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Cognitive correlates of verbal memory and verbal fluency in schizophrenia, and differential effects of various clinical symptoms between male and female patients

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ABSTRACT

Background: Impairment of higher cognitive functions in patients with schizophrenia might stem from perturbation of more basic functions, such as processing speed. Various clinical symptoms might affect cognitive efficiency as well. Notably, previous research has revealed the role of affective symptoms on memory performance in this population, and suggested sex-specific effects.
Method: We conducted a post-hoc analysis of an extensive neuropsychological study of 88 patients with schizophrenia. Regression analyses were conducted on verbal memory and verbal fluency data to investigate the contribution of semantic organisation and processing speed to performance. The role of negative and affective symptoms and of attention disorders in verbal memory and verbal fluency was investigated separately in male and female patients.
Results: Semantic clustering contributed to verbal recall, and a measure of reading speed contributed to verbal recall as well as to phonological and semantic fluency. Negative symptoms affected verbal recall and verbal fluency in the male patients, whereas attention disorders affected these abilities in the female patients. Furthermore, depression affected verbal recall in women, whereas anxiety affected it in men.
Conclusions: These results confirm the association of processing speed with cognitive efficiency in patients with schizophrenia. They also confirm the previously observed sex-specific associations of depression and anxiety with memory performance in these patients, and suggest that negative symptoms and attention disorders likewise are related to cognitive efficiency differently in men and women.

1. Introduction

Meta-analyses in patients with schizophrenia have revealed impairments in a broad range of neurocognitive domains (Heinrichs and Zakzanis, 1998; Mesholam-Gately et al., 2009). Deficits in diverse high cognitive processes might possibly find a common basis in the deterioration of more elementary mechanisms. Verbal memory is a central cognitive function which has consistently been found to be substantially impaired in schizophrenia (Cirillo and Seidman, 2003). The inability to conduct effective encoding of information at the learning stage has long been recognized as a crucial cognitive factor of the observed recall deficiency (Koh, 1978). Indeed, several studies have revealed that the number of words that patients are able to recall is related to the extent to which they have spontaneously organised these words, when semantic clustering is possible (Brébion et al., 1997; Holthausen et al., 2003; Brébion et al., 2004; Hill et al., 2004; Roofeh et al., 2006; Gsottschneider et al., 2011). More recently, decreased processing speed in these patients has been proposed as an underlying factor for impairment not only in verbal memory, but also in various other neurocognitive functions such as visual memory and verbal fluency (Rodriguez-Sanchez et al., 2007; Brébion et al., 2011; Ojeda et al., 2012). Processing speed and organisational encoding strategy might make joint contributions to the efficiency of verbal recall, while processing speed may be an essential performance factor in various other cognitive domains.

Clinical symptoms also contribute to the observed cognitive deficits in patients. Notably, negative symptoms are usually found to be moderately related to impaired neuropsychological functioning (Ventura et al., 2009). Clinically-rated attention disorders, which are generally considered to be distinct from negative symptomatology, might also influence cognitive efficiency in schizophrenia. Although affective symptoms have been far less investigated in this population, their role in verbal memory

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has emerged in a few studies (Lysaker et al., 2000; Brébion et al., 2001; Sanfilipo et al., 2002; Moser et al., 2006; Brébion et al., 2007, 2009). We recently observed, using a visual memory task, that the effect of affective symptoms was modified by gender. Impaired visual memory was related to depression in women and to anxiety in men (Brébion et al., under review). Given that this dissociation was unexpected, we conducted retrospective analyses of two other independent schizophrenia samples, in an attempt to determine whether the gender-specific effect of affective symptoms could be replicated. Sex group re-analysis of our previously published verbal memory data indeed revealed the same differential effect of anxiety in men and depression in women (re-analyses of both datasets are reported in Brébion et al., under review, see discussion). The fact that this differential pattern of associations was observed in three independent schizophrenia samples from three different cultures (USA, United Kingdom, and Spain), and in verbal as well as visual memory measures, suggests that the effect was not a chance finding. Differences between male and female patients in the way other clinical symptoms relate to cognition have been reported as well (Karilampi et al., 2011). However, gender effects in relation with symptomatology are generally not examined, and there is not a clear pattern of the way negative symptoms, affective symptoms, and attention disorders might affect cognitive performance differently in male and female patients.

To further investigate the role of clinical symptoms in cognitive impairment in schizophrenia, we conducted a post-hoc analysis of a large cognitive database held by the Parc Sanitari Sant Joan de Déu. We focused on the factors affecting verbal memory and verbal fluency. Our objective was twofold: 1) to confirm the role of processing speed in these two functions, as well as the additional role of encoding strategy in verbal memory efficiency; and 2) to investigate gender differences in the way clinical symptoms are related to verbal memory and verbal fluency. Following our previous observations we predicted that depression affects verbal memory –and possibly verbal fluency– in women, while it is anxiety that affects these in men. Potential differences in the way negative symptoms and attention disorders might play a role in men and women were explored.

2. Method

2.1. Subjects

Eighty-eight outpatients with schizophrenia (DSM-IV-TR) were included in the study. They were randomly selected from a computerized register of five Community Mental Health Centres (CMHC) from Sant Joan de Déu Mental Health Services in Barcelona. Exclusion criteria were mental retardation, substance abuse, and neurological disorders. The study was approved by the Sant Joan de Déu-Mental Health Services Ethics Committee. All patients provided written informed consent to participate in the study after receiving a complete description by their psychiatrist. The sociodemographic and clinical characteristics of the sample are presented in Table 1.

Table 1
Sociodemographic and clinical data for the 88 schizophrenia patients (mean and standard deviation).

Age	41.2 (12.0)
Sex	59 males, 29 females
Education level	3.43 (.93)[a]
WAIS vocabulary score	29.7 (11.4)
Disease duration (years)	18.7 (11.3)
Number of psychiatric admissions	3.5 (4.4)
PANSS total	59.2 (12.7)
PANSS positive symptoms	13.5 (4.5)
PANSS negative symptoms	19.6 (6.2)
PANSS depression	1.8 (1.1)
PANSS anxiety	1.9 (1.1)
PANSS attention	1.7 (1.0)

[a] Fewer than 9 years of education on average.

2.2. Clinical ratings

The Positive and Negative Syndrome Scale (PANSS) for Schizophrenia (Spanish version, Peralta and Cuesta, 1994) was administered to all patients. The items of interest for this analysis were negative symptom score, depression, anxiety, and attention disorders.

2.3. Material and procedure

The patients had been administered a broad neuropsychological battery. This analysis focuses on verbal memory, verbal fluency, and processing speed. We therefore selected the following tasks:

- The Test de Aprendizaje Verbal España Complutense (TAVEC), used to assess verbal memory. This is a Spanish equivalent of the California Verbal Learning Test. A list of 16 words organisable into 4 semantic categories (list A) was read aloud, and the subjects were required to recall as many words as they could immediately after learning. Then the procedure was repeated four times with the same list. After the 5th recall of list A, a second semantically-organisable list was administered once (list B, the interference list), before the subjects were again required to recall the words from list A. The measures used for this analysis were the number of words recalled at the 1st presentation of list A, the number of words recalled from list B, an index of serial clustering in free recall (reflecting the propensity to learn the list by rote rehearsal) for list A and for list B, and an index of semantic clustering in free recall (reflecting the propensity to encode the words from the list according to their semantic properties) for list A and for list B.
- The phonological fluency and semantic fluency tasks. Subjects were required to produce as many words as possible starting with the letters F, A, and S within 1 min for each letter (phonological fluency), and as many names of animals as possible within 1 min (semantic fluency).
- The Stroop naming component of the Stroop test. Subjects had to read a list of names of colour aloud, as quickly as possible. The reading speed score obtained was used as a measure of processing speed.

Clinical assessment and cognitive testing were conducted the same day or within a couple of days by two trained psychologists (κ index of inter-rater reliability above .80).

2.4. Statistical analysis

2.4.1. Associations with cognitive factors

Regression analyses were conducted on the numbers of words recalled from list A (1st recall) and list B. The cognitive predictors were the serial and semantic clustering indices and the Stroop reading speed measure. Age, sex and vocabulary score were also entered among the predictors to control for their potentially confounding effect. The regression analyses were then conducted on phonological and semantic verbal fluency measures, after removal of the serial and semantic clustering indices from the predictors.

2.4.2. Associations with clinical symptoms

Regression analyses were conducted in each sex group on the numbers of words recalled from list A (1st recall) and list B, and on both types of verbal fluency. Negative symptom score, depression, anxiety, and attention disorders were entered as predictors. Age and vocabulary score were entered as well.

3. Results

The mean numbers of words recalled were m = 3.9 (sd = 1.7) for the 1st recall of list A, and m = 3.4 (sd = 1.8) for list B. The verbal fluency scores were m = 21.5 (sd = 11.1) for phonological fluency, and m = 14.3 (sd = 4.3) for semantic fluency.