

# Processing speed mediates the relationship between verbal memory, verbal fluency, and functional outcome in chronic schizophrenia

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## Abstract

Verbal fluency and verbal memory have been reported to be diminished in patients with schizophrenia. These deficits could partially predict functional disability in this pathology. However, processing speed often mediates the relationship among cognitive processes in the disorder. Our goal was to analyse the influence of processing speed as mediator of the relation between verbal fluency–verbal memory and functional disability in chronic schizophrenia. We examined 90 hospitalized patients and 30 healthy controls (matched for gender, age and years of education). The neuropsychological battery included tests for verbal fluency, verbal memory, motor speed and processing speed. Outcome measures included Disability Assessment Schedule (DAS-WHO) and number of hospitalizations (NH). Results confirmed chronicity on clinical symptoms (PANSS total  $X=48.94+14.97$  PANSS negative  $X=27.81+10.18$ , PANSS positive  $X=23.51+10.81$ ) and impairment on functional disability (DAS-WHO  $X=13.62+4.28$ ). As expected, verbal fluency was severely impaired in patients and significantly predicted functional outcome. Immediate and Delayed Verbal Memory were also severely impaired and predicted functional outcome. However, when processing speed was entered in the regression analyses the significance of verbal fluency and verbal memory decreased significantly. Sobel's equation was significant, suggesting full mediation. Our findings suggest that processing speed may be a central factor in the relation between cognitive symptoms and functional outcome in chronic schizophrenia.

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## 1. Introduction

The presence of cognitive deficits in schizophrenia has been extensively reported as a core feature of the disorder (Heinrichs and Zakzanis, 1998; Wilk et al., 2005), and

the average impairment can reach 2 standard deviations below normal performance (Bilder et al., 2000; Harvey and Keefe, 1997).

The suggested evidence of cognition as best predictor of functional outcomes and disability in schizophrenia including work functioning and independent living (Gold et al., 2002; Hofer et al., 2005) provided further relevance to the study of these deficits, specially after the published weak relation with clinical symptoms (Green, 1996). Green additionally characterized the association between specific neurocognitive domains and different measures

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of outcome: 1. verbal memory (VM) associated with all types of functional outcome, 2. vigilance related to social problem solving and skill acquisition, and 3. executive functioning with community functioning. Bowie and Harvey (2005) also found a positive relation among neurocognitive domains and adaptive/social skills, suggesting that negative symptoms and neurocognitive domains are distinct and have differential pathways of change with treatment.

Since Green's findings of verbal memory as related to all functional outcomes, the interest to analyse it deeply has increased. Several studies have shown that both verbal memory (VM) and verbal fluency (VF), as well as the processing speed (PS), are related to different measures of outcome: Bryson and Bell (2003) found that VM was associated to the improvement in work performance, while clinical symptoms did not. Dickerson et al. (1999) found that VM, VF and performance on trail making test predicted changes in social and community outcome. Gold et al. (2002) reported that semantic fluency, VM, and some measures of processing speed (PS) (as TMT-A and Stroop) predicted job tenure, but not fine motor speed (Purdue Pegboard). Jaeger et al. (2003) discovered that VF, attention and VM predicted work, school, and independent living, even after controlling for negative symptoms. In a more specific analysis Velligan et al. (2000) replicated Green's finding on VM predicting all measures of community outcome, vigilance predicting social outcomes, and executive functioning predicting work and activities of daily living (ADLs). Daily problem solving skills have also been found to be dependent on VM abilities, VF, and processing speed (PS) both, in a testing setting (Keefe et al., 2006; Revheim et al., 2006) or in a real context (Rempfer et al., 2003). Furthermore, some authors concluded that PS is strongly related to VM (Brébion et al., 2006) and VF (Van Beilen et al., 2004) in chronic schizophrenia.

The strong role played by PS in relation to VF and VM has been previously addressed. However, none of these studies analysed profoundly this interaction related to functional outcome. Given the reported relevance of processing speed (PS), we hypothesized PS to be a putative mediator between the verbal memory (VM), verbal fluency (VF) and functional disability (FD) in chronic schizophrenia. That is to say, the association among VM, VF, and functional outcomes (FO) could be (at least partially) attributed to the mediation effect of PS. Therefore, we aim first, to describe the role played by VM and VF, in FO in patients with chronic schizophrenia. Secondly, analyse the possible interaction between PS and VM–VF as real predictors of FO.

## 2. Materials and methods

### 2.1. Participants

90 hospitalized patients were recruited from Alava Psychiatric Hospital (76 males, 14 females; years of education =  $10.17 + 2.8$ ), ranged in age from 18 to 65 (age =  $36.09 + 10.68$ ). Mean time of hospitalization for patients was very variable on the sample ( $646.24 + 1648.72$  days).

Subjects met diagnostic criteria for schizophrenia according to the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) (APA, 1994) criteria, using the Structured Clinical Interview for DSM-IV (SCID-I). At time of recruitment all were under antipsychotic medication. Exclusion criteria included previous history of lack of consciousness (>1 h), mental retardation, relevant neurological condition including cerebrovascular disease, hypertension, and significant sensorial deficits.

All participants underwent a general medical evaluation, and cognitive assessment described below. Patients additionally completed psychiatric interview and psychiatric evaluation including Positive and Negative Symptom Scale (PANSS), Brief Psychiatric Rating Scale (BPRS), Calgary Depression Scale, and Young Mania Scale.

Thirty healthy comparison participants were recruited and screened to rule out past or current history of psychiatric disorder, medical conditions relevant to central nervous system, and significant sensorial deficits. The two groups did not significantly differ on age ( $t = -0.64$ ,  $p = 0.53$ ), gender distribution ( $\chi^2 = 3.03$ ,  $p = 0.08$ ) or years of education ( $t = 0.21$ ,  $p = 0.83$ ). All subjects were voluntary and gave written informed consent form approved by the institutional review board to participate in the study.

### 2.2. Measures

#### 2.2.1. Verbal memory test

The Spanish version of Logical Memory I and II (WMS-III) was used (Wechsler, 1987). In this test, the examiner reads two stories, stopping after each reading for an immediate free recall. Then, after 20 min the subject is asked to recall the two stories read before. Two measures are obtained: Immediate Verbal Memory (IVM) and Delayed Verbal Memory (DVM).

#### 2.2.2. Verbal fluency from test

Barcelona (Peña-Casanova, 1990); reliability (concurrent validity with ADAS (Alzheimer's Disease Assessment Scale)  $r = 0.87$ ,  $r^2 = 0.76$ ; test–retest reliability:  $r = 0.92$ , interrater  $r = 0.99$ ).

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