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Involvement of the mirror neuron system in blunted affect in schizophrenia

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ABSTRACT

Blunted affect is a relatively enduring schizophrenic symptom and its presence brings about poor functioning and outcomes. Functional impairment in the mirror neuron system which is involved in both motor execution and imitation may be a neural basis of blunted affect, but it is not proved yet. Fifteen patients with schizophrenia and 16 healthy controls performed the facial expression task during functional magnetic resonance imaging. The task was to reproduce facial expressions in response to the face or word stimuli for happiness, sadness, and meaningless expression. Brain activities during facial expressions in patients compared with controls and their relationship with affective flattening were analyzed. Compared to controls, patients exhibited decreased activity in the widespread dorsal frontal regions and increased activity in the ventral frontal and subcortical regions. Patients also demonstrated significant negative correlation of the severity of affective flattening with activities in the mirror neuron system, such as the premotor cortex, motor cortex, and inferior parietal lobule. Emotional expression in patients with schizophrenia may be related to hypoactivity of the dorsal system and hyperactivity of the ventral system. An imbalance of these two systems may contribute to blunted affect. Directly addressing blunted affect using emotional expression provides a new perspective that functional disturbance of the mirror neuron system may play an important role in manifestation of blunted affect in schizophrenia.

1. Introduction

Blunted affect, a severe reduction in the intensity of externalized feeling tone, has been considered a core symptom in schizophrenia. It is a relatively enduring symptom that responds poorly to treatment (Kirkpatrick et al., 2001), and thus its presence brings about poor functioning and outcomes (Gur et al., 2006). Most behavioral studies about blunted affect have used facial expressions, because the face is the most emotionally expressive part of the body (Tremeau, 2006). Facial expressions can be classified into two types: voluntary/posed expression (e.g., when one imitates a facial expression in a photograph) and involuntary/evoked expression (e.g., when one remembers a personal experience), which use cortical/pyramidal and subcortical/extrapyramidal circuits, respectively (Ekman, 2003). Many different methods, including film clips, still pictures, cartoons, music, food, and social interactions, have been used to evoke emotional expressions, and have consistently indicated that poor facial expression is a characteristic of schizophrenia (Kring and Moran, 2008).

Previous neuroimaging studies about blunted affect have used indirect approaches like emotional appraisal or experience rather than a direct method like facial expressions. For example, more severe blunted affect was correlated with greater amygdala activation for misidentified fearful faces (Gur et al., 2007) and with higher amygdala and parahippocampal activities during emotion perception (Lepage et al., 2011). In the comparison between with- and without-blunted-affect groups, blunted affect was associated with failing to activate the dorsal prefrontal cortex and anterior cingulate during passive viewing of emotional stimuli (Fahim et al., 2005; Stip et al., 2005). Although the process of emotional appraisal or experience may affect the subsequent expression process (Scherer and Ekman, 1984), these two processes are discrete. Therefore, a neural basis of blunted affect needs to be explored using the facial expression task, but this approach has not been addressed yet.

Because facial expression is a motor behavior, blunted affect can be regarded as a motor abnormality (Dworkin et al., 1996). The finding that the subjective experience of emotion was relatively intact despite decreased levels of expressivity in schizophrenia (Aghevli et al., 2003) further supports the motor dysfunction hypothesis of blunted affect. Another motor aspect includes an imitation behavior because it plays an important role in diverse forms of social learning (Shea, 2009). The mirror neuron system (MNS) is a set of neurons that become active

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during motor action, the observation of another individual's motor action, and imitation (Rizzolatti and Craighero, 2004). Recent studies demonstrated that poor performance of the imitation task was correlated with the severity of negative symptoms (Park et al., 2008; Matthews et al., 2013). Taken together, motor and imitation dysfunctions seem to have a connection with blunted affect. Nonetheless, these abnormalities have not been addressed yet in functional neuroimaging studies.

The current study was designed to investigate the neural basis of blunted affect in schizophrenia using an fMRI. Because we considered facial expression to be most appropriate in investigating functional correlates of blunted affect, we used evoked and posed facial emotional expression tasks rather than employing the emotion processing task. We expected that patients with schizophrenia would exhibit poorer performances in all facial expression variables compared to healthy controls. In addition, given that schizophrenia is associated with deficits in motor execution and imitation, we hypothesized that impaired performance of facial expressions in patients with schizophrenia would be related to altered activities in the prefrontal-limbic circuits and MNS.

2. Methods

2.1. Subjects

Fifteen patients with schizophrenia and sixteen healthy controls participated in this study (Table 1). The Structural Clinical Interview for DSM-IV (First et al., 1996) was used for the diagnosis of schizophrenia in patients, who were recruited in the psychiatric outpatient clinic, and the exclusion of any psychiatric disorders in controls, who were recruited by poster advertisements. The exclusion criteria included the presence of a neurological or significant medical illness, and current or past substance abuse or dependence. All participants were right-handed (Anett, 1970). There were no significant group differences in gender, age, and intellectual function assessed using Raven's Progressive Matrices (Raven et al., 1988). All patients were taking antipsychotics; the mean chlorpromazine-equivalent dose was 454.5 ± 316.9 mg. Other medications were anticholinergic drugs ($n = 3$), propranolol ($n = 2$), and benzodiazepines ($n = 5$). The study was approved by the institutional review board, and written informed consent was obtained from all participants.

2.2. Clinical measurements

Patients were examined using the Positive and Negative Syndrome Scale (PANSS) for clinical symptoms (Kay et al., 1987). The Modified Prosocial Scale was derived from some PANSS items to rate social functioning (Docherty et al., 2010). In order to amplify the variance of measures for blunted affect and demonstrate its diversity, the affective flattening subscale scores of the Scale for the Assessment of Negative Symptoms (SANS AF) (Andreasen, 1984) were summed to produce the total score. Motoric neurological soft signs were measured using motor coordination (MOCO) and motor sequencing (MOSE) scores of the Brief Motor Scale (BMS) (Jahn et al., 2006). Antipsychotics-induced side effects were assessed using the Rating Scale for Extrapyramidal Side Effects (RSEPS) (Simpson and Angus, 1970). Depression was rated using the Montgomery–Åsberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979).

Table 1
Demographics and clinical data.

	Patients ($n = 15$)	Controls ($n = 16$)	t/χ^2	p value
Gender (M/F)	9/6	10/6	0.02[a]	0.89
Age (years)	36.7 (8.1)	36.8 (6.3)	−0.01	1.00
Education (years)	12.6 (1.5)	14.8 (2.8)	−2.67	0.01
Raven's progressive matrices	44.9 (8.1)	49.9 (6.8)	−1.85	0.08
MADRS	7.5 (3.9)	3.2 (2.9)	3.49	0.002
BMS, motor coordination	2.8 (1.7)	0.7 (0.6)	4.51	<0.001
BMS, motor sequencing	2.1 (1.8)	0.1 (0.3)	4.52	<0.001
PANSS positive/negative/general	9.7 (2.8)/12.6 (3.4)/24.4 (6.1)	NA		
Modified Prosocial Scale	7.3 (2.4)	NA		
SANS, affective flattening	14.3 (5.9)	NA		
RSEPS	2.1 (1.8)	NA		
Duration of illness (years)	10.9 (7.3)	NA		

Abbreviations: MADRS, Montgomery-Åsberg Depression Rating Scale; BMS, Brief Motor Scale; PANSS, Positive and Negative Syndrome Scale; SANS, Scale for the Assessment of Negative Symptoms; RSEPS, Rating Scale for Extrapyramidal Side Effects.
[a] Pearson's chi square value.

2.3. Experimental task

During fMRI scanning, participants performed a pre-trained facial expression task (Fig. 1), in which a trial contained three different phases: "watching," "expressing," and "returning." A visual stimulus with six different conditions was presented as a cue during each 0.5-s watching phase. The face stimuli from 9 different persons (5 males) consisted of three different expressions: happiness, sadness, and meaningless expression (raising the eyebrows and pouting the lips). The word stimuli were three different Korean words meaning "happiness," "sadness," and "eye mouth" for meaningless expression. During the expressing phase lasting 3.5 s, the word "express" was presented, and participants were asked to imitate the facial stimuli (posed expression) or make a facial expression as the word stimuli indicated (evoked expression). To stop making an expression and return to the neutral expression, a neutral cartoon face was presented for the returning phase of 1 s. A total of 180 trials, with 30 trials in each condition, were arranged in an event-related design and were divided into two sessions. The null events were varied from 1.25 s to 10 s. The total task time was 21 min 29 s. An MR-compatible video camera for monitoring a whole face recorded facial movements throughout the scanning. For the task validity, subjective responses to the face stimuli were measured as valence and arousal after the scanning.

2.4. Image acquisition

MRI data were acquired on a 3 T scanner (Intra Achieva; Philips Medical System). Thirty-eight contiguous 3.5-mm-thick axial slices were collected using an echo planar imaging sequence depicting the blood-oxygenation-level-dependent signal (echo time = 30 ms; repetition time = 2500 ms; flip angle = 90°; field of view = 220 mm; and image matrix = 128 × 128). Axial 1.2-mm-thick T1-weighted images (echo time = 4.6 ms; repetition time = 9.673 ms; flip angle = 30°; field of view = 220 mm; and image matrix = 256 × 256) were also collected.

2.5. Behavioral data analysis

Facial expressions were coded independently by two coders who were blind to the contents of the video clips using the Facial Expression Coding System (Kring and Sloan, 2007). Valence, intensity, frequency, and duration of the expression were rated, and the intraclass correlation coefficients were 0.91, 0.86, 0.89, and 0.78, respectively. The mean scores from the two coders were used for the following analyses. The facial responses were classified as "relevant" or "irrelevant" according to the correspondence of valence between the stimuli and participants' expressions. The missing and irrelevant response rates were counted for each condition. Because all pairs of the variables were significantly correlated ($p < 0.001$), composite scores were computed. Z scores for intensity, frequency, and duration of each condition were summed. The sum of composites for only relevant expressions was referred to as the "facial expression score," whereas that for all expressions was referred to as the "facial movement score."