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The Puzzle of Processing Speed, Memory and Executive Function Impairments in Schizophrenia: Fitting the Pieces Together

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Abstract

Background—Substantial impairment in digit-symbol substitution task performance in schizophrenia is well established, which has been widely interpreted as denoting a specific impairment in processing-speed ability. However, other higher-order cognitive functions might be more critical to performance on this task. To date, this has not been rigorously investigated in schizophrenia.

Methods—One-hundred and twenty-five schizophrenia cases and 272 controls completed neuropsychological measures of processing speed, memory and executive functioning. We implemented a series of confirmatory factor and structural regression modeling in order to build an integrated model of processing speed, memory and executive function with which to deconstruct digit-symbol substitution task and characterize discrepancies between cases and controls.

Results—The overall structure of the processing speed, memory and executive function model was the same across groups ($\chi^2 = 208.86$, $p > .05$) but the contribution of the specific cognitive domains to coding task performance differed significantly. When completing the task controls relied on executive function and, indirectly, on working memory ability; while schizophrenia

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cases utilized an alternative set of cognitive operations whereby they relied on the same processes required to complete verbal fluency tasks.

Conclusions—Successful coding task performance is predominantly reliant on executive function, rather than processing-speed or memory abilities. Schizophrenia patients perform poorly on this task due to an apparent lack of appropriate executive function input, they rely instead on an alternative cognitive pathway.

Keywords

Keywords: schizophrenia; neuropsychology; processing speed; information processing; structural equation modeling; digit-symbol substitution

Introduction

Neuropsychological research has established that individuals with schizophrenia exhibit impaired performance when completing numerous cognitive tasks (1). The task on which patients appear to be most impaired is the digit-symbol substitution task (2-4). This finding has been interpreted as denoting a substantial impairment in processing speed in schizophrenia. However, this interpretation only holds true if those cognitive processes, which are required to complete the digit-symbol substitution task, are truly synonymous with processing-speed ability. Indeed evidence is now accruing which suggests that perhaps digit-symbol substitution performance is reliant on more complex cognitive abilities such as memory and executive function (5-9). Were this the case it would necessitate a re-evaluation of the meaning of the digit-symbol substitution impairment in schizophrenia. The goal of the present study was to disentangle both the cognitive underpinnings of the digit-symbol substitution task in healthy individuals and to postulate a model for understanding the impairments exhibited by schizophrenia patients when completing this task. In so doing we hoped to appropriately frame the digit-symbol substitution impairment in schizophrenia and moreover generate testable hypotheses for the origins of the impairment.

Salthouse (1996) defined processing-speed as the number of correct responses an individual is able to make within a finite amount of time. Thus, on the face of it at least, the digit-symbol substitution task indexes processing-speed ability where participants are required to correctly substitute symbols and digits using a key under timed conditions (10). However, several lines of evidence suggest that coding tasks may, in fact, overlap with tests of memory and executive function. In factor analytic research, processing speed factors typically comprise the digit-symbol substitution task alongside the Trail Making Tests and verbal fluency both of which encapsulate distinct elements of executive function and memory 6. Knowles and colleagues (2012) extended this finding. Using a confirmatory factor model of processing speed comprising factors of varying degrees of cognitive complexity they demonstrated that the digit-symbol substitution task completion is reliant not on basic psychomotor speed but instead on processes more associated with memory and also executive functioning 7. This finding is in line with studies using linear regression models which have shown that both memory and executive function make significant contributions to performance 5 and also with work from the field of experimental psychology which has highlighted memory deficits in schizophrenia as a contributing factor

to the coding-task impairment (11). These lines of evidence suggest that the digit-symbol substitution task may be much more than a mere test of processing speed, but no study has made a detailed examination of the role of processing speed along with memory and executive function in task completion. Doing so would allow an integrated model of the cognitive impairment in schizophrenia to be developed.

We report data from a large sample of schizophrenia cases and community controls that completed multiple measures of processing speed, memory and executive function. We applied confirmatory factor analyses to these measures, followed by structural regression modeling techniques. The aims of this study were threefold: (a) to establish the structure of processing speed, memory and executive function abilities and also, where the digit-symbol substitution best fitted within that structure; (b) to investigate the hierarchical relationships within the structure and the digit symbol-coding task; and (c) examine whether differences between controls and cases in the structure and/or the hierarchy could explain the coding-task deficit in schizophrenia. The present investigation is, to our knowledge, the largest rigorous study of the causes of the processing-speed impairment in schizophrenia using a comprehensive model of cognition.

Methods

Participants

Participants comprised 125 schizophrenia patients (average age = 31.58 (range 20–67) years, 68% males) and 272 controls (average age = 40.96 (range 17–65) years, 34% male). For the schizophrenia group the mean SAPS (scale for the assessment of positive symptoms) score was 10.97 (SD=16.11) and the SANS (scale for the assessment of negative symptoms) was 28.89 (SD=23.56). The sample used in the present paper is the same as used in a previous paper of which the present paper is an extension (7).

Neuropsychological Assessment

A comprehensive neuropsychological battery was administered to all participants including: visual scanning (12), simple motor speed (12), number sequencing (12), letter sequencing (12), number-letter switching (12), letter and category fluency (12), spatial span forward and backward (10), visual pattern task (10), listening memory span (10), letter-number sequencing (10), digit span forward (10), tower test (10), Wisconsin card sorting task (10), switching fluency (12), and the digit symbol substitution task.

Working memory measures were included if they assessed the maintenance and manipulation of verbal and visuospatial information (13-15); and executive function measures were included that assessed shifting, updating and inhibition. Tests of processing speed were selected in accordance with the theoretical and empirical work of Salthouse (16) and which covered abilities previously suggested to be involved in DSST completion including psychomotor speed, visual scanning, sustained attention and coordination of elementary operations (17). Further details of the processing-speed measures chosen for inclusion can be found in (7).

Statistical Analysis and Model Building

Data were carefully screened for outliers and there was no evidence of potential bias. In terms of statistical power, Monte Carlo simulations of structural equation modelling suggest that samples of at least one-hundred cases are required to confer enough power for models to converge with a good degree of accuracy (18).

Confirmatory factor analysis was implemented using Analysis of Momentary Structure (AMOS) 18.0 software (19) to test a six-factor theory-based model of processing speed, memory and executive function. The processing-speed portion of this model was established previously (7) while the memory and executive portion, which was built specifically for this paper, was based on theoretical and experimental work by Baddeley which has consistently shown that memory is composed of separate verbal and visuospatial elements alongside an executive component. The executive component was modelled on the work of Miyake and colleagues, which demonstrated that executive function ability incorporates three fundamental elements: shifting, updating and inhibition (20). Full details of model building, assessment and comparison can be found in the supplemental materials. We used structural equation modeling (SEM) to examine the degree to which each of the latent variables contributes to performance on the digit-symbol substitution task by comparing alternative nested models (models with different combinations of paths from each latent variable to the digit-symbol substitution task) using the specification search function in AMOS (19). This analysis was done separately in cases and controls. This analysis is akin to a complex multiple regression analysis where the latent variables can be conceived as predictor variables and the digit-symbol substitution task the dependent variable. The specification search selects the model that fits the data best, which is analogous to selecting the most parsimonious and best-fitting multiple regression model i.e. that model that can account for a significant portion of the variance in the dependent variables using the fewest predictor variables in the equation (20).

Results

Descriptive Statistics and Group Comparisons

Table 1 presents the performance of cases and controls on the measures of processing speed, memory and executive function. Cases performed significantly worse than controls on all measures (all p-values <0.001). The most severe impairment was on the digit symbol-coding task ($d = -1.51$), followed by the semantic fluency measure ($d = -1.18$). The observed effect sizes are similar to those reported in recent meta-analyses (2-3).

Confirmatory Factor Analysis

The memory, executive function and processing-speed model (see blue portion of Figure 1, and also see Table 2 for the correlations between factors) fit was good in both controls ($\chi^2 = 92.88_{83}$, $p=0.22$; RMSEA=0.021; CFI=.99 and NFI=0.94) and cases ($\chi^2 = 106.96_{88}$, $p=0.08$; RMSEA=0.044; CFI=.97 and NFI=0.86). Furthermore, an exploratory factor analysis suggested a similar factor structure (Table S1). Multigroup comparison indicated that neither the factor structure ($\chi^2 = 196.45_{170}$, $p=0.080$, RMSEA =.020, CFI =.99, NFI =.961) nor the factor loadings ($\chi^2 = 208.86_{178}$, $p=0.057$, RMSEA =.021, CFI =.98, NFI =.91)

differed significantly between controls and cases, suggesting that the basic structure is the same across groups.

Structural Model Specification

Next we examined which factors of the processing speed, memory and executive function model best predicted coding task performance. Table 3 presents the results of the specification search used to select the best combination of factors in controls and cases. In the control group ($\chi^2 = 90.45_{73}$, $p=0.081$, $BCC_0 = 0.00$, $AIC_0 = 0.00$) the best fitting model was a two path model with a path from Executive Function (β -coefficient = .39, $p<.05$) and a path from Shifting and Sequencing (β -coefficient = -.35, $p<.05$) to the digit-symbol coding task. In cases ($\chi^2 = 90.68_{77}$, $p=0.136$, $BCC_0 = 0.00$, $AIC_0 = 0.00$) the best fitting model was also a two-path model but with a path from Shifting and Sequencing (β -coefficient = -.37, $p<.05$) and a path from Verbal Fluency (β -coefficient = .51, $p<.01$) to the digit-symbol coding task (see yellow portion of Figure 1).

Exploratory Structural Model of Processing Speed, Memory and Executive Function

Structural regression modelling was implemented to develop a hierarchical model of processing speed, memory and executive function where the digit-symbol substitution task was placed at the top of the hierarchy. A hierarchical model of processing speed, memory and executive function is shown in Figure 2, this model fitted the data well in both controls ($\chi^2 = 106.38_{110}$ $p=.36$, $AIC = 242.38$, $CFI = 1.00$, $NFI = .93$, $RMSEA = .013$) and cases ($\chi^2 = 132.33_{110}$ $p=.07$, $AIC = 252.330$, $CFI = .97$, $NFI = .87$, $RMSEA = .040$). The upper portion of the model (including the digit-symbol coding task) differed between controls and cases. Nested model comparisons showed that in controls the best fitting model was a two-path model ($\chi^2 = 106.38_{102}$ $p=.36$, $AIC = 242.38$, $CFI = 1.00$, $NFI = .93$, $RMSEA = .035$), with a path from Executive Function (β -coefficient = .33, $p<.05$) and one from Shifting and Sequencing (β -coefficient = -.39, $p<.01$). In cases the best fitting model was a one-path model ($\chi^2 = 132.33_{110}$ $p=.07$, $AIC = 252.33$, $CFI = .97$, $NFI = .87$, $RMSEA = .040$), with a path from Verbal Fluency (β -coefficient = .89, $p<.001$). Thus the paths in the upper portion of the model where factors connected directly to the digit-symbol substitution task differed in controls and cases. However, the characterisation of the model below these directly connecting factors was the same in both groups (including the relationships between psychomotor speed, visuo-spatial memory, verbal memory, shifting and sequencing and verbal fluency) except that in cases the path between Phonological Memory and Verbal Fluency was dropped because it was not significant.

Discussion

It is well established that digit-symbol substitution task performance is substantially impaired in schizophrenia, a finding that has been widely interpreted as denoting a specific impairment in processing-speed ability. However, the results of the present study challenge this view. By building an integrated model of processing speed, memory and executive function this study has revealed that the digit-symbol substitution task is best described as a measure of executive function (rather than processing speed or memory) and by developing an exploratory model the present study generates a tentative but testable hypothesis for why

schizophrenia patients underperform on this task, namely that in cases (as compared to controls) there is a discrepancy in the level of executive function input.

The confirmatory factor model shown in Figure 1 demonstrates that the same basic structure of executive, memory and processing speed cognitive functions existed in healthy controls and schizophrenia patients with a factor model comprising psychomotor speed, visuo-spatial memory, phonological memory, executive function, shifting and sequencing, and verbal fluency fitting equally well in both groups. It is of note that this model is very similar to one generated by an exploratory factor solution (Table S1) – the digit-symbol substitution task was not included in this analysis as this end goal was to use this factor structure to deconstruct the task. This is important to note as it supports the idea that this model is truly one that represents the data rather than representing, for example, the authors' expectations for how the measures should group together. Upon using the confirmatory factor analysis to deconstruct the primary cognitive influences on digit-symbol substitution task performance it became apparent that the way in which the constituent cognitive functions were applied to the digit-symbol coding task completion differed between groups. Healthy controls appeared to rely on executive function and shifting and sequencing abilities to complete the task, while schizophrenia patients relied on sequencing and shifting and verbal fluency. First, this finding mirrors that of Knowles and colleagues, which was that digit-symbol substitution performance is more closely allied to those dimensions of processing speed associated with memory and executive function rather than with basic psychomotor speed. Secondly, the findings of the present study extend those of Knowles and colleagues (7) by showing that in schizophrenia the level of executive function input is insufficient for successful digit-symbol coding task performance.

The exploratory model presented in this study, where the confirmatory factor model was re-specified to as hierarchical, is not being proposed as the definitive model of cognition in schizophrenia rather it represents an attempt to disentangle the underlying cognitive underpinnings of the digit-symbol substitution deficit in schizophrenia and moreover an attempt to generate hypotheses for future work in the field. What it proposes is that given a hierarchical structure of cognition there appears to be one or more pathways in schizophrenia which are defunct and this leads to patients employing an alternative strategy to controls, one which seemingly leads to a decrement in digit-symbol substitution task performance. Of course, this hypothesis should be thoroughly tested in future, perhaps using experimental psychology techniques where digit-symbol themed paradigms could be employed, for example by relaxing the time constraints for digit-symbol testing; suggesting strategies; using dual task designs which might be used to partial out the working memory or executive function components of the task, and so on. Nonetheless the results here suggest that when completing the digit-symbol substitution task, schizophrenia patients depend upon cognitive abilities typically associated with verbal fluency rather than executive functioning. Successful performance on executive function measures is characterised by on-line, seamless integration of multiple abilities including planning, inhibition, set-shifting and updating, all of which must be adaptively applied as the task progresses. Verbal fluency requires participants to make laboured searches of long-term memory under timed conditions with application of inhibition (17). Given this it is unsurprising that controls outperform schizophrenia patients on the digit-symbol substitution task, a measure which

accounting for approximately 15% of the variance. Furthermore a measure of executive functioning significantly predicted coding task performance after the effects of motor speed, perceptual speed, and visual scanning had been partialled out (5). Other experimental work examining the conceptual and procedural overlap and differences between fluency tasks and coding tasks under variable time constraints would be valuable.

This study has some potential limitations. It might be argued that the model presented in the current paper is not necessarily the definitive model of processing speed, memory and executive function as alternative specifications may fit the data equally well. Although both the confirmatory factor and hierarchical models explained a substantial amount of the variance in digit-symbol coding task performance in both controls (49% and 50% for the confirmatory and hierarchical models respectively) and in cases (70% and 78%) as denoted by the squared multiple correlations of the digit-symbol coding task (44). It could also be argued that the results presented here are a reflection of testing methodology rather than underlying cognitive structure. However, the current model specification is supported by an exploratory factor analysis which resulted in a six factor solution (see Table S1). Moreover the final groupings of measures were a result of exploratory and also confirmatory factor analysis whereby alternative groupings were carefully considered. Another potential limitation of the present study is the difference in gender distribution in controls and cases (34% male and 68% male respectively) which may affect the results given that previous research has shown that brain structure may vary between genders. However, the fit of the six-factor model was equally as good when using data residualised for the effects of age and sex. A caveat of the results of the present paper is that the hierarchical model is exploratory. However, this model serves to support the findings of the confirmatory factor analyses rather than as a stand alone finding. Another potential limitation of the present study is that it is possible that in different, perhaps more symptomatic patient groups the model may be characterized differently, for example in a first-episode versus a chronic group; this could be explored in future studies. Furthermore, it would be of interest to attempt to replicate these findings under an experimental psychology paradigm. For example, Elahipanah and colleagues demonstrated that schizophrenia patients adopt an inefficient visual search strategy when completing the digit-symbol substitution task (45) – a finding that is compatible with the overall view presented in the present manuscript, which is that patients are not adopting an optimal executive strategy when completing the task.

In conclusion, the results of the present study that the digit-symbol substitution task is better characterised as a measure of executive function than processing speed or memory; and the pronounced digit-symbol substitution task impairment in schizophrenia appears to be due to a lack of appropriate executive function input.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

The final confirmatory factor model of processing speed, memory and executive functioning. The measurement model is shown on the right in blue and consists of six factors. The structural model is shown on the left in orange and consists of a two-path solution in both controls and cases. However, the path combination differs in each group. In controls there are paths from Executive Functioning and Sequencing & Shifting, and in cases paths from Sequencing & Shifting and Verbal Fluency to the digit-symbol substitution task.

Figure 2.

The exploratory hierarchical model of processing speed, memory and executive functioning in controls and cases. There is little difference between controls and cases in the relationships in the lower half of the model but the upper half of the model differs significantly. While in controls Executive Functioning and Shifting & Sequencing significantly predict digit-symbol substitution task performance in cases only the Verbal Fluency factor predicts performance on the digit-symbol task.

Table 1Standardized Scores for Processing Speed, Memory and Executive Function Measures for Controls and Cases^a.

Task	Control (N=272)		Schizophrenia (N=125)		Difference (Control _{mean} -Schizophrenia _{mean})
	Mean	SD	Mean	SD	
Digit Symbol Substitution					
Task	0.37	0.79	-0.85	0.93	1.21
Semantic Fluency	0.28	0.90	-0.77	0.84	1.05
Number Sequencing	-0.32	0.61	0.73	1.29	-1.05
Listening Memory Span	0.28	0.90	-0.77	0.81	1.04
Switching Fluency	0.30	0.86	-0.68	0.95	0.99
Letter Fluency	0.25	0.91	-0.71	0.90	0.96
Letter Sequencing	-0.28	0.75	0.68	1.19	-0.96
Letter Number					
Sequencing	0.26	0.87	-0.67	0.98	0.93
Visual Scanning	-0.28	0.64	0.64	1.33	-0.92
Number-Letter					
Sequencing	-0.23	0.82	0.64	1.16	-0.88
Spatial Span Backward	0.23	0.89	-0.63	1.03	0.86
Visual Pattern Task Span	0.19	0.96	-0.52	0.92	0.71
Tower Task	0.21	0.85	-0.55	1.15	0.76
WCST	0.15	0.99	-0.45	0.88	0.60
Spatial Span Forward	0.14	0.98	-0.39	0.96	0.53
Digit Span Forward	0.16	0.99	-0.38	0.90	0.55
Simple Motor Speed	-0.14	0.85	0.36	1.24	-0.50

^a Based on Table 2 in Knowles and colleagues (2012).

Table 2

Correlations Between Factors in the Memory and Processing Speed Model in Controls (Lower Half) and Cases (Upper Half).

	Psychomotor Speed	Visuo-Spatial Memory	Phonological Memory	Executive Functioning	Shifting and Sequencing	Verbal Fluency
Psychomotor Speed	1	-.59	-.43	-.94	.86	-.79
Visuo-Spatial Memory	-.49	1	.84	.88	-.78	.58
Phonological Memory	-.42	.86	1	.75	-.63	.53
Executive Functioning	-.65	.64	.76	1	-.92	.85
Shifting and Sequencing	.83	-.65	-.58	-.82	1	-.77
Verbal Fluency	-.50	.42	.56	.32	-.63	1

Table 3

Specification Search Results for Controls and Cases.

	Model	df	χ^2	p	BCC ₀	AIC ₀
Controls	Executive Functioning & Shifting and Sequencing	73	90.45	.081	0.000	0.000
	Executive Functioning	74	92.79	.069	0.207	0.334
	Executive Functioning, Shifting and Sequencing & Verbal Fluency	72	88.82	.076	0.491	0.364
	Executive Functioning & Verbal Fluency	77	90.68	.136	0.000	0.000
Cases	Visuo-Spatial Memory, Phonological Memory & Verbal Fluency	76	89.13	.144	0.782	0.452
	Visuo-Spatial Memory, Shifting and Sequencing & Verbal Fluency	76	90.24	.127	1.887	1.557