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
Motivation and Cognition in Schizophrenia

Schizophrenia is a severe mental illness characterized by a constellation of signs and symptoms, including positive (e.g., delusions), negative (e.g., lack of motivation), and cognitive (e.g., 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, and it 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 (i.e., computational processes) and motivational influence (i.e., 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 (i.e., 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.

Figure 1. Illustration of the Components of Cognitive Test 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 and the primary findings 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
first phase of the trial, 1493 patients were randomized to receive olanzapine, perphenazine, quetiapine fumarate, risperidone, or ziprasidone hydrochloride under double-blind conditions and were followed up for 18 months or until treatment was discontinued for any reason.33 Patients had monthly visits with study physicians. The primary sample for the present study included individuals who were clinically stable, operationalized as no change in antipsychotic regimen for the preceding 6 months. This inclusion criterion was implemented to increase the generalizability of the present findings to other outcome studies and clinical trials focused on cognitive end points, both of which typically examine stable patients.35

The study inclusion criteria have been reported previously.35 Briefly, participants were eligible if they were aged 18 to 65 years and had a diagnosis of schizophrenia confirmed using the Structured Clinical Interview for DSM-IV Axis I Disorders.36 Participants were excluded if they had a diagnosis of schizoaffective disorder, mental retardation, pervasive developmental disorder, delirium, dementia, amnesia, or other cognitive disorders; if they had only 1 episode of schizophrenia; if they were pregnant or breast-feeding; or if they had a serious and acutely unstable medical condition.

The study was approved by the institutional ethics review board at each site, and written informed consent was obtained from the patients or their legal guardians. All participants demonstrated adequate decision-making capacity in regard to participating in the study as determined by the MacArthur Competence Assessment Tool for Clinical Research.37

Instruments and Procedure

The neuropsychological tests that constituted the CATIE cognitive battery have been described in detail in a previous report.39 Scores on individual tests were converted to z scores and combined to construct the following cognitive domain scores: (1) processing speed, calculated as the mean score of the Digit Symbol Test39 from the Revised Wechsler Adult Intelligence Scale, Grooved Pegboard,40 and the mean score of the Controlled Oral Word Association Test41 and Category Instances scale42; (2) working memory, measured by the mean score of the Letter-Number Sequencing test42 and a computerized test of visuospatial working memory43; (3) verbal memory, assessed with the mean score of 3 trials from the Hopkins Verbal Learning Test44; (4) vigilance, evaluated by the d-prime summary score from the Continuous Performance Test45; and (5) reasoning, measured by a mean score from the Mazes subtest of the Revised Wechsler Intelligence Scale for Children46 and a computerized version of the Wisconsin Card Sorting Test.47,48 These domains are all assessed by the MATRICS (Measurement and Treatment Research to Improve Cognition in Schizophrenia) Cognitive Consensus Battery.49,50

We then calculated the mean of the 5 domain scores to create a cognitive composite score. Details on the baseline characteristics of neurocognition47 and response to treatment51 in the CATIE study have been published previously.

Intrinsic motivation was evaluated using the sum of the following 3 items from the Intrinsic Psychiatric Foundations subscale of the Heinrichs-Carpenter Quality of Life Scale52: sense of purpose, motivation, and curiosity. These items measure general traitlike motivation and tap into core constructs within self-determination theory, which defines intrinsic motivation as the interest in, drive toward, and enjoyment of activities and goals for their own sake (ie, even in the absence of specific extrinsic rewards).53 Although no criterion standard instrument for the assessment of intrinsic motivation schizophrenia exists, this derived 3-item measure has been used in numerous empirical studies examining this construct in patients with schizophrenia.23,24,54–59 The measure demonstrated good internal consistency in the present sample (Cronbach α = 0.80). The Heinrichs-Carpenter Quality of Life Scale is a clinician-administered instrument that evaluates various functional domains during the past 4 weeks.

Other measures of interest included the Clinical Global Impression–Severity Scale to assess overall clinical severity,60 Positive and Negative Syndrome Scale (PANSS) to assess psychopathology,61 Calgary Depression Scale for Schizophrenia to assess depressive symptoms,62 and the Heinrichs-Carpenter Quality of Life Scale, excluding the Intrapsychic Foundations domain, to assess psychosocial and community functioning.52

Statistical Analysis

Bivariate relationships were examined using Pearson product-moment correlation coefficients. To test the robustness of these correlations, 95% bias-corrected accelerated confidence intervals (CIs) were estimated using 10 000 bootstrap samples, drawn by randomly resampling with replacement from the original data set.63 Next, partial correlations were conducted to examine the relationship between intrinsic motivation scores and cognitive test performance while statistically controlling for other clinical variables (eg, Clinical Global Impression–Severity Scale). Potential differences in magnitude of association between the variables were calculated using the Steiger test for dependent correlation coefficients.64,65

The relationship between change in level of intrinsic motivation and change in cognitive test performance was also examined through a partial correlation analysis, controlling for baseline scores in the primary sample of patients with stable disease. Analyses were conducted on patients with stable schizophrenia who served as the primary sample in the present study; however, we also confirmed these relationships in the full CATIE sample to examine generalizability of findings to a larger and more heterogeneous sample of patients and in a subsample of patients who were free of antipsychotics at baseline. Statistical tests were considered significant at P < .05 (2 tailed). All analyses were conducted using commercially available software (SPSS Statistics, version 20; IBM Corp.).

Results

Patient Characteristics

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,\textsuperscript{23-24,56-59} 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 ($r = 0.57$; $P < .001$), vigilance ($r = 0.29$; $P = .004$), and working memory ($r = 0.41$; $P = .02$; 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 Impress–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 ($r = 0.26$; $P < .001$), PANSS general psychopathology subscale ($r = 0.30$; $P < .001$), 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 partialed 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 ($r = 0.20$; $P < .001$), sex ($r = 0.33$; $P < .001$), race ($r = 0.32$; $P < .001$), or years of education ($r = 0.27$; $P < .001$). The 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.\textsuperscript{5} Because functional status was related to motivation ($r = 0.57$; $P < .001$) and cognition ($r = 0.22$; $P < .001$), we reexamined the association between these variables after statistically account-
Supplement); however, controlling for change in functional status remained after accounting for the change in clinical variables, in motivation and change in cognitive test performance relating 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

<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>

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).

Discussion

The present study examined the association between intrinsic motivation and cognitive performance in individuals with schizophrenia. Our results reveal that poor motivation is significantly associated with worse performance on tests of processing speed, working memory, verbal memory, vigilance, and reasoning, suggesting that cognitive impairments in schizophrenia may be partly secondary to amotivation. This association between motivation and performance cannot be explained by the severity of psychopathology or by shared variance with functioning scores.

We wish to emphasize that the present results do not suggest that the full extent and degree of cognitive impairment in schizophrenia result from motivational impairments; previous work has shown cognitive deficits even in patients who invest adequate effort.29 Nonetheless, an association in the moderate effect size range was elucidated. Intrinsic motivation levels predicted from 6% to 16% of the variance in global cognitive performance scores.

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 (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.

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>
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<td>Working memory</td>
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Abbreviation: CATIE, Clinical Antipsychotic Trials of Intervention Effectiveness.

a Includes a sample of 1321 patients.

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
suffice for this purpose. Future studies should empirically establish an instrument to assess motivation specifically in the context of cognitive testing in patients with schizophrenia.

Our results have important implications regarding our understanding of cognitive deficits in schizophrenia. First, they suggest that cognitive performance should change by simply enhancing the intrinsic value of the testing procedures. Some preliminary evidence of this enhancement exists, in that offering task instructions in a gamelike fashion, thus increasing the intrinsic value of the task, has been found to increase learning in patients with schizophrenia.73 At the same time, variables that undermine motivation such as defeatist beliefs, which may decrease the intrinsic value ascribed to a task, have been found to be associated with lower cognitive performance.74 These findings, of course, also have implications for cognitive training or remediation programs.79 Second, although not directly related to intrinsic motivation, these results leave open the possibility that increasing motivation more broadly defined (which includes extrinsic motivation76) will increase performance. Several older studies77–80 have confirmed this assertion. Similarly, interventions that affect 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.81–83 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 schizophrenia84; we have used this specific measure in a previous study and the results are consistent with those presented herein.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 scores51 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 schizophrenia77–79; 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 motivation 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.


54. Saperstein AM, Fiszdon JM, Bell MD. Intrinsic motivation as a predictor of work outcome after vocational rehabilitation in schizophrenia. J Nerv Ment Dis. 2011;199(9):672-677.


74. Grant PM, Beck AT. Defeatist beliefs as a mediator of cognitive impairment, negative symptoms, and functioning in schizophrenia. Schizophr Bull. 2009;35(4):798-806.


