Forward and Backward Visual Masking in Unaffected Siblings of Schizophrenic Patients

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Background: Visual masking tasks assess the earliest stages of visual processing. This study examined visual masking performance for forward and backward masking tasks in siblings of schizophrenic patients and healthy comparison subjects.

Methods: A staircase method was used to ensure that unmasked target identification was equivalent across subjects to eliminate differences due to discrimination of simple perceptual inputs. Four computerized visual masking tasks were administered to 43 siblings of patients and 42 normal comparison subjects. The tasks included: 1) locating a target; 2) identifying a target with a high-energy mask; 3) identifying a target with a low-energy mask; and 4) a paracontrast/metacontrast procedure with nonoverlapping target and mask.

Results: Across masking conditions, there was a significant group by forward/backward interaction, meaning that siblings showed a larger difference from control subjects in backward versus forward masking. This group difference was more pronounced in the location condition.

Conclusions: These results support the theory that visual masking procedures may be indicators of vulnerability to schizophrenia. The pattern of findings in this report (larger group differences on backward versus forward masking and on the location condition) suggests that the activity of transient visual channels may be particularly linked to vulnerability.

Key Words: Visual masking, schizophrenia, vulnerability, visual processing, backward masking, siblings

Visual masking has proved to be a highly versatile means to probe perceptual abnormalities in schizophrenia. In visual masking, the visibility of a briefly presented target is reduced by a mask that is presented very shortly before or after the target (Breitmeyer 1984; Breitmeyer and Ogmen 2000). If the mask follows the target in time, the effect is called backward masking; if the mask precedes the target, it is called forward masking. Schizophrenic patients consistently demonstrate performance deficits on visual masking tasks, meaning that they have more difficulty than comparison subjects in identifying the target in the presence of a mask (Cadenhead et al 1998; Green and Walker 1986; Rund 1993; Saccuzzo and Braff 1981).

Visual masking deficits in schizophrenia are not related to concurrent positive psychotic symptoms (Green and Walker 1986), nor are they related to antipsychotic medications (Braff 1981; Butler et al 1996). They are, however, related to other clinical features of schizophrenia, including negative symptoms (Green and Walker 1986; Slaghuis and Curran 1999; Weiner et al 1990), formal thought disorder (Perry and Braff 1994), and poor premorbid functioning (Knight 1992). The masking deficits are not diagnostically specific to schizophrenia and have been reported in chronic bipolar disorder (Green et al 1994a) but not in depression (Rund et al 2004). In addition, a study from our laboratory showed that visual masking performance was related to the performance of schizophrenic patients on a measure of social perception (i.e., ability to perceive a social context from brief vignettes) (Sergi and Green 2002).

There is evidence that performance on visual masking procedures may be a trait marker that reflects vulnerability to schizophrenia, as opposed to signs of clinical illness. One line of supporting evidence comes from studies that have reported masking deficits in patients who are in clinical remission (Green et al 1999; Miller et al 1979). A second line of evidence that is reflected by the current study comes from studies of first-degree relatives of patients (Bedwell et al 2003; Green et al 1997; Keri et al 2001; Lieb et al 1996).

Visual masking performance is frequently interpreted in terms of an interaction between two key visual channels that form the basis for complex visual processing and object perception (Van Essen et al 1992). In our previous papers, we have referred to these as transient and sustained channels, consistent with a large literature on visual masking. These terms are largely interchangeable with the anatomically based terms magnocellular and parvocellular (also called the M and P) channels. According to the Breitmeyer model, the sustained channel activity elicited by the target conveys relevant information that is needed to identify targets. Masking results from disruption of this target information by the transient and/or sustained channels of the mask (Breitmeyer 1984; Breitmeyer and Ganz 1976).

Convergent findings from several laboratories have suggested that the visual masking deficit in schizophrenia may be linked to an abnormality in transient channels (Cadenhead et al 1998; Green et al 1994b; Schechter et al 2003; Schuck and Lee 1989). Recent studies have used specialized procedures to separate the role of transient and sustained visual channels, including masks of different spatial frequency (Butler et al 2002, 2005), manipulating the color of stimuli (Schechter et al 2003), and the Vernier task that measures minimal level of detectable spatial displacement of stimuli (Keri et al 2004). These tasks have usually, though not always, implicated an abnormality in transient channels in schizophrenia. The study using the Vernier procedure also reported deficits in unaffected siblings of schizophrenic patients (Keri et al 2004). While studies have suggested transient channel abnormalities, it appears unlikely that sustained channels are fully normal in schizophrenia. We have noted abnormalities in gamma activity during visual masking (Green et al 2003a; Wynn et al, in press), and according to the

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model of Purushothuman et al (2000), this activity is a product of the sustained channels.

Evidence from the first-degree relatives suggests that aberrant transient channels may be a vulnerability indicator for schizophrenia. Two studies that found backward masking deficits in unaffected siblings of schizophrenic patients (Green et al 1997; Keri et al 2001) observed trends for the group differences to be more pronounced in tasks that placed a greater emphasis on transient channels (e.g., tasks that required subjects to locate, instead of identify, the target). Similarly, a recent study of 28 relatives of schizophrenic patients (including siblings, parents, and children) showed decreased sensitivity on a masking task for relatives versus control subjects when background color was changed from gray to red (Bedwell et al 2003). Because red light suppresses the transient system, the authors interpreted the pattern of results in which the performance of control subjects, but not relatives, was reduced to reflect an abnormality in the transient channels in relatives. Also, the relatives showed a more nonlinear masking function compared with control subjects on the location task when it was administered with neutral background. This pattern was viewed as additional evidence for aberrant transient channels in relatives. One additional study (Lieb et al 1996) failed to find masking deficits in a small sample ($n = 17$) of adolescents who were considered to be at high risk for schizophrenia because they were offspring of a parent with the illness. The two groups did not differ in overall performance.

The evidence for visual masking deficits in first-degree relatives of patients is suggestive but not fully consistent across studies. It is notable that three of the four studies suggest that differences between relatives and control subjects may be more apparent when the task places particular emphasis on the role of the transient channels.

The studies to date have two notable methodological limitations. First, no study has examined forward masking in relatives of patients. Whereas backward masking involves both transient and sustained channels, forward masking involves sustained channels almost entirely (Breitmeyer 1984). Hence, if siblings show deficits on backward but not forward masking, it would strengthen the argument that performance differences may reflect abnormalities in transient channels. A second limitation is that no study of siblings so far has examined visual masking deficits after equating groups for initial sensory input. All of the studies have used a suprathreshold target, meaning that subjects could identify the target easily in the absence of the mask. If the groups were to differ in unmasked target detection, the differences would be more accurately characterized as a basic problem in visual perception, as opposed to a specific visual masking deficit. A direct way to address this question is to use a thresholding procedure that equates subjects on perceptual input of an unmasked target.

With these limitations in mind, the goals of the current study were to examine visual masking deficits for forward and backward masking procedures in a sample of siblings of schizophrenic patients and healthy comparison subjects. We used computerized versions of four different masking conditions and we employed a staircase procedure to equate subjects in their unmasked performance.

Methods and Materials

Subjects

All participants in this study were part of the project, “Early Visual Processing in Schizophrenia” (M.F. Green, Principal Investigator). All subjects gave written informed consent after the procedures were fully explained. Human subject procedures were approved by the Institutional Review Boards of UCLA and the VA Greater Los Angeles Healthcare System. Subjects in the sibling group shared both biological parents with a patient whose diagnosis of schizophrenia was verified by project staff. The patient probands of the siblings were primarily recruited from the mental health clinics of the VA Greater Los Angeles Healthcare System. The procedures and visual masking results from the patient participants are presented elsewhere (Green et al 2003b; Rassovsky et al 2004, 2005). The control subjects in this current study are a subgroup of those from Green et al (2003b). Our earlier study included a subsample of recent-onset patients and their matched control subjects, and those control subjects are not part of the current study.

A total of 43 siblings of patients and 42 normal comparison subjects were assessed on the masking procedures. All subjects received a diagnostic interview with the Structured Clinical Interview for DSM-IV (SCID) (First et al 1997) and selected sections of the Structured Clinical Interview for DSM-IV Axis II Disorders (First et al 1996). All SCID interviewers were trained to administer the SCID by the Diagnosis and Psychopathology Unit of the UCLA Clinical Research Center for Schizophrenia. Interviewers were trained to a minimum kappa of .75 for key psychotic and mood items.

Four of the siblings were considered to have disorders in the schizophrenia spectrum and were excluded from the primary analyses. Two of these siblings had a diagnosis of schizophrenia, one had a diagnosis of schizoaffective disorder, and one had delusional disorder. Normal comparison subjects were recruited through flyers at various locations in the UCLA and VA medical centers and from notices in local newspapers. Potential participants were excluded if they had a history of any psychotic disorder, recurrent depression, bipolar disorder, substance dependence, or if they met criteria for any of the following Axis II disorders: avoidant, borderline, paranoid, schizoid, and schizophrenotypal. Mean age was 42.3 (SD = 9.1; range = 19–60) years and 35.9 (SD = 8.2; range = 22–54) years for the siblings and control subjects, respectively. Mean education was 13.6 (SD = 2.0; range = 10–19) and 13.5 (SD = 1.1; range = 12–16) for siblings and control subjects, respectively. The sibling group was 47% male subjects and the control group was 48% male subjects. The groups differed significantly on age ($p < .01$) but not on any other demographic variable.

Masking Procedures

We used specially developed computerized masking procedures that will be briefly summarized here and have been described in more detail elsewhere: for a description of the general methods, see Green et al (2002); for a description of the paracontrast and metacontrast procedures, see Rassovsky et al (2004). Prior to the visual masking trials, subjects were equated for unmasked performance with a psychophysical staircase method (Wetherill and Levitt 1965). In this thresholding procedure, target duration was constant at 13.3 milliseconds. We used a monitor that was driven at 150 Hz or 6.67 milliseconds for each sweep of the screen; so, 13.3 milliseconds represents two sweeps. The contrast of the target (i.e., gray scale value) was systematically varied both upward and downward, based on whether the subject’s response was correct or not. This method yields a contrast level at which all subjects are performing at roughly 84% accuracy for unmasked stimuli. By matching subject unmasked performance in this manner, any subsequent differences between groups can be attributed more clearly to masking deficits, instead of problems in basic visual input. The deter-
The target for all conditions was a square with a gap at the top, bottom, or left. The target could appear at any one of four locations on the screen (upper left, lower left, upper right, lower right). The mask for three of the masking conditions (location, identification, with a high-energy mask; identification with a low-energy mask) consisted of clusters of boxes that covered all possible target locations. For the paracontrast/metacontrast condition, the mask was a square that surrounded, but did not overlap, all possible target locations.

The target for all masking conditions (shown in Figure 1) was a square with a gap on one of three sides (up, down, or left) that could appear in any one of four locations on the screen (upper left, upper right, lower left, lower right). The subjects were asked to state the location of the gap on the target (for identification conditions) or the location of the target on the screen (for the location condition). To reduce response errors, subjects gave their response by speaking aloud and the test administrator entered the response on the computer. For the first three masking conditions, the mask consisted of adjacent boxes that appeared in the same area as the target (e.g., overlapping target and mask). For the last masking condition, the mask was a square that surrounded, but did not overlap, the possible target locations.

In this situation of nonoverlapping stimuli, forward masking is called paracontrast and backward masking is called metacontrast. A fixation point was presented starting 400 milliseconds before target presentation and ending 100 milliseconds before each target presentation. Each target location was 1.03° of visual angle from fixation and each target subtended 0.27° of visual angle. Stimulus onset asynchrony (SOA) was presented in randomized fashion and 12 trials were presented for each SOA, so that the three targets and four locations were counterbalanced. Twelve unmasked trials were interspersed in each masking condition to examine whether subjects were showing signs of fatigue during a session.

Four masking conditions were used that rely to differing degrees on sustained and transient channels (Breitmeyer and Ogmen 2000). The first condition, location, places more reliance on the transient channels. The first two conditions generate a “monotonic” masking function in which performance increases with increasing SOA for the backward portion of the masking function. The last two conditions typically generate a nonmonotonic masking function in which the backward masking portion is U-shaped. The U-shaped masking functions can occur when the mask is relatively weak compared with the target (as in the low-energy condition) or when the mask does not overlap the area of the target (as in paracontrast and metacontrast). The significance of a U-shaped masking function is that it suggests that primary masking mechanism involves interruption (i.e., the disruption of the sustained channels of the target by the transient channels of the mask) as opposed to integration (i.e., fusing of the sustained channel activity from both target and mask).

1. Location task with a high-energy mask. In this condition, subjects indicated where a target appeared but did not need to identify the target. The energy of the mask was twice that of the target (four screen sweeps for the mask; two for the target). The “energy” of a stimulus reflects the strength of a visual stimulus and it is determined by duration x intensity. Aside from the interspersed unmasked trials, this condition used 13 SOAs from -80 milliseconds to 80 milliseconds. This range in SOAs is smaller than the other conditions because location is typically an easier task than identification and it yields a more compressed masking function.

2. Identification task with a high-energy mask. In this condition, subjects identified a target when the energy of the mask was half the energy of the target (one screen sweep for the mask; two for the target). This condition used 15 SOAs from -120 milliseconds to 120 milliseconds.

3. Identification task with a low-energy mask. In this condition, subjects identified a target when the energy of the mask was equal to the energy of the target (two screen sweeps for both). We administered two blocks of trials for this masking condition (total of 24 trials per SOA). To make the number of trials comparable across the four masking conditions, we only used data from the first block of trials. This condition used 15 SOAs from -80 milliseconds to 120 milliseconds.

4. Identification paracontrast and metacontrast. In this condition, the subjects identified the target when the mask surrounded but did not spatially overlap the target. The energy of the mask was equal to the energy of the target (two screen sweeps for both). We administered two blocks of trials for this masking condition (total of 24 trials per SOA). To make the number of trials comparable across the four masking conditions, we only used data from the first block of trials. This condition used 15 SOAs from -80 milliseconds to 120 milliseconds.
it was included as a covariate in subsequent analyses. Initial analyses that included all four conditions were followed up with separate analyses for each of the four masking conditions.

**Results**

The critical stimulus intensity (the gray scale values that yielded 84% unmasked performance) was comparable for siblings and control subjects. Mean values (and SDs) for contrast levels were 28.0 (10.2) for siblings and 27.7 (9.3) for control subjects (a value of 1 is the lightest and 44 the darkest).

Results for siblings and control subjects for each of the four masking conditions are shown in Figures 2 through 5. Percent correct is shown on the y-axis and stimulus onset asynchronies (SOAs) are shown on the x-axis. Chance performance is 25% accuracy. Forward masking intervals are shown as negative numbers on the left and backward masking as positive numbers on the right.

Mixed model analyses were conducted excluding any sibling \((N = 4)\) with a diagnosis in the schizophrenia spectrum. There was no significant main effect for group, but there was a significant group by forward/backward interaction \((F = 4.88, df = 1,79, p = .03)\). In addition, the analyses revealed a main effect

**Figure 2.** Location condition: results for siblings of patients and control subjects. The siblings are shown with open circles and control subjects are shown with filled circles. Performance (percent correct) is shown on the y-axis and stimulus onset asynchronies (SOAs) are shown on the x-axis. Chance performance is 25% accuracy. Forward masking intervals are shown as negative numbers on the left and backward masking as positive numbers on the right.

**Figure 3.** Identification with high-energy mask: results for siblings of patients and control subjects. The siblings are shown with open circles and control subjects are shown with filled circles. Chance performance for this and the other identification conditions is 33% accuracy.

**Figure 4.** Identification with low-energy mask: results for siblings of patients and control subjects. The siblings are shown with open circles and control subjects are shown with filled circles.

**Figure 5.** Identification with paracontrast and metacontrast: results for siblings of patients and control subjects. The siblings are shown with open circles and control subjects are shown with filled circles.
for forward versus backward masking ($F = 185.1$, $df = 1.79$, $p < 0.001$), an effect of condition ($F = 65.3$, $df = 3,232$, $p < 0.0001$), but no group by condition interaction ($F < 1$, $df = 3,232$, ns). The group by forward/backward interaction can be viewed in Figures 2 through 5: siblings showed a larger difference from control subjects in backward as compared with forward masking.

Although the three-way interaction was not significant, we examined the four masking conditions separately with mixed model analyses to evaluate if the effects were pronounced in some conditions but absent in others, because such effects have theoretical importance for locating the disturbed visual channels. The general finding described above was most notable in one condition, location. There was a significant group by forward/backward interaction for this condition ($F = 4.59$, $df = 1.79$, $p < 0.05$) but not for any other condition. As in the overall analysis, the groups showed a larger difference in backward than forward masking. The overall three-way interaction test is relatively weak in this case because the group by forward/backward interaction occurred only in one of the four masking conditions. In fact, a specified contrast to examine backward versus forward masking revealed a group difference for the location condition that was significantly larger than the group difference averaged over the other three conditions ($t = 2.96$, $df = 232$, $p < .005$). Group main effects and the group by forward/backward interactions were not significant in any of the other three conditions ($p$-values ranged from .39 to .98).

Because the groups differed in age, we conducted another mixed model ANCOVA with age as a covariate. Age was related to masking performance and did not interact with group. The results were virtually identical to those reported above, and the key finding of a group by forward/backward interaction remained significant.

**Discussion**

In this study, we examined both forward and backward masking performance in siblings of schizophrenic patients and a control sample. In an initial thresholding procedure, the contrast level of the stimuli was adjusted to match subjects on their ability to perceive unmasked stimuli. We did not find differences in the contrast levels for the two groups, but we observed an overall group by forward/backward interaction for the masking conditions. The interaction was a result of larger group difference (with siblings performing more poorly) on backward versus forward masking, and this was true in the location condition when considered separately but not the other conditions. Because differences between siblings and control subjects were present after subjects were equated for unmasked performance, the masking differences are not attributable to problems in basic detection or perceptual input. Thus, while equating for unmasked performance may reduce the overall size of the observed performance deficit compared with prior sibling studies that did not include this refinement, it does allow the deficit to be attributed more clearly to visual masking.

The fact that the effect was more pronounced in the location condition is consistent with two previous findings (Green et al. 1997; Keri et al. 2001). Information about the location of targets can be carried by transient channels, whereas information for identification of the targets needs to be conveyed by the sustained visual channels that are more sensitive to high spatial frequency information (Breitmeyer 1984). We interpret the data to suggest an abnormality in the transient channels of unaffected siblings of patients.

The methods in the current study do not directly implicate specific brain regions that could underlie the difference in masking between siblings and control subjects. A separate component of this research program is focused on the regional brain activity that underlies visual masking. In the first paper from this line of investigation, we successfully adapted visual masking procedures for the functional magnetic resonance imaging (fMRI) scanner and identified several regions that seem to be related to masking effects, including the lateral occipital complex (visual region LO) (Green et al. 2005). We are currently applying these procedures to patients, siblings, and comparison subjects.

The current study is unable to address the question of whether the masking deficits are indicators of vulnerability to schizophrenia in particular or psychosis in general. Clearly, the masking deficits are not diagnostically specific, as they have been found in chronic bipolar patients (Green et al. 1994a, 1994b). Data from Keri et al. (2001) reported deficits in siblings of schizophrenic patients but not siblings of bipolar patients, tentatively suggesting that visual processing deficits may reflect trait and state factors in schizophrenia but only state factors in bipolar disorder.

The performance of the siblings on the backward masking location task is similar in pattern to that seen with patients (Green et al. 2003b). However, unlike patients with schizophrenia, the siblings in this study did not show deficits on forward masking. Some studies have reported selective deficits in patients on backward masking (Saccuzzo et al. 1996; Slaghuis and Bakker 1995). However, when we carefully examined this question using the same masking methods as those used in the current study, we found comparable levels of deficits in patients for forward and backward masking (Green et al. 2003b). Forward masking involves sustained channels to a greater extent than backward masking. Hence, this pattern of results suggests abnormalities in both transient and sustained channels (i.e., both forward and backward masking) for patients with schizophrenia but mainly in transient channels (backward masking only) for their siblings. Thus, it is possible that the vulnerability-linked component of masking involves transient channels, while sustained channel dysfunction is more tied to active symptomatic states. Hence, by using refined visual masking procedures, we may be able to separate out vulnerability indicators from episode indicators in schizophrenia (e.g., Nuechterlein and Dawson 1984; Zubin and Spring 1977).

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