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Sex differences in verbal memory in schizophrenia patients treated with “typical” neuroleptics

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Abstract

The relationship between sex and verbal learning and memory was investigated in 70 males and 36 females with a diagnosis of schizophrenia. Ninety-seven percent of the sample was receiving typical neuroleptic medication as treatment and had never received atypical medications. Selected scores from the California Verbal Learning Test (CVLT) [Delis, D.C., Kramer, J.H., Kaplin, E., Ober, B., 1987. The California Verbal Learning Test—Research Edition. Psychological Corporation, New York] were dependent variables in a series of hierarchical multiple regression analyses. Predictors comprised demographic, clinical and general cognitive measures. Sex was the most powerful predictor of both cumulative learning (Trial A5 recall) and the absolute number of words recalled after 20 min (Long-Delay Free Recall), accounting for 14% and 16% of score variance, respectively. Chlorpromazine-equivalent dose was negatively related to learning and recall. However, recall savings (Percent Retention) was unrelated to any predictor. This pattern of results parallels sex differences observed in the general population, albeit at a lower overall level of performance and with the suggestion of greater relative deficit in males. Schizophrenia does not eliminate and may even increase the advantage women demonstrate over men in some aspects of verbal memory.

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During the past two decades, there has been a resurgence of interest regarding the issue of sex and gender differences in schizophrenia. This issue is relevant to understanding the heterogeneity of the illness and the influence of sex on treatment, course, outcome, and etiology (Canuso et al., 1998). Studies have addressed a broad range of topics, including sex and gender differences in premorbid social functioning

(Goldstein et al., 1990; Childers and Harding, 1990), age of illness onset (McGlashan and Bardenstein, 1990), symptom expression (Leung and Chue, 2000), outcome (Murray and Van Os, 1998), and genetic risk (Goldstein et al., 1990).

In the domain of cognition, verbal memory dysfunction is probably the most prevalent impairment in schizophrenia (Aleman et al., 1999; Heinrichs and Zakzanis, 1998). The new generation of antipsychotic drugs and reduced need for anticholinergic medication may have enhanced verbal memory abilities in the patient population (Kern et al., 1999). However, deficits persist and research samples are often overwhelm-

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ingly male, while little is known about the differential performance of male and female patients. [Goldberg et al. \(1995\)](#) found no evidence for differential verbal memory performance in male and female patients and this was echoed by [Hoff et al. \(1998\)](#) and by [Bilder et al. \(2000\)](#). On the other hand, [Goldstein et al. \(1998\)](#) reported that only male patients were impaired in verbal memory. [Lewine et al. \(1997\)](#) and [Gruzelier et al. \(1999\)](#) argued that sex differences in memory and other aspects of cognition were present in schizophrenia, but were mediated by age-of-illness onset and clinical syndrome effects. There is also a report by [Lewine et al. \(1996\)](#) suggesting that sex differences in verbal memory exist, but in the unexpected direction, with male patients superior to females on performance indices. Apart from inconsistent results, evolving medication practices are a complicating issue in attempts to understand the role of gender in schizophrenic cognition and little information is available concerning memory in patients never treated with newer medications.

Studies of brain morphology relevant to verbal memory, including volumetric studies of the cerebral ventricles, periventricular area and left medial temporal lobe, contribute little clarity to the issue of sex differences. Thus, [Bogerts et al. \(1990a,b\)](#) showed that male schizophrenia patients had a significantly greater reduction in left hippocampal tissue volume than females. Similarly, [Nopoulos et al. \(1997\)](#) reported greater ventricular enlargement in male patients. However, [Lauriello et al. \(1997\)](#) found that cortical gray matter and ventricular abnormalities were present equally in male and female schizophrenia patients. Moreover, [Gur et al. \(2000\)](#) reported hippocampal reductions related to memory function in both sexes and [Goldstein et al. \(2002\)](#) failed to find any sex differences in subcortical gray matter regions.

It is evident that no definite conclusion can be drawn from the recent literature on sex differences and verbal memory in schizophrenia, although the preponderance of studies seems to favor the view that this cognitive function is about equally compromised in men and women with the illness. In contrast, verbal memory comparisons of healthy men and women have suggested that women generally demonstrate greater proficiency on many indicators ([Bleecker et al., 1988; Kramer et al., 1997; Lewin et al., 2001](#)). It has long been proposed that this superior performance is the result of the greater utilization by females of verbally

based learning strategies ([Bolla-Wilson and Bleecker, 1986; Sundet, 1986](#)). In an effort to establish specific areas of differential performance in verbal memory and learning, [Kramer et al. \(1988\)](#) found that women consistently outperformed men on measures of immediate and delayed recall. However, sex differences were not found in many other areas of memory functioning, including rate of learning, retention, types of errors, and recognition. Superior recall in women has been attributed both to better retrieval strategies as well as to more effective organization of verbal material during initial learning ([Kramer et al., 1988](#)).

The purpose of the present study was to increase knowledge regarding sex differences in neurocognitive functioning in schizophrenia, with specific reference to the domain of verbal memory and patients treated with standard neuroleptics and never exposed to the newer “atypical” medications. These issues were addressed using the California Verbal Learning Test (CVLT; [Delis et al., 1987](#)), a multifaceted measure of many qualitative and quantitative aspects of memory function including learning, delayed recall, and retention. In addition, extensive age and sex norms are available for the CVLT. Therefore, it is possible to compare the performance of males and females with schizophrenia and also to compare patients to normal males and females on various indices of verbal learning and memory. Our basic question was: is the putative superiority of healthy, non-schizophrenic women in verbal learning and recall tasks also present in the schizophrenia patient population? And more specifically, is there evidence for sex differences in verbal learning and recall in schizophrenia patients once key demographic, general cognitive and clinical variables are taken into account? A multiple regression approach was adopted to answer these questions within the context of outpatients treated with standard neuroleptic medication in the early 1990s and prior to the widespread application of “atypical” drugs later in the decade.

1. Methods

1.1. Subjects

Seventy males and 36 females with a diagnosis of schizophrenia, who were outpatients at the Queen

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