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Revisiting the Backward Masking Deficit in Schizophrenia: Individual Differences in Performance and Modeling With Transcranial Magnetic Stimulation

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Abstract

Background—Deficits in backward masking have been variably reported in schizophrenia patients, but individual differences in the expression of these deficits have not been explicitly investigated. In addition, increased knowledge of the visual system has opened the door for new techniques such as transcranial magnetic stimulation (TMS) to explore these deficits physiologically.

Methods—Patients with schizophrenia and healthy controls were tested using a backward masking paradigm. In order to examine the functionality of visual pathways involved in backward masking, subjects were retested on a backward masking paradigm using single pulse TMS applied to occipital cortex in lieu of the masking stimuli.

Results—Compared with controls, patients had significantly delayed recovery from visual backward masking. However, 23.5% of patients (compared to 5% of controls) never recovered to levels approaching unmasked performance. When these subjects were segregated from the analysis, group differences vanished. In addition, stimulus masking with occipital TMS followed the same pattern in both patients and controls.

Conclusions—Observations of individual differences in visual masking performance may identify a subgroup of schizophrenia patients. The TMS data suggest that this deficit may not localize to the occipital cortex. However, TMS can be a useful tool for localizing processing deficits in schizophrenia.

Keywords

Individual differences; occipital cortex; schizophrenia; transcranial magnetic stimulation; visual masking

Schizophrenia patients have been shown to have visual information processing deficits as assessed by visual masking paradigms. In backward masking, a target visual stimulus is rapidly followed by a masking visual stimulus, which, if shown temporally close enough to the target, will interfere with the identification of the target. In the first report of backward masking in schizophrenia, patients and healthy controls were shown a high contrast pattern mask at varying interstimulus intervals (ISIs; 50 to 300 msec) after the target presentation (Saccuzzo *et al.* 1974). Schizophrenia patients were less accurate than both healthy controls

and nonschizophrenia psychiatric patients at all ISIs beyond 100 msec. This basic experiment has been repeated, with a similar result: schizophrenia patients required much longer ISIs before their performance returned to an unmasked level (for a review, see Braff *et al.* 1991). This deficit may be attentional or represent slowed processing speed characteristic of schizophrenia patients (Braff and Saccuzzo 1985; Saccuzzo and Miller 1977; Saccuzzo *et al.* 1996).

A backward masking abnormality may also be informative about pathways involved in visual processing. Physiological research suggests that afferent visual information segregates into two parallel channels based on temporal and spatial characteristics. A 'transient' channel conducts information for fast orientation of the visual system to the location of a visual stimulus. A slower processing 'sustained' channel conducts information needed for detailed analysis and identification of the visual object. As a mechanism to explain the interruptive effects of backward masking, Breitmeyer and Ganz (1976) suggested that fast transient perception of the mask interferes with ongoing pattern analysis of the target information arriving via the sustained channel. The hypothesized interference between visual channels would occur using a mask with an ISI of 30-100 msec. On this suggestion, Green *et al.* (1994a, 1994b) manipulated the visual properties of the targets and masks presented to patient and control groups in order to study masking at short ISIs. Group differences were found at all ISIs between 20 and 100 msec.

The presence of masking deficits over a broad range of ISIs (short [Green *et al.* 1994a, 1994b] and long [Saccuzzo *et al.* 1974, 1996]) may be due to heterogeneity amongst patients, differences in testing paradigms or deficits involving multiple stages of visual processing (Green *et al.* 1997; Michaels and Turvey 1979). Alternatively, the lack of temporal specificity may be due to more general attentional or motivational factors in schizophrenia patients. In visual processing tasks like backward masking, it is assumed that subjects are motivated, maintaining a constant level of concentration throughout the trials. This is problematic in a symptomatic patient group. Furthermore, poor or chance performance by a small subgroup can create the appearance of a deficit in the group as a whole. Researchers have long been aware of the difficulty in distinguishing nonspecific deficits from those specific to visual information processing (e.g., Braff and Saccuzzo 1985; Braff *et al.* 1991; Saccuzzo *et al.* 1996). However, individual subject task performance has not been explicitly scrutinized in prior work.

In the present study, we assessed visual processing pathways during backward masking in schizophrenia patients. Accuracy criteria were applied to identify extremely poor performers in order to gauge their effect on group differences. Subjects also performed forward masking tasks as a closely related control task (Chapman and Chapman 1978), since schizophrenia patients have not demonstrated deficits in forward masking performance (Saccuzzo and Braff 1981; Saccuzzo *et al.* 1996; Slaghuis and Bakker 1995). In addition, rather than using stimulus duration to equate target visibility in participants, a staircase procedure involving luminance changes was employed, while stimulus duration was kept constant. Previous studies have equalized target visibility across subjects by varying the duration of target presentation in the unmasked condition. The critical stimulus duration (CSD) is determined for each subject by increasing the target stimulus duration until performance reaches an accuracy criterion. Schizophrenia patients often require a CSD that is double that of healthy control groups, and can be many tens of msec greater for an individual patient than for controls (Saccuzzo *et al.* 1996). Use of CSDs that vary widely between both individuals and experimental groups may be a serious confound in masking tasks, where timing between stimuli is the variable being researched (Macknik and Livingstone 1998).

A further procedure was used in order to examine the anatomy of a masking deficit. Backward masking can occur both proximally and distally within the nervous system. In the retina, stimuli occurring closely together in time can be combined into a single image, resulting in masking by integration. Interruption is the interference with ongoing analysis of the target by later incoming mask information and takes place centrally in the visual cortex. Vulnerability to a backward mask in schizophrenia is thought to be due to the central effect of interruption (Cadenhead *et al.* 1998; Green *et al.* 1994a). In order to probe the central processing pathways that underlie masking deficits in schizophrenia patients, transcranial magnetic stimulation (TMS) was administered to replace the masking stimulus.

TMS uses an alternating magnetic field to induce current flow in underlying biological tissue. The magnetic field passes through the scalp and cranium essentially unimpeded, allowing the field to focally stimulate the superficial cortex without appreciable distortion. TMS has been found to affect visual processing in primary visual cortex (i.e. V1) in a characteristic, time-dependent manner (e.g., Amassian *et al.* 1989; Corthout *et al.* 1999; Masur *et al.* 1993; Miller *et al.* 1996). A single pulse from a magnetic coil placed over the occipital cortex can successfully mask a target stimulus when the magnetic pulse follows the visual presentation by 80 to 100 msec. This window corresponds to the time when target information reaches V1. A properly timed TMS pulse can increase the threshold of stimulus visibility by disrupting processing of the incoming retinal signal (Kammer and Nusseck 1998). Here, TMS was applied to both healthy control and schizophrenia groups at ISIs between 14 and 196 msec. If V1 is a locus of the schizophrenia backward mask deficit, then TMS neural stimulation may simulate the effect of a backward mask and disrupt target recognition, more so for patients relative to healthy controls. While the interruption of processing caused by TMS might not necessarily be the same as that caused by a visual mask, a direct effect of disruption specific to V1 would suggest that early deficits observed in backward masking in schizophrenia patients have a nexus in abnormal early perceptual processing in V1.

Methods and Materials

Subjects

Seventeen patients (5 female) were recruited from the New York State Psychiatric Institute (NYSPI) Schizophrenia Research Unit. All received diagnoses of schizophrenia according to DSM-IV criteria using the Diagnostic Interview for Genetic Studies (Nurnberger *et al.* 1994). Eleven of the patients were diagnosed with paranoid schizophrenia, two as disorganized, and four as undifferentiated. Seven patients were medication-free. The average age of onset of schizophrenia was 23.1 ± 7.3 years, and the mean duration of illness was 6.4 ± 6.6 . The mean Brief Psychiatric Rating Scale (BPRS) for the group was 29.1 ± 4.7 . Twenty healthy participants (9 female) were recruited from the local community. Subjects were excluded if they had an Axis I DSM-IV disorder (Structured Clinical Interview for the DSM-IV, Nonpatient version, SCID-NP). None had a first degree relative with a history of psychotic disorder. In addition, subjects were excluded from participating in the TMS session if they had a history of neurological disorder, seizures, loss of consciousness, any metallic implants or devices, or hearing loss. All subjects signed informed consent and all had normal or corrected-to-normal vision. This study was approved by the local Institutional Review Board (IRB). Group characteristics are shown in Table 1. Patient and Healthy Control groups were similar in age ($t = .5$, $df = 34$, $p < .62$) and gender ($\chi^2 = 1.5$, $df = 1$, $p < .22$), but differed in level of education ($t = 5.6$, $df = 34$, $p < .001$).

Testing Procedures

The visual stimuli for the masking tasks were displayed on a Dell Ultrascan monitor (17" screen), controlled by a Dell Dimension P200V computer (Dell Inc., Round Rock, Texas). The monitor had a 70 Hz refresh rate. Stimulus presentation was locked with the vertical synch signal to the monitor, so that stimuli appeared at the same point in each refresh cycle. Although the refresh cycle lasted 14.3 msec, the actual duration of both the target and the mask stimuli was about 2 msec, equivalent to the phosphor decay rate of the monitor. Target stimuli were Landolt 'Cs', with the gap facing one of four orientations. The Cs were presented at the center of the computer screen. With participants seated 50 cm away, each had a diameter of .4 degrees of visual angle. The masks were filled circles with the same diameter as the target C.

Target Luminance—The luminance of the target was determined using a staircase procedure (Wetherill and Levitt 1965). Participants were seated facing the monitor in a darkened room, using a chin rest that stabilized the distance from the eyes to the target at 50 cm. They were instructed to press one of four numbers on the number pad of the keyboard in response to a stimulus presentation: "2" meaning the gap in the C was open downward; "8" for upward; "4" when on the left; and "6" when on the right. A fixation cross at .5 degrees of visual angle and luminance of 2.41 cd/m² preceded each target presentation, against a background luminance of 2.11 cd/m². The cross lasted 500 msec, with the target C presented 400 msec after it disappeared. Beginning with a target luminance of 2.91 cd/m², luminance was changed in steps of .054 cd/m², with an increment if an error was made and a decrement if three consecutive correct responses were made. The staircasing continued until nine changes in direction had occurred (approximately 45 to 65 trials), providing an estimate for the 78% accuracy level of performance for that participant. Masks were approximately 1.7 times target luminance.

In the first session, after the 78% unmasked performance level was ascertained, four blocks of visual masking trials were run. Two blocks used forward masking, and two, backward masking, presented in an ABBA order, counterbalanced between subjects. The ISI between target and mask was one of 11 durations (14, 21, 29, 36, 43, 57, 71, 86, 114, 143, 200 msec). ISI varied pseudorandomly over each 110 trial block, until 10 trials had been presented at each. Subjects were given as much time as necessary to respond before the next trial was begun.

TMS—In the second session, the task remained the same, except TMS pulses were substituted for the visual masks. Single pulse TMS was administered using a MagStim 200 stimulator (MagStim Company, Limited, Dyfed, United Kingdom) with a 90 mm round coil. Each subject was seated comfortably in the same chair and in the same setting as the previous session. Ear plugs were worn throughout the testing to decrease sound exposure. The optimal stimulation site and stimulation intensity were determined during the first block of trials. Three sites were assayed for coil placement: on the back of the head centered on the midline, with the bottom edge 2 cm above the inion (Amassian *et al.* 1989) and 2 cm above and below it. With the stimulus luminance set at the 78% accuracy level found in the first session, single magnetic pulses were applied 86 msec after the target C. If three of five correct target identifications were made, the coil was moved to one of the other two sites, where the process was repeated. The initial TMS field intensity was set at 65% of the capacity of the Magstim device. If three errors did not occur at any site, the intensity was increased by 5%. Trials continued until three of five errors were made at a site. Five to ten more trials were performed to see if the errors persisted. If so, that location and TMS intensity were used for the rest of the session. Two blocks of 110 trials each were run.

Eleven target-TMS pulse ISIs (0, 43, 57, 71, 86, 100, 114, 129, 143, 171, 200 msec) were used, pseudorandomly ordered such that 10 trials at each ISI occurred in each block.

Analysis

Multivariate repeated measures analysis of variance (MANOVA) was conducted on the accuracy measures obtained at each ISI. In the model, the between-subject term was group (patient vs. healthy control). The *F*-value associated with Wilk's Lambda was used for significance testing. Significant multivariate findings were followed by post-hoc *t*-tests at each ISI. Analyses were initially done with Years of Education (the only demographic which differed between healthy controls and patients) as a covariate. These are not reported, as Education had no effect on any of the dependent measures.

Criterion for Unresponsive Subjects

Subjects were classed as unresponsive if they showed no sign of recovery from the mask with increasing ISI. In a typical masking function, accuracy increases with increasing target-to-mask ISI until it approaches unmasked levels. Two criteria were used to identify subjects who did not improve over time. First, the mean percentage accuracy over the four longest ISIs (84 to 196 msec) was less than 50%. Second, the subject did not attain a 70% accuracy level (i.e., approach the 78% no mask performance level) at any of the ISIs used. The masking function of a subject meeting these criteria was essentially flat, at a level of accuracy well below the unmasked level.

Results

Performance on Luminance Staircase

The mean percentage luminance for the patient group was 19.2 ± 8.5 and 16.8 ± 5.7 for the controls. The difference between the group means was not significant ($t = 1.0$, $df = 34$, $p = .34$). When the unresponsive performers were excluded (see below), the gap between the means narrowed, with group means of $17.8 \pm 7.0\%$ and $17.1 \pm 5.8\%$ for patients and controls respectively. The four patients who were unresponsive performers on the backward masking task had a mean percentage luminance of 23.5 ± 12.4 . This was not significantly different from the mean of those who performed adequately in the masking task ($t = 1.2$, $df = 15$, $p = .26$).

Backward Masking Performance

Four patients (out of 17) and one healthy control (out of 20) were unresponsive performers on the backward masking task. When patient characteristics between nonperformers and performers were examined, the only demographics that might have been significant were there a large enough *n*, were gender and age. Four of the five nonperformers were men, whereas in the performer group nine out of 13 were men and mean ages were 21.0 and 31.8 respectively; i.e. the nonperformers were more likely to be young men. There was no obvious difference between nonperformers and performers on medication status (three on, one off, one questionable vs. nine on and four off respectively), age of illness onset (20.8 vs. 23.8), years of education (12.8 vs. 13.0), positive symptom severity (13.0 vs. 12.3) and negative symptom severity (19.5 vs. 17.4). We did not review the DSM diagnosis subtypes as these were unstable and unlikely to be revealing.

When all participants were included, the MANOVA yielded a Group effect ($F(1,35) = 4.3$, $p < .05$) and a main effect of ISI ($F(10,26) = 18.9$, $p < .0001$). In post hoc tests, the healthy control group was significantly more accurate than the patient group at ISIs of 14 msec ($t = 2.5$, $df = 35$, $p < .02$), 140 msec ($t = 2.5$, $df = 35$, $p < .02$) and 196 msec ($t = 2.3$, $df = 35$, $p < .03$). When unresponsive performers were excluded, MANOVA revealed only a main

effect of ISI ($F(10, 21) = 23.3, p < .0001$), with no Group effect. Figure 1A plots the percentage accuracy across ISI for three groups: patient and control subjects who were above criterion and subjects (patient and control) who performed below criterion. When these three groups were submitted to a MANOVA, main effects of Group ($F(2,34) = 15.1, p < .0001$) and ISI ($F(10, 25) = 13.5, p < .0001$), as well as a trend in Group by Time interaction ($F(20, 50) = 1.7, p < .07$) were found. Follow-up ANOVAs were significant at all ISIs beyond 28 msec (except 43 msec). At each of the seven ISIs that showed a Group difference, post hoc pairwise comparisons (Tukey-Kramer HSD) showed significant differences between the unresponsive performers and the other two groups. The high performing patient and control groups were indistinguishable.

Forward Masking Performance

In the forward masking task, three controls were classified as unresponsive, including the control who was unresponsive in the backward masking task. The same group of four patients who were classed as unresponsive in backward masking was also unresponsive performers in forward masking. In addition, one patient declined participation in the task.

When all participants were included, the MANOVA detected only a main effect of ISI ($F(10,25) = 11.9, p < .0001$), with no Group effect. The same was found when unresponsive subjects were removed: there was a main effect of ISI ($F(10,18) = 15.9, p < .0001$), with no Group effect. As in the previous figure, Figure 1B plots the percentage accuracy across ISI for the three groups. ISIs are reported as negative numbers: the duration between target and mask subtracted from a target onset time of zero. When these three groups were submitted to a MANOVA, main effects of Group ($F(2,33) = 11.8, p < .0001$) and ISI ($F(10, 24) = 10.9, p < .0001$), as well as a Group by Time interaction ($F(20, 48) = 2.1, p < .02$) were found. Follow up ANOVAs were significant at all ISIs except three ($-21, -28$, and -71 msec). At all ISIs from -36 to -200 (except -71 msec, post hoc pairwise comparisons (Tukey-Kramer HSD) showed significant differences between the unresponsive performers and the other two groups. The high performing patient and control groups were indistinguishable except at -14 and -196 msec, where patients were better than controls.

TMS Masking Performance

Fourteen of the 17 subjects in the patient group underwent the TMS procedure: two declined to participate and one was ruled out due to a history of loss of consciousness. Eleven of these 14 demonstrated TMS masking effects. Of the other three, one did not demonstrate TMS masking at any ISI, and TMS masking in the other two was unclear due to poor performance at all ISIs. One of these latter two was an unresponsive performer in the visual masking session as well. For the control group, 18 of the original 20 received TMS, one had declined to participate and the other was excluded due to a history of concussion. Of those that participated, 15 showed TMS masking effects, two performed poorly at all ISIs and one did not demonstrate TMS masking at any ISI.

TMS thresholds averaged $84.7 (\pm 1.9)\%$ and $87.7 (\pm 2.5)\%$ of total stimulator output for control and patient groups respectively. Poor performers averaged $87.3 (\pm 1.8)\%$ as well. The TMS thresholds were not related to patient or control groups or gender ($F(3,22) = .8, p < .49$). When subjects were grouped by masking performance, they also showed no relationship with threshold ($F(2,23) = .4, p < .65$). Threshold was also not correlated with luminance threshold ($r = .24, p < .21$). The variable expected to be most important in determining the TMS threshold was the distance of the TMS coil to the regions in V1 containing the foveal representation, dependent on factors like skull and scalp thickness.

The mean group accuracy for each ISI is shown in Figure 2A. A U-shaped function, typical of previous studies using this TMS paradigm (Amassian *et al.* 1989; Corthout *et al.* 1999; Masur *et al.* 1993; Miller *et al.* 1996), was observed for both control and patient groups. The greatest effect on accuracy was between target-to-TMS intervals of 57 and 129 msec. Beyond 150 msec, both groups showed recovery to unmasked accuracy levels. Accuracy at ISIs less than 50 msec were decreased from unmasked levels in both groups. MANOVA revealed only a main effect of ISI ($F(10, 15) = 9.3, p < .0001$). No significant Group or Group by ISI interactions were found. The actual degree of TMS-induced disruption in accuracy varied considerably across participants, most likely due to differences in skull thickness and in the anatomy of area V1, both of which can be considerable (Stensaas *et al.* 1974). In an attempt to vitiate the influence of these differences, the accuracy of each individual was normalized to a range between 0 (the lowest accuracy across ISIs) and 1 (the highest accuracy obtained). The normalized group mean accuracy across ISIs are shown in Figure 2B. A MANOVA performed on the normalized data again showed no group differences. Figure 2B illustrates that the TMS effect is similar between the two groups.

Discussion

Our psychophysical investigation explored a backward masking deficit as a model for sensory processing deficits in schizophrenia. However, we did not find a backward masking deficit in our sample. In fact we found that an initial abnormality was attributable to a subset of patients who could not perform the task adequately. When we compared poorly performing patients to both patients and controls, significant differences were found. The extremely poor performers on the backward masking task did not exhibit a temporal pattern of accuracy performance interpretable as a recovery from the interfering effects of the mask. Instead, their masking curves stayed flat across ISIs, suggesting a range of possible explanations, from an extremely long-lasting early perceptual deficit to impaired attention.

Despite the absence of a backward masking specific processing deficit, there is substantial evidence implicating visual processing deficits in schizophrenia. In particular, the visual pathway carrying transient channel information has been cited (Butler *et al.* 2001, 2005; Chen *et al.* 1999; O'Donnell *et al.* 1996). We attempted to selectively probe this pathway by targeting V1. Although we were able to adequately use TMS as a 'visual mask,' we were again not able to detect a difference in performance between patients and healthy controls. However, this finding does not rule out deficits in other portions of the transient pathway in visual processing in schizophrenia and TMS could be further utilized to explore this circuitry.

Separation of Biological from Methodological Causes of Backward Masking Deficits

In some of the earliest studies of backward masking, it was also found that schizophrenia patients did not reach unmasked performance levels (e.g., Saccuzzo *et al.* 1974). Braff and Saccuzzo (1985) attributed this poor performance to floor and ceiling effects. By extending the mask ISI to 700 msec, where patients and controls had similar mean accuracy, they were able to reveal deficits specific to backward masking. However, poor general performance in a small subset of patients could also have explained those results. Saccuzzo and Schubert (1981) entertained the possibility of low motivation in patients resulting in flat masking functions, but rejected it based on considerations of the group means. However, means may have varied due to a group of outliers. Poor performing outliers may represent a separate group of individuals who cross different diagnoses. Moreover, backward masking deficits have been identified in manic and schizoaffective patients, further blurring the notion of a disease specific deficit (Saccuzzo *et al.* 1996). Furthermore, another recent study also demonstrated backward masking effects attributable to a small number of unresponsive participants (Rothfeld 2001). In that study, 30 patients with schizophrenia and 39 healthy

controls identified target letters with backward masks presented at four ISIs: 60, 120, 240 and 480 msec. The normal control group was significantly more accurate than the patient group at the two longer ISIs but not at the shorter ISIs. However, when subjects who performed at chance at all ISIs (8 patients and 3 controls) were excluded, there were no differences between patient and normal control groups. Here, as in the present study, about one-quarter of the patients, because they were not performing the tasks in a meaningful way, generated the appearance of a “deficit” in patients relative to normal controls. Both studies highlight that an analysis of individual patient behavior is essential.

The need for this analysis was underscored by the results of the forward masking task. When all subjects were included in the analysis, group differences were seen in backward but not forward masking tasks. The presence of a deficit based on task would have been taken as evidence of a schizophrenia vulnerability specific to backward masking. However, there were no task specific differences in patients and healthy controls once unresponsive subjects were segregated from the analyses.

The present results, and those of Rothfeld (2001), do not imply that previous findings of backward masking deficits in schizophrenia are due only to methodological problems rather than actual physiological deficiencies. There is a great deal of evidence, independent of backward masking data, implicating a schizophrenia deficit specific to the processing of transient visual information, which would lead to backward masking deficits. The visual stimuli of the present study were chosen for their previous effectiveness in TMS masking studies (e.g., Amassian *et al.* 1989) rather than for properties which might elucidate specific transient visual channel abnormalities. On the other hand, the visual properties chosen were not dissimilar to those used in a number of studies which reported a patient specific deficit. The important result here and in Rothfeld is that individual performance must be scrutinized before group deficits can be concluded.

In addition to the absence of group differences on backward masking performance, there were no group differences in target luminance between schizophrenia patients and healthy controls, unlike the increases in CSD in patients typically found. Stimulus duration and target luminance determine target visibility, or stimulus energy, and can be used interchangeably to vary stimulus energy up to 100 msec (Bloch's Law). Extended CSDs for schizophrenia patients may artificially create a masking deficit by interference of the longer target with the backward masking task itself. Although ISI remains constant with varying CSDs, timing between stimulus events (the most relevant parameter) is not necessarily dependent on ISI (Macknik and Livingstone 1998). Furthermore, the standard method used to determine CSD has been criticized as over-conservative, often forcing an artificially elevated result (Badcock *et al.* 1988). In response to that criticism, a psychophysical staircasing procedure was recommended to achieve a more accurate measure. In at least one study of backward masking, when careful staircasing procedures were applied to measures of CSD, schizophrenia patients still had significantly longer CSDs than controls (Saccuzzo and Braff 1981).

In addition to procedural issues, a prolonged stimulus duration has biological implications. A dissociation between target duration and luminance may be attributable to a peripheral, possibly retinal, deficiency in visual processing in schizophrenia. A direct comparison of stimulus duration and luminance in the same individuals, both healthy controls and with schizophrenia, may be necessary to settle this question.

Probing Visual Pathways for Deficits Using TMS

Explanations for the backward masking deficit in schizophrenia were initially framed within stage theories of information processing. The slower rising masking function in patients may

have been the result of a comparative slowness in processing, in which the target information was not successfully transferred from the sensory register to higher centers before the mask icon arrived (Saccuzzo and Schubert 1981). As the complexity of the visual system has been uncovered over the past few decades, it has become clear that modeling human information processing in terms of serial stages is inadequate. However, psychophysical and physiological evidence have been accumulating in favor of a defect in the visual pathways that utilize the information provided by transient visual channels (Bedwell *et al.* 2003; Butler *et al.* 2001, 2005; Chen *et al.* 1999; O'Donnell *et al.* 1996). Green *et al.* (1994a, 1994b) have suggested that the masking deficits observed at short ISIs reflect overactive transient visual channels. This was suggested in the context of the masking mechanism proposed by Breitmeyer and Ganz (1976) in which the influx of fast traveling transient information from the mask may interfere with slower ongoing pattern processing of the target representation.

The anatomical substrate carrying the transient visual information is thought to be the magnocellular pathway, which together with the parvocellular pathway carrying slower-processed pattern information supply the visual input to V1. Beyond V1, a major portion of the transient visual information follows a dorsal route from occipital to parietal cortex, while pattern information is sent on a ventral route into temporal cortex. It is not clear at what points along these routes transient overactivity might disrupt visual processing. The first cortical location where the two pathways significantly interact is V1, and thus a possible locus for the masking mechanism proposed by Breitmeyer and Ganz (1976). In the simplest interpretation, the influx of transient information from the mask may interfere with the target representation already being processed in V1, and may happen to a greater degree in schizophrenia patients than healthy controls. The comparative vulnerability to disruption of V1 target processing between schizophrenia and control groups was tested here using TMS, on the assumption that a TMS pulse would disrupt sustained processing in V1 like a visual mask. This assumption is supported by a comparison of psychophysical and TMS studies in which it was concluded that there is strong evidence that TMS to occipital cortex produces masking effects akin to those produced by a visual mask (Breitmeyer *et al.* 2004). Given this assumption, the similarity in how the two groups recovered from occipital TMS application suggests that there is no deficit in V1 processing in schizophrenia patients. This conclusion is in line with evidence that the deficit in schizophrenia in handling transient visual information may be later in the dorsal stream (Chen *et al.* 2003; Keri *et al.* 2000).

On the other hand, the way the deficit manifests may be based on other neural processes interacting with fast transient information. One crucial role for this information stream may be to prime the ventral pattern-processing pathway, framing the visual scene (Doniger *et al.* 2002; Schroeder *et al.* 1998). This may occur in conjunction with nonspecific input from the intralaminar thalamic nuclei (e.g. Bachman 1997), with higher-level control processes (Enns and Di Lollo 2000; Ramachandran and Cobb 1995), or with oscillatory processes involved with the integration or binding of perceptual features into objects (Green *et al.* 1999). The deficits seen in schizophrenia in backward masking might be due to abnormal interactions of transient information and any of these theoretical mechanisms, at any number of cortical locations, beginning with V1.

While the present study provided a demonstration of the need to explicitly explore individual differences in visual masking performance in patient populations, further studies are needed to validate and extend its findings. Present results indicate that patient differences in methods of assessing target visibility using luminance and duration staircasing should be investigated. In addition, the visual stimuli used in the present study were of the type known to be effectively masked by TMS. In the future, individual differences should be studied in masking paradigms using targets and masks whose properties are specifically

designed to preferentially affect the different visual streams in order to assess the generality of the present findings. The present study also provided a demonstration of the use of TMS to investigate visual pathways. However, targeting TMS on specific sites can be improved upon. Here, targeting a round coil was achieved using scalp landmarks. In the future, the use of coils with more focused magnetic fields, along with MRI guided coil registration and targeting based on imaging task-related activations on an individual basis, would make exploration of the dorsal pathway more efficient. Replication of the present TMS results using a greater number of subjects would help extend their generality. Overall, TMS may be an invaluable tool for the examination of neuropsychological function and dysfunction in schizophrenia as well as other psychiatric and neurologic illnesses.

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Figure 1.

The mean percentage accuracy across interstimulus interval (ISI) for three groups for backward (**A**): and forward (**B**): masking: healthy controls with above-criterion performance (open circles), patients with above-criterion performance (black circles), and subjects (patients and controls): with below-criterion performance (black squares).

Figure 2.

The mean accuracy (**A**): and normalized accuracy (**B**): across the target-to-TMS pulse intervals for healthy controls (open circles): and patients (black circles). TMS, transcranial magnetic stimulation.

Table 1

Characteristics of the Patient and Healthy Control Groups

Group	<i>n</i>	Gender (% male)	Age	Education ^a (years)
Patients	17	70.6	31.9 ± 9.0	12.9 ± 2.5
Controls	19	52.6	30.4 ± 8.9	18.9 ± 3.7

^aSignificant difference between patient and healthy control groups ($p < .001$).