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Pupillary Responses and Attentional Allocation Problems on the Backward Masking Task in Schizophrenia

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Abstract

Deficits in the early stages of visual information processing have consistently been found on the backward masking task in patients with schizophrenia, but the nature of this impairment remains unclear. Pupillography was used to measure attentional allocation during visual backward masking task performance in patients with schizophrenia (n=16) and nonpsychiatric controls (n=16). Schizophrenia patients detected significantly fewer targets than controls only when the stimulus onset asynchrony (SOA) between targets and masks reached 317 msec. For both groups, peak pupil dilation responses were also significantly larger in the 317 msec SOA condition relative to a no-mask condition, suggesting that the processing load of the 317 SOA masking condition was greater than the no-mask condition. In addition, a principal components analysis of pupillary response waveforms identified time-related components that appeared to differentially index attentional allocation to targets versus masks. Patients with schizophrenia showed less dilation than controls on a middle component that appeared to index attentional allocation to targets, but patients showed greater dilation than controls on a late component that appeared to index attentional allocation to masks. That is, controls attended more to targets than to masks, but patients attended more to masks than to targets. These findings suggest that masking impairments at SOA intervals greater than 100-200 msec may be due to abnormalities in attentional allocation mechanisms.

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Information-processing (IP) models provide a strong theoretical basis for stimulating research on cognitive impairment in schizophrenia. These models also offer established laboratory tasks that are highly sensitive to cognitive impairment in schizophrenia (Nuechterlein & Dawson, 1984). One well-studied task, the visual backward masking task, taps the time course of information passing through the sensory register. A target stimulus (e.g., letter) is visually presented and rapidly followed by a mask (e.g., patterned or random lines) at varying stimulus onset asynchronies (SOA) between the target and the mask (e.g., 10 to 700 msec). When the mask follows the target, it is called backward masking. Subjects typically must identify the target or its location. The masking stimulus is thought to interfere with the accurate identification or localization of the target, because it takes time for information to be transferred from the sensory register to short-term memory. If the mask is presented before this information transfer is completed, the target is less likely to be correctly identified.

When the mask is of similar energy (e.g., duration and luminance) to the target, studies have consistently reported impaired target identification at SOAs of about 120-350 msec in medicated and unmedicated, acute and remitted schizophrenia patients in more than 20 studies (Balogh & Merritt, 1987; Braff & Saccuzzo, 1981; Green, Nuechterlein & Mintz, 1994; McClure, 2001; Miller, Saccuzzo & Braff, 1979; Rund, Landro & Orbeck, 1993). This masking deficit has also been found in schizophrenia-spectrum subjects with schizotypal or psychosis prone traits (Steronko & Woods, 1978; Balogh & Merritt, 1985; Saccuzzo & Schubert, 1981) and in unaffected siblings of schizophrenia patients (Green, Nuechterlein & Breitmeyer, 1997). Masking task deficits, therefore, may reflect vulnerability or predisposition for schizophrenia, rather than the symptoms of the illness itself.

Despite consistent findings of masking task deficits in patients with schizophrenia, the nature of this impairment remains unclear. In particular, attention mechanisms have received surprisingly little study as a possible source of masking deficits in schizophrenia. When the masking interval is greater than 100 msec, identification of stimulus meaning is thought to occur in short-term visual memory (Phillips, 1974). At this point, limited controlled processes must be shifted and shared between targets.
Pupillary Responses

and masks to identify both stimuli, so attentional allocation to one or the other stimulus is required (Loftus, Hanna & Lester, 1988; Michaels & Turvey, 1979; Phillips, 1974). Michaels and Turvey (1979) referred to this as “replacement,” whereby target information is replaced by mask information as the main focus of attention. This is the first stage in early visual processing when masking deficits are attributed to attentional mechanisms or the allocation of processing resources. Target identification suffers after 100 msec intervals, not because of the quality of the target icon is degraded (e.g., by integration or interruption), but because target and mask icons compete for common stimulus identification algorithms. Backward masking task impairments in schizophrenia, which are most-commonly observed at masking intervals greater than 100 msec, may be due abnormalities in these attentional allocation mechanisms in short-term visual memory (Knight, 1992; 1993). Wasteful allocation of processing resources to mask processing would leave fewer resources available for accurate target identification (Braff, Saccuzzo & Geyer, 1991; Nuechterlein & Dawson, 1984).

Pupillometry methods can be used to examine attentional allocation during backward masking tasks. For many decades, the pupillary response has been used as a reliable and sensitive psychophysiological index of “mental effort” or the amount of processing resources allocated to a cognitive task (Beatty, 1982; Beatty & Lucero-Wagoner, 2000; Kahneman, 1973). Increased pupil dilation during cognitive task performance reflects increased allocation of processing resources to the task. In numerous studies (for a review, see Beatty, 1982; Beatty & Lucero-Wagoner, 2000), increased task processing load (e.g., more difficult perceptual discriminations, greater sentence syntax complexity, more arithmetic multiplicands) reliably evoked greater pupillary dilation responses, regardless of the cognitive domain tapped by different tasks.

In our previous research (Verney, Granholm & Dionisio, 2001; Verney, 2001; Verney, Granholm, Marshall, Malcarne & Saccuzzo, submitted), task-evoked pupillary responses of nonpsychiatric participants were recorded during a visual backward masking task. By comparing pupillary responses recorded in masked and no-mask conditions, it was possible to identify the amount
of processing allocated to targets versus masks, because pupil dilation in the no-mask condition reflected only target processing and pupil dilation in masked conditions reflected both target and mask processing. Pupil dilation were significantly greater in longer (317 and 717 msec) SOA conditions than in the no-mask condition, suggesting the mask only demanded additional processing when it was presented more than 100 msec after the target. This finding is consistent with masking models that predict attentional demands are highest in SOA conditions greater than 100-200 msec, because attention must be shifted and shared between targets and masks in order to identify both stimuli in short-term visual memory (Loftus, Hanna & Lester, 1988; Michaels & Turvey, 1979; Phillips, 1974).

A principal components analysis (PCA) of pupillary response waveforms was also computed in these studies (Verney, 2001, Verney et al., submitted). PCA is often used as a method of reducing the large number of time points in psychophysiological data to a small number of meaningful factors. Three time-linked factors were found: Early (0 to 0.7 s), middle (0.7 to 1.55 s), and late (1.55 to 3.0 s) components. The early factor occurred when pupil constrictions to light (e.g., from the computer display) typically peak (Loewenfeld, 1999) and likely indexed the pupillary light reflex. The middle factor occurred when pupil dilation responses to discrete trials of a cognitive task typically peak and correlate with task processing load (Beatty, 1982; Beatty & Lucero-Wagoner, 2000; Steinhauer & Hakerem, 1992). In addition, dilation on the middle factor tended to be greater in the no-mask condition (target processing only) relative to masking conditions (target and mask processing), especially for shorter SOA conditions. In contrast, dilation on the late factor was significantly greater in masking (target and mask processing) relative to no-mask (target processing only) conditions, especially in the longer SOA conditions. This pattern of results suggested that the middle factor indexed attentional allocation to targets, while the late factor indexed attentional allocation to masks.

In the present study, the pupillary responses of patients with schizophrenia and age- and education-comparable healthy control participants were recorded during performance of a target-identification version of the visual backward masking with an equal-energy mask. Consistent with
previous studies using similar masking tasks, we predicted that schizophrenia patients would show target identification deficits only in a longer (317 msec) SOA condition. We also predicted that the PCA factor structure for pupillary response waveforms found in our previous masking task research (Verney, 2001; Verney et al., submitted) would be replicated and that the patients with schizophrenia would show less dilation than controls on the middle (target) component and greater dilation than controls on the late (mask) component. This finding would be consistent with the hypothesis that attentional allocation problems (over-allocation to masks) at least partially contribute to masking task deficits in schizophrenia.

Method

Participants

Outpatients who met Diagnostic and Statistical Manual (fourth edition, or DSM-IV; American Psychiatric Association, 1994) criteria for a diagnosis of schizophrenia based on the Structured Clinical Interview for DSM-IV or SCID-patient version (First, Spitzer, Gibbon & Williams, 1995) were recruited. These patients were recruited from the Veterans Affairs San Diego Healthcare System, University of California, San Diego, Outpatient Psychiatry Services, San Diego County Mental Health Services, and private physicians. All patients were community-dwelling outpatients (i.e., not institutionalized). Symptom severity ratings were acquired for the patients using the Scales for the Assessment of Positive and Negative Symptoms (SAPS: $M = 5.2; SD = 5.1$; and SANS: $M = 6.0, SD = 4.1$; Andreasen & Olsen, 1982). Nonpsychiatric controls with no DSM-IV diagnoses of past or current mood or psychotic disorders (based on the SCID-Nonpatient Version; First et al., 1995) were also recruited to match the age and education of the patients. These participants were recruited from the general community, using local advertisements.

Patients and nonpsychiatric comparison participants were excluded for the following: (1) Neurological disorders (e.g., seizure disorder; head injury with loss of consciousness $> 30$ minutes); (2) history of any alcohol or substance dependence diagnosis (DSM-IV criteria) other than nicotine or
caffeine in the past year; (3) uncorrected/corrected visual acuity less than 20/50 based on a Snellen wall chart exam; (4) ocular medications, diseases or surgery that might affect pupil function; (5) near-chance performance in the no-mask condition (2 patients with 55% and 65% accuracy and 2 controls with 45% and 50% accuracy); and (6) abnormal pupil measurements (resting diameter and/or pupillary response outliers > 2 $SD$ or excessive artifacts in recordings). Table 1 displays the demographic characteristics of the final sample of 16 patients and 16 controls. Controls did not differ significantly from patients on age, $t(30) = 0.51$, $p > .05$, education, $t(30) = 0.00$, $p > .05$, Wechsler Adult Intelligence Scale – Revised Vocabulary subtest scaled scores (Wechsler, 1981; missing for 2 patients and 3 controls), $t(25) = 1.26$, $p > .05$, gender, $X^2(1) = 2.33$, $p > .05$, or ethnicity (Caucasian vs. Non-Caucasian), $X^2(1) = 0.53$, $p > .05$.

Eleven patients were taking typical antipsychotic medications, two were taking atypical antipsychotic medications, seven were taking anticholinergic medications, and two were not taking any psychotropic medications. Medication status was unavailable for one patient. The following current medication values were calculated: (1) Average daily dosage (mg) of antipsychotic medication as clinically recommended chlorpromazine equivalents (CPZE; Ereshefsky & Richards, 1990; Sadock & Sadock, 2000); and (2) average daily dosage (mg) of anticholinergic medication as clinically recommended benztropine equivalents (BZTE: Ereshefsky & Richards, 1990; Sadock & Sadock, 2000). The mean current daily dosage of CPZE for the 13 patients receiving antipsychotic medications was 309.8 mg ($SD = 247.0$) and the mean current daily dosage of BZTE for the 7 patients receiving anticholinergic medications was 3.4 mg ($SD = 1.4$).
Apparatus

A PC-compatible microcomputer and standard 15-inch color monitor was used to administer the masking task and store responses. A standard joystick equipped with two response buttons was used to collect responses. Participants sat facing the monitor with their head stabilized in a chin rest to maintain a distance of 77 cm between the subject and the computer monitor. Pupil area was recorded from the left eye using a Micromeasurements System 1200 corneal-reflection-pupil-center infrared pupillometer (Micromeasurements, Inc., Farmington, CT). A video camera sensitive to infrared light and an infrared light source were positioned 24 cm from the participant below the field of view between the participant and computer monitor. Analog pupil area was digitized at a 60 Hz sampling rate and saved for later offline processing. For consistency with the literature, area was then converted to diameter for all analyses. The resolution of the pupillometer was 0.05 mm diameter.

Procedure

On the backward masking task, two vertical lines of different length (2 cm & 3 cm) were presented side-by-side 3 cm apart randomly offset (i.e., not aligned at the top or bottom) in the center of the monitor. Subjects were asked to identify the longer of the two lines by pressing either the right or left response button corresponding to the right and left line. The targets were randomly and equally distributed to the right and left side. Both detection accuracy and speed was emphasized with the instruction, “Try to be as accurate as you can, but also be as fast as you can.” The target stimuli were followed by longer masking lines of 4 cm presented in the same locations as the target stimuli. In addition to a no-mask condition, the interval between the onset of the target and onset of the mask (stimulus onset asynchrony, or SOA) was 50, 67, 100, 134, 317 msec, for a total of 6 conditions. These SOA’s were chosen to be similar to those used in previous studies, within the constraints of the video refresh rate of the monitor (approximately 17 msec cycles). Due to the video refresh rate limitations, targets and masks were each presented for 17 msec.
Prior to the masking task, a calibration was conducted to ensure participant-pupillometer agreement on center of visual field. At the beginning of each trial, a green fixation square (0.85 cm x 0.85 cm, 0.63 degrees of visual angle, and 7 lux) was presented in the center of the monitor (with a black screen background) along with a high-pitched tone (1500 Hz for 500 ms). The fixation square and tone served as visual and auditory cues to warn the participant to prepare for the trial’s target stimulus. When the participant’s left pupil was detected as fixating on the green square for at least 200 ms, the program would terminate the fixation square and administer the trial. This procedure ensured that the participant was attending to the center of the screen, where stimuli were presented, and not blinking when the targets were flashed. Three seconds after the onset of the target stimulus, a low-pitched tone (800 Hz for 500 ms) served as an auditory cue signaling the end of the trial. Participants were asked to try to refrain from blinking during this trial period and only blink during a 3 second inter-trial interval.

Following 24 practice trials (4 per condition), 20 trials per condition were randomly presented, for a total of 120 test trials. The practice trials began with the easiest conditions, namely, two No-Mask trials followed by two 317 msec SOA trials. The SOA durations of the remaining 20 practice trials were randomly blocked. For the first half of the practice, computer-automated feedback was provided regarding correctness of participant’s response. Feedback was not provided during the test phase of the study. During test trials, a moment of rest was allowed after each presentation of 6 trials since the computer required time to periodically save strings of pupillary response data. In addition, each participant was allowed a few minutes to rest halfway through the test. The entire task (i.e., instructions, practice, and test) typically required less than 30 minutes. The percentage of correct target identifications and median response time for the 20 trials for each condition were recorded.

Data Analysis

Graphic displays of raw pupil diameter data were first visually inspected for gross artifacts by a trained technician and discarded for major artifacts and excessive blinking. A computer algorithm was
then used to remove eye blinks and other minor artifacts from other trials by linear interpolation. A 7-point smoothing filter was then passed over the data. For each participant, an average pupillary-response waveform was then calculated for the artifact-free trials of each SOA and no-mask condition. To remove individual differences in resting pupil size, baseline pupil size for each condition waveform (i.e., average of 5 pupil diameter samples recorded 100 msec prior to onset of the target display) was then subtracted from all subsequent samples for that waveform. Peak dilation for each condition waveform was then determined by picking the largest pupil dilation sample (change from baseline) within a 500-2500 msec window after onset of the target display. A principal components analysis (PCA) with varimax rotation was also performed on the 180 time point samples (i.e., three seconds) of the pupillary response waveform in each of the six conditions for each participant. Three factors were expected based on our previous research (Verney, 2001; Verney et al., submitted).

To test the hypothesis that the patients would show significantly impaired detection accuracy in longer (317 msec), but not shorter, SOA conditions, planned group comparisons of detection accuracy within each condition were computed using Bonferroni-corrected, independent samples, one-tailed t-tests. Pupillary responses were examined by computing a separate 2 (groups) X 6 (conditions) analysis of variance (ANOVA) for baseline pupil size and peak dilation. In addition, a 2 (groups) X 6 (conditions) X 3 (PCA components) analysis of variance ANOVA was computed for the factor scores from the pupil waveform PCA. Greenhouse-Geisser correction was used when sphericity assumptions were violated. To follow-up significant interaction effects for each ANOVA, Dunnett’s procedure was used to compare each masked condition with the no-mask condition, because the difference in processing demands between masked and no-mask conditions was of primary interest. Finally, a planned 2 (groups) X 2 (middle vs. late PCA factors) contrast was computed to test the hypothesis that the patients with schizophrenia would show less pupil dilation than controls on the middle (target) factor, but greater dilation than controls on the late (mask) factor.

Results
Backward Masking Task Performance

Figure 1 presents detection accuracy in each condition for each group. As predicted, the patients with schizophrenia detected significantly fewer targets than controls in the 317 msec SOA condition, t(30)=2.56, p<.05, but the groups did not differ significantly in any other masking condition. The patients with schizophrenia also detected fewer targets than controls in the no-mask condition, t(30)=3.08, p<.05. To control for this group difference in the ability to accurately perceive the target lines even when no mask was present, the groups were again compared in the 317 msec condition using no-mask condition detection accuracy as a covariate, and the groups still differed significantly, F(1, 29)=2.86, p=.05.

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Baseline Pupil Size

Baseline pupil size (see Table 2) did not differ significantly between the groups, F(1, 30)=0.49, p > .05, η² = .016, or across conditions, F(5,150) = 0.49, p > .05, η² = .016, and the group X conditions interaction was not significant, F(5, 150)=0.28, p > .05, η² = .009. The groups, therefore, did not differ significantly in baseline, resting pupil size.

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Insert Table 2 about here
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Pupillary Responses

Figure 2 shows the pupillary response waveforms and Table 2 shows peak dilation scores for all conditions for each group. Patients with schizophrenia showed significantly smaller overall peak dilation relative to controls, F(1, 30) = 6.96, p < .05, η² = .188. Peak dilation also differed significantly across SOA conditions, F(3.4, 150) = 2.61, p < .05 (Greenhouse-Geisser corrected), η² = .080, but the
group X condition interaction was not significant, $F(3.4, 150) = 1.57$, $p > .05$ (Greenhouse-Geisser corrected), $\eta^2 = .050$. The significant condition effect was examined using Dunnett’s tests to compare each masking condition with the no-mask condition for the combined sample of both groups.

Consistent with our previous research (Verney et al., 2001), peak dilation was significantly greater in the 317 msec SOA condition than in the no-mask condition ($p < .05$), but peak dilation in all other masking conditions did not significantly from the no-mask condition.

Pupillary Response Waveform Factor Structure

Consistent with our previous research (Verney, 2001; Verney et al., submitted), three prominent stable PCA components accounting for 97.0% of the variance in the pupillary response data. All factors were internally consistent and well defined by the data (the lowest of the squared multiple correlations for factors from data was .69). The three components formed a linear time course of the pupillary response waveform (see Figure 2): (1) An early light reflex component from 0 to 0.7 seconds (eigenvalue = 6.8); (2) A middle component from 0.7 to 1.62 seconds (eigenvalue = 21.8); and 3) a late component from 1.62 to 3.00 seconds (eigenvalue = 68.4). Table 2 presents PCA factor scores in each condition for both groups.

The 2 (groups) X 6 (masking conditions) X 3 (PCA factors) ANOVA showed significant effects for the condition X PCA factor interaction, $F(10,300) = 2.93$, $p < .01$, $\eta^2 = .089$, and the group X PCA factor interaction, $F(2,60) = 3.92$, $p < .05$, $\eta^2 = .116$. None of the other main effects or interactions were significant. The significant condition X PCA factor interaction was examined using Dunnett’s tests ($p < .05$) to compare each masking condition with the no-mask condition for the combined sample of both groups. For the early factor (see Table 2), no masking condition differed significantly from the
no-mask condition. For the middle factor (see Table 2 and Figure 3), significantly less pupil dilation was found for all masking conditions relative to the no-mask condition ($p<.05$). In contrast, for the late factor (see Table 2 and Figure 3), pupil dilation tended to be greater in all masking conditions relative to the no-mask condition, but the only difference to reach statistical significance was the 317 SOA vs. no-mask comparison ($p<.05$). The middle and late factors, therefore, showed the opposite pattern of dilation responses relative to the no-mask condition: Less dilation was shown for masking relative to no-mask conditions for the middle factor, and greater dilation was shown for masking relative to no-mask conditions for the late factor, especially in the longest SOA condition.

The significant group X PCA factor interaction was due to the different pattern of middle and late factor scores shown by the two groups (see Figure 4). Consistent with the study hypothesis, controls showed greater overall dilation (collapsing across conditions) than patients with schizophrenia on the middle (target) factor, but showed less overall dilation than patients with schizophrenia on the late (mask) factor, $F(1,30) = 8.75$, $p < .01$, $\eta^2 = .226$. For patients with schizophrenia, overall dilation on the late factor was significantly greater than on the middle factor, $t(15) = 3.78$, $p < .01$, whereas for controls, overall dilation on the middle factor was marginally greater than on the late factor, $t(15) = 1.65$, $p = .12$. Groups did not differ significantly on the early factor, and overall dilation for the early factor did not differ significantly from the middle or late factors for either group ($p > .05$).

Medication and Symptom Effects
Patients receiving anticholinergic medications (n=7) did not differ significantly (two-tailed t-tests) from patients not receiving these medications (n=9) on baseline pupil size, detection accuracy, peak dilation or any PCA factor score in any condition. In addition, current daily dosage of anticholinergic medication (BZTE) did not correlate significantly with any of these dependent variables in the patients. Similarly, daily dosage of antipsychotic medication (CPZE) did not correlate significantly with any of these dependent variables, except that greater CPZE dosage was associated with a smaller (more normal) factor score on the early (light reflex) factor, $r = -.50$, $p < .05$. Positive symptom severity (SAPS total) was not significantly correlated with any dependent variable. Greater negative symptom severity (SANS total) was significantly correlated with poorer detection accuracy in the 67 msec SOA condition, rho = -.54, $p < .05$. In summary, no meaningful, consistent associations between medications or symptoms and any of the dependent measures were found.

Discussion

The pupillary responses of patients with schizophrenia and healthy nonpsychiatric participants were recorded while they performed a target-identification version of the visual backward masking task with an equal-energy mask. Consistent with numerous previous studies using similar types of masking tasks, patients with schizophrenia showed impaired detection accuracy only in the 317 msec SOA condition (Balogh & Merritt, 1987; Braff & Saccuzzo, 1981; Braff, Saccuzzo & Geyer, 1991; Green et al., 1994; McClure, 2001; Miller et al., 1979; Rund et al., 1993). To investigate the role of attentional mechanisms in producing this commonly observed impairment, pupillary responses were recorded as an index of attentional allocation to targets and masks. Consistent with our previous research with healthy undergraduates (Verney, Granholm & Dionisio, 2001; Verney, 2001; Verney et al., submitted), peak dilation was significantly greater in the 317 msec SOA condition than in the no-mask condition. This finding is consistent with masking models that predict attentional demands are highest in SOA conditions greater than 100-200 msec, because selective attention must be shifted and shared between targets and masks in order to identify both stimuli in short-term visual memory.
(Loftus, Hanna & Lester, 1988; Michaels & Turvey, 1979; Phillips, 1974). Taken together, these behavioral and psychophysiological data indicate that the greatest masking task impairment was found in the SOA condition with the highest processing load. This suggests that masking impairments at SOA intervals greater than 100-200 msec may be due abnormalities in resource allocation and/or resource availability (Nuechterlein & Dawson, 1984).

The PCA findings provide additional evidence that attentional allocation deficits may contribute to masking task impairments in schizophrenia. The present study replicated the PCA factor structure found for pupillary response waveforms in two previous masking studies of healthy undergraduates (Verney, 2001; Verney et al., submitted). Three time-linked factors found were: Early (0 to 0.7 s), middle (0.7 to 1.62 s), and late (1.62 to 3.0 s) components. The early factor likely indexed the pupillary light reflex, because this factor occurred when pupil constriction to light is typically found (i.e., in response to light from stimuli on the computer screen; Loewenfeld, 1993). No interesting group or condition differences were found for this factor. The middle factor occurred when the extent of task-evoked peak pupil dilation is typically found to reflect the processing load associated with key task operations (Beatty, 1982; Beatty & Lucero-Wagoner, 2000; Steinhauer & Hakerem, 1992). The late factor occurred after this task processing load factor. Importantly, the middle and late dilation factors showed the opposite pattern of results when masking and no-mask conditions were compared. Less dilation was found for masking relative to no-mask conditions for the middle factor, but greater dilation was found for masking relative to no-mask conditions for the late factor, especially in the longest SOA condition. In the no-mask condition, only target processing was required and near-perfect target identification accuracy was found. In masking conditions, both target identification and mask processing was required and poorer target identification accuracy was found. Therefore, an index of target processing should show greater processing load in the no-mask condition, while an index of mask processing should show greater processing load in masking conditions. This was exactly the pattern of results found for the middle and late factors, respectively.
This interpretation of the late factor as indicating mask processing is consistent with the Michaels and Turvey (1979) “replacement” hypothesis that target processing is replaced by mask processing at SOAs greater than about 100-200 msec. Late (mask) factor dilation was greater in longer SOA conditions and differed significantly from the no-mask condition only in the longest (317 msec) SOA condition. This finding is also consistent with Phillips’ (1974) hypotheses that masking impairments after about 100 msec SOAs are due to limitations on controlled processes that select inputs to short-term visual memory where they are identified.

The nonpsychiatric participants showed greater dilation on the middle (target) factor than on the late (mask) factor, suggesting they selectively attended to targets more than masks. In contrast, patients with schizophrenia showed less dilation on the middle factor than on the late factor, suggesting they selectively attended more to masks than to targets. That is, patients with schizophrenia wastefully allocated more processing resources to masks, leaving fewer resources spared for target identification.

In the language of the Michaels and Turvey (1979) model, target processing was “replaced” by mask processing to a greater extent for patients relative to controls. This finding is consistent with an attentional allocation problem that occurs in a later stage of processing (e.g., short-term visual memory) when inputs compete for stimulus identification resources (Knight, 1992; 1993). This finding is also consistent with the hypothesis of Green et al. (1997) of an “attentional disengagement” deficit that occurs at interstimulus intervals greater than 70 msec. Thus, an attentional allocation problem in schizophrenia may partially contribute to masking task deficits on this type of masking task.

Research on the nature of masking task deficits in schizophrenia has typically focused on two other masking mechanisms: integration and interruption (or inhibition; Breitmeyer, 1984; Breitmeyer & Ganz, 1976; Breitmeyer & Ogmen, 2000). Integration is the fusing together of the target and mask representations into an indecipherable image and is maximal at shorter (e.g., 20 ms) intervals. Interruption occurs when processing of the target is disrupted by the incoming processing signals of the mask, resulting in only partial processing of the target, and typically occurs between 20 and 70 ms.
Pupillary Responses 17

intervals. In a neural system model of these two factors (Breitmeyer, 1984; Breitmeyer & Ganz, 1976; Breitmeyer & Ogmen, 2000), a transient visual pathway (magnocellular tract) rapidly detects and transmits low spatial frequency information about stimulus onset, offset and location, while a sustained visual pathway (parvocellular tract) responds more slowly and transmits high spatial frequency information about the finer details of stimulus processing. Integration occurs when information about the target and mask combine in sustained channels, and interruption occurs when transient mask activity inhibits sustained target activity, which inhibits correct identification of the target. There is some evidence that masking task deficits in schizophrenia may involve deficits in transient magnocellular pathways (Butler et al., 2001; Cadenhead, Serper & Braff, 1998; Green et al., 1994). However, a more recent expanded masking model (Breitmeyer & Ogmen, 2000; Purushothaman, Ogmen, & Bedell, 2000) emphasizes that synchronized gamma frequency oscillations in sustained channels may bind features of visual stimuli together, and there is some evidence that aberrant gamma range activity in schizophrenia may lead to sustained channel deficits (Green & Nuechterlein, 1999; Green, Nuechterlein & Breitmeyer, 1997; Kwon et al., 1999). Deficits in both channels may also be present.

The question of whether transient or sustained channel deficits or attentional resource allocation deficits better account for masking impairments centers on the question of whether input stages (e.g., quality of initial icon representation formation) or subsequent stages (e.g., competition for and allocation of higher cortical stimulus identification resources) can better account for deficits. This is an old controversy about peripheral versus more central deficits in schizophrenia research, which may be a meaningless distinction (Saccuzzo, 1977). For example, from the bottom-up, the magnocellular (transient) pathway helps orient attention toward salient stimuli, so overactive transient channel activity may be one mechanism by which a second input orients processing resources away from sustained processing of earlier relevant inputs (Butler et al., 2001; 2002). From the top-down, attention manipulations are known to modulate masking effects (Ramachandran & Cobb, 1995; Havig, Breitmeyer & Brown, 1998). Of note, patients with schizophrenia show normal performance on forward masking
Pupillary Responses

studies (i.e., when the mask precedes the target; Slaghuis & Bakker, 1995; Saccuzzo, Cadenhead & Braff, 1996), and Saccuzzo et al. (1996) suggest this indicates a centrally, rather than peripherally, mediated impairment. Other studies have also implicated central rather than transient channel deficits in schizophrenia (Keri, Antal, Szekeres, Benedek & Janka, 2000). In addition, based on animal studies, Sherman and Friedlander (1988) concluded that there are no significant inhibitory interneurons from magnocellular to parvocellular tracts. This suggests there is no neuroanatomic mechanism for a peripheral deficit in schizophrenia involving magnocellular (transient) inhibition of the parvocellular (sustained) tract. Further research is needed to reconcile this discrepancy between neuroanatomic animal studies and clinical studies of schizophrenia that implicate transient channel deficits. Regardless of the specific nature of the deficit, this study suggests a mechanism that results in an abnormal over-allocation of attention to masks rather than targets in schizophrenia.

Bachmann (1994; 1997) described a neurophysiological masking model that emphasizes the role of attention and activation mediated by thalamic reticular systems (Bachmann, 1994; 1997). In this model, identification and conscious awareness of a stimulus requires both a specific (SP) input carrying content information (e.g., orientation, color, form, spatial frequency, etc.) through classic visual pathways to visual cortex and a nonspecific (NSP) input from the thalamic reticular system. The NSP input is required to raise the level of activation of SP inputs to a level sufficient for awareness and identification. Because the NSP input is slower than the SP input, the timing of some masking intervals can lead to enhancement of mask SP inputs by target NSP inputs on backward masking tasks. Consistent with this model, several thalamic mechanisms are known to selectively enhance transfer and processing of sensory-perceptual data, such as sensory gating by the nucleus reticularis thalami (Scheibel, 1980; Crick, 1984) and cortical activity synchronization in cortico-thalamic loops (Alexander, DeLong & Strick, 1986; Crick, 1984). Interestingly, gamma oscillations that may be involved in masking effects can be produced by stimulus-driven activation of cortico-thalamic loops (Tallon-Baudry, Bertrand, Delpuech & Perneir, 1997).
It is possible that pupillary responses reflect these reticular-thalamic activation inputs. Pupil dilation is a function of the balance of activity between opposing sympathetic and parasympathetic systems. The brainstem nuclei driving these autonomic systems receive extensive inhibitory input from the reticular system and structures in cortico-thalamic loops. For example, electrical stimulation of the midbrain reticular formation in animals results in pupillary dilation (Loewenfeld, 1993). It is through these reticular connections that pupillary responses may provide an index of central brain systems that govern selective enhancement of sensory-perceptual inputs or attentional allocation (Beatty, 1986). In the present study, the reduced overall pupillary responses and abnormal distribution of pupillary responses between targets and masks found in patients with schizophrenia may implicate dysfunction in the general level of reticular system activation and/or the allocation of activation among inputs. Several investigators have emphasized thalamic mechanisms and cortico-thalamic loop dysfunction in schizophrenia (Andreasen, Arndt, Swayze, Cizadlo, Flaum, O’Leary, Ehrhardt & Yuh, 1994; Carlsson & Carlsson, 1990; Swerdlow & Koob, 1987).

Poor premorbid status and severe negative symptoms have been found to be associated with poorer masking task performance in other studies (Knight, 1992; 1993; Green & Walker, 1986). Perry and Braff (1994) also found that poorer masking task performance was associated with more severe thought disorder. In the present study, no significant associations were found between positive or negative symptoms and masking task performance or pupillary responses. The patients in the present study, however, were community-dwelling outpatients with relatively mild symptoms, so restricted range of symptom severity may have reduced symptom correlations. We also did not find any effect of medications on performance. Some previous studies found better performance in patients taking antipsychotic medications (Braff & Saccuzzo, 1982; Butler, Harkavy-Friedman, Amador & Gorman, 1996), but one found no differences between patients on and off medications (Butler et al., 2002). Consistent with previous studies (Granholm, Chock & Morris, 1998; Granholm, Morris, Asarnow,
Chock & Jeste, 2000; Granholm, Morris, Sarkin, Asarnow & Jeste, 1997; Steinhauer & Hakerem, 1992), medications also did not significantly impact pupillary responses in the present study.

This study had several limitations. For example, a standard target exposure duration was used in this study, because the limitations of our computer display did not permit matching participants for no-mask detection accuracy using a critical stimulus duration (CSD) procedure. At the exposure used, the patients with schizophrenia detected significantly fewer targets in the no-mask condition. This suggests that the patients may not have received the same amount of target information in the no-mask condition. Any group might show masking deficits relative to another group, if not provided with an equivalent amount of target information. We attempted to account for this by using no-mask detection accuracy as a covariate in group comparisons, and still found impairment in the longer SOA condition. However, masking effects are less ambiguous when no-mask performance is equated using a CSD or other procedure (e.g., graded increase in the difference in length between target lines). Future studies should also further validate our interpretations of the pupil waveform PCA factors found in our masking studies. Additional evidence that the late component reflects mask processing would be provided by manipulating the information value of the mask or using a procedure that required greater attention to masks and testing for increased dilation on the late factor with increased mask load. These studies are currently under way in our laboratory.
References


_Dissertation Abstracts International_.


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Table 1. Demographics of the Two Participant Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (years)</th>
<th>Education (years)</th>
<th>WAIS-R Vocabulary Scaled Score</th>
<th>Gender (% male)</th>
<th>Ethnicity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenia Patients (n=16)</td>
<td>50.0 (8.4)</td>
<td>12.8 (2.3)</td>
<td>10.2 (3.7)</td>
<td>81%</td>
<td>Caucasian 69%</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>African Am. 6%</td>
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<td></td>
<td></td>
<td>Hispanic 6%</td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Asian Am. 0%</td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td>Other/Unknown 19%</td>
</tr>
<tr>
<td>Nonpsychiatric Participants (n=16)</td>
<td>48.1 (12.6)</td>
<td>12.8 (1.3)</td>
<td>11.9 (3.0)</td>
<td>56%</td>
<td>Caucasian 56%</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>African Am. 25%</td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Hispanic 13%</td>
</tr>
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<td></td>
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<td></td>
<td>Asian Am. 0%</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Other/Unknown 6%</td>
</tr>
</tbody>
</table>

Notes: Values represent means (with standard deviations) and percentages where indicated. WAIS-R = Wechsler Adult Intelligence Scale–Revised (nonpsychiatric: n=13; schizophrenia: n=14). The groups did not differ significantly on any variable.
Table 2. Average median response times in each condition for each group

<table>
<thead>
<tr>
<th>SOA Condition</th>
<th>50 ms</th>
<th>67 ms</th>
<th>100 ms</th>
<th>134 ms</th>
<th>317 ms</th>
<th>No Mask</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenia</td>
<td>954(169)</td>
<td>979(192)</td>
<td>927(141)</td>
<td>917(140)</td>
<td>1017(239)</td>
<td>825(137)</td>
</tr>
<tr>
<td>Nonpsychiatric</td>
<td>936(310)</td>
<td>877(260)</td>
<td>856(268)</td>
<td>853(257)</td>
<td>842(272)</td>
<td>716(170)</td>
</tr>
</tbody>
</table>

Notes:
Values represent means (with standard deviations).

Table 3. Pupillary Response Measures for the Two Participant Groups

<table>
<thead>
<tr>
<th>Dependent Measure</th>
<th>SOA Condition</th>
<th>50 ms</th>
<th>67 ms</th>
<th>100 ms</th>
<th>134 ms</th>
<th>317 ms</th>
<th>No Mask</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Schizophrenia</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Baseline (mm)</td>
<td>3.92 (.73)</td>
<td>3.90 (.75)</td>
<td>3.92 (.72)</td>
<td>3.90 (.74)</td>
<td>3.93 (.75)</td>
<td>3.91 (.73)</td>
<td></td>
</tr>
<tr>
<td>Peak Dilation (mm)</td>
<td>.16 (.09)</td>
<td>.15 (.08)</td>
<td>.15 (.08)</td>
<td>.15 (.07)</td>
<td>.16 (.09)</td>
<td>.15 (.08)</td>
<td></td>
</tr>
<tr>
<td>Early PCA Factor</td>
<td>.29 (.36)</td>
<td>.29 (.23)</td>
<td>.27 (.47)</td>
<td>.26 (.57)</td>
<td>.24 (.39)</td>
<td>.33 (.46)</td>
<td></td>
</tr>
<tr>
<td>Middle PCA Factor</td>
<td>-.31 (.43)</td>
<td>-.41 (.43)</td>
<td>-.40 (.45)</td>
<td>-.35 (.42)</td>
<td>-.42 (.48)</td>
<td>-.28 (.64)</td>
<td></td>
</tr>
<tr>
<td>Late PCA Factor</td>
<td>-.14 (.40)</td>
<td>-.03 (.62)</td>
<td>-.09 (.45)</td>
<td>-.19 (.34)</td>
<td>-.09 (.33)</td>
<td>-.23 (.24)</td>
<td></td>
</tr>
<tr>
<td><strong>Non-psychiatric</strong></td>
<td></td>
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<td></td>
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<td></td>
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</tr>
<tr>
<td>Baseline (mm)</td>
<td>3.76 (.69)</td>
<td>3.76 (.68)</td>
<td>3.77 (.68)</td>
<td>3.76 (.67)</td>
<td>3.75 (.70)</td>
<td>3.74 (.67)</td>
<td></td>
</tr>
<tr>
<td>Peak Dilation (mm)</td>
<td>.21 (.09)</td>
<td>.20 (.07)</td>
<td>.22 (.07)</td>
<td>.23 (.08)</td>
<td>.25 (.09)</td>
<td>.23 (.08)</td>
<td></td>
</tr>
<tr>
<td>Early PCA Factor</td>
<td>.25 (.29)</td>
<td>.34 (.24)</td>
<td>.25 (.34)</td>
<td>.33 (.33)</td>
<td>.37 (.23)</td>
<td>.37 (.29)</td>
<td></td>
</tr>
<tr>
<td>Middle PCA Factor</td>
<td>-.24 (.20)</td>
<td>-.27 (.19)</td>
<td>-.26 (.19)</td>
<td>-.24 (.19)</td>
<td>-.26 (.21)</td>
<td>-.18 (.22)</td>
<td></td>
</tr>
<tr>
<td>Late PCA Factor</td>
<td>-.36 (.21)</td>
<td>-.34 (.26)</td>
<td>-.31 (.22)</td>
<td>-.32 (.21)</td>
<td>-.24 (.23)</td>
<td>-.36 (.23)</td>
<td></td>
</tr>
</tbody>
</table>
Figure Captions

Figure 1. Percent correct target detections in each masking and no-mask condition for each participant group. Error bars are ± 1 S.E.

Figure 2. Pupillary response waveforms recorded during a visual backward masking task are shown in each masking and no-mask condition for healthy controls (left) and patients with schizophrenia (right). Waveforms are divided into early, middle and late time-linked PCA components.

Figure 3. Middle (left) and late (right) pupillary response PCA factor scores in masking and no-mask conditions for the combined sample of both groups. Error bars are ± 1 S.E.

Figure 4. Overall (collapsing across masking and no-mask conditions) middle and late pupillary response PCA factor scores for each group. Error bars are ± 1 S.E.
Detection Accuracy (%) vs. Interstimulus Interval (msec)

- **Nonpsychiatric Controls**
- **Patients with Schizophrenia**

Data points for both groups show an increasing trend as the interstimulus interval increases.