The speed of visual attention in schizophrenia: Electrophysiological and behavioral evidence

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Abstract

Schizophrenia is characterized by a substantial slowing of manual response times and by impairments in attention. However, prior research has not investigated whether attention itself is slowed in schizophrenia, and this was the goal of the present study. In Experiment 1, the N2pc component of the event-related potential waveform—an electrophysiological correlate of the focusing of attention—was recorded from 24 schizophrenia spectrum patients and 13 control subjects. Although behavioral response times were delayed by over 100 ms in the patient group, the onset latency of the N2pc component was virtually identical across groups, and no reduction in N2pc amplitude was observed in the patient group. In Experiment 2, a new cueing paradigm was developed to provide a behavioral measure of the speed of attention in 22 schizophrenia spectrum patients and 13 control subjects. We found that the average time required to allocate attention to a cued location was only 19 ms greater for the patient group than for the control group, with most patients within the range of the control subjects. Together, these experiments revealed little or no slowing of the allocation of visual–spatial attention in patients with schizophrenia. Thus, the mechanisms responsible for allocating attention to salient visual targets appear to be largely unaffected by the illness, and the well-documented slowing of manual response times in schizophrenia cannot easily be explained by a slowing of attention.

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Keywords: Schizophrenia; Attention; Event-related potential; ERP; N2pc; Speed of processing

1. Introduction

Deficits in attention have been viewed as a core element of schizophrenia since the first clinical descriptions of the disorder (Bleuler, 1911; Kraepelin, 1919), and empirical studies have documented robust impairments in attention (Nuechterlein and Dawson,
However, attention is a complex cognitive construct that can be defined in many ways (Zubin, 1975), and it has been difficult to pinpoint the precise nature of the attention deficit in schizophrenia. Other research has pointed to a general slowing of processing, which can be seen most dramatically in the pervasive finding of slowed manual response times (RTs) in discrimination tasks (reviewed by Nuechterlein, 1977) and in impaired performance on traditional psychometric measures of processing speed such as Digit Symbol and Trailmaking (Dickinson et al., 2004; Heaton et al., 2001). Indeed, Cancro et al. (1971) have called RT slowing the “closest thing to a north star in schizophrenia research.”

It is possible that the deficit in attention and the slowing of processing actually represent the same underlying impairment, namely a slowing in the allocation of attention. However, there has been no systematic exploration of whether schizophrenia involves a slowing of shifts of attention. Many studies have compared the effects of various attentional manipulations on the task performance of schizophrenia patients and control subjects (e.g., Carr et al., 1998; Posner et al., 1988), but the vast majority of these studies have not directly measured the time required to allocate or shift attention. It is entirely possible that attention is less effective in patients but still operates with the same speed, and it is also possible that the speed of allocation would be slowed in patients with no reduction in the ultimate effectiveness of attention. Thus, measurements of the effectiveness of attention do not speak to the speed of attention allocation.

Special procedures are necessary to measure the speed of attention from behavioral data. Moreover, although timing information is an intrinsic part of event-related potential (ERP) recordings, ERP studies of schizophrenia have not typically focused on components that reflect specific attention mechanisms. For example, although many studies have examined the latency of the P3 wave (reviewed by Jeon and Polich, 2003), and some researchers have argued that P3 amplitude can be used as an indirect index of the amount of resources allocated to a given stimulus (e.g., Isreal et al., 1980; Kramer et al., 1988), there is no evidence suggesting that the P3 wave itself reflects the operation of an attention mechanism (unless attention is defined so broadly that it includes all controlled cognitive processing). Thus, the goal of the present study was to measure the speed of attention shifts in schizophrenia patients and control subjects using behavioral and ERP methods that were designed for this specific purpose.

Two converging experiments were conducted, one using a an ERP component that directly indexes the allocation of visual–spatial attention and another using a behavioral paradigm that was designed to measure the time course of attentional orienting. The advantage of the ERP measure is that it provides a millisecond-by-millisecond measure of the allocation of attention, directly revealing the time course of shifts of attention. The advantage of the behavioral measure is that it is more directly related to the ultimate function of the system. Together, these two measures provide strong converging evidence regarding the speed with which visuospatial attention can be allocated.

2. Experiment 1

In this experiment, we focused on the N2pc (N2-posterior-contralateral) component of the ERP waveform, an extensively studied and well validated correlate of the focusing of visual attention (Eimer, 1996; Luck et al., 1997; Luck and Hillyard, 1994a,b). When subjects focus attention onto a target item in a bilateral stimulus array, the N2pc component is observed as a negative-going deflection at contralateral electrode sites between 200 and 300 ms post-stimulus. An initial study of event-related magnetic fields (ERMFs) showed that the N2pc component is generated in lateral occipitotemporal cortex (Hopf et al., 2000), and a more recent study combining ERMFs, ERPs, and functional magnetic resonance imaging (fMRI) has shown more specifically that it arises from the human homologues of monkey inferotemporal cortex and area V4 (Hopf et al., 2006). In addition, studies of functional similarities have provided evidence that the N2pc component is a human ERP homologue of attentional modulations of single-unit activity that have been observed in these same areas in macaque monkeys (Chelazzi et al., 1998, 2001; Luck et al., 1997).

A major advantage of the N2pc component is that its contralateral scalp distribution allows it to be isolated from the rest of the ERP waveform, which is largely
bilateral when bilateral stimulus displays are used. Specifically, the N2pc component can be isolated by presenting a lateralized target within a bilateral stimulus array and by computing difference waves in which the response at a given electrode for an ipsilateral target is subtracted from the response at that electrode for a contralateral target. The resulting difference waveform reflects only the lateralized N2pc component and not the many bilateral ERP components that would otherwise overlap with the N2pc component (see Chapter 2 in Luck, 2005 for a general discussion of this approach). Moreover, although many ERP components are lateralized when unilateral stimuli are presented, these components are bilateral in response to bilateral stimulus arrays; consequently, these components are also eliminated by this subtraction procedure. Thus, the use of bilateral stimulus arrays containing a lateralized target makes it possible to accurately measure N2pc onset latency, which provides a precise measure of the time at which perceptual processing becomes focused onto the target item (Woodman and Luck, 2003a,b). A similar procedure is widely used to isolate the lateralized readiness potential, a measure of response preparation (e.g., Dehaene et al., 1998; Gratton et al., 1988; Hsieh and Yu, 2003; Miller and Hackley, 1992; Osman et al., 2003). By using this procedure, it is possible to isolate the N2pc component from other ERP components that are unrelated to shifts of attention, yielding a highly precise means of measuring the speed with which attention can be deployed to a target item. If schizophrenia involves a slowing in the speed with which attention can be shifted to a target item, then the onset latency of the N2pc component should be delayed in patients relative to matched control subjects.

For the sake of comparison with other studies, we also compared the overall ERP waveforms between the patient and control groups. However, it is very difficult to isolate specific ERP components in this manner (Luck, 2005), so strong conclusions about specific cognitive processes cannot easily be drawn from these waveforms.

2.1. Method

2.1.1. Participants

Twenty-two patients meeting DSM-IV criteria for schizophrenia (7 paranoid, 1 residual, 13 undifferentiated) or schizoaffective disorder (1) and 13 healthy control subjects participated in this experiment. Diagnosis was established for each patient using a best estimate approach combining information from past medical records, collateral informants (when available), and the results of a Structured Clinical Interview for DSM-IV. The patients were clinically stable outpatients living alone, with families or in residential settings. Symptom ratings and demographic information are presented in Table 1. Five of the patients were employed or enrolled in school full time; five worked part-time; and 12 were unemployed or participated in day programs. The patients, on average, were not highly symptomatic. Sixteen patients were receiving second-generation antipsychotic medications, five were receiving traditional antipsychotic medications, and one was receiving both. All patients had been receiving the same medication, at the same dose, for at least 8 weeks prior to study participation. The control subjects were recruited from the same community, but had no current Axis I or Axis II spectrum disorder and no

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Participant demographics</th>
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<tr>
<td></td>
<td>Experiment 1</td>
</tr>
<tr>
<td>Patients</td>
<td>Controls</td>
</tr>
<tr>
<td>Age</td>
<td>43.1</td>
</tr>
<tr>
<td>Education</td>
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<tr>
<td>Father’s education</td>
<td>13.5</td>
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<tr>
<td>Male/Female</td>
<td>19:3</td>
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<tr>
<td>AA/A/H/C/O</td>
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<td>WRAT-3</td>
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<td>SANS—total score</td>
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<tr>
<td>BPRS—total score</td>
<td>30.0</td>
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<tr>
<td>BPRS-anxiety/depression</td>
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<td>BPRS-negative symptoms</td>
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<tr>
<td>BPRS-positive symptoms</td>
<td>9.6</td>
</tr>
<tr>
<td>BPRS-activation</td>
<td>3.8</td>
</tr>
<tr>
<td>BPRS-hostility/suspicion</td>
<td>4.3</td>
</tr>
</tbody>
</table>


※ Data are unavailable for 1 patient in Experiment 1.
\[\text{ }\]

※ Data are unavailable for 4 patients and 1 control subject in Experiment 1 and for 2 control subjects in Experiment 2.

※ Data are missing for 3 patients and 1 control.

※ Data are missing for 6 patients in Experiment 1 and 4 patients in Experiment 2 for the BPRS and SANS.
family history of psychotic disorder. The two groups did not differ on demographic variables other than Wide Range Achievement Test (WRAT) scores (see Table 1).

All subjects provided informed consent, and the protocol was reviewed by the Institutional Review Board of the University of Maryland School of Medicine.

2.1.2. Stimuli and task

The stimuli are illustrated in Fig. 1. They were viewed from a distance of 100 cm and presented on a CRT with a dark gray background and a continuously visible fixation cross. Each stimulus array consisted of 12 items in the left visual field (LVF) and 12 items in the right visual field (RVF). All of the items were white, except for one red item and one green item. The red and green items appeared on opposite sides of the array, and the color on a given side varied randomly from array to array. Consequently, the location of the target was unpredictable. Each item was a \(0.36 \times 0.36\) outlined square with a \(0.26\) gap on one side. The gap was on the left or right side of the white squares (randomly determined), and it was on the top or bottom of the colored squares (randomly and independently determined; see Fig. 1 for stimulus spacing information).

At the beginning of each trial block, the subject was instructed to attend either to the red item or to the green item, which served as the target for that block. They were further instructed to press the top button on a game controller, using the index finger, if the target square contained a gap on the top and to press the bottom button, using the middle finger, if the target square contained a gap on the bottom.

Each array was presented for 2000 ms, followed by an intertrial interval of 1000 ms. Arrays were presented in blocks of 128 trials, with three 26-s rest breaks interposed within each block and a long break between blocks. Each subject completed three attend-red blocks and three attend-green blocks in alternating order, with the starting color selected at random. A total of 192 trials were presented for each combination of attended color and target side. Accuracy was measured as the proportion of trials on which the correct response was emitted, and RT was summarized as the median of the individual correct-response RTs for each subject.

2.1.3. Recording and analysis

The EEG was recorded from tin electrodes in an elastic cap using a subset of the International 10/20 System sites (F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, T3, T4, T5, T6, O1, O2, and left earlobe) and two nonstandard sites (OL, halfway between O1 and T5; and OR, halfway between O2 and T6). These electrodes were recorded using a right earlobe reference electrode, and the signals were re-referenced offline to the average of the left and right earlobes (Luck, 2005; Nunez, 1981). The horizontal electro-oculogram (HEOG) was recorded as the voltage between electrodes placed 1 cm lateral to the external canthi and was used to measure horizontal eye movements. The vertical EOG was recorded from an electrode beneath the left eye, referenced to the right earlobe, and was used to detect blinks. The EEG and EOG were amplified by a Neuroscan Synamps amplifier with a gain of 5,000 and a bandpass of 0.05–100 Hz, and the amplified signals were digitized at 500 Hz and averaged offline with a 200-ms prestimulus baseline. A digital low-pass filter was applied offline (Gaussian impulse response function,
half-amplitude cutoff = 18.5 Hz, full width at half maximum = 23 ms). Trials with incorrect behavioral responses or EEG/EOG artifacts were excluded from the averages using our standard procedures (Woodman and Luck, 2003b).

Ocular artifacts led to the rejection of 32% of trials in the patient group and 29% of trials in the control group. We also examined the averaged HEOG waveforms after artifact rejection to ensure that the averaged ERP waveforms were not contaminated by small eye movements that escaped rejection. These residual eye movements averaged less than 0.2°, causing negligible distortion of the ERP waveforms.

To isolate the N2pc component, we constructed difference waves in which the waveforms for trials with an ipsilateral target (relative to the electrode site) were subtracted from the waveforms for trials with a contralateral target. To eliminate any hemispheric asymmetries that were unrelated to attention, we then averaged the difference waves across left- and right-hemisphere electrode pairs. N2pc amplitude was measured from these difference waves as the mean amplitude between 200 and 400 ms at the posterior electrode sites (P3/4, O1/2, OL/R, T5/6). Latency measures can be highly sensitive to noise, and we therefore averaged together the difference waves across these posterior electrode sites and applied a low-pass filter before measuring N2pc latency (Gaussian impulse response function, half-amplitude cutoff = 5.8 Hz, full width at half maximum = 75 ms). Peak latency was measured as the local peak latency between 175 and 400 ms (Luck, 2005), and onset latency was measured as the time point at which the voltage reached 50% of the local peak amplitude (Miller et al., 1998).

The amplitudes of the other ERP components were measured from waveforms in which contralateral and ipsilateral targets were combined. Mean amplitude measurements were taken at the posterior electrode sites (P3/4, O1/2, OL/R, T5/6) for four time periods, 100–200 ms, 200–300 ms, 300–400 ms, and 400–500 ms.

Analysis of variance (ANOVA) was used for all statistical tests with an alpha level of .05, and probability values were adjusted when appropriate with the Greenhouse–Geisser epsilon correction for nonsphericity (Jennings and Wood, 1976). In analyses of behavioral data and N2pc latency, group (patient versus control) was a between-subjects factor, and target color was a within-subjects factor. The N2pc amplitude analysis included these two factors and an additional within-subjects factor of electrode site (P3/4, O1/2, OL/R, T5/6). The analyses of the other ERP components included these three factors and another within-subjects factor of electrode hemisphere.

2.2. Results

2.2.1. Behavioral results

The top two rows of Table 2 summarize the behavioral results and statistical analyses of these results, and Fig. 2A shows the individual median RTs along with group means and 95% confidence intervals. Mean accuracy was greater than 90% correct in both the patient and control groups. The mean of the median RTs was 137 ms slower in the patient group than in the control group. Both groups were approximately 40 ms faster when discriminating red targets than when discriminating green targets, indicating that the red item was more salient than the green item.

To provide a more detailed view of the RT data, Fig. 2B shows the probability distribution of RT for red and green targets in the patient and control groups. For both groups, the distribution for green targets was shifted rightward compared to the distribution for red targets, indicating that the color of the target influenced the minimum amount of time required to perform the task. Similarly, the RT distributions for the patient group were shifted rightward compared to the RT distributions for the control group, indicating that the minimum amount of time to perform the task was greater for the patient group than for the control group. In addition, the RT distribution was somewhat broader for the patient group than for the control group, indicating that RT was more variable in the patient group.

2.2.2. N2pc results

Grand average ERP waveforms are shown in Fig. 3 for the parietal, posterior occipital, lateral occipital, and posterior temporal electrode sites. Separate waveforms are shown for contralateral and ipsilateral targets relative to the hemisphere of the recording electrode. For both the patient and control groups, the N2pc component can be seen as a more negative (i.e., less positive) voltage beginning at approximately 200
ms poststimulus for red targets and beginning at approximately 250 ms for green targets. To isolate the N2pc component from the overlapping bilateral ERP components, Fig. 4A shows contralateral-minus-ipsilateral difference waves. N2pc amplitude, onset latency, and peak latency were measured from these waveforms, and group means are shown in Table 2, along with the essential statistical analyses. Mean N2pc onset latency is also shown in Fig. 4B, along with the individual-subject values and 95% confidence intervals. For both the patient and control groups, N2pc onset latency (like behavioral RT) was approximately 50 ms earlier for schizophrenia patients compared to control subjects. No significant effects were found for the main effects and interactions that are not listed here.

Table 2
Descriptive statistics (mean ± standard error) and major statistical results for each behavioral and N2pc variable in Experiment 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control subjects</th>
<th>Schizophrenia patients</th>
<th>Color main effect</th>
<th>Group main effect</th>
<th>Color × group interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reaction time (ms)</td>
<td>Attend green</td>
<td>Attend red</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attend green</td>
<td>808 ± 39</td>
<td>760 ± 36</td>
<td></td>
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<tr>
<td>Attend red</td>
<td>939 ± 32</td>
<td>903 ± 35</td>
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<td></td>
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<tr>
<td>Percent correct</td>
<td>94.8 ± 1.1</td>
<td>95.0 ± 1.0</td>
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</tr>
<tr>
<td>N2pc onset latency (ms)</td>
<td>283 ± 11</td>
<td>229 ± 9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N2pc peak latency (ms)</td>
<td>324 ± 13</td>
<td>292 ± 18</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N2pc amplitude (µV)</td>
<td>−0.46 ± 0.18</td>
<td>−0.66 ± 0.15</td>
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<td></td>
</tr>
</tbody>
</table>

F(1, 33) = 25.62, p < .0001
F(1, 33) = 6.19, p = .0181
F(1, 33) = 0.52, p = .4753
F(1, 33) = 0.09, p = .7672
F(1, 33) = 0.01, p = .9114
F(1, 33) = 0.33, p = .3344
F(1, 33) = 0.40, p = .5301
F(1, 33) = 0.28, p = .5991

No significant effects were found for the main effects and interactions that are not listed here.
red than for green targets, leading to a highly significant main effect of target color (see Table 2). These results establish the accuracy and sensitivity of our N2pc latency measurements in this experiment.

N2pc onset latency was nearly identical for the patient and control groups, both for red targets and green targets. N2pc peak latency for red targets was approximately the same in the two groups, but it was somewhat later in patients than in control subjects for green targets. However, this difference did not approach statistical significance (see Table 2). Thus, schizophrenia patients are able to shift attention to a salient target object just as rapidly as control subjects.

Mean N2pc amplitude was 0.2–0.3 µV greater for red targets than for green targets, and this difference was significant. Mean N2pc amplitude was 0.1–0.2 µV greater for patients than for control subjects, but this difference did not approach statistical significance. Thus, schizophrenia patients exhibited no impairment in the magnitude of the N2pc component.

2.2.3. Other ERP components

The waveforms for the patient and control groups, averaged across ipsilateral and contralateral targets, are overlapped in Fig. 5. The waveforms are collapsed across red and green targets because the waveforms did not generally differ as a function of target color, except for the N2 wave as described later. The results of the main statistical analyses are shown in Table 3.

When considering these results, it is important to keep in mind that the ERP waveform consists of the sum of many underlying components that overlap in time, and it is difficult to determine the onset, peak, and offset times of the underlying components from the observed waveforms. This in turn makes it difficult to determine what changes in the underlying components were responsible for a given difference in waveforms between groups (see Luck, 2005). This problem was obviated for the N2pc component by using difference waves to isolate the N2pc component from other overlapping components, but it complicates the interpretation of the waveforms shown in Fig. 5. These waveforms and the following analyses are presented primarily to facilitate comparison with previous studies, and they should be interpreted with caution.

Three major differences between the patient and control groups can be observed in Fig. 5. First, there
was a difference between 100 and 200 ms, in the time range of the P1 and N1 waves. This difference was present primarily at the posterior and lateral occipital electrodes, leading to a significant group × electrode site interaction without a significant main effect of group (see Table 3). The most plausible interpretation of this difference is that it reflects a reduction in the amplitude of the P1 component for the patient group, as reported previously for schizophrenia patients (Foxe et al., 2001; Schechter et al., 2005). Assuming that the P1 wave partially overlaps the N1 wave in time (see Luck and Hillyard, 1990), this could also explain the apparent enhancement of N1 peak amplitude for the patient group compared to the control group. Other interpretations are possible (e.g., an earlier N1 latency for the patient group), but the results clearly show that sensory processing between 100 and 200 ms differs between the patient and control groups.

The second major difference between groups was observed in the 200–300 ms latency range, during which the voltage was more negative (less positive) for the control group than for the patient group, except at the posterior occipital electrodes. This led to a
significant group × electrode interaction without a significant main effect of group. The posterior P2 and N2 components overlap each other during this time range, and it is impossible to know whether the observed difference reflects an enhanced P2 wave or a reduced N2 wave for the patient group compared to the control group. Previous studies have found a reduction in visual N2 amplitude for schizophrenia patients (Alain et al., 2002; Bruder et al., 1998; Potts et al., 2002), and the difference observed here between 200 and 300 ms may reflect the same effect.

Although not reflected in the waveforms shown in Fig. 5, the N2 wave was more negative for the attend-green condition than for the attend-red condition in both the patient and control groups from approximately 250–400 ms. This was reflected in a significant color main effect in the 300–400 ms latency range and a significant color × electrode interaction in the 200–300 ms and 300–400 ms latency ranges. This pattern did not differ across groups ($F < 1$ for the group × color interaction and the group × color × electrode interaction in both latency ranges).

The third main difference between groups was evident in the P3 latency range. Specifically, P3 amplitude tended to be smaller for the patient group than for the control group, especially at posterior occipital electrodes. However, the group main effect and group × electrode interactions failed to reach significance in the 400–500 ms latency range. The lack of a reduction in P3 amplitude for the patient
group compared to the control group should not be surprising, because reductions in visual P3 amplitude for schizophrenia patients are much less robust than reductions in auditory P3 amplitude (e.g., Ford et al., 2001; Mathalon et al., 2000a; Pfefferbaum et al., 1989; Shelley et al., 1996). Moreover, targets in the present experiment were not rare and therefore generated relatively small P300 amplitudes. Furthermore, much of the activity in the P3 latency range probably reflected the occipital P3 component identified by Luck and Hillyard (1994a) – which is not probability-sensitive – rather than the conventional probability-sensitive P3b component that is typically assessed in studies of schizophrenia.

2.3. Discussion

Although RTs were more than 100 ms longer in the patient group than in the control group, there was no evidence of a difference in N2pc onset latency. Because the N2pc is lateralized with respect to the location of the target item, this result indicates that both patients and control subjects were able to localize the target item quite rapidly. Moreover, because of the extensive evidence linking the N2pc component to the focusing of attention (Luck and Ford, 1998; Luck et al., 1997; Luck and Hillyard, 1994a,b), we can further conclude that both patients and control subjects were able to shift attention rapidly to the target location. In addition, N2pc amplitude is associated with the amount of attention allocated to an object (Luck et al., 1997), and we observed that N2pc amplitude was slightly and nonsignificantly larger in the patients than in the control subjects. Thus, the attentional mechanism reflected by the N2pc component appears to be unimpaired in schizophrenia, both in terms of the time required to shift attention and the amount of attention that can be allocated. Thus, the significant slowing of patient RTs documented here and in many previous studies does not appear to be caused by a slowing in the allocation of visual attention.

This conclusion relies on accepting the null hypothesis that there were no differences in N2pc onset latency between patients and controls. Could this null result be explained by measurement error in quantifying N2pc onset latency or by an insensitivity of N2pc onset latency to variations in the time required to shift attention? The large and highly

### Table 3

<table>
<thead>
<tr>
<th>Time Range</th>
<th>Group main effect</th>
<th>Color main effect</th>
<th>Electrode main effect</th>
<th>Group × electrode interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>100–200 ms</td>
<td><em>F</em>(1, 33)=0.118 p = 0.733</td>
<td><em>F</em>(3, 99)=3.64 p &lt; 0.05</td>
<td><em>F</em>(1, 33)=0.22 p = 0.64</td>
<td><em>F</em>(3, 99)=0.15 p = 0.85</td>
</tr>
<tr>
<td>200–300 ms</td>
<td><em>F</em>(1, 33)=5.88 p &lt; 0.05</td>
<td><em>F</em>(3, 99)=5.85 p &lt; 0.05</td>
<td><em>F</em>(1, 33)=3.25 p &lt; 0.05</td>
<td><em>F</em>(3, 99)=5.52 p &lt; 0.01</td>
</tr>
<tr>
<td>300–400 ms</td>
<td><em>F</em>(1, 33)=19.09 p &lt; 0.001</td>
<td><em>F</em>(3, 99)=13.92 p &lt; 0.001</td>
<td><em>F</em>(1, 33)=2.47 p = 0.11</td>
<td><em>F</em>(3, 99)=6.41 p &lt; 0.01</td>
</tr>
<tr>
<td>400–500 ms</td>
<td><em>F</em>(1, 33)=0.01 p = 0.9098</td>
<td><em>F</em>(3, 99)=35.55 p &lt; 0.001</td>
<td><em>F</em>(1, 33)=2.70 p = 0.072</td>
<td><em>F</em>(3, 99)=0.15 p = 0.8843</td>
</tr>
</tbody>
</table>

When appropriate, *p*-values are adjusted by the Greenhouse–Geisser epsilon. No significant effects were found for the main effects and interactions that are not listed here.
reliable differences in N2pc onset latency between red and green targets indicate that measurement error and insensitivity are not plausible explanations. That is, the effect of target color was just as large and robust for N2pc onset latency as it was for RT, indicating that N2pc onset latency provides a precise and sensitive measure of the speed of attention.

Another possible explanation for the lack of an N2pc onset latency difference is sampling error. That is, we may have sampled–by chance–an unusually slow group of control subjects or an unusually fast group of patients. However, the difference in RTs between groups was comparable to the differences observed in previous comparisons between patients and control subjects (Carr et al., 1998; Elvevag et al., 2000; Sereno and Holzman, 1996), making this explanation quite unlikely. In addition, N2pc onset latencies for both groups were comparable to the onset latencies observed in previous studies of healthy young adults (Luck and Hillyard, 1994a,b; Woodman and Luck, 2003b).

We also observed several statistically significant differences in other ERP components between the patient and control groups, which demonstrates the statistical power of our comparisons between these groups. The differences in the 100–200 ms latency range are consistent with prior reports of impaired sensory ERP components in schizophrenia (Foxe et al., 2001; Schechter et al., 2005). One might expect that an impairment in sensory processing would lead to a delay in the allocation of attention, and yet this was not observed. This can be explained by the existence of multiple parallel visual processing streams. In particular, Javitt and his colleagues have proposed that the reduced sensory ERP responses reflect a specific deficit in the magnocellular processing stream (Butler et al., 2005; Schechter et al., 2005), and this stream presumably plays relatively little role in the visual search task used here. Thus, the present experiment is consistent with previous studies in showing reduced early sensory ERP responses and delayed RTs, indicating that the patient and control groups used in the present experiment were comparable to those used in previous experiments. The unique contribution of the present experiment is that it shows that these deficits are accompanied by strikingly normal processing at a well-defined intermediate processing stage.

It is important to ask what it means for the N2pc component to show no sign of abnormality in patients when earlier components do show significant abnormalities. The human visual system consists of several processing streams that operate in parallel (Goodale and Milner, 1992; Ungerleider and Mishkin, 1982), and this general principle is also true of cognitive processing in general (Meyer and Kieras, 1997; Rumelhart and McClelland, 1986). In such a complex, parallel system, it should be no surprise that a deficit in a specific process at one point in time is not propagated to different processes at later points in time, because the later processes may be a part of a different parallel processing stream. Indeed, the purpose of the present experiment was to use a highly specific measure of a well-defined attentional processes, with the ultimate goal of determining exactly which processes are and are not impaired in schizophrenia.

When interpreting ERP results such as these, it is important to consider the limitations that arise from looking at averaged data. In particular, the onset of an ERP component in an averaged ERP waveform tends to reflect the trials with the shortest onset latencies and does not always reflect the average onset latency (see chapter 6 in Luck, 2005). Indeed, although N2pc onset time was virtually identical in the patient and control groups, N2pc peak latency tended to be somewhat later in the patient group, although this difference did not approach significance. The N2pc results cannot, therefore, rule out the possibility that although patients frequently shift attention as fast as control subjects, they occasionally shift attention much more slowly. This pattern could not fully explain the RT difference between groups, because the fastest RTs produced by the patients were slower than the fastest RTs produced by the control subjects (see Fig. 2B). However, it could be at least partly responsible for the greater RT variance observed in the patient group.

It should also be noted that the patients were medicated while being tested. This could be a reasonable explanation if we had observed decreased N2pc amplitudes or increased N2pc latencies, but it cannot easily explain the finding of intact N2pc amplitudes and latencies in the patient group. Antipsychotic medications do not typically fully ameliorate the cognitive deficits observed in schizophrenia.
(see meta-analysis by Woodward et al., 2005), and we observed a typical degree of RT slowing despite the medications. It is therefore unlikely that the medications eliminated a slowing of N2pc latency that would have been observed if we had tested unmedicated patients.

3. Experiment 2

Experiment 2 used a behavioral paradigm to provide converging evidence about the speed of attention. This is important for two reasons. First, the conclusions drawn from Experiment 1 depend on the absence of a difference between groups, and converging evidence will therefore be useful for showing that this was not a statistical anomaly. Second, visuospatial attention can operate in multiple cognitive subsystems (Luck and Vecera, 2002; Vogel et al., 2005), and it is possible that schizophrenia involves a slowing of the operation of attention within a subsystem that is not reflected by the N2pc component. Behavioral outputs are more likely to reflect contributions from multiple mechanisms of attention and may therefore reveal effects that are absent for a given ERP component.

The paradigm used in Experiment 2 was a variant of the widely used Posner spatial cueing paradigm (Posner, 1980; Posner et al., 1980) and was modeled on the study of Lyon (1990). As illustrated in Fig. 6A, a circular array of letters was presented for 1000 ms and then masked. At a variable interval prior to the mask, one of the letters was cued by the disappearance of a location marker box, and subjects simply indicated the identity of this letter. If subjects can shift attention to the cued letter before it disappears and is replaced by a mask, then they should be able to report the identity of the letter. If attention arrives at the cued letter after it has been replaced by the mask, then subjects will be unable to accurately report the letter’s identity. By varying the time between the cue and the onset of the mask array, it is possible to determine how much time is required for attention to shift to the cued letter.

Note that, because the letter array was present for 1000 ms before the onset of the mask array, the masks could not interfere with the formation of a sensory representation of the letter array; instead, the masks served to eliminate any persistence of the letter array in iconic memory. Thus, it is unlikely that the exaggerated metacontrast masking effects that are often observed in schizophrenia patients (see Green, 1998) will influence the results of the present experiment.

With this experimental paradigm, the data from each subject can be plotted as a function in which accuracy (proportion correct) varies with the cue-mask delay interval (see Fig. 6B). The simplest interpretation of this function is that the proportion correct at a given delay interval reflects the probability that attention can shift within that period of time. This assumes that the subject will be 100% correct if attention has shifted prior to mask onset and will be 0% correct if attention has not shifted prior to mask onset. This is, of course, an oversimplification.

If the subject simply makes a guess when attention has not shifted in time, this guess would be correct on approximately 4% of trials (because the target is one of 26 different letters). Moreover, given the long duration of the letter array, it is possible for subjects to store some of the items in short-term memory and use this memory to identify the cued item even if the visual representation of the cued item was eliminated by the mask before attention was shifted. The ability to use this strategy presumably varies across subjects, and it is therefore necessary to eliminate the influence of memory (and other guessing strategies) when comparing the patient and control groups. This can be accomplished by assuming that accuracy at a delay of zero is based entirely on the use of memory and guessing strategies, which is a reasonable assumption given that no sensory information about the identity of the target is present after cue onset when the cue-mask delay is zero (see the broken line near the bottom of Fig. 6B).

In addition, even if attention could potentially shift to the cued item prior to the onset of the mask, subjects may occasionally have lapses of concentration that cause them to make errors even with very long cue-mask delays. This can be estimated from the asymptotic level of accuracy (see the broken line near the top of Fig. 6B).

To adjust for these two factors, which are unrelated to the speed with which attention can shift, we normalized the data for each subject according to the formula $N_t = (P_t - P_0)/(P_{\text{asymptote}} - P_0)$, where $N_t$ is the normalized proportion of correct responses at
cue-mask delay \( t \), \( P_t \) is the observed proportion of correct responses at delay \( t \), \( P_{\text{asymptote}} \) is the asymptotic proportion correct (the average for delays of 400–1000 ms), and \( P_0 \) is the observed proportion correct at delay 0. This is equivalent to stretching the function vertically so that it starts at 0 and asymptotes at 1 (see the \( y \)-axis scale at the right of Fig. 6B).

The function relating normalized proportion correct to cue-mask delay provides a means of quantifying the probability that attention can shift within a particular period of time. The time required to shift attention presumably varies from trial to trial, leading to a distribution of shift times. To quantify the speed of attention with a single value, we estimated the time at which the normalized proportion of correct responses reached a threshold value of 0.5 (this is the most commonly used threshold when performance ranges from 0.0 to 1.0). We call this time the attention-speed estimate, and it represents the amount of time required for a given subject to be able to shift attention to the cued item on 50% of trials. This value was estimated by means of a curve-fitting procedure, as described in the Method section.

To perform the task shown in Fig. 6A, subjects must not only shift attention before the mask is presented, they must also encode the identity of the letter at the cued location. High-contrast letters can be encoded in parallel with minimal capacity limitations (Schneider and Shiffrin, 1977), so it is likely that subjects encoded the letters prior to the appearance of the cue. Thus, the function relating accuracy to cue-mask delay is unlikely to be significantly influenced by the time required to encode the cued letter, at least in the control subjects. However, it is possible that this function may be shifted to the right for patients if they are unable to encode the letters prior to the onset of the cue.

3.1. Method

3.1.1. Participants

Twenty-four patients and 15 healthy control subjects participated in this experiment. Demographic

Fig. 6. (A) Example of the stimuli used in Experiment 2. Subjects simply reported the identity of the letter indicated by the cue. (B) Example of the function relating accuracy to cue-mask delay in this experiment.
information and patient symptom ratings are provided in Table 1. The patients, on average, were not highly symptomatic. Six of the patients were employed or enrolled in school full time; four worked part-time; and 14 were unemployed or participated in day programs. Twenty patients were receiving second-generation antipsychotic medications and five were receiving traditional antipsychotic medications. Five patients and seven control subjects had previously participated in Experiment 1.

3.1.2. Stimuli and task

The stimuli are illustrated in Fig. 6A. Stimuli were viewed from a distance of 70 cm and presented on a CRT with a gray background. Each trial began with a 500-ms blank interval, followed by a 500-ms presentation of a fixation cross and 8 location-marker boxes (1.74 × 1.74°). The boxes were equally spaced along an invisible circle with a radius of 3.0°, and adjacent boxes were separated by 1.2° (center to center). The array of boxes was followed by a 1000-ms presentation of an array of 8 white letters (each subtending approximately 1.0 × 1.1°), selected at random without replacement from the set of all upper-case letters. Each mask consisted of the digits 2–9 overlapped within a 1.0 × 1.3° region.

A location was cued by extinguishing a randomly selected location marker box prior to the onset of the mask array. The delay between the offset of the box and the onset of the mask was 0, 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, or 1000 ms, varying unpredictably across trials. A question mark was presented 500 ms after the onset of the mask array, and the subject verbally named the cued letter, guessing if necessary. Responses were unspeeded. The experimenter—who did not see the stimulus display—typed the subject’s response into the computer, and then the next trial began. The trials were divided into 4 blocks of 130 randomly ordered trials, yielding a total of 30 trials at each cue-mask delay interval.

3.1.3. Data analysis

As described above, we computed the normalized proportion correct at each delay for each subject. To obtain the attention-speed estimate, we fit each subject’s normalized data with a generalized exponential function, \( t^v/(t^v+(1-w)^v) \), where \( t \) is the cue-mask delay time and \( v \) and \( w \) are free parameters. This function is similar to a cumulative normal function, but it does not assume that the left and right halves of the function are symmetrical and is thus not distorted by skewness. The free parameters of this function were estimated by minimizing the mean-square error between the fit and the observed data for each subject, and we then computed the time \( t \) at which this function reached a value of 0.5. The purpose of this curve-fitting procedure was solely to provide a reliable measure of the threshold value, and we do not assume that it mathematically represents the processes involved in performing the task.

The function fit the single-subject data very well, accounting for an average of 98.0% of the variance in the patient group and an average of 98.9% of the variance in the control group. All fits accounted for at least 92.7% of the variance.

The raw and normalized data were analyzed with ANOVAs, and the \( p \)-values were adjusted when appropriate with the Greenhouse–Geisser correction.

3.2. Results

Fig. 7 summarizes the data from this experiment, showing the mean proportion correct and mean normalized proportion correct at each cue-mask interval. The attention-speed estimate is also shown for each subject, along with the means and 95% confidence intervals for the patient and control groups.

For both groups, accuracy rose quickly between the 0- and 200-ms cue-mask delay intervals and then reached an asymptote. As is commonly observed for discrimination tasks, the nonnormalized mean proportion correct was somewhat lower for the patient group than for the control group. This difference was somewhat greater at short cue-mask delays than at long cue-mask delays, which may reflect a better use of short-term memory by the control subjects (memory is useful primarily at short delays). However, there was also a clear reduction in asymptotic accuracy in the patient group compared to the control group. Supporting this description of the means, a two-way ANOVA yielded significant main effects of group \([F(1, 37)=12.54, \ p<.0001]\) and cue-mask delay interval \([F(12, 444)=439.56, \ p<.0001]\), along with a significant group × interval interaction \([F(12,
Follow-up comparisons at each delay interval using the pooled error term from the omnibus ANOVA showed a significant reduction in patient accuracy compared to control accuracy \( p < .05 \) for all intervals except those between 400 and 750 ms.

After the data were normalized, some modest differences could be observed between the patient and control groups in the growth of accuracy over delay intervals. Specifically, accuracy rose somewhat more rapidly in the control group than in the patient group. However, the group × cue-mask delay interval interaction was only marginally significant in an ANOVA on the normalized data \( [F(12, 444)=2.43, p = .07] \). The main effects of group and cue-mask delay interval were both significant \( [F(1, 37)=5.65, p < .05 \text{ and } F(12, 444)=530.91, p < .0001, \text{ respectively}] \). Follow-up comparisons at each delay interval using the pooled error term from the omnibus ANOVA showed a significant reduction in patient accuracy compared to control accuracy \( p < .05 \) only for the intervals between 100 and 200 ms.

The mean attention-speed estimate was 83 ms for the control group and 102 ms for the patient group. A one-way ANOVA indicated that this 19-ms difference was marginally significant \( [F(1, 37)=3.99, p = .053] \). An inspection of the individual-subject data (Fig. 7C) suggests that most of the difference between groups can be attributed to four patients whose values were well beyond those of the rest of the patient group. Moreover, most of the attention-speed estimates for the patient group overlapped with the range of attention-speed estimates for the control group.

The normalized proportion correct function shown in Fig. 7B reflects the probability that attention shifted at or before a particular point in time. To provide an estimate of the probability that attention shifted at a particular point in time (but not before), Fig. 8 shows the derivatives of the functions shown in Fig. 7B. That is, the value at each time point is equal to the difference between the normalized accuracy at that time point and the previous time point, divided by the number of milliseconds between the time points. This function is can be compared directly to the RT probability histogram from Experiment 1 (see Fig. 2B). As in the RT probability histogram, the function shown in Fig. 8 is shifted to the right for the patient group compared to the control group, along with a modest increase in the

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Fig. 7. (A) Mean proportion of correct responses at each cue-mask delay for the two groups. (B) Mean normalized proportion of correct responses at each cue-mask delay for the two groups. (C) Attention-speed estimate for each subject (filled circles), along with the mean and 95% confidence interval for each group.
width of the function. However, the magnitude of these effects (in milliseconds) was quite a bit smaller for the attention-shift data shown in Fig. 8 than for the RT data shown in Fig. 2B.

The attention-speed estimates shown in Fig. 7C suggest that four of the patients were outliers and formed a distinct subgroup. To assist in assessing this possibility, Fig. 9A shows proportion correct as a function of cue-mask delay for each patient, with the data from four outlier patients drawn in thick solid lines and the data from the other patients drawn in thin broken lines. The data from the 20 non-outlier patients show an impressive degree of similarity, and the data from the four outlier patients are distinctly different, showing no improvement in accuracy over the first 100 ms of the function. Three of the four outlier patients also exhibited unusually low asymptotic accuracy values.

Mean proportion correct is shown for the control subjects, the non-outlier patients, and the outlier patients in Fig. 9B. Although the non-outlier patients exhibited reduced accuracy at the shortest cue-delay intervals compared to the control subjects, accuracy increased rapidly in these patients as the cue-mask delay increased. This similarity can be seen more clearly in Fig. 9C, which uses normalized proportion correct to factor out differences in initial and asymptotic accuracy. The normalized functions were nearly identical for the non-outlier patients and for the control subjects. In contrast, the function was clearly shifted rightward in the four outlier patients.

Fig. 8. Derivative of the function shown in Fig. 7B. The value at each point was calculated by subtracting the accuracy at that point from the accuracy at the previous point and then dividing by the time difference between the two points. The value at time zero was set to zero.

Fig. 9. (A) Proportion correct at each cue-mask delay for individual outlier (solid lines) and non-outlier patients (broken lines). (B and C) Mean proportion correct (B) and mean normalized proportion correct (C) at each cue-mask delay for the control subjects, the non-outlier patients, and the outlier patients.
Although the data shown in Fig. 9 reflect a post-hoc division of the patients into two subgroups, there was an extremely high degree of consistency within each subgroup and a large gap between the two subgroups. These factors strongly suggest that this grouping reflects a real underlying difference in cognitive processing rather than an arbitrary division of a single continuous distribution of performance.

The four outlier patients did not differ substantially from the rest of the patients in terms of schizophrenia subtype, medication, race, handedness, sex, age, education, father’s education, and most symptom ratings. However, WRAT scores were quite a bit lower in these four patients (mean = 86.0) compared to the main patient sample (mean = 96.6), and this difference nearly reached statistical significance (p = .054, Mann–Whitney U-test). This suggests a difference in premorbid scholastic abilities, also supported by a modest difference in years of education (12.5 years for the outlier patients, 14.0 years for the non-outlier patients). The outlier group also showed reduced scores on the BPRS Hostility/Suspicion subscale (mean = 3.8) compared to the main patient sample (mean = 6.3); this reached statistical significance (p = 0.05, Mann–Whitney U-test), but the direction of this effect suggests that it is spurious. Two of the four outlier patients were on traditional antipsychotic medications and two were on second-generation antipsychotic medications. Thus, with the exception of a possible difference in premorbid functioning, there were no obvious differences between the outlier and non-outlier subjects on a wide range of demographic, symptom, and treatment variables. Additional research will be necessary to determine if this slowing of attention is accompanied by similarly distinctive patterns of performance in other cognitive tasks.

3.3. Discussion

In this experiment, a small and marginally significant amount of slowing was observed in the patient group compared to the control group. Moreover, much of the slowing of attention in the patient group appeared to be caused by a small number of patients, with most patients falling within the range of the control group. Even including the four “slow” patients, the magnitude of the overall group effect was very small (19 ms) compared to the degree of RT slowing typically observed in speeded discrimination tasks (e.g., 137 ms in Experiment 1). The small magnitude of the slowing of attention in this experiment relative to the slowing of RTs in Experiment 1 is evident when comparing mean attention-speed estimates with mean RTs and also when comparing the distribution of attention shift times from the present experiment (Fig. 8) with the distribution of RTs from Experiment 1 (Fig. 2B).

We therefore conclude that schizophrenia does not involve a substantial and consistent slowing of visual–spatial attention. This conclusion is consistent with findings from more conventional spatial cueing experiments in which subjects make speeded responses to simple targets after being cued to the target’s location or to a different location. That is, although some studies have found differences in hemispheric asymmetries in this task (e.g., Posner et al., 1988), patients do not consistently show overall deficits in the ability to shift attention to a cued target in most studies (e.g., Bustillo et al., 1997; Fuentes et al., 1999; Gold et al., 1992; Maruff et al., 1996; Moran et al., 1992; Nestor et al., 1992; Strauss et al., 1991).

Behavioral measures of attention typically reflect the operation of multiple attention-related processes, and this can be both a strength and a weakness. In the present experiment, this attribute of behavioral measures is a strength because it means that the lack of a substantial slowing of attention is in some ways more remarkable than the lack of a slowing of N2pc latency observed in Experiment 1. That is, even though many stages of processing contributed to the attention-speed estimates in the present experiment, providing many opportunities for slowing to be observed, very little slowing was in fact observed. The corresponding weakness, however, is that it is more difficult to pinpoint the causes of the slight slowing that was observed in the present experiment. That is, it is impossible to know whether the patients who exhibited slowing were impaired in the initial shift of perceptual attention (as would be reflected by a delayed N2pc onset), in the perceptual encoding of the cued item, or in the transfer of this encoded representation into working memory. However, this weakness of the present experiment is relatively minor given that the attention-speed estimates for most
patients were within the same range as the attention-speed estimates for the control subjects.

4. Symptom correlations

We performed non-parametric correlational analyses (Spearman’s rho) between symptom ratings and N2pc amplitude, N2pc onset latency, Experiment 1 RT, and attention speed estimates (see Table 4). Symptom variables included the total score from the Schedule for the Assessment of Negative Symptoms (SANS; Andreasen, 1983) (all items omitting the global scores, the attention scores, and poverty of content of speech), along with the total score and five factor scores from the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1962): anxiety/depression; negative symptoms; positive symptoms; activation; and hostility/suspiciousness.

None of the correlations were significant (all \( p < 0.10 \)), although this may reflect the modest sample sizes in these experiments. The largest correlations were between negative symptoms—as measured with the SANS—and the RT and N2pc latency measures from Experiment 1. However, the negative symptom subscale from the BPRS was largely uncorrelated with the RT and N2pc latency measures, suggesting that any relationship between these measures and negative symptoms is weak. A modest correlation was also observed between BPRS positive symptoms and N2pc amplitude, but greater symptoms were associated with larger rather than smaller N2pc amplitudes. This pattern of correlations suggests that the symptomatic dimensions of the illness are not associated with the specific attentional processes assessed in these two experiments, as is commonly the case with measures of cognitive function (Gold and Green, 2005; Rund et al., 2004).

5. General discussion

The goal of this study was to determine whether the allocation of visuospatial attention is slowed in schizophrenia, potentially playing a major role in the pervasive and substantial slowing of patient RTs. Although attention-related task impairments have been widely documented in schizophrenia (see reviews by Nestor and O’Donnell, 1998; Zubin, 1975), none of these studies has directly and precisely measured the speed with which attention can be oriented. Using an electrophysiological measure of the operation of attention in visual cortex, Experiment 1 provided clear evidence that patients can shift attention to a peripheral target quite rapidly. Using a behavioral measure of attention, Experiment 2 indicated that patients can shift attention to a cued location almost as rapidly as control subjects. Thus, we conclude that schizophrenia does not involve a substantial slowing in the allocation of visuospatial attention and that any slowing of attention is too small to play a significant role in the slowing of patient RTs.

One important caveat is necessary, however. Specifically, the present experiments were designed to provide the subjects with salient bottom-up information about which location should be attended. That is, the to-be-attended location was indicated by a clear difference in color (Experiment 1) or the sudden removal of an object frame (Experiment 2). Under these conditions, attention is guided primarily by information that is readily available within visual cortex, requiring minimal control by prefrontal executive systems. In contrast, we have recently shown that visual search can be dramatically slowed in schizophrenia patients when the target is less salient (Fuller et al., in press). A hint of this was also observed in the present study. Specifically, N2pc peak

| Table 4 | Correlations (Spearman’s rho) between measures of clinical symptoms and variables of interest from Experiments 1 and 2 |
|-----------------|-----------------|-----------------|-----------------|
| Symptom rating  | N2pc latency \( \rho \) | N2pc amplitude \( \rho \) | Experiment 1 RT \( \rho \) | Speed of attention \( \rho \) estimate |
| SANS total      | .34             | -.02            | .40             | -.12            |
| BPRS total      | .18             | .08             | .19             | .07             |
| BPRS anxiety/  | -.02            | -.06            | -.07            | -.06            |
| depression      |                 |                 |                 |                 |
| BPRS negative   | .05             | -.01            | .14             | -.03            |
| symptom         |                 |                 |                 |                 |
| BPRS positive   | .26             | .39             | .31             | .18             |
| symptoms        |                 |                 |                 |                 |
| BPRS activation | -.25            | -.09            | -.22            | .07             |
| BPRS hostility/ | .21             | .14             | .21             | -.31            |
| suspicion       |                 |                 |                 |                 |

All \( p \) values were \( >0.1 \) without correction for multiple comparisons. Data are missing for 6 patients in Experiment 1 and 4 patients in Experiment 2 for the BPRS and SANS.
latency was somewhat delayed in patients for the less salient green targets in Experiment 1. Although this slowing was not statistically significant, it is at least consistent with the hypothesis that impairments in executive control could lead to a slowing of attention. That is, more attentional control should be necessary for allocating attention to the less salient of two targets. These results suggest that the neural systems for shifting attention may be largely intact in patients, but an impairment in prefrontal control mechanisms may lead to substantially slowed shifts of attention under conditions that require intensive top-down control.

It is also important to note that the allocation of attention might be substantially but intermittently slowed in schizophrenia patients. The experimental paradigms used in this study were primarily sensitive to the fastest shifts of attention, and it is possible that attention was slowed by a large amount on a small subset trial in the patients. Even if this was true, however, the present results still provide clear evidence that the patients possess the neural circuitry necessary to execute rapid shifts of attention on a large proportion of trials.

Other ERP studies have provided evidence that is consistent with the proposal that the slowing of patient RTs is not due to a slowing of attention. In particular, many ERP studies have shown that the latency of the P300 wave is increased in patients, which accompanies the widely known reduction in P300 amplitude (see review by Jeon and Polich, 2003). However, the increase in P300 latency is typically found only in older patients, with little or no difference in younger patients (Mathalon et al., 2000b; O’Donnell et al., 1995; Wang et al., 2003). Because Experiment 1 of the present study did not include a probability manipulation, it was not possible to provide a meaningful measure of P3 latency. However, on the basis of previously published regression equations (Mathalon et al., 2000b; Wang et al., 2003), the average slowing of P300 latency in Experiment 1 should have been approximately 20–30 ms, which is much smaller than the observed slowing of RT. Thus, these prior results suggest that the cognitive events that lead up to the P300 are not sufficiently slowed to account for the large increases in manual RT.

What, then, accounts for the slowing of manual RT in schizophrenia? Extensive research by cognitive psychologists over the past 15 years indicates that much of the time required to perform simple discrimination tasks is taken up by a highly capacity-limited central bottleneck process (see reviews by Pashler, 1994, 1998). In particular, the process of determining which response should be emitted once a stimulus has been perceived appears to be highly capacity limited, operating in many cases as a single-channel bottleneck in the information processing stream. Processes prior to this stimulus–response translation stage may show capacity limitations, but they are not typically as severe as those in the central bottleneck stage. In particular, relatively easy perception and categorization tasks occur prior to the central bottleneck (Luck, 1998; Pashler and Johnston, 1989), as do shifts of visuo-spatial attention (Pashler, 1991).

It is plausible that the slowing of RTs in schizophrenia is largely caused by a slowing in the process of stimulus–response translation. This hypothesis is consistent with the results of the present study, in which minimal slowing of visuo-spatial attention was observed. It is also consistent with the finding of minimal slowing of P300 latency, because the P300 wave primarily reflects processes that occur prior to the stimulus–response translation process (Luck, 1998; Magliero et al., 1984). This hypothesis is also consistent with prior RT studies in schizophrenia, which have shown that RTs are particularly slowed when the stimulus–response translation process is made more difficult (e.g., Hemsley, 1976; Marshall, 1973; Wykes et al., 1992). Other studies of schizophrenia patients point to other causes of slowing (see review by Nuechterlein, 1977), but this may reflect the use of non-optimal procedures for isolating specific stages of processing.

A deficit in the basic process of stimulus–response translation would be expected to impact performance of a variety of speeded performance tasks, and deficits on elementary processing speed tasks such as Digit Symbol Substitution are well documented in the schizophrenia literature. Indeed, there is compelling evidence from meta-analyses and structural equation modeling that: a) processing speed deficits are among the largest (if not the largest) and most reliable impairments observed in schizophrenia; b) that the impairment in processing speed cannot be explained on the basis of generalized impairment; and c) the extent of processing speed impairment is related to
functional outcome in the illness (Bellack et al., 1999; Dickinson and Coursey, 2002; Dickinson and Gold, in press; Dickinson et al., 2004; Wilk et al., 2005; Wykes et al., 1992). Moreover, it is possible that the cognitive system that is responsible for stimulus–response translation is involved in a variety of cognitive control processes, which may play a role in the overall pattern of cognitive dysfunction in schizophrenia. Similarly, it is possible that schizophrenia does not involve a specific deficit in the stimulus–response translation system, per se, but that this system is particularly vulnerable to impairments in a more general, low-level process. Additional research is necessary to explore these possibilities.

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