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Early visual processing deficits in patients with schizophrenia during spatial frequency-dependent facial affect processing

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ABSTRACT

Abnormal facial emotion recognition is considered as one of the key symptoms of schizophrenia. Only few studies have considered deficits in the spatial frequency (SF)-dependent visual pathway leading to abnormal facial emotion recognition in schizophrenia. Twenty-one patients with schizophrenia and 19 matched healthy controls (HC) were recruited for this study. Event-related potentials (ERP) were measured during presentation of SF-modulated face stimuli and their source imaging was analyzed. The patients showed reduced P100 amplitude for low-spatial frequency (LSF) pictures of fearful faces compared with the HC group. The P100 amplitude for high-spatial frequency (HSF) pictures of neutral faces was increased in the schizophrenia group, but not in the HC group. The neural source activities of the LSF fearful faces and HSF neutral faces led to hypo- and hyper-activation of the frontal lobe of subjects from the schizophrenia group and HC group, respectively. In addition, patients with schizophrenia showed enhanced N170 activation in the right hemisphere in the LSF condition, while the HC group did not. Our results suggest that deficits in the LSF-dependent visual pathway, which involves magnocellular neurons, impair early visual processing leading to dysfunctional facial emotion recognition in schizophrenia. Moreover, it suggests impaired bottom-up processing rather than top-down dysfunction for facial emotion recognition in these patients.

1. Introduction

Abnormal facial affect perception and processing have been widely documented in patients with schizophrenia, both behaviorally and physiologically, as measured by event-related potentials (ERPs). Over the last few decades, studies have revealed that face-related ERPs generally show reduced or delayed activation in patients with schizophrenia during facial emotion recognition or tasks related to face perception (McCleery et al., 2014). P100, a component reflecting early visual perception, was reduced in response to facial stimuli in patients (Campanella et al., 2006; Caharel et al., 2007), while some studies reported no differences between normal controls (Herrmann et al., 2004; Wynn et al., 2008; Jung et al., 2012). The N170 component has been consistently reported to show reduced amplitude and delayed latency that reflects altered decoding stages of facial features (Herrmann et al., 2004; Johnston et al., 2005; Turetsky et al., 2007; Lee et al., 2010). Some studies report that the late ERP components of facial emotional processing (N250 or P300) are altered in schizophrenia (Streit et al., 2001; Turetsky et al., 2007; Wynn et al., 2008); however, there are also results suggesting intact amplitudes and latencies in such components (Herrmann et al., 2004; Johnston et al., 2005; Turetsky et al., 2007).

Facial affect recognition involves complex visual processing that combines the global emotional expression of the face with detailed features. Such visual features are transferred from the retina to the visual cortex through two major parallel pathways: the magnocellular pathway and parvocellular pathway (Livingstone and Hubel, 1988; Tobimatsu and Celesia, 2006). Each pathway processes different aspects of facial features; global information and coarse emotional cues are related to the low-spatial frequency (LSF) features and thus, more dominantly processed through the magnocellular pathway, whereas high-spatial frequency (HSF) features like precise recognition of identity and detailed analysis of facial traits is more dominantly processed by the parvocellular pathway (Obayashi et al., 2009; Silverstein et al., 2010; Calderone et al., 2013; Laprevote et al., 2013).

Researchers have found meaningful abnormalities of such visual pathways in schizophrenia patients. These deficits include increased visual thresholds (Schechter et al., 2003; Caharel et al., 2007), greater sensitivity to backward masking (Saccuzzo and Braff, 1986; Braff, 1993; Butler et al., 1996; Green and Nuechterlein, 1999; Schechter et al., 2003), decreased contrast sensitivity (Slaghuis and Curran,

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1999; Keri et al., 2002; Butler et al., 2005), or motion perception (Chen et al., 1999; Schwartz et al., 1999; Li, 2002). Such findings indicate impairments in both magnocellular and parvocellular pathway, but a more dominant impairment in the magnocellular pathway seems to be evident. Thus, the deficit in perceptual organization or ability to process global form information may be responsible for inaccurate facial expression recognition in schizophrenia (Frith et al., 1983; Turetsky et al., 2007; Laprevote et al., 2010; Silverstein et al., 2010). However, there is insufficient evidence to confirm this hypothesis.

Since the parvocellular and magnocellular pathways have different dominancy in processing spatial frequencies (SF), it is possible to arouse each visual pathway using SF-manipulated facial images according to their dominancy. To the best of our knowledge, only one ERP study has used SF-manipulated facial images to investigate which visual pathway is responsible for abnormal emotion recognition in schizophrenia (Obayashi et al. (2009). Although they found that schizophrenia patients have deficits in SF-dependent visual processing, they failed to demonstrate any change in emotional processing due to SF differences. Therefore, the relationship between visual pathway deficits and altered facial affect recognition by patients with schizophrenia is still unclear.

In the current study, we investigated how deficits in the visual pathway alter face affect processing in schizophrenia using SF-manipulated facial images as stimuli. Patients with schizophrenia show more inaccurate understanding in negative emotions (Bell et al., 1997); therefore, we used fear and neutral facial pictures in different SF conditions. We hypothesized that visual pathway deficiencies would be dominant for LSF fearful face pictures expressed as reduced amplitude of the ERP components or reduced source activation of pathway-related brain areas.

2. Methods

2.1. Participants

We recruited 21 patients (10 women) aged 37.57 ± 11.37 years who were diagnosed with schizophrenia (SPR) based on the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) Axis I Psychiatric Disorders (First et al., 1997b). All patients were on stable doses of atypical antipsychotic medications. The patient's psychiatric symptoms were evaluated using the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987).

Eighteen healthy controls (HC; 10 women) were recruited from the local community through advertisements in local newspapers and posters. Their mean age was 40.83 ± 12.07 years. They were initially screened for any signs that might have affected the experiment. After initial screening, controls were interviewed using the SCID for DSM-IV Axis II Disorders to exclude those with any personality disorders (First et al., 1997a).

The details of the study were explained to the participants and they signed a written consent form, approved by the Institutional Review Board of Inje University Ilsan Paik Hospital. Detailed demographic data of our participants are listed in Table 1.

Table 1
Demographic data and symptom ratings of the participants.

		Schizophrenia ($n = 21$)	Healthy controls ($n = 18$)	p value
Age (years)		37.57 ± 11.37	40.83 ± 12.07	0.391
Male:Female		11:10	8:10	0.751
Education duration (years)		12.44 ± 2.33	14.17 ± 4.13	0.133
Number of accepted epochs				
BSF Fear		39.14 ± 11.62	40.56 ± 12.43	0.716
BSF Neutral		39.76 ± 12.43	42.11 ± 8.46	0.502
HSF Fear		37.38 ± 12.69	41.06 ± 9.74	0.323
HSF Neutral		37.19 ± 11.84	41.39 ± 9.20	0.230
LSF Fear		38.00 ± 11.41	40.33 ± 10.42	0.512
LSF Neutral		38.67 ± 11.72	40.17 ± 9.93	0.672
Number of hospitalizations		3.23 ± 7.83		
Dosage of medication (CPZ equivalents, mg)		394.12 ± 283.88		
PANSS	Positive score	15.70 ± 6.11		
	Negative score	20.20 ± 8.06		
	General score	39.55 ± 12.38		
	Total score	75.45 ± 23.86		

2.2. Stimuli

A total of 104 faces (52 fearful and 52 neutral facial expressions) were selected from the Korea University Facial Expression Collection (KUFEC) (Lee et al., 2006). The pictures were converted into gray scale. HSF and LSF pictures were obtained by applying high-pass (>24 cycles/image) and low-pass (<8 cycles/image) filters, respectively. The filtering procedures were done using the MATLAB software version 7.9 (The MathWorks, Natick, MA, USA). A statistical test using repeated measures ANOVA was used to ensure that the average intensity of each gray scale image did not differ between the SF and emotion (SF: (F[1.730,88.210] = 3.149, p = 0.055; emotion: F[1,51] = 1.959, p = 0.168). Example images and their amplitude spectrum of the facial stimuli used in the current study are illustrated in Fig. 1.

2.3. Experimental procedure

The participants were seated in a comfortable chair facing a 17-in. CRT monitor in a sound-attenuated room. The experiment consisted of three sessions. In each session, the participant was presented with two facial stimuli, a fearful and a neutral face, and an irrelevant stimulus (picture of a chair). The SF of the facial stimuli in a session was set to be either broad spatial frequency (BSF), HSF, or LSF, which was maintained during each session. The participants were instructed to focus on the stimuli appearing on the screen. To ensure that the participants were concentrating on the stimulus, they were instructed to press a button whenever a chair stimulus were presented. Each session was composed of 100 facial (50 fearful and 50 neutral faces) and 20 chair stimuli appearing in a random order. Each trial began with a fixation cross for 200 ms, followed by a blank screen for 500 ms. The face or chair stimuli were presented for 500 ms afterwards, followed by a blank screen with an interval between 1200 and 1800 ms.

2.4. EEG acquisition

EEG were amplified and recorded using NeuroScan SynAmps2 amplifier (Compumedics USA, El Paso, TX, USA). We recorded EEG using QuikCap (Compumedics USA, El Paso, TX, USA) with two additional bipolar electrodes to record vertical and horizontal electrooculogram. The signals were referenced to both mastoids and grounded to AFz. Impedances were maintained below 5 kΩ for all electrodes. The sampling rate was set to 1000 Hz and a 0.1–100 Hz online filter with 60 Hz bandstop filter were applied to the initial recording.

2.5. EEG preprocessing and ERP analysis

All preprocessing was done with the Scan 4.3 software (Compumedics USA, El Paso, TX, USA). A trained person inspected the recordings to reject artifact blocks induced by gross movements or other possible artifacts. Ocular artifacts were reduced using the mathematical procedure implemented in the preprocessing software (Semlitsch et al., 1986). The artifact-corrected data were re-referenced to average reference and epoched from −200 ms pre-stimulus to 900 ms post-stimulus. Each epoch was baseline-corrected and filtered using a 0.1 Hz to 30 Hz bandpass filter. Any epoch with amplitude exceeding ±75 μV was considered as a physiological artifact and was rejected from the analysis. Finally, the remaining artifact-free epochs were averaged across each stimulus condition and group. The number of epochs used

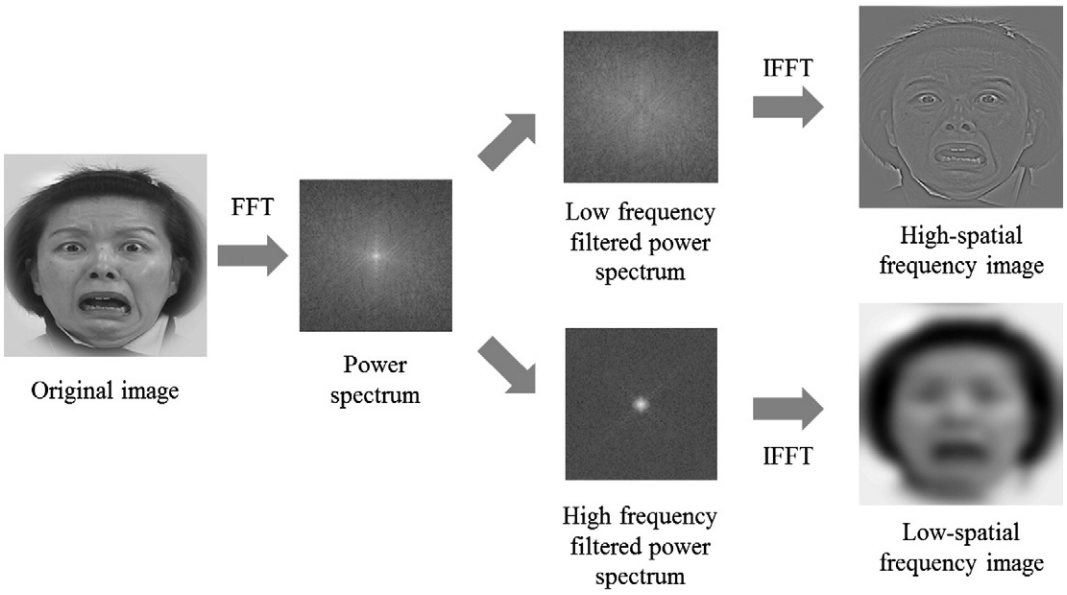

Fig. 1. Example images and their amplitude spectrums of the facial stimuli. The facial image was filtered to high-spatial frequency (HSF) image or low spatial frequency image (LSF).

to average for each participant did not significantly differ between stimuli conditions and groups (Table 1).

Using the averaged ERP waveform of each participant, we identified four ERP components (P100, N170, N250, and P300) (Streit et al., 1999; Onitsuka et al., 2006; Blau et al., 2007; Turetsky et al., 2007; Wynn et al., 2008). The latency and amplitude of each ERP component was identified using the following criterion: P100 as the maximum peak in electrodes O1/O2 between 50 and 150 ms; N170 as the minimum peak in electrodes P7/PO7/PO8/P8 between 120 and 220 ms; N250 as the minimum peak in F1/FC1/FC3/F2/FC2/FC4 between 150 and 350 ms; and P300 as the maximum peak in electrodes F1/FC1/F2/FC2 between 300 and 450 ms.

2.6. ERP source localization using sLORETA

Standardized low-resolution brain electromagnetic tomography (sLORETA) is widely used for solving the EEG inverse problem to estimate neural activation of the brain (Pascual-Marqui, 2002; Wagner et al., 2004). sLORETA assumes that the source activation of one voxel is synchronized to that of the surrounding voxels to calculate a particular solution.

In the current study, the source activations for each ERP component were estimated using the realistic head model based from the MNI152 standard template. The source space was restricted to the cortical gray matter, which provided us with 6238 voxels with $5 \times 5 \times 5$ mm resolution. The source activation for each ERP component and condition used its own time range for estimation ([mean ERP latency] $\pm$ [1 SD]) to represent different latencies between conditions or group (Kim et al., 2013). All source estimation procedures were done using the free sLORETA software (http://www.uzh.ch/keyinst/loretaOldy.htm).

2.7. Statistical analysis

To compare demographic variables between groups, the independent *t*-test and Chi-square test were used. The amplitude and latency of each ERP component was compared using repeated measures ANOVA, with within subject factors of laterality (left and right), frequency (BSF, HSF, and LSF), and emotion (neutral and fear), and group (SPR and HC) as the between-subjects factor. Green–Geisser correction was used to correct for non-sphericity. For any significant effect, we performed a post hoc analysis adjusting the *p* values using Bonferroni correction for multiple comparison.

To compare sLORETA source images, we used the statistical package implemented in the sLORETA software. We used log of ratio of averages as the statistical comparison method for each condition with statistical non-parametric mapping method that uses a randomization test for multiple comparison correction.

3. Results

3.1. Demographical data

Table 1 summarizes the demographical data and its statistical results. There were no differences in age, education, and gender between the two groups. The number of epochs used for analysis did not differ for SF ($F[2,74] = 0.575$, $p = 0.565$) or emotion ($F[1,37] = 0.962$, $p = 0.333$).

3.2. P100 component

Fig. 2 shows the P100 waveform according to the stimuli conditions. The amplitudes and latencies averaged across each facial expression are summarized in Table 2. RMANOVA revealed that P100 had a significant main effect of SF ($F[2,74] = 11.374$, $p < 0.001$) and a significant interaction of SF $\times$ emotion $\times$ group ($F[2,74] = 5.044$, $p = 0.009$).

To investigate the interaction between SF $\times$ emotion $\times$ group, post hoc analysis was performed using the averaged P1 amplitude over both hemispheres for each SF, emotion, and group condition. A significant group difference was found between LSF conditions ($p = 0.045$) when the fear stimuli were presented. SPR exhibited significant differences between the SFs in the fearful condition (BSF > HSF, $p = 0.006$; BSF > LSF, $p = 0.010$), also in the neutral condition with a different trend (BSF > HSF, $p = 0.017$; LSF > HSF, $p = 0.008$). HC demonstrated significant differences in P100 amplitude between SF as LSF > HSF ($p = 0.005$) in the fearful condition and no significant differences in neutral condition (Fig. 3).

The latency of the P100 showed a significant main effect of SF ($F[1.440,53.286] = 3.645$, $p = 0.031$) but not of any other main effects or interaction involving group differences.

3.3. N170 component

Fig. 4 shows the mean waveform averaged across each emotion (combined fearful and neutral) according to their left and right

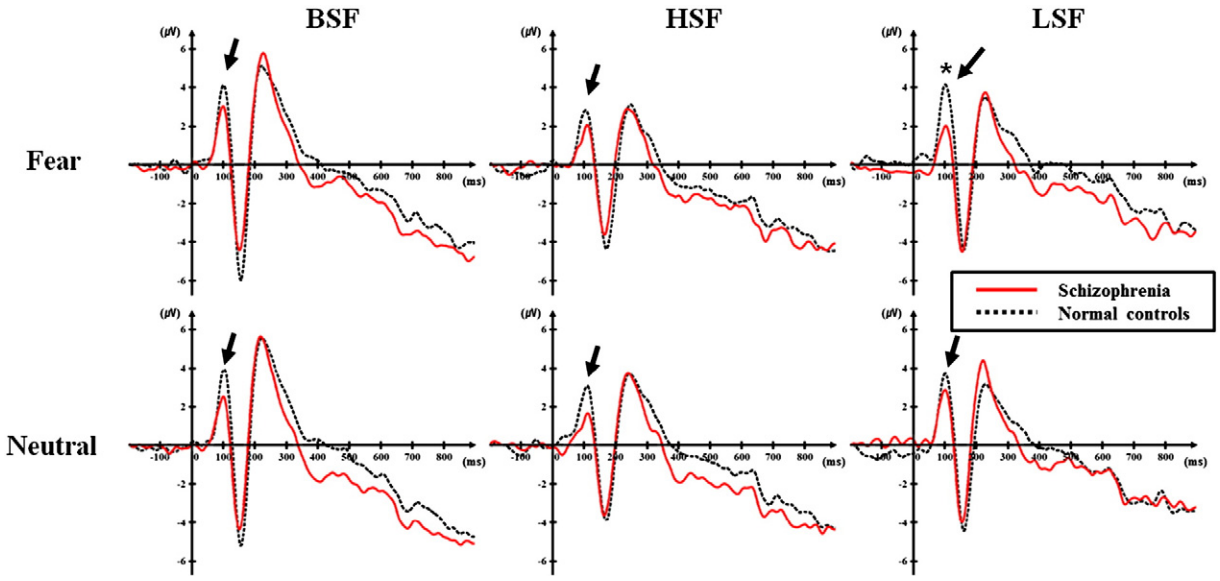

Fig. 2. P100 waveform of each condition and group. Statistical analysis revealed a significant between-group difference ($p = 0.045$) in LSF fear condition (marked as an asterisk), and a SF × emotion × group interaction ($p = 0.016$). The arrows indicate the P100 component.

hemisphere. Table 2 summarizes the N170 amplitude and latencies averaged across each hemisphere. There was a significant main effect of SF ($F[2,74] = 9.671$, $p < 0.001$) and a significant laterality × SF × group interaction ($F[1.468,54.310] = 3.704$, $p = 0.044$). As the more negative amplitude corresponds to enhanced activation for negative ERP components, we denote the inequality sign according to their absolute values.

The post hoc analysis to investigate the laterality × SF × group interaction, we performed the post hoc analysis using the averaged N170 amplitude over emotion for each laterality, SF, and group. The results demonstrated that both groups showed enhanced activation in BSF when compared with HSF and LSF in the left hemisphere (SPR: BSF > HSF, $p = 0.008$; BSF > LSF, $p = 0.005$; HC: BSF > HSF, $p = 0.005$; BSF > LSF, $p = 0.020$). In the right hemisphere, SPR showed a significant enhancement in the LSF condition when compared to HSF, and a marginal difference between BSF (LSF > HSF, $p = 0.037$; LSF ≥ BSF, $p = 0.068$). HC showed differences where BSF > HSF ($p = 0.030$) but no differences between other conditions. To summarize, the left hemisphere showed a consistent trend of BSF > HSF = LSF in both groups. In the right hemisphere, schizophrenia patients revealed a significant LSF > HSF activation; however, normal controls showed BSF > HSF differences (Fig. 5). Such different trends in the right hemisphere demonstrates that SPR shows a relatively enhanced activation of the LSF N170 component.

The latency of the N170 showed a significant main effect of SF ($F[1.259,46.592] = 50.788$, $p < 0.001$) but there were no other main or interaction effects involving group differences.

3.4. N250 and P300 component

The N250 component showed a significant main effect of SF ($F[1.719,63.619] = 24.750$, $p < 0.001$) and emotion ($F[1,37] = 4.214$, $p = 0.047$). The latency of the N250 showed a significant main effect of SF ($F[2,74] = 10.149$, $p < 0.001$) and a significant latency × emotion × group interaction ($F[1,37] = 6.662$, $p = 0.014$).

The P300 amplitude or latency had neither significant main effects nor group interactions.

Table 2
Mean amplitude and latencies of P100, N170, N250, and P300 and the standard error of each spatial frequency (low spatial frequency, LSF; broad spatial frequency, BSF; and high spatial frequency, HSF) and emotion (fear and neutral).

		Schizophrenia			Healthy Controls		
		LSF	BSF	HSF	LSF	BSF	HSF
Amplitude	(μV)						
P100	Fear	3.12 ± 0.61	4.35 ± 0.50	2.92 ± 0.50	4.96 ± 0.65	4.64 ± 0.54	3.49 ± 0.55
	Neutral	3.90 ± 0.55	3.78 ± 0.60	2.73 ± 0.59	4.29 ± 0.59	4.45 ± 0.65	3.99 ± 0.64
N170	Fear	−5.75 ± 0.65	−6.12 ± 0.81	−4.63 ± 0.65	−4.83 ± 0.70	−6.36 ± 0.88	−5.05 ± 0.70
	Neutral	−5.41 ± 0.83	−5.91 ± 0.78	−4.93 ± 0.76	−4.99 ± 0.90	−5.71 ± 0.85	−4.60 ± 0.82
N250	Fear	−3.16 ± 0.35	−4.21 ± 0.38	−2.92 ± 0.38	−2.58 ± 0.38	−3.51 ± 0.41	−2.44 ± 0.41
	Neutral	−3.22 ± 0.34	−4.22 ± 0.42	−3.26 ± 0.36	−2.70 ± 0.37	−3.88 ± 0.45	−2.84 ± 0.39
P300	Fear	2.27 ± 0.61	2.00 ± 0.50	2.59 ± 0.53	1.51 ± 0.66	1.42 ± 0.54	2.24 ± 0.57
	Neutral	2.23 ± 0.61	2.58 ± 0.61	2.29 ± 0.65	1.52 ± 0.65	1.57 ± 0.66	1.70 ± 0.70
Latency	(ms)						
P100	Fear	103.12 ± 2.71	100.29 ± 2.51	108.81 ± 2.69	105.23 ± 3.01	102.69 ± 2.71	104.81 ± 2.91
	Neutral	102.81 ± 2.42	101.36 ± 2.51	105.29 ± 3.42	103.03 ± 2.61	103.25 ± 2.72	107.67 ± 3.69
N170	Fear	160.12 ± 2.33	153.74 ± 2.11	168.79 ± 2.98	163.03 ± 2.52	155.33 ± 2.28	172.69 ± 3.22
	Neutral	157.29 ± 2.13	152.91 ± 2.28	167.93 ± 2.78	163.36 ± 2.30	155.53 ± 2.46	157.29 ± 2.13
N250	Fear	234.67 ± 7.07	225.98 ± 5.06	243.93 ± 7.27	243.25 ± 7.63	235.64 ± 5.46	255.19 ± 7.85
	Neutral	228.60 ± 6.59	231.88 ± 5.45	252.00 ± 6.33	245.17 ± 7.12	234.50 ± 5.89	248.75 ± 6.84
P300	Fear	390.52 ± 5.69	394.62 ± 9.01	396.24 ± 7.00	384.81 ± 6.15	371.22 ± 9.73	383.86 ± 7.57
	Neutral	394.21 ± 6.33	398.33 ± 6.37	396.95 ± 5.18	379.39 ± 6.83	376.78 ± 6.88	389.61 ± 5.59

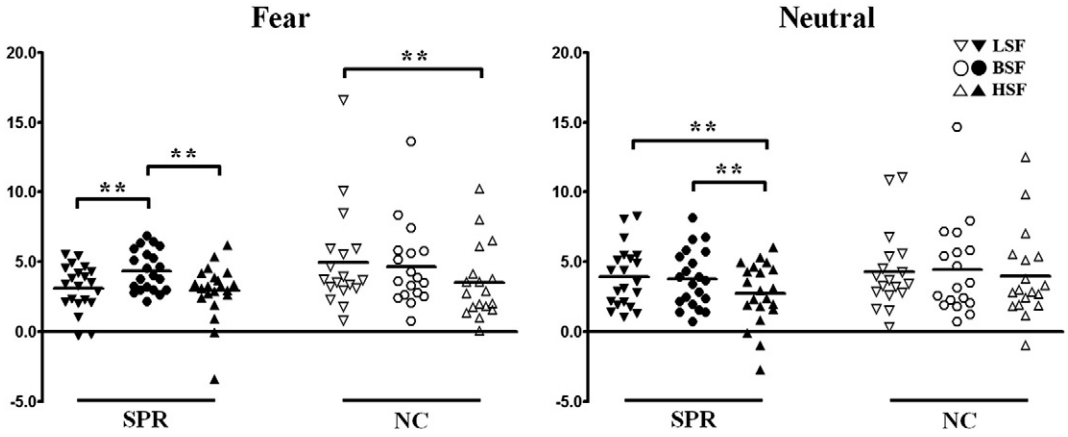

Fig. 3. P100 amplitude comparison between each emotion, group, and frequency. In fearful faces, healthy controls showed a significant difference in amplitude between conditions, with HSF < LSF, while schizophrenia patients showed an LSF < BSF difference. In the neutral condition, HSF activation was significantly lower compared to LSF and BSF in patients with schizophrenia.

3.5. sLORETA analysis

We found a significant group interaction between SF × emotion × group in P100 and SF × laterality × group interaction in N170. Therefore, we compared the following source images between groups: 1. Fear LSF P100; 2. Fear HSF P100; 3. LSF N170; 4. HSF N170.

Between-group comparisons on LSF source activation revealed significantly reduced activation in SPR P100 Fear condition (medial frontal gyrus, BA6; paracentral lobule, BA31; cingulate gyrus, BA24; Fig. 6, top). On the other hand, enhanced activation in medial frontal gyrus (BA10) in HSF condition were demonstrated in SPR when compared to NC (Fig. 6, bottom). The significant voxels are listed in Table 3.

4. Discussion

In this study, we examined deficits in the visual pathway for face affect processing in patients with schizophrenia using SF-manipulated facial images. For fearful face stimuli, the P100 amplitude was reduced in SPR compared to NC in LSF stimuli. In the case of neutral face stimuli, SPR showed reduced P100 amplitude for HSF faces compared to BSF and LSF, while these differences were not observed in NC. P100 source activity revealed reduced activation of the medial frontal gyrus, paracentral lobule, and cingulate gyrus in the LSF fear condition and enhanced activation of the medial frontal gyrus in the HSF neutral condition. In addition, SPR showed significantly enhanced N170 activation for LSF faces compared to HSF faces in the right hemisphere, while HC did not show these differences.

Pourtois et al. (2005) found that the P1 component is enhanced by LSF fearful faces in healthy subjects. They interpreted that an early P1 response to fear expression depends on a visual pathway preferentially tuned to coarse-magnocellular inputs. Obayashi et al. (2009) reported that HC tend to show augmented amplitudes in P100 in response to LSF faces; however, the augmented patterns were not observed in SPR.

In line with previous studies, we found decreased activation in P100 processing, indicating abnormalities in early visual processing in both LSF and HSF conditions. We also found significant emotion effects presented as reduced activation in the LSF fear condition and a decreasing trend in the HSF neutral condition. The reduced P100 activation seems to be consistent with the fact that SPR shows both magnocellular and parvocellular pathway deficiencies, and this deficit is more dominantly

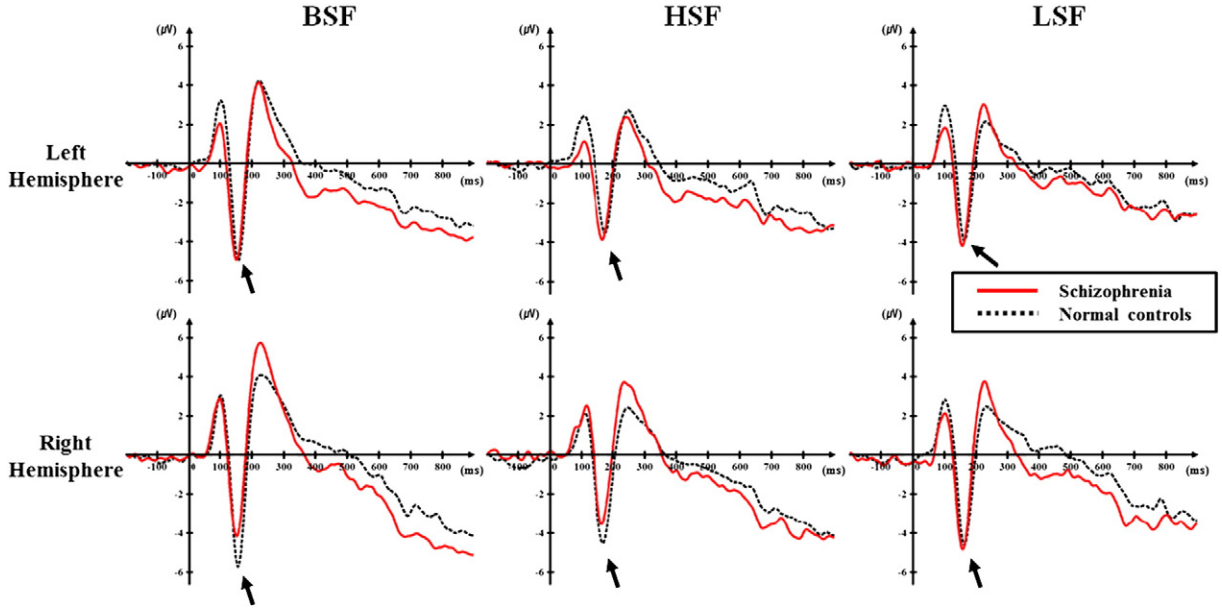

Fig. 4. The mean waveform averaged across each emotion (combined fearful and neutral) according to their left and right hemispheres. Statistical analysis revealed a significant SF × laterality × group interaction ($p = 0.004$). No significant group differences were found in any condition. The arrows indicate the N170 component.

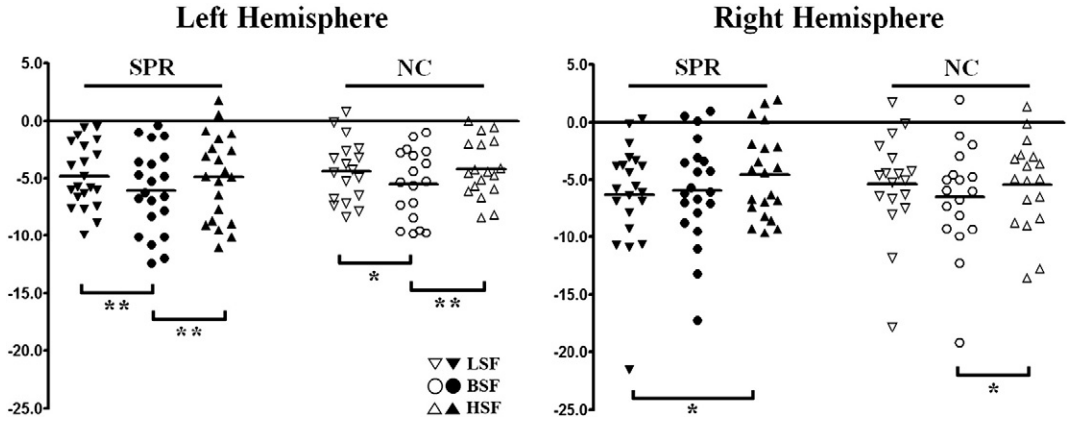

Fig. 5. N170 amplitude (combined fearful and neutral) comparison between each group, and frequency. In the left hemisphere, N170 BSF amplitude was enhanced in healthy controls compared to HSF and LSF (left). In the right hemisphere, patients with schizophrenia showed reduced activity in the HSF than in the LSF, whereas healthy controls showed a significant increase in amplitude in the BSF condition than in the HSF condition (right).

pronounced in the magnocellular pathway (Butler et al., 2001, 2005; Kim et al., 2005; Schechter et al., 2005; Campanella et al., 2006).

The source activity of LSF P100 was reduced in the medial frontal gyrus and paracentral lobule in SPR compared to HC. The ventromedial cortex receives magnocellular projections originating from the amygdala (Porrino et al., 1981). In addition, the magnocellular pathway supports the rapid transformation of LSF information to subcortical regions such as the amygdala (Pessoa and Adolphs, 2010). Moreover, the amygdala plays a critical role in the perception and regulation of emotion, especially fear (Davidson et al., 2000; Hariri et al., 2003), and can regulate the frontal cortex and visual processing regions (Hariri et al., 2003; Vuilleumier and Pourtois, 2007). Therefore, decreased activation of the medial frontal gyrus in the LSF fear condition explains the secondary effect of magnocellular pathway deficiencies affecting the perception of fear emotion. In addition, since studies repeatedly reported reduced gray matter volume (Borgwardt et al., 2010; Hirjak et al., 2014; van Lutterveld et al., 2014) and reduced functional connectivity (Liu et al., 2011) related to paracentral lobule in schizophrenia patients, this area could be an important anatomical region that might reflect a deficit of early visual processing in SPR.

In contrast, enhanced activation of the medial frontal gyrus (BA 10) in the HSF P100 is consistent with the fMRI study of Calderone et al. (2013). They found enhanced activation of these areas in the HSF condition, suggesting that SPR preferentially utilizes HSF information rather than LSF while constructing a frame for an object stimulus or to compensate for the deficits in LSF information. In addition, behavioral studies show that SPR tend to perceive neutral faces as fearful and this may cause hyperactivation in the medial frontal gyrus due to the additional emotional engagement (Kohler et al., 2003).

The N170 component represents structural decoding of the face; therefore, enhanced N170 amplitude in the right hemisphere in the LSF condition could be a compensatory effect associated with the reduced LSF P100 amplitude. Impaired processing of global information in earlier stages provides weakened form information reaching the fusiform face area in schizophrenia patients, which leads to insufficient signal strength to process face stimuli (Silverstein et al., 2010). This is in line with previous studies showing that patients require longer stimuli duration or increased signal strength to process face stimuli (Butler et al., 2008; Chen et al., 2009). Moreover, the primary neural source of the N170 component is thought to be the fusiform gyrus, in particular the right fusiform gyrus, which is thought to be more sensitive to faces (Kanwisher et al., 1997). Our findings showing increased N170 LSF amplitude in the right hemisphere might represent a delayed processing of the LSF features due to earlier insufficient P100 activation in LSF processing or insufficient HSF processing to decode detailed facial features.

We did not find any amplitude differences, including group interactions in the later components. This suggests that the altered emotion

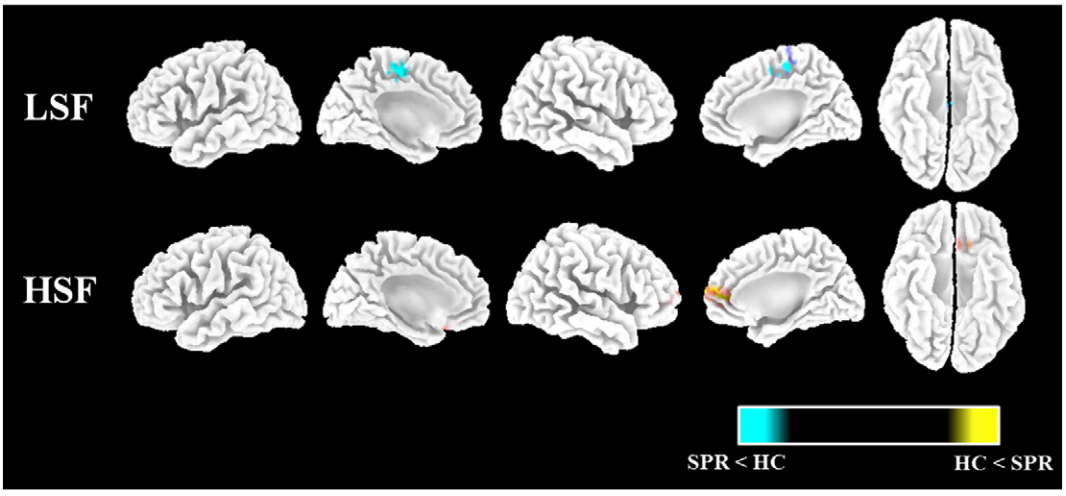

Fig. 6. Between-group comparisons of P100 source activity in LSF and HSF conditions using sLORETA. In the P100 LSF fear condition (top), patients with schizophrenia showed reduced activation in the medial frontal gyrus (BA6), precuneus (BA31), and cingulate gyrus (BA24). In the P100 HSF neutral condition (bottom), patients with schizophrenia showed enhanced activation in the medial frontal gyrus (BA10).

Table 3
List of voxels showing significant differences between group in each condition. (BA: Brodmann Area).

Condition	Structure	BA	MNI-coordinates			Cluster size (voxels)	
			x	y	z		
P100 LSF fear	Medial frontal gyrus	6	0	-20	55	36	$p < 0.05$
	Paracentral lobule	31	0	-20	50	6	$p < 0.05$
	Cingulate gyrus	24	5	-10	50	1	$p < 0.05$
P100 HSF neutral	Medial frontal gyrus	10	10	55	15	5	$p < 0.05$

recognition in schizophrenia is due to impaired bottom-up processing at a relatively early stage rather than a top-down dysfunction (Butler et al., 2007). There are competing theories that emphasize top-down (Cohen and Servan-Schreiber, 1992; Weinberger and Gallhofer, 1997; van der Stelt et al., 2004) versus bottom-up deficiencies (Doniger et al., 2002; Gonzalez-Hernandez et al., 2003; Butler et al., 2005; Johnston et al., 2005) in schizophrenia; however, our results suggests dominant bottom-up dysfunction in the early stages, which leads to altered emotional processing.

There are some possible limitations of the current study. First, we could not exclude a medication effect in our study. There are studies indicating that the amplitude of the ERP is influenced by antipsychotic medication. However, we did not find any significant correlation between the medication dose and ERP amplitude. Second, our paradigm did not assess behavioral responses to evaluate the emotions evoked by the stimuli. As mentioned previously, patients with schizophrenia tend to perceive neutral emotion as more fearful than healthy controls; therefore, it is not clear whether the patients with schizophrenia perceived each emotion as expected.

In the current study, we found altered visual processing in the early stage ERP amplitudes. These were more biased towards a magnocellular pathway deficit as shown by group differences in the P100 LSF fear condition. Different source activation patterns suggest that impairments of the magnocellular pathway are also related to emotional processing at a subcortical level, and lead to impairments in the visual pathway. In addition, the absence of a later ERP component deficit suggests that the deficit in emotion recognition in patients with schizophrenia is implicated with early stage bottom-up visual processing.

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Contributors

Do-Won Kim designed the study and wrote the manuscript. Seung-Hwan Lee designed the study and wrote the protocol. Miseon Shim and Myeong Ju Song helped the data management and calculated the current source densities from the data set. Chang-Hwan Im supervised the study process and manuscript writing. All authors contributed to and have approved the final manuscript.

Conflict of Interest

All the authors declare that they have no conflicts of interest.

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