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Abbreviated neuropsychological assessment in schizophrenia:

Prediction of different aspects of outcome

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Abstract

The aim of this study was to identify the best subset of neuropsychological tests for prediction of several different aspects of functioning in a large ($n = 236$) sample of older people with schizophrenia. While the validity of abbreviated assessment methods has been examined before, there has never been a comparative study of the prediction of different elements of cognitive impairment, real-world outcomes, and performance-based measures of functional capacity. Scores on 10 different tests from a neuropsychological assessment battery were used to predict global neuropsychological (NP) performance (indexed with averaged scores or calculated general deficit scores), performance-based indices of everyday-living skills and social competence, and case-manager ratings of real-world functioning. Forward entry stepwise regression analyses were used to identify the best predictors for each of the outcomes measures. Then, the analyses were adjusted for estimated premorbid IQ, which reduced the magnitude, but not the structure, of the correlations. Substantial amounts (over 70%) of the variance in overall NP performance were accounted for by a limited number of NP tests. Considerable variance in measures of functional capacity was also accounted for by a limited number of tests. Different tests constituted the best predictor set for each outcome measure. A substantial proportion of the variance in several different NP and functional outcomes can be accounted for by a small number of NP tests that can be completed in a few minutes, although there is considerable unexplained variance. However, the abbreviated assessments that best predict different outcomes vary across outcomes. Future studies should determine whether responses to pharmacological and remediation treatments can be captured with brief assessments as well.

Keywords

Schizophrenia; Disability; Neuropsychological assessment; Functional capacity; Abbreviated assessments

Impaired performance on neuropsychological (NP) tests is correlated with a variety of deficits in everyday living and social outcomes across a variety of neuropsychiatric conditions (Heaton & Pendleton, 1981). These impairments predict worse outcomes in terms of a range of everyday behaviors, including social functioning (Smith, Hull, Romanelli, Fertuck, & Weiss, 1999), self-

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care (Harvey et al., 1998), community-living skills (Palmer et al., 2002), and employment (McGurk & Meltzer, 2000). Much of this research has been focused on people with schizophrenia, and there has been some debate about whether relationships between impairments in different cognitive ability domains and aspects of disability are specific or more generalized. For instance, in a study of people with schizophrenia attentional performance was shown to predict early occupational success, while sustained work performance was better predicted by episodic-memory performance (Bryson & Bell, 2003). In contrast, other studies have found correlations of essentially similar magnitude between multiple components of a cognitive assessment battery and a number of aspects of everyday functional outcomes (Evans et al., 2003; McGurk, Mueser, Harvey, LaPuglia, & Marder, 2003; Twamley et al., 2002).

If the relationships between multiple cognitive impairments and different elements of functional disability are similar, then it is possible that a detailed and lengthy neuropsychological assessment may not be required to provide a reasonable estimate of disability. For instance, research-oriented neuropsychological assessments of patients have employed as many as 38 different cognitive tests (Bilder, Mukherjee, Rieder, & Pandurangi, 1985). Several abbreviated assessment batteries have been developed to assess intelligence (Wechsler, 1999) and screen for dementia (Randolph, 1998). In the area of schizophrenia, it has been suggested that the results of abbreviated cognitive assessments may also explain a considerable proportion of the variance in the total scores of longer assessment batteries (Keefe et al., 2004; Keefe, Poe, Walker, & Harvey, 2006b). Several abbreviated cognitive assessment procedures have been developed previously, and these batteries have been validated either against the results of longer NP assessments (Keefe et al., 2004) or against aspects of functional disability (Velligan et al., 2004). These studies have generated consistent findings indicating that the total scores on longer NP assessment batteries can be very well predicted by performance on a small subset of the elements of the battery, a finding also produced in studies of people with HIV infection (Carey et al., 2004b).

Abbreviated batteries may be appealing for several reasons. From the research perspective, shorter assessments have been shown empirically to lead to fewer missing data and to have a generally higher completion rate (Keefe et al., 2004). Rates of completion of baseline assessments have been directly linked to overall attrition from research studies. This is exemplified by the results of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) baseline NP assessment, where some of the assessments in that fairly lengthy (approximately 90 min) battery were missing on as many as 25% of the cases at baseline (Keefe et al., 2006a), with similar rates of incremental missing data across two subsequent follow-up assessments (Keefe et al., 2007). A recent meta-analysis indicated that a single, rapidly completed NP measure, Digit Symbol from the Wechsler Adult Intelligence Scale (WAIS), is the test that is most impaired in people with schizophrenia (Dickinson, Ramsey, & Gold, 2007). Interestingly, this was also the single NP measure that was the strongest correlate of global performance scores on the CATIE battery at baseline, accounting for 61% of the variance in both stepwise and hierarchical predictor models of the total score. Several widely used NP measures, including the Wisconsin Card Sorting Test (WCST; Heaton, Chellune, Talley, Kay, & Curtiss, 1993) and the Continuous Performance test (Cornblatt, Lenzenweger, & Erlenmeyer-Kimling, 1989), accounted for as little as 2% of the variance in that same total score. From a clinical perspective, the more abbreviated the NP battery, with less specialized competence required to administer and interpret the assessment, the more accessible is the assessment of patients with schizophrenia treated at nonacademic practice sites.

A recent development in the assessment of disability in schizophrenia is the clear separation of assessment of functional capacity (i.e., what the individual can do under optimal conditions: his/her competence) and real-world outcomes (what the individual actually does in day-to-day living: his/her performance). It has been found that NP performance has a complex relationship

with disability, with substantial correlations between NP ability areas and measures of functional capacity (Bowie, Reichenberg, Patterson, Heaton, & Harvey, 2006; Twamley et al., 2006; Velligan et al., 2007) and a smaller, more delineated correlation between NP measures and everyday outcomes, above and beyond the influences of functional capacity (Bowie et al., 2008; Bowie et al., 2007; Keefe, Poe, Walker, & Harvey, 2006). In a recent study, we found different correlational relationships between different aspects of functional capacity, real-world outcomes, and NP performance in a sample of people with schizophrenia (Bowie et al., 2008). These relationships were more complex than the results of a previous study where NP performance was examined as a single composite score (Bowie et al., 2006). Further, when we examined only functional-capacity measures, without reference to everyday outcomes (McClure et al., 2007) we found that working memory and verbal skills predicted social competence more efficiently than processing speed and that processing speed was more specifically related to performance on measures of living skills than it was to social skills. In that study, the two functional-capacity measures used in this study were found to load on a single canonical root, indicating high levels of factorial integrity.

The divergence in correlational findings when NP performance was considered as a single global score or as a series of different NP ability areas may indicate that different abbreviated assessments of NP performance are required to predict different outcomes relevant to functional status: global NP scores on comprehensive assessments, indices of functional capacity, and measures of everyday real-world outcomes. While multiple studies of abbreviated assessment have been performed, there has never been a comprehensive study of the NP ability domains that best predict global NP performance, functional capacity (social and living skills), and real-world outcomes. Further, there have been questions raised about whether the results of other abbreviated assessment procedures accurately capture score produced with longer assessment batteries (Axelrod, 2002).

In this paper, we report the results of a set of analyses evaluating this issue. Using a large sample of people with schizophrenia who received a comprehensive neuropsychological assessment, we identified the best subset of NP tests to predict two different “global” scores for NP performance: an averaged composite score reflecting average levels of performance on the battery and a general deficit score that reflects the number and severity of deficits identified by the battery. We also identified the predictors of two measures of functional capacity: performance on a measure of social competence and total scores on a performance-based assessment of everyday-living skills, as well as measuring real-world outcomes indexed by total scores on a case-manager rating scale examining a variety of elements of real-world outcomes. We expected that the best single predictor of composite NP performance would be processing speed, but also expected that there might be different primary or secondary predictors of deficits in social and everyday-living outcomes, based on our previous findings of differential correlations with competence measures in social skills and everyday-living domains.

METHOD

Participants

The participants in this study were older schizophrenia or schizoaffective outpatients enrolled in a longitudinal study of cognitive and functional status. Exclusion criteria consisted of a primary DSM-IV (*Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition*; American Psychiatric Association, 1994) Axis I diagnosis other than schizophrenia or schizoaffective disorder, Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) score below 18, Wide Range Achievement Test, Third edition (WRAT-3; Wilkinson, 1993) reading grade equivalent of Grade 6 or less, or any medical illnesses that might interfere with the assessment of cognitive functioning. The relatively low MMSE cutoff

score was based on previous studies showing substantial impairments in institutionalized patients; no patients that we screened failed this criterion. All participants met DSM-IV criteria for schizophrenia or schizoaffective disorder. The Comprehensive Assessment of Symptoms and History (CASH; Andreasen, Flaum, & Arndt, 1992) was completed by a trained interviewer, and diagnoses were confirmed at a consensus meeting by an experienced clinician. In addition, patient data were used in these analyses only if they were receiving case management services and actively involved in psychiatric rehabilitation services. The case managers were used as informants for real-world functional-status ratings. Study participants were also required to have evidence of continued illness at the time of recruitment, as evidenced by meeting at least one of three criteria: (a) an inpatient admission for psychosis in the past two years; (b) an emergency room visit for psychosis in the past two years; or (c) a score on the Positive and Negative Syndrome Scale (PANSS; Kay, Fiszbein, & Opler, 1987) positive symptoms items delusions, hallucinations, or conceptual disorganization of 4 (moderate) or more at the time of their baseline assessment. Outpatient status was defined as living outside of any institutional setting, including a nursing home. Recruitment was conducted at clinics at Veterans' Affairs Hospitals, a New York State psychiatric hospital, or Mount Sinai School of Medicine.

All patients were receiving treatment with antipsychotic medications at the time of assessment. All participants signed a written informed consent form approved by the institutional review board at each research site, after the testing procedures were fully explained.

Measures

All participants completed the test battery in a fixed order, following the screening measures described above. All interviewers received extensive training in performing all assessments, and every three months their performance was evaluated through rerating of training tapes, dual ratings of the functional-status measures with Christopher R. Bowie, and quality assurance assessments of all testing. These raters were trained to adequate reliability on symptom ratings with two full days of training, four standardized video tapes, and in-person interviews that yielded intraclass correlation coefficients (ICCs) from .86 to .92.

Performance-based measure of functional capacity—The University of California, San Diego (UCSD) Performance-Based Skills Assessment Battery (UPSA; Patterson, Goldman, McKibbin, Hughs, & Jeste, 2001a) is designed to directly assess functional skills competence among the severely mentally ill. This test was designed for older outpatients and measures performance in a number of domains of everyday functioning through the use of props and standardized skills performance situations. In this study, the UPSA-B (Mausbach, Harvey, Goldman, Jeste, & Patterson, 2007) was used, which contains two of the original UPSA domains, based on two recent studies suggesting that these two subscales alone correspond excellently with the total score. In the finance domain, the patient must count out given amounts from real currency, make change, and fill out a check to pay a utility bill. The communication domain involves a series of role-play situations that require the patient to make emergency calls, call directory assistance to request a telephone number, call the number, and then reschedule a medical appointment. We standardized the scores to a 100-point scale, like the original 5-subtest UPSA, thus allowing comparisons to previous results. This total score was used as our dependent measure.

The Social Skills Performance Assessment (SSPA; Patterson, Moscona, McKibbin, Davidson, & Jeste, 2001b) is a measure of social competence that was created for use with schizophrenia patients. After a brief practice, the patients initiate and maintain a conversation for three minutes in each of two situations: greeting a new neighbor and calling a landlord to request a repair for a leak that has gone unfixed after a previous request. These sessions were audiotaped

and scored by a different trained rater who was unaware of diagnosis (patient or healthy control as part of a larger study) and scores on all other measures. Dimensions of social skills scored include fluency, clarity, focus, negotiation ability, persistence, and social appropriateness. The raters' assessment of these skills were compared to the gold standard ratings of the instrument developers ($ICC = .86$), and high interrater reliability was maintained at three months ($ICC = .87$). The mean of the ratings on these variables across the two measures was used in this study.

Real-world functional outcomes—In order to examine everyday functioning in the real world, the Specific Level of Function Scale (SLOF; Schneider & Streuening, 1983) was employed. This scale is a 43-item observer-rated report of a patient's behavior and functioning on the following domains: physical functioning (e.g., vision, hearing), personal care (e.g., toileting, eating, grooming), interpersonal relationships (e.g., initiating, accepting and maintaining social contacts; effectively communicating), social acceptability (e.g., verbal and physical abuse, repetitive behaviors), participation in community activities (e.g., shopping, using telephone, paying bills, use of leisure time, use of public transportation), and work skills (e.g., employable skills, level of supervision required, punctuality). Ratings are made on a 5-point Likert scale by a third-party informant on the basis of the amount of assistance that the patient requires to perform real-world skills (personal care, activities), effects on daily living (physical functioning), or frequency of the behavior (interpersonal relationships, social acceptability, work skills). For all participants in this study, a caseworker or other high-contact clinician for the patient completed the SLOF in order to obtain information on real-world performance. All informants indicated that they knew the patient at least "very well" (4 or more) on the SLOF's 5-point Likert scale and were unaware of any of the other data on the patient. The scale has excellent interrater reliability, factorial validity, and internal consistency and has been previously shown to be related to NP performance and scores on functional-capacity measures (Bowie et al., 2008; Bowie et al., 2006; Bowie et al., 2007). The interviewers who completed and scored all other aspects of assessment were unaware of the case managers' SLOF ratings.

Cognitive assessment—Neuropsychological tests were selected from a larger battery to represent diverse but nonoverlapping cognitive domains that were previously shown to be the most consistently correlated with functional outcomes (Green, 1996; Green, Kern, Braff, & Mintz, 2000). These tests included the Wisconsin Card Sorting Test (Heaton et al., 1993), the Trail Making Test Parts A and B (Reitan & Wolfson, 1993), Learning Trials 1-5 from the Rey Auditory Verbal Learning Test (RAVLT; Spreen & Strauss, 1998), the Consortium to Establish a Registry for Alzheimer's Disease (Morris et al., 1989) version of animal naming, the constructional praxis assessment, and their 15-item version of the Boston Naming Test, and the Digit Span, Letter-Number Sequencing, and Digit Symbol Coding subtests of the Wechsler Adult Intelligence Scale, 3rd edition (WAIS-III; Psychological Corporation, 1998). We also collected vocabulary scores from the WAIS-III and reading subtest scores from the WRAT-3.

Creation of composite cognitive scores—All raw scores on the NP tests were converted to age- and, when possible, education- and gendercorrected standardized scores using published norms. In the total-score approach to the composite cognitive performance, these standardized scores were averaged to create a single unweighted score. We did not include vocabulary and WRAT scores in these composites, reserving those two indices to estimate the influence of premorbid functioning on current performance. The Global Deficit Score (GDS) approach was also used as a measure of impairments in NP performance (Carey et al., 2004a). This approach is different from an averaging approach in that it focuses on the number and severity of NP impairments. In so doing, it weights the NP data in a similar manner to clinical ratings by considering both the number and the severity of deficits in an individual's performance throughout the test battery, giving no weight to performance within and above

the normal range (Heaton et al., 2001; Heaton et al., 1994). The GDS approach begins by converting the standard scores described above to deficit scores that reflect the presence and severity of impairment. T scores greater than or equal to 40 represented no impairment (deficit score = 0); whereas a deficit score of 1 reflects mild impairment (T score = 39 to 35); deficit score of 2 reflects mild to moderate impairment (T score = 34 to 30); 3 reflects moderate impairment (T score = 29 to 25); 4 reflects moderate to severe impairment (T score = 24 to 20), and 5 reflects severe impairment (T score <20). Deficit scores on all tests were then averaged to create the GDS. In previous studies of diverse neuropsychiatric populations a GDS greater than or equal to 0.5 has accurately predicted expert clinical ratings of overall impairment (Carey et al., 2004a; Heaton et al., 2001). A GDS at this cutoff indicates that, on average, an individual was mildly impaired on half of the NP test measures in the battery. The GDS method appears to be relatively unaffected by modifications in test batteries.

Statistical analyses

The primary analyses that we performed were regression analyses, predicting the various outcome variables with performance on each of the NP assessments. We used a forward entry stepwise regression procedure, with a $p < .05$ criterion for entry. We then repeated these analyses after adjusting each of the outcomes domain scores for WRAT-3 reading scores. In this analysis we entered the reading scores as the first predictors of the outcome variable and repeated the forward entry stepwise analysis by entering the block of predictors into the equation second.

RESULTS

Descriptive characteristics of the patients and performance on the NP measures are presented in Table 1. The mean GDS score of the overall sample was 1.39 ($SD = 0.83$), reflecting moderate impairment, and 82% of the cases had GDS scores in the impaired range, even when estimates of decline from premorbid functioning were not considered.

We next examined the correlations among two different estimates of premorbid intellectual functioning, the WRAT-3 and WAIS-III vocabulary, with total PANSS scores, individual NP tasks, and functional performance variables. The correlations for vocabulary and NP performance ranged from a low of $r = .19$, *ns* (WCST errors) to a high of $r = .50$, $p < .001$, (Digit Span backwards). Correlations of WRAT-3 scores were slightly smaller for every variable, ranging from a low of $r = .11$, *ns* (WCST errors) to a high of $r = .48$, $p < .001$ (Digit Span backwards). Correlations were slightly higher with UPSA-B, $r = .63$, $p < .001$, for vocabulary, and $r = .58$, $p < .001$, for WRAT-3. Correlations between these two variables and SSPA performance and SLOF scores were smaller but statistically significant. Total PANSS scores did not correlate significantly ($p > .05$) with any NP or functional-outcomes measures and as a result were not entered into analyses predicting these variables.

Table 2 presents the results of the regression analyses predicting NP performance, with the average-based composite score presented on the top of the table and the GDS-based analyses on the bottom. In the composite score analysis, six variables entered, accounting for 71% of the variance. These included three different indices of processing speed, as well as two indices of verbal working memory and episodic memory. For the GDS-based analyses, nine variables entered the equation and accounted for 78% of the variance in the predicted score. Interestingly, two separate indices of processing speed entered the equation first and between them accounted for 67% of the total variance. Table 3 presents the results of the regression analyses for the UPSA-Brief total score, the SSPA, and the results for the everyday outcomes measure: the SLOF. For the UPSA-B, six variables entered the equation, accounting for 46% of the variance. Again, a measure of processing speed entered the equation first and accounted for substantial variance in the UPSA total score. For the SSPA, three variables predicted 36% of the variance,

with two elements of processing speed, Digit Symbol and animal naming, entering followed by RAVLT total learning. Finally, for prediction of real-world functioning with the SLOF total scores, two variables entered the equation, accounting for 22% of the variance. Two different putative measures of processing speed—Trail Making Test Part A and animal naming—accounted for the majority of the variance.

When we repeated the regression analyses after entering the WRAT-3 scores into the equation first, we found a very similar pattern of results. The variance accounted for in the prediction was reduced, but the order of entry of the variables was completely unaffected. For the averaged NP composite, the R^2 accounted for by the block of predictors was reduced to .45, for GDS the reduction was also to .45, for UPSA-B the reduction was to .44, for SSPA it was reduced to .22, and for the SLOF the reduction was to .12.

DISCUSSION

Systematic consideration of the prediction of functional outcomes as well as cognitive impairments makes this study unique, and the results of this study suggest that prediction of overall cognitive functioning and some aspects of functional disability in people with schizophrenia can be accomplished with high efficiency with relatively abbreviated assessments, consistent with earlier work. In fact, 67% of variance in the cognitive General Deficit Score classifications is accounted for by two different processing-speed measures. When real-world outcomes were considered, the only predictors in the stepwise analyses were indices of processing speed. Processing-speed measures predominated as the significant predictors of both functional outcomes and total NP performance. Real-world outcomes were predicted with considerably less accuracy than NP performance or measures of functional capacity, and within functional capacity, everyday-living skills were predicted much better than social functioning. It appears as if different sets of predictors might be required in order to best predict different aspects of outcome.

Limitations of the study include the fact that the patients were older, which might be argued to increase the salience of processing speed in the prediction of overall performance. It has been shown, however, in multiple samples that were exclusively nongeriatric that performance on digit symbol constitutes the single largest effect size for impairments compared to healthy individuals (Dickinson et al., 2007). While the analyses we used are exploratory, they expand on previous studies using regression analyses where only overall NP ability was the criterion variable. Finally, while the current NP assessment was quite broad, it did not include an assessment of vigilance or visual memory. In the previous CATIE analyses, vigilance performance accounted for 2% of the variance in total NP scores in the context of an overall battery.

From a practical point of view, these results suggest that for clinicians who are interested in a general, but quite predictive, understanding of NP impairments and functional capacity, a very abbreviated cognitive assessment procedure may give an excellent estimate. The two processing-speed measures that predicted two thirds of the variance in general cognitive deficits are well normed and can be administered in about 6 minutes. Although these cross-sectional data do not address the potential sensitivity of these measures to treatment-related change, two recent studies suggest that processing-speed measures are the indices most sensitive to treatment-related changes associated with atypical antipsychotic medications (Harvey, Patterson, Potter, Zhong, & Brecher, 2006) and cholinesterase inhibitors (Buchanan et al., 2008).

The level of prediction of performance on measures of functional capacity and ratings of real-world outcomes was not nearly this great. Thus, it seems that a reasonable conclusion is that

global NP deficits are well predicted in schizophrenia by a very small subset of NP measures and that the prediction of disability, in terms of both functional capacity and real-world outcomes, requires a slightly different assessment approach. Adjusting for estimates of premorbid functioning that are sensitive to verbal IQ reduced the total variance accounted for, but did not eliminate the predictability of cognitive impairments, functional capacity, or everyday outcomes. These findings suggest that there are specific NP abilities, related to but not completely subsumed by, global intellectual functioning, that are particularly relevant to the overall severity of NP impairment in schizophrenia.

Another issue of importance is the general predictability of real-world outcomes by cognitive-performance variables. Several recent studies have suggested that other individual-differences variables such as social cognitive abilities add to the prediction of real-world outcomes. Further, societal variables such as disability insurance and demographic factors such as ethnicity affect employment outcomes (Rosenheck et al., 2006). We (Leung, Bowie, & Harvey, 2008) also showed that NP ability scores were much better predictors of residential functioning (i.e., independence in living) than employment or social outcomes in this same sample of people with schizophrenia. It may be that an abbreviated assessment of cognitive functioning is most suited to prediction of cognitive impairments and everyday-living skills than other outcomes, which may be affected by other external variables. Finally, we (Bowie & Harvey, in press) also found that impairments in communication, indexed by scores on a clinical assessment of formal thought disorder, were as strongly related to social outcomes as NP deficits.

The last, and quite important, issue raised by these data is the significance of processing speed as a major predictor of global cognitive impairments. While it had been argued in the past that processing-speed measures such as WAIS Digit Symbol are most impaired in people with schizophrenia because of their sensitivity to multiple cognitive domains (learning, speed, praxis, attention), it has recently been argued that such measures may actually be measuring the severity of impairments that arise from generalized factors (Dickinson et al., 2007). These factors, including inflammatory processes, abnormalities in glucose transport, or changes in white matter connectivity, have the potential to induce impairments in multiple elements of cognitive functioning, with processing speed being most salient. It is not possible in a single-sample study to determine whether differences in predictability of different outcomes found in different indices of processing speed (e.g., Digit Symbol vs. Trail Making) reflect subtle meaningful differences between tests or simple statistical artifacts.

In conclusion, abbreviated cognitive assessment predicts global indices of NP performance well in people with schizophrenia and manifests a pattern of prediction that is more efficient for NP performance than for functional impairment. The reduced predictability of certain aspects of functional disability may be related to the general predictability of these areas of functioning more than the abbreviated nature of the assessment. Processing-speed indices manifested the best prediction of overall impairments, and it seems clear that more assessments will be required in any battery that is designed to predict multiple features of outcome.

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APPENDIX

Conflict of interest statement

Philip D. Harvey has served as an advisor or consultant to: Astra-Zeneca Pharmaceuticals, Bristol-Myers Squibb, Eli Lilly and Company, Johnson and Johnson, Inc., Memory Pharmaceuticals, Novartis Pharmaceuticals, Pfizer, Inc., SolvayWyeth Alliance, and the Sanofi-Aventis Group. He has current or immediately prior grant or contract support from: Astra-Zeneca Pharmaceuticals, Bristol Myers Squibb, Johnson and Johnson, Inc., and Pfizer, Inc.

Richard S. E. Keefe: Past (1-2 years): Abbott (advisory board, as of 1/26/07); Astra-Zeneca (advisory board, as of 5/20/06; Speaker, as of 10/20/06); Gabriel Pharmaceuticals (consulting, as of 7/25/06); Otsuka (consulting, as of 5/15/07); Pfizer (research funding, as of 5/15/07); Saegis (advisory board, as of 5/25/06; consulting, as of 5/25/06). *Current/active*: Acadia (consulting); Astra Zeneca (unrestricted educational funding); Bristol Myers Squibb (consulting); Cephalon (consulting); Cortex (consulting); Cyberonics (consulting, as of 10/2006); Dainippon Sumitomo Pharma (consulting, as of 3/25/07); Eli Lilly Laboratories (advisory board; consulting; research funding; Speaker); Johnson & Johnson (consulting; research funding, pending); Lundbeck (consulting); Memory Pharmaceuticals (advisory board; consulting); Merck (consulting); Orexigen (consulting); Organon Pharmaceuticals (advisory board; unrestricted educational funding); Pfizer (consulting); Sanofi/Aventis (advisory board; consulting); Xenoport (consulting). *Royalties received*: Brief Assessment of Cognition (BACS); Measurement and Treatment Research for Improving Cognition in Schizophrenia (MATRICS) Battery (BACS Symbol Coding). *Personal stake*: Director of Neurocognitive Assessment Unit for CATIE Project; Member of MATRICS Neurocognition Committee; Director of Treatment Units for Reducing Neuropsychological Symptoms (TURNS) Chief Neuropsychologists Group.

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Thomas L. Patterson and Robert K. Heaton have no current conflicts.

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TABLE 1

Demographic characteristics and test performance

<i>Variable</i>	<i>M</i>	<i>SD</i>	<i>%</i>
<i>Demographic</i>			
Age (years)	57.1	7.3 ^d	
Years of education	12.8	2.2	
WRAT-3 Reading	44.43	8.59	
WAIS-III Vocabulary	35.51	13.76	
Sex (% male)			70.4
<i>Ethnicity</i>			
			64
Caucasian			22
African American			10
Hispanic			4
Other			
<i>Cognitive performance</i>			
<i>Cognitive domain</i>			
<i>Intellectual functioning</i>			
Test			
WAIS-III Vocabulary	34.51	13.76	
WRAT-3 Reading	44.43	8.60	
WCST Errors	74.22	14.14	
RAVLT Learning	33.18	11.04	
Trail Making Part A Time	69.80	41.04	
Trail Making Part B Time	159.91	60.32	
WAIS-III Digit Symbol	38.11	16.04	
WAIS-III Digit Span Forward	8.93	2.22	
WAIS-III Digit Span Backward	5.16	2.28	
WAIS-III Letter-Number Sequencing	6.31	3.11	
<i>Verbal skills</i>			
Animal Naming	16.23	5.65	
Boston Naming Test	13.34	1.79	
Praxis Test Total Score	8.75	1.78	
SSPA Total Score	3.89	1.36	
UPSA-Brief Total Score	68.80	19.57	
SLOF Total Score	193.14	23.86	
PANSS Total Score	55.32	14.73	
<i>Functional and clinical variables</i>			

Note. *N* = 236. WRAT-3 = Wide Range Achievement Test-Third Edition. WAIS-III = Wechsler Adult Intelligence Scale-Third Edition. WCST = Wisconsin Card Sorting Test. RAVLT = Rey Auditory Verbal Learning Test. SSPA = Social Skills Performance Assessment. UPSA = UCSD Performance-Based Skills Assessment Battery. SLOF = Specific Level of Function Scale. PANSS = Positive and Negative Syndrome Scale.

^aRange 50-75.

TABLE 2
Regression results predicting global estimates of cognitive performance

Score	Step	Variable	R ²	R ² change	F	p
Composite cognitive score	1	Trail Making Part B	.54	.54	256.10	.001
	2	RAVLT Learning	.62	.08	45.42	.001
	3	Digit Span Backward	.66	.04	26.97	.001
	4	Digit Symbol	.69	.03	18.98	.001
	5	Trail Making Part A	.70	.01	7.78	.005
	6	Letter-Number Sequencing	.71	.01	5.32	.02
GDS cognitive score	1	Trail Making Part B	.58	.58	294.24	.001
	2	Digit Symbol	.67	.09	57.76	.001
	3	Letter-Number Sequencing	.71	.04	36.71	.001
	4	Digit Span Backward	.74	.03	17.97	.001
	5	Praxis Total	.75	.01	12.72	.001
	6	RAVLT Learning	.76	.01	9.47	.002
	7	Digit Span Forward	.77	.01	7.71	.005
	8	Animal Naming	.78	.01	5.32	.02

Note. GDS = Global Deficit Score. RAVLT = Rey Auditory Verbal Learning Test.

TABLE 3

Regression results predicting measures of functional disability

Score	Step	Variable	R ²	R ² change	F	p
UPSA Total Score	1	Digit Symbol	.27	.27	90.04	.001
	2	Boston Naming	.39	.12	34.46	.001
	3	Digit Span Forward	.41	.02	16.62	.001
	4	Letter-Number Sequencing	.43	.02	10.17	.002
	5	Praxis Total Score	.45	.02	7.05	.005
	6	RAVLT Learning	.46	.01	4.39	.05
SSPA Total Score	1	Digit Symbol	.24	.24	38.98	.001
	2	Animal Naming	.34	.10	14.44	.001
	3	RAVLT Learning	.36	.02	9.77	.002
SLOF Functional Score	1	Trail Making Part A	.17	.17	31.62	.001
	2	Animal Naming	.22	.05	9.33	.003

Note. UPSA = UCSD Performance-Based Skills Assessment Battery. SSPA = Social Skills Performance Assessment. SLOF = Specific Level of Function Scale. RAVLT = Rey Auditory Verbal Learning Test.