Working Memory Consolidation Is Abnormally Slow in Schizophrenia

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This study reports evidence that patients with schizophrenia demonstrate a slowing of working memory (WM) consolidation, which is the process of transforming transient perceptual representations into durable WM representations. Sixteen schizophrenia patients and 16 healthy control participants performed a task measuring the visual WM consolidation rate in a change-detection paradigm. A target display containing 3 colored squares was followed by a variable delay of 17–483 ms, a pattern mask, and then a test stimulus. This pattern mask does not interfere with perception but disrupts WM consolidation. Control participants reached no-mask performance by 250 ms, indicating completed WM consolidation, whereas patients failed to reach no-mask performance by 483 ms. Slowed consolidation may play an important and largely unrecognized role in schizophrenia.

Keywords: working memory, schizophrenia, change-detection paradigm, cognitive impairments, cognitive performance

Cognitive impairments are important correlates of functional outcome in schizophrenia (Green, 1996). Of these impairments, working memory (WM) has been the focus of extensive research effort because it plays a central role in virtually every domain of cognition, including reasoning, language comprehension, and cognitive control (Miyake & Shah, 1999). Therefore, an impairment of WM in schizophrenia would be expected to have a significant negative impact on many different aspects of cognitive performance, an inference supported in the schizophrenia literature by evidence that the extent of WM impairment is related to deficits in problem solving (Gold, Carpenter, Randolph, Goldberg, & Weinberger, 1997), language comprehension (Condray, Steinhauer, van Kammen, & Kasparek, 1996), and planning (Hutton et al., 1998). Further, WM impairments have also been related to some of the symptomatic manifestations of the illness, including negative symptoms (Carter et al., 1996) as well as disorganization (Daban et al., 2003; Perlstein, Carter, Noll, & Cohen, 2001). Thus, there is converging evidence that WM impairment may play a critical role in mediating some of the cognitive and symptomatic disturbances of the illness.

However, given that WM paradigms involve at least three phases—target encoding, target maintenance, and response selection—it is not clear which specific cognitive processes are responsible for the performance deficits observed in schizophrenia. It is possible, however, to narrow the search from a consideration of the accumulated literature. First, impairments have been documented on visual, auditory, and haptic stimuli, suggesting some form of amodal impairment (Coleman et al., 2002; Fleming et al., 1997; Fleming, Goldberg, Gold, & Weinberger, 1995; Javitt, Strous, Grochowski, Ritter, & Cowan, 1997; Park & Holzman, 1992; Tek et al., 2002). Second, it appears unlikely that a deficit in WM maintenance processes is the major or sole locus of impairment because deficits are typically found on the shortest interval tested (see, e.g., Tek et al., 2002, with impairments at 250 ms), and there is inconsistent evidence across studies that increasing the delay substantially magnifies the patient impairment relative to control participants (Javitt et al., 1997; Lencz et al., 2003; Tek et al., 2002). These findings do not rule out a WM maintenance deficit but instead suggest that it is difficult to explain the entire schizophrenia WM deficit on the basis of a maintenance deficit alone. Third, limitations in storage capacity also have difficulty accounting for the literature because patients are impaired with target arrays including only a single item (Park & Holzman, 1992), a storage demand that is not plausibly beyond capacity (see also Gold, Wilk, McMahon, Buchanan, & Luck, 2003). Similarly, a deficit limited to retrieval-related operations is unlikely given that deficits have been observed using two alternative forced-choice response formats (Sullivan, Shear, Zipursky, Sagar, & Pfefferbaum, 1997), which make minimal demand on strategic retrieval operations.

Given that the schizophrenia WM deficit cannot be fully explained by impairments in maintenance, storage capacity, or re-
sponse selection, this leaves impairments of encoding processes as a likely candidate. Two stages of encoding can be distinguished. First, the raw sensory input must be transformed into a coherent perceptual representation; we refer to this variety of encoding as perceptual analysis. Second, because perceptual representations decay rapidly and may be overwritten by new sensory inputs, the transient perceptual representation of an object must be transformed into a durable WM representation that can be maintained over time. This variety of encoding is often called short-term consolidation to make an analogy with the consolidation of representations in long-term memory (Jolicoeur & Dell’Acqua, 1998). This process has also been called vulcanization to make an analogy with the process used to make raw rubber more durable (Vogel, Woodman, & Luck, in press), and it is this process that is the focus of the current study.

Several studies have suggested that impairments at the initial stage of encoding—perceptual analysis—may contribute to WM impairments in schizophrenia (Javitt et al., 1997; Knight, Elliott, & Freedman, 1985; O’Donnell et al., 1996). Although patient WM performance may be degraded with perceptually challenging stimuli, impaired performance has also been observed with very simple, highly discriminable targets such as a single spatial location presented on an uncluttered display (Park & Holzman, 1992) or an array of colored rectangles (Gold et al., 2003). In addition, the temporal dynamics of perceptual analysis may be functionally slowed in schizophrenia, as documented in the substantial literature examining visual backward masking. Multiple studies have demonstrated that patients remain vulnerable to masks far longer than control participants, possibly implicating a dysfunctional interaction between transient and sustained pathways in early visual processing (Cadenhead, Serper, & Braff, 1998; Green, Nuechterlein, Breitmeyer, & Mintz, 1999; Green, Nuechterlein, & Mintz, 1994a, 1994b; Rund, 1993). Thus, it is possible that impairments in the precision or temporal dynamics of perceptual analysis contribute to WM deficits in schizophrenia, but it is unlikely that impaired perceptual analysis can account for deficits documented using highly discriminable stimuli presented without any masks.

There is also suggestive evidence of slowing of postperceptual processing in schizophrenia, as shown by Knight and colleagues (Knight et al., 1985), using masking tasks and in four recent studies using rapid serial visual presentation (RSVP) techniques. Two studies used variants of the attentional blink paradigm, in which a series of 15–20 letters are presented rapidly one at a time at fixation and participants must identify two targets. Although participants accurately identify the first target, the second target is often missed, especially if it follows the first target by 200–400 ms (Chun & Potter, 1995; Raymonds, Shapiro, & Arnell, 1992). It is thought that the encoding and transfer of the first target into WM inhibits or postpones consolidation of the second target, leaving the second target vulnerable to being overwritten by the next item in the stream (Giesbrecht & Di Lollo, 1998). There is compelling behavioral and electrophysiological evidence that participants form an accurate perceptual representation of the second target even though they cannot accurately report it, suggesting that the attentional blink is not simply a new form of perceptual-level masking but instead implicates WM consolidation processing (Luck, Vogel, & Shapiro, 1996; Vogel & Luck, 2002; Vogel, Luck, & Shapiro, 1998). Two studies have shown that patients with schizophrenia have a more severe and prolonged attentional blink compared with healthy participants, (Cheung, Chen, Chen, Woo, & Yee, 2002; Li et al., 2002), and two additional RSVP studies have shown that patients with schizophrenia remain vulnerable to interference for a longer duration than control participants, suggesting a slowing of WM consolidation (Gagnon, Everett, LaJeunesse, Gosselin, & Lavoie, 2000; Park & Hooker, 1998). However, RSVP paradigms are not optimal for examining WM consolidation because many processes contribute to the “blink,” processes that may also be impaired in schizophrenia, such as the requirement to carry out two simultaneous tasks (remembering one target and preparing a response while searching for another target). Thus, the evidence from attentional blink paradigms can only be considered as suggestive evidence of slowed or incomplete consolidation in patients with schizophrenia.

The present study used a paradigm (described below) that was recently developed by Vogel et al. (in press) to measure the rate at which perceptual representations are consolidated into more durable WM representations. We hypothesized that patients with schizophrenia would demonstrate a slowing of WM consolidation. In addition, the resulting WM representations may be abnormally fragile, making them prone to disruption by subsequent distracting stimuli and internal noise. Thus, a deficit in consolidation may provide an integrative account of many of the impairments documented in the schizophrenia WM literature.

Method

Participants

Sixteen patients meeting Diagnostic and Statistical Manual of Mental Disorders (4th ed., DSM-IV; American Psychiatric Association, 1994) criteria for schizophrenia (12 undifferentiated and 4 paranoid subtype), and 16 healthy control participants participated in the study. Diagnosis was established for each patient using a best estimate approach combining information from past medical records, collateral informants (when available), and the results of a Structured Clinical Interview for DSM–IV diagnosis. Diagnosis was established at a consensus conference involving clinical staff who worked with the patient, chaired by a senior research psychiatrist, or by one of the present authors (J.M.G.). The patients were clinically stable outpatients: 12 were receiving new generation antipsychotics, 2 were receiving traditional antipsychotics, and 2 were receiving both. All patients had been receiving the same medication, at the same dose, for at least 8 weeks prior to study participation. A total of 16 healthy control participants were recruited from the community through newspaper advertisements, wall notices, and word of mouth. All control participants were screened using the complete Structured Clinical Interview for DSM–IV Axis I Disorders (SCID–I; First, Spitzer, Miriam, & Williams, 1997a) and the Structured Clinical Interview for DSM–IV Axis II Personality Disorders (SCID–II; First, Spitzer, Miriam, & Williams, 1997b). All control participants were free of a current or past history of major psychiatric illness and denied a family history of psychotic disorders in first-degree relatives. All participants (patients and control participants) were free of other medical or neurologic comorbidity that might interfere with test performance, including substance abuse or dependence within the last 12 months. All participants were between the ages of 18 and 55 years of age.

Demographic features are shown in Table 1. Although the two groups differed on years of education and Wide Range Achievement Test (WRAT; Wilkinson, 1993) scores, they did not differ on fathers’ years of education...
or on any other demographic variables. The patient group’s RBANS (Repeatable Battery for the Assessment of Neuropsychological Status) score was 72.25. This is slightly above the mean RBANS score of 70.54 (SD = 14.80) based on 575 schizophrenia cases drawn from the Maryland Psychiatric Research Center (University of Maryland School of Medicine) and two Maryland private psychiatric hospitals (Wilk et al., 2004). Thus, the group of patients with schizophrenia in this study can be viewed as representative of a larger schizophrenia sample.

**Task Overview**

In this experiment, participants performed a change-detection task, as illustrated in Figure 1. On each trial, participants were presented with a target array containing three colored squares that were followed, after a brief delay, by a test array. The task was to indicate whether the target and test arrays were identical or differed in the color of one item. On unmasked trials, the delay interval between target and test arrays was unfilled, providing plenty of time for consolidation of the target array. On masked trials, an array of pattern masks was presented at varying intervals following the offset of the target array. The stimuli and timing parameters were designed to avoid perceptual masking. Specifically, the stimuli were simple and highly discriminable, and at least 117 ms of uninterrupted processing time was available before mask onset.

In a nearly identical paradigm, Vogel et al. (in press) found that accuracy was highly impaired when the mask array appeared shortly after the target array but that performance gradually recovered as the mask was delayed. The size and duration of the masking effect was large for arrays of four objects and became progressively smaller as the number of objects decreased, with no masking effect for single-object arrays. This pattern indicates that the consolidation process makes use of a limited-capacity resource, and there is some evidence that this resource is modality non-specific (Jolicoeur, 1999).

Vogel et al. (in press) also used a perceptual control condition to demonstrate that the masks did not interfere with the perception of the

<table>
<thead>
<tr>
<th>Demographic features</th>
<th>Control group</th>
<th>Patients</th>
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<tbody>
<tr>
<td>Age</td>
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<td>40.4, 6.4</td>
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<tr>
<td></td>
<td>t = 0.32</td>
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<td></td>
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<td>Years of education</td>
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<td>12.7, 2.1</td>
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<tr>
<td></td>
<td>t = 2.87</td>
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<td></td>
<td>df = 30</td>
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<td>Father’s years of education</td>
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<td>14.3, 3.6*</td>
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<td></td>
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</tr>
<tr>
<td></td>
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<tr>
<td>Left:Right (hand)</td>
<td>1:15</td>
<td>2:14</td>
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<tr>
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<td>χ² = 0.001</td>
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<td>WRAT</td>
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<td></td>
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<td>25</td>
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<td></td>
<td>df = 25</td>
<td>p &lt; .05</td>
</tr>
</tbody>
</table>

*Note.* AA = African American; A = Asian; H = Hispanic; W = White; WRAT = Wide Range Achievement Test.

a Data are missing for 3 control participants. b Data are missing for 4 patients. c Data are missing for 5 control participants.

**Table 1**

**Demographic Features of Sample**

![Figure 1](image-url)  
*Figure 1.* The stimuli for the working memory condition. There were 120 mask trials—24 at each interval—and 24 no-mask trials.
target array, and the present study also includes this control condition (described below). Once perceptual masking is ruled out, this experimental paradigm provides a relatively pure means of assessing WM consolidation (see the Discussion section for more details).

**Stimuli**

The stimuli were presented within a 9.8° × 7.3° region on a computer monitor with a gray background viewed from a distance of 70 cm. Each WM target array consisted of three colored squares that were placed randomly in this region with the constraint that the squares were separated from each other and from the central fixation cross by at least 2° (center to center). Each square subtended 0.65° × 0.65° of visual angle, and the color of each square was randomly selected without replacement from a set of seven highly discriminable colors: red, white, black, blue, green, pink, and yellow. The test array was identical to the target array, except that on 50% of trials one square changed to a new color that had not been present at any location in the target array. Each mask consisted of four colored squares, each of which subtended 0.65° × 0.65° of visual angle, joined to make a larger square centered over the location where the target square had been. The four colors were chosen randomly without replacement from the same set of colors used for the memory stimuli with the constraint that the mask did not contain the color used for the target square or the test square presented at a given location.

**Procedure**

After giving informed consent, all participants performed the WM and perceptual control conditions during a single experimental session that lasted approximately 35 min. The perceptual control condition was administered first, followed by the WM condition.

**WM condition.** The WM condition is illustrated in Figure 1. A fixation cross appeared in the center of the screen at the beginning of each trial and remained visible throughout the trial. After a delay of 2,000 ms, a target array consisting of three colored squares was presented for 100 ms. Following a variable delay of 17, 133, 250, 367, or 483 ms during which only the fixation cross was visible, an array of three masks appeared for 100 ms, with one mask at each location of the preceding target array. Note that, although the interstimulus interval (ISI) delay ranged from 17–483 ms, the stimulus onset asynchrony (SOA) between the target array and the pattern mask ranged from 117–583 ms. The test array appeared 1,000 ms after the offset of the target array; the delay between mask offset and target array onset therefore depended on the SOA between the target array and the mask (see Figure 1). The test array remained visible for 3,000 ms, during which time the response was collected. On 50% of the trials, the test array was identical to the target array; on 50% of the trials, the color of one square was different in the test array than in the target array. Participants indicated whether the two displays were the same or different by pressing one of two labeled buttons on a response box. Task directions explicitly emphasized response accuracy with no mention of response speed. There were 120 mask trials in the WM condition, that is, 24 at each interval, equally distributed and randomly presented in 2 blocks of 60 trials.

The 24 no-mask trials were identical to the mask trials, except that the masks were not presented (the interval between target array offset and test array onset remained 1,000 ms, allowing for 1 s of uninterrupted consolidation and maintenance time). They were administered first so that the participants would not mistake the test array for a mask array.

The current study differs from the original Vogel et al. (in press) study in one significant way. The participants in the Vogel et al. study performed a simultaneous verbal distractor task to block rehearsal. This method was not used in the current study because we were concerned that patients might have difficulty performing two concurrent tasks or might adopt a different strategy than control participants on how to meet this demand, thereby introducing a potential confound in the interpretation of the WM condition. In addition, allowing verbal encoding does not have a substantial impact on performance in this type of task (Vogel, Woodman, & Luck, 2001).

**Perceptual control condition.** The perceptual control condition is illustrated in Figure 2. This condition was designed to have the same perceptual requirements as the WM condition but did not require WM consolidation. Specifically, a target stimulus was shown at the beginning of the trial, and the participants determined whether this target stimulus was...
present in the target array. The target array was masked, just as in the WM condition, so any effect of masking on perception should impair performance in the control condition. Vogel et al. (in press) found no effect of the masks on performance in this condition using healthy young adult observers, but some effect might be expected at the shortest masking interval in the present study given the different population of participants.

Each trial in this condition began with a 2,000-ms fixation period, followed by the presentation of a colored square in the center of the screen for 1,000 ms to indicate the target color for that trial. This was followed by a 1,000-ms delay and then a 100-ms test array consisting of three colored squares. This was followed by a variable delay of 17, 133, 250, 367, or 483 ms and then either a 100-ms array of masks or a 100-ms blank interval in the no-mask trials. A response screen followed in which the fixation point was replaced by a question mark, and participants made an unspeeded button-press response to indicate whether the target color was present in the test array. The target color was present in the test array in 50% of the trials.

A total of 120 mask trials were administered in the control condition, 24 at each delay interval. Twelve masked trials from each delay interval were presented in random order in two blocks of 60 trials. The 24 no-mask trials were presented before the masked trials.

**Statistical Methods**

The major dependent variable was \( A' \), a measure of sensitivity (similar to \( d' \)) that is widely used in signal detection experiments. To compute \( A' \), we first quantified the hit rate (H) as the proportion of correct responses for trials in which the sample and test arrays were identical, and the false-alarm rate (F) was quantified as the proportion of incorrect responses in which the two test stimuli were different. \( A' \) scores were calculated using the following formulas: \( A' = 0.5 + (H – F)(1 + H – F)/4H(1 – F) \), when \( H \geq F \), and \( A' = 0.5 – (F – H)(1 + F – H)/4F(1 – H) \), when \( F > H \) (Stanislaw & Todorov, 1999, Equation 2). Extreme values of \( H \) or \( F \) were adjusted by replacing zero values with 0.5/n and values of 1.0 with \((n – 0.5)/n \), where \( n \) is the number of trials. The control and WM conditions were analyzed separately using the repeated measures analysis of variance (ANOVA) model: \( A' = \) Masking Condition + Group + Group \( \times \) Masking Interval. This repeated measures model was fitted using the generalized estimating equation method (Liang & Zeger, 1986). With this method, model parameters are estimated using a working correlation model (in this case, compound symmetry) of the within-subject correlations of the repeated measures; residuals from the fitted model are then used to correct the standard errors of the model parameters for lack of fit between the working correlation model and the actual within-subject correlation structure.

In the control condition, we were interested in identifying the longest interval at which perceptual-level masking effects might confound interpretation of differences observed between healthy control participants and patients when masking was used in the WM encoding condition. Accordingly, we examined each time interval at which masking was applied to determine whether the control participant versus patient difference was significantly different from that observed in the no-mask trials (separate test for Diagnosis \( \times \) Masking interaction comparing the no-mask trials separately with each masking interval). All tests were performed using contrasts among parameters estimated from the overall ANOVA model, using the pooled error estimate.

For the analysis of the WM condition, we omitted observations from the masking interval identified as showing potential perceptual-level masking effects in the control experiment. If a Group \( \times \) Interval interaction was significant, we performed planned contrasts among parameters estimated from the overall ANOVA model using the pooled error estimate. First, we ran separate tests for the Group \( \times \) Masking interaction (no mask vs. masking) at each masking delay interval to determine at which delay intervals masking increased control participant versus patient differences compared with the no-mask trials. These tests also measured the corresponding estimates of the magnitude of the control participant versus patient differences at each interval. Second, within each group, we compared \( A' \) in the no-mask and masking trials at each masking delay interval to determine at what delays masking no longer had an effect on encoding.

We calculated effect sizes using the pooled standard deviation.

To assess the psychometric properties of the WM masking trials relative to the WM no-mask trials, we calculated the true score variance for each masking interval. This was done by multiplying the observed variance by the reliability for each masking interval (no-mask, 17 ms, 133 ms, 250 ms, 367 ms, and 487 ms; Chapman & Chapman, 1973, 1978). Reliability was calculated using Cronbach’s alpha, on the basis of a split of even and odd trials for each interval. These analyses were performed in order to address the possibility that differences in task sensitivity in the masking trials relative to the no-mask trials could confound the interpretation of study results.

**Results**

**Perceptual Control Condition**

The goal of the perceptual control condition was to determine which masking intervals were free from perceptual masking effects and could therefore be used in the analysis of the WM condition. The results from the perceptual control condition are shown in Figure 3. For both groups, accuracy increased between the 17-ms and 133-ms masking intervals but then remained stable, near the no-mask level of performance. Overall accuracy was lower in the patient group than in the control group, and the impairment at 17 ms was substantially larger for the patients than for the control participants. Thus, masking appeared to be present only at the 17-ms interval.

The overall ANOVA model for this condition showed significant effects of group, \( F(1, 30) = 7.92, p = .008 \); masking interval, \( F(5, 150) = 12.50, p < .0001 \); and Group \( \times \) Masking Interval interaction, \( F(5, 150) = 2.39, p = .04 \). We interpreted the significant Group \( \times \) Masking Interval interaction as indicating the presence of perceptual-level masking effects at some intervals and performed post hoc tests comparing the group differences at different masking delay intervals to the group difference in the no-mask trials.

In the no-mask control trials, control participants had significantly higher \( A' \) scores than patients (\( M \pm SE = 0.972 \pm 0.004 \) vs. \( 0.954 \pm 0.006 \)), \( F(1, 148) = 6.82, p = .01 \). Post hoc tests of the Group \( \times \) Interval interaction were performed to compare performance at each masking interval with no-mask performance. These tests were statistically significant for the 17-ms delay, \( F(1, 148) = 11.15, p = .001 \), but not for the other intervals (minimum of \( p > .22 \) for any interval). This suggests that, although patient accuracy was generally lower than control accuracy, this effect did not differ between the mask and no-mask trials except at the 17-ms masking interval. Moreover, the Group \( \times \) Masking Interval effect from the omnibus ANOVA was no longer significant (\( p = .75 \)) when we dropped the 17-ms interval from the analysis. Further, because the magnitude of the control participant versus patient difference in \( A' \) seemed similar in all intervals from 133 ms to 483 ms (see Table 2 and Figure 3), we compared the average between-groups difference across these four intervals with the no-mask condition and found no significant effects of masking, \( F(1, 148) = 0.72, p = .40 \) (95% confidence interval for change in difference because of the
masking effect = −0.013–0.034). That is, the between-groups effects observed from 133 to 483 ms do not appear to result from perceptual-level masking effects. Instead, it appears that patients demonstrate an elevated error rate in both the no-mask and masked intervals relative to control participants.

**WM Condition**

The results from the WM condition are shown in Figure 4. For both groups, performance was highly impaired at the shortest masking delay and increased systematically as the delay increased. Consistent with the previous results of Vogel et al.’s (in press) study, control participants neared asymptotic performance by the 250-ms delay, and their asymptotic performance was near their no-mask performance. In contrast, patients never reach an asymptote, and their performance at the longest masking interval was substantially lower than their no-mask performance.

![Figure 3](image)

*Figure 3.* The results of the perceptual control condition are presented as A’ values. Control participants (squares) and patients (triangles) were impaired at the 17-ms interval compared with their no-mask performance, but the groups did not differ from no-mask performance at any other intervals. Error bars represent the standard error of the mean.

The control participants and patients were not significantly different on no-mask trials ($M \pm SE = 0.941 \pm 0.010$ vs. $0.926 \pm 0.012$), $F(1, 118) = 1.01, p = .32$. Note that the actual magnitude of the between-groups difference on the no-mask trials of the WM condition is quite similar to that observed above on the no-mask trials of the perceptual control condition: The differing effect sizes reflect the different degrees of variability observed in these two conditions.

1 In addition, paired t tests revealed that the patient and control groups’ performance in the 17-ms interval differed significantly from their no-mask performance (for patients, $p < .001$; for control participants, $p = .003$), but no other interval differed significantly from the no-mask performance for either group (all $ps > .10$), providing further evidence that perceptual masking was not present in the intervals greater than 17 ms.
Because of the backward masking effects observed at 17 ms in the perceptual control condition, we omitted the 17-ms interval from the data analysis for the WM condition. In the overall ANOVA for the WM condition, statistically significant effects were found for group, $F(1, 30) = 7.52, p = .01$; masking interval, $F(4, 120) = 9.63, p < .001$; and Group $\times$ Masking Interval, $F(4, 120) = 2.65, p = .035$. Moreover, planned comparisons indicated that the differences in $A^*$ between control participants and patients were statistically significant at each masking interval ($p < .05$ for each interval).

To determine whether the significant Group $\times$ Masking Interval interaction supported our hypothesis of slowed WM consolidation in patients, we performed a set of planned tests comparing the group difference in the no-mask trials with the group difference at each masking interval. Separate tests comparing each masking delay with the no-mask trials yielded significant ($p < .05$) Group $\times$ Delay Interval interactions at all intervals except 483 ms, $F(1, 118) = 3.26, p = .073$, evidence of impaired consolidation in patients. Because the result for the 483-ms interval is marginal, we cannot rule out continued, but slightly attenuated, masking effects at this interval as well.

To further evaluate the time course of the masking effects, we also separately compared the mean $A^*$ within each group at each masking delay interval with the mean $A^*$ attained in the no-mask trials. In control participants, $A^*$ at the 133-ms masking delay was significantly less than $A^*$ in the no-mask trials ($M \pm SD = 0.941 \pm 0.011$ vs. $0.885 \pm 0.024$), $F(1, 118) = 8.16, p = .005$, but there were no significant differences between the masked and no-mask trials at longer intervals (minimum $p = .26$). Thus, in control participants, there is no detectable effect of masks on WM encoding after 133 ms. In patients, however, $A^*$ was significantly less in the masked than in the no-mask trials at all masking delay intervals, including at 483 ms ($p < .05$ for all delays). At all delay intervals between 133 ms and 483 ms, the effect size for the difference between control participants and patients was 2–3 times the effect size for the difference between control participants and patients in the no-mask trials of the WM condition (see Table 2).

As a final test of slowed consolidation, we conducted a Group $\times$ Masking Interval comparison that excluded the no-mask trials (as well as the 17-ms trials). In addition to significant main effects of group, $F(1, 118) = 131.57, p < .001$, and masking interval, $F(3, 118) = 12.78, p < .001$, this ANOVA yielded a significant Group $\times$ Masking Interval interaction, $F(3, 118) = 3.16, p = .027$. These findings indicate that accuracy changed over masking intervals in a different way for patients and control participants, consistent with a slowing of the consolidation process.

Examination of the true score variance associated with the no-mask and masking trials (see Table 2) enhances confidence that the patient deficit is not an artifact of the discriminating power of the task interacting with the generalized deficit of the illness. Greater true score variance enhances the discriminating power of a task condition, leading to the expectation that the magnitude of between-group differences should track the magnitude of the true score variances associated with each condition if the psychometric properties of the measures were responsible for the overall pattern of effects. However, the true score variances observed in the 250-, 367-, and 483-ms intervals are all lower than in the no-mask trials (where the groups did not differ). Therefore, the deficits observed in these later masking intervals cannot be explained on the basis of psychometric artifact, indicating that the masking deficits are not likely to be explained on the basis of the generalized deficit observed in the illness.

**Discussion**

The results of this study demonstrate a marked deficit of WM consolidation processes in patients with schizophrenia. It appears that patients require at least twice as long as healthy participants to fully consolidate material into WM in this paradigm: Whereas control participants reach their no-mask performance level with a 250-ms delay between target and mask, patients continue to demonstrate significant masking effects at the longest interval tested, 483 ms. It remains for future experimental work to determine the full duration of this vulnerability. Abnormal slowing of WM consolidation in schizophrenia was previously implicated by the early work of Knight and colleagues (Knight et al., 1985) and by more recent studies using the attentional blink paradigm (Cheung et al., 2002; Li et al., 2002). However, the simplicity and within-

**Table 2**

<table>
<thead>
<tr>
<th>Mask delay (ms)</th>
<th>C vs. SZ effect size</th>
<th>Diagnosis $\times$ Delay</th>
<th>True score variance (C only)</th>
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<tr>
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<td>0.89**</td>
<td>0.34</td>
<td>2.47</td>
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<tr>
<td>17 ms</td>
<td>1.31***</td>
<td>0.35</td>
<td>10.03</td>
</tr>
<tr>
<td>133 ms</td>
<td>0.53</td>
<td>0.77**</td>
<td>7.75</td>
</tr>
<tr>
<td>250 ms</td>
<td>0.56</td>
<td>1.10*</td>
<td>1.45</td>
</tr>
<tr>
<td>367 ms</td>
<td>0.86*</td>
<td>0.87*</td>
<td>0.80</td>
</tr>
<tr>
<td>483 ms</td>
<td>0.70*</td>
<td>0.74*</td>
<td>2.02</td>
</tr>
</tbody>
</table>

Note. The 17-ms delay interval was omitted from analysis of the working memory condition because of the evidence of backward masking at this delay seen in the control condition.

* $p < .05$. ** $p < .01$. *** $p < .001$. 

Greater true score variance enhances the discriminating power of a task condition, leading to the expectation that the magnitude of between-group differences should track the magnitude of the true score variances associated with each condition if the psychometric properties of the measures were responsible for the overall pattern of effects. However, the true score variances observed in the 250-, 367-, and 483-ms intervals are all lower than in the no-mask trials (where the groups did not differ). Therefore, the deficits observed in these later masking intervals cannot be explained on the basis of psychometric artifact, indicating that the masking deficits are not likely to be explained on the basis of the generalized deficit observed in the illness.
experiment comparisons of the current paradigm make it possible to rule out contributions from impairments in perception and attention switching that complicate the interpretation of prior studies in this area.

A key element of the present experimental design is that it can differentiate between the effects of masking on the formation of perceptual representations and the effects of masking on WM consolidation. Consistent with previous studies of perceptual masking in schizophrenia, we found evidence of exaggerated backward masking effects in the perceptual control condition, at a longer SOA than is typical of the schizophrenia literature. Thus, deficits in perceptual functioning appear to be a reliable feature of schizophrenia and may contribute to impaired WM performance in paradigms that burden perceptual analysis. However, it does not appear possible to attribute the consolidation impairment documented here to perceptual deficits, given the pattern of patient performance observed in the control condition. Simply described, patients are able to effectively search a three-item array much more rapidly than they are able to consolidate information from a three-item array into WM. No perceptual-level masking effects were evident in the patient group by 133 ms, whereas consolidation-related impairments were still evident at 483 ms. Thus, our results implicate deficits in both perceptual analysis processes and postperceptual consolidation processes in schizophrenia.

It is important to consider whether consolidation is actually slowed in schizophrenia or whether consolidation is simply ineffective such that WM representations are never as fully consolidated in patients as in control participants. If consolidation is simply slowed, then given sufficient time, patients would form an accurate and durable WM representation. In contrast, if consolidation is not fully effective in schizophrenia, then the WM representations would be vulnerable to masks and other distractions at any time point. The present data indicate that at least part of the

Figure 4. The results of the working memory condition are presented as A' values. Results from the 17-ms interval are shown for reference only; they were not included in the analyses. Control participants (squares) reached their no-mask performance by the 250-ms interval whereas patients (triangles) showed impaired performance in the 483-ms interval compared with their no-mask performance. Error bars represent the standard error of the mean.
performance deficit is due to a slowing of consolidation: Performance was near asymptote by 250 ms in the control group, whereas performance steadily increased up to 483 ms in the patient group. However, it is possible that consolidation is generally impaired—indeed, independent of time—in schizophrenia because masked performance was worse than no-mask performance for patients at the longest masking interval tested (483 ms). Of course, the speed of consolidation and the ultimate effectiveness of consolidation may be interrelated. For example, if consolidation is sufficiently slow, then the perceptual representation of the sensory input will have faded before consolidation is complete, and consolidation will be ineffective no matter how much time has passed. Further work will be needed using a variety of masking durations and stimulus types in order to further characterize the nature of the deficit documented here.

An impairment of WM consolidation is likely to have significant consequences for many other cognitive operations and everyday visual behavior. In essence, patients’ perceptual representations remain vulnerable for a prolonged period to the interfering impact of subsequent environmental stimuli and internal “noise.” Theoretically, the addition of such noise may decrease the precision of WM representations, thereby contributing to deficits observed on tasks requiring very fine perceptual discriminations of WM targets (Javitt et al., 1997; Lenz et al., 2003). Similarly, impaired consolidation may contribute to deficits documented on tasks that require rapid updating of large amounts of information in WM, such as high-load versions of the N-back task (Callcott et al., 1998). If the deficit in visual WM consolidation found here generalizes to other cognitive domains, it would likely compromise the performance of other tasks that involve the rapid creation and transformation of WM representations (such as language comprehension and reasoning). Thus, it is possible that a specific deficit in WM consolidation would decrease the overall efficiency of the WM system. Clearly, other impairments could also compromise WM capacity and efficiency, and we are not claiming that impaired consolidation is the sole cause of WM failure in schizophrenia. However, poor consolidation may well play an important, and largely unrecognized, role in the genesis of WM impairment.

It is often difficult to link experimentally observed deficits in specific cognitive operations to everyday behavior. However, visual WM consolidation may be unusual in this regard because this process is implicated in the basic process of perceiving and exploring the visual environment. In essence, every time a person makes a saccadic eye movement, the new sensory input will mask the previous percept unless it has been consolidated in some way. An impairment in this consolidation process should be evident in several different aspects of visual behavior. First, in an effort to compensate for the deficit, one would expect that patients would make fewer exploratory eye movements when inspecting new visual scenes and that gaze times would be prolonged. Several studies have documented this pattern of exploratory eye movements in schizophrenia (Kojima et al., 1992; Matsushima et al., 1992, 1998; Ryu, Morita, Shoji, Waseda, & Maeda, 2001). Second, one would expect that patients would have difficulty integrating information from different parts of a visual scene in order to form a conceptual level of representation. A number of studies have demonstrated abnormalities in perceptual organization in patients with schizophrenia consistent with this notion (Place & Gilmore, 1980; Silverstein et al., 1996; Wells & Leventhal, 1984). Thus, there is converging evidence from other aspects of visual processing that are consistent with impaired WM consolidation in the schizophrenia literature.

Single-cell recording data obtained from nonhuman primates during the performance of WM tasks provide a rich set of observations that can be speculatively related to the present results. These studies have demonstrated that multiple cortical areas have the ability to represent information about the identity of target stimuli (but note that only a few cortical areas have been mapped using these techniques, and the full extent of the network that contributes to WM performance remains unknown). Miller, Erickson, and Desimone (1996) demonstrated that single cells in both inferior temporal cortex and prefrontal cortex maintain stimulus-selective, sustained activity over a delay interval. However, the sustained selective activity in inferior temporal neurons can be eliminated by the presentation of intervening stimuli during the delay period. In contrast, sustained delay activity in prefrontal neurons is much more robust in the face of distracting, intervening stimuli. It is therefore possible that consolidation occurs primarily for prefrontal WM representations and not for inferotemporal WM representations.

Similarly, Chao and Knight (1995) reported that patients with prefrontal lesions show greater interference from distractors than patients with temporal-parietal lesions or healthy control participants at all delay intervals, with greater impairment with increasing delays. Applied to the current paradigm, it appears likely that the pattern masks engage the same inferotemporal networks that represent the target information, effectively overwriting, or replacing, the task-relevant information. Therefore, successful performance on masked trials is dependent on access to prefrontal representations. It appears that patients with schizophrenia have an impairment that limits the rapid formation of precisely this type of representation.

The extent to which the performance deficits documented here can be attributed to specific failures of prefrontal level representations is admittedly uncertain, as dysfunction in other aspects of the network could also compromise performance. However, our proposed account would be consistent with other evidence of prefrontal abnormalities in schizophrenia that includes alterations in brain structure, metabolic activity in response to cognitive challenge, and a range of cognitive deficits commonly attributed to this area (Barch et al., 2001; Carter et al., 1998; Fletcher et al., 1998; Perlstein et al., 2001; Weinberger, Berman, & Zec, 1986).

Cognitive studies in schizophrenia must inevitably consider the role of two potential confounds: medication effects and the role of generalized cognitive impairment. We are unaware of any studies directly addressing the role of antipsychotic medications on WM consolidation. Several lines of indirect evidence suggest that medication effects are unlikely to be responsible for the deficit documented here. First, a number of studies have documented medication-related enhancements on a variety of attention and WM tasks (such as the N-back, the continuous performance task [CPT], and the digit span distractibility task) that bear some relationship to the task studied here (Nestor, Faux, McCarley, & Sands, 1991; Oltmanns, Ohayon, & Neale, 1978; Spohn, Lacoursiere, Thompson, & Coyne, 1977; Spohn & Strauss, 1989; Weickert et al., 2003). In addition, there are numerous reports that...
clinically unaffected (and unmedicated) first-degree relatives of patients demonstrate impairment on a number of WM tasks (Conklin, Curtis, Katsanis, & Iacono, 2000; Glahn et al., 2003; MacDonald, Pogue-Geile, Johnson, & Carter, 2003; Park, Holzman, & Goldman-Rakic, 1995; Tuulio-Henriksson et al., 2002), including impairment on a repetition blindness task, a type of RSVP paradigm (Park & Hooker, 1998). In that study, unmedicated, non-schizophrenic family members showed similar impairments to those observed in their ill medicated relatives, strong evidence that the behavioral deficit was not secondary to treatment effects. Thus, although the available evidence is indirect and we cannot conclusively dismiss the possibility of a treatment artifact, this possibility appears unlikely.

Patients with schizophrenia demonstrate impairments across most complex forms of cognition, a generalized pattern of impairment. Thus, it is always possible that any claim for a specific type of deficit, such as the masking deficit proposed here, simply reflects this more general impairment. The true score variance data in Table 2 suggest that the masking deficit is not a psychometric artifact and therefore is not easily accounted for by the generalized deficit. That is, we can be confident that the different pattern of accuracy observed for patients is not just an artifact of a combination of poorer overall performance and different levels of sensitivity in the different masking intervals. Instead, the results reflect a specific impairment that causes a greater performance deficit in some masking intervals than in others. However, it is still possible that the observed consolidation deficit is just one facet of a somewhat broader deficit. Indeed, the fact that Vogel et al. (in press) demonstrated that consolidation is a capacity-limited process raises the possibility that a reduction in attentional resources could account for a compromise of consolidation, a possibility that cannot easily be discounted. However, in our view, it is of little concern whether this deficit occurs as part of a broader impairment or as a focal abnormality: The implications for other aspects of cognitive function remain the same. That is, slowed WM consolidation is likely to significantly compromise multiple aspects of cognitive performance whether it occurs in isolation or as part of a broader pattern of impairment.

Summary

This study found evidence that patients with schizophrenia require at least twice as long as control participants to fully consolidate three items into visual WM, even when the study design controlled for potential perceptual differences. The implication of these results is that people with schizophrenia are subject to disruption of the formation of WM representations for a prolonged period compared with healthy individuals, an impairment that would have a profound effect on any cognitive tasks requiring the storage and retention of information in WM.

References

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