Motivational Deficits and Cognitive Test Performance in Schizophrenia

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**IMPORTANCE** Motivational and cognitive deficits are core features of schizophrenia, both closely linked with functional outcomes. Although poor effort and decreased motivation are known to affect performance on cognitive tests, the extent of this relationship is unclear in patients with schizophrenia.

**OBJECTIVE** To evaluate the association between intrinsic motivation and cognitive test performance in patients with schizophrenia.

**DESIGN, SETTING, AND PARTICIPANTS** Cross-sectional and 6-month prospective follow-up study performed at 57 sites in the United States, including academic and community medical treatment centers, participating in the Clinical Antipsychotic Trials of Intervention Effectiveness study. The primary sample included 431 stable patients with a *DSM-IV* diagnosis of schizophrenia currently receiving a stable medication regimen.

**INTERVENTIONS** Cognitive performance and intrinsic motivation were evaluated using a comprehensive neuropsychological test battery and a derived measure from the Heinrichs-Carpenter Quality of Life Scale, respectively. Symptom severity and functional status were also assessed.

**MAIN OUTCOMES AND MEASURES** The primary outcome variable was global neurocognition. Individual domains of cognition were also evaluated for their association with motivation.

**RESULTS** Level of intrinsic motivation was significantly and positively correlated with global cognitive test performance, a relationship that held for each domain of cognition evaluated (correlation range, 0.20-0.34; *P* < .001). This association was found to be reliable after statistically accounting for positive, negative, depressive, and overall symptom severity (*P* < .05) and after accounting for community functioning (*P* < .001). The relationship between motivation and cognitive performance also remained significant after controlling for antipsychotic dose (*P* < .05). Prospective increase in motivation during the 6-month follow-up was also found to be significantly related to improvement in global cognitive performance (*P* < .05).

**CONCLUSIONS AND RELEVANCE** The present findings provide strong support for a robust and reliable relationship between motivation and cognitive performance and suggest that test performance is not purely a measure of ability. Future studies assessing cognition in patients with schizophrenia should consider potential moderating variables such as effort and motivation. Implications for the assessment and interpretation of cognitive impairment based on neuropsychological test measures in schizophrenia are discussed, especially in the case of clinical trials for cognition-enhancing treatments.

**TRIAL REGISTRATION** clinicaltrials.gov Identifier: NCT00014001
Schizophrenia is a severe mental illness characterized by a constellation of signs and symptoms, including positive (eg, delusions), negative (eg, lack of motivation), and cognitive (eg, attention) symptoms. Cognitive impairments and negative symptoms are considered core features of schizophrenia that also represent key predictors of functional outcomes. Although these 2 domains of psychopathology are considered distinct and separable, the influence of motivation rather than broadly defined negative symptoms on cognitive performance remains unclear.

Cognitive ability is taken to be a stable feature of schizophrenia, has been found to predict future development of the disorder in unaffected youth, and has been suggested to have the potential to serve as an endophenotype. These notions rest on the assumption that performance on standard neuropsychological tests is a valid proxy for cognitive ability. However, numerous factors have the potential to influence test performance, such as the internal drive to perform well. Therefore, cognitive test performance reflects variance related to core cognitive processing ability and other external factors, such as the motivation to complete the testing procedures (Figure 1). Indeed, this parsing of cognitive test performance into core cognitive information processing (ie, computational processes) and motivational influence (ie, energetic processes) has been described by many authors. Given the prominence of motivational deficits in schizophrenia and the link between motivation and cognition, we can reasonably postulate that cognitive impairments seen in patients with the illness are, to some extent, secondary to motivational impairment.

Although the notion of motivation and effort influencing performance has been established in healthy individuals and patients with neurologic conditions, the concept is less well understood in schizophrenia. One study has demonstrated that a significant and sizeable portion of the variance in cognitive test performance can be explained by poor mental effort, as assessed by an instrument often used to detect suboptimal effort, a finding that has been replicated. Furthermore, 2 studies have shown that intrinsic motivation levels are significantly associated with cognitive performance. The negative symptom of avolition (ie, apathy) has also been shown to be associated with poorer cognitive performance.

Our own pilot work suggests that motivation specifically ascribed to test taking accounts for a significant and sizeable portion of the variance in cognitive test scores in patients with schizophrenia. However, some findings are conflicting. Specifically, one study reported a lack of association between cognitive test performance and intrinsic motivation levels related to approach or to avoidance behavior in patients with schizophrenia, as assessed by a personality questionnaire; interestingly, that study found a relationship between these measures in healthy volunteers. A subsequent study also failed to find a significant association between self-reported motivation and performance on working memory tests in patients using the same questionnaire. Notwithstanding these inconsistent findings, motivation seems to affect cognitive test performance in patients with schizophrenia; however, this relationship needs to be confirmed (or disproved) in a sufficiently large sample of patients and tested across multiple domains of cognitive functioning. Given the surge of interest in cognition in schizophrenia, highlighted by the emergence of several recent clinical trials evaluating the effects of pharmacotherapy on cognitive performance, the role of potentially mediating or moderating variables such as motivation and effort on cognitive test performance in schizophrenia need to be better understood.

The present study examined the relationship between intrinsic motivation and cognitive test performance in a large and heterogeneous sample of patients with schizophrenia. We evaluated the associations between motivation and global cognition and individual domains of cognition. We hypothesized that the level of intrinsic motivation would be significantly related to performance on cognitive tests; specifically, lower levels of motivation would be associated with greater cognitive impairment globally and for each individual cognitive domain. We further hypothesized that the relationship between motivation and cognitive performance would be independent of clinical severity or functional status. In addition, longitudinal increases in motivation were hypothesized to be significantly related to improvements in cognitive performance.

Methods
Participants
Data were drawn from the limited-access datasets of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study for chronic schizophrenia, supported by the National Institutes of Health. Details of the study design and rationale have been presented elsewhere. The primary purpose of the CATIE study was to compare the effectiveness of atypical and conventional antipsychotics through a randomized clinical trial conducted from January 2001 through December 2004, at 57 sites in the United States (16 university clinics, 10 state mental health agencies, 7 Department of Veterans Affairs medical centers, 6 private nonprofit agencies, 4 private-practice sites, and 14 mixed-system sites). In the
Cognitive, symptom, and functioning data were available for 431 patients with schizophrenia who received the same medication for 6 months. Sociodemographic and clinical characteristics of the sample are presented in Table 1. The mean level of...
intrinsic motivation for the present sample was comparable with that reported in other schizophrenia samples, which reflects moderate deficits in intrinsic motivation.

**Association Between Motivation and Cognition in Stable Patients**

Level of intrinsic motivation was significantly and positively correlated with the cognitive composite score and scores from each individual domain of cognition (Figure 2 and the eFigure in the Supplement). Further, each individual item within the intrinsic motivation measure was significantly and positively correlated with the cognitive composite score and scores from each individual domain of cognition (eTable 1 in the Supplement). Level of motivation was more strongly associated with processing speed performance than scores on tests of reasoning (z = 3.25; P = .001), vigilance (z = 2.95; P = .003), and working memory (z = 2.41; P = .02); the magnitude of the association between motivation and other cognitive domains did not differ (P > .05 for all). Intrinsic motivation was found to be associated with cognitive test performance for individuals using each antipsychotic medication, even after controlling for dose (eTable 2 in the Supplement).

The relationship between intrinsic motivation and cognitive test performance remained after individually controlling for severity of illness as indexed by the Clinical Global Impression–Severity Scale (r = 0.29; P < .001), PANSS total score (r = 0.28; P < .001), PANSS positive subscale (r = 0.31; P < .001), PANSS negative subscale (r = 0.26; P < .001), or the Calgary Depression Scale for Schizophrenia (r = 0.34; P < .001). The association between motivation and cognitive performance also remained significant when controlling for other clinical variables such as years of antipsychotic treatment (r = 0.28; P < .001) or presence of medical comorbidity (r = 0.31; P < .001). This relationship also held when the variance attributed to all indices of illness severity was partialled out together (r = 0.20; P < .001), suggesting that this relationship is not secondary to symptom severity.

Motivation continued to demonstrate a significant relationship with cognitive test performance when sociodemographic variables were statistically accounted for such as age (r = 0.30; P < .001), sex (r = 0.33; P < .001), race (r = 0.32; P < .001), or years of education (r = 0.27; P < .001). This relationship also held when all these sociodemographic variables were controlled concurrently (r = 0.23; P < .001).

Previous work has suggested that 2 constructs may be related not because they are inherently linked, but rather because of a shared relationship with distal outcome variables. Because functional status was related to motivation (r = 0.57; P < .001) and cognition (r = 0.23; P < .001), we reexamined the association between these variables after statistically account-

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**Figure 2. Graphical Depiction of the Strength of the Bivariate Relationship Between Intrinsic Motivation Level and Each Cognitive Domain Score**

Data are reported from 431 patients with schizophrenia. Level of motivation was correlated with the cognitive composite score (r = 0.33; P < .001; 95% bias-corrected accelerated CI, 0.25-0.40), verbal memory (r = 0.22; P < .001; 95% bias-corrected accelerated CI, 0.18-0.34), vigilance (r = 0.22; P < .001; 95% bias-corrected accelerated CI, 0.13-0.33), processing speed (r = 0.34; P < .001; 95% bias-corrected accelerated CI, 0.26-0.42), reasoning (r = 0.20; P < .001; 95% bias-corrected accelerated CI, 0.10-0.29), and working memory (r = 0.25; P < .001; 95% bias-corrected accelerated CI, 0.17-0.33).

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**Table 1. Sociodemographic and Clinical Characteristics of 431 Study Patients**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Data*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>41.7 (11.0) [18-66]</td>
</tr>
<tr>
<td>Sex, male, %</td>
<td>75.9</td>
</tr>
<tr>
<td>Race, white, %</td>
<td>62.6</td>
</tr>
<tr>
<td>Patient’s educational level, y</td>
<td>12.1 (2.2) [3-21]</td>
</tr>
<tr>
<td>Duration of antipsychotic therapy, y</td>
<td>14.6 (11.4) [0-56]</td>
</tr>
<tr>
<td>Unemployed, %</td>
<td>82.8</td>
</tr>
<tr>
<td>CGI-S score</td>
<td>3.9 (1.0) [1-7]</td>
</tr>
<tr>
<td>PANSS score</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>63.3 (15.9) [30-109]</td>
</tr>
<tr>
<td>Positive</td>
<td>14.2 (4.9) [7-30]</td>
</tr>
<tr>
<td>Negative</td>
<td>17.8 (5.8) [7-14]</td>
</tr>
<tr>
<td>General</td>
<td>31.3 (8.3) [16-58]</td>
</tr>
<tr>
<td>CDSS total score</td>
<td>2.9 (3.5) [0-16]</td>
</tr>
<tr>
<td>QLS mean score</td>
<td>2.9 (1.1) [0.3-6.0]</td>
</tr>
<tr>
<td>Intrinsic motivation score</td>
<td>8.6 (4.2) [0-18]</td>
</tr>
</tbody>
</table>

Abbreviations: CDSS, Calgary Depression Scale for Schizophrenia; CGI-S, Clinical Global Impression–Severity Scale; PANSS, Positive and Negative Syndrome Scale; QLS, Heinrichs-Carpenter Quality of Life Scale excluding the Intrapsychic Foundations subscale.

*Unless otherwise indicated, data are expressed as mean (SD) [range].
Supplement); however, controlling for change in functional status, albeit at a level trending toward significance (eTable 4 in the Supplement), remained after accounting for the change in clinical variables, in motivation and change in cognitive test performance related to improvements in cognitive performance on tests from individual cognitive domains remained significant while controlling for sociodemographic, clinical, and functioning variables (eTable 3 in the Supplement).

Last, prospective increases in motivation were found to be significantly related to improvements in cognitive performance (Table 2). This relationship between longitudinal change in motivation and change in cognitive test performance remained after accounting for the change in clinical variables, albeit at a level trending toward significance (eTable 4 in the Supplement); however, controlling for change in functional status nullified this association.

Exploring Relationships in the Full CATIE Sample

Next, we wanted to explore whether this relationship would be observed in the entire CATIE sample by examining baseline data (n = 1322). Even in this large and heterogeneous group of patients, intrinsic motivation had a significant association with cognitive test performance (Table 3). This relationship held for a subsample of 351 patients free of antipsychotics for at least the preceding 2 weeks (r = 0.31; P < .001).

Table 2. Effect of Longitudinal Change in Intrinsic Motivation on Change in Cognitive Test Performance

<table>
<thead>
<tr>
<th>Cognitive Domain</th>
<th>Correlation With Change in Intrinsic Motivation, r</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite score</td>
<td>0.10</td>
<td>.04</td>
</tr>
<tr>
<td>Verbal memory</td>
<td>0.10</td>
<td>.05</td>
</tr>
<tr>
<td>Vigilance</td>
<td>0.11</td>
<td>.04</td>
</tr>
<tr>
<td>Processing speed</td>
<td>0.09</td>
<td>.08</td>
</tr>
<tr>
<td>Reasoning</td>
<td>0.09</td>
<td>.06</td>
</tr>
<tr>
<td>Working memory</td>
<td>0.08</td>
<td>.10</td>
</tr>
</tbody>
</table>

Table 3. Bivariate Correlations Between Level of Intrinsic Motivation and Cognitive Scores for 1322 CATIE Participants With Available Data

<table>
<thead>
<tr>
<th>Cognitive Domain</th>
<th>Intrinsic Motivation (95% Bias-Corrected Accelerated CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite score</td>
<td>0.33 (0.29-0.38)</td>
</tr>
<tr>
<td>Verbal memory</td>
<td>0.29 (0.24-0.33)</td>
</tr>
<tr>
<td>Vigilance</td>
<td>0.21 (0.16-0.27)</td>
</tr>
<tr>
<td>Processing speed</td>
<td>0.32 (0.27-0.37)</td>
</tr>
<tr>
<td>Reasoning</td>
<td>0.20 (0.15-0.25)</td>
</tr>
<tr>
<td>Working memory</td>
<td>0.26 (0.21-0.31)</td>
</tr>
</tbody>
</table>

Abbreviation: CATIE, Clinical Antipsychotic Trials of Intervention Effectiveness.

One possible mechanistic explanation for the link between motivation and cognitive performance is that amotivation and cognitive deficits in schizophrenia result at least partially from impairments in the computation of effort demands.66 In the case of apathy, these impairments are related to physical effort, whereas for cognition they are related to mental effort costs. Cognitive functioning has been shown to carry inherent action costs,67 and patients with schizophrenia have been found to invest less effort during cognitive tests than healthy individuals.68 In addition, deficits in patients’ willingness to expend physical effort have been found to be related to their performance on cognitive tests.69,70 Although one study71 did not find such a relationship using a different measure of effort-related motivation. Having motivation and cognitive deficits linked to aberrant effort computations suggests that both of these domains are associated with a common neural architecture, likely related to dopamine signaling and frontostriatal circuit functioning.66 Some evidence in fact supports this theory; for example, one study72 has shown that activity within the ventral striatum is associated with cognitive performance in healthy volunteers, although not in patients with schizophrenia. Whether compromised cognitive performance is due to motivational deficits, increased task difficulty, or an interaction between both is generally difficult to disentangle, and studies wishing to assess one construct independent of the other will need to select tasks carefully. Nevertheless, future studies evaluating cognition in schizophrenia should examine potential mediating/moderating variables such as effort and motivation. This concern becomes particularly important in clinical trials evaluating interventions that putatively enhance cognition.73 In such trials, whether changes in cognitive performance can be ascribed to change in core cognitive functioning or to peripheral changes in level of motivation/effort should be elucidated (Figure 1). We also recommend that individuals who demonstrate poor motivation should be identified in such trials, and that subanalyses should be conducted excluding individuals identified as putting forth suboptimal effort. Although no criterion standard for how to detect such cases among individuals with schizophrenia exists, perhaps a stringent threshold on 1 or more performance validity tests could...
motivation and effort should also affect cognitive performance. To this point, increasing dopaminergic transmission via amphetamine, which is well known to affect motivation and reward processing, has been shown to improve performance on cognitive tests. \cite{73-80} These findings taken together clearly demonstrate an association of level of motivation and cognitive test performance in schizophrenia.

In evaluating the present study, limitations should be mentioned. First, the measure used to assess intrinsic motivation was derived from the Heinrichs-Carpenter Quality of Life Scale rather than being a stand-alone measure. Recently, an intrinsic motivation inventory has been developed for and validated in patients with schizophrenia\cite{84}; we have used this specific measure in a previous study and the results are consistent with those presented herein. \cite{79} Second, our assessment of intrinsic motivation relied on a single measure. Although this measure included 3 distinct items and each demonstrated a relationship with cognitive performance, future studies should examine whether multiple indicators of motivation and effort (eg, performance validity tests) might explain a greater portion of variance in cognitive test performance. Third, the relationship between change in intrinsic motivation and change in cognitive test performance, although statistically significant, was of a modest effect size. This effect may be owing in part to the relatively small improvement in cognition scores\cite{51} and level of intrinsic motivation (estimated mean difference, 0.53; paired sample test, \(t_{28} = 2.65; P = .008\) seen after antipsychotic treatment; a more robust relationship might be observed after more substantive changes in cognitive performance and motivation. Fourth, although the present results are interpreted as intrinsic motivation affecting cognitive performance scores, directionality cannot be established with the present set of analyses. The possibility that cognitive impairment undermines volition remains. Finally, the influence of motivation and effort on cognitive test performance is not specific to individuals with schizophrenia\cite{17-19}; however, the prevalence of motivational deficits in this disorder suggests that this relationship may be particularly salient and ought to be taken into account.

**Conclusions**

The present results strongly encourage the assessment of variables such as motivation and effort when evaluating cognitive performance in schizophrenia. Taking these other variables into account may enhance the discovery of variables (eg, genetic) that are specifically related to core neurocognitive ability. At the very least, our results suggest that poor cognitive test performance scores should not be inferred at face value to reflect impairment purely in neural processes subserving the cognitive process in question (ie, neuroanatomical localization). In addition, our findings suggest that in the ongoing search for therapeutics to improve functional outcomes among individuals with schizophrenia, a greater focus on motivational and effort-based deficits and their underlying neurobiology, or indeed the shared mechanisms underlying the motivation-cognition relationship, may facilitate efforts aimed at ameliorating these impairments and improving outcomes.
Disclaimer: This study reflects the views of the authors and may not reflect the opinions or views of the CATIE study investigators or the National Institutes of Health.

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Criteria.


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