

Verbal Working Memory Impairment in Schizophrenia Patients and Their First-Degree Relatives: Evidence From the Digit Span Task

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Objective: The evidence for verbal working memory deficits in schizophrenia has been inconsistent. Few studies have evaluated verbal working memory in the first-degree relatives of schizophrenia patients, who likely share the genetic diathesis for schizophrenia but not the potential confounds associated with chronic mental illness. **Method:** The Wechsler Digit Span Task was used to investigate verbal working memory in 52 schizophrenia patients, 56 of their first-degree relatives, and 73 nonpsychiatric comparison subjects. **Results:** The nonpsychotic relatives showed no impairment on the forward digit span task, a measure of general attention, but did show impairment on the backward digit span task, a measure of verbal working memory. Schizophrenia patients showed impairment on both the forward and backward digit span tasks. **Conclusions:** These results indicate that the forward and backward digit span tasks tap different cognitive abilities that are differentially associated with the diathesis for schizophrenia. Working memory deficits associated with schizophrenia appear to be generalized and not limited to the spatial modality.

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Working memory deficits in schizophrenia may have important implications both for the localization of underlying neurologic impairment and for explanations of disparate cognitive deficits associated with this disorder (1). Findings that suggest spatial working memory deficits in schizophrenia have been well-replicated (2). In contrast, findings indicative of verbal working memory deficits have been less consistent (3). It is unclear whether working memory deficits in schizophrenia are limited to the spatial modality or whether the working memory dysfunction is more generalized and includes other domains.

Reports of cognitive deficits in schizophrenia are open to some criticism because multiple factors associated with chronic mental illness (e.g., lower education levels or medication effects) could potentially color performance and thus limit the conclusions that can be drawn. If cognitive deficits reflect the underlying genetic risk for schizophrenia, it would be beneficial to study first-degree relatives, since they likely share some

of the genetic diathesis for schizophrenia without the aforementioned complications.

This report examines verbal working memory, as measured by performance on the backward digit span task, in schizophrenia patients and their biological relatives. Among schizophrenia studies that report separate performance data for the forward and backward tasks, Stratta et al. (4) and Stefansson and Jonsdottir (5) found schizophrenia patients to perform significantly worse than nonpsychiatric comparison participants on both the forward and backward digit span tasks. In contrast, Park and Holzman (6) failed to find a difference between schizophrenia patients and nonpsychiatric comparison participants in performance on either subtest. None of these studies included first-degree relatives of schizophrenia patients. We propose that a task as quickly and easily administered as the backward digit span task provides invaluable working memory information. Impaired performance on this task in asymptomatic individuals could potentially serve as an indicator of genetic predisposition for schizophrenia.

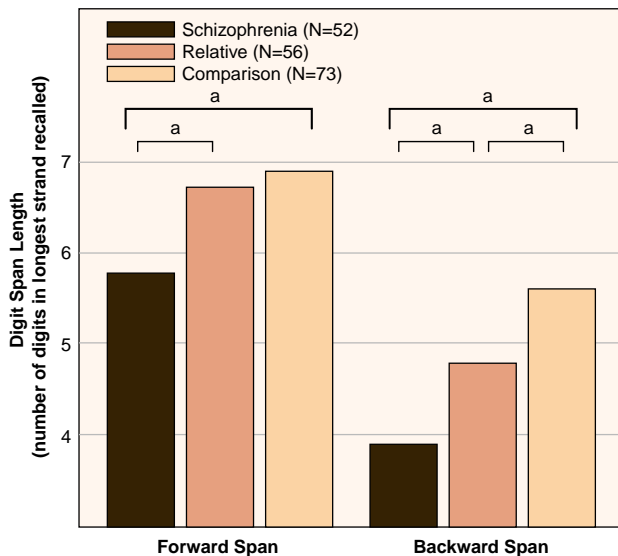
METHOD

Fifty-two schizophrenia inpatients (37 men; mean age=32.1 years, SD=9.1; mean education=12.4 years, SD=2.3) were recruited from

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FIGURE 1. Forward and Backward Digit Span Task Performance of Patients With Schizophrenia, Their First-Degree Relatives, and a Nonpsychiatric Comparison Group



^a Brackets depict significant differences between groups as determined by honestly significant difference post hoc analyses.

acute-care psychiatric units of a regional metropolitan hospital. All patients met DSM-IV criteria for schizophrenia according to the Structured Clinical Interview for DSM-IV (SCID) and chart reviews. The patients were between the ages of 18 and 65, spoke English fluently, were not currently using drugs or alcohol, had not recently undergone ECT treatment, and had no history of neurological disease, systemic disease known to involve CNS functioning, clinically significant head injury, or mental retardation.

Seventy-three nonpsychiatric comparison participants (27 men; mean age=35.7 years, SD=13.2; mean education=15.6 years, SD=2.2) were recruited from the community through advertisement posters placed at several regional hospital clinics and community vocational/technical schools. Comparison participants were excluded for the same general and medical criteria as the schizophrenia patients. They were additionally excluded for any past or present psychiatric or substance dependence disorders, as determined by the SCID, as well as if they reported that a first-degree relative had sought psychiatric treatment.

Fifty-six first-degree relatives of the schizophrenia inpatients (24 men; mean age=42.3 years, SD=13.1; mean education=14.1 years, SD=2.1) participated. They were excluded for the same general and medical criteria as the schizophrenia patients and the nonpsychiatric comparison participants. Diagnostic information was obtained by interview using the SCID. All participants provided written informed consent and were paid for their participation.

All participants were administered the Wechsler Digit Span Task. This test requires the examiner to verbally present digits at a rate of one per second. The forward test requires the participant to repeat the digits verbatim. The backward test requires the participant to repeat the digits in reverse order. The number of digits increases by one until the participant consecutively fails two trials of the same digit span length.

RESULTS

A chi-square analysis that compared the proportion of men and women in each group indicated that the groups were not balanced for gender ($\chi^2=15.19$, $df=2$, $p<0.0005$), with the schizophrenia group being dispropor-

tionately male. Separately computed t tests for each group failed to reveal any significant gender differences in either forward or backward digit span performance. The groups differed significantly in age ($F=9.98$, $df=2$, 178 , $p<0.001$), with post hoc tests (all post hoc tests used Tukey's honestly significant difference, $p<0.05$) indicating that the first-degree relatives were significantly older than both the schizophrenia patients and the nonpsychiatric comparison participants, who did not differ in age. Age was not correlated with performance on either the forward or backward digit span task within any group or when groups were combined. Since neither gender nor age was related to digit span performance in this study, they were not considered as factors in the remaining analyses. Education level differed significantly among the groups ($F=33.18$, $df=2$, 178 , $p<0.0001$), with post hoc tests indicating that the schizophrenia patients had fewer years of education than the first-degree relatives, who, in turn, had fewer years of education than the nonpsychiatric comparison participants. Higher education was associated with better digit span performance ($r=0.44$, $df=179$, $p<0.001$).

Figure 1 shows the mean group differences in performance on the forward and backward digit span tasks, as measured by the number of digits in the longest strand recalled. Since adequate normative data for the forward and backward digit span tasks as separate measures do not exist, the dependent variable used was the number of digits in the longest strand recalled (i.e., digit span length). Analyses were repeated by using Wechsler scoring procedures, assigning one point for each correctly recalled strand; both main effects and post hoc comparisons yielded the same results as digit span length.

There was a significant difference among groups in forward digit span length ($F=15.51$, $df=2$, 178 , $p<0.0001$), with honestly significant difference post hoc tests indicating that schizophrenia patients had a shorter forward digit span length than both the first-degree relatives and the nonpsychiatric comparison participants, who did not differ. There was a significant difference among groups in backward digit span length ($F=25.68$, $df=2$, 178 , $p<0.0001$), with honestly significant difference post hoc tests indicating that schizophrenia patients had a shorter backward digit span length than their first-degree relatives who, in turn, had a shorter backward digit span length than the nonpsychiatric comparison participants. When analyses were repeated, applying the rigorous inclusion criteria of the nonpsychiatric comparison participants to the first-degree relatives (which omitted 18 relatives from the analyses), all findings remained the same.

In order to show that the significant differences among groups in backward digit span performance were not attributable to group differences in education or forward digit span performance, separate analyses of covariance were computed with education and forward digit span performance as covariates. The pattern of significant results was the same as when no covariates were used. Because the observations were not

independent (e.g., some of the first-degree relatives were from the same family), we adjusted the denominator degrees of freedom by replacing the number of individuals with the number of families and recomputed the p values. All of the statistical tests reported remained significant (all p values <0.001).

DISCUSSION

Schizophrenia patients as well as their first-degree relatives showed impairment on the backward digit span task, with both groups differing significantly in performance from nonpsychiatric comparison participants. In contrast, only schizophrenia patients showed impairment on the forward digit span task. These results indicate that the forward and backward digit span tasks tap different cognitive abilities that are differentially associated with the diathesis for schizophrenia. Consistent with current conceptualizations of working memory, performance on the backward digit span task measures verbal working memory by requiring internal manipulation of mnemonic representations of verbal information in the absence of external cues. If we accept forward digit span performance as a measure of general attention, our group comparisons of backward digit span performance, while statistically controlling for performance on the forward digit span task, allowed us to specifically target the performance variance attributable to verbal working memory.

Most important, the nonpsychotic first-degree relatives of the schizophrenia patients exhibited impaired verbal working memory. This finding cannot be attrib-

uted to lower education levels, distractibility due to active psychotic symptoms, or medication effects. Impaired performance on the backward digit span task, a simple measure of verbal working memory, appears to be associated with the diathesis for schizophrenia and may be a valuable indicator of susceptibility for this disorder. Additionally, performance on the backward digit span task may be used as an endophenotypic marker for the schizophrenia genetic diathesis. Coupled with other known endophenotypic markers, such as impaired smooth pursuit eye movements, it may be possible to develop a multivariate high-risk phenotype that could be used to assist genetic linkage analyses (7).

REFERENCES

1. Goldman-Rakic PS, Selemon LD: Functional and anatomical aspects of prefrontal pathology in schizophrenia. *Schizophr Bull* 1997; 23:437-458
2. McDowell JE, Clementz BA: Ocular-motor delayed response task performance among schizophrenia patients. *Neuropsychobiology* 1996; 34:67-71
3. Granholm E, Sarkin AJ, Morris SK, Asarnow RF, Jeste DV: Pupillary responses index overload of working memory resources in schizophrenia. *J Abnorm Psychol* 1997; 3:458-466
4. Stratta P, Daneluzzo E, Prosperini P, Bustini M, Mattei P, Rossi A: Is Wisconsin Card Sorting Test performance related to "working memory" capacity? *Schizophr Res* 1997; 27:11-19
5. Stefansson SB, Jonsdottir TJ: Auditory event-related potentials, auditory digit span, and clinical symptoms in chronic schizophrenic men on neuroleptic medication. *Biol Psychiatry* 1996; 40:19-27
6. Park S, Holzman PS: Schizophrenics show spatial working memory deficits. *Arch Gen Psychiatry* 1992; 49:975-982
7. Iacono WG, Grove WM: Schizophrenia reviewed: toward an integrative genetic model. *Psychol Sci* 1993; 4:273-276