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Neural response to the second stimulus associated with poor speed discrimination performance in schizophrenia

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Abstract

Visual motion processing is compromised in schizophrenia (SZ), but it is uncertain what neural deviations account for their motion analysis abnormalities. Neural activations were measured with dense-array electroencephalography while 14 medicated SZ and 14 healthy persons performed a paired-stimuli forced choice speed discrimination task. SZ had (a) worse-at-speed discrimination, replicating previous findings, (b) normal early extrastriate neural activity (N1) to both motion stimuli, (c) reduced later extrastriate activity (P2) specifically to the second stimulus, and (d) following P2, an enhanced later N2 over parietal cortex. Stronger P2 and N2 responses were associated with better speed discrimination performance across groups. These findings indicate that the neural correlates of poor motion analysis in SZ may not be an early visual analysis abnormality but a problem with efficient use of speed information later in cognitive processing.

Descriptors: Evoked potentials, Visual, Motion, Smooth pursuit, Parietal cortex

The smooth-pursuit system provides for maintaining foveation and clear vision of slowly moving objects (Robinson, 1965). Successful smooth pursuit requires sufficient extrastriate cortex-mediated motion perception abilities (Lisberger, Morris, & Tychsen, 1987; Stanton, Friedman, Dias, & Bruce, 2005) and use of that perceptual information to generate correct frontal cortex- and cerebellar-dependent motor responses (Lencer & Trillenberg, 2008). Problems with smooth-pursuit eye movement performance have been consistently observed among schizophrenia subjects (e.g., Clementz & McDowell, 1994; Hutton & Kennard, 1998), but these abnormalities could result from dysfunction of perceptual and/or motor output functions.

Behavioral studies are consistent with a motion perception deficit in schizophrenia (Chen, Bidwell, & Holzman, 2005; Chen, Levy, Sheremata, & Holzman, 2004; Chen, Nakayama, Levy, Matthysse, & Holzman, 2003; Clementz, McDowell, & Dobkins, 2007; Kim, Wylie, Pasternak, Butler, & Javitt, 2006; O'Donnell et al., 2006; Slaghuis, Bowling, & French, 2005; Stuve et al., 1997). Blood flow-based functional neuroimaging studies (measuring the blood-oxygen-level dependent [BOLD] response) also are consistent with this thesis because people with schizophrenia have lower activity in cortical motion processing area V5 during smooth pursuit (Hong et al., 2005; Lencer, Nagel, Sprenger, Heide, & Binkofski, 2005) and speed discrimination tasks (Chen et al., 2008). People with schizophrenia also have shown reduced activity in frontal and supplemental eye fields and anterior cingulate cortex during smooth pursuit (Hong et al., 2005), revealing involvement of motor output structures and enhanced activity in the inferior convexity of prefrontal cortex during speed discrimination (Chen et al., 2008), perhaps indicating invocation of compensatory mechanisms for a primary motion processing deficit. The temporal resolution of fMRI, with a sampling rate slower than the visual pathway's neural transmission time, however, limits the determination of when, during the course of pretrial preparation, motion processing, response generation, and post-trial evaluation, these deviations in brain function occur.

Wang, Brown, Dobkins, McDowell, and Clementz (2010) directly measured neural activity with dense-array electroencephalography (EEG) during performance of a task where only a simple motion direction judgment of a grating stimulus was required (e.g., Chen et al., 2003). Stimuli were presented within the context of a visual oddball design (one motion direction, specifically, centrifugal motion, defined as the target, was infrequent and required a button press when perceived). During this task, Wang et al. (2010) found that people with schizophrenia had enhanced early visual cortex activity (90 ms after stimulus onset; see also Dakin, Carlin, & Hemsley, 2005), but lower detection rates of the target motion and deficient target-detection–related late neural activity over parietal cortex (400 ms after stimulus onset). There was no indication of generally reduced neural activations to motion stimuli; rather, people with schizophrenia showed an association (accounting for 36% of performance variance) between detection of target motion and target-detection–related brain activity in parietal cortex.

Kim et al. (2006) proposed that motion processing deficits in schizophrenia are caused by impaired bottom-up early magnocellular pathway input to motion processing areas, a reasonable suppo-

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sition since this pathway provides majority input to V5 motion areas (Maunsell, Nealey, & DePriest, 1990). Wang et al. (2010), and other data (Clementz, 1996; Gutherie, McDowell, & Hammond, Jr., 2006; Kim, Thaker, Ross, & Medoff, 1997), are inconsistent with this thesis by indicating that at least some V5-supported functions (Dursteler & Wurtz, 1988; Newsome, Wurtz, Dursteler, & Mikami, 1985) are normal. Wang et al.'s (2010) results were more consistent with abnormalities in later stages of processing in schizophrenia (see also Chen et al., 2004), perhaps beyond extrastriate cortex (V5), involving dysfunction of stimulus classification, target detection, and/or template matching (Alain, Hargrave, & Woods, 1998; Clementz, Wang, & Keil, 2008; van der Stelt, Frye, Lieberman, & Belger, 2004) rather than problems generating the proper neural response to motion stimuli (see also Braus, Weber-Fahr, Tost, Ruf, & Henn, 2002). Whether there is a motion perception problem in schizophrenia and at what neural processing stage this dysfunction is manifest, therefore, is uncertain.

To assess smooth-pursuit–related motion processing, variations of speed discrimination tasks (see Nakayama, 1985) are used because speed discrimination performance, among healthy humans, is closely related to actual smooth-pursuit abilities (Kowler & McKee, 1987). During speed discrimination, paired motion stimuli are presented in close temporal proximity (separated by 500 ms), and subjects make a forced choice judgment comparing their speeds. Such studies indicate elevated speed discrimination thresholds in schizophrenia (Chen, Levy, et al., 1999; Chen, Palafox, et al., 1999; Clementz et al., 2007). Requirements in such tasks are different from those of Wang et al. (2010), where only direction of motion was essential, although stimulus classification, target detection, and/or template matching are important components of performance in both paradigms.

The present study will build upon previous studies (Clementz et al., 2007; Wang et al., 2010) by directly measuring brain activity using EEG during a speed discrimination task. With only behavior measurements from previous studies, it was impossible to determine what neural activity differences account for poor speed discrimination judgments in schizophrenia. Under the thesis of a bottom-up motion processing problem, neural deviations during motion processing should occur early (in the first 150 ms) and be independent of target presentation order.

Materials and Methods

Participants

Sixteen chronic outpatients with DSM-IV (American Psychiatric Association, 1994) schizophrenia (mean age = 42 years; *SD* = 8; range = 26–56; 6 females) and 15 healthy persons (mean age = 41 years, *SD* = 8; range = 27–55; 5 females) participated. All participants were right handed and had normal or corrected-to-normal vision. We conducted a SCID interview (Structured Clinical Interview for DSM-IV Axis I Disorders, see First, Spitzer, Gibbon, & Williams, 1995) to confirm diagnoses and rule out Axis I disorders in healthy subjects. No neurological hard signs, clinically confounding treatments, history of head trauma, and current psychoactive substance use disorders were found in participants. Three participants (1 healthy, 2 schizophrenia) did not meet a minimal performance criterion of 60% correct on the motion processing tasks and were not used in data analysis. All remaining patients were clinically stable (Global Assessment of Functioning *M* = 35, *SD* = 4) on antipsychotic medications (12 on atypical and 2 on typical; mean chlorpromazine (CPZ) equivalent dose = 497 mg, *SD* = 226) for > 8 weeks prior to participation (i.e., based on diagnostic interview, patients' clinical and medication status had not changed during this period). Previous studies indicate that visual processing deficits in schizophrenia are not associated with antipsychotic medications (see, e.g., Butler et al., 2007, for a discussion). There were no significant associations here between CPZ equivalent dose and any dependent measure among persons with schizophrenia. After the study, participants were paid $15/h for their participation. The University of Georgia Institutional Review Board approved this study, and participants provided informed consent prior to testing.

Stimuli and Procedure

Stimuli were presented on a 21″ high resolution flat surface color monitor with a refresh rate of 100 Hz that was 60 cm from the participants' eyes. A centrally located diamond, on which subjects were instructed to remain fixated, was visible throughout testing. The relevant visual stimulus was a light/dark, vertically oriented sinusoidal grating (0.5 cycles/degree), 2.5 × 5 degrees, presented at 100% contrast with a mean luminance of 20 cd/m^2 against a 0.1 cd/m^2 background (see Figure 1). The gratings, when they appeared, had their inside edge at central fixation. Within the 2.5 × 5 degree aperture, the grating moved horizontally, in the direction away from fixation, at a specified speed for 500 ms. Unlike the simple motion direction detection task used by Wang et al. (2010), a standard 2-alternative forced-choice design was used (Clementz et al., 2007). Each trial consisted of two motion stimuli, a "standard" speed (10 degrees/s) and a "test" speed that randomly differed from the standard by −30%, −20%, −10%, 0%, 10%, 20%, 30% [differential speed = (test speed − standard speed)/standard speed]. We employed relatively slower stimuli since speed discrimination at higher speeds may depend on changes in perceived contrast in addition to motion processing (Pantle, 1978). A trial began with the central fixation diamond. After a brief interval

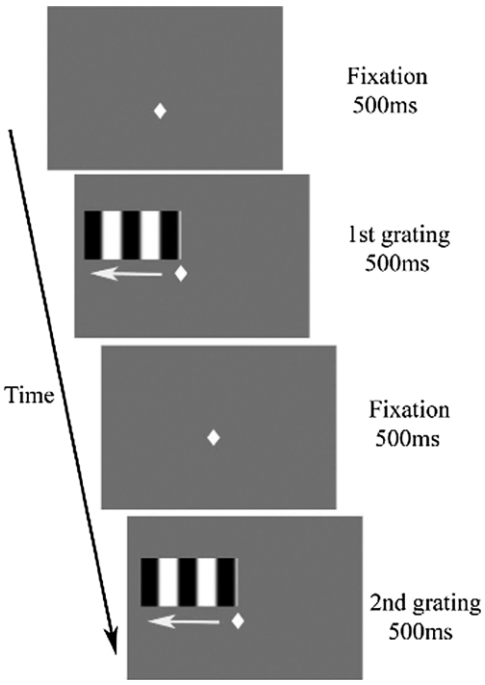

Figure 1. Illustration of the stimuli.

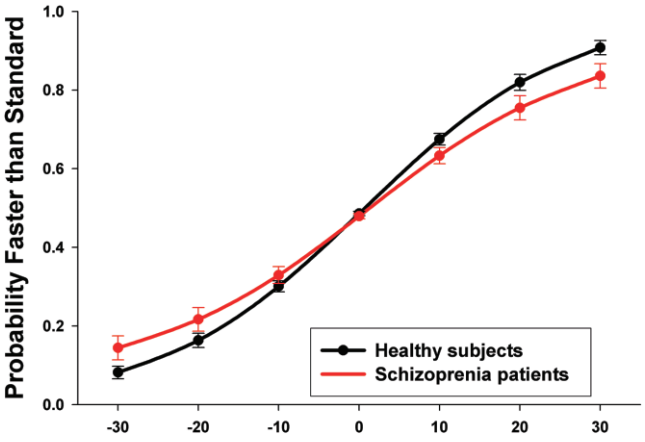

Figure 2. Plot of the psychometric function (mean probabilities (±1 SEM) across different speed percent deviation from standard speed) for schizophrenia (red) and healthy (black) participants for speed discrimination.

(500 ms), the standard (or test) grating appeared randomly on either the left or right side of fixation for 500 ms. After 500 ms interstimulus interval (ISI), the test (or standard) grating was displayed for 500 ms. At the end of each trial, subjects judged which grating (first or second) was fastest. No feedback was provided on response accuracy. The presentation order of the two types of gratings (standard, test), location (left, right), and the speed of the test stimulus were randomized across trials. Each participant completed 420 total trials (60 trials for each differential speed; half in each direction), meaning that they viewed 840 total moving gratings.

EEG Recording

EEG data were measured using a 256-channel Geodesic Sensor Net and NetAmps 200 amplifiers (Electrical Geodesics Inc. [EGI], Eugene, OR). Recordings were referenced to the vertex sensor (Cz). As is standard with high input impedance amplifiers like those from EGI, sensor impedances were below 50 kΩ. Data were analog-filtered from 0.1 to 100 Hz, digitized at 250 Hz, stored on disk for later offline analysis, and recorded continuously throughout the testing.

Behavioral Analyses

For each test speed, the percentage of trials for which the subject perceived the test speed as faster than standard speed (Y axis) was plotted against the test speed (X axis), and the data (which ranged from 0%–100%) were fit with a cumulative normal function using probit analysis (Clementz et al., 2007; McKee, Klein, & Teller, 1985; see Figure 2). Speed discrimination threshold was computed as the test speed corresponding to 75% on the Y axis minus the test speed corresponding to 25%, divided by 2. In addition, a "bias" measure was computed as the test speed that yielded 50% on the Y axis (if there is no bias, this value should be 10 degrees/s, i.e., the same as the standard speed). Reaction time was calculated only for trials with correct responses.

EEG Analyses

Raw data were checked for bad channels (less than 5% for any participant), which were replaced using a spherical spline interpolation method (as implemented in BESA 5.1; MEGIS Software, Gräfelfing, Germany). Data were transformed to an average reference and digitally filtered from 1–50 Hz (12 db/octave rolloff, zero-phase). Ocular, muscle, and cardiac artifacts were identified via sensor distributions using the independent component analysis (ICA) toolbox in EEGLAB 4.515 (Delorme & Makeig, 2004) under Matlab (Version 7.0, MathWorks, Natick, MA).

Trials of 700 ms duration (with 200 ms prestimulus interval) were averaged separately for the standard and each test speed. Trials with activity greater than 75 μV were automatically eliminated. Grand averages were baseline corrected using the 200 ms prestimulus period. The similarities in spatial distributions of visual evoked potentials (VEP) components within and between groups were determined by calculating Pearson correlations between stimuli presented on left and right visual field using the sensors as observations and voltage as the dependent variable. For both schizophrenia and healthy groups, VEPs between left and right visual-field stimuli had highly similar spatial distributions over the 257-sensor array (healthy: N1 $r = .91$, P2 $r = .97$, N2 $r = .88$; schizophrenia: N1 $r = .91$, P2 $r = .91$, N2 $r = .83$; all $ps < .01$; see Figure 3). Therefore, in the following analysis, trials were averaged across left- and right-presented stimuli.

VEP component latency identification was performed using programs written in Matlab and modeled after Wang et al. (2010). To identify components above baseline noise level, global field power (GFP) plots were derived for every subject and condition. The only identifiable components in the GFP plots for all subjects in all conditions were the N1, P2, and N2 (see Figure 3). The latency for the N1, P2, and N2 component for each condition were determined from the peak in the individual GFP plots. Magnitudes of the N1, P2, and N2 (in uV) were quantified at the peak latency of the component (±4 ms) by using the highest negative (N1, N2) or positive (P2) voltage sensor over posterior cortex and then averaging over five sensors that included and surrounded this sensor. For statistical comparisons, the negative voltage component amplitudes were multiplied by −1 so that they indicated magnitude in the same direction as the positive voltage component.

Statistical Analyses

To investigate the influence of grating speed, presentation order (standard speed grating first or second), and speed differences between the standard and test gratings on motion processing, data were analyzed in two ways. First, three categories of trials were created based on whether the test grating speed was actually faster or slower (relative deviation) than the standard grating speed (standard speed, test speeds slower than standard, test speeds faster than standard). Trials were then averaged as a function of presentation order (whether a grating speed occurred first or second), creating 6 total averages per subject. Second, four categories of trials were created as a function of absolute deviation from the standard grating speed (standard speed = 0%; test speed deviations of ±10%, ±20%, and ±30%). Trials were then averaged as a function of presentation order (whether a standard grating speed occurred first or second), creating 8 total averages per subject. Analysis of variances (ANOVAs) with group as a between-subjects factor and speed and order as repeated-measures factors were used for hypothesis testing. These analyses were conducted separately on each VEP peak (N1, P2, N2). Where appropriate, Huynh-Feldt–adjusted degrees of freedom correction was used when the sphericity assumption was violated (Mauchly's test of sphericity; Cardinal & Aitken, 2006).

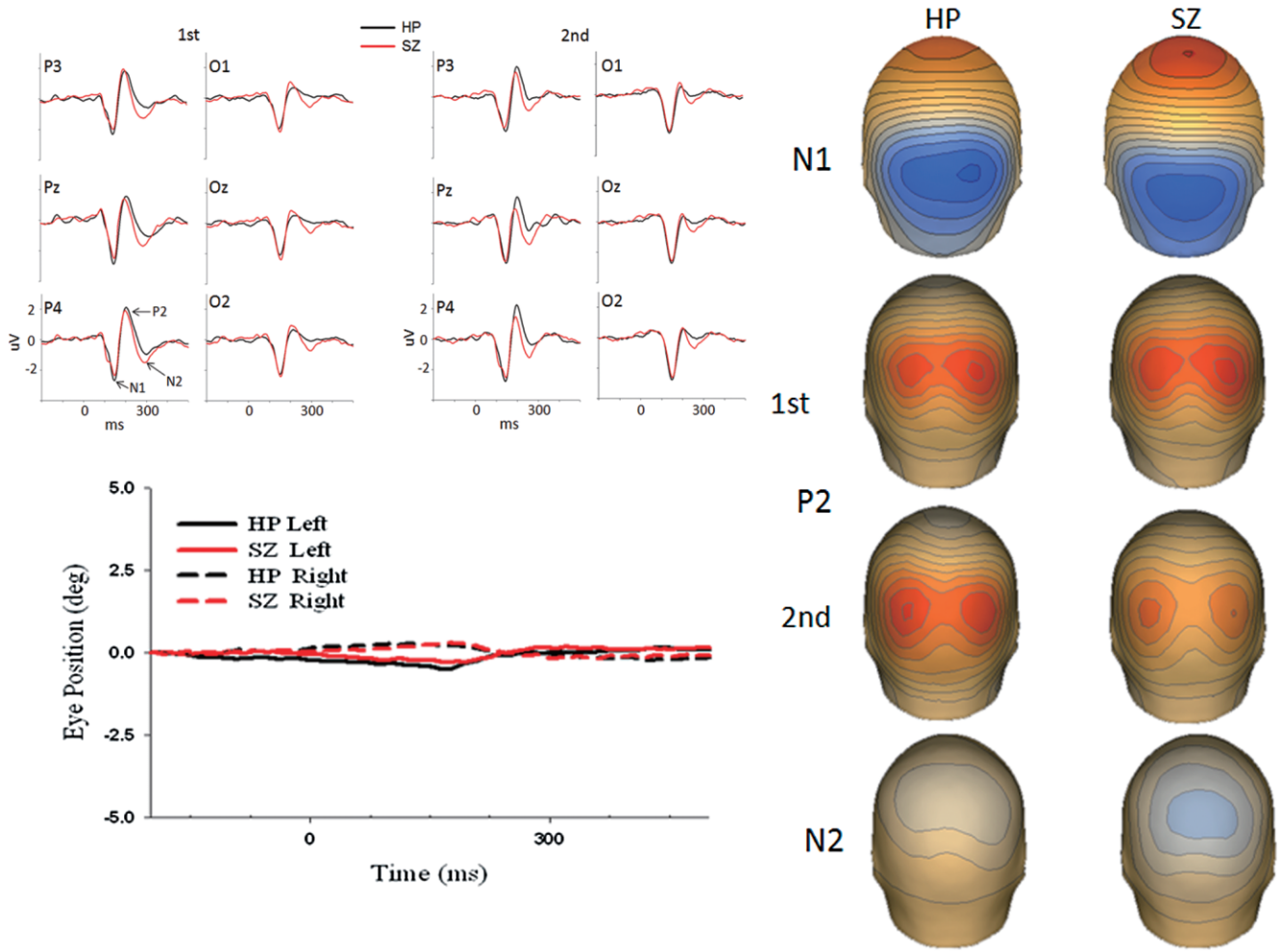

Figure 3. Neural activities associated with VEP components during speed discrimination task. The upper VEP waveforms at selected electrode sites (P3, Pz, P4, O1, Oz, O2) show the N1, P2, and N2 time courses for healthy participants (HP) and schizophrenia patients (SZ) separately to first and second presented stimuli. The lower time by voltage plot shows horizontal eye movements in response to left and right stimuli and illustrates that both schizophrenia and healthy participants followed the instruction to maintain central fixation. The right panel shows neural activities of N1, P2, and N2 and is seen from the occipital view. The N1 voltage topography shows HP has no difference from SZ. The P2 voltage topography shows HP have no difference from SZ to first stimulus but larger P2 to the second stimulus. The N2 voltage topography shows SZ have stronger N2 compared to HP.

Results

Behavior

There was no difference between groups on the number of usable trials (schizophrenia $M = 419$, $SD = 3$; healthy $M = 417$, $SD = 6$). Significantly higher speed discrimination thresholds (poorer speed discrimination performance) were observed for schizophrenia subjects ($M = 22.2\%$, $SD = 12$) than for healthy subjects ($M = 15\%$, $SD = 5.1$), $t(26) = 2.17$, $p = .039$, reflected by the shallower psychometric function for persons with schizophrenia in Figure 2. There was no group difference on "bias," the speed difference yielding 50% of reports of the test speed being faster than the standard, $t(26) = 0.99$, $p = .329$.

On reaction time, there was a significant Group × Speed interaction, $F(2,52) = 8.15$, $p = .003$, $\varepsilon = 0.70$. When the test speed equaled the standard speed, healthy persons ($M = 1300$ ms, $SD = 342$) were significantly slower than participants with schizophrenia ($M = 1136$ ms, $SD = 162$). The two groups did not differ significantly, however, when the test speed was either slower (healthy $M = 1095$ ms, $SD = 229$; schizophrenia $M = 1078$ ms, $SD = 152$) or faster (healthy $M = 1106$ ms, $SD = 218$; schizophrenia $M = 1054$ ms, $SD = 154$) than the standard.

VEP Effects (Table 1)

Relative deviation from standard speed. First, we investigated group differences on latencies and amplitudes as a function of test relative speed (faster vs. slower) versus the standard. For N1, there were no significant effects involving group membership on either latency ($M = 148$ ms, $SD = 8$) or amplitude ($M = 3.8$ μV, $SD = 1.7$). There was a significant effect, however, of presentation order on N1 amplitude, $F(1,26) = 11.1$, $p = .003$, with N1 to the second grating ($M = 4.1$ μV, $SD = 1.9$) being significantly larger than to the first grating ($M = 3.4$ μV, $SD = 1.8$). For P2 latency, there were no significant effects involving group membership ($M = 198$ ms, $SD = 12$). For P2 amplitude, there was a significant presentation order by group interaction, $F(1,26) = 7.6$, $p = .011$, which was driven by the fact that P2 amplitudes to the first grating did not

Table 1. *Mean Amplitude (uV) and Latency (ms) of Event-Related Potentials for Healthy (HP) and Schizophrenia (SZ) Participants*

	N1 amplitude		N1 latency		P2 amplitude		P2 latency		N2 amplitude		N2 latency	
	1st	2nd	1st	2nd	1st	2nd	1st	2nd	1st	2nd	1st	2nd
HP	3.6 (2.0)	4.3 (2.2)	146 (9)	146 (11)	3.2 (1.8)	**3.2 (1.8)**	201 (14)	199 (15)	**1.8 (0.8)**	**1.4 (0.5)**	**293 (21)**	**277 (24)**
SZ	3.3 (1.5)	3.9 (1.4)	150 (6)	149 (8)	3.2 (1.7)	**2.4 (1.5)**	201 (11)	194 (12)	**2.3 (0.8)**	**2.1 (0.7)**	**285 (11)**	**255 (17)**

Notes. *SD* values are included in parentheses. Effects with significant group differences are highlighted in bold.

differ between schizophrenia ($M = 3.2$ μV, $SD = 1.7$) and healthy ($M = 3.2$ μV, $SD = 1.8$) participants, but higher P2 amplitudes to the second grating were observed in healthy ($M = 3.2$ μV, $SD = 1.8$) compared to schizophrenia ($M = 2.4$ μV, $SD = 1.5$) participants. Inspection of the P2 topographies (see Figure 3) suggested that this between-groups difference on P2 amplitude in response to the second grating was accounted for by greater occipital-parietal cortex activity among the healthy subjects.

For N2 latency, there was a significant main effect of Group, with healthy participants being slower to generate a N2 ($M = 285$ ms, $SD = 20$) than persons with schizophrenia ($M = 270$ ms, $SD = 12$), $F(1,26) = 5.5$, $p = .027$. For N2 amplitude, there was also a significant main effect of Group, with healthy persons ($M = 1.6$ μV, $SD = 0.6$) having smaller amplitude responses than persons with schizophrenia ($M = 2.2$ μV, $SD = 0.7$), $F(1,26) = 6.1$, $p = .021$. Inspection of the N2 topographies (see Figure 3) suggested that this between-groups difference on N2 amplitude was accounted for by greater parietal cortex activity among the persons with schizophrenia (see Wang et al., 2010, for a similar parietal cortex signal during motion processing).

Absolute value of deviation from standard speed. Second, we investigated group differences on latencies and amplitudes as a function of test absolute speed (percent deviation: 0%, ±10%, ±20%, ±30%) versus the standard. For N1, there were again no significant effects involving group membership on either latency or amplitude. There were significant effects of absolute test deviation from the standard, however, on both N1 latency, $F(3,78) = 2.8$, $p = .046$, and amplitude, $F(3,78) = 5.6$, $p = .002$. The latency effect was driven by N1 peaks to the standard speed being later ($M = 149$ ms, $SD = 9$) than those to the 30% deviation test speeds ($M = 146$ ms, $SD = 9$), $t(27) = 2.9$, $p = .007$. The amplitude effect was driven by the N1 to standard speed ($M = 3.6$ μV, $SD = 1.8$) being significantly smaller than to all of the test speeds, ts$(27) > 3.0$, ps $< .006$, with the test speed means across absolute deviations not significantly differing (overall $M = 4.1$ μV, $SD = 1.8$). For P2 and N2 latency and amplitude, the group effects paralleled those observed in the relative deviation analyses (no group difference for P2 latency, but a main effect of Group on N2 latency: schizophrenia $M = 277$, $SD = 12$; healthy $M = 291$, $SD = 15$; $F(1,26) = 6.75$, $p = .015$). In addition, for P2 and N2 amplitudes, there were significant main effects of absolute deviation from the standard, Fs$(3,78) > 6.76$, ps $< .001$, εs < 1.07. The amplitude of responses to the standard speed stimuli (P2: $M = 2.8$ μV, $SD = 1.5$; N2: $M = -1.8$ μV, $SD = 0.7$) were significantly smaller than the amplitude of responses to the test speed stimuli (overall P2: $M = 3.3$ μV, $SD = 1.7$; overall N2: $M = 2.1$ μV, $SD = 0.8$), ts$(27) > 2.6$, ps $< .015$, with the test speed means across absolute deviations not significantly differing for either P2 or N2.

Relationships Between Behavior and Brain Activity

Bivariate correlations (linear and quadratic effects; quadratic fits did not significantly increase R^2 in any instance) were used to describe relationships between the five measures that significantly differentiated groups (reaction time, speed discrimination threshold, P2 amplitude to the second stimulus, and N2 latency and amplitude to the second stimulus). There were two classes of significant associations: (1) among brain activations, and (2) between brain activations and speed discrimination threshold. Among brain activations, there was a significant association between P2 and N2 amplitudes to the second stimulus for both healthy, $r(14) = 0.55$, $p = .02$, and schizophrenia participants, $r(14) = 0.48$, $p = .04$. These correlations did not significantly differ between groups (based on Fisher's z).

Given the significant correlation between P2 and N2, we investigated whether P2 and N2 may be indexing a single process in the speed discrimination decision using two additional analyses[1]. First, we calculated the S2 voltage difference from the P2 peak to the N2 peak for each individual, and performed ANOVAs with Group as a between-subjects factor and Speed as a repeated measures factor. There were no significant effects involving group membership on this variable. Second, we calculated the S2 latency difference between P2 and N2 for each individual, and then performed the same ANOVAs. There was a significant group main effect on this latency difference, $F(1,26) = 5.38$, $p = .029$. Healthy participants had larger P2-N2 latency differences ($M = 86$ ms, $SD = 18$) than participants with schizophrenia ($M = 73$ ms, $SD = 11$).

Regarding performance, there was a significant association between reaction time and N2 amplitude for schizophrenia, $r(14) = -.58$, $p = .029$, but not healthy subjects, $r(14) = .05$, $p = .87$, and the magnitude of these associations significantly differed, Fisher's $z = 1.67$, $p < .05$. When N2 amplitude was larger, schizophrenia participants made correct speed discrimination responses more promptly (Figure 4). There were also significant associations for speed discrimination threshold and P2 amplitude for participants with schizophrenia, $r(14) = -.46$, $p = .048$, but not healthy subjects, $r(14) = -.39$, $p = .080$, although the magnitude of these associations did not differ, Fisher's $z = -0.2$, $p > .05$. Participants were better at detecting between-stimuli speed differences when P2 amplitude to the second stimulus was larger (see Figure 4). Similarly, for healthy persons there also was a significant association between speed discrimination threshold and N2 amplitude, $r(14) = -.55$, $p = .020$; this same correlation for schizophrenia was marginally significant, $r(14) = -.45$, $p = .054$, but the magnitude of these relationships did not differ between groups, Fisher's $z = -0.31$, $p > .05$. Participants were better at detecting between-stimuli speed differences when N2 amplitude was larger

1. As requested by an anonymous reviewer.

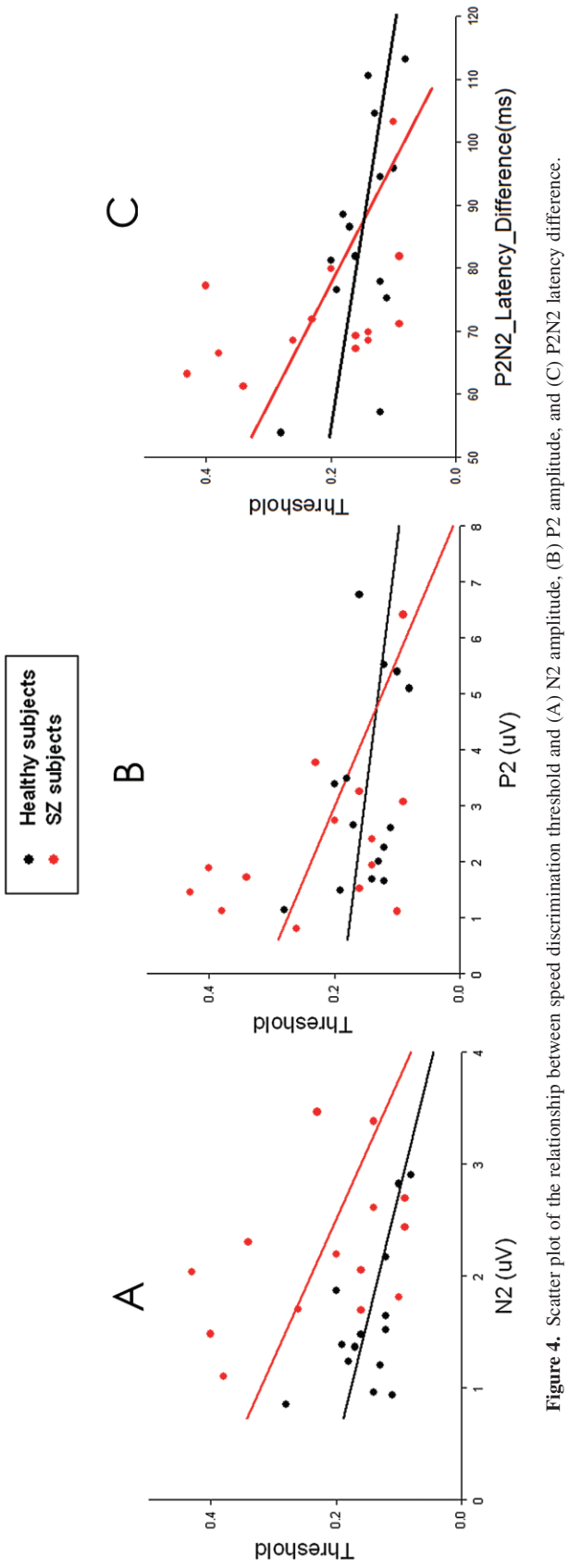

Figure 4. Scatter plot of the relationship between speed discrimination threshold and (A) N2 amplitude, (B) P2 amplitude, and (C) P2N2 latency difference.

(see Figure 4). Finally, there was a significant association between speed discrimination threshold and the P2-N2 latency difference for healthy persons, $r(14) = -0.55$, $p = .042$); this same correlation was not significant for participants with schizophrenia, $r(14) = -0.45$, $p = .103$, although the magnitude of these correlations did not differ between groups, Fisher's $z = 0.3$, $p = .76$. The shorter the P2-N2 latency difference, therefore, the worse was an individual's speed discrimination performance (see Figure 4).

Discussion

The present study examined the neural correlates of motion processing in schizophrenia during speed discrimination. Consistent with previous literature (Chen, Levy, et al., 1999; Clementz et al., 2007), schizophrenia patients had higher speed discrimination thresholds (worse performance) than healthy participants, an abnormality that was not a function of excessive eye movements (see Figure 3 herein; Hong et al., 2009). Higher speed discrimination thresholds in schizophrenia do not seem attributable to relatively early neural processing deficits (Kim et al., 2006) because patients had normal initial N1 responses (at 150 ms) to both the first and second motion gratings. About 50 ms later, however, schizophrenia participants had reduced P2 activity specifically to the second motion grating, an effect that was associated with worse speed discrimination ability. These data are most consistent with the theory of a late stage deficit in motion processing abnormalities in schizophrenia (Chen et al., 2004; Wang et al., 2010).

Despite poor speed discrimination performance, there were two indications that this abnormality was not a function of deficient early (more perception-related) neural activations. First, schizophrenia brain activations to the N1 were normal to both stimuli, indicating unimpaired early registration of the speed stimuli at the time of initial activation of V5 (Martinez-Trujillo, Cheyne, Gaetz, Simine, & Tsotsos, 2007). Second, healthy and schizophrenia participants had statistically similar reductions in N1 amplitude and increases in N1 latency to the standard compared to the test stimuli. The visual N1 is sensitive to speed differences (e.g., Maruyama, Kaneoke, Watanabe, & Kakigi, 2002; Müller, Göpfert, Breuer, & Greenlee, 1998), so our N1 effects indicate that both groups implicitly differentiated the most common stimulus (the standard) from the test stimuli. Intact implicit memory has been shown for schizophrenia using multiple paradigms (e.g., Kazes et al., 1999; Sponheim, Steele, & McGuire, 2004), and is related to intact implicit learning in schizophrenia (Danion, Meulemans, Kauffmann-Muller, & Vermaat, 2001). These findings suggest that difficulties with speed discrimination occur at a later neural processing stage (beyond V5).

Previous studies reporting early visual processing deficits in schizophrenia typically used low contrast stimuli to favor magnocellular inputs and high contrast to favor the parvocellular pathway (Butler & Javitt, 2005; Butler et al., 2005). Our stimuli were high contrast (100%), which possibly saturated early magnocellular responses, perhaps resulting in relatively normal early visual event-related potentials (ERPs). We used such stimuli because schizophrenia patients have abnormally low signal-to-noise responses for visual stimuli early in sensor processing (e.g., Clementz et al., 2008). With low contrast stimuli, therefore, it would be difficult to differentiate low response magnitude secondary to excess neural noise from a primary problem with motion perception. In addition, Chen et al. (2004) reported significantly poor velocity discrimination in schizophrenia using both low and high contrast stimuli and

suggested contrast had little effect on improving schizophrenia patients' speed discrimination performance. In addition, both of these papers evaluated neural response to speed independent of stimulus contrast. Medial temporal cortex might also help support such a specific function. For instance, Sclar, Maunsell, and Lennie (1990) reported that the middle temporal visual area (MT) has a steep contrast sensitivity response curve and could be saturated at high contrast. We did observe reduced bilateral parietal activation in schizophrenia specifically correlated to poor speed discrimination performance.

Stimulus salience can be modulated by exogenous (e.g., color saturation; Claeys, Lindsey, De Schutter, & Orban, 2003) or endogenous factors (e.g., attention; Lu, Lesmes, & Sperling, 1999). In the present study, the second moving grating elicited a larger N1 than did the first, an indication of enhanced attention/salience to the second stimulus (Hopfinger & West, 2006). Although both groups demonstrated a salience effect, only healthy persons seemed able to efficiently apply it to speed judgments, which was associated with enhanced neural activity at the time of P2 among participants with better (lower) discrimination thresholds. In contrast, schizophrenia participants had enhanced N2 activity over parietal cortex. A similar N2 component has been observed during visual motion processing when performing smooth-pursuit eye movements (Haarmeier & Thier, 1998). The significant correlation between N2 amplitude and speed discrimination threshold also indicates that N2-related neural computations, like P2, contributed to the speed discrimination decision. P2 and N2 were also significantly correlated within groups, indicating a functionally complementary relationship between these VEP components.

Multiple interpretations are possible, but perhaps speed template matching occurred most efficiently at the time of P2 among healthy persons; schizophrenia participants who managed this early comparison operation also showed better speed discrimination ability. Given their sluggish consolidation abilities, however, it was more likely participants with schizophrenia nominally performed a less efficient compensatory speed comparison operation at the time of N2, a thesis consistent with recent fMRI data (Chen et al., 2008). Late stage processing of motion information, as was evident for schizophrenia participants in the present study, is likely part of the 'salience-driven' motion processing system involving brain regions beyond V5 (Claeys et al., 2003).

Inadequate storage of early physical stimulus properties also could lead to compromised neural activation of higher-level operations needed for speed discrimination and deleteriously affect behavioral judgments. In response specifically to the second motion grating, when the comparison operation was required, schizophrenia patients not only had larger N2 responses, past the point when healthy participants seemingly performed the template matching operation, but increased the frequency of their neural oscillations (i.e., they had a shorter P2-N2 latency difference, which effectively resulted in oscillatory activity during this narrow time window at around 13.5 Hz, compared to 11.5 Hz for healthy persons). Indeed, for all participants a shorter P2-N2 interval was associated with worse speed discrimination performance (see Figure 4). Perhaps this indicates an attempt to sample additional information from the environment to perform the required matching operation, which is also consistent with schizophrenia subjects having larger N2 responses in relation to the second stimulus. This ostensible compensatory strategy also apparently was used by healthy persons who had subpar speed discrimination performance. Understanding the mechanisms underlying these relationships could provide useful insights into the nature of what we currently understand as information processing abnormalities in schizophrenia.

In summary, the present study reported on the neural substrates supporting speed discrimination performance among participants with schizophrenia. Abnormal neural activations in schizophrenia are not strictly associated with their poor speed discrimination abilities. Consistent with Wang et al. (2010), the present data indicate normal registration of an initial motion stimulus (including normal implicit memory for the most frequently presented speed) and a late stage processing abnormality in schizophrenia. In addition, there is evidence from these data that poor speed discrimination among schizophrenia participants is also a function of a sluggish neural comparison operation at the time of presentation of the second stimulus. This high-level deviation in motion comparison operations (at the level of parietal cortex) is additional evidence for a theory of later stage, post-V5 deficits in schizophrenia (Chen et al., 2004; Wang et al., 2010). The later stage deficit may imply impaired utilization of stimuli with high relative salience in schizophrenia (Federspiel et al., 2006) that require compensatory neural activations in an attempt to meet the demands of current behavioral requirements (Chen et al., 2008).

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