

General and Specific Cognitive Deficits in Schizophrenia: Goliath Defeats David?

Dwight Dickinson, J. Daniel Ragland, James M. Gold, and Ruben C. Gur

Background: Our earlier work suggested that the cognitive performance impairment in individuals with schizophrenia relative to healthy control subjects was generalized, cutting across narrower cognitive ability dimensions. Current analyses sought to extend these findings.

Methods: Seventeen neuropsychological variables, available for 148 schizophrenia subjects and 157 control subjects, were subjected to structural equation modeling. Analyses incorporated a hierarchical model, grouping the variables into six familiar cognitive domains and linking these to a higher-order, general cognitive ability factor. We added diagnosis to the model as a grouping factor and estimated loadings from diagnosis to the general cognitive factor and, separately, to the domain factors.

Results: The fit of the final model was good (e.g., Non-Normed Fit Index [NNFI] = .988). Approximately 63.6% of the diagnosis-related variance in cognitive performance was mediated through the general factor, with smaller direct effects on verbal memory (13.8%) and processing speed (9.1%).

Conclusions: The schizophrenia cognitive deficit is largely generalized across performance domains, with small, direct effects of diagnostic group confined to selected domains. This generalized deficit sometimes has been seen as a function of the psychometric limitations of traditional cognitive test batteries. Alternatively, it may be a fundamental manifestation of schizophrenia, with similarly general neurobiological underpinnings.

Key Words: Cognitive deficit, neuropsychological testing, processing speed, schizophrenia, structural equation modeling, verbal memory

A large literature supports a multifactor structure of neuropsychological test performance among individuals with schizophrenia. Deficits in episodic memory, sustained attention, working memory, processing speed, and reasoning/problem solving have been reported frequently (1). However, these separable dimensions are strongly correlated, reflecting their shared relationship with a common cognitive ability factor (2,3), referred to as “g” (4). Most of the schizophrenia factor analytic literature has addressed the “within-group” structure of cognition. The structure of “between-groups” cognitive deficit evident in comparisons of schizophrenia patients and healthy control subjects has been less studied. Using structural equation modeling (SEM), we found that most of this deficit was generalized across cognitive dimensions—in essence, a “deficit g”—and that domain-specific effects of diagnosis were selective and small in magnitude (5).

Generalized deficit findings are a challenge to domain-specific interpretations of neuropsychological findings in clinical trials and studies of schizophrenia genetics, and may raise fundamental questions about the neural underpinnings of cog-

nitive dysfunction in this illness. However, the 2004 analysis used a simplified model of cognitive structure and was limited to measures drawn from the Wechsler intelligence and memory scales. To confirm and extend these findings, we analyzed data from a comprehensive neuropsychological battery administered to large schizophrenia and control samples (6). We examined whether the between-groups performance deficit is better understood as a single, generalized deficit; a number of discrete domain-specific deficits; or some combination of generalized and specific effects. Based on our earlier work, we hypothesized that the deficit would be mediated mainly through a common cognitive ability factor, with smaller direct effects on selected cognitive domains.

Methods and Materials

Participants

Patients and control subjects were assessed and followed by the Schizophrenia Research Center at the University of Pennsylvania. Data for the present analyses were collected from January 1993 to May 1998, as described previously (6). Patients had DSM-III-R diagnoses of schizophrenia established by clinical examination and structured clinical interview but were free of other psychiatric conditions. Control subjects were free of psychiatric disorders in themselves and their first-degree relatives. Patients and control subjects were between the ages of 18 and 45 and had no medical conditions or head injury history that might affect cognitive functioning. All schizophrenia participants were stable outpatients. Forty-two schizophrenia participants were in their first episode of illness with little medication history at the time of testing, 77 were on stable doses of antipsychotic medication, and 29 were missing medication information. One-way analyses of variance (ANOVAs) showed no significant differences among these patient subgroups on any of the cognitive test variables (all p s > .05, all but one p > .25).

Statistical Analysis

Data from 148 schizophrenia patients and 157 healthy control subjects were analyzed. These samples were nonover-

From the VA Capitol Health Care Network Mental Illness Research, Education and Clinical Center (DD, JMG), Education and Clinical Center; Psychiatry Department (DD, JMG), University of Maryland School of Medicine; and Maryland Psychiatric Research Center (JMG), Baltimore, Maryland; Department of Psychiatry and Behavioral Sciences (JDR), University of California at Davis, Sacramento, California; and Psychiatry Department (RCG), University of Pennsylvania School of Medicine; and the Philadelphia Veterans Administration Medical Center (RCG), Philadelphia, Pennsylvania.

Address reprint requests to Dwight Dickinson, Ph.D., Mental Illness Research, Education and Clinical Center, Suite 6A (BT/MIRECC), 10 North Greene Street, Baltimore, MD 21201; E-mail: Dwight.Dickinson@va.gov.

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Table 1. Grouping of Individual Neuropsychological Variables into Cognitive Domains

Cognitive Domain	Individual Cognitive Tests/Variables ^a
Executive/Working Memory	WCST Categories, WCST Perseverative Errors, Trail Making Test B, WAIS Digit Span
Verbal Ability	WAIS Vocabulary, MAE Naming
Spatial Ability	WAIS Block Design, Benton Judgment of Line Orientation
Verbal Learning and Memory	WMS Logical Memory I, WMS Logical Memory II, CVLT Trials 1–5, CVLT Delayed Free Recall
Visual Learning and Memory	WMS Visual Reproduction I, WMS Visual Reproduction II
Processing Speed	Trail Making Test A, Symbol Cancellation, Category Fluency

CVLT, California Verbal Learning Test; MAE, Multilingual Aphasia Examination; WAIS, Wechsler Adult Intelligence Scale; WCST, Wisconsin Card Sorting Test; WMS, Wechsler Memory Scale.

^aSpecific citations for the neuropsychological measures referred to in this article are available in standard neuropsychological reference works (9).

lapping with those analyzed for the 2004 report. LISREL 8.8 (7), with maximum likelihood estimation, was used to estimate parameters and evaluate model fit. Our primary analyses incorporated a hierarchical six-factor model of cognitive performance for patients and control subjects validated in our earlier analyses of within-group cognitive structure in these same samples (6). Central premises of the hierarchical model are that cross-domain associations between individual cognitive test variables actually reflect the interrelationships among a smaller number of latent cognitive domain factors (e.g., processing speed, verbal memory) and that these interrelationships are caused, in turn, by the shared relationship of the domain factors to a higher-order latent factor representing general cognitive ability or *g* (8). Consistent with these ideas, each of the 17 cognitive variables was assigned (by consensus of the authors) to load exclusively on the factor indicated in Table 1, and these factors were assigned to load on the common factor.

To examine the structure of the between-groups deficit, we added diagnostic group to the hierarchical model (Figure 1, bracket b). We first estimated a common factor model with no independent paths from diagnosis to individual cognitive domain factors. Then, we added direct paths (e.g., the curved arrow in Figure 1), one at a time, and re-estimated. The model was considered final when additional direct diagnosis factor paths no longer contributed significantly to model fit. The goodness-of-fit index (GFI) (10), non-normed fit index (NNFI) (11), and root mean square error of approximation (RMSEA) (12) were used to assess overall goodness of fit of the estimated model variance-covariance matrix to the observed matrix. Interpretation of these indices is described in our earlier report (6).

Results

Sample Characteristics

Patients were significantly older than control subjects, more likely to be male, and less likely to be Caucasian. Patients also had fewer years of education, although parental education was statistically equivalent between groups (Table 2). To reduce the impact of

demographic differences, all analyses covaried age, sex, race/ethnicity, and mother's/father's education.

The schizophrenia deficit was significant for every neuropsychological variable (all *ps* < .01). Wechsler Adult Intelligence Scale (WAIS) Vocabulary and Digit Span standard scores indicated that the control subjects were above average in intellectual performance, while the schizophrenia group was below average. The performance discrepancy between groups on these intellectual measures was comparable with other schizophrenia/control group comparisons on similar measures (13,14).

Modeling Results

A model with all diagnosis effects mediated through the common factor fit the data marginally (Table 3, Model 1). Model fit improved significantly with the addition of a path representing the direct effects of diagnosis on verbal memory (Table 3, Model 2) and improved further with the addition of a direct processing speed path (Table 3, Model 3). No other direct paths from diagnosis to cognitive factors significantly improved model fit. Figure 2 shows the final model and

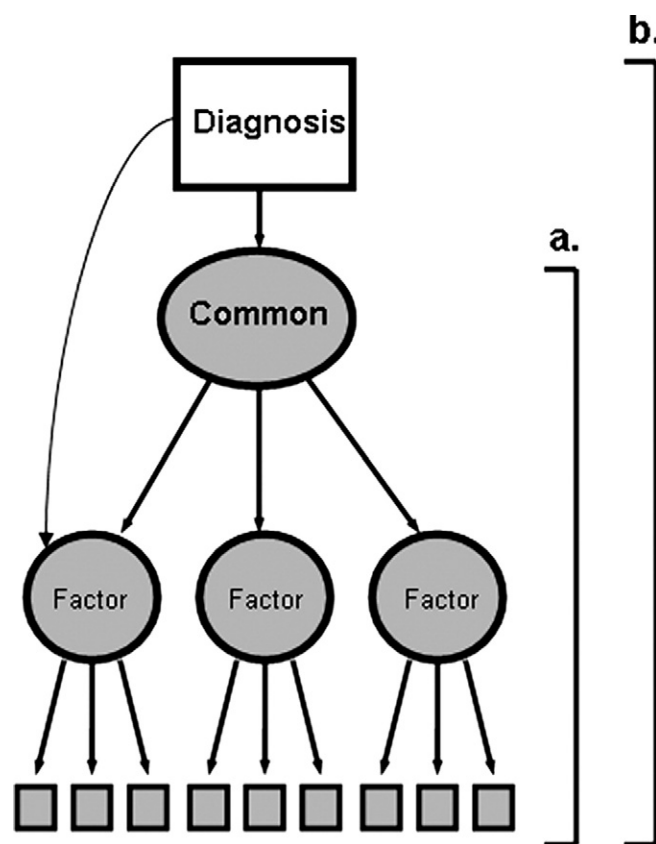


Figure 1. Illustration of the hypothesized model and structural equation modeling methodology. The part of the figure indicated by the bracket labeled "a" illustrates the hierarchical measurement model. Performance on observed variables (boxes) is assumed to be driven by domain-specific latent factors. These factors are determined, in turn, by the common cognitive ability factor. The whole figure (indicated by bracket "b") illustrates the overall structural model for current analyses. These analyses test whether the effects of diagnostic grouping (i.e., schizophrenia vs. healthy control status; represented by the unshaded box marked "Diagnosis") on the observed cognitive variables is mediated through the common factor or whether diagnosis affects observed variables through direct effects on domain-specific factors.

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