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Saccadic eye movements and regional cerebral blood flow in schizophrenic patients

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Abstract This study examined saccadic eye movements, using simple stationary targets, in schizophrenic patients. The targets were eight black points or eight arabic-numbered points placed in randomized order on the circumference of a circle. Self-paced eye movements during clockwise tracking of these points, by 23 patients and 23 controls, were recorded using an infrared eye-mark recorder. Then the relationship between the saccades and clinical symptoms was investigated. Finally, the relationship between the performance of the saccades and resting regional cerebral blood flow (rCBF) was examined using single photon emission computed tomography with ^{99m}Tc-hexamethyl propyleneamine oxime (HMPAO). The results indicate that patients track with significantly fewer correct scores and more deviant scores than controls, in agreement with our previous study. There were two groups of patients: an ordinary group who obtained a full-target-hitting score at a 200-ms setting and a fast group who obtained the full score at 100 ms but not at 200 ms. Some patients displayed significantly more hypermetria than controls. Significant correlations were found between hallucination and delusion symptoms and correct score. With respect to relative rCBF, fast-group patients showed significantly decreased rCBF in the left limbic and inferior parietal areas as compared with ordinary group patients. These findings suggest that some schizophrenic patients view the stationary targets too fast and this may be related to dysfunction in the limbic-parietal association area in the left hemisphere.

Key words Schizophrenia · Eye movement · Regional cerebral blood flow · Clinical symptoms · Parietal lobe

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Introduction

Several studies have indicated disturbance of saccadic eye movements in schizophrenic patients using a variety of tasks (Schmid-Burgk et al. 1982, 1983; Reischies et al. 1988, 1989; Fukushima et al. 1990; Paus 1991; Park and Holzman 1992; Matsui and Kurachi 1995). Matsui and Kurachi (1995) examined elementary eye movements in a simple saccadic tracking task using stationary targets. It was found that schizophrenic patients track with significantly fewer correct scores and more deviant scores than controls, and that superfluous fixations in the patients improved significantly when numbered points were placed on targets. In that study, under numbered-point conditions, the patients showed fewer target hittings than controls when a fixation point had been defined as a point at which the gaze is held for more than 200 ms, but there was no significant difference between patients and controls at the 100-ms setting; i.e. it was found that some patients viewed the targets too fast. This may possibly be due to the subjects being able to anticipate the next number because the arabic numbers were placed in order from 1 to 8. The first aim of the present study was to reexamine the experiment done by Matsui and Kurachi (1995), using numbered points placed in randomized order, in another cohort of patients. The second aim was to investigate the relationship between saccadic eye movements and clinical symptoms.

Saccades have been shown to be controlled by various cortical and subcortical regions. Some studies have reported changes in regional cerebral blood flow (rCBF) during various saccadic tasks in humans (Melamed and Larsen 1979; Fox et al. 1985; Frith et al. 1992; Petit et al. 1993; Paus et al. 1993; Anderson et al. 1994). Brain regions mentioned in these studies were the frontal lobes, frontal eye field, supplementary motor area, anterior cingulate, parietal cortex, thalamus, basal ganglia, hippocampus, and cerebellum. In such studies on schizophrenic patients, Nakashima et al. (1994) reported that the left dorsolateral prefrontal cortex was not activated during voli-

tional saccades in patients, but was activated in normal controls. The relationship between the eye-movement parameters and resting rCBF in schizophrenic patients has also been reported. Tsunoda et al. (1992) showed that the mean duration of fixation on the Benton visual retention test was negatively correlated with rCBF in the left superior frontal area and left basal ganglia, and the mean scan path was positively correlated with the left superior frontal area. Matsui et al. (1993) reported that the number of "eye transfers" on eye movement from one element area of the figure to another in the WAIS picture completion test was positively correlated with rCBF in the left anterior cingulate and left thalamus. Thus, the third aim of this study was to examine the relationship between the performance of eye movements during a saccadic tracking task and resting rCBF in schizophrenic patients.

Subjects and methods

Twenty-three schizophrenic patients recruited from the inpatient and outpatient clinics of Toyama Medical and Pharmaceutical University Hospital participated in this study. All patients fulfilled DSM-III-R criteria for schizophrenia (10 males and 13 females). Their mean age was 27.9 ± 8.6 (SD) years (range 15–43 years), and their mean duration of illness was 7.3 ± 5.3 years. The mean daily chlorpromazine-equivalent dosage was 821.5 ± 808.6 mg. Table 1 shows all medication. The control subjects consisted of 23 healthy volunteers (14 males and 9 females) and with a mean age of 25.4 ± 3.9 years (range 23–40 years). Neither age nor gender differed significantly between patients and controls. The purpose and procedures of the study were explained to the subjects, and their informed consent was obtained. Symptoms were assessed using the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen 1984a) and the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen 1984b).

Saccadic tracking procedure

The subject sat on a chair equipped with a Nac V-type eye-mark recorder, a device that detects corneal reflections of infrared light. The subject's head was held in place by a chin rest and lateral supports. Two saccadic tracking figures were projected individually onto a translucent screen located 1.2 m directly in front of the subject's eyes. Eight points of 1 angular degree in size were placed on the circumference of a circle having a diameter of 20 angular degrees (Fig. 1). One figure contained eight black points, whereas the other had eight points with arabic numbers (1–8) in randomized order. The subject was first instructed to look at the center (+) of each figure. Then he/she was asked to scan each of the eight points once in clockwise order by moving the eyes. The order of the two figures was counterbalanced across subjects. Each task was self-paced. Eye movements during two tracking tasks were recorded on video tape using the eye-mark recorder. The recording system was as described in the previous report by Matsui and Kurachi (1995). This technique enables us to see the eye-fixation points and eye movements on the figure simultaneously. Data for two figures recorded with the eye-mark recorder were analyzed by computer.

Measurement of eye movement

The analysis of eye-movement behaviour was based on the following measures, as previously described by Matsui and Kurachi (1995). We analyzed the data at two settings; firstly, when the fix-

Table 1 The medication of all patients

Patient no.	Butyrophenones	Phenothiazines	Benzamides	Others
1				
2	Pimozide 1 mg	Chlorpromazine 5 mg		
3	Haloperidol 2.25 mg			
4	Haloperidol 2.25 mg	Levomepromazine 40 mg		
5	Haloperidol 4.5 mg			
6	Haloperidol 3 mg	Chlorpromazine 12.5 mg	Sulpiride 150 mg	
7	Haloperidol 5.25 mg			
8		Levomepromazine 35 mg	Nemonapride 6 mg	
9			Nemonapride 9 mg	
10	Pimozido 2 mg	Fluphenazine 6 mg	Sulpride 75 mg	
11	Bromperidol 9 mg			
12	Pipamperone 300 mg		Nemonapride 9 mg	
13	Haloperidol 15 mg			
14	Haloperidol 12 mg	Fluphenazine 4 mg		
15	Bromperidol 18 mg			
16	Haloperidol 9 mg	Levomepromazine 175 mg		Zotepine 75 mg
17		Chlorpromazine 150 mg	Nemonapride 30 mg	
18	Timiperone 6 mg	Levomepromazine 10 mg		Clocapramine 75 mg
19		Levomepromazine 220 mg	Nemonapride 30 mg	
20				Clocapramine 150 mg
21		Levomepromazine 150 mg, chlorpromazine 35 mg	Nemonapride 30 mg	Mosapramine 150 mg
22	Haloperidol 15 mg	Levomepromazine 100 mg, chlorpromazine 37.5 mg	Sulpride 600 mg, sultopride 600 mg	Mosapramine 150 mg
23		Chlorpromazine 30 mg	Nemonapride 30 mg	Clocapramine 250 mg zotepine 75 mg

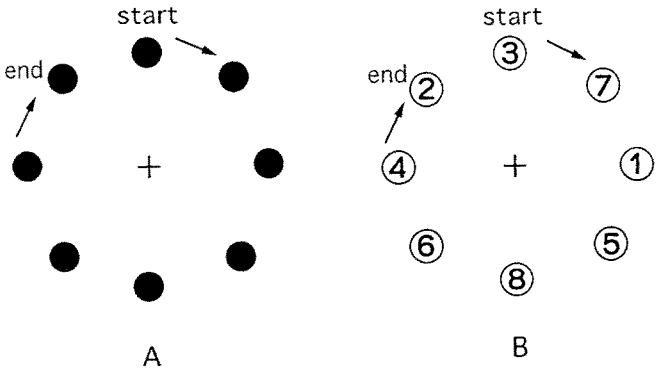


Fig. 1 A saccadic tracking task on **A** eight black-point and **B** randomized numbered-point targets. The subject was instructed to look at the center (+) of the figure first. He/she was then asked to scan the eight points clockwise, in order

ation point was defined as the point at which the gaze was held for at least 200 ms, and secondly when the gaze was held for at least 100 ms. Eye movements were assessed using the following parameters:

1. Correct score: composed of the number of target hits plus normal paths. The maximum possible score is 15 points. *Target hitting:* When a fixation hits a target, a one-point score is given. The maximum possible score is 8 points. *Normal path:* Normal saccade lines (straight lines from one point to the next point) are scored as one point each. The maximum possible score is 7 points.
2. Deviant score: composed of the number of superfluous fixations plus aberrant paths. *Superfluous fixation:* Some fixations occur elsewhere and do not hit a target. The total number of such events is the score. *Aberrant path:* A path deviating from the normal paths. The total number of such paths is the score.

Fig. 2 Location of regions of interest. Single photon emission computed tomography (SPECT) images from a representative patient. *1* Anterior cingulate; *2* superior frontal area; *3* middle frontal area; *4* inferior frontal area; *5* orbital area; *6* supplementary motor area; *7* basal ganglia; *8* thalamus; *9* limbic area; *10* superior temporal area; *11* middle and inferior temporal area; *12* posterior cingulate; *13* superior parietal lobule; *14* inferior parietal lobule

The cue effect was defined as attainment of a significantly higher correct score or lower deviant score under numbered-point conditions than black-point conditions.

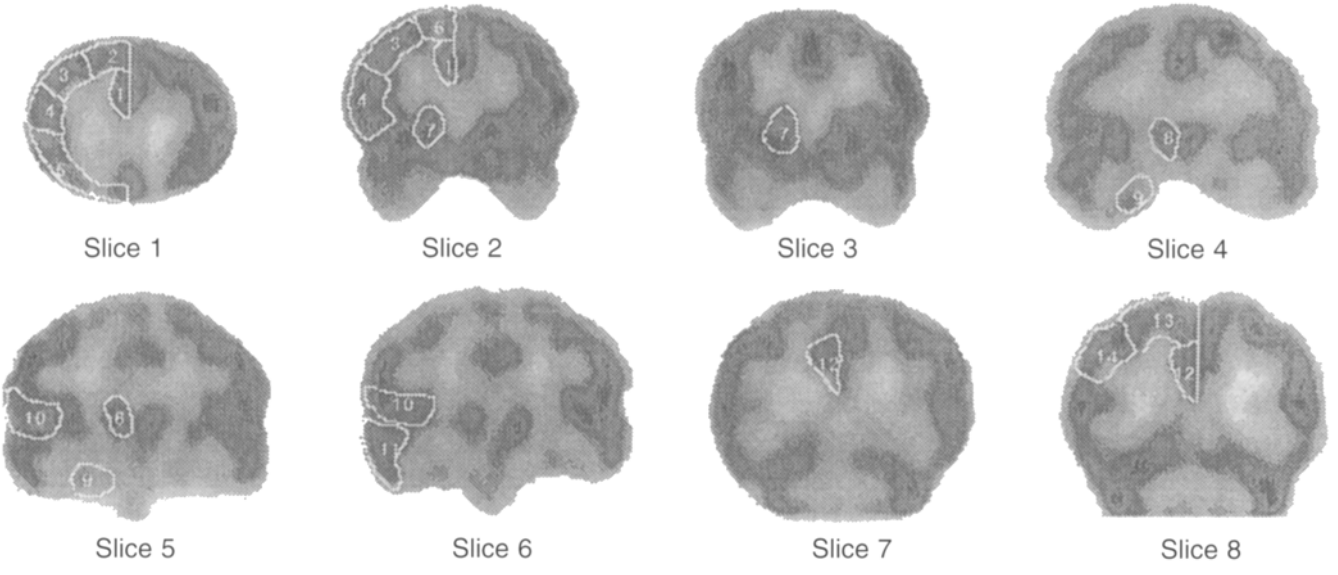
In addition, eye-movement errors were analyzed according to the following classification:

1. *Omitting.* Eye movements omitted a target.
2. *Hypermetria.* A fixation went at least 3 angular degrees beyond a target and then returned to the target.
3. *Centering.* Paths directed toward the center point.
4. *Return.* Paths returned to a point just anterior to the target.
5. *Slipping.* A fixation hit at least 3 angular degrees away from a target and thereafter went to the next target.
6. *Superfluity.* All superfluous fixations other than hypermetria, return, and centering.

Single photon emission computed tomography

Procedure

Measurements were taken in a dimly lit room with background noise from cooling fans. The subjects sat quietly with their eyes open for 10 min after intravenous injection of 555 MBq (15 mCi) ^{99m}Tc-hexamethyl propyleneamine oxime (HMPAO). Single photon emission computed tomography (SPECT) was performed with a three-head rotating gamma camera system (GCA9300A, Toshiba, Tokyo, Japan) by employing high-resolution fan beam collimators combined with a minicomputer (GMS550U; Toshiba, Tokyo, Japan). The resolution is 7 mm full width at half maximum in the center of the reconstructed slice when the rotating radius is 13.2 cm. The computer slice width is 6.8 mm. The SPECT data were obtained in a 128×128 format for 30 angles in a 120° arc for each camera at 60 s per angle. The total period of data acquisition was 30 min. The filtered-back projection method was used for SPECT image reconstruction after preprocessing projection data with a Buttherworth filter. A series of 5.1-mm thick coronal slices, approximately vertical to the orbitomeatal (OM) line was obtained with each scan. How to analyze rCBF was based on Matsui et al. (1993) and Yuasa et al. (1995). Fourteen regions of interest (ROIs) were drawn in each hemisphere on eight slices by referring to the individual magnetic resonance imaging scan with 5.1-mm slices. Counts/voxel of each ROI were determined, and, to reduce artifacts, the values of ROI from two contiguous slices were averaged. Then, a regional index, i.e., the percentile ratios between the value of the ROI and the mean value of all 14 regions, was calculated for each hemisphere. Thus, the regional indices of the 14 ROIs were obtained in each hemisphere: superior frontal area, middle frontal area, inferior frontal area, anterior cingulate area, supplementary



motor area, orbital area, posterior cingulate area, superior temporal area, middle and inferior temporal area, limbic area (amygdala plus hippocampus), basal ganglia, thalamus, superior parietal lobule, inferior parietal lobule (Fig. 2).

Clinical symptoms and eye movements in patients were assessed within 2 weeks of SPECT. Relationships between eye-movement parameters and rCBF were analyzed for 21 patients, because 2 patients could not undergo SPECT within the 2-week period.

Statistical analysis

Differences between eye-movement parameters in controls and patients were examined using the Mann-Whitney U-test. The Sign Test was performed to determine the effects of conditions or settings within the same group of subjects. Fisher's exact test was performed for differences in frequency between groups on the error score. The same descriptive statistics as Matsui and Kurachi (1995) were used to examine these main analyses for the first purpose. Differences in rCBF between the two groups of patients were examined using Student's *t*-test. Regarding the significance of these differences, correction for multiple comparisons was not performed following the recommendations of Rothman (1990), and Michels and Rosner (1996). Spearman's rank correlation test was used for correlations between eye-movement parameters and clinical symptoms or drug dosage. Bonferroni corrections were used to analyze these correlations.

Results

Analysis of eye movements

Table 2 shows the group means and standard deviations for eye-movement parameters under both conditions (black points/randomized numbered points) in the saccadic tracking task. At the 200-ms setting, the schizophrenic patients showed significantly fewer correct scores ($P < 0.01$) and more deviant scores ($P < 0.01$) than the normal controls under both conditions. There were significant differences in all other subparameters (target hitting, normal path, superfluous fixation, aberrant path) between controls and patients. Under the black-point condition at the 100-ms setting, there was no significant difference between patients and controls in target hitting. Patients, however, still showed fewer correct scores 19 < 0.01: both conditions) and more deviant scores than controls ($P < 0.01$ under the black-point condition; $P < 0.05$ under the numbered-point condition). Neither the schizophrenic patients nor the normal controls exhibited a significant cue effect, i.e., there was no significant difference in any of the parameters between numbered-point conditions and black-point conditions.

Comparison between eye movements at the 200-ms and 100-ms settings

Under the black-point condition, the patients had more correct scores ($P < 0.05$), more target hittings ($P < 0.01$), and more aberrant paths ($P < 0.01$) at the 100-ms setting than at the 200-ms setting. Both controls and patients also had more deviant scores ($P < 001$) and more superfluous fixations ($P < 0.01$) at the 100-ms setting.

Under the numbered-point condition, patients had more target hittings ($P < 0.05$) at the 100-ms setting than at the 200-ms setting. Both the normal controls and the patients had more deviant scores ($P < 0.01$ each), more

Table 2 Eye movements during a saccadic tracking task in controls and schizophrenic patients (mean ± SD)

Conditions	Eye-movement parameters					
	Correct score	Target hitting	Normal path	Deviant score	Superfluous fixation	Aberrant path
200-ms setting						
Black points						
Normal controls	14.8 ± 0.6	7.9 ± 0.3	6.9 ± 0.3	0.2 ± 0.5	0.2 ± 0.5	0
Schizophrenic patients	12.8 ± 2.3**[a]	7.1 ± 1.1**[a]	5.7 ± 1.3**[a]	3.3 ± 5.8**[a]	1.9 ± 3.0**[a]	1.5 ± 2.9**[a]
Randomized numbered points						
Normal controls	14.9 ± 0.5	8.0 ± 0.2	7.0 ± 0.3	0.3 ± 0.8	0.1 ± 0.5	0.1 ± 0.3
Schizophrenic patients	12.7 ± 2.5**[a]	7.0 ± 1.2**[a]	5.7 ± 1.3**[a]	2.6 ± 4.6**[a]	1.3 ± 2.7**[a]	1.3 ± 2.0*[a]
100-ms setting						
Black points						
Normal controls	14.8 ± 0.5	8.0 ± 0	6.8 ± 0.5	1.6 ± 2.8**[b]	1.0 ± 1.3**[b]	0.8 ± 2.1
Schizophrenic patients	14.0 ± 1.2**[a]; *[b]	7.9 ± 0.3**[b]	6.1 ± 1.0**[a]	6.8 ± 6.9**[a]; **[b]	3.9 ± 3.6**[a]; **[b]	2.9 ± 3.6**[a]; **[b]
Randomized numbered points						
Normal controls	14.8 ± 0.5	8.0 ± 0	6.8 ± 0.5	2.4 ± 2.2**[b]	1.2 ± 1.4**[b]	1.2 ± 1.0**[b]
Schizophrenic patients	13.5 ± 1.8**[a]	7.7 ± 0.5*[a]; *[b]	5.8 ± 1.4**[a]	7.0 ± 9.0*[a]; **[b]	3.6 ± 4.9**[b]	3.5 ± 3**[b]

A perfect correct score is 15 points (number of target hits plus normal paths)
The deviant score equals the number of abberant paths plus superfluous fixations

[a] Mann-Whitney U-test, controls vs patients
[b] Sign Test, 200-ms setting vs 100-ms setting in the same group
* $P < 0.05$
** $P < 0.01$

Table 3 Numbers of subjects who made each type of eye-movement error

Subject	Schizophrenic patients				Normal controls			
Condition	Black		Number		Black		Number	
Setting (ms)	200	100	200	100	200	100	200	100
Error type								
Omitting	10*	1	9**	3	2	1	1	0
Hypermetria	4	10*	2	8	0	2	0	7
Centering	1	1	2	2	0	0	0	0
Return	1	1	2	3	0	0	0	1
Slipping	4	1	2	2	0	0	0	1
Superfluity	13**	18	10	17	3	12	4	10

* $P < 0.05$
** $P < 0.01$ (Fisher's exact test was used to evaluate control and patient scores)

superfluous fixations ($P < 0.01$ each), and more aberrant paths ($P < 0.01$ each) at the 100-ms setting than at the 200-ms setting.

These results indicate that some patients viewed the targets correctly at more than 100 ms but less than 200ms, whereas almost all control subjects viewed the targets correctly at more than 200 ms.

Error analysis of eye movements

Table 3 shows the number of subjects who made each type of error in eye movements. Under the black-point condition at the 200-ms setting, 10 of the 23 patients presented the omitting-type error, whereas only 2 of the 23 normal controls manifested this error type ($P < 0.05$). Thirteen patients and only 3 controls presented the superfluity-type error ($P < 0.01$). Under the numbered-point condition, 9 patients, but only 1 control, presented the omitting-type error ($P < 0.01$).

Under the black-point condition at the 100-ms setting, hypermetria was evident in 10 patients, whereas only 2 controls showed hypermetria. None of the normal controls showed hypermetria at the 200-ms setting. Two patients, but none of the controls, showed centering.

Relationship of eye-movement parameters with regional cerebral blood flow

The difference in rCBF between the two groups of patients was examined: the ordinary group (group O) who obtained full-target-hitting scores at the 200-ms setting under the black-point condition and the fast group (group F) who obtained full-target-hitting scores at the 100-ms setting, but not at 200 ms, under this condition (Table 4). The group F patients showed significantly more deviant scores at the 100-ms setting as compared with the 200-ms setting. The group-F patients showed decreased rCBF in the left limbic and inferior parietal areas as compared with the group O patients ($P < 0.05$, each) (Fig. 3). There were no significant differences between the two groups in rCBF in other brain regions.

Relationship of eye-movement parameters with clinical syndromes and neuroleptic dosage

Hallucinations score ($r = -0.59$, $P = 0.0031$) and delusions score ($r = -0.68$, $P = 0.0004$) in SAPS correlated negatively with the correct score under the numbered-

Table 4 Eye movements in two groups of schizophenic patients under black-point conditions (mean ± SD)

	Eye-movement parameters					
	Correct score	Target hitting	Normal path	Deviant score	Superfluous fixation	Aberrant path
Group O ($n = 10$)						
200-ms setting	14.5 ± 0.7	8.0 ± 0	6.5 ± 0.7	5.0 ± 8.4	2.8 ± 4.3	2.2 ± 4.1
100-ms setting	14.5 ± 0.7	8.0 ± 0	6.5 ± 0.7	6.4 ± 9.7	3.7 ± 5.0	2.7 ± 4.8
Group F ($n = 9$)						
200-ms setting	11.7 ± 2.6**[a]	6.4 ± 1.3**[a]	5.2 ± 1.3**[a]	1.3 ± 1.6	0.8 ± 1.0	0.6 ± 1.1
100-ms setting	14.1 ± 0.9*[b]	8.0 ± 0**[b]	6.1 ± 0.9	5.6 ± 3.1*[b]	3.4 ± 2.0*[b]	2.1 ± 2.1*[b]

Group O: patients who obtained the full-target-hitting score at the 200-ms setting
Group F: patients who obtained the full-target-hitting score at the 100-ms setting, but not at the 200-ms setting
A perfect correct score is 15 points (number of target hits plus normal paths)
The deviant score equals the number of abberant paths plus superfluous fixations
[a] Mann-Whitney U-test. group O vs group F
[b] Sign Test, 200-ms setting vs 100-ms setting in the same group
* $P < 0.05$
** $P < 0.01$

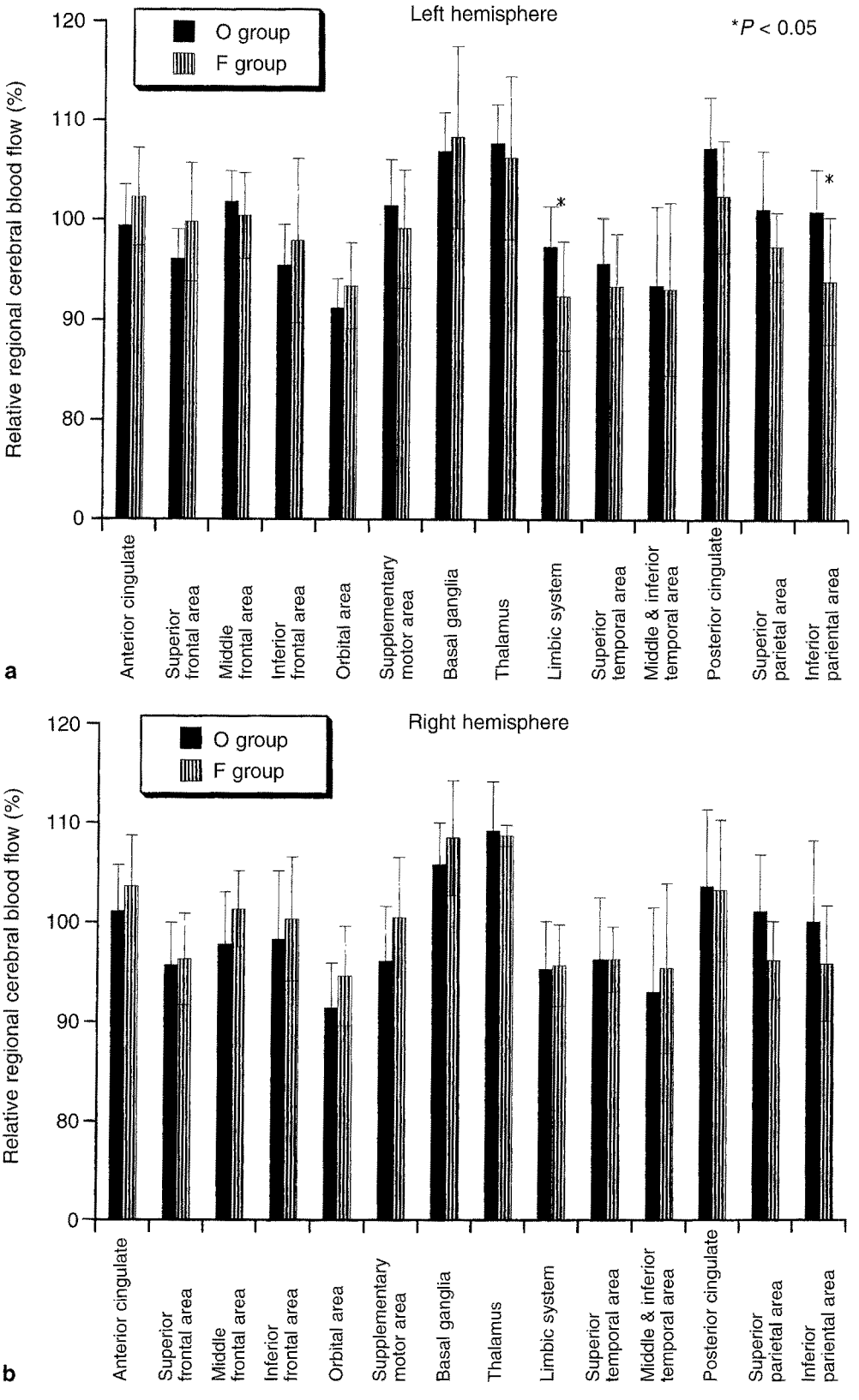


Fig. 3 Relationship of eye-movement parameters with regional cerebral blood flow. **a** Left hemisphere; **b** right hemisphere. *O* Patients who obtained the full-target-hitting score at the 200-ms setting ($n = 10$); *F* patients who obtained the full-target-hitting score at the 100-ms setting, but not at the 200-ms setting ($n = 9$). $P < 0.05$ (t-test; O vs F, in the same region of interest)

point condition at the 200-ms setting. There were no significant Bonferroni-corrected correlations between other symptom scores and the correct score or the deviant score.

Assessment of the effect of neuroleptics on eye-movement parameters showed no significant correlation between eye-movement parameters and total chlorpromazine-equivalent dosage, butyrophenones, phenothiazines, or benzaminedes dosage.

Group-F patients did not differ significantly from group O in the severity of any symptoms or in neuroleptic dosage.

Discussion

The results of this study confirm that schizophrenic patients show fewer correct scores and more deviant scores than normal controls in saccadic tracking of stationary targets, in agreement with the previous findings of Matsui and Kurachi (1995). Furthermore, Matsui and Kurachi (1995) showed that the deviant scores in patients improved significantly under numbered-point conditions in serial order. However, defective saccadic tracking in patients did not improve with the use of targets on which the numbers had been placed in randomized order. Shagass et al. (1976) reported that eye-tracking performance (smooth-pursuit eye movement) is markedly improved in both patients and normal subjects by replacing the fixation dot on the pendulum with pseudorandomly displayed numbers. The numbers on the pendulum presumably enhanced the attentiveness of the patients by adding a simple perceptual-cognitive act, the recognition of digits. In contrast, randomized numbers on the stationary targets may have been burdensome for patients. Optimal conditions for patients to enhance attentiveness in a saccadic tracking task may be arabic numbers placed in order from 1 to 8. Contrary to our prediction that the patients would view the target during the full time, in the situation in which the subjects were unable to anticipate the next number, patients showed significantly more target hitting at the 100-ms setting than at the 200-ms setting. This was true not only under the black-point condition, but also under the randomized numbered condition, suggesting that some patients still view the target too fast. Consistent with this, at the 200-ms setting, the number of patients who made omitting-type errors did not decrease under the randomized numbered condition as compared with the black-point condition.

Concerning the relationships between eye movements and rCBF, the group-F patients, i.e., the patients who viewed the target too fast, showed decreased rCBF in the left inferior parietal and limbic area as compared with the group-O patients who viewed the targets at a presumably normal duration (over 200 ms). The inferior parietal area in the present study overlaps the posterior parietal cortex. The posterior parietal cortex constitutes, along with the frontal eye field, the two main areas involved in triggering saccades, and there are direct connections between the two areas (Kennard et al. 1994). Mountcastle et al. (1975) found neurons in the simian posterior parietal cortex that discharge before and in association with saccades. The posterior parietal cortex has the role of visuospatial integration and saccadic initiation, whereas the prefrontal cortex inhibits unwanted saccades and selects significant saccadic eye movements (Pierrot-Deseilligny et al. 1991a, 1991b). Nakashima et al. (1994) showed that left dorsolateral prefrontal cortex activation and correlative left posterior parietal cortex activation were observed during volitional saccades in normal controls but not in schizophrenic patients. They suggested that the dorsolateral prefrontal cortex associates with the posterior parietal cortex during saccadic eye movements. In addition, the visual fixation neurons that accelerate discharge synchronously with fixation on a visual object have been recorded in the simian inferior parietal lobule (Lynch et al. 1977). Clinically, square-wave jerks, i.e., sporadic horizontal saccades followed after an interval by corrective saccades, during fixation have been reported to occur in subjects with presenile dementia (Feldon and Langston 1977) and in patients with parietal lesions (Sharpe et al. 1982).

The parietal cortex also has direct connections with the limbic (parahippocampal) cortex (Pandya and Kuypers 1969; Van Hoesen 1982). There is growing evidence that schizophrenic patients have abnormalities in the medial temporal lobe (Roberts 1991). Decreased volumes of medial temporal lobe structures (amygdala, hippocampus, and parahippocampal gyrus) in schizophrenic patients have been reported by both postmortem histopathological evaluation and antemortem magnetic resonance imaging (MRI, Bogerts et al. 1985; Suddath et al. 1989). Patients with schizophrenia showed a significantly lower regional cerebral glucose metabolic rate in the hippocampus and the anterior cingulate cortex than did normal controls (Tamminga et al. 1992). Frith et al. (1992) reported that the rCBF in the left hippocampus and parahippocampal gyrus increased during the internal monitoring of eye movements in normal subjects. Thus, it seems possible that the overly fast fixation in the saccadic task in some schizophrenic patients is related, at least in part, to dysfunction in the inferior parietal and limbic areas. In 1 of the 2 patients who showed centering, atrophy of the right parietal lobe was observed on MRI. She also had several deviant scores and belonged to group O. The possibility that impaired saccades may be related to morphological brain change should be studied in the future. The limitation of the present study is that rCBF was measured in the resting state rather than the activation state. However, as performance on the Wisconsin card-sorting test in schizophrenic patients has been reported to correlate with prefrontal rCBF in the resting state (Sagawa et al. 1990) as well as the activated state (Weinberger et al. 1986), studies on resting rCBF provide clues to the selection of adequate tasks for an activation study. Further research is needed to elucidate the differences in rCBF among normal controls, group O, and group F.

The error analysis of eye movements revealed that some patients displayed hypermetria. Several other studies (Schmid-Burgk 1982, 1983; Mather and Puchat 1983) have also reported hypermetria in schizophrenic patients. As to the neural mechanisms underlying the eye movements observed, it has been suggested that the cerebellum contributes to saccadic eye movements (Kase et al. 1980; Bruce and Goldberg 1985; Mano et al. 1991). Cerebellar atrophy in schizophrenic patients has been documented by computed tomography (CT), MRI (Weinberger et al. 1982; DeLisi et al. 1986; Rossi et al. 1993) and postmortem studies (Weinberger et al. 1980). Based on these findings, the hypermetria displayed in schizophrenic patients may be related to impairment of the neural network which involves the cerebellar hemisphere.

Schlenker and Cohen (1995) showed that smooth-pursuit eye-tracking impairment was associated with performance in psychomotor soft signs. This may show that impaired smooth pursuit in schizophrenic patients is a general deficiency in motor control. The present saccadic tracking also should clarify the relation with general motor ability in future.

With regard to the relationship between clinical syndromes and eye movements, significant negative correlations were found between hallucinations and delusions symptoms and correct scores. Impairment of saccadic eye movements in the present task may be attributable to failure to monitor the intended eye movements, and this failure may be related to passivity experiences (disturbance of the self) as proposed by Frith et al. (1992).

There was no correlation between drug dosage and eye-movement parameters. However, most patients in this study had already received neuroleptic drugs when eye-movement tests and SPECT were performed. Strictly, the influence of the treatment to the results of eye movements and rCBF remains to be elucidated. Further studies need to replicate the present findings in drug-naive patients.

In conclusion, the present findings suggest that some schizophrenic patients view stationary targets too fast and this may be related to dysfunction in the limbic-parietal association area in the left hemisphere.

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