INTRODUCTION

Eye movement recordings are useful to investigate the biological characteristics of information processing in mental disorders such as schizophrenia [1,2]. In particular, exploratory eye movements (EEMs) were established by Kojima et al. [3-5], who indicated that the scanning length and RSS (responsive search score) are trait markers in schizophrenic patients. EEMs are the movements that are required to scan or search a picture or a drawing. The movements can be measured by tracking the gazing point using an eye marker (e.g., nac: EMR-8). The movement is considered to be a sensory motor component of visual recognition. In addition, Loughland et al. [6] indicated that eye scanning is a trait marker in schizophrenic patients.

Facial affect recognition is the ability to identify the emotion expressed on a face. Facial affect recognition is an important function in human social relation-
ships. Thus, the effects of facial affect must be studied in schizophrenic patients because such patients have been reported to have a deficit in facial recognition [6,7]. To date, few studies on the effect of facial affect have been reported, and little is known about the effect of facial affect on eye movements in healthy subjects and schizophrenic patients. Schizophrenic patients have been shown to manifest a significant deficit in the ability to correctly identify the emotions associated with facial expressions [2]. Such patients have distinctive deficits in emotional appropriateness, and an impaired ability to identify facial affect correctly might contribute to this deficit. Loughland et al. [6] reported that the scanning was specifically impaired for positive emotion rather than negative emotion.

It has been reported that schizophrenic patients have a dysfunction in left eye scanning [8-11]. Healthy controls first scan the left field of a screen, but schizophrenic patients were found to hardly scan the left field at all. This scanning behaviour may be specific to schizophrenic patients.

The present study compared the effects of emotional stimuli on EEMs in schizophrenic patients and healthy controls. The first aim was to determine whether or not there are different responses in eye movements to an emotionally loaded task in the two groups. The second aim was to evaluate the laterality in the manner of patients’ eye movements.

METHODS

Subjects

This study was conducted with 40 schizophrenic patients (included 27 paranoid type, 13 non-paranoid type: disorganized type 9, catatonic type 1, undifferentiated type 3) and 40 age-matched healthy controls. All patients with schizophrenia were diagnosed using the Structured Clinical Interview of the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition [12]. They were treated as inpatients or outpatients at the Department of Psychiatry, Kurume University Hospital. The clinical state of all patients was assessed using the Positive and Negative Symptom Scale [13] by two psychiatrists within 1 week after eye movement recording. When scores differed between the two psychiatrists, the final scores were determined by consensus before being analyzed as data. All patients were treated with neuroleptics. All controls had no history of psychiatric or neurological diseases or drug addiction. All subjects were right-handed as determined by the Edinburgh Handedness Inventory [14], and had normal vision. This study was approved by the Ethics Committee of Kurume University, and written informed consent was obtained from all subjects prior to the experiments. The demographic and clinical characteristics of all subjects are shown in Table 1.

<table>
<thead>
<tr>
<th>TABLE 1. Profile of subjects</th>
<th>Schizophrenia (40)</th>
<th>Healthy controls (40)</th>
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</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>28.0±8.5</td>
<td>30.6±6.5</td>
</tr>
<tr>
<td>Sex (F/M)</td>
<td>28/12</td>
<td>20/20</td>
</tr>
<tr>
<td>Duration of education (year)</td>
<td>13.1±1.7</td>
<td>14.4±1.3</td>
</tr>
<tr>
<td>Duration of illness (year)</td>
<td>5.6±5.5</td>
<td>–</td>
</tr>
<tr>
<td>Equivalents of CPZ(mg)</td>
<td>369.0±194.8</td>
<td>–</td>
</tr>
<tr>
<td>PANSS Total score</td>
<td>50.9±6.6</td>
<td>–</td>
</tr>
<tr>
<td>Positive subscale</td>
<td>24.8±5.5</td>
<td>–</td>
</tr>
<tr>
<td>Negative subscale</td>
<td>20.5±4.2</td>
<td>–</td>
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</table>

Apparatus and stimuli

We used two symmetrical babies’ faces to expand the eye scanning field and increase the number of gaze points. For primary study, healthy subjects (N=194) were asked, “How do the smiling or crying babies feel?” All subjects answered that the smiling babies feel pleasure and the crying babies feel sad. Picture 1: Two symmetrical smiling babies with laughing sounds (70 dB, SPL) were used to study the effect of possible positive emotion. Picture 2: Two symmetrical crying babies with crying sounds (70 dB, SPL) were used to study the effect of negative emotion. The pictures were projected onto a screen to form images 120 cm wide and 90 cm high. The maximum angles of sight lines were 40° horizontally and 24° vertically.

Eye movements were recorded using an eye-mark recorder (nac, EMR-8, Tokyo, Japan). Movement >1° with duration >100 ms was scored as an eye movement. Recorded data were assessed by computer-assisted analysis in terms of two parameters related to total eye scanning length (TESL) between gazing points [15-17], which was calculated from the distance between two eye gazing points as reported previously. In the present study, we subdivided the total number of gaze points (TNGP) into the left and right halves of the screen (left and right TNGP) [9,10]. Each session consisted of a series of two pictures, each presented for 15 sec.
EMOTIONAL EYE SCANNING IN SCHIZOPHRENIA

Procedure

In a darkened room, where visual and auditory sensory stimuli were attenuated, eye movement was recorded using an eye-mark recorder. Subjects were instructed to identify each picture exactly as it was presented. They were also instructed to fix their gaze at several corner points to check their eye movements in order to evaluate neurological deficits and low-level eye movement as a reflex organic saccade. No subjects showed deficits under the procedure.

The recording was performed as follows. At first, all subjects were instructed, “Look at the picture in front of you carefully and memorize it. After recording, I will ask you to check the picture you saw”.

Session 1 (S1): Each subject was instructed, “Please imagine something pleasurable”. After the subject said, “Yes, I am imagining something pleasurable”, we said, “Look at the pictures in front of you”, after which the eye mark was recorded. Session 2 (S2): The subject was instructed, “Please imagine something sad”. After they said, “Yes, I am imagining something sad”, we said “Look at the picture in front of you”, and then the eye mark was recorded. Session 3 (S3): The subject was instructed, “Please imagine the saddest thing you can think of”. After they said, “Yes, I am imagining the saddest thing I can think of”, we said “Look at the picture in front of you”, and then the eye mark was recorded. Session 4 (S4) and session 5 (S5) were performed as which S1 again. Subjects rested for one between S3 and S4.

The degree of the emotion recalled was measured on a seven-point scale. The affect scales ranged from 0 (not at all) to 6 (very much). No significant difference was observed between the two groups in terms of positive (controls, 5.20 ± 0.80; patients, 5.05 ± 0.86) and negative (controls, 4.94 ± 0.72; patients, 5.01 ± 0.76) recall. Furthermore, all subjects were asked about the events imagined after the experiment.

Data from the right and the left eyes were analyzed and found to be similar. No significant difference was obtained between the right and the left eyes.

Statistical analysis

One-way repeated ANOVA (stimuli, fields) was

Fig. 1. A: presented pictures. B, C: typical series of exploratory eye movements in a healthy subject (B) and a schizophrenic patient (C). Each dot indicates a gaze point and each line, a movement.
used to compute the main session effects performed for each group (patients or controls). Post hoc analyses were conducted using Scheffe tests. The Pearson correlation coefficient was used to identify significant relationships between symptom scores, measures of eye movements, and dose of medication. A level of $p<0.05$ was accepted as statistically significant. The data for all subjects’ responses to the pleasurable events were analyzed.

RESULTS

Eye movements

Gaze points shifted between the left and right fields around the babies’ eyes and mouth, like two reversed triangles at S1 (smiling babies: imagining pleasurable events). Gaze points were progressively reduced when viewing crying babies while imagining sad and saddest events in both controls and patients. Note that gaze points were further reduced at S4 (smiling babies: imagining pleasurable events again) in patients but increased in controls.

Total eye scanning length (TESL; Table 2; Fig. 2)

There was a significant main session effect of TESL in both controls ($F=23.1, p<0.001$) and patients ($F=8.5, p<0.001$). TESL was reduced significantly for S2 ($p<0.001$) and S3 ($p<0.001$) compared to that for S1:Smile 333.9±178.1 23.2±5.5 468.0±139.5 26.3±4.8
S2:Cry 243.0±155.6 19.1±5.2 322.6±126.4 22.6±5.4
S3:Cry 219.1±165.0 19.2±4.9 297.6±129.3 21.4±4.6
S4:Smile 210.4±124.8 19.4±5.0 440.1±150.9 24.5±4.9
S5:Smile 237.6±124.7 19.9±5.2 449.4±168.1 25.6±5.4

**TABLE 2.**

Measure of eye movements

Means and standard deviation of the mean are given

<table>
<thead>
<tr>
<th></th>
<th>Schizophrenia (40)</th>
<th>Healthy controls (40)</th>
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<tbody>
<tr>
<td></td>
<td>TESL (cm)</td>
<td>TNGP (n)</td>
</tr>
<tr>
<td>S1:Smile</td>
<td>333.9±178.1</td>
<td>23.2±5.5</td>
</tr>
<tr>
<td>S2:Cry</td>
<td>243.0±155.6</td>
<td>19.1±5.2</td>
</tr>
<tr>
<td>S3:Cry</td>
<td>219.1±165.0</td>
<td>19.2±4.9</td>
</tr>
<tr>
<td>S4:Smile</td>
<td>210.4±124.8</td>
<td>19.4±5.0</td>
</tr>
<tr>
<td>S5:Smile</td>
<td>237.6±124.7</td>
<td>19.9±5.2</td>
</tr>
</tbody>
</table>

**Fig. 2.** Left panel: Total eye scanning length (TESL; ordinate) was plotted against sessions (abscissa) in control group (○) and schizophrenia group (●). Right panel: Total number of gaze points (TNGP; ordinate) was plotted against sessions (abscissa) in control group (□) and schizophrenia group (■). Means and standard errors of the mean are given. Asterisks indicate significant differences. ***: $p<.001$, **: $p<.01$. 

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S1 in both controls and patients. No significant difference was observed between S1 and S4 or S5 in controls; thus, TESL recovered to the original values when viewing smiling babies again while imagining pleasurable events (S4, S5) in controls. In patients, significant differences were observed between S1 and S4 (p < 0.001) or S5 (p < 0.01).

TESL in controls was significantly larger than that in patients for S1 (F = 27.6, p < 0.001), S2 (F = 12.5, p < 0.001), S3 (F = 11.2, p < 0.001), S4 (F = 110.9, p < 0.001), and S5 (F = 81.9, p < 0.001).

**Total number of gaze points (TNGP; Table 2; Fig. 2)**

There was a significant main session effect of TNGP in both controls (F = 13.1, p < 0.001) and patients (F = 8.8, p < 0.01). TNGP was reduced significantly for S2 (p < 0.001) and S3 (p < 0.001) compared to that for S1 in controls. In patients, TNGP was reduced significantly for S2 (p < 0.001), S3 (p < 0.001), S4 (p < 0.01), and S5 (p < 0.01) compared to that for S1.

TESL in controls was significantly larger than that in patients for S1 (F = 14.2, p < 0.001), S2 (F = 17.4, p < 0.001), S3 (F = 8.0, p < 0.01), S4 (F = 42.2, p < 0.001), and S5 (F = 44.5, p < 0.001).

**Left and right total number of gaze points (left TNGP, right TNGP; Fig. 3)**

There was a significant main session effect of left TNGP in both controls (F = 6.45, p < 0.001) and patients (F = 4.07, p < 0.01). Left TNGP was reduced significa-

### Table 3.

**Relationship between eye measures and symptom scores**

<table>
<thead>
<tr>
<th></th>
<th>Negative scores</th>
<th>Positive scores</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>TESL (cm)</td>
<td>Left TNGP (n)</td>
</tr>
<tr>
<td>S1:Smile</td>
<td>-0.496 (p&lt;0.001)</td>
<td>-0.367 (p&lt;0.05)</td>
</tr>
<tr>
<td>S2:Cry</td>
<td>-0.523 (p&lt;0.001)</td>
<td>-0.406 (p&lt;0.05)</td>
</tr>
<tr>
<td>S3:Cry</td>
<td>-0.420 (p&lt;0.001)</td>
<td>-0.219</td>
</tr>
<tr>
<td>S4:Smile</td>
<td>-0.639 (p&lt;0.001)</td>
<td>-0.511 (p&lt;0.001)</td>
</tr>
<tr>
<td>S5:Smile</td>
<td>-0.537 (p&lt;0.001)</td>
<td>-0.424 (p&lt;0.05)</td>
</tr>
</tbody>
</table>

**Fig. 3.** Total number of gaze points (TNGP; ordinate) was plotted against sessions for left field of screen (Left TNGP) and right field of the screen (Right TNGP) in control group (□) and schizophrenia group (■). Means and standard errors of the mean are given. Asterisks indicate significant differences. **:** p < .001, **:** p < .01, *: p < .05.
significantly for S2 (p<0.05) and S3 (p<0.001) compared to that for S1 in controls. In patients, Left TNGP was also reduced significantly for S2 (p<0.01), S3 (p<0.01), S4 (p<0.01), and S5 (p<0.01) compared to that for S1.

Left TNGP in controls was significantly larger than that in patients for S1 (F=18.8, p<0.001), S2 (F=26.7, p<0.001), S3 (F=10.5, p<0.01), S4 (F=95.7, p<0.001), and S5 (F=46.9, p<0.001).

There was a significant main session effect of right TNGP in controls (F=6.55, p<0.001) and in patients (F=3.66, p<0.05). Right TNGP was reduced significantly for S2 (p<0.001) and S3 (p<0.001) compared to that for S1 in controls. In patients, Right TNGP was also reduced significantly for S2 (p<0.05) and S3 (p<0.01) compared to that for S1. There were no significant differences in right TNGP between S1 and S4 or S5 in both controls and patients.

Right TNGP in controls was similar to that in patients for all sessions. No significant difference was observed between patients and controls in all sessions.

**Relationship between eye measures and symptom scores**

The most significant correlation was obtained between the TESL and negative symptom scores for S4 when viewing smiling babies while imagining pleasurable events the second time. Left TNGP at S4 was also significantly and negatively correlated with negative symptom scores, as seen in Table 3. There was no significant correlation between eye measures and positive symptom scores. There was also no significant correlation between dose of antipsychotic and symptoms.

**DISCUSSION**

The most important finding of the present study was that EEMs clearly differed between schizophrenic patients and healthy controls under the emotional loading task, and the difference was evident when viewing smiling babies while imagining pleasurable events the second time only at the left field of the screen; this suggests that EEMs under the emotional loading task are a useful biologic marker for clinical evaluation.

Kojima et al. [5] investigated EEMs using specially constructed S-shaped geometric figures, demonstrating that EEMs were a useful biologic marker of visual cognitive function in patients with psychiatric disorders such as schizophrenia, and reported that EEMs might be a trait marker for schizophrenic patients. In the present study, we found that EEMs of schizophrenic patients showed properties similar to the results of Kojima et al. The present study also examined the effects of affective stimuli in different scanning fields, as the left or the right scanning fields of a screen. Specific aspects of this study are discussed below.

**Total eye scanning length (TESL)**

TESL for patients was significantly shorter than that for controls in all sessions. Previous studies have reported that schizophrenic patients produced relatively restricted scanpaths to all face stimuli [2,6,8,9]. In the present study, TESL in patients was significantly shorter than that in controls for both smiling and crying babies, consistent with previous evidence. The decreased TESL for schizophrenic patients suggests a reliance on serial processing strategies, resulting from the failure to achieve an integrated percept of the face.

TESL was reduced significantly when viewing the crying babies while imagining sad events in both controls and patients. TESL was recovered when viewing the smiling babies while imagining pleasurable events the second time in controls, but not in patients. These findings suggest that the recovery from a negative emotional state (imagining sad events) observed in controls may be a useful measure to evaluate the effects of emotion and also the resistance to negative emotion. Thus, the present protocol may be a useful technique for determining how visual cognitive function reflects the effects of emotion, especially the control of negative and positive emotions. The significant reduction in TESL when viewing smiling babies while imagining pleasurable events again (S4, S5) may mostly indicate the vulnerability of schizophrenic patients to emotional load. The findings might reflect the method of visual response assessment, but one should note that these results indicate a dysfunction of schizophrenic patients relative to controls.

Loughland et al. [6] reported that schizophrenic patients showed an impairment of scanning and this was evident for happy and neutral faces. In the present study, the poor recovery of patients might mostly reflect an impairment in response to happy faces, especially after negative emotional loading. The authors concluded that the impairment of scanning in schizophrenic patients might reflect a failure to integrate face stimuli due to dysfunction in the synchronization between local and global processing. Indeed, the eye movements reflected gazing at a narrow field of the screen.

**Total number of gaze points (TNGP)**

In the present study, a difference of TNGP under loaded emotion was clear in the left field of the screen, but not in the right field. TNGP in patients was sig-
nificantly smaller than that in controls at S1, S2, S4, and S5, with differences only in the left field of the screen, indicating dysfunction of the right brain.

The effects of unilateral corpus callosum brain lesions show that the right hemisphere is superior to the left in perceiving facial emotional expression and mood [18-20]. In addition, in healthy individuals, the emotional expression of the left side of a face seems to be processed preferentially [21]. Phillips and David reported that schizophrenic patients had difficulty in redirecting their initial focus of attention to the left field of stimuli and proposed left specific scan paths as a marker of attention processes in schizophrenic patients [8]. The right brain has been considered to subserve emotional function, while the left brain has symbolic functions [22]. In a previous study, Nishiura et al. [9] reported that viewing images with positive content reduced left TNGP in schizophrenia. Moreover, we also reported that the left TNGP was smaller in schizophrenic patients under positive affect with voice [11]. The present finding that TNGP was significantly smaller and did not recover after the second viewing of smiling babies only in the left field is consistent with previous findings of abnormal left field scanning in schizophrenia during viewing of positive emotional stimuli. Thus, the present observations in which the effects of emotion were significant only at the left field of the screen may be useful for evaluating the hemispheric function of the brain. The present positive and negative emotional stimuli are considered to show the degree of healthy cognitive function between right and left brain.

**Symptoms and eye movements**

Negative psychiatric symptoms have been reported to correlate negatively with exploratory eye movements. A significant negative correlation between TESL and negative symptom scores was also observed in the present study. This suggests strongly that EEMs are useful for clinical application and reflect negative symptoms such as blunted affect, passive/apathetic withdrawal, and emotional withdrawal. Minassian et al. [23] suggested that such visual organization impairments might be related to cognitive inflexibility and frontal dysfunction.

**Conclusions and psychophysiological significance**

The left visual field of the screen under an emotionally loaded task might be the most important for characterizing the vulnerability of schizophrenic patients to emotional stress. This may result from three factors. 1) One is the dysfunction of the scanning property in which humans first scan the left field. This dysfunction is due to the impairment of major set to event processing. 2) The second is that schizophrenic patients may have an impairment of the right frontal cortex especially under pleasurable condition because the left inner position is innervated from the right brain. 3) Third, the amygdala shows increased activation when viewing smiling babies only in patients with schizophrenia [24]. From these hypotheses, schizophrenic patients may have an impairment of the right cortex, especially under pleasurable emotion. This dysfunction could cause difficulty in relationships with other humans. Rehabilitation concerned with pleasure should be given priority for schizophrenic patients to help them recover or improve their social life.

There are several limitations in this study that should be taken into consideration. First, we didn’t measure an emotionally neutral loading task. However, in our previous study using similar pictures, EEMs of schizophrenic patients were smaller than those of healthy controls when viewing pictures of smiling babies and open circles (neutral stimuli), but no significant difference was observed when viewing pictures of crying babies [9]. Furthermore, we think that the series of protocols used in this study is most important. EEMs recovered to the level of S1 after re-loading with positive emotion (S4, S5) in the controls. However, EEMs did not recover to the level of S1 in schizophrenic patients. The trend is especially seen in the left visual field. These results are considered to represent the vulnerability of schizophrenic patients to emotional stress. Second, we did not assess the intelligence of the subjects. It is possible that the intelligence level of the subjects might affect the results of the tasks. Thus, a detailed examination that takes intelligence into consideration will be required in the future. Third, other psychotic disorders (ex., brief psychotic disorder, delusional disorder, schizoaffective disorder etc.) were not assessed in the present study. It is necessary to study EEMs in other psychotic disorders to determine whether the present observed dysfunction is specific to schizophrenia or not. Further, regarding the influence of drugs, almost all patients received atypical anti-psychotic drugs. In this study, EEMs were not correlated with anti-psychotic dose. Although the relationship between medication effects and EEMs is unclear, future study should be done to clarify this issue.

Finally, with regard to EEMs in the left field of a screen, the emotionally loaded task provided an index for comparing the recovery ability of schizophrenic patients and healthy controls. Thus, EEMs appear to constitute clinical and hemispheric functional markers.
that may be useful for exploring human visual cognition.

REFERENCES