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Working memory and schizophrenia: evidence for slowed encoding

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Abstract

Previous studies have found impairments in working memory in individuals with schizophrenia, but have not identified the underlying information processing deficit. Because schizophrenia is associated with slowed cognitive processing, deficits on working memory tests may be due to decreased speed of encoding rather than an inability to maintain information over time. This hypothesis was examined using a Delayed Match to Sample (DMTS) Test. Task difficulty under 0-delay conditions was equated by individually establishing the stimulus presentation time needed to reach approximately 80% accuracy. Schizophrenia participants required longer presentation durations, but there were no group differences under delay conditions when performance was equated in the 0-delay condition. These results suggest that poor working memory performance in schizophrenia results from slowed encoding processes.

Keywords: Schizophrenia; Working memory; Slowing; Cognition

1. Introduction

Deficits in working memory, the ability to simultaneously hold and manipulate information in a short-term store, are well documented in individuals with schizophrenia (see Keefe, 2000, for a review). Furthermore, working memory impairments appear to represent a marker of the disorder. Deficits have been observed in individuals with residual symptomatology, in their first-order relatives, and in individuals with schizotypal personality characteristics (Park et al., 1995a,b, 1999). In addition, spatial working memory is one of the best discriminators of genetic relatedness in samples of discordant and control twins (Cannon et al., 2000). From a neuroanatomical perspective, working memory deficits have been linked to dysfunction in the structures that form the frontal–striatal and limbic systems (Bilder and Szeszko, 1996; Buchsbaum, 1990), and from a neuropsychological perspective, they may help explain impairments in higher level executive function (Cohen and O'Reilly, 1995; Dehaene and Changeux, 1991; Hartman et al., 2001; Kimberg and Farah, 1993). Thus, an understanding of working memory in schizophrenia holds the promise of explaining a core symptom of this disorder.

Despite the evidence for working memory deficits in schizophrenia, it is not yet known which compo-

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nents of this complex memory system are most impaired. The most widely used conceptualization of working memory, the model developed by Baddeley and collegues, posits separate short-term buffers for verbal and visuospatial information as well as a central executive (Baddeley and Hitch, 1994; see also Cohen and Servan-Schreiber, 1992; Cohen et al., 1999; Goldman-Rakic, 1991; Nuechterlein et al., 1994). The central executive allocates limited attentional resources to carry out a range of functions, such as controlling input to the buffers, inhibiting irrelevant information, coordinating competing cognitive demands, and maintaining or manipulating information held in the buffers.

Studies of working memory in schizophrenia have focused either on global impairments in working memory or on the processes involved in simple storage of information. In the former set of studies, deficits are generally interpreted as evidence for reduced central executive capacity. In the latter, reduced performance is often taken to mean impairments of the verbal and visuospatial buffers, although the tests may also draw on the central executive when the capacity of the buffers is exceeded or when interference is present. With regard to global tests of working memory, the most commonly used tasks are measures of complex span that make simultaneous demands on storage and processing. In most versions of these tasks, test-takers process a series of sentences for comprehension, after which they must recall the last word of each sentence (Daneman and Carpenter, 1980). Working memory capacity is represented by the length of the longest series for which recall is successful. Individuals with schizophrenia are consistently impaired on this type of task (Condray et al., 1996; Morice and Delahunty, 1996; Stone et al., 1998), as well as on other complex working memory tasks such as the Letter–Number Sequencing Test, the *n*-back task, and random generation of digits and letters (Artiges et al., 2000; Carter et al., 1997, 1998; Gold et al., 1997; Huguelet et al., 2000; Salamé et al., 1998). Unfortunately, the complexity of these tasks makes it difficult to identify the specific deficits that lead to poor performance. On the complex span tasks, for example, it is not clear whether the source of difficulty is reduced performance on the individual components of the task, such as simple storage of incoming information and sentence processing, or whether the deficit results from central executive dysfunction affecting the ability to coordinate the various task demands and inhibit irrelevant information. It is equally difficult to tease apart the cognitive components of the other complex working memory tests.

A number of studies have attempted to isolate one component of the central executive by testing whether the coordination of dual tasks is the source of impairment in individuals with schizophrenia. These have produced mixed results. Some studies have shown increased costs in dual-task as compared to single-task conditions for individuals with schizophrenia (Bressi et al., 1996; Cornblatt et al., 1985), but several others have not (Salamé et al., 1998; Spindler et al., 1997). There is no obvious explanation for the conflicting results; indeed, the two studies that controlled for task difficulty of single tasks and used similar types of procedures reached different conclusions (Bressi et al., 1996; Salamé et al., 1998).

Findings regarding simple storage deficits in working memory have been more consistent and perhaps more informative. Span measures using locations, colors, and objects as stimuli have shown deficits in every study in which they have been used (e.g., Salamé et al., 1998; Spindler et al., 1997). A recent meta-analysis of studies using the Digit Span test (Wechsler, 1997) suggests a significant deficit in individuals with schizophrenia with this task as well (Heinrichs and Zakzanis, 1998), although not all studies have shown impairments. The Brown–Peterson task (Brown, 1958; Peterson and Peterson, 1959), which tests for retention of three verbal stimuli after a distraction-filled delay, also shows reduced performance across studies (Fleming et al., 1995; Goldberg et al., 1998; Randolph et al., 1992; Stuss et al., 1982; Weinberger and Cermak, 1973). Thus, a simple storage deficit appears to contribute to at least some of the working memory deficit in this population.

Further investigation of simple storage tasks has focused on delayed response (DR) tasks. These tests were first used by neurobiologists studying models of memory in non-human primates (see Fuster, 1989, for a review). The basic task in these animal studies requires subjects on each trial to remember one of two spatial locations over an unfilled delay period. Research using DR tasks to study schizophrenia has utilized more complex versions of the task for the most part, increasing the number of possible locations, and sometimes introducing distraction-filled delay intervals in order to disrupt mnemonic strategies (Keefe, 2000). Without these modifications, ceiling effects have been observed (Seidman et al., 1995). Research has also been expanded to include tests of working memory for the identity rather than location of a stimulus. In the experiment reported here, we had participants remember colors, and in keeping with the animal literature, we refer to these identity-based DR tasks as Delayed Match to Sample (DMTS) tasks.

DR and DMTS tasks show consistent evidence of a storage deficit in schizophrenia,[1] and shed further light on the nature of this deficit. Storage may be thought of as comprising a minimum of two components: encoding and maintenance. Encoding in working memory is distinct from sensation and perception in that it involves attending to a stimulus, selecting it for entry into working memory, and activating its internal representation. Maintenance in working memory comprises the ability to sustain activation of information in working memory over time and in the face of distraction. Additional retrieval mechanisms may also play a role in storage tasks, although they have not been studied independently of encoding and maintenance in schizophrenia.

Evidence for reduced encoding comes from studies that separate initial encoding from the ability to maintain information once it is in working memory. These studies can be divided into two types, both examining the effects of delay length. One type includes conditions in which memory is tested immediately after the study stimulus is removed; these studies compare the 0-delay condition to delay conditions. The other type compares delays of varying length, for example, comparing 5- to 30-s delay conditions. Most studies of the first group found significant impairment even in the 0-delay condition (Carter et al., 1996; Fleming et al., 1997; Keefe et al., 1995). Exceptions appear due to ceiling effects (Javitt et al., 1997; Snitz et al., 1999). Conditions with a delay between study and test generally revealed increased impairment compared to 0-delay conditions, but in all cases interpretation was problematic because high levels of performance at the 0-delay artificially compressed the group difference in this condition and thus reduced its sensitivity to impairment (Carter et al., 1996; Javitt et al., 1997; Keefe et al., 1995). For studies comparing delays of different lengths, most found no interaction between delay length and group (Javitt et al., 1997; Keefe et al., 1995; McDowell and Clementz, 1996; Park and Holzman, 1992; Ross et al., 2000). When group differences did increase as a function of delay length, again ceiling effects in the easier condition tended to obscure clear interpretation (Snitz et al., 1999). The absence of greater impairments with longer delay intervals suggests that the source of the deficit lies in the encoding of the stimuli, rather than the maintenance of information once it enters working memory.

Additional findings supporting this conclusion demonstrate that poor sensory discrimination and failures to understand the task cannot explain the working memory impairments in schizophrenia. These results come from experimental conditions in which the study stimulus remained present during the entire trial. In these non-memory conditions, there was generally no significant group difference because performance was at ceiling for both schizophrenia and control groups (Park and Holzman, 1992, 1993; Park et al., 1999; Stratta et al., 1999). Two studies in which performance was below ceiling in the non-memory conditions were informative, however. In a task that required participants to detect a change in pitch of a single tone, Javitt et al. (1997) found an impairment. Similarly, Park and Holzman (1992) found a significant group difference in the simultaneous condition when the time between onset and response was long (30 s). Taken together, these findings suggest that while failures to perceive cannot account for impairments in working memory, impairments in identifying sensory input may exist and contribute in some studies to deficits in working memory.

Further evidence for the importance of encoding comes from a consideration of the role of distraction. As noted above, studies have sometimes utilized distraction-filled delay periods, but even with unfilled delays, impairments are consistently found. Furthermore, several studies have directly compared filled and unfilled delay intervals. One of these (Javitt et al.,

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[1] To our knowledge, the only exception is a study by Stevens et al. (1998), who found impairments on a verbal task but not a tonal task. This study involved participants who were pre-selected for intact attention and ability to encode tones, however, raising the possibility that more impaired individuals were excluded.

1997) found similar impairments under both conditions; the other found impairment only with distraction-filled delay (Snitz et al., 1999), but ceiling effects in the unfilled delay condition leave open the possibility that the effect of distraction was similar for individuals with schizophrenia and controls. Thus, at present there is little evidence for greater effects of distracting information in schizophrenia, at least once information has entered working memory.

In summary, the existing literature leads to the conclusion that the working memory deficit in schizophrenia results from reduced encoding of stimuli into working memory. Individuals with schizophrenia appear to have a reduced ability to use information that has been fully perceived to create a stable, internal representation in working memory. Once encoded into working memory, however, they have no more difficulty than healthy individuals in maintaining that information, even in the face of distraction. Nevertheless, this explanation has not been adequately tested in previous studies. It was the goal of the current study to test it directly.

In the study reported here, we predicted that individuals with schizophrenia would show impaired encoding of information into working memory. More specifically, we hypothesized their impairment to be the result of cognitive slowing. The slowing hypothesis is consistent with other results showing slowed information processing in individuals with schizophrenia. For instance, several recent studies have shown that impairments in working memory can be accounted for after statistically controlling for performance on independent measures of speed that do not involve working memory. Thus, reduced articulation rate (Salamé et al., 1998) as well as slowing on Digit Symbol and the color naming portion of the Stroop Color-Word Test (Brebion et al., 1998, 2000) have been linked to deficits on simple span tasks as well as in dual task performance.

In order to provide a strong test of the slowing hypothesis, we first administered a pretest to each participant to determine the amount of study time needed to produce an accuracy rate of approximately 80% in the 0-delay condition. Having thus equated the level of encoding for all participants, we then used the individualized study time on additional DMTS trials administered under two conditions: (1) a 0-delay condition, in which memory was tested immediately, and (2) a 6-s-delay condition, which introduced a distraction task between study and test. This procedure was expected to keep performance below ceiling in both 0-delay and delay conditions, but at the same time allow us to observe possible group differences in forgetting across a delay interval.

The slowing hypothesis predicted that individuals with schizophrenia would need more time to study target information, but would not show additional deficits after a distraction-filled delay. In contrast, if there were a deficit in the maintenance of information, group differences should increase with the introduction of a distraction-filled delay, even if performance were equated under 0-delay conditions.

A secondary goal of this study was to examine the relationship between working memory impairments and other cognitive functions. This relationship was explored in two ways. First, correlations between individual display times for the DMTS task and neuropsychological test performance were examined. The latter covered a range of cognitive functions, including vocabulary, attention, language, visuospatial construction, auditory memory, calculations, reasoning, and executive function. Although no direct measures of processing speed were included, it was our expectation that slowing in working memory would be significantly correlated even with tests that have minimal speed requirements. Second, neuropsychological test performance was compared for subgroups of individuals with schizophrenia who displayed either low and high accuracy on the DMTS pretest with a display time of 2000 ms. A final component of the study examined working memory performance in relationship to behavior characteristics of the schizophrenia group: clinician ratings of maladaptive behavior observed during testing, length of illness, the presence of negative symptoms, and medication type.

2. Methods

2.1. Participants

Participants included individuals with confirmed schizophrenia and a matched healthy control group. All participants were fluent in English as their first language.

2.1.1. Participants with schizophrenia

Participants with schizophrenia were recruited from either an admissions or rehabilitation unit while they were hospitalized at John Umstead Hospital, which is a state psychiatric facility in Butner, NC. They included 16 individuals (4 women and 12 men; 10 White and 6 African American participants), who were initially diagnosed with schizophrenia by the attending psychiatrist. In addition, all participants met DSM-IV (American Psychiatric Association, 1994) criteria for schizophrenia, based on chart review and diagnostic interview using the Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Version (SCID-I/P, Version 2.0; First et al., 1996). A doctoral-level clinical psychologist conducted all diagnostic interviews. Diagnoses included disorganized ($N=3$), paranoid ($N=9$), and undifferentiated ($N=4$) subtypes of schizophrenia.

Participants were excluded for any significant past or present central nervous system disorders (e.g., seizure disorder, cerebral vascular disease), traumatic brain injury, loss of consciousness for 10 min or longer, learning disability, attention deficit/hyperactivity disorders, multiple repeated grades, mental retardation, or dementia. Participants were also excluded if they had a history of behavioral or conduct problems that were not consistent with schizophrenia.

Additional exclusion criteria involved alcohol and other substance use. Those meeting DSM-IV criteria for either current or lifetime alcohol or polysubstance dependence were eliminated from the study. Lifetime abuse/dependence was defined as (1) a period of dependence or abuse lasting 1 year or longer, or (2) more than three episodes of alcohol dependence lasting longer than 6 months within a 5-year period. Other criteria for exclusion included a reported pattern of drinking more than two alcoholic drinks in a 24-h period on three or more days per week. Use of injection drugs, PCP, Ecstasy, or other synthetic agents more than twice over the lifetime was also a criterion for exclusion. Chart review, interviews, and information from area mental health programs that was available in the course of treatment planning revealed that no participants had documented use of illicit substances for at least 3 months prior to testing and that three reported no history of any use.

Screening was also used to rule out significant hearing and vision impairment as well as color blindness. In addition, use of cold or allergy medications within 72 h prior to testing was grounds for exclusion. Finally, any potential participant who had participated in a medication study and/or used experimental psychiatric medications in the last 6 months was removed from the initial participant pool.

All participants except two were receiving neuroleptic treatment at the time of interview and testing. Eight were taking standard psychotropic medications, while six were being treated with atypical anti-psychotic medication. Prescribed psychotropic medications included clozapine ($N=2$), olanzapine ($N=1$), risperdal ($N=3$), haloperidol ($N=3$), fluphenazine (Prolixin) ($N=3$), thiothixene (Navane) ($N=1$), quetiapine (Seroquel) ($N=1$), lithium ($N=1$), fluoxetine (Prozac) ($N=2$), valproic acid (Depakote) ($N=2$), trihexyphenidyl (Artane) ($N=1$), and benztropine (Cogentin) ($N=3$).

The age of onset of schizophrenic symptoms had a mean of 21.4 years (SD = 6.5, range = 14–38), and the average duration of illness was 13.8 years (SD = 10.1 years, range = 2–32). Participants had been hospitalized an average of 4.3 times (SD = 2.2, range = 1–8).

The constellation of deficit symptoms was determined using the Schedule for the Deficit Syndrome (SDS; Kirkpatrick et al., 1989), a measure that quantifies and clusters persistent deficit symptoms in the absence of active psychosis. Participants were almost equally split on this measure (Deficit syndrome = 9, No deficit syndrome = 7).

2.1.2. Control participants

The 16 participants who comprised the control group were recruited from the surrounding community and were paid for their participation (4 women and 12 men; 12 White, 3 African American, and 1 Asian participant). They were screened for lifetime episodes of affective, substance use and all psychotic disorders using the Structured Clinical Interview for DSM-IV Axis I Disorders-Non-Patient Version (SCID-NP, Version 2.0; First et al., 1996). Exclusion criteria included the same general and medical criteria as for the participants with schizophrenia. Exclusion criteria for alcohol use in controls were as follows: (1) heavy drinking or problems controlling alcohol intake in the past 6 months, (2) drinking four or more days per week in the past month, (3) drinking seven or more drinks in a 24-h period in the last month, or (4) intoxication four or more days in the last month. Use of injection drugs, PCP, Ecstasy, or other synthetic agents more than twice over the lifetime was also a criterion for exclusion.

2.1.3. Comparisons of schizophrenia and control participants

Healthy controls were matched with participants with schizophrenia on age, years of education, and gender. Participants with schizophrenia had a mean age of 34.6 years (SD = 11.2, range = 18–53) and an average of 13.4 years of education (SD = 2.1, range = 10–18 years), while healthy controls had a mean age of 31.9 years (SD = 10.9, range = 19–38) and an average of 14.0 years of education (SD = 2.53, range = 10–20 years). There were no statistical differences between groups in either variable.

2.2. Tasks

2.2.1. Delayed Matching to Sample (DMTS)

The DMTS task consisted of a memory task presented on an IBM-clone computer using Micro Experimental Laboratory software (MEL; Schneider, 1988). On each trial, participants had to learn a set of three colors, selected from a set of five (green, dark blue, light blue, red, and magenta). Memory was tested by means of a forced-choice test, in which one of the initially presented target stimuli was presented again along with two foils. Thus, all five possible stimuli appeared on each trial, three as the target stimuli and the other two as foils on the memory test. Participants completed two blocks of 15 trials in the 0-delay condition and two blocks with a 6-s distraction-filled delay between study and test. One block of each was administered at the beginning and again at the end of the testing session. The second block in each condition was included in order to establish the stability of working memory function and to increase the reliability of the results.

The sequence of events for each trial was as follows: A ‘get ready’ signal consisting of three ‘+++’ was presented for 500 ms, followed by a blank screen for 150 ms. The stimuli to be remembered were presented next. They consisted of three colored rectangles 1.4 × 0.7 cm in size, arranged vertically on the screen. The colors were selected pseudo-randomly from the five possible colors so that across trials each color appeared approximately an equal number of times in each position on the screen. The target stimuli remained on the screen for a duration determined individually through pre-testing, which will be described below.

In the 0-delay condition, the memory test followed immediately after a 500-ms blank screen. (The blank screen was inserted because it was found in pilot testing that without it test-takers were not always sure when the study stimuli had switched to the test stimuli.) In the delay condition, the memory test appeared after a 6-s filled delay. In both conditions, the test contained three colored test items, one of which matched a studied color from that trial. The stimuli were again positioned vertically on the screen, and the location of the correct response varied pseudorandomly but was never the same as at the time of study. Participants were required to point to the correct response, and the experimenter recorded the response. There was no time limit for responding, and no feedback about accuracy was given. An inter-trial interval of 1000 ms followed each response. At the end of this interval, the next ‘get-ready’ signal appeared.

The distraction task used during the delay interval comprised a screen filled with 16 pairs of letters, arranged in four columns with four pairs in each column. Each pair consisted of two identical or two different uppercase letters (e.g., GG or PX). Participants were asked to scan down each column starting at the upper left, saying ‘yes’ or ‘no’ aloud for each pair, depending on whether it contained letters that were the same or different, respectively. Instructions stressed the importance of responding accurately to as many pairs as possible before the screen was cleared.

2.2.2. Cognistat (Northern California Neurobehavioral Group, 1995)

The Cognistat is a brief neuropsychological screening measure that identifies moderate to severe neurocognitive deficits in six functional domains: orientation, attention, language, visuospatial construction, auditory memory, calculations, and reasoning.

2.2.3. Peabody Picture Vocabulary Test-R—Form M (PPVT-R; Dunn and Dunn, 1981)

The PPVT-R is a vocabulary test that uses a forced-choice format. For each item, the test-taker must select from four pictures the one that is associated with a word spoken by the examiner. Individuals can make verbal or non-verbal responses; no feedback is given to participants about their responses. The test is scored using individually determined basal and ceiling scores after six of eight consecutive items are missed.

2.2.4. *Wisconsin Card Sorting Test (WCST; Heaton et al., 1993)*

The Wisconsin Card Sorting Test is a measure of concept formation and cognitive flexibility commonly used in schizophrenia research. Participants performed the WCST under two conditions: the standard administration and one with modifications designed to evaluate the role of memory in explaining impairments in individuals with schizophrenia. One deck of 64 cards was used for each condition. The conditions were administered in counterbalanced order, separated by approximately 15 min. Only the results of the standard administration will be discussed here. See Hartman et al. (2000) for further discussion of the modified WCST.

2.2.5. *Clinician Ratings of Test Behavior*

This measure is designed to quantify behavioral observations of the participant's approach to testing. It was developed by two of the authors (MCS, SGS) to record testing behavior for later scrutiny, in many cases by investigators or clinicians who did not gather the data directly. It has been used with over 600 inpatients in clinical settings and in several previous research studies (Silva et al., 1994, 1995, 1999). The measure evaluates the validity of testing results based on six categories of behavior, including arousal, distractibility, confusion, general motivation, fatigue, and psychomotor agitation. Each category of behavior is rated on a 1 to 4 scale, with lower scores indicating more compromised test behavior. Each rating is anchored by means of written descriptions so as to produce independent ratings. In the current study, clinician ratings were based on observations made during formal testing and were made after all testing was finished. All individuals administering tests in this study were trained and monitored for consistency in ratings on this measure by one of the investigators (MCS).

2.3. *Procedure*

All interviewing and testing was conducted in a clinical or research office. After obtaining informed consent, each participant in the schizophrenia group was administered screening and diagnostic instruments. These were followed by completion of the neuropsychological battery within 3 days. Each control participant provided background information, and completed the psychiatric screening (SCID-NP) and neuropsychological testing on the same day. Time to complete testing was approximately 2–3 h, depending on participant efficiency and the need for breaks.

The testing battery was administered in a standardized order for all participants. Testing began with the DMTS. Participants first received practice on the distraction task that was used in the delay condition. Following this practice, a pretest consisting of two to six blocks of 10 0-delay trials each was administered in order to determine the display time needed to reach an accuracy rate of approximately 80%. Based on pilot testing, an initial duration of 2000 ms was used for participants with schizophrenia and 600 ms for control participants. Presentation times were altered after each block depending on the participant's performance. Possible presentation times were selected from a pre-established set of study times, ranging from 67 to 3600 ms. At the end of the pretest, a study time was selected for use on the critical trials. This time represented the shortest study time from the pretest at which the participant achieved 80% accuracy or better. At this point, the first set of critical DMTS trials was administered; these comprised one 15-trial block in the 0-delay condition and one 15-trial block in the 6-s delay condition. Three additional practice trials were given before each block.

Additional testing continued with the Cognistat, followed by the first administration of the WCST. The second set of critical DMTS trials was then administered. It again included one 15-trial block of the 0-delay condition and one 15-trial block of the 6-s delay condition; they were administered using the same study time as in the first set. The PPVT-R and the second WCST administration comprised the last set of tasks. A debriefing explaining the intent of the study was followed by completion of the Clinician Ratings of Test Behavior.

3. Results

Non-directional hypotheses were tested, and the level of significance was set at 0.05 for all analyses

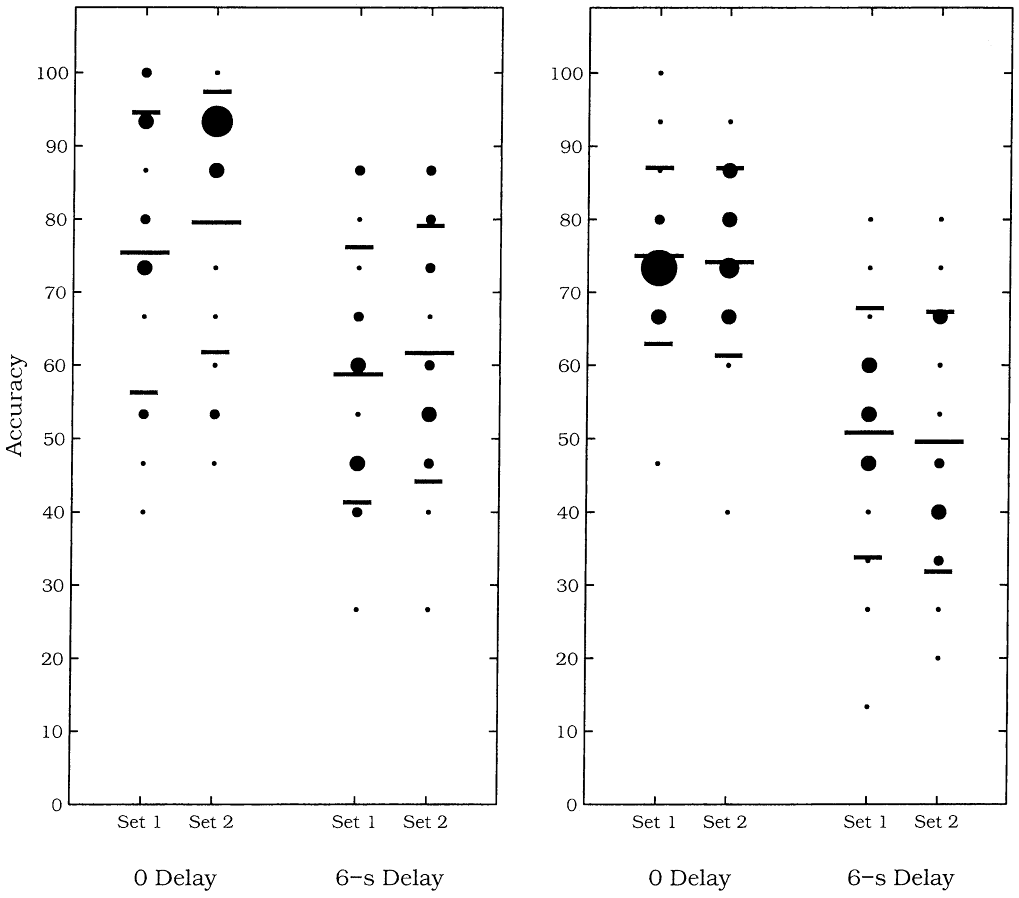

Fig. 1. Accuracy (percentage correct) on the Delayed-Match-to-Sample Test for the schizophrenia (left panel) and control (right panel) groups. Dots represent individual participant data, with the size of the dots reflecting the number of observations at each point. The horizontal lines indicate the mean, plus and minus one standard deviation.

except in the case of multiple comparisons, where the Rom modification of the Bonferroni procedure was used to determine the appropriate *p*-value (Olejnik et al., 1997).

3.1. Delayed Match to Sample (DMTS)

The pretest resulted in the selection of significantly slower study times for individuals with schizophrenia compared with control participants [M (SD) = 2163 (457) ms vs. 421 (473) ms, $t(30) = 10.58$, $p < 0001$]. The schizophrenia group required approximately a fivefold increase over controls in the amount of time needed to effectively encode stimuli into working memory.

Accuracy on the DMTS test was measured in terms of the percentage of correct responses in each condition (see Fig. 1). Under 0-delay conditions, accuracy was approximately 76%, and was reduced to approximately 55% under delay conditions. This level of performance was significantly greater than chance (i.e., 33%).[2] Analysis of DMTS test performance was carried out by means of a three-way ANOVA, with group as a between-subjects variable and set (first

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[2] When data analysis was conducted without the participants whose performance was at or close to chance (two participants in the control group and four in the schizophrenia group), the pattern of results was identical.

vs. second) and delay length (0 vs. 6-s) as within-subjects variables. Results indicated a significant effect of delay, with both groups showing lower accuracy under delay conditions, $F(1, 30) = 57.70$, $p < 0.0001$. No effects involving group or set even approached significance ($ps > 0.10$). Thus, performance remained stable across two administrations of the test. More importantly, individuals with schizophrenia had no difficulty in maintaining information in working memory if they were given enough time to encode it.

In order to determine whether this conclusion held even for the most impaired individuals, we conducted additional analyses with the schizophrenia group divided into two subgroups based on performance during the 0-delay pretest. A high-accuracy ($n = 7$) and a low-accuracy group ($n = 9$) were created using a median split based on the average accuracy at the 2000 ms study time (see Table 1). All participants with schizophrenia received at least one block of trials with this study time. A *t*-test comparison confirmed the difference in accuracy between these two groups in the pretest [$t(14) = 3.79$, $p = 0.002$; M(SD) = 92.4% (2.5) vs. 70.0% (15.4)]. Analysis of DMTS test critical trials was then conducted with subgroup as a between-subjects variable (high-accuracy vs. low-accuracy schizophrenia), and set and delay length as within-subjects variables. This ANOVA revealed significant effects of subgroup, $F(1, 14) = 9.23$, $p = 0.009$, and delay, $F(1, 14) = 17.01$, $p = 0.001$. Of greater importance, there was no interaction between group and delay length ($F < 1$), showing that even for the lowest-performing individuals, the rate of information loss during the distraction-filled delay was similar to that of higher performing individuals.

Table 1
Accuracy (percentage correct) on the Delayed-Match-to-Sample Test for high and low accuracy schizophrenia subgroups

Group	0-delay		6-s delay	
	Set 1	Set 2	Set 1	Set 2
High accuracy				
M	81.9	91.4	70.5	69.5
SD	12.0	8.4	15.8	14.8
Low accuracy				
M	70.4	70.4	49.6	55.6
SD	22.6	18.0	13.0	17.6

3.2. Neuropsychological test performance and its relationship to the DMTS task

On the Cognistat, 9 of the 16 individuals with schizophrenia were impaired on at least one subtest, with six of these scoring in the moderately impaired range. In contrast, there were only three control participants with scores in the impaired range; all of the impairments in this group were in the mild range. Statistical analysis showed significant impairments in the schizophrenia group on three of the subtests: Constructional Ability, $t(30) = 2.07$, $p = 0.047$, Similarities, $t(30) = 2.48$, $p = 0.02$, and Judgment, $t(30) = 2.34$, $p = 0.03$, with a trend towards reduced performance on the Memory subtest ($p < 10$) (see Table 2). With *p*-values corrected for multiple comparisons, the *t*-test for Similarities remained significant; the *t*-test for Judgment just missed significance. There were no significant group differences for Orientation, Attention, Comprehension, Repetition, Naming, and Calculation ability.

On the PPVT-R, individuals with schizophrenia had reduced vocabulary scores, $t(30) = 3.27$, $p = 0.003$ [M(SD) standard scores = 90.9 (16.1) vs. 112.1 (20.2)]. On the WCST, they completed fewer categories [M(SD) = 2.4 (2.0) vs. 4.1 (1.5), $t(30) = 2.67$, $p = 0.01$], made more non-perseverative errors [M(SD) = 11.1 (7.7) vs. 5.8 (5.0), $t(30) = 2.34$, $p = 0.03$], and showed a trend towards making more perseverative errors [M(SD) = 11.8 (8.9) vs. 7.1 (3.7), $p < 0.07$]. The overall pattern of neuropsychological test results indicates impairments among individuals with schizophrenia in executive function and conceptual abilities, as well as in vocabulary.

Cognistat test scores also showed significant Pearson correlations with slowing on the DMTS test. Three of the Cognistat subtests were significantly and negatively correlated with the amount of study time needed for encoding on the DMTS test: Memory ($r = -0.38$, $p = 0.03$), Constructional Ability ($r = -0.44$, $p = 0.01$), and Similarities ($r = -0.40$, $p = 0.02$). There was a near significant trend for Orientation as well ($r = -0.50$, $p = 0.06$). When *p*-values were corrected for multiple comparisons, the correlation with Memory was no longer significant. Study time was also related to PPVT-R scores ($r = -0.56$, $p = 0.001$) and to WCST performance (categories: $r = -0.54$, $p = 0.001$; perseverative errors: $r = 0.56$, $p = 0.0008$;

Table 2
Performance on the Cognistat

	Schizophrenia	Control
Orientation		
M	11.4	11.9
SD	1.1	0.3
Memory[a]		
M	10.6	11.6
SD	1.9	0.9
Attention		
M	7.8	7.9
SD	1.0	0.3
Comprehension		
M	6.0	6.0
SD	0.0	0.0
Repetition		
M	11.9	12.0
SD	0.3	0
Naming		
M	7.7	7.9
SD	0.6	0.3
Constructional ability[b]		
M	4.7	5.4
SD	1.2	0.8
Calculations		
M	3.7	3.8
SD	0.8	0.5
Reasoning: similarities[b]		
M	6.1	7.5
SD	2.0	0.9
Reasoning: judgment[b]		
M	4.3	5.3
SD	1.4	0.9

Higher scores indicate better performance.

[a] $p < 0.10$.

[b] $p < 0.05$.

non-perseverative errors: $r = 0.45$, $p = 0.009$). Thus, slowing of working memory encoding was related to impairments in a range of other cognitive functions, including executive function and visuospatial ability.

Accuracy on the DMTS task was also associated with impaired neuropsychological test performance. This was demonstrated by analyses of neuropsychological test results conducted with the schizophrenia group divided as before into high and low accuracy subgroups. In these ANOVAs, subgroup (high-accuracy vs. low-accuracy schizophrenia) was a between-subjects variable. There were no reliable subgroup differences on the Cognistat, except for Naming [M(SD) = 7.4 (0.7) vs. 8.0 (0.0), $F(1, 14) = 4.89$, $p = 0.046$]. However, the low-accuracy subgroup performed significantly more poorly than the high-accuracy subgroup on the PPVT-R [M(SD) = 82.3 (13.8) vs. 102.0 (11.8), $F(1, 14) = 9.02$, $p = 0.001$], and achieved fewer categories [M(SD) = 1.6 (1.7) vs. 3.6 (1.8), $F(1, 14) = 5.10$, $p = 0.04$] and made more non-perseverative errors [M(SD) = 14.6 (7.8) vs. 6.7 (5.3), $F(1, 14) = 5.17$, $p = 0.04$] on the WCST. There was a trend towards more perseverative errors on the WCST [M(SD) = 15.1 (9.9) vs. 7.4 (5.2), $p = 0.09$].

3.3. Relationship of DMTS slowing to participant characteristics

Clinician ratings of observable test-taking behavior are reported in Table 3. Mean ratings for the schizophrenia group ranged from 3.3 to 3.8, indicating a mild level of behavioral dysfunction, as would be expected in a group of individuals willing and able to complete a full testing session. Differences between individuals with schizophrenia and controls were first examined by means of a MANOVA, which indicated an overall effect of group, $F(6, 25) = 5.44$, $p = 0.001$. Follow-up ANOVAs showed that the schizophrenia group had lower scores on all ratings except Motivation. Thus, individuals with schizophrenia were less alert, $F(1, 30) = 9.30$, $p = 0.005$, more distractible, $F(1, 30) = 4.31$, $p = 0.047$, and more confused, $F(1, 30) = 15.00$, $p = 0.0005$. They also showed more fatigue, $F(1, 30) = 12.0$, $p = 0.002$, and agitation, $F(1, 30) = 7.74$, $p = 0.009$.

Spearman correlations examining the relationship between the clinician ratings and DMTS test performance were calculated using the total of all ratings and stimulus presentation times for the DMTS test. Compromised behavior in the testing session was significantly correlated with longer study times for the DMTS test ($r_S = -0.76$, $p < 0.0001$). The correlations were significant for each of the six individual ratings as well (r_Ss: -0.38 to -0.52). After correcting for multiple comparisons, Motivation and Dis-

Table 3
Clinician Ratings of Test Behavior

	Schizophrenia	Control
Total[a]		
M	21.4	23.9
SD	1.8	0.3
Arousal/Alertness[a]		
M	3.5	3.9
SD	0.5	0.3
Distractibility[a]		
M	3.7	4.0
SD	0.6	0.0
Confusion/Comprehension of instructions[a]		
M	3.5	4.0
SD	0.5	0.0
Motivation		
M	3.8	3.9
SD	0.4	0.3
Fatigue from testing[a]		
M	3.3	4.0
SD	0.8	0.0
Psychomotor agitation[a]		
M	3.6	4.0
SD	0.6	0.0

Clinician Ratings are made on a 1–4 scale, with lower scores indicating behavioral dysfunction.

[a] $p < 0.05$.

tractibility were no longer significant, however. An ANOVA was also conducted on the total clinician ratings with the schizophrenia group divided into high and low accuracy subgroups. Results showed a significant effect of subgroup, $F(1,\ 14) = 5.38$, $p = 0.04$, with significantly more abnormal test behavior in the low-accuracy group [M(SD) = 20.6 (1.7) vs. 22.4 (1.4)].

Examination of characteristics of schizophrenia in relation to test performance indicated a near significant difference in chronicity for individuals in the low vs. high-accuracy subgroups. [M(SD) = 17.9 (10.9) vs. 8.4 (6.2) years, $p = 0.06$], but no correlation between chronicity and DMTS study times. A Chi-square test used to examine the relationship between type of psychotropic medications (typical vs. atypical neuroleptics) and accuracy on the DMTS showed no significant association between these variables. In addition, there was no correlation between DMTS study times and medication type. Similar null results were obtained in tests of the hypothesis that the deficit syndrome would be associated with differences in DMTS performance.

4. Discussion

Results of the current study revealed a number of noteworthy findings. First, individuals with schizophrenia showed slowed encoding of stimuli into working memory. They required approximately five times as much time to view the stimuli in order to reach the same level of performance as controls in a 0-delay condition of the DMTS task. Although not all previous studies have reported impairments under 0-delay conditions, several have (Javitt et al., 1997; Park and Holzman, 1992). Those that did not find an impairment for the most part had near perfect performance for both schizophrenia and control subjects. Although high performance under 0-delay conditions in earlier studies ensured that the schizophrenia group was able to perform non-memory components of the task, the presence of ceiling effects may have masked deficits in encoding. In the current study, we avoided ceiling effects and demonstrated a significant impairment in the schizophrenia group in the ability to encode information into working memory.

Our results also demonstrated that after equating for differences in encoding speed, individuals with schizophrenia showed no greater loss of information over a 6-s, distraction-filled delay than controls. Both groups performed more poorly after the delay, but the drop in accuracy was similar for both groups. It is unlikely that insufficient statistical power accounted for the lack of impairment, given that control participants showed slightly greater loss of information than participants with schizophrenia (24% vs. 17%). In addition, intact maintenance of information in working memory was observed even for the schizophrenia subgroup who performed most poorly on the 0-delay condition of the task. Thus, working memory deficits among individuals with schizophrenia cannot be explained by an inability to maintain information over time. They also cannot be attributed to greater susceptibility to distraction once information is in working memory. Together, the pattern of results points to a deficit in encoding into working memory.

Working memory deficits in the schizophrenia group were observed in the context of additional cognitive impairments. In addition to slowed encoding, these individuals showed reduced functioning in a number of domains: executive functions such as concept formation and cognitive flexibility, as well as vocabulary and reasoning ability. Although the specific measures that correlated with measures of speed and accuracy of DMTS performance differed to a certain extent, executive function was consistently related to both aspects of working memory. This finding is consistent with previous results in the schizophrenia literature. For instance, Snitz et al. (1999) also found that performance on a DR task was correlated with the category score on the WCST, and other studies have reached the same conclusions with other measures of working memory and executive function (e.g., Gold et al., 1997; Huguelet et al., 2000; Randolph et al., 1992). Our findings raise the possibility that inefficient encoding into working memory may also underlie impairments in executive function in individuals with schizophrenia.

In addition to its relation to executive function, working memory was also associated in the current study with observable dysfunctional behaviors: greater distractibility, confusion, fatigue, and agitation, as well as reduced alertness and motivation. These ratings probably reflect both the attentional impairments seen specifically in schizophrenia, as well as more general impairments associated with severe psychiatric disorders. Working memory was more strongly related to these measures of behavioral disturbance than to measures of negative symptomatology, type of medication, or length of illness.

In summary, the current study has localized the working memory impairment in schizophrenia to the encoding of information, and suggests that the mechanism involved is a reduction in the speed of creating a stable representation in working memory. Although we have no direct evidence, we hypothesize that the impairment observed here reflects generalized slowing. If so, one would expect a significant relationship between working memory encoding speed and other measures of cognitive processing speed. This prediction remains to be tested in the future. Nevertheless, it is consistent with results of a number of studies showing that slowed information processing can account for deficits in a range of higher level cognitive functions in schizophrenia (Brebion et al., 1998, 2000; Salamé et al., 1998). Previous studies have reached this conclusion using a correlational approach, by demonstrating that statistical control of group differences in cognitive processing speed can account for the deficits in working memory, executive function, and memory. In contrast, the current study used an experimental approach, showing that equating group differences in encoding speed eliminates other differences in working memory.

Although the hypothesis of slowed encoding is consistent with our findings and with previous research, other possible explanations must be considered. One candidate explanation is slowed perceptual processing. Indeed, the literature on sensory-perceptual abilities shows significant deficits in the early stages of stimulus identification among individuals with schizophrenia (Asarnow and MacCrimmon, 1981; Braff, 1989; Buchanan et al., 1997; Green and Walker, 1984; Green et al., 1994; Nuechterlein et al., 1994; O'Donnell et al., 1996). Another alternative explanation involves impairments of attention. For instance, there is evidence for impairments in the ability to orient to the onset of a stimulus among individuals with schizophrenia (Öhman et al., 1986). Nevertheless, the large amount of extra study time needed by the schizophrenia group in the current study suggests impairments beyond inefficient identification of the stimuli or poor orienting. It would be useful in future research, however, to have independent measures of perceptual speed and orienting deficits in order to separate their contributions from the effects of impaired working memory encoding.

A final possible explanation of slowing on the DMTS is an impairment in interference control. Other researchers have found increased interference from recent but irrelevant stimuli with other tasks. For instance, individuals with schizophrenia often show increased proactive interference with the Brown–Peterson paradigm (Fleming et al., 1995; Goldberg et al., 1998; Weinberger and Cermak, 1973). Nevertheless, Randolph et al. (1992) have shown that proactive interference can be predicted from first trial performance, suggesting that it is the consequence rather than cause of poor performance on tasks with multiple test trials. Interference as an explanation is also inconsistent with some findings in the literature showing that individuals with schizophrenia are unimpaired in their ability to coordinate dual tasks (Salamé et al., 1998; Spindler et al., 1997). It is also incompatible with the finding in the current study that distraction during the delay interval did not differentially impact individuals with schizophrenia. Thus, explanations other than slowed encoding seem insufficient to account for the impairments observed on the DMTS task.

5. Conclusions

The pattern of results in this study supports the hypothesis that working memory impairments in individuals with schizophrenia result from slowed encoding. The current findings also suggest that impaired encoding may be a factor in reduced executive function and observable behavior disturbance. Furthermore, although these individuals are likely to be slower to perceive stimuli and to have attention deficits, these impairments appear inadequate as accounts of their working memory impairments. Future research will be necessary to corroborate these conclusions, of course. In addition, our results regarding the relationship between slowing and psychiatric variables such as symptom constellation need additional investigation. In particular, the small sample size of the current study precluded strong conclusions regarding the relationship of working memory to negative symptoms. A number of previous studies have shown an association of negative symptoms with greater degrees of working memory impairment (Carter et al., 1996; Park et al., 1999). One study of working memory also found a significant relationship with the positive symptom of formal thought disorder (Spitzer, 1993) and another reported a trend towards an association with positive symptoms (Park et al., 1999). Thus, future studies may benefit from more extensive analysis of both positive and negative symptoms in relation to slowing in working memory. Similarly, our finding that individuals with longer histories of illness demonstrated more impaired working memory suggests the need for additional work on the course of schizophrenia with respect to slowed encoding in working memory.

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