.33	165	0.185	
% male	77	59.7	91	73.6	3.65	1	0.056	
% Caucasian	77	48.1	91	53.8	0.80	2	0.671	
% Hispanic ethnicity	77	16.9	91	25.3	1.74	1	0.187	
% schizophrenia	73	57.5	89	67.4	1.68	1	0.195	
% prescribed antipsychotic medication	76	97.4	88	98.9	0.51	1	0.476	
% living independently	77	77.9	91	68.1	4.43	3	0.219	
% employed	77	9.1	91	11.0	1.73	3	0.630	
% never married	70	47.1	75	53.3	7.53	6	0.275	
WRAT-III reading total	77	43.2 (6.9)	89	44.6 (6.9)	1.26	164	0.210	
Koren accuracy score	73	0.5 (0.2)	86	0.5 (0.2)	−1.26	157	0.208	0.00
Mazes score	77	37.3 (7.9)	90	39.9 (8.2)	2.11	165	0.036	0.32
PANSS positive symptoms total	76	17.6 (5.7)	88	14.9 (5.5)	−3.09	162	0.002	0.49
PANSS negative symptoms total	76	16.9 (6.3)	89	15.6 (6.3)	−1.30	163	0.195	0.21
BDI-II total	76	20.3 (11.7)	88	10.4 (9.5)	−5.87	144.08	<0.001	0.94
UPSA-B total	75	67.9 (13.9)	89	68.0 (16.5)	0.04	162	0.966	0.01

Note. Significant differences are indicated in bold font. BDI-II = Beck Depression Inventory, second edition; PANSS = Positive and Negative Syndrome Scale; UPSA-B = UCSD Performance-based Skills Assessment, Brief; WRAT-III = Wide Range Achievement Test, third edition.

Exploratory analyses of domain-specific neurocognitive awareness among all participants yielded no statistically significant correlations between the attention and memory domains of the MIC-SR and their objective cognitive counterparts (MIC-SR attention and CPT-IP $r = .069$; $p = .325$; MIC-SR memory and HVLt t-score $r = -.013$; $p = .854$). There was no significant relationship between MIC-SR executive function and Mazes ($r = -.123$; $p = .077$), though participants who reported more problems with executive functioning scored significantly higher on Koren accuracy ($r = .147$; $p = .038$).

4. Discussion

These results are consistent with previous research showing that the majority of people with schizophrenia demonstrate neuropsychological impairment (Palmer et al., 1997), and that a large proportion of those individuals minimally endorse cognitive problems (Medalia and Thysen, 2008). Indeed, more than half of participants with objectively measured cognitive impairment demonstrated impaired neurocognitive insight. This finding is consistent with previous literature suggesting that many individuals with schizophrenia are poor raters of their own cognition (Johnson et al., 2011; Keefe et al., 2006; Medalia et al., 2008; Medalia and Lim, 2004; Moritz et al., 2004; Poletti et al., 2012; Saperstein et al., 2012) and everyday functioning (Durand et al., 2015; Sabbag et al., 2012).

The first and second hypotheses, that impaired neurocognitive insight would be related to poorer executive functioning and functional capacity performance, were not supported. Our measures of executive functioning were not comprehensive, and included only a reasoning task and a speeded planning task; thus, constructs such as switching and inhibition were not measured. It is possible that these latter tasks are more related to neurocognitive insight, but it is also possible that neurocognitive insight is unrelated to executive skills and the ability to carry out tasks of daily living. We generally found no evidence of domain-specific neurocognitive insight; cognitive symptom complaints in specific domains were mostly unrelated to actual neurocognitive performance, except that greater executive functioning symptoms were weakly related to better executive performance.

The third hypothesis had mixed support; as hypothesized, participants with intact neurocognitive insight reported more severe depressive symptoms, which is consistent with numerous previous studies examining insight and depression (Medalia et al., 2008; Moritz et al., 2004; Sellwood et al., 2013). These findings are also in line with previous research demonstrating that more severe self-rated depression

was associated with underestimation of functional abilities (Bowie et al., 2007) as well as higher self-reported disability (Sabbag et al., 2012). In the current study, participants with intact insight did not differ from those with impaired insight, however, on negative symptom severity. Unexpectedly, participants with intact neurocognitive insight reported more severe positive symptoms of psychosis. Item analysis demonstrated that the groups significantly differed on delusions, hallucinatory behavior, suspiciousness, and hostility, though on average the ratings were no greater than “mild”. As voices and related delusional ideation are conceptualized in the cognitive-behavioral model as negative cognitions about oneself reflecting interpersonal vulnerability (Beck and Rector, 2005), perhaps those with intact awareness are more confronted with their cognitive problems via voices. Additional investigation is warranted to examine the relationship between neurocognitive insight and positive symptom severity.

This study is limited by characteristics of the sample (e.g., outpatient status, middle-age, chronic psychosis); these results may not generalize to inpatients and/or first-episode schizophrenia patients. The narrow measurement of executive functioning and functional capacity, and the exclusion of a social cognition measure, may have also limited our ability to detect significant differences between participants with impaired versus intact neurocognitive insight. In addition, although classification of participants into groups reflecting “intact” and “impaired” insight was conducted using a statistically sound technique and for the purpose of comparing groups on other relevant variables, we acknowledge that neurocognitive insight (like other types of insight) likely exists on a continuum and is not simply an all-or-none feature of schizophrenia. A similar limitation in characterizing neurocognitive insight is that the MIC-SR does not probe all of the cognitive domains represented in the MCCB. Therefore, participants’ subjective evaluation of abilities related to speed of processing, working memory, and visual learning were not specifically assessed, which could have affected the relationship between subjective and objective cognitive functioning and resulting classification into ‘impaired’ versus ‘intact’ neurocognitive insight. Finally, the MIC-SR is a relatively new measure and its psychometrics were not examined within this sample; given a construct as complex as insight, its reliable and valid measurement may prove challenging.

Looking ahead, as the concept of neurocognitive insight becomes better characterized and understood, investigation of its role in neurocognitive treatment adherence and outcome will be critical. Just as patients with low levels of clinical insight are less likely to adhere to their prescribed medication regimen (McEvoy et al., 2006), those with low levels of neurocognitive insight may be less likely to be interested in or adherent to cognitive training interventions. In fact, in a recent treatment study (Keefe et al., 2015), treatment with enceniclene, an alpha-7 nicotinic partial agonist, was found to lead to improvements in performance on the MCCB as well as informant-rated cognitive performance. Critically, self-reports of cognitive functioning were not sensitive to treatment with enceniclene despite beneficial effects detected with both objective and informant-based rates of cognitive change. Because individuals tend to be poor raters of their own cognitive functioning, particularly when they show evidence of objective cognitive impairment, it may be helpful to provide education and feedback regarding cognitive performance to increase awareness of cognitive impairment (Medalia et al., 2012), as well as incorporate motivational interviewing techniques addressing impaired cognition and its impact to increase adherence to cognitive remediation treatment (Fiszdon et al., 2015). Future studies may emphasize clinical features of those lacking neurocognitive insight, as well as the relationship between neurocognitive insight at baseline and outcome following cognitive remediation treatment. As more treatments with efficacy for cognition are developed, it will become critical to assist patients in detecting their cognitive impairments at baseline and their treatment-related improvements in order to optimize treatment of cognitive deficits and to reduce cognition-related everyday disability.

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Contributors

Authors Harvey, Patterson, and Twamley wrote the VALERO protocol. Authors Burton and Twamley designed this study. Author Burton managed the literature searches and statistical analyses, and wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

Dr. Harvey has received consulting fees from Boehringer Ingelheim, Forum Pharmaceuticals (En Vivo), Lundbeck Pharma, Otsuka America Pharma, Sanofi Pharma, Sunovion Pharma, and Takeda Pharma during the past year. The other authors have declared that there are no conflicts of interest in relation to the subject of this study.

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