Neural correlates of blunted affect in patients with schizophrenia: an fMRI study

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Directed by Professor Jae-Jin Kim

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<TABLE OF CONTENTS>

LIST OF FIGURES

LIST OF TABLES

ABSTRACT

Neural correlates of blunted affect in patients with schizophrenia: an fMRI study

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Objectives: Blunted affect may be associated with motor and social dysfunction in schizophrenia. This study was designed to investigate the neurobiological basis of blunted affect in patients with schizophrenia specifically in limbic regions and brain regions related to motor and social functioning.

Methods: Fifteen patients with schizophrenia and 16 healthy controls were asked to reproduce facial expressions during functional magnetic resonance imaging (fMRI) scanning for three conditions: happy, sad and unmeaningful facial movement (UFM) conditions. Blunted affect was rated using the affective flattening subscale of the Scale for the Assessment of Negative Symptoms (SANS AF). Facial expressions were videotaped and rated using the Facial Expression Coding System (FACES).

Results: Compared to healthy controls, the patient group was impaired for all expressive variables. The patient group exhibited decreased activity in the left premotor cortex, right superior parietal lobule, left insula and right cerebellum compared to the control group during the expression of happy and sad emotion relative to UFM condition. The percent signal change in the left premotor cortex was correlated with total facial expression score rated by FACES in the patient group. After controlling for facial movements, the patient group showed decreased activity in the right dorsolateral prefrontal cortex (DLPFC), right

supplementary motor area, left motor cortex, right superior parietal lobule, left insula and right cerebellum compared to the control group during the expression of happy and sad emotion relative to UFM condition. The percent signal change in the left insula was correlated with the SANS AF score. The percent signal changes in the right DLPFC and right cerebellum were correlated with the Social Anhedonia Scale score.

Discussion: These findings suggest that motor coordination problem may affect blunted affect in patients with schizophrenia. This study also provides evidence that blunted affect in schizophrenia may be influenced by the functional disturbance of the interconnected networks including the insula. In addition, the association of decreased activities in the DLPFC and cerebellum with increased social anhedonia found in this study suggests possible involvement of altered cortico-cerebellar circuit in social anhedonia in patients with schizophrenia.

Key words: blunted affect, social anhedonia, motor coordination, social functioning, insula, dorsolateral prefrontal cortex, cerebellum

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I. INTRODUCTION

1. Previous studies about blunted affect in schizophrenia

Historically, blunted affect, defined as a disturbance of affect manifested by a severe reduction in the intensity of externalized feeling tone, has been considered as an essential part of schizophrenia. For example, Bleuler viewed blunted affect as a fundamental symptom of schizophrenia, whereas hallucinations and delusions were regarded as accessory symptoms.[1] Following Bleuler's early observation, numerous researches have provided evidences about the importance of blunted affect. Blunted affect has been shown to be discriminating between schizophrenia and other psychiatric disorders,[2] and it is associated with diagnosis of schizophrenia across a number of diagnostic systems.[3] Like other negative

symptoms, blunted affect is a relatively enduring symptom that is generally resistant to treatment.[4] Furthermore, the presence of this symptom is associated with poor functioning and outcome.[5]

The most studies about blunted affect in schizophrenia was using facial expression, because the face is the most expressive and specific part in the body where emotions are expressed.[6] Facial expressions can be divided into two types: voluntary/posed and involuntary/spontaneous expressions.[6] Many different methods were used to evoke emotion, including film clips, still pictures, cartoons, music, foods and social interactions.[7] The extent of facial expression was measured using observational coding system, such as the Facial Action Coding System,[8] the Facial Expression Coding System,[9] and Specific Affect Measure.[10] Although diverse methods and measures were used to assess blunted affect in schizophrenia, the findings consistently indicate that patients with schizophrenia display fewer positive and negative facial expressions compared to healthy controls.[7]

Previous models of blunted affect proposed various etiologies, including repression,[11] impaired social relations[12] and institutionalization.[13] However, more recent studies have suggested that blunted affect is related to functional abnormality during emotional processing. Several studies found that the severity of negative symptoms including blunted affect was correlated with measures of emotion processing.[14-15] Furthermore, a behavioral study demonstrated that patients with blunted affect showed greater impairment in emotion processing task

than patients without blunted affect, and that blunted affect ratings uniquely predicted performance on emotion processing task compared with other negative symptoms.[5] In addition, recent neuroimaging studies support the relationship between blunted affect and abnormalities of emotion processing in patients with schizophrenia. Gur et al.[16] investigated neural activity during the emotional identification task. They found that greater amygdala activation for misidentified fearful faces was highly correlated with more severe blunted affect in patients with schizophrenia. More recently, Lepage et al.[17] examined neural correlates of facial emotion perception during the gender decision task for sad, happy and neutral faces. They demonstrated that the severity of blunted affect in patients with schizophrenia was correlated with neural activity in the amygdala and parahippocampal region. Taken together, these studies suggest that blunted affect can be affected by neural activity in multiple limbic regions during emotion processing.

Antipsychotics are related to extrapyramidal symptoms, of which akinesia can be confused with blunted affect in patients with schizophrenia. However, there is some debate about the influence of antipsychotics on blunted affect in schizophrenia. While some studies demonstrated an adverse effect of antipsychotics on facial expression,[18-19] others found no clear effect of antipsychotics use on expressivity.[20-21]

2. Blunted affect and motor dysfunction

Subtle motor and sensory dysfunctions or neurological soft signs (NSS) are present in a substantial proportion of patients with schizophrenia in multiple studies.[22] A recent meta-analysis indicated that a majority of patients with schizophrenia (73%) performed outside the range of healthy controls on aggregate NSS measures.[23] The occurrence of NSS is independent of demographic and antipsychotic treatment,[24] suggesting that NSS could be regarded as a trait feature of schizophrenia. Conventionally defined as non-localizing neurological abnormalities that cannot be related to impairment of a specific brain region, NSS involves observable defects in sensory integration, motor coordination and inhibition. NSS are significantly correlated with a poor premorbid functional state, early onset of the disease, and poor outcome.[25-26] Because increased NSS scores have been found in non-affected first degree relatives of patients with schizophrenia[27] and have been shown to precede the onset of the disease,[22] NSS have been considered a genetic vulnerability factor of schizophrenia.

It was proposed that blunted affect might reflect the motor abnormalities rather than affective deficits, because the behaviors assessed in measures of blunted affect are all motor behaviors. This is partly supported by the findings that the subjective experience of emotion is relatively intact despite decreased levels of expressivity in patients with schizophrenia.[28-29] Moreover, several studies demonstrated that measures of blunted affect were correlated with measures of

motor abnormalities in patients with schizophrenia,[30-31] supporting the motor dysfunction hypothesis.

3. Blunted affect and social functioning

Impairment of social functioning has long been regarded as a core feature of schizophrenia. The term "social functioning" implies overall performance across many everyday domains (e.g., independent living, employment, interpersonal relationships, and recreation).[32] Deterioration of social functioning is one of the defining characteristics of schizophrenia specified by the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, Text Revision (DSM-IV-TR).[33] Social isolation and withdrawal are frequently reported prodromal symptoms, as well as characteristic markers of the defect state.[34] Social dysfunction seems to be exacerbated by the chronic course of the disorder, but there are considerable data suggesting that may adult patients showed maladaptive interpersonal relationship beginning in childhood.[35] The consequences of social dysfunction may lead to severe impairments in multiple areas of role functioning (e.g., friendship, marriage and employment).[36] Social dysfunction also seems to affect the long-term outcome and course of schizophrenia.[37] Poor premorbid social adjustment at the onset the disorder is one of the best prognostic indicators.[38]

Blunted affect in patients with schizophrenia was suggested to be an index of social functioning.[39] Eye contact, facial expressiveness, vocal inflection,

and affective responsivity, which are rated by measures of blunted affect, are all social behaviors that facilitate communication. It is plausible that poor eye contact or a lack of vocal inflections is influenced by a social deficit rather than an affective problem. In fact, the correlations between blunted affect and social functioning were significant in several studies.[40-42] However, motor and social dysfunction were not considered in the neuroimaging studies of blunted affect in patients with schizophrenia yet.

4. Neural correlates of motor and social functions

There are many brain regions involved in motor function, which includes the motor cortex, premotor cortex, supplementary motor area (SMA), posterior parietal cortex, cerebellum and basal ganglia.[43] The motor cortex is involved in generating neural impulses that pass down to the spinal cord and control the execution of movement.[43] The premotor cortex is responsible for the sensory guidance of movement and the direct control of some movements with an emphasis on proximal and trunk muscles of the body.[43] The SMA has many proposed functions including the planning of complex movements and the coordination of bi-manual movement.[43] The posterior parietal cortex is thought to be involved in transforming multisensory information into motor commands and motor planning.[44] The cerebellum and the basal ganglia are dedicated to motor control. The basal ganglia generate the actual motor programs, while the

cerebellum is involved in the timing and coordination of the motor programs.[45]

Neuroimaging studies demonstrated that there was a circumscribed set of brain regions dedicated to social functioning. The major components of social brain were the medial prefrontal cortex (MPFC), dorsolateral prefrontal cortex (DLPFC), frontal polar cortex (FPC), superior temporal sulcus, temporoparietal junction and insula.[46-47] The MPFC has been consistently activated during a wide range of tasks which required participants to think about mental states such as mentalizing and theory of mind.[48] The DLPFC has been implicated in volitional control of emotional response and reward-based learning in social interactions.[46] The FPC has been known to be responsible for overriding ongoing processing to explore new options in nonstationary environments.[49] The superior temporal sulcus and temporoparietal junction have been involved in seeing the world from another's point of view (i.e., perspective taking).[50] The insula has been found to be activated in a large number of studies that involve the empathic feeling of others' emotions.[51]

5. Blunted affect and social anhedonia

Anhedonia, a reduced ability to experience pleasure in normally pleasurable situations, is one of the core clinical features[52] and a significant determinant of functional disability in schizophrenia.[53] Moreover, anhedonia has been considered a genetic vulnerability factor of schizophrenia.[54] Despite clinical

significance of anhedonia, research on this emotional disturbance has provided inconsistent set of findings. On the one hand, patients generally report experiencing lower levels of pleasure than normal controls on self report measure of trait anhedonia.[55-56] On the other hand, patients have reported experiencing normal levels of pleasant emotions in controlled laboratory studies using emotionally evocative stimuli.[7] Thus, there appears to be a disjunction between trait and state assessments of pleasurable experiences in schizophrenia. One of the theories that could explain the state-trait disjunction is a social-specific deficit theory, which means that state emotion deficits are restricted to social domain.[57] In support of this hypothesis, longitudinal studies have shown that social anhedonia is predictive of the onset of schizophrenia-spectrum disorders.[58-59]

Social anhedonia may be related to blunted affect in patients with schizophrenia. Deficits in emotion processing are thought to play a central role in blunted affect and social anhedonia in patients with schizophrenia.[5, 60] Poor social functioning was also related to greater social anhedonia[52] and more severe blunted affect[40-42] in patients with schizophrenia. Moreover, severe social anhedonia was associated with low level of emotional expression in patients with schizophrenia[61] and nonclinical individuals.[62] Therefore, we could assume that common neural correlates of blunted affect and social anhedonia would be found.

6. The present study

This study was designed to investigate the neurobiological basis of blunted affect in patients with schizophrenia. While previous studies employed emotion processing task, we used evoked and posed facial expression task for happy, sad and unmeaningful facial movement conditions because we have considered facial expression task to be most appropriate in investigating functional correlates of blunted affect. According to previous studies, we hypothesized that patients with schizophrenia would exhibit poorer performances in all facial expression variables compared to healthy controls, and that impaired performance in facial expression would be related to motor and social dysfunctions. In addition, we hypothesized that patients with schizophrenia would show altered activation in limbic regions and brain regions related to motor and social functioning, and that the altered activation would be associated with the severity of blunted affect and social anhedonia. To test these hypotheses, we used event-related functional magnetic resonance imaging (fMRI) to identify the regional deficit of brain activity in patient with schizophrenia during facial emotional expression. The correlations between the deficient regional activities and the severity of blunted affect and social anhedonia in schizophrenia were computed.

II. MATERIALS AND METHODS

1. Subjects

Fifteen patients with schizophrenia (9 males, 6 females) and sixteen healthy controls (10 males, 6 females) participated in the study. The patients were recruited from psychiatric outpatient clinics and were in a stable phase of the illness. The exclusive diagnosis of schizophrenia in the patient group and the exclusion of any psychiatric disorder in the control group were made by a skilled psychiatrist using the Structural Clinical Interview for DSM-IV (SCID-IV).[63] All participants were right-handed, as assessed by the Annett Handedness Inventory.[64] Exclusion criteria included the presence of a neurological or significant medical illness, and current or past substance abuse or dependence. As shown in Table 1, there were no significant differences between the patient and control groups by gender and age (36.7±8.1 years and 36.8±6.3 years, respectively). The mean years of education differed significantly between the patient and control groups at 12.6±1.5 and 14.8±2.8 years, respectively (t= −2.67, df=23.72 p=0.01). Intellectual function assessed using Raven's Progressive Matrices[65] was not significantly different between the patient and control groups (111.6±20.7 and124.4±15.0, respectively).

Anhedonia was assessed by the Physical Anhedonia Scale (PAS) and the Social Anhedonia Scale (SAS).[66] The PAS and the SAS consisted of 61 and

48 true/false questions, respectively, with higher scores representing greater anhedonia. The patient group had significantly higher PAS scores than the control group (patients: 16.2±6.5, controls: 11.0±7.4; t=2.08, df=29, p=0.05), whereas the SAS scores did not differ significantly between the patient and control groups (11.1±5.0 and 8.4±4.1, respectively). Anxiety and depression were rated using the State Trait Anxiety Inventory (STAI)[67] and Montgomery-Åsberg Depression Rating Scale (MADRS).[68] The STAI is a 40-item self-reported measure of state (item 1−20) and trait (item 21−40) anxiety. State anxiety refers to transitory emotional reactions at the time of assessment, whereas trait anxiety deals with individual differences to anxiety proneness. Each item is rated on a 4-point Likert scale (from 1 to 4), with higher score representing severe anxiety. State and trait anxiety was not significantly different between the patient and control groups (state anxiety: 42.3±6.7 and 39.3±5.3; trait anxiety: 44.7±8.1 and 42.3±7.8, respectively). The MADRS is a 10-item clinician-rated scale and each item is rated from 0 to 6. Higher scores of the MADRS indicate increasing depressive symptoms. The patient group had significantly higher MADRS scores than the control group (patients: 7.5±3.9, controls: 3.2±2.9; t=3.49, df=29, p=0.002). The Positive and Negative Affect Schedule (PANAS)[69] was used to measure current affects, and it contains 20 mood-descriptive adjectives; 10 concerning positive affects (PA) and 10 on negative affects (NA). Rating is on a 5-point Likert scale ranging from 1 (‘not at all/very little’) to 5 (‘very much’); and higher sum-scores indicate increasing

level of current affect. The PANAS NA score in the patient group was significantly higher than that in the control group (patients: 23.4±6.7, controls: 14.9±7.2; t=3.40, df=29, p=0.002), whereas the PANAS PA score did not differ between the patient and control groups (26.9±6.8 and 29.1±8.2, respectively).

Motoric neurological soft signs were investigated by a skilled psychiatrist using the Brief Motor Scale (BMS).[70] The BMS is a 10-item measure of motor coordination and motor sequencing. The BMS motor coordination (MOCO) (patients: 2.8±1.7, controls: 0.7±0.6; t=4.51, df=17.19, p<0.001) and motor sequencing (MOSE) (patients: 2.1±1.8, controls: 0.1±0.3; t=4.51, df=14.5, p<0.001) subscale scores in the patient group were significantly higher than those of the control group. Neuroleptic induced side effect was examined by means of the following instruments: the Rating Scale for Extrapyramidal Side Effects (EPS),[71] Abnormal Involuntary Movement Scale (AIMS),[72] and Barnes Akathisia Rating Scale (BARS).[73] The mean scores of the EPS, AIMS and BARS in the patient group were 2.1±1.8, 1.9±0.7 and 0.7±1.4, respectively. Blunted affect in the patient group was assessed by the affective flattening subscale of the Scale for the Assessment of Negative Symptoms (SANS AF)).[74] The mean SANS AF score in the patient group was 14.3±5.9. Clinical symptoms were rated by a skilled psychiatrist using the Positive and Negative Syndrome Scale (PANSS).[75] The mean ratings of positive, negative, and general symptom subscale scores of the PANSS in the patient group were 9.7±2.8, 12.6±3.4 and 24.4±6.1, respectively. Social functioning

was examined using the Modified Prosocial scale which was derived that consists of four PANSS items, including “active social avoidance”, “emotional withdrawal”, “passive/apathetic social withdrawal” and “difficulty in abstract thinking”. The mean Modified Prosocial scale score of the patient group was 7.3±2.4. The patient group’s mean duration of illness was 10.9±7.3years. Twelve patients were taking one atypical antipsychotic drug and 3 patients were taking one typical antipsychotic drug. The mean chlorpromazine-equivalent dose for the patient group was 454.5±316.9 mg. The study was approved by the Yonsei University College of Medicine Institutional Review Board. Written informed consent was obtained from all participants before the study began.

Table 1 Demographic and clinical data

	Patients (n=15)	Controls (n=16)	t/χ^2	*p*
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
Gender (M/F)	9/6	10/6	0.02[a]	0.89
IQ	111.6±20.7	124.4±15.0	-1.98	0.06
PAS	16.2±6.5	11.0±7.4	2.08	0.05
SAS	11.1±5.0	8.4±4.1	1.64	0.11
State STAI	42.3±6.7	39.3±5.3	1.36	0.18
Trait STAI	44.7±8.1	42.3±7.8	0.85	0.40
MADRS	7.5±3.9	3.2±2.9	3.49	<0.01
PANAS Positive Affect	26.9±6.8	29.1±8.2	-0.81	0.43
PANAS Negative Affect	23.4±6.7	14.9±7.2	3.40	<0.01
BMS motor coordination	2.8±1.7	0.7±0.6	4.51	<0.01
BMS motor sequencing	2.1±1.8	0.1±0.3	4.52	<0.01
PANSS positive	9.7±2.8	–		
PANSS negative	12.6±3.4	–		
PANSS general	24.4±6.1	–		
Modified Prosocial scale	7.3±2.4	–		

SANS affective flattening	14.3±5.9	–
AIMS	1.9±0.7	–
EPS	2.1±1.8	–
BARS	0.7±1.4	–
Duration of illness (years)	10.9±7.3	–
Chlorpromazine-equivalent dose (mg)	454.5±316.9	–

[a]Pearson's chi square value

IQ was estimated using Raven's Progressive Matrices.

PAS: Physical Anhedonia Scale, SAS: Social Anhedonia Scale, STAI: State-Trait Anxiety Inventory, PANAS: Positive Affect and Negative Affect Scale, MADRS: Montgomery-Å sberg Depression Rating Scale, BMS: Brief Motor Scale, PANSS: Positive and Negative Syndrome Scale, SANS: Scale for the Assessment of Negative Symptoms, AIMS: Abnormal Involuntary Movement Scale, EPS: Rating Scale for Extrapyramidal Side Effects, BARS: Barnes Akathisia Rating Scale

2. Design and Procedure

A. Stimuli

We recruited fourteen healthy volunteers (8 males and 6 females, ages from 28 to 35 years). They were introduced to the concept of the seven basic emotions (anger, contempt, disgust, fear, happiness, sadness and surprise) and the relationships of different emotions with characteristic facial muscle contractions and trained to contract and relax different facial muscles associated with the seven emotions.[76] The volunteers were requested to express happy and sad emotions according to the directed facial actions for each emotion while pictures were obtained (e.g., Fig 1-A). Another 20 healthy subjects selected a single emotion form seven basic emotions that best described the emotion portrayed while viewing the pictures of the volunteers. The happy and sad pictures of 9 volunteers (5 males and 4 females) with more than 70% agreement were chosen as emotional picture stimuli. The 9 volunteers were instructed to raise the eyebrows and pout the lips while the pictures were taken and the pictures were selected as an unmeaningful facial movement (UFM) stimuli (e.g., Fig 1-A). All pictures were taken using a Canon PowerShot G10 digital camera. The pictures were edited using Adobe Photoshop 7.0. All pictures were converted to grayscale and mounted on the same grey background.

As shown in Fig 1-B, the word stimuli were “happiness”, “sadness” and “eye mouth”. All the stimuli were words with two syllables in Korean.

B. Tasks

Before fMRI scanning, subjects practiced the tasks until complete understanding of the instructions. Fig 1-D illustrates the structure of one experimental trial. After the word or picture stimuli were presented, the word "express" appeared and subjects were given instructions to imitate the facial expression of the picture stimuli (posed facial expression task) or to make a facial expression as the word stimuli indicated (evoked facial expression task). After the word "happiness" or "sadness" was presented, subjects were told to express happy or sad emotions. After the word "eye mouth" was presented, subjects were instructed to raise the eyebrows and pout the lips like the UFM picture. After the word "express" was presented, a neutral cartoon face (Fig 1-C) appeared and subjects were asked to return to the neutral facial expression. Thirty trials in each condition were conducted in an event-related design. The order of stimulus presentation was counterbalanced across subjects, and the 180 trials were divided into two runs and an intermission of a few minutes was positioned between runs to maintain subjects' motivation and concentration. Because a set of faces of three different individuals was used as the picture stimuli for each condition, each individual's face was displayed ten times for each condition. Each trial consisted of the word or picture stimuli presentation of 500 ms duration, making a corresponding facial expression of 3500 ms duration and neutral facial expression of 1000 ms duration. The null events were added in varying durations from 1250 ms to 10000 ms, and the total session time was 21

min 29 s. Following scanning, all subjects rated the valence (from -4 to 4) and arousal (from 0 to 8) of the pictures.

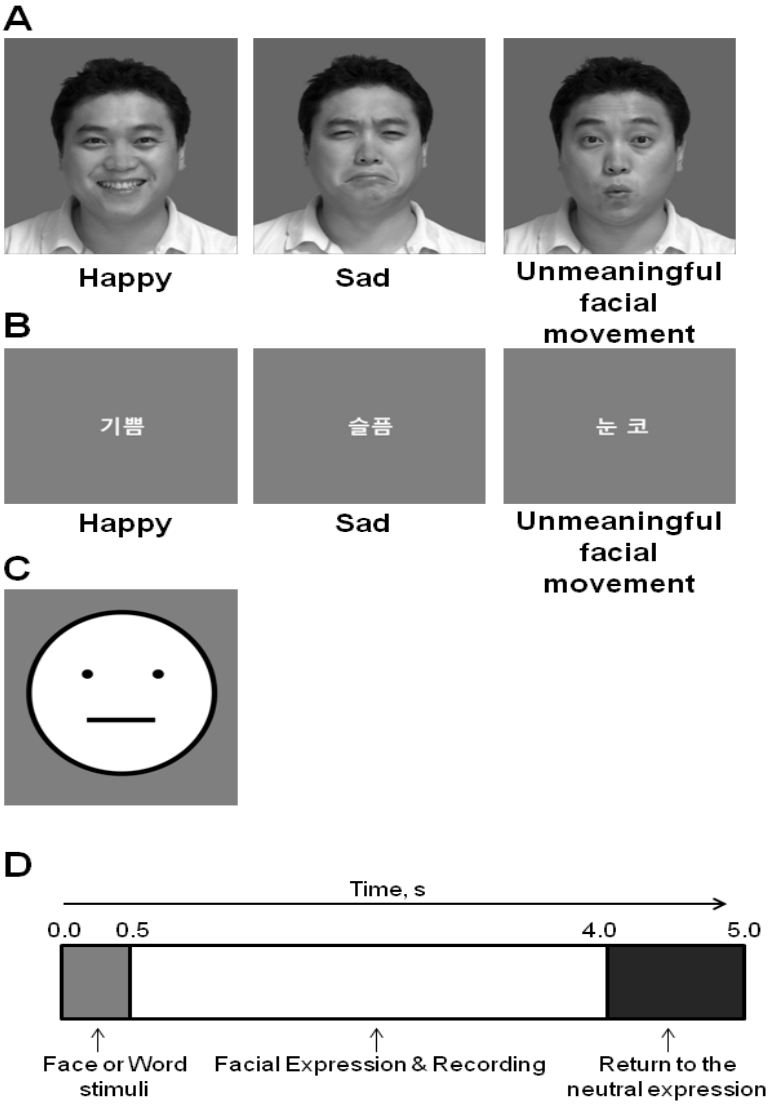

Fig 1. Examples of picture stimuli (A), word stimuli (B) and neutral cartoon face (C). From left to right, the words are “happiness”, “sadness” and “eye mouth” in Korean (B). The structure of one experiment trial is illustrated in (D).

C. Facial recording

Subjects were requested to avoid head movements during the fMRI measurements but were told that they need not suppress their facial movements. To minimize head movements, subjects' heads were restrained in a frame with bilateral padding. A MR compatible video camera (12M; MRC systems, Heidelberg, Germany) attached to the head coil monitored facial movements. The video camera used a wide-angle lens to monitor a whole face area and it recorded facial movements throughout the entire session.

D. Coding facial expressions

Subjects' facial expressions were coded independently by two coders using the Facial Expression Coding System (FACES).[9] In FACES, facial expressions in video segments are coded for frequency, duration, valence (positive or negative), and intensity (1=low, 4=very high). Facial expressions corresponding to the UFM stimuli were also coded for frequency, duration and intensity. The facial expression corresponding with each condition was coded as relevant, and that not corresponding with each condition as irrelevant. The agreement between raters' scores was high for the patient (mean ICC: valence 0.93, intensity 0.96, duration 0.77) and control groups (mean ICC: valence 0.89, intensity 0.74, duration 0.80). The FACES ratings were averaged between the two coders. Coders

were blind to the hypotheses of the study and to the nature and names of the film clips.

Correlations between the individual FACES variables within each condition were very high ($p<0.001$ for all pairs of FACES variables). Because of this, and to reduce the number of dependent variables, composite variables were computed. To do this, Z scores were computed for each condition and were then summed to form composites. Total facial expression score was the sum of composites for relevant expressions. Total facial movement score was the sum of composites for relevant and irrelevant expressions.

E. Image acquisition

Functional and structural MRI data were acquired on a 3 T MR scanner (Intra Achieva; Philips Medical System, Best, Netherlands). Thirty-eight contiguous 3.5-mm-thick axial slices covering the entire brain were collected using a single-shot, T2*-weighted echo planar imaging sequence depicting the blood-oxygenation-level-dependent (BOLD) signal (TR=2500 ms; TE=30 ms; flip angle=90°; field of view=220 mm; image matrix=128×128). High-resolution T1-weighted MR images (axial slices with 1.2-mm slice thickness; TE=4.6 ms; TR=9.673 ms; flip angle=30°; field of view=220 mm; image matrix= 256×256) were collected prior to functional data acquisition.

3. Statistical Analysis

A. Behavioral data analysis

Demographic and clinical data were compared between groups with Student's *t*-test, except for the gender variable, for which a chi-square test was used. Repeated measure analysis of variance (ANOVA) with the group as the between-subject factor and the experimental condition (happy, sad, or UFM) as the within-subject factor was conducted to compare groups with respect to valence and arousal ratings for pictures. Repeated measure ANOVA with the group as the between-subject factor, and the experimental condition (happy, sad, or UFM) and stimulus type (word or picture) as the within-subject factor was conducted to compare groups with respect to total facial expression and movement scores. Correlation analyses were performed between the SANS AF, total facial expression score, BMS subscale scores and Modified Prosocial scale score in the patient group. Correlation analyses were also performed between the SANS AF, total facial expression score, SAS and other clinical variables in the patient group. Statistical significance was set at a threshold of $p<0.05$. Additionally, adjusted *p* values for multiple testing were considered using a sequential Holm–Bonferroni procedure.

B. Neuroimaging data analysis

Preprocessing and analysis of the neuroimaging data were performed using SPM8 (Statistical Parametric Mapping, version 8, Wellcome Department of Cognitive Neurology, London, UK). The first four volumes were discarded to allow for signal equilibration. After correcting slice acquisition time differences acquired in the interleaved sequence, head movement effects were corrected by realigning the images. After slice timing and realignment, the functional images were coregistered to the T1-weighted image for each subject, and then spatially normalized using nonlinear transformation functions obtained by registering individual T1-weighted images to a standard template. The spatially normalized functional data were smoothed with an 8 mm full-width-at-half-maximum Gaussian filter.

For the facial expression task, we defined six event types based on facial expression and stimuli type; namely word happy, word sad, word UFM, picture happy, picture sad, and picture UFM. The movement parameters obtained from the realignment procedure were included as regressors to account for any residual effects of head motion. All images were inspected visually for motion or other artifacts and artifact repair method was used to reduce residual errors in 6 patients and 5 controls (http://cibsr.stanford.edu/tools).[77] Linear contrasts of subject specific parameter estimates for conditions of interest were taken to a second-level random-effects model. Between-group comparisons were performed with a two-

sample *t*-test to find out regions showing significant group difference in activities during the expression of happy and sad emotion relative to UFM condition. Subsequent between-group comparisons were also performed with an ANCOVA using a total facial movement score during emotional condition as a covariate to rule out the confounding effect of facial movements. The effects of parkinsonian symptoms and dose of antipsychotics were examined by correlating the EPS scale score and dose of antipsychotics in chlorpromazine equivalents on the happy and sad *versus* UFM condition contrast. Between-group two-sample *t*-tests were performed to find out regions showing significant group differences in activities during the expression of happy or sad emotion relative to UFM condition. An exploratory analysis for screening activations in the a priori regions was done at a threshold of uncorrected $p < 0.001$ with more than 5 contiguous voxels, and the significant clusters in the a priori regions were used for secondary small volume correction (SVC) analysis, which was conducted at family wise error (FWE)-corrected $p < 0.05$ using 5-mm sphere with a fixation point at the local maxima. The percent signal change (PSC) in the clusters identified by the between-group comparisons were calculated using MarsBaR (version 0.42, http://marsbar.sourceforge.net/). Correlation analyses were performed between the PSC of significant clusters, the SAS and total facial expression scores in the patient and control groups, as well as between the PSC of significant clusters and the SANS AF scores in the patient group. Partial correlation analyses were also performed between the PSC of significant clusters, the SAS, total facial expression

scores and the SANS AF scores in the patient group, controlling for the chlorpromazine-equivalent dose of antipsychotics. Correlation analyses were performed between the PSC of significant clusters, the chlorpromazine-equivalent dose of antipsychotics and EPS scores in the patient group.

III. RESULTS

1. Behavioral data

The valence and arousal ratings of the pictures are presented in Table 2. For the valence of the pictures, there were significant main effect of condition [$F(2,28)=19.29$, $p<0.001$] and group X condition interaction [$F(2,28)=4.04$, $p=0.04$], but no significant main effect of group. In the patient group, there was no significant difference in the valence rating between happy and sad conditions, between happy and UFM conditions, or between sad and UFM conditions. In the control group, the valence for happy condition was significantly higher than those for sad and UFM conditions and the valence for sad condition was also significantly lower than that for UFM condition. The valence ratings for each condition did not differ significantly between the patient and control groups. For the arousal of the pictures, there was no significant main effect of group, main effect of condition or group X condition interaction.

The total facial expression scores for each condition are presented in Fig

2. For the total facial expression score, there was significant main effect of group [$F(1,29)=13.03$, $p=0.001$], but no significant main effect of stimulus or condition, and no significant group X stimulus, group X condition, stimulus X condition or group X stimulus X condition interaction. The total facial expression scores for all conditions differ significantly between the patient and control groups (word happy: $t=-3.19$, $df=15.96$, $p=0.006$; word sad: $t=-4.14$, $df=22.61$, $p<0.001$; word UFM: $t=-2.56$, $df=17.36$, $p=0.02$; picture happy: $t=-2.87$, $df=15.52$, $p=0.01$; picture sad: $t=-3.32$, $df=17.53$, $p=0.004$; picture UFM: $t=-3.23$, $df=15.92$, $p=0.005$). For the facial movement score, there was significant main effect of group [$F(1,29)=39.22$, $p<0.001$], but no significant main effect of stimulus or condition, and no significant group X stimulus, group X condition, stimulus X condition or group X stimulus X condition interaction. The total facial movement scores for all conditions differ significantly between the patient and control groups (word happy: patient -1.82±2.88 control 1.71±1.37, $t=-4.31$, $df=19.75$, $p<0.001$; word sad: patient -2.12±2.12 control 1.99±2.00, $t=-5.54$, $df=29$, $p<0.001$; word UFM: patient -2.02±2.84 control 1.89±1.22, $t=-4.92$, $df=18.73$, $p<0.001$; picture happy: patient -1.61±3.01 control 1.51±1.27, $t=-3.72$, $df=18.58$, $p=0.001$; picture sad: patient -2.07±2.52 control 1.94±1.50, $t=-5.33$, $df=22.56$, $p<0.001$; picture UFM: patient -2.24±2.46 control 2.10±1.33, $t=-6.06$, $df=21.20$, $p<0.001$).

The SANS AF ($r=0.51$, $p=0.05$) and total facial expression scores ($r=-0.55$, $p=0.03$) were correlated with the BMS MOCO score in the patient group at an uncorrected $p<0.05$, whereas they were not correlated with the BMS MOSE.

The SANS AF scores (r=0.65, p=0.01) were correlated with the Modified Prosocial scale score in the patient group at an uncorrected p<0.05, while the total facial expression scores did not show any correlation. The correlation between the SANS AF score and total facial expression score was not significant. The SANS AF and total facial expression scores were not also correlated with any other clinical variables including the years of education, levels of intelligence, PAS, SAS, STAI, MADRS, AIMS, EPS and BARS scores, while the SAS score (r=0.52, p=0.05) correlated with the EPS scores in the patient group at an uncorrected p<0.05.

Table 2 Valence and arousal ratings for the pictures

	Patients (n=15)	Controls (n=16)
Valence (-4 ~ 4)		
Happy	1.37±1.87	2.19±1.15
Sad	0.89±1.97	–1.27±2.01
UFM	0.53±1.40	0.28±1.25
Arousal (0 ~ 8)		
Happy	3.43±1.90	3.50±2.24
Sad	3.57±1.82	3.45±2.00
UFM	3.58±1.39	4.01±1.51

UFM: unmeaningful facial movement

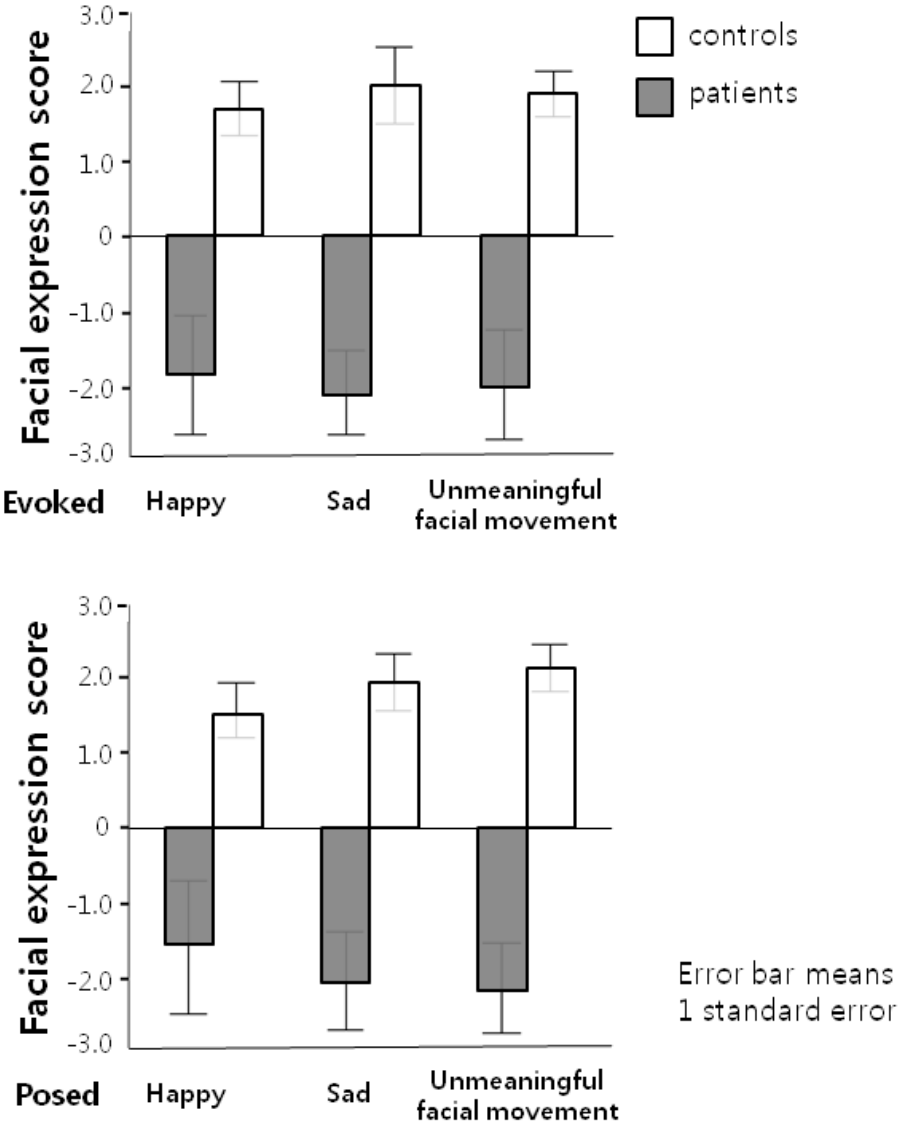

Fig. 2 Total facial expression scores for each condition. The patient group showed significantly decreased facial expression score for all conditions than the control group.

2. Neuroimaging data

As shown in Table 3, an analysis of the fMRI data examined the group difference in activation during the expression of happy and sad emotion relative to UFM condition. Compared to the control group, the patient group exhibited decreased activity in the left premotor cortex, right superior parietal lobule, left insula and right cerebellum. The patient group did not exhibit any significantly increased activity compared to the control group for this contrast. As shown in Fig 3, the activity in the left premotor cortex (r=0.54, p=0.04) was positively correlated with the total facial expression score in the patient group, while no correlation existed in the control group. The activity in the right cerebellum was negatively correlated with the SAS score in the patient (r=-0.60, p=0.02) and control groups (r=-0.55, p=0.03). After the dose of antipsychotics was controlled, the correlations between the correlation between the activity in the right cerebellum and the SAS score (r=-0.55, p=0.04) in the patient group remained significant, while the correlation between the activity in the left premotor cortex and the total facial expression score (r=0.53, p=0.05) did not remain significant. The activity in the right cerebellum also correlated with the EPS score in the patient group (r=-0.68, p=0.005). There was no significant correlation between the PSC of significant clusters and dose of antipsychotics.

When facial movements were controlled, the patient group showed decreased activity in the right dorsolateral prefrontal cortex (DLPFC), right

supplementary motor area (SMA), left motor cortex, right superior parietal lobule, left insula and right cerebellum compared to the control group during the expression of happy and sad emotion relative to UFM condition (Table 4). The patient group did not show any significantly increased activity compared to the control group for this contrast. As shown in Fig 4, the activities in the two clusters in the left insula were negatively correlated with the SANS AF score in the patient group (-38, -32, 22: r=-0.52, p=0.05; -40, 16, 16: r=-0.62, p=0.01). After the dose of antipsychotics was controlled, these correlations remained significant (-38, -32, 22: r=-0.59, p=0.03; -40, 16, 16: r=-0.57, p=0.04). As shown in Fig 5, the activities in the two clusters in the right DLPFC (44, 34, 24: r=-0.60, p=0.02; 46, 36, 12: r=-0.62, p=0.01) and the two clusters in the right cerebellum (30, -72, -24: r=-0.68, p=0.01; 36, -56, -24: r=-0.62, p=0.01) were negatively correlated with the SAS scores in the patient group, while no correlation existed in the control group. After the dose of antipsychotics was controlled, these correlations (DLPFC 44, 34, 24: r=-0.60, p=0.02; 46, 36, 12: r=-0.58, p=0.03; cerebellum 30, -72, -24: r=-0.63, p=0.01; 36, -56, -24: r=-0.57, p=0.03) in the patient group remained significant. The activity in the right cerebellum (36, -56, -24: r=-0.69, p=0.004) also correlated with the EPS score in the patient group. There was no significant correlation between the PSC of significant clusters and dose of antipsychotics.

As shown in Table 5, the activity in the right inferior parietal lobule showed a positive correlation with dose of antipsychotics. A negative correlation was observed between the activity in the left cerebellum and dose of

antipsychotics. There was no brain region which showed significant correlation with EPS score in the patient group.

Group differences in emotion-specific activity patterns were also examined, irrespective of stimulus type. The patient group showed decreased activity in the right DLPFC, right premotor cortex and right cerebellum compared to the control group during happy facial expression relative to UFM condition, while the patient group showed no increased activity (Table 6). The patient group showed decreased activity in the left DLPFC, left insula, left parahippocampal gyrus and cerebellum compared to the control group during sad facial expression relative to UFM condition, while the patient group showed no increased activity (Table 7).

Table 3 Regions showing significant difference in activities between the patient and control groups during the expression of happy and sad emotion relative to unmeaningful facial movement (UFM) condition

Regions, BA	Zmax	MNI coordinates			Nvox
		x	y	z	
Patient < Control					
L Premotor cortex, 6	3.40	-50	6	44	5
R Superior parietal lobule, 7	3.37	32	-48	66	8
L Insula, 13	3.71	-38	-22	18	33
R Cerebellum	3.61	36	-54	-24	10
	3.40	34	-72	-24	8
Patient > Control					
None					

BA: Brodmann area, Zmax: maxium Z value, MNI: Montreal Neurological Institute, Nvox: number of voxels, L: left, R: right

Noted in this table are those clusters of significant activation (FWE corrected $p<0.05$) after small volume correction analysis

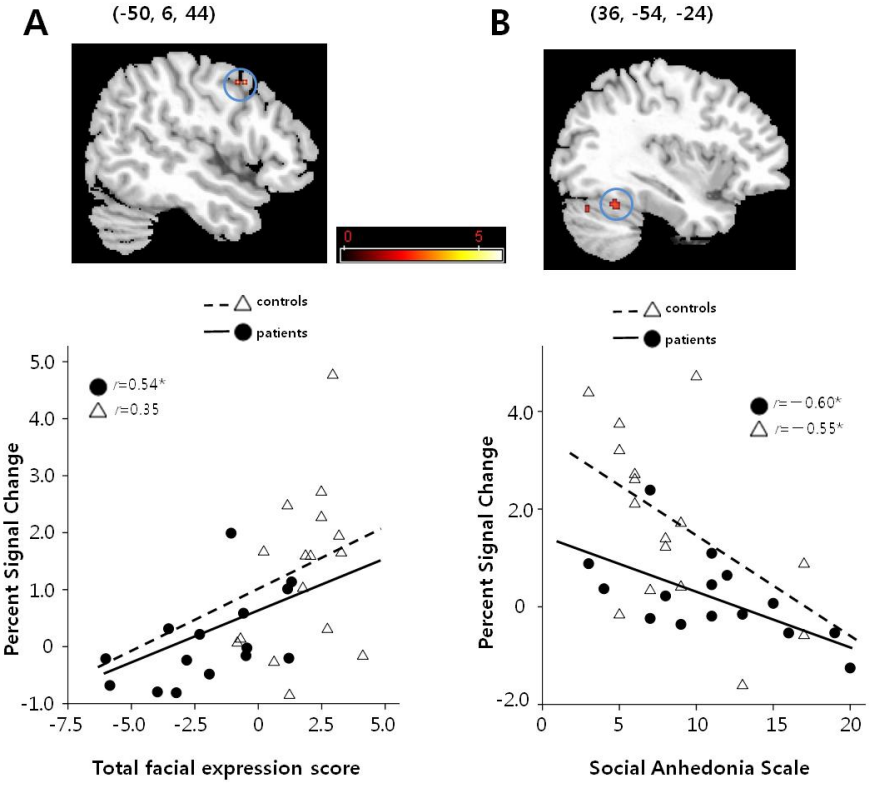

Fig 3. The activity in the left premotor cortex (A) was positively correlated with the total facial expression score in the patient group (r=0.54, p=0.04), while no correlation existed in the control group. The activity in the right cerebellum (B) was negatively correlated with the Social Anhedonia Scale score in the patient (r=-0.60, p=0.02) and control groups (r=-0.55, p=0.03). *Significant finding at an uncorrected p<0.05

Table 4 Regions showing significant difference in activities between the patient and control groups during the expression of happy and sad emotion relative to unmeaningful facial movement (UFM) condition after facial movements were controlled

Regions, BA	Zmax	MNI coordinates			Nvox
		x	y	z	
Patient < Control					
R Dorsolateral prefrontal cortex, 46	4.14	46	32	12	52
R Dorsolateral prefrontal cortex, 9	3.57	44	34	24	19
R Supplementary motor area, 6	3.33	4	6	58	7
L Motor cortex, 4	3.82	-38	-14	40	7
R Superior parietal lobule, 7	3.66	30	-48	66	6
L Insula, 13	4.23	-38	-32	22	220
	3.73	-40	16	16	38
R Cerebellum	3.40	36	-56	-24	9
	3.37	30	-72	-24	5
Patient > Control					
None					

BA: Brodmann area, Zmax: maxium Z value, MNI: Montreal Neurological Institute, Nvox: number of voxels, L: left, R: right

Noted in this table are those clusters of significant activation (FWE corrected $p<0.05$) after small volume correction analysis

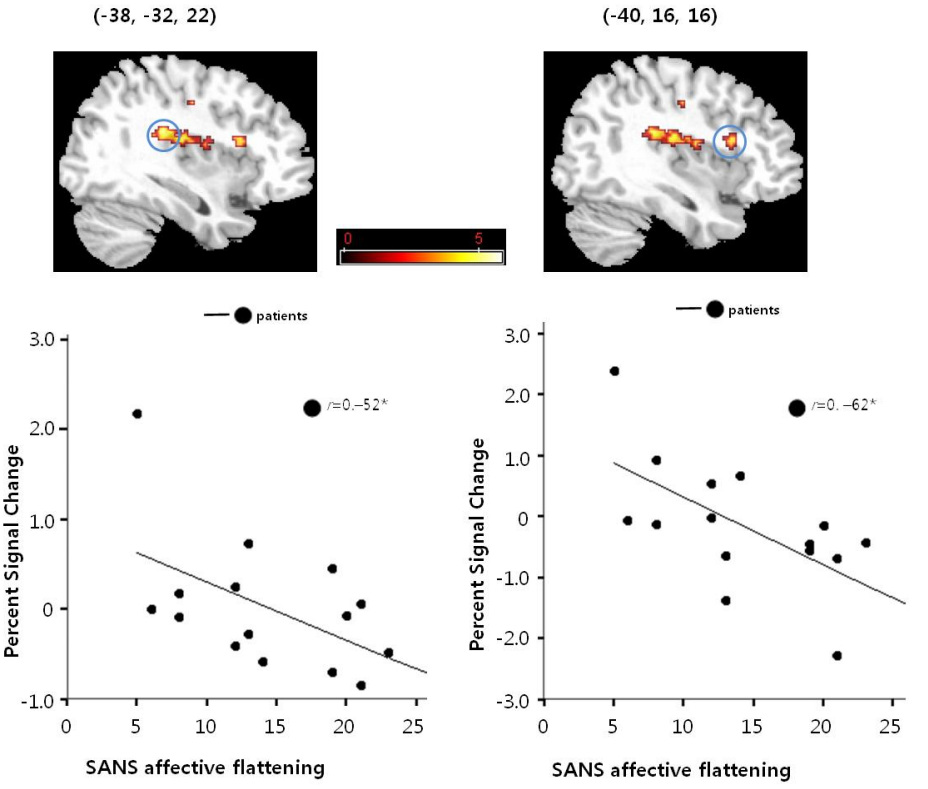

Fig 4. The activities in the two clusters in the left insula were negatively correlated with the affective flattening subscale score of the SANS in the patient group. *Significant finding at an uncorrected $p<0.05$

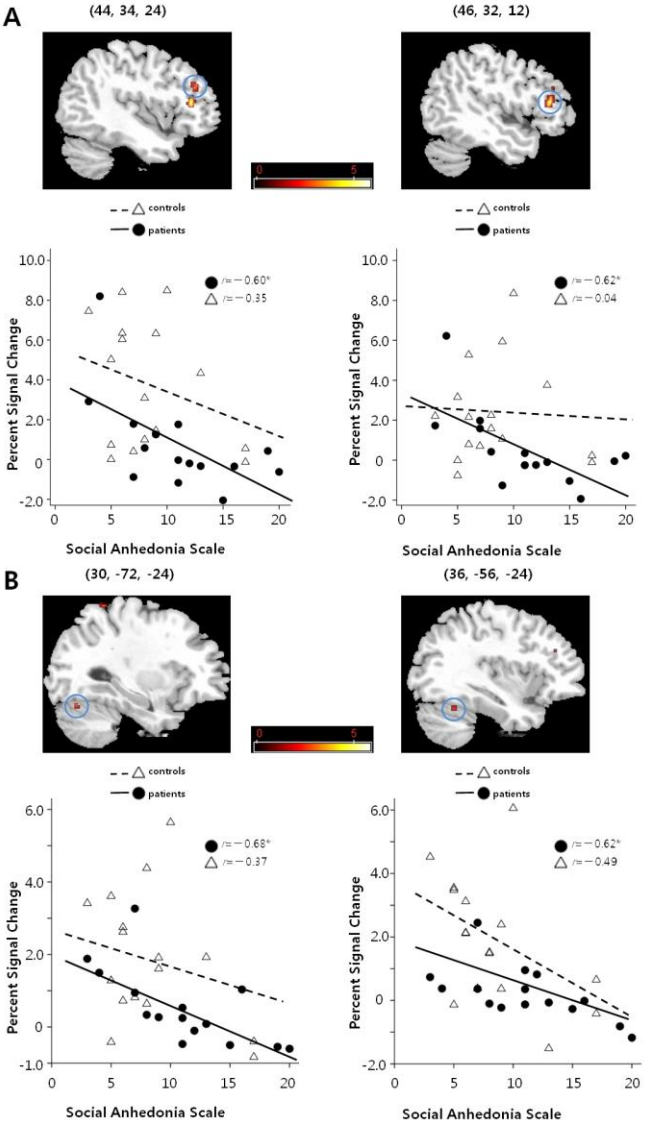

Fig 5. The activities in the two clusters in the right dorsolateral prefrontal cortex (A) and the two clusters in the right cerebellum (B) were negatively correlated with the Social Anhedonia Scale scores in the patient group. *Significant finding at an uncorrected $p<0.05$

Table 5 Results of voxelwise correlational analyses of antipsychotics dose in chlorpromazine equivalents and activities for the contrast emotional *versus* unmeaningful facial movement condition.

Regions, BA	Zmax	MNI coordinates			Nvox
		x	y	z	
Positive correlation					
R Inferior parietal lobule, 40	3.39	32	-46	36	8
Negative correlation					
L Cerebellum	3.52	-2	-68	-12	6

BA: Brodmann area, Zmax: maxium Z value, MNI: Montreal Neurological Institute, Nvox: number of voxels, L: left, R: right

Noted in this table are those clusters of significant activation (FWE corrected $p<0.05$) after small volume correction analysis

Table 6 Regions showing significant difference in activities between the patient and control groups during the expression of happy emotion relative to unmeaningful facial movement (UFM) condition

Regions, BA	Zmax	MNI coordinates			Nvox
		x	y	z	
Patient < Control					
R Dorsolateral prefrontal cortex, 9	3.45	46	34	24	16
R Premotor cortex, 6	3.48	54	4	42	6
R Cerebellum	3.30	2	-78	-14	8
Patient > Control					
None					

BA: Brodmann area, Zmax: maxium Z value, MNI: Montreal Neurological Institute, Nvox: number of voxels, L: left, R: right

Noted in this table are those clusters of significant activation (FWE corrected $p<0.05$) after small volume correction analysis

Table 7 Regions showing significant difference in activities between the patient and control groups during the expression of sad emotion relative to unmeaningful facial movement (UFM) condition

Regions, BA	Zmax	MNI coordinates			Nvox
		x	y	z	
Patient < Control					
L Dorsolateral prefrontal cortex, 9	3.31	-42	38	22	9
L Insula, 13	3.74	-36	-32	20	15
	3.61	-46	-10	14	7
L Parahippocampal gyrus, 28	4.00	-16	-18	-16	30
L Cerebellum	4.30	-16	-40	-14	56
	3.20	-12	-66	-14	10
R Cerebellum	4.06	36	-50	-26	57
	3.53	32	-70	-30	21
Patient > Control					
None					

BA: Brodmann area, Zmax: maxium Z value, MNI: Montreal Neurological Institute, Nvox: number of voxels, L: left, R: right

Noted in this table are those clusters of significant activation (FWE corrected $p<0.05$) after small volume correction analysis

IV. DISCUSSION

In this study, patients with schizophrenia were less facially expressive for both happy and sad emotions than healthy controls. This finding is in good agreement with previous studies which demonstrated that patients with schizophrenia displayed fewer positive and negative facial expressions.[7] However, the valence and arousal ratings for the picture stimuli in the patient group were not significantly different from those in the control group, suggesting similar levels of subjective affect. This is consistent with previous studies which have shown comparable degrees of positive and negative emotions in patients with schizophrenia than in normal controls.[6] These findings suggest that blunted affect in patients with schizophrenia may not stem from deficits in affective experience.

As expected, we found that the SANS AF and total facial expression scores were correlated with the BMS MOCO scores in patients with schizophrenia, although the correlations were not significant after a sequential Holm–Bonferroni procedure. This finding suggests that blunted affect in patients with schizophrenia may be associated with motor coordination problem. In addition, the lack of association between the SANS AF and total facial expression scores can be due to different context within which the ratings were made. Since the rating of the SANS are typically made during an interview, facial expression during the interview may have had more to do with an individual's social norm of communication. On the other hand, because facial expression during an fMRI

were made while the subjects lay alone in the scanner, the FACES ratings were relatively lacking of interpersonal context.

Consistent with our hypothesis, the SANS AF score showed significant correlation with the Modified Prosocial scale score in the patient group, although the correlation did not survive after the multiple testing corrections. This finding is consistent with previous studies which demonstrated the significant correlation between blunted affect and social functioning in patients with schizophrenia.[40-42] However, there is ambiguity about the direction of causal relationship. Therefore, future prospective studies could characterize the relationship between blunted affect and social functioning in patients with schizophrenia.

Using the event-related fMRI, we examined the functional abnormalities during the emotional expression in patients with schizophrenia. We found that the patient group showed decreased activities in various brain regions including the premotor cortex, insula and cerebellum. In particular, it was noteworthy that the patient group had reduced insula activation during emotional expression, in contrast to the control group. The patient group also exhibited decreased activity in the insula compared to the control group after controlling for facial movements. Furthermore, insular activity was correlated with the SANS AF scores in the patient group, suggesting the insula's role in emotional expression in patients with schizophrenia. Recent functional imaging studies have reported the involvement of the insula during imitating emotional facial expressions.[78-79] In addition, a neuroimaging study found that insula activity was correlated with magnitude of

facial muscular movement during emotional expression, which suggests the role of the insula in expressive aspects of emotional behavior.[79] Given that the insula serves as a link between the limbic system and the mirror neuron system (MNS),[80] the insula has been considered as an essential component for empathy by relaying action representation information to limbic area.[78] Conversely, the insula may play an important role in emotional expression by conveying emotional information processed by limbic system to the MNS, which plays a fundamental role not only in action understanding but also in action imitation.[81] Collectively, our findings suggest that blunted affect is not only related to impairments in limbic activity, but also related to the functional disturbance of the interconnected networks including the insula. But the specific role of the insula and limbic system and the relationship between them in blunted affect of schizophrenia would be subjects that need to be explored further.

The activities in the premotor cortex, superior parietal lobule and cerebellum during emotional expression were also decreased in the patient group than the control group. Specifically, the activity in the premotor cortex was correlated with total facial expression scores in the patient group, although the correlation was not significant after controlling for the dose of antipsychotics. Because the premotor cortex is consistently implicated in imitating emotional expression,[78-79] the premotor cortex may be considered as one of neural correlates of emotional expression. However, decreased premotor activity in the patient group could be due to poor facial expression during an fMRI, because the extent

of facial movement in the patient group was much lower than that in the control group. On the other hand, decreased activity in the superior parietal lobule (SPL) was also found after controlling for the extent of facial movement. The SPL plays a crucial role in many behaviors including the sensory-motor integration (i.e., the transformation of sensory information to motor commands),[82] visuospatial attention[83] and corporeal awareness[84], of which sensory-motor integration can be relevant to emotional expression. For example, an fMRI study demonstrated that the SPL were activated during sensory-motor transformations for eye and finger movements triggered by either somatosensory or visual cues.[85] Since facial emotional expression could be triggered by visual (e.g., other person's facial expression) or somatosensory (e.g., heartbeat) cues, the deficient activity in the SPL might play a role in blunted affect in patients with schizophrenia. The involvement of the SPL in facial emotional expression was also demonstrated by a previous fMRI study.[78]

Consistent with our hypotheses, the activities in the DLPFC and cerebellum showed significant correlations with the SAS score in the patient group. Although the DLPFC is known to play a principal role in executive function,[86] it has also been linked to affective processing. In particular, positive affect has been associated with activation of frontal regions including the DLPFC.[87-88] In addition, the impairments in using reward information to drive behaviors for obtaining desired outcomes might be the bases of negative symptoms including anhedonia in patients with schizophrenia, and the DLPFC has been regarded as one of the major

components of the system that link rewards with motivated behavior.[89] The cerebellum is traditionally considered as an organ that subserves balance and motor control; however, its involvement in affect has also been suggested.[90] In fact, patients with cerebellar lesions showed affective and behavioral disturbances which were characterized by inappropriate behavior and blunted affect.[91] The DLPFC and cerebellum forms reciprocally connected circuit, and a disruption in this circuitry produces "cognitive dysmetria", which is defined as difficulty in prioritizing, processing, coordinating and responding to information.[92-93] Given that "cognitive dysmetria" could be the basic cognitive abnormality that account for diverse symptoms in patients with schizophrenia, it could be the possible explanation about the involvement of the DLPFC and cerebellum with social anhedonia. However, the activity of a cluster in the cerebellum related to social anhedonia showed a correlation with the EPS scale score in the patient group. Moreover, the SAS score also correlated with the EPS scale score in patients with schizophrenia. These findings suggest that the association of cerebellar activity with social anhedonia may be partly due to neuroleptic induced parkinsonism, but future studies including drug-naïve patients are needed to come to firm conclusions about the relationship between cerebellar activity and blunted affect in patients with schizophrenia.

The activity in the inferior parietal lobule (IPL) in the patient group showed a positive correlation with the dose of antipsychotics. The IPL is involved in various functions including the perception of emotion,[94] understanding of

intention,[81] and coding of motor intention.[95] Since the current dose of antipsychotics usually reflects the recent severity of symptoms in patients with schizophrenia, the positive correlation may be due to compensatory activation of the IPL for the deficient activities of other regions related to severe symptoms. On the other hand, the correlation may be resulted from the beneficial effect[96] of antipsychotics to social cognition because the IPL can be related to social functioning as a component of mirror neuron system.[81]

We also observed patients' emotion-specific deficit of a number of other brain regions, including the DLPFC, premotor cortex, parahippocampal gyrus, insula and cerebellum. Of these regions, the activities of the insula and parahippocampal gyrus were decreased during the expression of sad emotion in the patient group compared with the control group. Each of these regions is implicated in processing of negative emotion: the insula has been found to be activated during processing of sad emotion[97-99] and the parahippocampal gyrus has also been related to unpleasant[100] or highly arousing emotion.[101] This is consistent with a previous neuroimaging study which revealed that patients with schizophrenia showed decreased activities in the insula and parahippocampal gyrus during the experience of unpleasant stimuli.[102] However, there is some question as to whether the deficient activities in these regions are only observed in relation to sad emotion in patients with schizophrenia. The decreased insular activity has been found during valence discrimination task for happy face in patients with schizophrenia.[103] In addition, patients with schizophrenia showed

significantly less activation than healthy controls in the parahippocampal gyrus during recognition task for happy face.[104] Therefore, further studies should be needed to draw firm conclusions about the relationship between the deficient activity of these regions and deficit in sad emotion expression in patients with schizophrenia.

Several limitations of this study should be acknowledged. First, the patients with schizophrenia in this study were taking antipsychotic medications. Given that antipsychotics are associated with extrapyramidal symptoms, which could influence emotional expression in patients with schizophrenia, it is possible that the antipsychotic medications may have affected the current findings. Although controlling for the dose of antipsychotics did not affect the most correlations between neural activities and emotional expression, future studies of emotional expression in patients with schizophrenia may benefit from including drug-naïve patients to avoid the possible confounding effects of medication. Second, there was a significant difference in years of education between the patient and control groups. However, the two groups did not differ in the levels of intelligence and the SANS AF and total facial expression scores did not show any associations with years of education. Third, the small sample size of the study could limit the generalization of these findings, thus further study with an extensive sample would be required.

V. CONCLUSION

The behavioral and neuroimaging findings suggest that motor coordination problem may affect blunted affect in patients with schizophrenia. This study also provides further evidence for the role of aberrant activity in the insula to blunted affect and the involvement of the DLPFC and cerebellum in social anhedonia in patients with schizophrenia. These findings suggest that blunted affect in schizophrenia may be influenced by the functional disturbance of the interconnected networks including the insula. In addition, the association of decreased activities in the DLPFC and cerebellum with increased social anhedonia found in this study suggests possible involvement of altered cortico-cerebellar circuit in social anhedonia in patients with schizophrenia.

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ABSTRACT(IN KOREAN)

조현병 환자에서 둔마된 정동의 신경매개체: fMRI 연구

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이 정 석

목적: 조현병 환자의 둔마된 정동은 운동 및 사회 기능장애와 연관될 가능성이 있다. 이 연구는 조현병 환자의 둔마된 정동 증상에 대한 신경생물학적 기초를 변연계 및 운동, 사회적 기능과 관련된 뇌영역에서 탐구하고자 하는 목적으로 설계되었다.

방법: 15명의 조현병 환자와 16명의 건강 대조군에게 fMRI촬영 중 행복, 슬픔, 무의미한 얼굴 움직임 조건에 해당하는 얼굴표정을 짓도록 하였다. 둔마된 정동은 SANS척도의 감정적 둔마 척도에 의해 평정되었다. 얼굴표정은 녹화되었으며 얼굴표정채점체계 (FACES)에 의해 얼굴표정 지음의 정도를 평정하였다.

결과: 건강 대조군에 비해 환자군은 모든 표정변수에서 장애를 보였다. 환자군은 감정표현 조건 시 좌측 전운동피질, 좌측 뇌섬엽, 우측 소뇌에서 대조군에 비해 저하된 활성을 보였다. 환자군에서 좌측 전운동피질의 퍼센트 신호 변화는 fMRI촬영 중 FACES로 채점된 얼굴표정점수와 상관성을 보였다. 얼굴 움직임을 통제했을 때 환자군은 감정표현 조건에서 우측 배외측 전전두피질, 우측 보완운동영역, 좌측 운동피질, 좌측 뇌섬엽, 우측 소뇌에서 대조군에 비해 저하된 활성을 보였다. 환자군에서 좌측 뇌섬엽의 퍼센트 신호 변화는 SANS의 감정적 둔마 척도와 상관성을 보였다. 환자군에서

우측 배외측 전전두피질과 우측 소뇌의 퍼센트 신호 변화는 사회적 무쾌감증 척도와 상관성을 보였다.

고찰: 이 결과들은 운동 협응의 문제가 조현병 환자의 둔마된 정동에 영향을 미칠 가능성을 시사한다. 이 연구는 또한 조현병 환자의 둔마된 정동이 뇌섬엽을 포함하는 상호연결된 신경망의 이상에서 영향을 받을 가능성을 제시한다. 이에 더해 배외측 전전두피질과 소뇌의 활성감소가 사회적 무쾌감증 증가와 관련성을 보인 사실은 피질-소뇌 회로의 장애가 사회적 무쾌감증에 관련되어 있을 가능성을 시사한다.

핵심되는 말 : 둔마된 정동, 사회적 무쾌감증, 운동 협응, 사회적 기능, 뇌섬엽, 배외측 전전두피질, 소뇌