

# Auditory Verbal Working Memory in Cognitive and Symptom Subtypes of Schizophrenia

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## Abstract

**Background:** Studies using a tone screening test to classify patients have found evidence for schizophrenia subtypes having either verbal working memory (WM) or generalized cognitive deficits. Given the importance of defining schizophrenia subtypes having distinct cognitive and pathophysiological abnormalities, this study aimed to replicate these findings in larger samples, define symptom features of subtypes, and examine medication effects.  
**Methods:** Patients with schizophrenia who passed the screening test (discriminators,  $n=60$ ) were compared to those who did not (nondiscriminators,  $n=23$ ), and healthy controls ( $n=52$ ) on a verbal WM test (word serial position test, WSPT) and other neurocognitive tests.  
**Results:** Performance on the WSPT and tone screening test did not differ between medicated and unmedicated patients. Patients who performed as well as controls on the tone screening test (i.e., Dsz) showed poorer performance on the WSPT and a deficit in verbal but not visual memory on the Wechsler Memory Scale-Revised. In contrast, NDsz patients showed overall poor performance on both verbal and nonverbal tests, consistent with a generalized deficit. Verbal WM deficits in Dsz patients were significantly correlated with auditory hallucinations and positive thought disorder ratings, but not with negative symptoms of schizophrenia. As predicted, Dsz patients having auditory hallucinations showed poorer verbal WM than nonhallucinators and controls.  
**Conclusions:** These findings are consistent with neuroimaging findings suggesting that verbal WM deficits in Dsz patients stem from dysfunction of language-related regions in left inferior frontal and temporal cortex, and confirm the value of the tone screening test for parsing schizophrenia into cognitive subtypes.

## Introduction

The clinical and neurocognitive heterogeneity of schizophrenia remains an obstacle to understanding its pathophysiology. We have addressed this issue in studies of working memory (WM) in schizophrenia. Wexler et al. (1998; 2002) divided schizophrenia patients into two subgroups on the basis of a screening test of auditory attention and perception: (1) patients who performed normally on the screening test (Discriminators) showed normal nonverbal WM, but poorer performance on a word serial position test (WSPT) of verbal WM; (2) patients who performed poorly on the screening test (Non-discriminators) had marked deficits on both word and tone serial position tests, suggestive of a generalized cognitive deficit. Bruder et al. (2004) confirmed the difference in WSPT performance between these subgroups and found that the verbal WM deficit in discriminators extended to the verbal memory scale on the Wechsler Memory Scale-Revised. The present study aimed to confirm these findings in a larger sample, and to rule out medication effects. Given the findings of reduced activity in language-related cortical regions of patients with auditory hallucinations (Wible et al., 2009), we also investigated whether or not there was a difference in verbal WM between discriminators with and without auditory hallucinations.

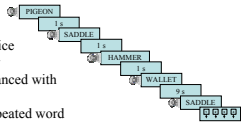
## Method

### Tone Discrimination Screening Test:

- 60 test trials in which tone pairs were presented
- Tones in pair were same or different
- If different, frequency ratio of 0.67, 0.75, 0.85, 0.90, or 0.95
- Half trials were same tones, half were different
- Each frequency ratio presented once per 10 trials
- Subjects indicated whether tones were the same or different

### Word Serial Position Test (WSPT):

- Thirty-six trials
- Four nouns presented in male voice
- One word repeated after 9s delay
- Trials randomly ordered and balanced with regard to serial positions
- Subjects indicated position of repeated word



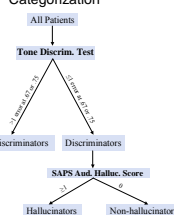
## Participants

### Demographics

Variable	Discriminators (n = 46, 35 male)		Nondiscriminators (n = 23, 14 male)		Controls (n = 52, 24 male)	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Age (years) <sup>a</sup>	39.4	8.8	36.6	10.3	26.7	6.3
Education (years)	14.4	2.5	13.5	2.5	16.1	2.1
Handedness	69.9	39.1	71.8	33.3	73.7	28.7
IQ <sup>b</sup>	22.1	6.8	22.1	6.7	75.7	22.1
Outset age (years)	8.5	8.2	8.5	9.6		
Total BPRS	35.9 <sup>c</sup>	13.3	35.6 <sup>d</sup>	10.8		
PANSS positive	15.9 <sup>e</sup>	7.1	14.2 <sup>f</sup>	5.7		
PANSS negative	14.3 <sup>g</sup>	4.0	16.6 <sup>h</sup>	5.9		

IQ: IQ test (range = 100 to 180); BPRS: Brief Psychiatric Rating Scale; PANSS: Positive and Negative Syndrome Scale.  
<sup>a</sup> Significant difference among groups in age,  $F(2,112) = 3.61, p < 0.05$  but Newman-Keuls comparisons were not significant.  
<sup>b</sup> Significant difference among groups in education,  $F(2,112) = 12.38, p < 0.001$ ; Newman-Keuls comparisons: Controls > Discriminators > Nondiscriminators.  
<sup>c</sup>  $n = 53$   
<sup>d</sup>  $n = 19$

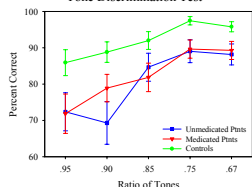
### Categorization



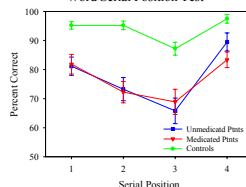
## Results

### Mean Percent Correct for Unmedicated Patients, Medicated Patients and Healthy Controls in Tone Discrimination Test and Word Serial Position Test

#### Tone Discrimination Test



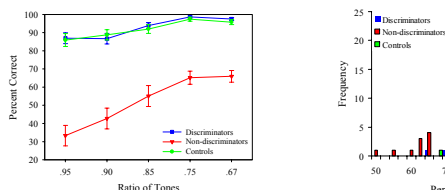
#### Word Serial Position Test



Healthy controls showed greater accuracy on the tone discrimination test than patients, but there was no difference in performance between medicated and unmedicated patients ( $F(2,129) = 4.32, p = 0.15$ ). Overall, subjects performed more accurately at the larger tone ratios ( $F(4, 516) = 28.84, p < 0.001, \epsilon = 0.667$ ).

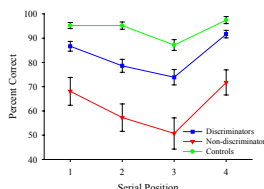
Healthy controls showed overall greater accuracy than patients on the WSPT but there was no difference in performance between medicated and unmedicated patients ( $F(2,129) = 21.29, p < 0.001$ ). There was also a significant difference in performance at the different serial positions ( $F(3,387) = 24.11, p < 0.001, \epsilon = 0.902$ ).

### Mean Percent Correct of Discriminators, Non-discriminators and Healthy Controls in Tone Discrimination Test



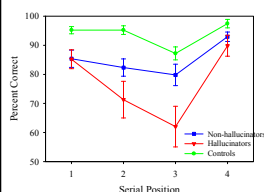
Non-discriminators performed significantly less accurately at all tone ratios than discriminators ( $F(1,129) \geq 60.03, p < 0.001$ ) and controls ( $F(1,129) \geq 62.74, p < 0.001$ ), but there was no difference between the performance of controls and discriminators. Subjects performed significantly more accurately at the larger tone ratios ( $F(4,516) = 36.18, p < 0.001, \epsilon = 0.688$ ); this effect was more pronounced in non-discriminators (Group by Tone Ratio interaction:  $F(8,516) = 3.74, p = 0.02, \epsilon = 0.688$ ).

### Mean Percent Correct of Discriminators, Non-discriminators and Healthy Controls in Word Serial Position Test



Non-discriminators and discriminators had significantly poorer accuracy than controls on the WSPT ( $p < 0.05$ ) and non-discriminators had poorer accuracy than discriminators ( $p < 0.05$ ; Group main effect:  $F(2,129) = 53.97, p < 0.001$ ). There was also a significant difference in performance as a function of serial position ( $F(3, 387) = 20.85, p < 0.001, \epsilon = 0.907$ ).

### Mean Percent Correct of Hallucinators, Non-hallucinators and Healthy Controls in Word Serial Position Test



There was a significant difference among groups ( $F(2,97) = 18.62, p < 0.001$ ). Group differences at the first 3 serial positions ( $F(2, 97) \geq 7.47, p < 0.001$ ) were more marked than those at the 4th position ( $F(2,97) = 3.95, p = 0.02$ ). Hallucinators had significantly poorer accuracy than controls at all serial positions ( $F(1,97) \geq 6.55, p < 0.01$ ), whereas nonhallucinators only performed significantly more poorly than controls at the first and second serial positions ( $F(1,97) \geq 11.32, p < 0.01$ ). Most importantly, hallucinators performed more poorly than nonhallucinators only at the middle serial positions 2 and 3, ( $F(1,97) \geq 5.26, p < 0.05$ ). There was also a significant difference in performance as a function of serial position ( $F(3,291) = 24.16, p < 0.001, \epsilon = 0.917$ ), and a Group by Serial Position interaction ( $F(6,291) = 3.45, p < 0.01, \epsilon = 0.917$ ).

### Neuropsychological Measures for Verbal and Nonverbal Tests

Variable	Discriminators (n = 39)		Nondiscriminators (n = 12)	
	Mean	S.D.	Mean	S.D.
WAIS-III				
Verbal IQ	104.3 <sup>a</sup>	14.6	88.1	15.8
Performance IQ	95.8 <sup>b</sup>	15.1	79.8	21.2
Wechsler Memory				
Verbal Memory	85.6	18.1	82.9 <sup>b</sup>	12.4
Visual Memory	99.3	19.8	88.5 <sup>b</sup>	21.0

<sup>a</sup>  $n = 35$   
<sup>b</sup>  $n = 11$

Nondiscriminators (NDsz) had lower verbal and performance WAIS-IQ scores than discriminators (Dsz), while Dsz patients had IQs in the normal range. On the WMS-R, Dsz patients performed as poorly as NDsz patients on the verbal memory index, but tended to show better visual memory. Dsz patients performed significantly more poorly on the verbal than visual memory index ( $t(38) = 4.36, p < 0.001$ ), whereas NDsz patients did not show a difference between their verbal and visual memory ( $t(10) = 0.83, ns$ ).

The WMS-R indexes were compared to norms from Wechsler, 1987. The verbal memory index for Dsz patients was between one and two SDs below the mean for the standardization sample ( $M = 107.6, SD = 14.7$ ), whereas their visual memory index was within a half a SD of the norms ( $M = 105.5, SD = 13.4$ ). The NDsz patients showed deficits on both the verbal and visual memory indexes, which were between one and two SDs below the norms.

## Conclusions

- Medication status did not play a role in performance on the tone discrimination or verbal WM test (WSPT).
- Patients who performed as well as controls on the tone discrimination test (Discriminators) showed a deficit on the WSPT. Patients who showed a deficit on the tone discrimination test (Non-discriminators) performed markedly poorer than controls and discriminators on the WSPT.
- The WMS-R results support the conclusion that the discriminator subgroup has a deficit in verbal but not nonverbal memory.
- The non-discriminator subgroup showed a deficit in both verbal and nonverbal memory; when combined with their poor performance on the tone discrimination test and WSPT, this suggests a more generalized deficit.
- Discriminators with auditory hallucinations showed poorer verbal working memory than non-hallucinators and controls.
- When considered together with neurophysiology studies, these findings suggest that deficits in a subgroup of schizophrenic patients (discriminators) stem from dysfunction of language-related regions in the left inferior frontal and parietotemporal cortex.
- The findings support the importance of parsing the heterogeneous disorder of schizophrenia into cognitive and symptom subtypes.

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