ORIGINAL ARTICLE

# Word and Tone Working Memory Deficits in Schizophrenia

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**Background:** Verbal memory deficits have been reported in many studies of patients with schizophrenia. We evaluated the specificity of these deficits by comparing patients and control subjects on several verbal and nonverbal auditory memory tests.

**Methods:** Performance of stable, medicated outpatients with *DSM-III-R* diagnoses of schizophrenia (N = 38) was compared with that of healthy subjects (N = 39) on a word list immediate recall task, tone delayed discrimination tasks, and word and tone serial position tasks. Before memory testing, patients were divided into 2 groups based on their ability to perform normally on a screening test requiring pitch discrimination and sustained attention.

**Results:** The nonverbal tests were more difficult for control subjects than the verbal tests. Despite this, patients who performed normally on the screening test of perception and attention performed normally on both nonverbal tests but had highly significant deficits on both verbal tests ($P<.001$ and $P=.02$). Patients who performed poorly on the screening test had highly significant performance deficits on all the memory tests.

**Conclusions:** One subgroup of patients with schizophrenia has a selective deficit in verbal memory despite normal motivation, attention, and general perceptual function. Another group has deficits in multiple aspects of cognitive function suggestive of failure in early stages of information processing.

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COGNITIVE DEFICITS are basic pathological characteristics of schizophrenia. Among these deficits, verbal memory dysfunction appears to be particularly severe. Saykin et al found that medicated[1] and drug-naive[2] patients were more impaired on verbal memory and learning than on 9 other dimensions of function, but also performed significantly more poorly than the controls on all dimensions. Deficits in immediate recall of word lists[3-6] and in verbal learning[7] have also been reported but were not compared with other cognitive deficits. Thus, while it is clear that verbal memory deficits are prominent in schizophrenia, it is not clear if they are part of a global cognitive dysfunction or, instead, constitute a central pathophysiological feature themselves.

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The present study pursued further the possibility of a selective deficit in verbal memory, addressing methodological issues critical to establishing the specificity of the deficit. In particular, we compared the performance of schizophrenic patients and healthy controls on a variety of auditory memory tasks with verbal and nonverbal memoranda. Care was taken to control for differences between tests other than the verbal-nonverbal distinction and to identify subjects who might do poorly because they could not attend to or discriminate among the stimuli they were required to recall.

## RESULTS

### VERBAL MEMORY

Immediate recall of the 16 words by controls (n = 30) averaged 8.0 ± 2.4 words, while DSz (n = 22) and NDSz (n = 14) patients recalled 6.0 ± 2.5 and 4.8 ± 1.8, respectively (**Figure 1**). Analysis of variance showed a main effect of group ($F_{2,63}=10.4$; $P<.001$). Post hoc tests indicated that scores for both patient groups were significantly lower than those for controls but were not significantly different from each other. Results were similar

## SUBJECTS AND METHODS

### SUBJECTS

Thirty-eight outpatients who met Structured Clinical Interview for *DSM-III-R*[8] criteria for schizophrenia and 39 controls without history of psychiatric illness were studied (**Table**). Subjects were excluded if they met criteria for substance abuse within the previous year, were currently using alcohol or drugs regularly, or had a history of neurologic illness. All patients were receiving psychiatric medications. Subjects were considered right or left handed if they wrote and performed 5 of 7 everyday tasks with that hand.[9] Patients and controls did not differ in age, sex, education, parental education, or handedness. All gave informed, written consent to participate.

### SCREENING TEST OF ATTENTION AND PERCEPTION

Two 300-millisecond pure tones were presented with 300 milliseconds between. Subjects indicated whether the tones differed in pitch. When different, the pitches were in 1 of 8 ratios ranging from 0.67 to 0.98. Subjects were considered to have failed the screening test if they did not score 100% at the 6 easiest levels. Twenty-five patients (referred to as *discriminators* [DSz]) passed and 13 (*nondiscriminators* [NDSz]) failed. The 2 patient groups did not differ in age, patient or parental education, or Positive and Negative Syndrome Scale[10] scores. Six of the 39 control subjects failed (ND controls). The controls who failed tended to be less educated ($t_{18} = 2.0$; $P = .07$) and to have less-educated fathers ($t_{19} = 2.0$; $P = .07$) than those who passed. Such poor performance on an easy test of attention and perception associated with lower educational achievement suggests that these subjects have attentional and learning problems. They were therefore not considered a primary comparison group.

### MEMORY TESTS

#### Verbal Tests

In the Word List Recall Test (WLRT), a list of 16 nouns was read to subjects.[11] Immediately afterward, subjects repeated words they could recall.

In the Word Serial Position Test (WSPT), each trial began with 4 nouns spoken with 1 second between words. One word was then repeated after a delay of 1, 5, or 9 seconds. Subjects were instructed to remember the 4 words in the order presented and to indicate the serial position of the repeated word by raising the appropriate finger of their right hand. There were 36 trials, balanced and ordered randomly with regard to the 3 retention intervals and 4 positions. No word appeared twice in the test.

#### Nonverbal Tests

In the Tone Delayed Discrimination Tests (TDDTs), there were 3 pitch-delayed match-to-sample tasks differing in difficulty. In the first (low load), two 300-millisecond tones were presented (ranging from 200-1200 Hz) separated by 1, 3, 5, 7, or 9 seconds. Subjects indicated by key press whether the tones were the same pitch. In the second, distraction was introduced by presenting 100-millisecond tones ranging in pitch from 105 to 1500 Hz, beginning 400 milliseconds after the first tone and ending 400 milliseconds before the second. In the third (high load), 3 tones were presented with a 400-millisecond intertone interval. After a delay, a fourth tone was presented and subjects indicated whether it was the same as any of the first 3. There were 30 trials in the first 2 tests and 40 in the third test.[12]

For the Tone Serial Position Test (TSPT), each trial began with three 300-millisecond tones (200-2500 Hz) separated by 400 milliseconds. One of the 3 was repeated after delays of 1, 3, 5, or 9 seconds, and subjects indicated whether it was the first, second, or third of the original 3. There were 36 trials balanced and ordered as in the WSPT.

### GENERAL PROCEDURE

Subjects were tested individually in 2 sessions with practice trials before all tests. In the first session, the WLRT, the screening test of perception and attention, and the TDDTs were given, in that order. In the second session, WSPT, TSPT, WLRT, and the screening test of perception and attention were given. The screening test was always given first; equal numbers of subjects took the WLRT before and after the 2 serial position tests and half took the WSPT before the TSPT. Eleven patients participated in both test sessions. (Only initial session scores were used on the WLRT. Ten had the same classification as DSz or NDSz on both occasions. One switched from DSz to NDSz and was assigned to the first group for session 1 tests and overall patient counts, and to the second group for session 2 tests.) Other subjects took 1 test session. This, together with rare technical difficulties, led to different numbers of subjects for different tests, ranging from 21 to 35 for patients and 17 to 38 for controls. None of the subgroups that were compared on experimental measures differed significantly from each other on any of the demographic measures except that patients who took the serial position tests were older than controls who took the serial position tests (42.8 ± 8.3 vs 36.7 ± 9.0 years). The ND controls were in the group that only took the serial position tests.

### DATA ANALYSES

Differences among DSz, NDSz, and controls were evaluated by analysis of variance. Scheffé 2-tailed tests were used for post hoc comparisons.

on the WSPT (**Figure 2**). Controls (n = 15) averaged 89% correct, while DSz (n = 17) and NDSz (n = 6) patients averaged 76% and 63% correct. Analysis of variance showed main effects of group ($F_{2,35} = 7.9$; $P<.002$) and serial position ($F_{3,105} = 7.8$; $P<.001$) but no interaction between the 2 ($F_{6,105} = 1.5$; $P<.20$). Post hoc tests again indicated that performances of both patient groups were significantly below that of controls but not significantly different from one another. No main effects or interactions of retention interval were detected. The ND controls performed significantly worse than other controls on the WSPT ($t_{40} = 8.0$; $P<.006$) and did not differ significantly from either patient group.

**Demographics of Subjects**

| Variable | Controls (n = 39) | Patients (n = 38) |
|---|---|---|
| Age, mean ± SD, y | 36.7 ± 12.3 | 42.9 ± 9.5 |
| Sex, No. | | |
| Male | 14 | 20 |
| Female | 25 | 18 |
| Education, mean ± SD, y | | |
| Subject | 14.7 ± 2.9 | 13.1 ± 2.4 |
| Mother | 13.0 ± 3.0 | 12.3 ± 4.0 |
| Father | 11.8 ± 3.6 | 12.3 ± 4.4 |
| Handedness, No. | | |
| Left | 1 | 2 |
| Right | 38 | 32 |
| Ambidextrous | 0 | 4 |
| Patient symptom ratings, mean ± SD* | | |
| Positive symptoms | NA | 16.5 ± 4.3 |
| Negative symptoms | NA | 20.1 ± 2.7 |
| General symptoms | NA | 37.4 ± 10.9 |

**Positive and Negative Syndrome Scale. NA indicates not applicable.*

## NONVERBAL MEMORY

Comparison of controls (n = 17) and DSz (n = 15) and NDSz (n = 10) patients on the TDDTs (Figure 1) yielded main effects of group ($F_{2,38} = 23.1$; $P<.001$) and test ($F_{2,76} = 60.6$; $P<.001$) but no interaction between the 2 ($F_{4,76} = 1.4$; not significant). Post hoc tests indicated that DSz patients performed as well as controls ($P = .80$), while NDSz patients performed significantly worse than controls and DSz patients ($P<.001$).

The TSPT yielded similar results (Figure 2). For controls (N = 17), this task proved more difficult than the WSPT (mean percentage correct, 67% vs 89%). Analysis of variance showed a trend for an effect of group ($F_{2,33} = 2.57$; $P<.10$). As with the TDDTs, DSz patients (n = 13) and controls performed similarly ($P>.34$), while NDSz patients (N = 6) performed significantly worse than controls ($P<.03$). Although NDSz patients again performed worse than DSz patients, the difference between them was not significant. The ND controls performed worse than other controls ($t_{38} = 9.7$; $P<.009$) and did not differ significantly from either patient group.

## COMMENT

In this study, most outpatients with schizophrenia displayed deficits in auditory verbal memory. This is consistent with earlier reports of deficits in immediate recall of aurally presented word lists in more acutely ill inpatients[5,6] and with reports of deficits in patients on other types of verbal memory tests.[2,7] Importantly, substantial deficits in auditory verbal memory were evident in patients who performed normally on an auditory nonverbal memory test. These patients did not suffer from global auditory processing problems, as might result from perceptual or attentional dysfunction, and their verbal memory deficits cannot be explained by nonspecific performance factors. Furthermore, the memory deficit itself is not global in those patients because their performance on the tone memory tests is intact.

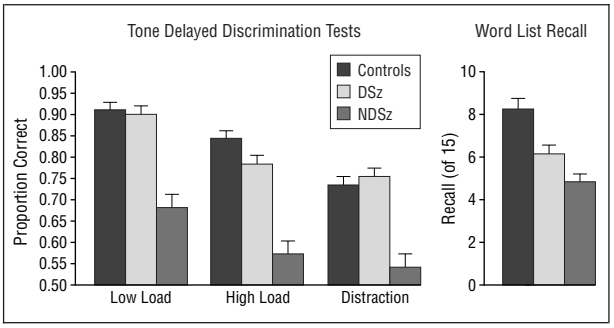


**Figure 1.** *Proportion correct on the 3 Tone Delayed Discrimination Tests (low load, high load, and low load with distraction) and number correct on the Word List Recall Test in healthy controls (n = 17 on the Tone Delayed Discrimination Tests and n = 30 on the Word List Recall Test), schizophrenic patients classified as discriminators (DSz) (n = 15 and 22, respectively), and schizophrenic nondiscriminators (NDSz) (n = 10 and 14, respectively).*

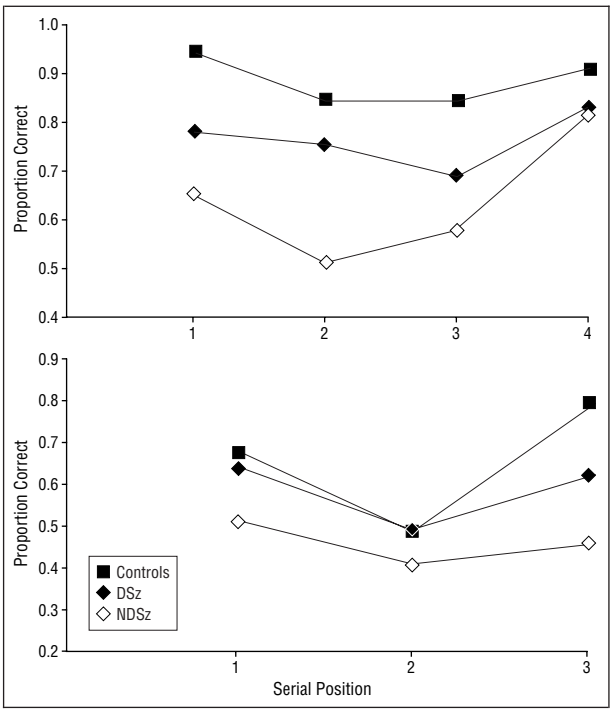


**Figure 2.** *Top, Proportion correct on the Word Serial Position Task in healthy controls (n = 15), schizophrenic patients classified as discriminators (DSz) (n = 17), and schizophrenic nondiscriminators (NDSz) (n = 6). Proportion correct is indicated separately for trials when the target word was in the first, second, third, or fourth position on the initial stimulus list. Bottom, Proportion correct on the Tone Serial Position Task in healthy controls (n = 17), DSz (n = 13), and NDSz (n = 6). Results are indicated separately for trials when the target tone was in the first, second, or third position on the initial stimulus list.*

Several methodological factors increase confidence in these conclusions. First, many patients who did poorly on a verbal test performed normally on a nonverbal task that for controls was more difficult than the verbal task. This rules out the possibility that patients did poorly on the verbal but not the nonverbal test simply because the verbal test was more difficult.[11] Second, results were similar with 2 types of verbal (WLRT, WSPT) and nonverbal (TDDTs, TSPT) tests. Third, 1 verbal and 1 nonverbal test (WSPT and TSPT) were virtually identical except for the nature of the stimuli, directly controlling in this manner for most differences

between tests other than the verbal-nonverbal distinction. Finally, before memory testing, patients were screened for their ability to attend to and perceive the nonverbal auditory stimuli they would be asked to remember. This made it possible to identify a subgroup of patients with relatively intact attention and perceptual function. Only in these patients is it reasonable to test memory per se, and only in these patients was the specific deficit in verbal memory evident. If results of all patients had been averaged together as in previous studies,[1,2] the group profile may have shown evidence of a relatively greater patient deficit in verbal memory, but only in the context of deficits on all tests.

The WSPT used in the present study is a test of working memory in that subjects keep in mind the original word list, usually through rehearsal, and use this information to locate the target word in the original sequence. In our companion article,[13] we report that healthy subjects activate the temporal lobe and prefrontal cortex while doing this task, precisely the network postulated to subserve verbal working memory.[14] Patients showed activation deficits in these areas,[13] which together with the performance deficits reported in this article suggest dysfunction in neural systems related to verbal working memory. Although the WLRT may draw on memory processes beyond those of working memory, deficits in the latter could also account for performance deficits on this test. Several studies have demonstrated the relative independence of auditory verbal and nonverbal working memory systems.[15,16] Thus, the dissociation of verbal and nonverbal memory function observed in DSz patients is consistent with this established feature of working memory.

Perception and encoding of auditory information is necessary before that information can enter working memory. In the present study, 1 group of patients (DSz patients) had deficits in auditory verbal working memory but performed normally on a screening test of attention and perception and on nonverbal working memory tests. The dissociation between verbal and nonverbal working memory in this group can be marked, as illustrated by 6 DSz patients (24% of the sample) who scored more than 2 SDs below the control mean on the WLRT but within 0.5 SD of the control mean on the TDDT. In these patients, the early stages of auditory processing appear to be intact. In contrast, a second group of patients (NDSz patients) was identified with deficits on the attention-perception test and both verbal and nonverbal memory tests. A parsimonious explanation of the performance deficits in this group is a perceptual or encoding dysfunction early in the information processing sequence.[17] Thus, while both groups of patients have a deficit in verbal auditory working memory and share the clinical manifestations of that deficit, they might arrive at the deficit as a result of quite different pathological and causative processes.

The present study is limited in the scope of neurocognitive assessment. Tests of other perceptual and cognitive functions shown previously to be abnormal in schizophrenia are necessary to determine the specificity of DSz deficits and the generality of NDSz deficits. Focused assessments of component aspects of language and verbal memory are necessary to specify the DSz deficit.

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