Visual masking procedures assess the earliest components of visual information processing (1). In visual masking, a subject’s ability to identify a visual stimulus (target) is reduced by another visual stimulus (mask) presented shortly before or after the target. Relative to healthy subjects, schizophrenia patients require longer time intervals between target and mask to identify the target (2). Despite the role of attentional deficits in schizophrenia (3), the effects of attentional manipulation on visual masking have not been explored.

The goal of the present study was to examine the effects of attentional manipulation on visual masking in schizophrenia. Schizophrenia patients and healthy comparison subjects completed a computerized masking task (4, 5). We cued attention to create a momentary enhancement of attentional allocation (i.e., increased readiness) by associating selected trials of the task with monetary reward. We predicted that cue manipulation would produce improved performance for both patients and healthy subjects.

Method

The present study included 105 schizophrenia outpatients (92% [N=97] of whom were male) and 52 nonpsychiatric comparison subjects (51% [N=27] of whom were male). The two groups are described in detail elsewhere (5). All patients were receiving antipsychotic medications (66% [N=70] were receiving second-generation antipsychotics). Mean illness chronicity was 13.6 years (SD=9.5). Patients’ average positive and negative symptom scores, according to the Brief Psychiatric Rating Scale, were 2.58 (SD=1.22) and 2.01 (SD=0.93), respectively. All participants gave written informed consent after receiving a full explanation of the research according to procedures approved by the institutional review boards of UCLA and the VA Greater Los Angeles Healthcare System.

A computerized system was used to administer the masking procedures (see reference 4 for a description of masking procedures, reference 5 for description of the metacontrast procedure). Initially, we equated participants’ unmasked target identification scores, according to the Brief Psychiatric Rating Scale, were 2.58 (SD=1.22) and 2.01 (SD=0.93), respectively. All participants gave written informed consent after receiving a full explanation of the research according to procedures approved by the institutional review boards of UCLA and the VA Greater Los Angeles Healthcare System.

A computerized system was used to administer the masking procedures (see reference 4 for a description of masking procedures, reference 5 for description of the metacontrast procedure). Initially, we equated participants’ unmasked target identification by using a staircase method (6). During this thresholding procedure, the contrast of the target (i.e., grey scale value) was systematically adjusted on the basis of the subject’s performance to achieve 84% performance accuracy. This contrast level was used for subsequent masking procedures. A metatraceout contrast masking procedure was used in which the mask surrounds, but does not spatially overlap, the target. The target was a square with a gap that could appear at the top, bottom, or left side (5). Targets could appear at any one of four locations on the screen (upper left, upper right, lower left, lower right). The mask was a square that surrounded all possible target areas. Stimulus onset asynchronies were spaced at 13.3-msec increments, with 24 trials administered at each stimulus onset asynchrony. On half the trials, the fixation was a small cross (standard trials); on the other half it was a star (cued trials). The fixation symbol appeared 900–100 msec before target onset. For the attentional manipulation, participants were instructed that a star indicated they would earn 5 cents if they got the next trial correct and they were paid upon session completion. Target type, location, and fixation type were randomized.

We used a factorial repeated measures analysis of variance. Diagnosis (schizophrenia versus comparison) was the between-subject factor. The within-subject design was a two-by-nine (standard versus cued trials by stimulus onset asynchrony) factorial. Primary interest focused on the interaction of diagnosis (schizophrenia versus comparison) and reward (standard versus cued trials).

Results

Analyses revealed a significant main effect for diagnosis (F=16.59, df=1, 155, p<0.0001), indicating that patients exhibited poorer performance than the comparison subjects during both standard and cued conditions. Patients demonstrated modest, but statistically significant, improvement in performance with the cuing (Figure 1). This improvement was not significant for the comparison subjects. The stimulus onset asynchrony-by-reward interaction was also significant for the schizophrenia patients (F=3.78, df=8, 832, p<0.0002) but not for the comparison subjects. We found a significant main effect for stimulus onset...
studies appears to increase momentary allocation of attentional resources during attentional manipulation and that the attentional enhancement effect was larger in patients than in comparison subjects. Thus, attentional manipulation in both schizophrenia patients and healthy comparison subjects demonstrated improved eye tracking during attentional manipulation and that the attentional enhancement effect was larger in patients than in comparison subjects. The fluctuating pattern of performance across stimulus onset asynchronies is likely a reflection of cortico-cortical oscillations in the gamma range (7).

Improvement in performance with cuing was not significant for the comparison subjects. The influence of attention on this particular measure appears quite limited. Top-down influences for patients with schizophrenia are likely to be greater in visual tasks that emphasize later stages or more complex stimuli. This finding is consistent with growing evidence for top-down attentional effects at the earliest levels of visual processing (9). The term “top-down influences” could refer to either the influences of attention on perception or the effect of re-entrant processes. These two effects may share similar circuitry and may be closely associated. As Posner has suggested (10), attention can have an effect either by amplifying the initial feed-forward activation at a given cortical site in the visual system or by enhancing the amount of reentrant activation. Typically, reentrant processing (11) is contrasted with feed-forward processing. According to feed-forward theories, perception is thought to occur through unidirectional processing of information from lower to higher levels in the brain. Reentrant processing, on the other hand, is accomplished through iterative exchanges of neural signals among levels (11). Communication between brain areas, according to the reentrant view, occurs as ascending and descending pathways form an iterative loop so that ascending stimuli would be influenced by descending top-down activity through the iterative loop process (12).

These findings that even the earliest stages of visual information processing are responsive to attentional manipulation in patients suggest very early top-down influences on the visual system. However, given the modest improvement in performance among patients and lack of improvement among comparison subjects, the influence of attention on this particular measure appears quite limited. Top-down influences for patients with schizophrenia are likely to be greater in visual tasks that emphasize later stages or more complex stimuli.

Discussion

Relative to the comparison subjects, patients exhibited poorer performance during both standard and cued conditions of a metacontrast procedure. Schizophrenia patients demonstrated modest, but statistically significant, improvement in performance with cuing. The improvement was not significant for the comparison subjects. The nonsignificant diagnosis-by-reward interaction indicated that the magnitude of patients’ improvement with cuing was not significantly greater than that of the comparison subjects. The fluctuating pattern of performance across stimulus onset asynchronies is likely a reflection of cortical oscillations in the gamma range (7).

Our findings are consistent with those from a study that examined the effects of attentional enhancement on eye tracking in recent-onset schizophrenia patients (8). Yee et al. found that both schizophrenia patients and healthy comparison subjects demonstrated improved eye tracking during attentional manipulation and that the attentional enhancement effect was larger in patients than in comparison subjects. Thus, attentional manipulation in both studies appears to increase momentary allocation of attention. The fact that attentional enhancement effects are either smaller or lacking among healthy subjects in these studies may indicate that comparison subjects are already using optimized attentional allocation during these tasks.

Our results offer modest support for “top-down” influences on visual perception in patients. This suggestion is consistent with growing evidence for top-down attentional effects at the earliest levels of visual processing (9). The term “top-down influences” could refer to either the influences of attention on perception or the effect of re-entrant processes. These two effects may share similar circuitry and may be closely associated. As Posner has suggested (10), attention can have an effect either by amplifying the initial feed-forward activation at a given cortical site in the visual system or by enhancing the amount of re-entrant activation. Typically, re-entrant processing (11) is contrasted with feed-forward processing. According to feed-forward theories, perception is thought to occur through unidirectional processing of information from lower to higher levels in the brain. Re-entrant processing, on the other hand, is accomplished through iterative exchanges of neural signals among levels (11). Communication between brain areas, according to the re-entrant view, occurs as ascending and descending pathways form an iterative loop so that ascending stimuli would be influenced by descending top-down activity through the iterative loop process (12).

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References

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In our previous 6-week acute study of ziprasidone and olanzapine in 269 patients with schizophrenia or schizoaffective disorder (1), both drugs showed comparable efficacy. Olanzapine, however, was associated with significant increases in body weight, total cholesterol, triglycerides, low-density lipoprotein cholesterol, and fasting insulin. Responders in the acute study (Clinical Global Impression [CGI] improvement score ≤2 or ≥20% reduction in symptom severity according to Positive and Negative Syndrome Scale total score) were enrolled in a 6-month, double-blind, multicenter continuation study, which compared the long-term efficacy and tolerability of these agents as maintenance treatment. After completion of the 6-month continuation study, patients could opt into a blinded extension study lasting up to 2 years. Data from the continuation study and extension study are reported here.

**Method**

Entry criteria for the acute study (1) included a primary DSM-IV diagnosis of schizophrenia or schizoaffective disorder. Enrollment criteria for the 6-month continuation study included 1) completion of 6 weeks’ double-blind treatment with ziprasidone or olanzapine, 2) a CGI improvement score of ≤2 or a ≥20% reduction in Positive and Negative Syndrome Scale total score at acute-study endpoint, and 3) outpatient status. Dosing for the continuation phase was flexible (ziprasidone, 40, 60, or 80 mg b.i.d.; olanzapine, 5, 10, or 15 mg/day) and based on investigators’ clinical judgment.