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# Impairment of verbal memory and learning in antipsychotic-naïve patients with first-episode schizophrenia

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## Abstract

**Background:** Verbal memory deficits are of interest in schizophrenia because of the potential relationship to functional and anatomic mesial temporal lobe pathology in this disorder. The goal of this study was to characterize the nature of verbal memory impairments in antipsychotic-naïve schizophrenic patients early in the course of illness. **Methods:** Neuroleptic-naïve patients with schizophrenia ( $n=62$ ) and healthy individuals ( $n=67$ ), matched on IQ, age, sex, and parental socioeconomic status, were administered the California Verbal Learning Test (CVLT). **Results:** Schizophrenia participants performed significantly worse than healthy individuals on measures of verbal learning, short- and long-term memory, and immediate attention. Deficits in recall were related to reduced use of organizational strategies to facilitate verbal encoding and retrieval. No group differences were found in rate of forgetting or susceptibility to proactive or retroactive interference. Memory deficits had minimal relation to positive or negative symptom severity. **Conclusions:** Schizophrenia is characterized by significant verbal memory dysfunction early in the course of illness prior to treatment with antipsychotic medications. Deficits in consistency of learning over several trials, as well as a strong relationship between semantic organizational strategies and reduced learning capacity, implicate prefrontal dysfunction as a contributor to verbal memory deficits in schizophrenia.

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**Keywords:** Schizophrenia; Verbal memory; Learning; Neuropsychology; Frontal lobes

## 1. Introduction

Verbal memory deficits are well-established in schizophrenia (Calev, 1984; Goldberg et al., 1989; Saykin et al., 1991). Some neuropsychological studies have found verbal memory deficits in schizophrenia to

be more severe than those evident in other neuropsychological domains (Censits et al., 1997; Dickerson et al., 1991; Saykin et al., 1994). Interest in verbal memory dysfunction has increased in recent years because neuroimaging and post-mortem studies have implicated left temporolimbic cortex as a site of neurophysiologic and neuroanatomic abnormalities in schizophrenia (Barta et al., 1990; Keshavan et al., 1998; Shenton et al., 1992). Indeed, verbal memory deficits have been linked to physiological abnormalities of mesial temporal cortex in schizophrenia

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patients (Mozley et al., 1996). In addition, verbal memory deficits have been linked to difficulties with self-generated organizational strategies in which patients fail to use semantic information to facilitate verbal encoding and retrieval (Brebion et al., 1997). This observation raises the possibility that prefrontal dysfunction also contributes to verbal memory impairments. Based on these findings and the significance of verbal memory deficits in day-to-day function (Green, 1996), an important aim of neuropsychological investigations of schizophrenia is to define the specific memory deficits associated with the disorder.

Studies of memory in schizophrenia have been of two general types. Some studies utilized summary scores of overall memory performance to contrast deficits in memory with those in other neuropsychological domains (Bilder et al., 2000; Gur et al., 1999; Riley et al., 2000; Saykin et al., 1991, 1994). Other studies assessed selective aspects of memory and learning. For example, a number of investigators have reported differential deficits in short- and long-term memory (Tamlyn et al., 1992) while others have reported rapid forgetting (Beatty et al., 1993). A pattern of preserved recognition memory despite impaired free recall was found by some authors (Bauman and Murray, 1968) while others found modest deficits in both recognition and recall memory (Caley, 1984; Gold et al., 1992). More recently, schizophrenia patients showed abnormal frontotemporal activation during verbal encoding relative to healthy participants, but no differences in word recognition were observed (Ragland et al., 2001). While these studies provide important findings, better understanding of the particular aspects of memory that are most impaired in schizophrenia is needed, particularly early in the course of the disorder prior to antipsychotic treatment which may affect verbal memory abilities (Bilder et al., 2002; Schuebach et al., in press).

The work of Paulsen et al. (1995) is one of few studies providing an in-depth evaluation of verbal memory and learning in schizophrenia. In addition to assessing traditional aspects of verbal memory such as overall learning, and short- and long-term retention, these authors utilized the California Verbal Learning Test (CVLT) to characterize learning styles, strategies, and rate of memory decay (i.e., forgetting). As Paulsen and her colleagues point out, these components

are differentially affected by disorders such as Alzheimer's and Parkinson's diseases, and by focal brain lesions to various cortical regions. They found learning, memory, and organizational deficits in their group of schizophrenia participants. However, duration of illness in this chronic sample was relatively long, all patients were apparently receiving antipsychotic medications, and 19% of patients were also receiving anticholinergic drugs that may impact memory performance (Strauss et al., 1990; Sweeney et al., 1991). Thus, it is difficult to ascertain whether the observed memory dysfunctions were related to the presence of schizophrenia, chronic effects of the illness, or iatrogenic effects of pharmacotherapy.

One strategy to avoid potential confounds of chronicity and antipsychotic treatment is to investigate schizophrenia early in the course of illness, *prior to treatment* with psychoactive medications. Previous reports of memory dysfunction in early phases of schizophrenia used summary scores of memory performance to contrast deficits in multiple neuropsychological domains (Hoff et al., 1992; Mohamed et al., 1999; Saykin et al., 1994). The goal of the present study was to describe the nature of verbal memory impairments in antipsychotic-naïve schizophrenia patients early in the course of illness by investigating the following aspects of memory: immediate retention; overall learning; short-term, long-term, and recognition memory; rate of forgetting; susceptibility to proactive and retroactive interference; and use of organizational strategies. Thus, this study examined components of memory that are linked to frontal (e.g., semantic organization) and temporal lobe function (e.g., recall; proactive and retroactive interference) to provide in-depth characterization of verbal memory deficits in schizophrenia.

## 2. Methods and materials

### 2.1. Subjects

Following hospitalization for first-episode psychosis, 62 individuals who met research diagnostic criteria for schizophrenia based on the Structured Clinical Interview for DSM-IV (SCID; APA, 1994) were recruited at the University of Pittsburgh Medical Center. Scheduled follow-up evaluations at 12 months

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