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Abnormal frontal activation during the perception of biological motion in patients with schizophrenia*

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Patients with schizophrenia have difficulty processing visual motion signals including biological motion (BM). A recent fMRI study found altered activation within the posterior superior temporal sulcus in patients with schizophrenia during BM perception. In addition, some frontal areas including ventral premotor cortex are known to be involved in biological motion perception in healthy individuals. However, it is unknown whether patients with schizophrenia have abnormal brain functioning in frontal areas while perceiving biological motion. The present study examined frontal activation associated with biological motion perception in patients with schizophrenia and healthy controls with fMRI data. In healthy controls, a portion of the ventral premotor area and the inferior frontal gyri exhibited specific activation to biological motion stimuli, which was not observed in schizophrenia patients. A dorsal portion of the superior frontal cortex was activated when non-biological motion was misperceived as biological in healthy controls while overall activation level was lower in schizophrenia. Anterior parts of the prefrontal cortex showed suppression during biological motion perception task in healthy controls, whereas no specific activation was observed in the patients with schizophrenia. These results indicate that schizophrenia patients exhibit abnormal frontal brain activation relative to healthy controls in biological motion perception, suggesting altered activities in frontal areas including the mirror neuron system.

Key words : Biological motion, Schizophrenia, Frontal cortex, Mirror neuron system, fMRI

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People are highly adept at recognizing biological motion (BM) including the movement of humans or other animals. Rapid and precise perception of such biological kinematics is essential for survival and everyday life. Even when BM is portrayed by a dozen of point-lights (Johansson, 1973) on the major joints of the body, observers can recognize it easily and effortlessly (Bertenthal & Pinto, 1994; Cutting, Moore & Morrison, 1988; Kim, Park, & Blake, 2011; Neri, Morrone, & Burr, 1998; see also reviews by Blake & Shiffrar, 2007; Kim, 2012). Often, observers are able to infer characteristics such as gender and affect from these simplified motion cues (Cutting & Kozlowski, 1977; Dittrich, Troscianko, Lea, & Morgan, 1996; Loula, Prasa, Harber, & Shiffrar, 2005; MacArthur & Baron, 1983).

A number of neuroimaging studies have investigated neural mechanisms underlying BM perception. The most consistently identified regions in these studies are the posterior superior temporal sulcus (pSTS) and its surrounding areas (Beauchamp, Lee, Haxby, & Martin, 2003; Gr èzes, Fonlupt, Bertenthal, Delon-Martin, Segebarth, & Decety, 2001; Grossman & Blake, 2001, 2002; Pelphrey, Mitchell, McKeown, Goldstein, Allison, & McCarthy, 2003; Michels, Lappe, & Vaina, 2005; Peuskens, Vanrie, Verfaillie, & Orban, 2005; Puce, Allison, Bentin, Gore, & McCarthy, 1998; Santi, Servos, Vatikiotis-Bateson, Kuratate, & Munhall, 2003; Vaina, Solomon, Chowdhury, Sinha, & Belliveau, 2001). In addition to the pSTS and surrounding visual areas, several imaging and lesion case studies found that frontal areas are also driven by the point-light BM; these areas include the ventral premotor cortex (vPMC), supplementary motor area (SMA) and parts of the inferior frontal gyrus (IFG) (Gilaie-Dotan, Kanai, Bahrami, Rees, & Saygin, 2013; Santi et al., 2003; Saygin, 2007; Saygin, Wilson, Halger, Bates, & Sereno, 2004; Vaina et al., 2001), suggesting that these areas respond to simplified motion cues of action (point-light BM) as well as natural scene of human action (Saygin, 2007; Saygin et al., 2004). Functionally these areas are classified as parts of the human mirror neuron system which is important for action understanding, imitation, or coding for the intention of behavior (Binkofski & Buccino, 2006; Buccino, Binkofski, & Riggio, 2004; Harrington, Siegert, & McClure, 2005; Iacoboni, Molnar-Szakacs, Gallese, Buccino, Mazziotta et al., 2005; Pineda, 2008; Rizzolatti & Craighero, 2004; Shamay-Tsoory, Shur, Barcai-Goodman, Medlovich, Harari, et al., 2007) and is thought to be involved in empathy, theory of mind and facial emotion processing (Rizzolatti & Craighero, 2004). Studies on BM perception and frontal activity, therefore, suggest effects of high-level frontal areas on visual perception (BM

perception, specifically) or vice versa (Saygin, 2007).

Schizophrenia, a well-known mental disorder, is characterized by abnormalities in visual perception, including the extended visual backward masking effect (Green, Nuechterlein, & Minz, 1994a,b), poor velocity discrimination (Chen, Palafox, Nakayama, Levy, Mattysse et al., 1999), impaired global coherent motion perception (Chen, Nakayama, Levy, Mattysse & Holzman, 2003b; Li, 2002), and impaired detection/discrimination of BM (Kim, Doop, Blake, & Park, 2005; Kim et al., 2011; Spencer, Sekuler, Bennett, & Christensen, 2013). Recent neuroimaging and EEG studies reported abnormal neural activation associated with BM perception in patients with schizophrenia (Kim et al., 2011; Singh, Pineda, & Cadenhead, 2011). Specifically, an fMRI study by Kim and colleagues (2011) revealed that selective activation to BM within the pSTS was lacking in patients with schizophrenia compared with healthy controls, and an EEG study (Singh et al., 2011) observed that first episode patients showed reduced mu wave suppression over sensorymotor cortex (including the STS) when viewing BM. However, it is not yet known whether the frontal activities associated with BM perception (e.g. vPMC and IFG) are also abnormal.

As mentioned earlier, the vPMC, IFG and some parietal areas comprise the mirror neuron system. Past research on the mirror neuron system have consistently reported functional abnormality or reduced mirror neuron activation in schizophrenia. An earlier imaging study indicated that patients with schizophrenia exhibit abnormal mirror neuron-related activation while viewing emotional stimuli (Quintana, Davidson, Kovalik, Marder, & Mazziotta, 2001). More recent electrophysiological studies demonstrated similar functional abnormality. For instance, patients with schizophrenia showed reduced motor-evoked potential (MEP) facilitation during the observation of action; MEP strength is thought to reflect the premotor mirror neuron activity (Enticott, Hoy, Herring, Johnston, Daskalakis et al., 2008; Mehta, Thirthalli, Basavaraju, Gangadhar, & Pascual-Leone, 2014) and such deficient mirror neuron activities appear to be correlated with impaired social cognition (Mehta et al., 2014). Considering results from previous studies pertaining to the involvement of the frontal areas in BM perception in healthy indiv iduals, and the function of the mirror neuron system in healthy individuals and those with schizophrenia, the frontal areas of patients with schizophrenia appear to exhibit different activation patterns from those of healthy controls while performing a BM perception tasks. Specifically, it is hypothesized that the ventral premotor cortex (vPMC) and inferior frontal

gyrus (IFG) of patients with schizophrenia would not demonstrate clearly selective activation for BM compared to non-BM stimuli. To examine this issue, the present study analyzed whole-brain fMRI data collected in a previous BM perception study (Kim et al., 2011), focusing on the frontal areas activated by BM stimuli and their activation patterns, as well as differences between groups.

Methods

Participants Ten outpatients who met DSM-IV criteria (American Psychiatric Association, 1994) for schizophrenia (4 females) were recruited from the outpatient clinic of Vanderbilt Psychiatric Hospital in Nashville, TN, USA. Diagnosis was determined on the basis of the Structured Clinical Interview for DSM-IV (SCID; Spitzer & Williams, 1985). Clinical symptoms at the time of testing were assessed with the Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962). Positive and negative symptoms were assessed using the Scale for Assessment of Positive Symptoms (SAPS; Andreasen & Olsen, 1982) and the Scale for Assessment of Negative Symptoms (SANS; Andreasen & Olsen, 1982), respectively. Mean illness duration was 18.6 (SD 8.67) years. All patients were taking atypical antipsychotic medication including risperidone, clozapine, or olanzapine. Mean CPZ dose (dosage equivalent to chlorpromazine, Bezchlibnyk-Butler & Jeffris, 1999) was 235.57 (SD 90.29) mg/day.

Ten healthy controls (matched on age, education, and IQ; 5 females) were recruited from the local community in Nashville, TN, USA. Healthy controls were excluded if they had a past or present DSM-IV Axis I/II disorder,or a family history of psychotic illness. Additionally, healthy controls were screened to rule out schizotypal personality using the Schizotypal Personality Questionnaire (SPQ; Raine, 1991) before the experiment. According to Raine 's report (1991), 10% of the population scored above 41 (out of 74) and those individuals may have an elevated risk for schizotypal personality disorder. Mean SPQ score of healthy participants was 14.3 (SD 9.0), which was well below the cut-off score. All participants had normal or corrected-to-normal vision and were provided with complete description of the procedure and gave written consent. The participants were the same people who took part in a previously published study (Kim et al., 2011).

Stimuli Point-light biological motion (BM) and scrambled motion consisting of black dots against a white background were presented on a CRT monitor (120Hz, TOTOKU Calix CDT2141A, Japan) controlled by a Macintosh computer running Matlab (Mathworks Inc.

Table 1. Demographic information

	Controls (n=10)	Patients (n=10)	*t*	*p*
Age	38.7 (7.2)	41.7 (9.4)	-.8	.43
Sex (M/F)	5/5	6/4	χ^2=.20	.65
Education (years)	15.7 (2.7)	14.3 (2.45)	1.22	.87
IQ	101.9 (11.8)	100.3 (27.9)	.17	.87
SPQ	14.3 (9.0)			
BPRS		14.9 (6.6)		
SAPS		19.6 (15.24)		
SANS		28.8 (14.9)		
Hand (L/R/Bi)	0/10/0	2/7/1	χ^2=3.52	.17
Illness duration (years)		18.6 (8.67)		

SPQ: Schizotypal Personality Questionnaire. BPRS: Brief Psychiatric Rating Scale.
SAP(N)S: Scale for Assessment of Positive(Negative) Symptoms.

Natick, USA) and the psychophysics toolbox (Brainard, 1997; Pelli, 1997). Biological motion animations consisted of 12 dots denoting the locations of the head, torso, and joints of a human body. Each BM stimulus engaged in one of 24 distinct activities including walking, running, jumping or kicking. Scrambled motion animations were created by spatially randomizing the initial dot positions of the corresponding BM stimulus; the local motion trajectories of each dot remained unchanged, but the global organization was disrupted. There was the third category of the stimuli, which was partially (37%) scrambled motion. However, the data associated with these stimuli were excluded from analyses because of the participants' biased response. Each PL animation fell within a virtual rectangular region subtending 3.0 × 6.0° visual angle. Each animation consisted of 20 frames and was played for 1 second in each trial.

Event-related fMRI scan During the fMRI scan, all participants performed a task of discriminating BM and scrambled motion. The task comprised nine runs; each run contained 24 trials (8 BM, 8 scrambled, and 8 partially scrambled motion in random order). The inter-stimulus interval (ISI) was 11 seconds, and it was long enough for the hemodynamic response to return to baseline. A fixation cross was always on at the center of the screen and changed its size 2 seconds before each event so that the participants ready for the next trial. The participants judged whether the given

motion depicted human action or not in each trial by pressing one of the pre-assigned buttons of the hand-puck. The total number of trials was 216. After finishing the task, the behavioral responses were classified into four signal-detection categories according to the combinations of stimulus and response: (1) “hits” or “human” response to BM, (2) “misses” or “non-human” response to BM, (3) “false alarms” or “human” response to scrambled motion, and (4) “correct rejections” or “non-human” response to scrambled motion. By counting the number of hits and false alarms, an unbiased discrimination sensitivity d' (=|z(hits) - z(false alarms)|) for each participant was calculated. Partially scrambled motion trials were excluded from this classification because there was no ‘correct’ answer for this type of stimulus.

Image acquisition All brain images were collected on a Phillips Intera Achieva 3T MRI scanner located at VU medical center, Nashville, Tennessee, USA. Before functional scans, high-resolution T1 anatomical images were collected for each participant (170 slices, 1.0×1.0×1.0mm). Functional images were collected across the entire brain (single-shot EPI, TR=2000ms, TE=25ms, flip angle=90°, FOV=240×240mm), parallel to AC-PC line (25 slices, 1.875×1.875mm in plane, 4.5mm thick with 0.45mm gap). During the scans, stimuli were back-projected onto a screen located at the participant’s feet and viewed through a periscope mirror attached to the head coil.

Image analysis Imaging data were preprocessed and analyzed using Brain Voyager QX 2.8.0 (Brain Innovations, Maastricht, The Netherlands). Anatomical images were transformed into Talairach stereotaxic space (Talairach & Tournoux, 1988) on which functional images were aligned. Functional volume preprocessing includes three-dimensional motion correction, linear detrending, high-pass temporal frequency filtering and spatial smoothing with a 4mm FWHM spatial filter. After preprocessing, the general linear model (GLM) was applied to the time-series of task-related functional volumes with the design matrix (reference time course) was defined to include 4 predictors based on behavioral responses (i.e. hit, miss, false alarm, and correct rejection). The voxels coupled with the event-related trials were averaged to create a single time-series for each condition (predictor); the percent change in BOLD signal was defined as the difference between baseline (activation level at the stimulus onset) and the average activation within a time window ranging from 6 to 8 seconds after the stimulus onset.

To localize the regions where the two participant groups showed significantly different

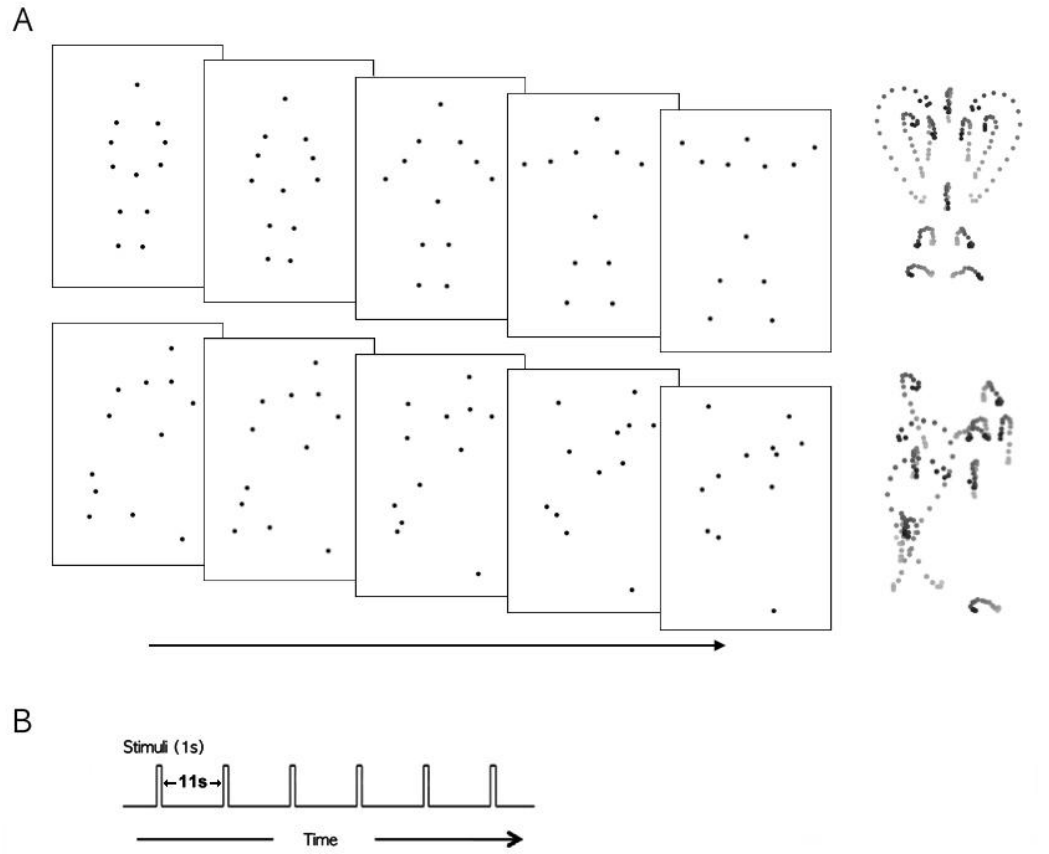

Figure 1. A (top): Exemplar frames of the animation (left) and motion trajectory (right) of a point-light (PL) biological motion ("jumping jack"). Light-gray indicates dots in earlier frames and dark-gray represents positions at later frames in the trajectory figure. A (bottom): Scrambled motion frames and the dot trajectory. B: Schematic structure of the trials in the event-related design.

activation in the BM processing, the BOLD signals associated with successful BM perception ("hit" trials) were compared between groups (i.e. controls - patients) at a false discovery rate (FDR) of $q<0.001$ (corrected $p<0.000163$). Those regions are listed in Table 2. Then, within the regions showing significant group difference, the event-related BOLD signal change for each predictor was examined in each group. Among the 4 predictors, "miss" trials were excluded from analysis because of the paucity of the trials in both groups.

Results

Behavioral performance In discriminating

BM and scrambled motion, the patients with schizophrenia performed significantly worse compared to healthy controls. Mean (*SE*) discrimination sensivity (d´) was 2.54 (0.4) in patients and 3.82 (0.32) in healthy controls and this difference was statistically significant (*t(18)*=2.45, *p*=0.024). With respect to accuracy rate for the stimulus-response categories, both group had comparable hit rate (controls 98.38 (*SE*=1.08)%, patients 94.57 (*SE*=3.42)%), but the patients had higher false alarm rates (37.7%, SE=9.7) than healthy controls (19.7%, *SE*=5.8). This difference in the incidence of false alarms did not reach statistical significance (*t(18)*=-1.59, *p*=0.13), although the effect size was high (Cohen's *d*=0.75).

The behavioral performance (d´) of the patients was not significantly correlated with their symptom severity indexed by BPRS (*r*=-0.56, *p*=0.09), SAPS (*r*=-0.24, *p*=0.49), or with SANS (*r*=0.01, *p=0.98*); the behavioral performance (d´) of the patients was also not significantly correlated with medication (*r*=-0.032, *p*=0.94). The SPQ score in healthy controls did not significantly correlate with d´ (*r*=-0.014, *p*=0.97).

fMRI results To localize the frontal areas where healthy controls and patients with schizophrenia demonstrated significantly different activation while processing BM stimuli, the BOLD signals associated with successful BM perception ("hit" trials) were compared between the two groups (i.e. controls - patients). In Table 2, the list of the frontal areas localized by group comparison is presented. Also as shown in Figure 2A, healthy controls exhibited greater activation for BM than patients with schizophrenia in several frontal areas. These areas included the bilateral ventral premotor cortex (vPMC), the bilateral inferior frontal gyrus (IFG), and the dorsal portion of the superior frontal gyrus (SFG). In addition, the contrast maps in Figure 2A also show that patients with schizophrenia had relatively greater activation in the anterior portion of the SFG and some prefrontal cortices compared with healthy controls.

For the localized frontal areas through the group comparison, the average % BOLD signal changes associated with each type of behavioral responses (hits, correct rejections, and false alarms) from the BM discrimination task were examined (Figure 2B). "Miss (non-BM response to BM)" trials were not included.

Among the areas where controls > patients was observed, the bilateral vPMC area showed greater activation to BM stimuli (hits) than to scrambled motion (correct rejections) in healthy controls (Figure 2B-a). Such BM-selective activation in healthy group was also observed in the bilateral inferior frontal gyri (Figure 2B-b).

Table 2. Frontal regions with different BM-associated activations between healthy controls and patients with schizophrenia

Area	L/R	Talairach Coordinates			CO vs. SZ	cluster size (# voxel)	*t*	corrected *p**	BA
		x	y	z					
vPMC	L	-53	0	22		130	8.26	0.000163	6
	R	48	7	31		312	5.80		6
IFG	L	-37	24	3	CO > SZ	57	6.63		45
	R	47	18	5		86	6.92		45
SFG	R	2	17	51		166	9.06		8
SFG	L	-17	45	45		35	-5.66	0.000163	8
PFC	L	-16	54	30	CO < SZ	22	-5.23		9
	R	11	-60	-9		9	-3.55		10

* Multiple comparison correction: False discovery rate (q(FDR)) < 0.001. vPMC: ventral premotor cortex, IFG: inferior frontal gyrus, SFG: superior frontal gyrus, PFC: prefrontal cortex, CO: Healthy controls, SZ: Patients with schizophrenia. BA: Brodmann Area

Follow-up within group analysis for the only healthy controls yielded significant activation difference between hit and correct rejection trials in the right hemisphere vPMC (peak: 59,1,26, 28 voxels, t=3.07, p<0.003, corrected with $q(FDR)$<0.05) and in the left IFG (peak: -53,18,8; 42 voxels, t=3.93, p<0.003, corrected with $q(FDR)$<0.05). In both the vPMC and IFG areas, activations for the error trials (false alarm) were similar to or greater than those for correct BM perception (hits), although the variances were large. In the patients with schizophrenia, on the other hand, both the vPMC and IFG areas were less activated across all the response types compared with healthy controls. Furthermore, these two areas in the patients did not show significant activation difference between hits and correct rejection trials, indicating a lack of BM-selective activity that was observed in healthy controls.

In the dorsal portion of the SFG (Figure 2B-c), healthy controls exhibited greater activation than the schizophrenia patients in general. However, activations for hits and correct rejections were not significantly different each other. Within the healthy group, the false alarm-associated activation was greater than activations for the other two response types (peak: 0,17,50, 104 voxels, t=4.50, p<0.0005 corrected with $q(FDR)$<0.01). In the schizophrenia patients, activations were similar across the three response types. In more anterior

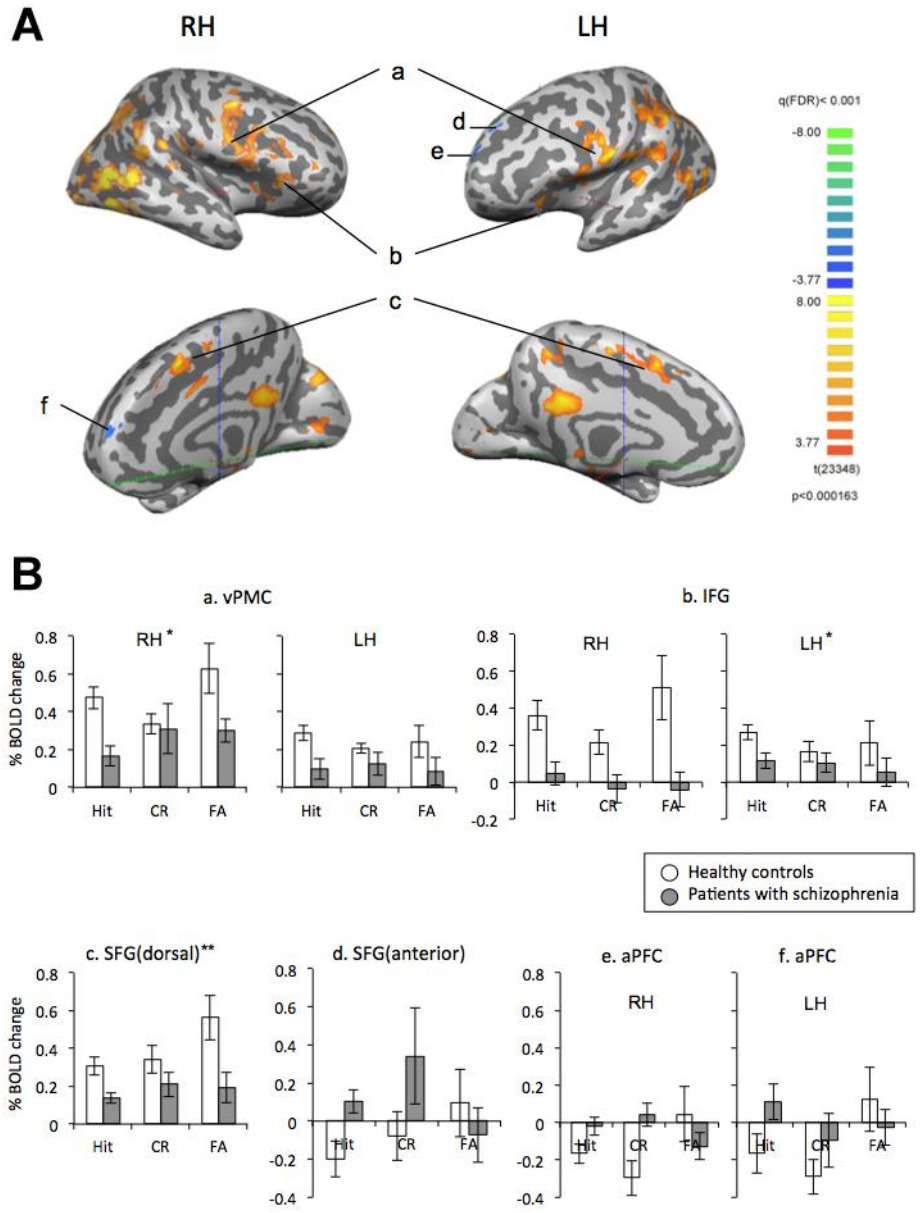

Figure 2. A: The regions showing activation difference between controls and patients with schizophrenia while viewing BM stimuli. B: Averaged peak activities associated with each type of response in the regions of interest from A. Error bar indicates standard error of the mean (SE). CR: correct rejection, FA: false alarm.

*:significant difference between hits- and correct rejections-related activation within the healthy controls in the right vPMC and the left IFG.

**:significant difference between FA and the other responses within healthy controls in the dorsal SFG.

parts of the superior and prefrontal cortex, activations for hits and correct rejections (note that these are correct responses) were suppressed (below the baseline) in healthy controls while the patients with schizophrenia showed small amount activation (Figure 2B-d) or no specific activation (Figure 2B-e and f), which made the contrast that looks like greater activation in schizophrenia than healthy controls. (Figure 2A). In the false alarm trials, activation was small, and both groups was associated with similar activation levels.

Discussion

The present study investigated activation differences in the frontal areas between healthy controls and patients with schizophrenia while they performed a BM discrimination task, using data collected for a previous study (Kim et al., 2011).

To summarize the results, the participants' behavioral performance indicated that the patients with schizophrenia had significantly lower discrimination sensitivity than controls and their behavioral performance was not correlated with clinical symptoms or medication. Imaging analyses revealed that the two groups demonstrated different frontal activations: healthy controls showed greater activation than the patients in the vPMC, IFG and the dorsal portion of the SFG. Among these areas, the vPMC and the IFG of healthy controls showed selectively greater activation to BM stimuli (hit trials) than to scrambled motion stimuli (correct rejection trials). In contrast, the patients with schizophrenia did not demonstrate any selective activation for BM stimuli. In the dorsal portion of the SFG, there was also group differences (controls > patients) in activation: however, BM-selective activation was not observed in either group. This area was strongly activated when scrambled motions were misjudged as BM in healthy controls. Lastly, healthy controls exhibited suppressed activity in the anterior part of the PFC while the patients did not show specific activation.

The ventral premotor cortex and the inferior frontal gyrus in BM perception

The main finding of this study is that different activation pattern was observed in the area of vPMC and IFG between the healthy controls and the patients with schizophrenia. Consistent with the previous findings (Santi et al., 2003; Saygin, 2007; Saygin et al., 2004; Vaina et al., 2001), these two areas activate more in response to BM stimuli than to non-biological scrambled motion stimuli in healthy individuals. On the other hand, the patients with schizophrenia did not show BM-selective activation in the vPMC and the IFG, and overall activation level in

patients with schizophrenia was also lower than of healthy controls. These results, therefore, suggest that the frontal function involved in BM processing is also compromised in schizophrenia in addition to abnormal function within the visual areas (e.g. pSTS; Kim et al., 2011; Singh et al., 2011).

Given that overall activation level is lower compared with controls, it could be argued that the abnormality within the vPMC and the IFG reflects patients' lack of attention on the visual task. Although this is not entirely impossible, this is unlikely. Behavioral results indicated that patients made more false alarm responses but the number of miss response was as small as that of controls. It is expected that schizophrenia patients would make more errors regardless of stimulus type if they had attention problems. Moreover, the previous study (Kim et al., 2011) revealed comparable (or somewhat stronger) activation than controls within the visual area (pSTS) from the same patients, discounting the explanation of hypoactivation reflecting poor attention.

Rather, the results from the vPMC and the IFG area could be discussed in consideration of the functions of the human mirror neuron system. As mentioned earlier, the vPMC and the IFG are part of the human mirror neuron system, and it is well known that the activities of the human mirror neuron system are driven by observing and understanding others' actions (Buccino et al., 2004; Umilta, Kohler, Gallese, Fogassi, Fadiga et al., 2001), learning of imitation (Rizzolatti, Fogassi, & Gallese, 2001), and expressing empathy (Leslie, Johnson-Frey, & Grafton, 2004; Rizzolatti & Craighero, 2004). Although out of the field of the vision science, a large body of literature has reliably reported abnormal neural activities within the mirror neuron system in patients with schizophrenia, mostly related with social stimuli. For instance, an fMRI study (Quintana et al., 2001) investigated the mirror neuron activities with a simple working memory task in which facial emotion diagrams or color circles were used; the inferior frontal cortex (IFC) activated in only normal controls for the facial diagrams. EEG studies also consistently reported reduced mirror neuron activities in schizophrenia on action observation (Enticott et al., 2008; McCormick, Brumm, Beadle, Paradiso, Yamada, et al., 2012) and theory of mind (Mehta et al., 2014).

Therefore, the patients' abnormal activation of the vPMC and the IFG in BM perception seems to reflect dysfunction of the mirror neuron system, and it is unlikely to be a result of deficient visual motion processing independent of the mirror neuron functions: these areas showed similar activation across the schizophrenia patients and healthy controls for random dot cinematograms (Chen, Grossman, Bidwell,

Yurgelun-Todd, Gruber et al., 2008). Because the point-light BM not only has visual motion cues but also has socially-relevant information, it may activate action recognition in the mirror neuron system of the normal brain. In other words, the results from the healthy group suggest that the function of action understanding of the vPMC and IFG is not restricted to natural motion scenes but extends to simple biological motion cues (Saygin et al., 2004), and the patients with schizophrenia may have abnormal neural activitiy with respect to this type of function.

Other frontal areas: superior and prefrontal cortex Beyond the vPMC and IFG, the two groups evidenced activation differences of other frontal areas: the SFG and PFC as presented in Table 2 and Figure 2. The activation patterns and group difference in these areas appear to reflect higher cognitive processes to perform perceptual/cognitive tasks in general and their abnormality, respectively, rather than indicating specific BM-related activities.

In the dorsal portion of the SFG, healthy controls exhibited greater overall activation than schizophrenia patients. This area corresponds to the Brodmann area (BA) 8 which overlaps the frontal eye field (FEF). BA 8 is known as subserving motor planning (Crozier, Sirigu, Lehéricy, van de Moortele, Pillon, et al., 1999) and visuospatial attention (Cheng, Fujita, Kanno, Miura, & Tanaka, 1995). In addition, this area is also activated by uncertainty (Volz, Schubotz, & von Cramon, 2003, 2004, 2005). Unlike the vPMC and the IFG, BM-selective activation was not observed in healthy controls while the greatest activation was associated with false alarm responses in this area. The reason for strong false alarm associated activation is unclear. One speculation is that healthy controls might have experienced uncertainty when they viewed scrambled motion. If so, they might have recruited resources from the SFG for making decision (even if they made errors). Such putative cognitive process may not work well for the patients group: the false alarm associated activation was similar to the other responses (hit and correct rejection) related activation. Because this is a highly speculative interpretation, more research is needed in the future to examine this issue with more ambiguous and sophisticated visual motion stimuli. It should be also noted that the number of false alarm trials was relatively small, and it is also possible that the group difference in this area might have demonstrated widely observed 'hypofrontality' in patients with schizophrenia.

In the anterior portion of the PFC, healthy controls exhibited suppression (negative % BOLD change) in hits and correct rejection trials (to remind, both are correct responses) while

schizophrenia patients did not show meaningful activation linked with any response type. To speculate, the anterior PFC may be responsible for higher level processing for generating correct response and its related activities might be manifested as suppression in the healthy group, whereas this putative suppression of inhibiting irrelevant response might be lacking in patients with schizophrenia. Even within the healthy controls, suppression was not observed when errors were made (false alarms), which supports this interpretation. Similar results have been observed in another study, although the task was quite different: a recent fMRI study with working memory paradigm (Kim, Matthews, & Park, 2010) reported anterior PFC suppression when healthy participants made correct response, which was not observed in patients with schizophrenia. Suppression did not occur when healthy participants failed to maintain the target stimulus, which is similar to the present results, too. Therefore, the results from the anterior PFC may reflect inhibition of irrelevant response (healthy controls) and inhibition failure (schizophrenia) rather than activity directly linked with BM processing. Further research focusing on inhibition or decision making in patients with schizophrenia would is needed to more clearly understand this issue.

Limitations There were a few limitations in the present study. First, all patients with schizophrenia were taking antipsychotic medications at the time of testing. The possibility of medication effects is not entirely excluded. However, past research suggest no explicit or specific effect on cortical excitability (e.g. Boroojerdi, Topper, Foltys, &Meincke, 1999; Daskalakis, Christensen, Chen, Fitzgerald, Zipursky, et al., 2003; Davey, Puri, Lewis, & Ellaway, 1997; Fitzgerald, Brown, Daskalakis, & Kulkarni, 2002) and on perceptual/cognitive ability (e.g. Allen, Gilbertson, van Kammen, Kelly, Gurklis, et al., 1997; see also Chen, Levy, Sheremata, Nakayama, Matthysse, et al., 2003a). In addition, the behavioral performance was not significantly correlated with medication in the present study. It is unlikely, therefore, that medication effect may be a critical confounding factor in interpreting the current data. Second, the sample size was relatively small. Regardless, group difference in behavioral performance was statistically significant with large effect sizes, and a conservative statistical criterion (false discovery rate of < 0.001) was used to find group difference in activation maps. Third, overall activation in patients with schizophrenia was lower than the healthy controls in most frontal areas except the anterior regions. These results do not exclude the possibility of a more general frontal dysfunction that appears common to schizophrenia (e.g. Okugawa, Nobuhara, Minami,

Takase, Sugimoto, et al., 2006). However, even if this were the case, it does not necessarily invalidate the mirror neuron explanation of aspects of schizophrenia, but rather that, at least, abnormal BM-associated activation may have been manifested along with broader neural deficits.

Conclusion The present study revealed different activation patterns of the frontal areas between healthy controls and the patients with schizophrenia while performing the BM discrimination task. Consistent with past research, it was confirmed that successful BM perception was associated with selective activities in the vPMC and the IFG (e.g. Saygin et al., 2004). However, the patients with schizophrenia have neural dysfunction within these two areas, which is a new finding and appears to be related with deficient mirror neuron functions. Taken together, the results from the present study exhibit that individuals with schizophrenia have abnormal neural activities linked with BM perception across a wide range of network including the frontal area beyond the visual area (e.g. pSTS), and future research focusing on connectivities among the areas could provide further understanding on the neural abnormalities related with behavioral outcome in schizophrenia.

References

Allen, D. N., Gilbertson, M. W., van Kammen, D. P., Kelly, M. E., Gurklis, J. A. Jr., & Barry, E. J. (1997). Chronic haloperidol treatment does not affect structure of attention in schizophrenia. *Schizophrenia Research, 25*, 53-61.

American Psychiatric Association (1994). *DSM-IV: Diagnostic and Statistical Manual of Mental Disorders (Ed. 4)*. Washington DC: American Psychiatric Press.

Andreason, N. C., & Olsen, S. (1982). Negative v positive schizophrenia. Definition and validation. *Archives of General Psychiatry, 39*, 789-794.

Beauchamp, M. S., Lee, K. E., Haxby, J. V., & Martin, A. (2003). fMRI responses to video and point-light displays of moving humans and manipulable objects. *Journal of Cognitive Neuroscience, 15*, 991-1007.

Bertenthal, B. I., & Pinto, J. (1994). Global processing of biological motions. *Psychological Science, 5*, 221-225.

Bezchlibnyk-Butler, K. Z., & Jeffris, J. J. (1999). *Clinical handbook of psychotropic drugs, 9th edition.* Hogrefe and Huber Publishers, Seattle.

Binkofski, F., & Buccino, G. (2006). The role of ventral premotorcortex in action execution and action understanding. *Journal of Physiology-Paris, 99,* 396-405.

Blake, R., & Shiffrar, M. (2007). Perception of human motion. *Annual Review of Psychology,*

58, 47-73.

Boroojerdi, B., Topper, R., Foltys, H., & Meincke, U. (1999). Transcallosal inhibition and motor conduction studies in patients with schizophrenia using transcranial magnetic stimulation. *British Journal of Psychiatry, 175*, 375-379.

Brainard, D. H. (1997). The psychophysics toolbox. *Spatial Vision, 10,* 443-446.

Buccino, G., Binkofski, F., & Riggio, L. (2004). The mirror neuron system and action recognition. *Brain and Language, 89*, 370-376.

Chen, Y., Grossman, E. D., Bidwell, L. C., Yurgelun-Todd, D., Gruber, S. A., Levy, D. L., Nakayama, K., & Holzman, P. S. (2008). Differential activation patterns of occipital and prefrontal cortices during motion processing: Evidence from normal and schizophrenic brains. *Cognitive, Affective,* & *Behavioral neuroscience, 8,* 293-303.

Chen, Y., Levy, D. L., Sheremata, S., Nakayama, K., Matthysse, S., & Holzman, P. S. (2003a). Effects on typical, atypical, and no antipsychotic drugs on visual contrast detection in schizophrenia. *American Journal of Psychiatry, 160,* 1795-1801.

Chen, Y., Nakayama, K., Levy, D., Mattysse, S., & Holzman, P. S. (2003b). Processing of global, but not local, motion direction is deficient in schizophrenia. *Schizophrenia Research, 61*, 215-227.

Chen, Y., Palafox, G. P., Nakayama, K., Levy, D. L., Mathysse, S., & Holzman, P. S. (1999). Motion perception in schizophrenia. *Archives of General Psychiatry, 56,* 149-154.

Cheng, K., Fujita, H., Kanno, I., Miura, S., & Tanaka, K. (1995). Human cortical regions activated by wide-field visual motion: an $H^2(15)O$ PET study. *Journal of Neurophysiology, 74*, 413-427.

Crozier, S., Sirigu, A., Lehéricy, S., van de Moortele, P. F., Pillon, B., Grafman, J,. Agid, Y., Dubois, B., & LeBihan, D. (1999), Distinct prefrontal activations in processing sequence at the sentence and script level: an fMRI study. *Neuropsychologia, 37,* 1469-1476.

Cutting, J. E., & Kozlowski, L. T. (1977). Recognizing friends by their walk: Gait perception without familiarity cues. *Bulletin of the Psychonomic Society, 9*, 353-356.

Cutting, J. E., Moore, C., & Mossison, R. (1988). Masking the motions of human gait. *Perception and Psychophysics, 44,* 339-347.

Daskalakis, Z. J., Christensen, B. K., Chen, R., Fitzgerald, P. B., Zipursky, R. B., et al. (2003). Effect of antipsychotics on cortical inhibition using transcranial magnetic stimulation. *Psychopharmacology, 170*, 255-262.

Davey, N. J., Puri, B. K., Lewis, S. W., & Ellaway, P. H. (1997). Effects of antipsychotic medication on electromyographic responses to transcranial magnetic stimulation of the motor cortex in schizophrenia. *Journal of Neurology, Neurosurgery, and Psychiatry, 63*, 468-473.

Dittrich, W. H., Troscianko, T., Lea S. E. G., &

Morgan, D. (1996). Perception of emotion from dynamic point-light displays represented in dance. *Perception, 25,* 727-738.

Encicott, P. G., Hoy, K. E., Herring, S. E., Johnston, P. J., Daskalakis, Z. J., & Fitzgerald, P. B. (2008). Reduced motor facilitation during action observation in schizophrenia: a mirror neuron deficit? *Schizophrenia Research, 102*, 116-121.

Fitzgerald, P. B., Brown, T. L., Daskalakis, Z. J., & Kulkarni, J. (2002). A transcranial magnetic stimulation study of inhibitory deficits in the motor cortex in patients with schizophrenia. *Psychiatry Research and Neuroimmunology, 114*, 11-22.

Gilaie-Dotan, S., Kanai, R., Bahrami, B., Rees, G., & Saygin, A. P. (2013). Neuroanatomical correlates of biological motion detection. *Neuropsychologia, 51,* 457-463.

Green, M. F., Nuechterlein, K. H., & Mintz, J. (1994a). Backward masking in schizophrenia and mania: I. Specifying a mechanism. *Archives of General Psychiatry, 51*, 939-944.

Green, M. F,. Nuechterlein, K. H., & Mintz, J. (1994b). Backward masking in schizophrenia and mania: II. Specifying the visual channels. *Archives of General Psychiatry, 51*, 945-951.

Grèzes, J., Fonlupt, P., Bertenthal, B., Delon-Martin, C., Segebarth, C., & Decety, J. (2001). Does perception of biological motion rely on specific brain regions? *NeuroImage, 13*, 775-785.

Grossman, E. D., & Blake, R. (2001). Brain activity evoked by inverted and imagined biological motion. *Vision Research, 41*, 1475-1482.

Grossman, E. D., & Blake, R. (2002). Brain areas active during visual perception of biological motion. *Neuron, 35*, 1157-1165.

Harrington, L., Siegert, R. J., & McClure, J. (2005). Theory of mind in schizophrenia: a critical review. *Cogntive Neuropsychiatry, 10,* 249-286.

Iacoboni, M., Molnar-Szakacs, I., Gallese, V., Buccino, G., Mazziotta, J. C., & Rizzolatti, G. (2005). Grasping the intentions of others with one's own mirror neuron system. *PLoS Biology, 3*, e79.

Johansson, G. (1973). Visual perception of biological motion and a model for its analysis. *Perception and Psychophysics, 14*, 201-211.

Kim, J. (2012). Biological motion: Perceptual processing, neural mechanisms and clinical application. *The Korean Journal of Cognitive and Biological Psychology, 24*(4), 357-392.

Kim, J., Doop, M. L., Blake, R., & Park, S. (2005). Impaired visual recognition of biological motion in schizophrenia. *Schizophrenia Research,* 77, 299-307.

Kim, J., Matthews, N. L., & Park, S. (2010). An Event-Related fMRI Study of Phonological Verbal Working Memory in Schizophrenia. *PLoS ONE, 5*(8), e12068

Kim, J., Park, S., & Blake, R. (2011). Perception of biological motion in schizophrenia and healthy individuals: A behavioral and fMRI

study. *PLos ONE, 6*: e19971.

Leslie, K. R., Johnson-Frey, S. H., & Grafton, S. T. (2004). Functional imaging of face and hand imitation: towards a motor theory of empathy. *Neuroimage, 21*, 601-607.

Li, C. S. (2002). Impaired detection of visual motion in schizophrenia patients. *Progress in Neuropsychopharmacology & Biological Psychiatry, 26*, 929-934.

Loula, F., Prasad, S., Harber, K., & Shiffrar, M. (2005). Recognizing people from thier movement. *Journal of Experimental Psychology: Human Perception and Performance, 31,* 210-220.

MacArthur, L. Z., & Baron, M. K. (1983). Toward an ecological theory of social perception. *Psychological Review, 90,* 215-238.

McCormick, L. M., Brumm, M. C., Beadle, J. N., & Paradiso, S. (2012). Mirror neuron function, psychosis, and empathy in schizophrenia. *Psychiatry Research: Neuroimaging, 201*, 233-239.

Mehta, U. M., Thirthalli, Jl., Basavaraju, R., Gangadhar, B., & Pascual-Leone, A. (2014). Reduced mirror neuron activity in schizophrenia and its association with theory of mind deficits: Evidence from a transcranial magnetic stimulation study. *Schizophrenia Bulletin, 40*, 1083-1094.

Michels, L., Lappe, M., & Vaina, L. M. (2005). Visual areas involvedin the perception of human movement from dynamic form analysis. *Neuroreport, 16*, 1037-1041.

Neri, P., Morrone, C., & Burr, D (1998). Seeing biological motion. *Nature, 395,* 894-896.

Okugawa, G., Nobuhara, K., Minami, T., Takase, K., Sugimoto, T., Saito, Y., Yoshimura, M., & Kinoshita, T. (2006). Neural disorganization in the superior cerebellar peduncle and cognitive abnormality in patients with schizophrenia: a diffusion tensor imaging study. *Progress in Neuro-Psychopharmacology, 30,* 1408-1412.

Overall, J. E., & Gorham, D. R. (1962). The brief psychiatric rating *scale. Psychological Reports, 10,* 799-812.

Pelli, D. G. (1997). The video toolbox software for visual psychophysics: transforming numbers into movies. *Spatial Vision, 10,* 437-442.

Pelphrey, K. A., Mitchell, T. V., McKeown, M. J., Goldstein, J., Allison, T., & McCarthy, G. (2003). Brain activity evoked by the perception of human walking: Controlling for meaningful coherent motion. *Journal of Neuroscience, 23*, 6819-6825.

Peuskens, H., Vanrie, J., Verfaillie, K., & Orban, G. A. (2005). Specificity of regions processing biological motion. *European Journal of Neuroscience, 21*, 2864-2875.

Pineda, J. A. (2008). Sensorimotor cortex as a critical componentof an 'extended' mirror neuron system: Does it solve the development, correspondence, and control problems in mirroring? *Behavioral and Brain Functions, 4*:47. Doi: 10.1186/1744-9081-4-47

Puce, A., Allison, T., Bentin, S., Gore, J. C., & McCarthy, G. (1998). Temporal cortex activation in human viewing eye and mouth

movements. *Journal of Neuroscience, 18*, 2188-2199.

Quintana, J., Davidson, T., Kovalik, E., Marder, S. R., & Mazziotta, J. C. (2001). A compensatory mirror cortical mechanism for facial affect processing in schizophrenia. *Neuropsychopharmacology, 25,* 915-924.

Raine,A. (1991). The SPQ: a scale for the assessment of schizotypal personality based on DSM-III-R criteria. *Schizophrenia Bulletin, 17*, 556-564.

Rizzolatti, G., & Craighero, L. (2004). The mirror-neuron system. *Annual Review of Neuroscience, 27*, 169-192.

Rizzolatti, G., Fogassi, L., & Gallese, V. (2001). Neurophysiological mechanisms underlying the understanding and imitation of action. *Nature Reviews Neuroscience, 2*, 661-670.

Santi, A., Servos, P., Vatikiotis-Bateson, E., Kuratate, T., & Munhall, K. (2003). Perceiving biological dissociating visible speech from walking. *Journal of Cognitive Neuroscience, 15,* 800-809.

Saygin, A. P. (2007). Superior temporal and premotor brain areas necessary for biological motion perception. *Brain, 130,* 2452-2461.

Saygin, A. P., Wilson, S. M., Hagler, D. J. Jr. Bates, E., & Sereno, M. I. (2004). Point-light biological motion perception activates human premotor cortex. *Journal of Neuroscience, 24,* 6181-6188.

Shamay-Tsoory, S. G., Shur, S., Barcai-Goodman, L., Medlovich, S., Harari, H., & Levkovitz, Y. (2007). Dissociation of cognitive from affetive components of theory of mind in schizophrenia. *Psychiatry Research, 149,* 11-23.

Singh, F., Pineda, J., & Cadenhead, K. S. (2011). Association of impaired EEG mu wave suppression, negative symptoms and social functioning in biological motion processing in first episode of psychosis. *Schizophrenia Research, 130*, 182-186.

Spencer, J. M., Sekuler, A. B., Bennett, P. J., & Christensen, B. K. (2013) Contribution of coherent motion to the perception of biological motion among persons with Schizophrenia. *Frontiers in Psychology, 13;4*: 507. doi: 10.3389/fpsyg.2013.00507

Spitzer, R. L., & Williams, J. D. W. (1985). *Structured Clinical Interview for DSM III-R.* New York State Psychiatric Institute Biomedical Research Division, New York.

Talairach, J., & Tournoux, P. (1988). Co-planar stereotaxic atlas of the human brain. *Thieme*, New York.

Umilta, M. A., Kohler, E., Gallese, V., Fogassi, L., Fadiga, L., Keysers, C., & Rizzolatti, G. (2001). I know what you are doing: a neurophysiological study. *Neuron, 31*, 155-165.

Vaina, L. M., Solomon, J., Chowdhury, S., Sinha, P., & Belliveau, J. W. (2001). Functional neuroanatomy of biological motion perception in humans. *Proceedings of the National Academy of Sciences of the United States of America, 98,* 11656-11661.

Volz, K. G., Schubotz, R. I., & von Cramon, D. Y. (2004). Why I am unsure? Internal and external attribution of uncertainty dissociated by fMRI. *Neuroimage, 21*, 848-857.

Volz, K. G., Schubotz, R. I., & von Cramon, D. Y. (2003). Predicting events of varying probability: uncertainty investigated by fMRI. *NeuroImage, 19,* 271-280.

Volz, K. G., Schubotz, R. I., & von Cramon, D. Y. (2005). Variants of uncertainty in decision-making and their neural correlates. *Brain Research Bulletin,* 67, 403-412.

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조현병 환자의 생물형운동 지각 관련 전두 피질 활동의 이상

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조현병 환자들의 시지각 이상에는 생물형 운동(biological motion) 지각 결함이 포함된다. 최근의 기능적자기공명영상(fMRI)연구에서는 환자들의 생물형 운동 자극에 대한 측두엽의 후부상측두구(pSTS)의 활동패턴이 정상인과 다르게 나타난다는 결과가 보고되었다. 이와 함께, 생물형운동 지각에 관여하는 전두 피질 영역들의 위치와 기능 역시 정상인들의 뇌에서 확인되어 왔으나, 조현병 환자들의 뇌에서 이들 영역이 어떤 활동을 보이는지에 대해서는 알려지지 않았다. 이에 따라 본 연구에서는 생물형 운동 지각 과제를 실행하는 과정에서 정상인과 조현병 환자들의 전두 피질 영역 활동의 패턴과 그 차이를 알아보고자 하였다. fMRI 자료의 분석 결과, 정상인 집단에서는 복측전운동피질(vPMC)과 하전두회(IFG)의 일부 영역에서 생물형운동 자극에 선택적으로 강한 반응이 관찰된 반면, 조현병 환자 집단에서는 이러한 자극 선택적 활동이 관찰되지 않았다. 전두엽의 배내측에 위치한 상전두회(SFG) 영역에서는 정상인 집단에서 비생물형 자극을 생물형 자극으로 착각하는 경우 강한 활동이 보였으나 조현병 환자 집단에서는 전체적으로 약한 활동이 나타났다. 전전두피질(PFC)의 앞쪽 일부 영역에서는 지각과제 수행 중 활동의 억제가 정상인집단에서 나타났으나 조현병 환자 집단에서는 이러한 패턴이 보이지 않았다. 이 결과들은 조현병 환자들이 생물형운동 지각에 관련된 전두 피질에서도 정상인과 다른 방식의 신경활동을 보임을 나타내며, 거울뉴런체계의 기능 이상 및 적절한 자극 처리에 관여하는 인지 과정에서의 이상을 시사하는 것으로 보인다.

주요어 : 생물형운동, 조현병, 전두피질, 거울뉴런체계, 기능적자기공명영상법