The association between verbal memory, processing speed, negative symptoms and functional capacity in schizophrenia

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ABSTRACT

The aim of this paper is to explore the links among verbal memory, processing speed, negative symptoms, and functional capacity, using structural equation modeling techniques. Model A is a multiple regression model with cognitive and symptom variables as predictors and functional capacity as the latent outcome variable. Model B consists of three two mediator models that assess the ability of each variable to mediate the effect of the other variable on outcome conditional on the inclusion of the other mediator in the model. Ninety-eight community-dwelling patients with schizophrenia (mean age = 35.8 years, S.D. = 10.1) participated in the study. Results indicate that verbal memory, processing speed and negative symptoms significantly contributed to functional status. Verbal memory was at least partially mediated by processing speed in its effect on outcome, while the impact of processing speed on outcome was mediated by both verbal memory and negative symptoms. The influence of negative symptoms on functional capacity was partially mediated by processing speed. These findings enrich our understanding of the direct and indirect effects of these three interrelated variables and provide a basis for the development of intervention strategies.

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1. Introduction

Understanding the factors that are associated with functional outcome in schizophrenia is critical for developing targeted interventions to improve quality of life in this population. Currently, the literature identifies several factors that have a role in outcome, including cognitive impairment (e.g., Green et al., 2000), severity of symptoms (e.g., Ventura et al., 2009), verbal memory (e.g., Green, 1996), and processing speed (e.g., Ojeda et al., 2008). However, it is not yet known which of these factors is most important to outcome, and which is likely to be the most productive target for rehabilitation.

Verbal memory has been regarded as one of the most consistent associates or predictors of community functioning in both cross-sectional and longitudinal studies. For instance, Green (1996) in his classic review concluded that verbal memory acts as a ‘rate-limiting factor’ for functional capacity in patients with schizophrenia. Revheim et al. (2006) found that verbal memory, working memory and processing speed were moderately associated with independent living. McClure et al. (2007) and Bowie et al. (2008) indicated that verbal memory, processing speed, and executive functions were significantly correlated with performance-based tasks of everyday life; similar findings were obtained by Rempfer et al. (2003) who used grocery shopping skills as an outcome measure. Likewise, Shamsi et al. (2011) found that verbal memory contributed significantly to the prediction of residential status (independent living). Even after 15 years following memory testing, verbal memory remained the most prominent in predicting the level of community functioning, accounting for 45% of the variance (Fuji and Wylie, 2003).

In addition to this work on verbal memory, a number of studies have focused on highlighting the importance of processing speed in mediating the effect of verbal memory on functional performance (Ojeda et al., 2008; Sánchez et al., 2009). For example, Ojeda et al. (2008) suggested that processing speed exerted a full mediating effect on the relationship between verbal memory, verbal fluency and functional disability in hospitalized patients with schizophrenia. Sánchez et al. (2009) extended Ojeda et al.’s findings by showing that the association between cognitive dysfunction (i.e., verbal memory, executive function, and working memory) and aspects of functional disability (i.e., self-care, family contact, vocational outcome, and social functioning) at 6-month follow-up was mediated to varying degrees by processing speed. However, methodological limitations such as inclusion of only chronic hospitalized patients (Ojeda et al., 2008) and disproportionately small number of women (male–female ratio of 4.6:1) in the sample (Sánchez et al., 2009), may restrict the generalizability of these findings. Even so, these results imply that the two cognitive variables shared a considerable degree of explained variance for functional outcome.
Negative symptoms have also been found to be associated with both cognitive dysfunction and functional disability in schizophrenia (O’Leary et al., 2000; Dickinson and Coursey, 2002; Cirillo and Seidman, 2003; Bell and Mishara, 2006; Lipkovich et al., 2009). In addition, there are conflicting views concerning the relative role of processing speed and negative symptoms in the prediction of outcome. One line of work favors the superiority of negative symptoms over processing speed in predicting functional outcome. Dickinson and Coursey (2002) found that negative symptoms accounted for the largest variance in functional ratings, followed by working memory rather than processing speed. They speculated that the inclusion of negative symptoms attenuated the strength of the association between processing speed and community functioning.

Similar results were reported by Revheim et al. (2006) and Villalta-Gil et al. (2006). In contrast, other work supports the direct and mediated contributions of processing speed to functional status. Bowie et al. (2008) found that processing speed predicted community participation directly and indirectly through its effects on both social competence and living skills, while negative symptoms had an indirect effect through its relationship with social competence. Lipkovich et al. (2009) demonstrated that at baseline, processing speed affected functioning mainly indirectly via negative symptoms. In the same study, following sustained treatment with antipsychotic drugs, changes in processing speed affected changes in quality of life both directly and indirectly through negative symptoms. Along a similar vein, the results from a meta-analysis of 75 cross-sectional studies provided support for the partial mediation by negative symptoms of the relation between cognition (including verbal memory and processing speed) and community function (Ventura et al., 2009). However, none of these studies simultaneously investigated the interplay among verbal memory, processing speed, negative symptoms and functional outcome.

The present study examined these complex relations in a single group of patients, thus avoiding possible interpretation bias produced by comparing results across studies with different schizophrenia subsamples and different test measures. In view of the consistent, albeit modest relationship between cognition and negative symptoms (Keefe and Eesley, 2006), two related research hypotheses were formed: first, we predicted that verbal memory, processing speed and negative symptoms will have direct effects on functional capacity in patients with schizophrenia; and second, each variable will indirectly influence functional capacity via one or both of the other two variables. Fig. 1A and B depicts the proposed models that encompass these hypotheses in path diagrams.

2. Methods

2.1. Participants

Ninety-eight individuals who met the Diagnostic and Statistical Manual of Mental Disorders, 4th revision (DSM-IV) (American Psychiatric Association, 1994) criteria for schizophrenia or schizoaffective disorder confirmed by the treating psychiatrists using the Structured Clinical Interview (SCID) (First et al., 1996) and aged between 16 and 65 years were recruited from an outpatient clinic of the Department of Psychiatry at the Kaohsiung Medical University, Taiwan. Exclusion criteria included evidence of current substance abuse, mental retardation, or history of neurological illness and significant changes in clinical state or in drug treatment during the preceding 3 months. Written informed consent was obtained from each patient prior to data collection. This study was approved by the Kaohsiung Medical University Hospital Institutional Review Board.

2.2. Measures

2.2.1. Processing speed

The Chu’s Attention and Processing Speed Test (CAPST; Chu, 1997) is used routinely by occupational therapists in Taiwan for the assessment of processing speed in patients with psychiatric disabilities. It consists of one test sheet that contains 100 strings of 14 letters and symbols (e.g. a#***@&c#o@z#). One string appears as a single item in the top row and the remaining 99 items are arranged in 33 rows with three items in each. Each string begins with a two-digit number (e.g. 02 a#***@&c#o@z#); strings are arranged in a numerical sequence from left to right and top to bottom. The response sheet is composed of seven columns containing, in all, 200 small blank squares, each paired with a randomly assigned two-digit number (00–99; each number appears twice). The task is to fill in the empty spaces with the number of target symbols in each corresponding item from the test sheet as quickly as possible. Eight practice trials were administered before beginning the task. The total score is the number of squares filled in correctly in 10 min. Test–retest reliability of the CAPST was high (r = 0.84). The CAPST is correlated moderately with other measures of processing speed, including the Digit Symbol subtest of the Wechsler Adult Intelligence Scale—Third Edition (Wechsler, 1993) (r = 0.68, p < 0.0001), and total time scores of the Color Trails form A, parts I (D’ Ella et al., 1996) (r = 0.54, p < 0.0001) in 40 outpatients with schizophrenia (Tan, 2009). The CAPST also correlated with work performance (r = 0.44) and activities of daily living (r = 0.62) in patients with schizophrenia (Chu, 1997).

2.2.2. Verbal memory

The Logical Memory (I and II) subtest of the Chinese version of the Wechsler Memory Scale—Third Edition (WMS-III; Wechsler, 1997) was used to tap verbal memory. Logical Memory involves the oral presentation of two paragraphs to the participant for recall. This subtest has both immediate and 30-minute delayed-recall trials.

2.2.3. Symptom severity

The Positive and Negative Syndrome Scale (Kay et al., 1987) is a 30-item rating scale assessing the presence/absence and severity of positive symptoms (seven items), negative symptoms (seven items), and general psychopathology (16 items) of schizophrenia. Each item is rated from one (no evidence) to seven (extreme) based on the objective criteria.

2.2.4. Functional capacity

The Activities of Daily Living Rating Scale—Second Edition (ADLRS-II; Chu, 1993) is a five-subscale community functioning scale designed for use with patients with psychiatric disabilities. It addresses everyday math and vocabulary, general information, money management, transportation and communication, and social problem solving. The everyday math and vocabulary subscale contains nine items that assess abilities to identify and correct wrong words in an advertising phrase, fill out a checking withdrawal slip, and handle everyday math problems (e.g., making change, multiplication, division, and discount). The general information subscale includes 10 items that assess the awareness of use of office and household appliances and the latest current events. The money management subscale consists of 10 items that test knowledge of the food prices, monthly budget, and banking skills. The transportation and communication subscale comprises 10 items that evaluate knowledge of traffic signs, use of public transportation, emergency phone numbers, telephone use, and post office usage. The social problem solving subscale is made up of five items that assess abilities to generate three plausible solutions for each of the social contexts (e.g., job finding). The total raw score for each subscale was 10 points, while the total scale score was the sum of all subscale scores (maximum = 50). The total score was further divided into six performance levels based on normative data obtained from 210 patients with psychiatric disorders: normal, near normal (i.e., supervision required for weaker areas of functioning), mildly and moderately impaired (i.e., provision of partial assistance), and severely and profoundly impaired (i.e., provision of full assistance). The ADLRS-II showed high test–retest reliability (r = 0.85, p < 0.001) and correlations between the scale and real-world functional performance involving self-care and home management were moderate to high in magnitude (r = 0.45 to 0.68, p < 0.001).

2.3. Procedure

In all subjects, demographic and clinical data were collected first, followed by the administration of the cognitive and ADLRS-II tests. PANSS ratings were completed in a separate session by a board-certified psychiatrist (T.C.T.) within the same week as the cognitive and ADLRS-II assessment. All measures were administered according to standard procedures by a trained examiner (P.C.T.), a master’s level occupational therapist specializing in psychiatric rehabilitation, in a single session of approximately 2 h duration.

2.4. Statistical analysis

2.4.1. Factor scores

A factor score was calculated from the principal components analysis for verbal memory (comparing logical memory subtests I and II, immediate and delayed tests) and used in the subsequent path analyses as an independent variable. Factor loadings for logical memory I and II were 0.96, respectively.

2.4.2. Path analysis

Path analysis is an extension of multiple regression in which hypothesized models can be tested. Relations between variables (pathways) are proposed and these are termed path coefficients or beta weights. Each path coefficient expresses the single effect to response variables after controlling other variables. Four path-analytic analyses were conducted to test the hypothesized models of functional outcome (see
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