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

METHODS: Neuropsychological measures of processing speed, memory, and executive functioning were completed by 125 patients with schizophrenia and 272 control subjects. We implemented a series of confirmatory factor and structural regression modeling to build an integrated model of processing speed, memory, and executive function with which to deconstruct the digit-symbol substitution task and characterize discrepancies between patients with schizophrenia and control subjects.

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, control subjects relied on executive function and, indirectly, on working memory ability, whereas patients with schizophrenia used an alternative set of cognitive operations whereby they relied on the same processes required to complete verbal fluency tasks.

CONCLUSIONS: Successful coding task performance relies predominantly on executive function, rather than processing speed or memory. Patients with schizophrenia perform poorly on this task because of an apparent lack of appropriate executive function input; they rely instead on an alternative cognitive pathway.

Keywords: Digit-symbol substitution, Information processing, Neuropsychology, Processing speed, Schizophrenia, Structural equation modeling

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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 (DSST) (2–4). This finding has been interpreted as denoting a substantial impairment in processing speed in patients with schizophrenia. However, this interpretation holds true only if the cognitive processes that are required to complete the DSST are truly synonymous with processing speed. Accruing evidence suggests that DSST performance may rely on more complex cognitive abilities such as memory and executive function (5–9). In this case, a re-evaluation of the meaning of the DSST impairment in patients with schizophrenia may be needed. The goal of the present study was to disentangle the cognitive underpinnings of the DSST in healthy individuals and to postulate a model for understanding the impairments exhibited by patients with schizophrenia when completing this task. We hoped to frame the DSST impairment in patients with schizophrenia appropriately and generate testable hypotheses for the origins of the impairment.

Salthouse (10) defined processing speed as the number of correct responses an individual is able to make within a finite amount of time. On the face of it at least, the DSST indexes processing speed where participants are required to substitute symbols and digits correctly using a key under timed conditions (11). However, several lines of evidence suggest that coding tasks may overlap with tests of memory and executive function. In factor analytic research, processing speed factors typically comprise the DSST alongside the Trail Making Test and verbal fluency, both of which encapsulate distinct elements of executive function and memory (6). Knowles *et al.* (7) extended this finding. Using a confirmatory factor model of processing speed comprising factors of varying degrees of cognitive complexity, they demonstrated that DSST completion does not rely on basic psychomotor speed, but instead relies on processes more associated with memory and executive functioning (7). This finding is in line with studies using linear regression models that showed that both memory and executive function make significant contributions to performance (5) and with work from the field of experimental

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psychology that highlighted memory deficits in patients with schizophrenia as a contributing factor to the coding-task impairment (12). These lines of evidence suggest that the DSST may be much more than a 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. Such an examination would allow an integrated model of the cognitive impairment in patients with schizophrenia to be developed.

We report data from a large sample of patients with schizophrenia and control subjects from the community who 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: 1) to establish the structure of processing speed, memory, and executive function abilities and where the DSST best fitted within that structure; 2) to investigate the hierarchical relationships within the structure and the digit-symbol coding task (DSCT); and 3) to examine whether differences between control subjects and patients with schizophrenia in the structure or hierarchy, or both, could explain the DSCT deficit in patients with schizophrenia. To our knowledge, the present investigation is the largest rigorous study of the causes of impairment of processing speed in patients with schizophrenia using a comprehensive model of cognition.

METHODS AND MATERIALS

Participants

Participants were 125 patients with schizophrenia (average age, 31.58 years [range, 20–67 years]; 68% men) and 272 control subjects (average age, 40.96 years [range, 17–65 years]; 34% men). For the schizophrenia group, the mean Scale for the Assessment of Positive Symptoms score was 10.97 (SD = 16.11) and the mean Scale for the Assessment of Negative Symptoms was 28.89 (SD = 23.56). The sample used in the present study is the same sample that was used in a previous study, of which the present study is an extension (7).

Neuropsychological Assessment

A comprehensive neuropsychological battery was administered to all participants that included visual scanning (13), simple motor speed (13), number sequencing (13), letter sequencing (13), number-letter switching (13), letter and category fluency (13), spatial span forward and backward (11), visual pattern task (11), listening memory span (11), letter-number sequencing (11), digit span forward (11), tower test (11), Wisconsin Card Sorting Task (11), switching fluency (13), and the DSST.

Working memory measures were included if they assessed the maintenance and manipulation of verbal and visuospatial information (14–16). Executive function measures that assessed shifting, updating, and inhibition were included. Tests of processing speed were selected that were in accordance with the theoretical and empirical work of Salthouse (10) and that 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 Knowles *et al.* (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 modeling suggest that samples of at least 100 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), and the memory and executive portion of the model, which was built specifically for the present study, was based on theoretical and experimental work by Baddeley (14) that consistently showed that memory is composed of separate verbal and visuospatial elements alongside an executive component. The executive component was modeled on work of Miyake *et al.* (20), which demonstrated that executive function ability incorporates three fundamental elements: shifting, updating, and inhibition. Full details of model building, assessment, and comparison can be found in Supplement 1. We used structural equation modeling to examine the degree to which each of the latent variables contributes to performance on the DSST by comparing alternative nested models (models with different combinations of paths from each latent variable to the DSST) using the specification search function in AMOS (19). This analysis was done separately in patients with schizophrenia and control subjects. This analysis is akin to a complex multiple regression analysis in which the latent variables can be conceived as predictor variables and the DSST 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., the 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 patients with schizophrenia and control subjects on the measures of processing speed, memory, and executive function. Patients with schizophrenia performed significantly worse than control subjects on all measures (all $p < .001$). The most severe impairment was on the DSCT ($d = -1.51$), followed by the semantic fluency measure ($d = -1.18$). The observed effect sizes are similar to effect sizes reported in meta-analyses (2,3).

Confirmatory Factor Analysis

The memory, executive function, and processing speed model (Figure 1, Table 2) fit was good in control subjects ([$\chi^2 = 92.88_{83}$,