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Cognitive Factor Structure and Invariance in People With Schizophrenia, Their Unaffected Siblings, and Controls

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Introduction: **Separable, but positively correlated, factors emerge from analyses of cognitive test data in schizophrenia and control samples (eg, verbal memory and processing speed) and these factors guide data reduction. Additionally, data support a hierarchical model of cognitive performance, in which these correlations reflect the influence of a higher-order factor, referred to as "g." We tested these findings in large, carefully screened samples of people with schizophrenia (n = 496), their unaffected siblings (n = 504), and controls (n = 823). Furthermore, we tested the hypothesis that cognitive performance in schizophrenia is more generalized across domains than among siblings and controls.** ***Method*****: A combination of exploratory and confirmatory factor analyses (EFA and CFA) and multiple groups CFA (MCFA) was used.** ***Results:*** **EFA yielded factors for verbal memory, visual memory, processing speed, working memory span, nback performance, and card sorting. The solution was consistent across groups, in terms of the factor assignments of individual cognitive variables and the magnitude of loadings. Method variance may have contributed to the card sorting, visual memory, and nback factors. CFA indicated that the hierarchical model, incorporating a "g" factor, was a good fit for data from all groups. MCFA suggested that this hierarchical structure was fully invariant for controls and siblings. While the variable/factor loadings for the schizophrenia group also were invariant with comparison groups, factor/"g" loadings were higher in schizophrenia, as were correlations among factor-based composite scores.** ***Conclusions:*** **Cognitive variables sort into domains consistently in schizophrenia, unaffected siblings, and controls. However, performance in schizophrenia is more generalized and less domain specific.**

Key words: cognition/general cognitive ability/factor analysis/structure invariance/data reduction

Introduction

Recently, we reported the results of exploratory and confirmatory factor analyses (EFA and CFA) of cognitive data from 397 early participants in the genetics study of the Clinical Brain Disorders Branch, National Institute of Mental Health (CBDB Sibling Study).[1] With data now available for more than 4 times as many participants, we revisited and extended that work.

Across numerous factor analyses of schizophrenia sample data, separable factors emerge for cognitive performance domains, including learning and memory, processing speed, reasoning/problem solving, and working memory.[2] The factors are moderately correlated.[3] This structure is broadly consistent across schizophrenia and control groups[4] and our earlier analyses of "CBDB Sibling Study" data confirmed that the structure characterized unaffected siblings of people with schizophrenia as well.[1] This consistent factor structure serves as a basis for data reduction, allowing combination of subgroups of individual measures into composite scores representing the different cognitive domains. Given the large number of overlapping cognitive variables available in the CBDB Sibling Study database and the desire to avoid redundant statistical tests, data reduction was a principal aim of the current analyses.

In nonclinical populations, positive correlations among cognitive factors (eg, processing speed and working memory) are thought to reflect the influence of a higher-order factor, designated general cognitive ability or "g."[5,6] The idea of general cognitive ability is related to IQ, but somewhat broader, encompassing cognitive abilities like episodic memory and spatial working memory that are only indirectly tapped by the most widely used IQ tests.[7] This stratified structure of cognitive performance—with "g" influencing performance in cognitive domains and

domain factors influencing performance on individual cognitive tests—is known as the "hierarchical model."[7] In earlier work with a nonoverlapping sample, the model provided a good characterization of data from schizophrenia patients and healthy controls.[4]

Despite the consistency in factor structure across schizophrenia and control groups, it is clear that the structures are not fully invariant. Mean performance differs reliably between these groups, to take one obvious example. There is another less obvious respect in which the group factor structures appear to differ. Earlier analyses showed that, while the grouping of observed variables into cognitive factors was the same for people with schizophrenia and healthy controls, the correlations among these factors and among domain composites based on the factors were higher in the schizophrenia sample than in the controls.[4] This finding suggests that cognitive performance in schizophrenia is more generalized and less domain specific than in healthy groups, but it has not been replicated or investigated in unaffected siblings. Such differences could have implications regarding the nature of the cognitive impairment in schizophrenia, its relationship to genetic risk, and the use and interpretation of different indexes of cognitive performance in genetics, neuroimaging, and other studies. The current study had 3 aims: (a) to confirm and refine the cognitive factor structure derived in analyses of the first wave of the CBDB Sibling Study data in order to allow reduction of the number of variables used in analyses of these data; (b) to test for the presence in these data of a higher-order factor representing general cognitive ability or "g"; and (c) to examine dimensions of invariance for the proposed factor structure across our large samples of schizophrenia, unaffected sibling, and control volunteers.

Methods

Participants

Data for analyses was drawn from 1824 volunteers in 3 groups: 496 schizophrenia probands, 504 of their unaffected siblings, and 823 healthy controls. All were participants evaluated in the course of participation in the CBDB Sibling Study, which has been described previously.[8] Participants ranged in age from 18 to 60 years and were able to provide informed consent. All participants were medically screened and completed separate diagnostic interviews with 2 research psychiatrists.[9] Individuals were included in the schizophrenia group if they had schizophrenia, schizoaffective disorder, psychosis not otherwise specified, or schizoid personality disorder. Siblings were permitted to have a history of mood/anxiety (~37%) or personality (~5%) disorder, although the majority had no history (~58%). Controls were excluded if they had first-degree relatives with schizophrenia spectrum disorders, if they were currently diagnosed with an Axis I or Axis II disorder, or if they were taking psychotropic medication at the time of the study. Any person with schizophrenia, sibling, or control was excluded if he or she had a history of head trauma with extended loss of consciousness, alcohol, or drug abuse within the past 6 months, IQ less than 70, or evidence of learning disability. Schizophrenia participants were stable and receiving neuroleptic medications at the time of testing.

Neuropsychological Assessment

All participants were administered a neuropsychological battery and 25 variables from a larger set were examined in current analyses (table 1). The 25 variables were selected by consensus among experienced neuropsychologists (T.E.G., J.M.G., and D.D.). These variables were judged to satisfy 3 principal criteria: (1) they are variables that have been commonly used in schizophrenia research, representing key domains of performance impairment, (2) they had shown evidence of impaired performance in healthy siblings of patients with schizophrenia, suggesting that they might serve as intermediate cognitive phenotypes related to genetic risk for schizophrenia, and (3) they showed good distributional characteristics across each of the 3 CBDB Sibling Study subgroups in this data set. Variables not meeting these criteria (generally because of extreme floor or ceiling effects) included those from Gordon's Continuous Performance Test, Benton's Facial Recognition Test, and the 0-back condition from the N-back task.

Statistical Analysis

Exploratory Analyses. All analyses were conducted using SPSS v16.0 and AMOS v16.0 statistical software (SPSS, Inc., Chicago, IL, 2008). Separate exploratory analyses were conducted for schizophrenia participants, unaffected siblings, and healthy controls. Missing data were excluded pairwise rather than listwise to maximize our use of valid data (see Table 1 for counts of missing values).

Our first aim of data reduction shaped the choice of exploratory analyses.[10] Subgroup data were subjected to principal components analyses (PCA) followed by varimax rotation, an approach that has been frequently used in schizophrenia research.[2] PCA is not a true latent factor analysis technique and some commentators recommend that its use be restricted to data reduction.[10] Because we are interested in underlying structure in addition to data reduction, we conducted a parallel exploratory analysis using maximum likelihood estimation to check the sensitivity of our analysis to extraction method. In all analyses, factors with eigenvalues greater than 1.0 were retained. An individual variable was excluded and analyses were redone if the variable did not show a loading of at least 0.40 on any factor or if it showed a complex loading pattern (eg, loadings of at least 0.40 on 2 or more factors).[10]

Table 1. Demographic and Cognitive Characteristics of Sample

	Schizophrenia			Siblings			Controls			Effect sizes	
N	496			505			823				
Age*	35.5 (10.1)			36.7 (10.1)			32.6 (9.7)				
Female*, *n* (%)	127 (25.6)			301 (59.6)			458 (55.6)				
Education*	14.0 (2.2)			15.9 (2.4)			16.7 (2.5)				
C/AA/O, *n**	412/27/57			445/12/48			669/76/73				
Cognitive Variable**	Mean	SD	Msg	Mean	SD	Msg	Mean	SD	Msg	ES SZ<HC	ES Sib<HC
WAIS Digit Symbol****	8.0	2.3	26	11.6	2.5	11	12.5	2.5	25	−1.85	−0.36
Trails A T-score****	37.3	10.5	28	46.0	10.4	16	48.0	10.2	24	−1.04	−0.19
Trails B T-score****	39.6	11.0	35	49.6	9.9	15	52.2	10.2	24	−1.20	−0.26
WMS Digit Span Forward***	8.5	2.0	32	9.6	1.9	18	9.8	1.8	172	−0.69	−0.11
WMS Digit Span Backward***	6.4	2.3	32	7.8	2.2	17	8.1	2.2	175	−0.76	−0.14
WAIS Letter Number Sequence	9.4	2.7	225	11.9	2.8	249	12.3	2.4	132	−1.16	−0.16
WMS Logical Memory 1****	17.5	7.9	28	26.7	7.1	13	27.9	6.8	24	−1.44	−0.17
WMS Logical Memory 2****	12.6	7.9	32	22.3	8.0	15	24.0	7.5	28	−1.49	−0.22
WMS Verbal Paired Association***	16.2	4.7	51	19.8	3.3	46	20.2	2.9	346	−1.03	−0.13
CVLT Trials 1–5 Total***	41.4	12.7	102	58.7	9.5	69	59.2	8.9	156	−1.70	−0.05
WMS Visual Reproduction 1***	30.5	7.0	34	35.3	3.9	19	35.5	3.3	344	−0.92	−0.06
WMS Visual Reproduction 2***	25.2	9.3	37	33.1	5.1	19	33.7	4.4	347	−1.17	−0.13
WCST % Perseverative Errors T-score****	39.8	11.7	57	46.8	8.9	28	49.2	9.1	76	−0.93	−0.27
WCST Categories Over Trials****	0.04	0.02	49	0.06	0.02	23	0.07	0.02	52	−1.50	−0.50
WCST Correct Over Trials****	0.64	0.17	50	0.79	0.11	23	0.80	0.11	52	−1.18	−0.09
Nback One****	0.65	0.26	186	0.83	0.18	154	0.88	0.13	107	−1.28	−0.34
Nback Two****	0.49	0.22	190	0.69	0.20	151	0.76	0.18	99	−1.40	−0.38
Nback Three****	0.43	0.17	189	0.55	0.18	151	0.64	0.18	100	−1.19	−0.50
WAIS Arithmetic****	8.6	2.5	25	10.8	2.5	11	11.1	2.5	24	−1.00	−0.12
WAIS Similarities	9.7	2.5	25	11.1	2.5	11	10.9	2.1	25	−0.53	0.09
WAIS Picture Completion	8.9	2.6	25	10.5	2.5	11	10.3	2.5	25	−0.55	0.08
WRAT Reading Standard Score****	102	11.2	25	107	9.9	11	108	8.9	27	−0.61	−0.11
Benton Line	24.5	5.1	35	27.4	3.5	20	27.5	3.5	31	−0.72	−0.03
Letter Fluency****	34.4	11.2	29	42.3	11.2	15	44.8	10.8	24	−0.95	−0.23
Category Fluency****	37.7	11.1	30	51.1	10.3	15	52.7	10.5	24	−1.40	−0.15
Mean ES										−1.07	−0.17

Note: C/AA/O, Caucasian/African American/Other; SD, standard deviation, Msg, number missing; ES SZ<HC, effect size (Hedges' g) for the schizophrenia impairment relative to controls; ES Sib<HC, effect size (Hedges' g) for the sibling impairment relative to controls; WAIS, Wechsler Adult Intelligence Scale; WMS, Wechsler Memory Scale; CVLT, California Verbal Learning Test; WCST, Wisconsin Card Sorting Test; WRAT, Wide Range Achievement Test. "WCST Categories Over Trials" and 'WCST Correct Over Trials"—to equate different versions of the WCST used at different times, categories and correct variables were divided by the number of trials administered. "Nback One," "Nback Two," and "Nback Three" scores are proportions correct.

*Subgroup demographic differences significant at $P < .001$.

**Controlling for age, gender, and race/ethnicity, schizophrenia < sibling and control at $P < .001$ for all cognitive measures.

***Controlling for age, gender, and race/ethnicity, sibling < control at $P < .05$.

****Controlling for age, gender, and race/ethnicity, sibling < control at $P < .01$.

Confirmatory Analyses. CFA followed the PCAs in order to address the second and third aims of the study. Separate initial confirmatory analyses tested whether the hierarchical model of cognitive performance[7] provided a good characterization of data from the current samples of schizophrenia patients, unaffected siblings, and healthy controls (figure 1). The variables and first-order factors were from the final PCA and each observed cognitive variable was constrained to load exclusively on a single factor.

The hierarchical model contrasts with "correlated factors" models used in earlier studies.[11] Correlated factors models are less constrained (and therefore easier to fit) than hierarchical models. They allow each first-order factor to correlate freely with every other first-order factor, but include no general cognitive ability factor and are otherwise atheoretical about the reasons for factor interrelationships. A correlated factors model was used as the comparison model in current analyses. Standard measures (described in [4,12]) were used to index overall goodness of fit of the estimated model correlation matrix to the observed matrix. In addition, we report the parsimony-adjusted comparative fit index (PCFI), which incorporates a penalty for increasing model complexity (ie, larger numbers of parameters being estimated). The index is used here to highlight relative differences within subsets of related analyses.

Multiple Group CFAs. Further CFAs addressed the question of structure invariance. Invariance is tested

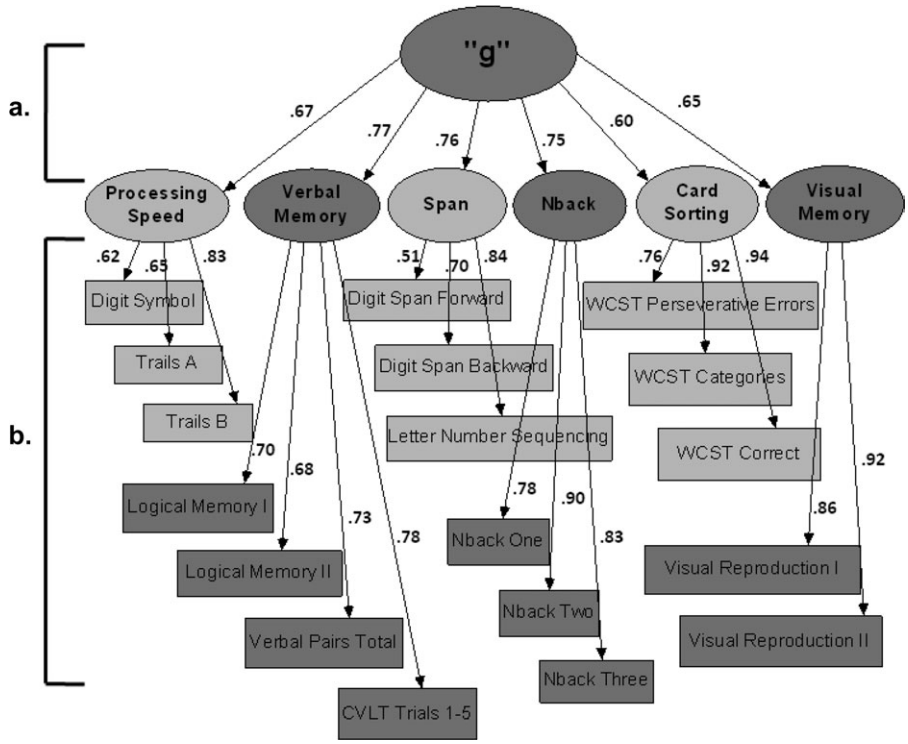

Fig. 1. Final data reduction model. Loadings are for the schizophrenia sample only ($n = 496$). The model parameters (ie, arrows) in the area indicated by bracket "a" are the factor/"g" loadings. The model parameters in the area indicated by bracket "b" are the variable/factor loadings.

through "multiple groups" CFA. These analyses proceed sequentially. First, all parameters are allowed to vary independently between groups. In the following analyses, sets of key parameters are constrained to be equal across groups. Significant deterioration in model fit with increasing equivalence constraints signals "noninvariance" and provides information about which parts of the model are noninvariant. For present purposes, the key dimensions of invariance are the variable/factor loadings and the factor/"g" loadings (figures 1a and 1b). We report 3 MCFAs: people with schizophrenia compared with healthy controls, people with schizophrenia versus their unaffected siblings, and unaffected siblings versus healthy controls. For each set, the initial unconstrained model (ie, with all parameters free to vary between groups) served as baseline. We then tested a model in which the CFA-derived variable/factor loadings were required to be equal across groups, followed by a model in which both variable/factor loadings and factor/"g" loadings were constrained to be equal. The chi-square difference test identified significant changes in model fit as additional model constraints were applied. Additional information about the magnitude and practical significance of group differences in the 2 key parameter dimensions was obtained through examination of changes in the values of the fit indexes described earlier.

Composite Correlations. Finally, composites were constructed to represent each factor for each individual with sufficient data. Scores on different measures were converted to *z*-scores using control means and standard deviations and then averaged within domains to yield a domain composite. Unit-weighted composites were used rather than loading-weighted factor scores because such composites generally correlate very highly with factor scores and because they are more replicable across laboratories and samples.[13] Raw domain composite scores were transformed as needed to enhance normality (ie, square or cube transformations to address negative skew). A "g" composite was derived in similar fashion. These values are intended to be used in future analyses of CBDB Sibling Study data. We calculated Pearson's correlations among the domain composites by subgroup and tested for differences in the magnitude of the correlations across subgroups using a multigroup adaptation of Fisher's test.[14]

Results

Participant Characteristics

Demographic statistics, cognitive variable performance for each group, and effect sizes for the impairments in schizophrenia participants relative to controls and unaffected siblings relative to controls are reported in table 1. All groups were predominantly Caucasian, which may limit the generalizability of findings to other racial and ethnic groups. It is important to note the smaller percentage of female participants in the schizophrenia group

compared with the other groups. All further analyses controlled for gender, age, and race/ethnicity, and sensitivity analyses explored whether gender differences between groups affected key findings. We did not control for education as it is confounded with illness in patients[15] and because current analyses are concerned mainly with associations among variables rather than mean performance levels. The schizophrenia participants were mildly symptomatic on average, as indicated by Positive and Negative Syndrome Scale scores (positive syndrome, mean = 13.5, SD = 6.4; negative syndrome mean = 19.3, SD = 9.6). They performed significantly worse than the sibling and control samples on all cognitive measures (all Ps $< .001$). The average effect size, the range of effects, and the maximal effect for Digit Symbol are all consistent with a recent meta-analysis.[16] Although the differences were generally small, unaffected siblings performed significantly worse than healthy controls on 17 of 25 variables, and numerically worse on 6 of the remaining 8 variables. The average effect (-0.17; range 0.09 to -0.50) was smaller than reported for relatives generally.[17] Part of the reason is that only age-matched siblings (and not parents) were included in the unaffected sibling sample here and siblings were carefully screened for schizophrenia spectrum diagnoses. In other ongoing work, we are examining the effects of nonschizophrenia spectrum diagnoses on cognitive performance in our sibling sample.[18] In general, however, the results are consistent with the growing body of evidence of small but reliable cognitive deficits in the close relatives of people of schizophrenia.

Exploratory PCA

In initial exploratory analyses, 7 of 25 variables showed complex and/or inconsistent loadings (the last 7 variables in table 1). Consequently, while these variables were retained for calculation of the "g" composite, they were eliminated from the PCA. Results of the PCA are in table 2.

For each subgroup, 6 parallel principal components were derived, accounting for 76.4% of overall variance in the schizophrenia group, 72.9% in the sibling group, and 71.3% in the control group (variance accounted for by each factor in each group is in table 2). Principal components for verbal memory, processing speed, and span measures emerged for each group. The remaining components were defined by particular cognitive tests, including a card sorting component, a component for the nback measures, and one for the 2 visual reproduction measures. Typical loadings above .70 for individual measures within components mean that the variables generally shared variance of 50% or more with the other variables in a given component set. No variable showed important secondary loadings. The primary loadings were consistent across measures within a component and across subgroups of people with schizophrenia, unaffected siblings, and controls.

The emergence of 3 factors defined by specific tests raised the question whether the test-based factors signify important, separable constructs, or reflect shared test methodology—so-called "method variance." To shed light on this question, we performed 2 further sets of factor analyses. In the first (alternative 1), we retained only one variable each from the card sorting, nback, visual reproduction groupings (Wisconsin Card Sorting Test [WCST] Perseverative Errors T-score, Nback Two, and visual reproduction 1), but held other aspects of the 6-component solution constant. In the second (alternative 2), we used the same 3 variables from the card sorting, nback and visual reproduction groupings as in alternative 1, but also added back the seven variables that had shown complex or inconsistent loadings in the prior analyses. In both solutions, memory, processing speed, and span components emerged for all groups (see table 3 for factor loadings from the alternative 1 solution). However, in other respects, these alternatives did not yield consistent, interpretable solutions across groups or variables. In alternative 1, for example, 4 factors emerged for controls, compared with only 3 for schizophrenia participants and their siblings. In the alternatives, loadings for the 3 variables retained from the card sorting, nback and visual reproduction groupings were split between factors and inconsistent from group to group. Predicted associations (eg, Nback Two and the span variables on a single working memory component) did not emerge. The overall variance explained by alternative 1 (55.5%–60.5%) and alternative 2 (56.0%–60.2%) dropped sharply compared with the six-component solution for all groups (71.3%–76.4%). There was also a dramatic decline in the variance in WCST Perseverative Errors T-score, Nback Two, and Visual Reproduction 1 explained jointly by the factors derived for alternative 1 and alternative 2 (ie, squared multiple correlations or communalities). For example, for the schizophrenia group, the preferred six-component solution explained variance in these 3 variables ranging from 77% to 89%, compared with 26%–40% for alternative 1 and 27%–53% for alternative 2. In short, these exploratory analyses did not point to a solution that was both interpretable and free of possible method variance.

Sensitivity analyses showed that our preferred 6-component solution is quite robust. Further subdividing our 3 groups by gender did not change the findings appreciably. The same 6-component solution held for all 6 groupings. Minor differences appeared only in the solution for the smallest subgroup (women with schizophrenia, $n = 127$; eg, complex California Verbal Learning Test loadings). It is likely that the differences were a function of limited sample size. Additional evidence of robustness came from the sensitivity analyses using maximum likelihood factor analysis rather than PCA. In these analyses, 6 factors corresponding to the 6 principal components

Table 2. Variable/Factor Loadings from Main Principal Components Analysis for Schizophrenia, Sibling, and Control samples

Factor	Verbal Memory			Card Sorting			Nback			Span			Processing Speed			Visual Memory		
Cognitive variable	Sz	Sb	Ct	Sz	Sb	Ct	Sz	Sb	Ct	Sz	Sb	Ct	Sz	Sb	Ct	Sz	Sb	Ct
WAIS Digit Symbol	0.12	0.13	0.15	0.08	0.12	0.14	0.27	0.27	0.29	0.04	0.11	0.04	**0.71**	**0.62**	**0.59**	0.10	0.09	0.11
Trails A T-score	0.02	−0.04	0.04	0.12	0.03	0.07	0.01	0.05	−0.03	0.09	−0.02	0.06	**0.86**	**0.84**	**0.81**	0.05	0.09	0.00
Trails B T-score	0.17	0.08	0.10	0.12	0.13	0.02	0.19	0.12	0.13	0.32	0.23	0.18	**0.71**	**0.77**	**0.78**	0.08	0.03	0.07
WMS Digit Span Forward	0.05	0.07	0.11	0.06	0.06	0.02	−0.01	0.08	0.06	**0.85**	**0.79**	**0.80**	0.07	0.05	0.00	0.10	−0.08	0.04
WMS Digit Span Backward	0.15	0.08	0.14	0.12	0.10	0.09	0.24	0.14	0.09	**0.77**	**0.80**	**0.80**	0.15	0.09	0.08	0.05	0.10	0.11
WAIS Letter Number Sequence.	0.28	0.23	0.14	0.16	0.12	0.07	0.25	0.16	0.12	**0.67**	**0.78**	**0.75**	0.20	0.15	0.22	0.10	0.12	0.02
WMS Logical Memory 1	**0.91**	**0.89**	**0.91**	0.12	0.09	0.04	0.09	0.12	0.08	0.10	0.10	0.12	0.03	0.00	0.04	0.09	0.00	−0.01
WMS Logical Memory 2	**0.90**	**0.90**	**0.92**	0.12	0.09	0.03	0.09	0.11	0.09	0.08	0.10	0.11	0.05	0.00	0.06	0.07	0.02	0.03
WMS Verbal Paired Association	**0.67**	**0.70**	**0.54**	0.13	0.00	0.14	0.11	−0.07	0.03	0.16	0.11	0.17	0.09	0.13	0.08	0.25	0.15	0.27
CVLT Trials 1–5 Total	**0.66**	**0.63**	**0.66**	0.15	0.04	0.16	0.21	0.27	0.17	0.15	0.09	0.09	0.22	0.04	0.16	0.18	0.26	0.10
WMS Visual Reproduction 1	0.19	0.12	0.08	0.09	0.15	0.16	0.22	0.13	0.10	0.13	0.03	0.08	0.11	0.11	0.04	**0.88**	**0.89**	**0.90**
WMS Visual Reproduction 2	0.28	0.18	0.17	0.15	0.13	0.10	0.17	0.19	0.18	0.11	0.06	0.06	0.11	0.09	0.11	**0.86**	**0.87**	**0.88**
WCST % Perseverative Errors T-score	0.08	0.01	0.03	**0.84**	**0.85**	**0.83**	0.18	0.07	−0.03	0.08	0.04	0.04	0.13	0.18	0.12	0.07	0.07	0.12
WCST Categories Over Trials	0.17	0.09	0.13	**0.87**	**0.89**	**0.89**	0.18	0.18	0.20	0.13	0.12	0.08	0.12	0.02	0.05	0.11	0.11	0.06
WCST Correct Over Trials	0.21	0.10	0.17	**0.89**	**0.89**	**0.91**	0.15	0.19	0.17	0.12	0.14	0.07	0.09	0.08	0.06	0.08	0.13	0.12
Nback One	0.11	0.17	0.12	0.17	0.11	0.08	**0.79**	**0.67**	**0.77**	0.09	0.18	0.05	0.25	0.13	0.03	0.14	0.22	0.09
Nback Two	0.15	0.09	0.09	0.21	0.15	0.12	**0.84**	**0.86**	**0.86**	0.15	0.14	0.12	0.14	0.16	0.12	0.12	0.09	0.08
Nback Three	0.17	0.06	0.10	0.16	0.17	0.08	0.81	0.81	0.80	0.18	0.09	0.10	0.07	0.14	0.15	0.18	0.07	0.11
% Variance accounted for by each factor:	16.2	14.9	14.4	14.1	13.8	13.6	13.6	12.4	12.6	11.4	11.5	11.1	11.2	10.3	9.8	9.8	9.9	9.7

Note: Abbreviations are explained in the first footnote to table 1. Bold values indicate the primary loading of each variable (rows) on the various factors (columns). Sz, schizophrenia; Sb, siblings; Ct, controls.

emerged for all 3 subgroups, with matching patterns of factor loadings.

Confirmatory Testing of the Hierarchical Model and "g"

Table 4a shows various indices of model fit for the single group CFAs. The hierarchical model, incorporating a "g" factor (figure 1), provided a good fit to the data for all 3 groups (eg, $\chi^2/df < 2.0$, Tucker Lewis Index > .95, root mean square error of approximation <.05). For all groups, all variable and factor loading parameters were significant (Ps < .001). In separate analyses by group, the 6 correlated factors model showed similarly good fit for all groups. Slight numerical disadvantages for the hierarchical model relative to the correlated factors model on some fit indices were offset by increased parsimony, as reflected in relatively better values for the PCFI. Again, sensitivity analyses considered these models within gender subgroups and again gender differences were minor. Figure 1 shows, for the full schizophrenia sample only, the maximum likelihood standardized regression weights (ie, loadings). The "g" loadings here are slightly smaller than those from the earlier report on the hierarchical model[4] but, in general, there is substantial consistency of results despite differences in the samples, the cognitive test batteries, and the subtest composition of cognitive domains.

The factor loadings for the associations of the broad cognitive ability factors with the general ability factor are slightly higher in each case in the schizophrenia group than in the sibling or control groups (data not shown). Consistent with this, when the factor groupings were used to create cognitive domain composites, the bivariate correlations

Table 3. Variable/Factor Loadings from "Alternative 1" Principal Components Analysis for Schizophrenia, Sibling, and Control Samples

Factor	Verbal Memory			Span			Processing Speed			Visual Reasoning/Memory (New, Controls Only)		
Cognitive Variable	Sz	Sb	Ct	Sz	Sb	Ct	Sz	Sb	Ct	Sz	Sb	Ct
WAIS Digit Symbol	0.13	0.12	0.16	0.06	0.14	0.06	**0.75**	**0.65**	**0.67**	xx	xx	0.15
Trails A T-score	−0.02	−0.09	0.02	0.05	−0.04	0.04	**0.81**	**0.75**	**0.77**	xx	xx	0.00
Trails B T-score	0.16	0.03	0.09	0.32	0.25	0.18	**0.72**	**0.71**	**0.77**	xx	xx	0.08
WMS Digit Span Forward	0.05	0.05	0.11	**0.83**	**0.80**	**0.81**	0.06	0.03	0.02	xx	xx	0.02
WMS Digit Span Backward	0.17	0.10	0.14	**0.79**	**0.80**	**0.80**	0.21	0.17	0.09	xx	xx	0.16
WAIS Letter Number Sequence	0.31	0.26	0.13	**0.70**	**0.77**	**0.75**	0.28	0.24	0.24	xx	xx	0.06
WMS Logical Memory 1	**0.90**	**0.88**	**0.92**	0.10	0.15	0.13	0.04	0.03	0.08	xx	xx	−0.04
WMS Logical Memory 2	**0.89**	**0.88**	**0.93**	0.07	0.14	0.12	0.06	0.02	0.09	xx	xx	−0.02
WMS Verbal Paired Association	**0.72**	**0.69**	**0.53**	0.17	0.07	0.16	0.15	0.09	0.05	xx	xx	0.36
CVLT Trials 1–5 Total	**0.70**	**0.70**	**0.66**	0.17	0.09	0.09	0.30	0.22	0.19	xx	xx	0.26
WMS Visual Reproduction 1	0.43	0.32	0.11	0.24	−0.06	0.11	0.28	0.47	0.01	xx	xx	**0.73**
WCST % Perseverative Errors T-score	0.24	0.06	0.03	0.16	0.09	−0.01	0.42	**0.50**	0.13	xx	xx	**0.72**
Nback Two	0.31	0.20	0.16	0.30	0.27	0.18	0.47	0.51	0.34	xx	xx	0.37
% Variance accounted for by each factor:	37.0	29.8	29.1	9.3	10.9	10.5	13.2	14.9	12.3	xx	xx	8.7

Note: Bold values indicate the primary loading of each variable (rows) on the various factors (columns). Sz, schizophrenia; Sb, siblings; Ct, controls.

between these domains were uniformly higher in the schizophrenia group than in the comparison groups (table 5).

The mean correlation for the schizophrenia sample ($r = .372$) was smaller than the mean composite score correlation found in our earlier meta-analysis (ie, $r = .45$), although within the confidence interval for that estimate (.35 to .54).[3] However, the schizophrenia mean was significantly larger than the mean correlations for the siblings ($r = .239$) or controls ($r = .245$; χ^2 [2 *df*] = 7.24, $P = .027$). There is a more restricted range of test performance among siblings and healthy controls than schizophrenia patients, most evident in the Visual Reproduction variables (table 1). This could reduce correlations in the sibling and control groups. However, removing the visual memory composite from the correlation analysis did not appreciably change the magnitude of the group mean correlations or the statistical significance of the group differences.

As a further test of the proposition that cognitive correlations are higher in schizophrenia, we examined the pattern of correlations among the 7 individual variables from the original 25 that were left out of the factor analysis. Importantly, performance variance in these 7 variables was similar across the 3 groups. The range of correlations across groups was slightly compressed in this comparison. However, the mean correlation in schizophrenia was largest ($r = .339$) and was significantly larger than the mean correlation among controls ($r = .245$; $z = 1.73$, $P = .042$). Correlations in siblings were intermediate ($r = .288$) and not significantly different from either the schizophrenia or control samples. This pattern of higher correlations in people with schizophrenia was preserved in gender subgroups. Women showed slightly higher correlations than men for all groups but, in both genders, all bivariate correlations for pairs of cognitive composites were higher in the schizophrenia subgroup than in the comparison groups.

Multiple Groups Analysis of Structure Invariance

Table 4b shows the fit indices associated with the various 2-group analyses. In each pair, the "unconstrained" model, with all parameters free to vary between the groups, serves as baseline. Because the hierarchical model provided a good fit to the data from each of the groups separately, it was expected that the unconstrained model for each 2-group contrast would provide a similarly strong fit. The second model for each contrast required that individual loadings of each observed variable on its designated first-order cognitive factor (figure 1, bracket b) be the same for both groups, but left the loadings of the domain factors on higher-order "g" (figure 1, bracket a) free to vary between the groups. In the analysis including controls and siblings, imposing this constraint improved parsimony slightly (as shown by the change in PCFI) and had no deleterious effect on model fit, resulting

Table 4. Confirmatory Factor Analysis Results

a. Single Group Models	χ^2	*df*	*P*	χ^2/df	TLI	RMSEA	PCFI
Schizophrenia only							
Hierarchical model	205.423	127	<.001	1.618	.975	.035	.729
Correlated factors model	182.457	118	<.001	1.546	.978	.033	.679
Healthy controls only							
Hierarchical model	238.227	127	<.001	1.876	.974	.033	.728
Correlated factors model	217.840	118	<.001	1.846	.975	.032	.678
Siblings only							
Hierarchical model	246.449	127	<.001	1.941	.957	.043	.719
Correlated factors model	218.249	118	<.001	1.850	.961	.041	.671
b. Multiple Group Contrasts	$\Delta\chi^2$	Δdf	ΔP				
Schizophrenia vs controls							
Unconstrained model	—	—	—	1.747	.974	.024	.729
Variable/factor loadings equal	106.611	12	<.001	2.069	.963	.028	.756
Additionally, factor/"g" loadings equal	934.472	35	<.001	4.769	.871	.053	.753
Schizophrenia vs siblings							
Unconstrained model	—	—	—	1.779	.975	.028	.724
Variable/factor loadings equal	57.669	12	< .001	1.916	.969	.030	.754
Additionally, factor/"g" loadings equal	677.415	35	< .001	3.908	.893	.054	.755
Controls vs siblings							
Unconstrained model	—	—	—	1.908	.967	.026	.725
Variable/factor loadings equal	12.487	12	.407	1.869	.969	.026	.759
Additionally, factor/"g" loadings equal	119.471	35	<.001	2.091	.961	.029	.817

Note: df, degrees of freedom; TLI, Tucker Lewis Index, RMSEA, root mean square error of approximation, PCFI, parsimony comparative fit index; Δ, delta. Smaller χ^2/df ratios indicate better model fit, with values around 2.0 showing good fit in an absolute sense. TLI values are better as they approach 1.0 and values above .95 indicate good model fit. Values for the RMSEA are better as they approach 0 and, below .05, are considered strong. The PCFI penalizes increasing model complexity (ie, larger numbers of parameters being estimated). Higher values are better, but there is no rule of thumb for interpretation. The index is used here to highlight *relative* differences within subsets of related analyses. For the multiple group analyses, $\Delta\chi^2$ and Δdf indicate, respectively, the change in χ^2 and the change in *df* with increasing invariance constraints. ΔP is the *P* value associated with the changes.

in a nonsignificant $\Delta\chi^2$ and values for other indexes similar to those derived for the unconstrained model. These results suggest that variable/factor loadings are consistent for healthy controls and unaffected siblings. In the separate comparisons of schizophrenia patients with controls and with unaffected siblings, $\Delta\chi^2$ values indicate a statistically significant reduction in model fit when variable/factor loadings are constrained to be equal. However, the improvement in parsimony and the small magnitude of change in main fit indexes after imposition of this constraint suggest that any deterioration was of limited practical significance. Thus, it is reasonable to consider loadings of individual variables on first-order cognitive domain factors to be consistent across the 3 groups.

The same reasoning applies in the comparison of siblings and controls when adding the requirement that loadings of the first-order factors on the higher-order "g" factor must be equal between groups. Again, $\Delta\chi^2$ is statistically significant but parsimony is improved with the additional constraint and changes in other fit index values are modest. It appears, then, that controls and siblings do not differ substantially in factor/"g" loadings. The same is not true for people with schizophrenia. In the analysis with controls and the parallel analysis with siblings, adding the constraint that factor/"g" loadings be equal yields significant $\Delta\chi^2$ values, no improvement in parsimony, and notable deterioration of other indexes of model fit. Factor/"g" loadings are higher for people with schizophrenia than they are for healthy controls or unaffected siblings.

Discussion

Complementary exploratory and confirmatory analyses of the CBDB Sibling Study data yielded factors for verbal memory, visual memory, processing speed, nback task performance, span task performance, and card sorting. The separation of individual cognitive test variables into factors was consistent across groups of individuals with schizophrenia, their unaffected siblings, and healthy controls, and these factor groupings were robust to sample differences in gender and other demographic variables. Analyses also showed that that the strength of the loadings of the individual variables on the separate components was comparable (table 2). A series of MCFAs confirmed this impression, showing that overall model fit deteriorated only slightly when the magnitude of the loading of each individual cognitive measure on the specified cognitive domain factor was constrained to be the same across

Table 5. Pearson's Correlations for Domain Composites, By Group

			Schizophrenia	Siblings	Controls
Processing speed	<–>	Verbal memory	.302	.144	.268
Processing speed	<–>	Span	.393	.240	.274
Processing speed	<–>	Nback	.421	.348	.307
Processing speed	<–>	Card sorting	.323	.215	.237
Processing speed	<–>	Visual memory	.305	.206	.197
Verbal memory	<–>	Span	.376	.222	.305
Verbal memory	<–>	Nback	.381	.239	.236
Verbal memory	<–>	Card sorting	.360	.127	.149
Verbal memory	<–>	Visual memory	.443	.259	.232
Span	<–>	Nback	.376	.349	.253
Span	<–>	Card sorting	.319	.242	.199
Span	<–>	Visual memory	.328	.097	.219
Nback	<–>	Card sorting	.450	.329	.249
Nback	<–>	Visual memory	.461	.323	.282
Card sorting	<–>	Visual memory	.339	.226	.294
	Mean		.372	.239	.245

groups. The finding of invariance in the factor measurement configuration supports the conclusion that we are measuring the same constructs in each of the groups.[19]

A possible weakness of the current analysis is that some of the derived factors represent variables from single cognitive tests and may be better thought of as "method factors" than as latent factors representing underlying constructs. Similar components or factors have appeared periodically in schizophrenia research, especially in regard to the WCST and Wechsler Adult Intelligence Scale Visual Reproduction.[11,20,21] We explored the issue here in separate analyses that included only one variable each from the WCST, nback, and Visual Reproduction. Consistent memory, processing speed, and span factors emerged in the further analyses, offering additional support for these groupings. However, the alternative analyses resulted in less variance explained than the 6-component solution—overall and in the 3 retained variables—and did not point to a consistent, interpretable solution across groups. Additionally, relationships that might have been hypothesized (eg, nback and span variables on a single working memory component, or Visual Reproduction with verbal memory measures on a single episodic memory component) did not emerge in the alternative analyses for any group. It would likely require additional measures, conceptually related to the variables underlying the card sorting, nback, and visual memory factors here, to determine whether these factors represent broader constructs that extend beyond the respective measurement methods used in this study. Although we cannot resolve the question with these data, our analyses suggest that card sorting, nback and Visual Reproduction, at least in the context of this battery of tests, tap aspects of cognitive performance that are, to a meaningful degree, separable from each other and from other elements of the battery. Furthermore, while method-influenced factors provide an incomplete approach to certain familiar constructs (eg, executive functioning and visual memory) and must be interpreted with caution, they nevertheless provide an empirical basis for the sorting of key variables in this large data set into separate composites in order to avoid redundant statistical testing in other studies. For these reasons, we settled on the 6-component solution as our preferred solution.

The foregoing illustrates some general points about the factor analytic literature in schizophrenia. On the one hand, factor analyses of schizophrenia data from any reasonably large, reasonably varied neuropsychological battery reliably yield multiple correlated factors.[2] Some variable groupings are particularly robust (eg, verbal memory and processing speed) and emerge across studies with quite different test batteries.[4,11] Such analyses can be used effectively to guide creation of factor-based composites and/or a general ability composite. The current samples and battery were carefully screened and selected and were suitable for these purposes. On the other hand, factor solutions vary somewhat as a function of the samples analyzed, the selection of cognitive tests, and variables within tests, and are likely to be influenced by testing methodology shared between variables.[21] Obviously, the current samples and battery are not immune from these criticisms. For example, it is not clear how our findings might have changed if our samples were not predominantly Caucasian, or if we had permitted individuals with IQ less than 70 to be analyzed, or if we had included one of the number of measures thought to associate most directly with general cognitive ability or "g" (eg, Raven's Progressive Matrices). Also, the culling process, which reduced the original 25 variables to 18, might not replicate in a different sample. Thus, while current analyses are consistent with broad findings of separable factors from previous schizophrenia factor analyses and provide a basis for data reduction in the current data set, not all of the detailed findings here will generalize to studies using different samples and test batteries.

Another limitation of current work results from the use of the EFA results to specify factor-based composites that were then analyzed using CFA in the same data set. This may have enhanced the fit of CFA models in the current analyses and may limit the generalizability of findings. Two points offer reassurance in this regard. First, because of differences in the gender composition of current study samples, EFA and CFA solutions were tested separately in gender subgroups. Very consistent 6-factor EFA solutions and hierarchical CFA models emerged for men and women across the samples. Second, independent evidence—based on nonoverlapping samples and different test batteries—offers general support for both the multifactor EFA solution[2] and the hierarchical CFA model.[4]

We have argued previously that there is a generalized cognitive deficit in schizophrenia[22,23] and findings from other groups are consistent.[24] The hierarchical model of human cognitive performance resolves any apparent inconsistency between general cognitive ability findings and findings emphasizing separable factors. In this model, a broad latent factor representing general cognitive ability or "g" is drawn from the associations among separable, but positively correlated, latent factors representing different cognitive domains.[7] This model has been shown to hold for nonclinical samples[7] and a nonoverlapping schizophrenia sample[4] and provides a conceptual foundation for calculation of widely used global cognitive performance composites. Current analyses confirmed the suitability of the model for unaffected siblings of schizophrenia patients as well as offering further support for its application to patients themselves and healthy controls.

The hierarchical model reinforces the obvious point that there are different levels of analysis of cognitive performance and suggests that a fixed cognitive battery, such as the MATRICS Consensus Cognitive Battery, will not be suitable for all circumstances. A global indicator of cognitive performance may be more appropriate for some purposes (eg, evaluating broad effects of antipsychotic treatment on cognitive performance[20,25] and predicting functional outcome[26]). One recent report[24] gives reason to think that a battery comprising just a few brief cognitive tests, carefully selected to yield a strong general ability composite, could serve research purposes while significantly reducing research participant burden. At the same time, there is heterogeneity in the profiles of cognitive impairment in subgroups of people with schizophrenia.[27,28] For work that capitalizes on this heterogeneity in an effort to identify more circumscribed pharmacological, neurophysiological, and molecular mechanisms,[29] factor-level indicators may prove more useful and will require more extensive cognitive test batteries.

In addition to the evidence of strong parallels, analyses highlighted group differences in the associations among first-order cognitive factors. In MCFAs, overall model fit was not affected when sibling and control groups were constrained to have identical "g" loadings on top of identical variable/factor loadings. However, fit deteriorated markedly when "g" loadings for the schizophrenia group were forced to be equal to "g" loadings for the sibling and control samples. The group differences were also reflected in correlations among the factor-based composites. On average, these were significantly higher in the schizophrenia sample than in either their unaffected siblings or healthy controls. We found corresponding relationships in a set of 7 distinct cognitive variables not included in the factor analysis. Furthermore, sensitivity analyses showed the same pattern across schizophrenia, sibling, and control groups separately in men and women, suggesting that gender does not moderate this effect.

These analyses add to the evidence that cognitive performance is more generalized in schizophrenia than in comparison groups. For the schizophrenia and control samples, the findings parallel findings from our earlier report.[4] The status of unaffected siblings of schizophrenia patients in this regard is less certain. Siblings showed correlations similar to controls when the analysis was confined to the 6 factor-based composites but showed correlations intermediate between patients and controls in analyses of 7 distinct cognitive variables. Thus, the increased generalization of cognitive performance in schizophrenia seems to relate to illness, at least in part, including the experience of chronic serious illness and the effects of treatment. Clarity about whether generalized cognitive impairment is also influenced by genetic and environmental risk factors shared with unaffected siblings awaits further research.

These findings seem not to result from frequently noted limitations of traditional cognitive measures (eg, their imprecision or multicomponent nature); obviously, the test battery analyzed here was the same for all groups. Analyses controlled for group differences in demographic variables. In terms of psychometrics, there was a slightly more restricted range of test performance among siblings and healthy controls than schizophrenia patients (table 1), but the differences were mostly minor and, where they were more pronounced (the Visual Reproduction variables), appeared to have little effect on the analysis of associations. In sum, factor analyses supported a consistent sorting of cognitive test variables into cognitive domains for people with schizophrenia, their unaffected siblings, and healthy controls, and consistent loadings of individual variables on specified factors across groups. The consistency supports the assumption that these constructs have similar meaning in the populations represented here. For siblings and controls, the associations of these separable cognitive factors with the higher-order general ability factor were also uniform. However, the factor/"g" loadings were higher in schizophrenia and translated into significantly more highly correlated cognitive domain composites for this group.

Current analyses add to earlier work showing more generalized cognitive performance in schizophrenia.[3,4]

It is possible that this could reflect a broad but definable effect of illness on cognitive performance (eg, overreliance on effortful and prefrontally mediated processing). However, in the context of a disorder that affects development holistically, generalized performance may be better interpreted as a fundamental reflection of a more unitary general ability than seen in comparison groups. It may be fair, therefore, to ask the question: is "g" quite the same construct in patients as it is in their siblings or controls?

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