DISTURBANCES IN THE CONTROL OF SACCADIC EYE MOVEMENT AND EYE–HEAD COORDINATION IN SCHIZOPHRENICS*  

Junko Fukushima,* Kikuro Fukushima,† Nobuyuki Morita,‡ and Itaru Yamashita‡  

College of Medical Technology, Departments of  †Physiology and  ‡Psychiatry,  
Hokkaido University Medical School, Sapporo 060, Japan  

Reprint address: Junko Fukushima, College of Medical Technology,  
Hokkaido University, West 5, North 12, Sapporo, 060 Japan  

Abstract — Some schizophrenic patients have been known to have frontal cortical dysfunction. In view of the evidence that voluntary purposive eye movements and rapid head movements involve areas of the frontal cortex, investigations of saccade performance have been carried out on schizophrenics in various laboratories. We have compared performance of schizophrenic patients in tasks involving inhibition of reflexive saccades (no-saccade) and initiation of saccades without target (memory-saccade) with performance in the antisaccade task. These measures were also compared with results of eye–head coordination tasks. Schizophrenics showed more errors and significantly longer latencies, with lower peak velocities at large amplitudes, in both the antisaccade task and the memory-saccade task. Performance with coordinated eye–head movement was basically similar, except for significantly longer latencies of head movement. These results suggest that schizophrenics may have a disturbance in initiating and executing purposive saccades without targets, and that dysfunction of the frontal cortex may contribute to this disturbance.

Keywords — saccade; antisaccade task; memory saccade task; schizophrenics: latency: error: peak velocity; eye–head coordination: CT scan; frontal cortical atrophy.

Introduction

Studies using regional cerebral blood flow and positron emission tomography have revealed that some schizophrenics have frontal cortical dysfunction (1–3). Electrophysiological studies (4–7) have shown that the frontal eye field and the dorsomedial frontal cortex control voluntary purposive saccadic eye movements.

Guitton et al (8), using an antisaccade task introduced by Hallett and Adams (9), which includes inhibition of reflexive saccades and initiation of purposive saccades, reported that patients with frontal lobe lesions showed abnormalities (more errors and longer latencies) in the antisaccade task but not in the simple saccade task. Recently it has been reported that many schizophrenic patients also revealed similar abnormalities in the antisaccade task, but not in the simple saccade task (10). Studies using CT (computed tomography) scans suggest that many schizophrenics with abnormalities in the antisaccade task showed frontal cortical atrophy, while none of the schizophrenics with normal antisaccades showed abnormalities (11).

In the present study, two more tasks (no-saccade and memory-saccade tasks) were assigned to schizophrenics in addition to the saccade and antisaccade tasks in order to study whether patients with abnormalities in the antisaccade task show disturbances in inhibition of reflexive saccades (in the no-saccade task) and initiation of saccades without target (in the memory-saccade task).

Large amplitude saccades usually accompany rapid head movements. Since it has also been suggested (12) that the frontal eye field...
and dorsomedial frontal cortex are involved in rapid head movements, eye-head coordinated saccade and antisaccade tasks on schizophrenics were also examined in order to compare the results in the saccade and antisaccade tasks in which head movement was not required with those in the eye-head coordinated tasks.

Subjects

Subjects consisted of 32 schizophrenics and 36 normal controls. Twenty-six male and 6 female subjects fulfilled DSM-III criteria for schizophrenia (18 to 41 years old; mean ± SD = 27 ± 7 years of age). The control group consisted of 36 age-matched healthy subjects (26 male and 10 female subjects; 18 to 42 years old; 25 ± 6 SD years of age) who had had no history of psychiatric disorders. No patient showed diagnosable neurological signs or alcohol or substance abuse. All the schizophrenics showed negative symptoms. Mild delusion and hallucination were present in 13 of the 29 schizophrenics. All the patients except one were receiving medication at the time of study, and they were in a state of relative stability. No side effects due to the medication (drowsiness, Parkinsonism, tardive dyskinesia) were present. Informed consent was obtained from all the subjects including patients.

Methods

Subjects were seated on a chair in the dark, facing a tangent screen placed 100 cm away from the subject’s eyes. In the initial series of the present study, visual targets consisted of 3 red light-emitting diodes (LEDs). One of them was used as a central fixation point. The other two were positioned 12° to the right and left of the central LED, and were used as target LEDs. When the LEDs were not turned on, their position could not be seen by the subjects. The methods of target presentation are summarized in Figure 1a. Subjects were asked to fixate on the central fixation light while it was turned on for 4 to 6 s randomly. Then either the right or left LED was presented randomly for 500 ms. Task 1: In the saccade task, subjects were told to look at the LED as quickly as possible. Task 2: In the antisaccade task, subjects were told not to look at the LED but to look immediately in the opposite direction at approximately equal distance from the fixation point. Task 3: In the no-saccade task, subjects were instructed not to look at the LED but to continue fixating on the point where the central LED had been. Task 4: In the memory-saccade task, subjects were instructed to look at the position where the target LED had been during fixation, immediately after the central LED was extinguished. A few practice presentations were given to subjects at the beginning of each task to be sure that the subjects understood the task correctly.

To examine peak velocities of saccades, LEDs were positioned at the following angles (4°, 8°, 12°, 17°, 26°, 29°) from the central fixation point, and tasks 1, 2, and 4 were assigned to the subjects.

Eye-head coordinated saccade and antisaccade tasks were examined in 5 schizophrenics and 5 controls; only the LEDs positioned at 29° were used as targets. Subjects wore a motorcycle helmet over the head tightly so that any head movement could be detected as movement of the helmet, which was attached to a pivot fixed to the chair. The pivot allowed only horizontal head turns. Head position was monitored by a potentiometer. Subjects were asked to perform each task with coordinated head movement. For comparison, subjects were also asked to perform each task without moving the head (eye only task, Figure 4b). Head movement was not otherwise blocked.

Eye movements were recorded electrooculographically (EOG). EOG and head movements were measured with DC with a high cut filter of 100 Hz. Electromyographic (EMG) activity of neck muscles was recorded from sternocleidomastoid and splenius muscles using surface electrodes. We judged it as an error when subjects made saccade to the target in the no-saccade and antisaccade tasks as shown in Figure 4c (indicated by arrows).
Figure 1. a. Schematic illustration of 4 tasks (1-4). R and L indicate right and left. b. Histograms of saccade amplitudes in the saccade, antisaccade, and memory-saccade tasks for 10 normal controls (upper graphs) and 13 schizophrenics (lower graphs).
Subjects were tested with 20 runs for each task. Eye velocities were derived by electronic differentiation of eye position records and were displayed on the screen of a computer (sampling clock 10 ms); latencies and peak velocities of saccades were measured in the saccade, antisaccade, and memory-saccade tasks when subjects performed tasks correctly. Mean and standard deviation (SD) of latencies and peak velocities of saccades when they performed correctly were calculated for each task.

CT scans were obtained from 28 schizophrenics using Somatom 2 scanners in the Department of Radiology, Hokkaido University Hospital. Evaluation of the CT scans on all the patients examined was done by two skilled neuroradiologists masked to this study.

Results

Latencies and Errors

Figure 1b summarizes amplitudes, latencies, and errors in the saccade, antisaccade, and memory-saccade tasks in which the target LEDs were positioned at 12° from the central fixation point. All the subjects, including schizophrenics, understood the tasks correctly and performed well, although saccade amplitudes in the saccade task of schizophrenics were smaller than those of controls.

Latencies of saccades in these 3 tasks and errors in the antisaccade task are summarized in Figure 2. No significant difference was observed between normal controls and schizophrenics in latencies of saccades in the saccade task (Figure 2a). As to errors of the antisaccade task (Figure 2b), only 11 of the 36 normal controls showed an error rate of 5% to 10%, and the remaining 25 showed no errors (mean error rate for the 36 was 2.1% ± 3.5% SD). The mean error rate for schizophrenics was 29.4% ± 21.7% SD (range 5% to 80% for individual patients), which was significantly higher than that of normal controls (P < 0.001). Latencies of antisaccades were also significantly longer for many patients than for controls (Figures 2c and 3b, mean 324.1 ms ± 73.4 ms SD compared with 255.3 ms ± 20.5 ms SD, P < 0.001). In the memory-saccade task, latencies of saccades in many schizophrenics were also significantly longer than in controls (Figure 2d, mean 400.7 ms ± 96.1 ms SD compared with 275.2 ms ± 42.9 ms SD). In the no-saccade task, none of control subjects showed errors, while 3 schizophrenics revealed error rates of 10%, 10%, and 25%.

Peak Velocities of Saccades

Mean amplitudes of saccades in the saccade task were plotted against mean ± SD values of peak saccade velocities in Figure 3a for normal controls and schizophrenics. There was no significant difference between the two in any saccades of different amplitude. However, as shown in Figure 3c and d, similar plots for saccades in the antisaccade and memory-saccade tasks reveal that peak velocities of saccades for schizophrenics are significantly lower than those of normal controls at saccade amplitudes larger than 17° despite the fact that the amplitudes of saccades were similar. An example is presented in Figure 3b for an antisaccade; the patient showed significantly slower saccade compared to the control.

Eye-head coordinated saccade and antisaccade tasks

Figure 4a summarizes mean latencies of onset of eye and head movement in schizophrenics and in normal controls in eye-head coordinated saccade and antisaccade tasks. Latencies of eye movement of schizophrenics were significantly longer in the antisaccade task (P < 0.01), but not in the saccade task, which is similar to the results obtained in the saccade task in which head movement was not required. However, schizophrenics showed longer latencies for head movement in both saccade and antisaccade tasks (Figure 4a). Activity of neck EMG recorded in 2 patients also showed longer latencies compared to normal controls in the saccade task.

Figure 4b summarizes error rates in eye-head coordinated antisaccades. Error rates
Figure 2. a, c, and d are mean latency histograms of saccades for individual controls (n = 36) and schizophrenics (n = 32) in the saccade, antisaccade, and memory-saccade tasks, respectively. b. Histograms of mean error rates in the antisaccade task for individual controls and schizophrenics. Ordinates indicate number of subjects. Overall mean ± SD values are indicated for each histogram. Dotted lines are overall mean values. Significance level for the values between normal controls and schizophrenics was tested with a t test for each task and is indicated. NS indicates no significant difference.
Figure 3. a, c, and d are mean amplitudes of saccades plotted against mean ± SD values of peak saccade velocities in the saccade, antisaccade, and memory-saccade tasks, respectively, for 10 controls and 13 schizophrenics. b shows examples of antisaccades in normal control and schizophrenic. Upward deflection for eye movement is toward left. CL and LL indicate center light and left light.
Figure 4. a. Latency histograms of onset of saccades and head movements in eye–head coordinated saccade and antisaccade tasks for 5 controls and 5 schizophrenics. Significance level for the values between control and schizophrenics was tested with a t test: * = P < 0.01; *** = P < 0.0001. b. Error rates in the eye–head coordinated antisaccade task and in the antisaccade task in which head movement was not allowed (eye only task) for individual schizophrenic patients and controls. c. Example of errors in the eye–head coordinated antisaccade task in control (1) and schizophrenic (2). Upward deflection for eye movement is toward right. Neck EMG was recorded from sternocleidomastoid muscle. CL and LL indicate center light and left light.
were significantly higher in schizophrenics than in controls, with values similar for individual patients irrespective of whether or not coordinated head movement was required (see Methods). Figure 4c presents examples of errors of a control subject and a schizophrenic patient. Although patients occasionally showed saccade errors with no detectable head movement, neck EMG showed activity coinciding with errors of eye movement (c(2) in Figure 4), suggesting that the error signal reached neck muscles also.

There was a significant correlation between the results of antisaccades and CT scans in schizophrenic patients. Of the schizophrenics with more errors and longer latencies in the antisaccade task, 73% revealed frontal cortical atrophy including dilatation of the interhemispheric fissure (an example is shown in Figure 5a). However, none of the schizophrenics with normal results in the antisaccade task showed abnormalities in CT scans (Figure 5b).

**Discussion**

Many schizophrenics showed not only more errors and longer latencies in the antisaccade task despite their normal performances in the antisaccade task, but they also showed longer latencies in the memory-saccade task. Peak saccade velocities in the antisaccade and memory-saccade tasks were significantly slower than those of the controls in large amplitude saccades. Since at least in smaller saccades the amplitudes and peak velocities of saccades in all three tasks (Figures 1b, 3a, 3c, and 3d) were comparable to those of normal controls,
it is unlikely that the abnormalities seen in schizophrenics were due to fatigue or drowsiness (13) or to a poor understanding of the task. Rather, the normal results in the simple saccade task on one hand (with a target) and the abnormal results in the antisaccade and memory-saccade tasks on the other (without a target for saccades) suggest that the abnormalities may be related to an impairment of initiating and executing purposive saccades without a target. The results in the no-saccade task may suggest that some schizophrenics could not keep purposive fixation without a target, allowing reflexive saccades to external stimuli.

Guitton et al (8) reported that patients with frontal lobe lesions showed errors and longer latencies in the antisaccade task despite the normal performances in the simple saccade task. Deng et al (14) found that peak velocities of memory-guided (but not visually elicited) saccades were decreased in alert monkeys after lesions of the frontal eye fields. Both results suggest an involvement of frontal cortex in initiating and executing purposive saccades without targets. Since there was a significant correlation between the results of antisaccades and the frontal cortical atrophy on CT scans in schizophrenics in the present study (compare reference 15), it is likely that the abnormalities in errors, latencies, and peak velocities in the antisaccade and memory-saccade tasks in the patients may be related to dysfunction of the frontal cortex.

It is unknown why the patients showed lower peak velocities only during saccades with amplitudes larger than $17^\circ$ in the antisaccade and memory-saccade tasks. Since amplitudes of spontaneous saccades in normal humans are reported to be mostly less than $15^\circ$ (16), it is possible that saccades with larger amplitudes ($>15^\circ$) are differently controlled by the brain. Deng et al (14) reported that lesions in the frontal eye field in alert monkeys caused lower peak velocities in memory-guided saccades over a wide range of saccade amplitudes, and suggested that the frontal eye field is involved not only in initiating purposive saccades but in the control of motor parameters in such saccades. It is possible that since smaller amplitude saccades are required in everyday life (for example, see reference 16), they had been compensated for in our patients and only uncompensated larger amplitude saccades were detected at the time of study. Since larger amplitude saccades were usually performed by eye–head coordination (17), we examined eye–head coordinated saccade and antisaccade tasks on schizophrenics. Our limited observations indicate that the performance of schizophrenics was basically similar with or without coordinated head movement, except for significantly slower latencies of head movement compared to the controls. Moreover, errors appeared not only in eyes but in neck EMG activities, suggesting that the error signal was sent to eyes and head simultaneously (18).

To summarize, the present results suggest that the abnormal performances of many schizophrenics in the antisaccade and memory-saccade tasks are related to disturbance in initiating and executing purposive saccades without targets, and that dysfunction of the frontal cortex may contribute to the abnormalities.

REFERENCES