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Disturbed Smooth Pursuit and Saccadic Eye Movements in Schizophrenia

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Summary. Smooth pursuit and saccadic eye movements of schizophrenic patients were examined. In a pendulum (0.5 Hz) tracking task schizophrenic inpatients had a slightly lower smooth pursuit gain than outpatients and controls, who showed no significant differences. The number of saccades, counter-saccades and velocity arrests occuring in a 20 s tracking epoque was the same in patients and controls, but patients made larger saccades. When tracking a stepping target by saccadic eye movements, schizophrenic inpatients, and to a lesser extent outpatients, exhibited longer reaction times than controls and had a higher incidence of "non-fixation" (saccades away from the target while the target is stationary). Schizophrenic patients also showed a significantly larger proportion of dysmetric saccades (undershooting the target). While similar changes of reaction time and non-fixation score were observed in manic-depressives and alcoholics, dysmetria was more often found in schizophrenics and possibly constitutes the expression of a specific impairment of attention.

Key words: Eye movements – Schizophrenia

Introduction

In 1908 Diefendorf and Dodge reported abnormal smooth pursuit eye movements in schizophrenic subjects which was rediscovered by Holzman et al. in 1973. Since then several groups have confirmed the occurrence of disturbed smooth pursuit eye movements (SPEM) in schizophrenic inpatients using both EOG and infrared recording techniques (Cegalis and Sweeney 1979; Mialet and Pichot 1981; Pivik 1979; Salzman et al. 1978; Shagass et al. 1974). How far the disturbances of SPEM in schizophrenic patients represent a trait characteristic

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for this disease is, as yet, an unresolved problem. A disturbance of SPEM resembling the one in schizophrenics can be induced in healthy subjects submitted to stress (Brezinova and Kendell 1977). In manic-depressive patients similar deficits of pursuit as in schizophrenic patients were reported by several authors (Levin et al. 1981; Shagass et al. 1974). Furthermore, SPEM seem to deteriorate with increasing age (Kuechenmeister et al. 1977). The majority of schizophrenic patients investigated so far received chronic treatment with neuroleptics. Though it has been shown that there are probably no short term effects (Holzman et al. 1975), it is still unclear, whether these drugs have long-term effects upon the oculomotor system that might account for the reported SPEM abnormalities.

The authors quoted above considered mainly smooth pursuit eye movements. Only Diefendorf and Dodge (1908) also mentioned changes in saccadic eye movements of schizophrenic patients. The present paper focuses on saccadic eye movements and demonstrates that saccades are also disturbed in these patients. A preliminary communication has been published elsewhere (Becker et al. 1982).

Patients and Methods

Stimuli

Two experimental tasks were given to the subjects (Ss):

(I) Pendulum Tracking Task. SPEM were induced by having the Ss track a luminous pendulum (gas-diode with a diameter of 3 mm) swinging at a frequency of 0.5 Hz with an amplitude of 15° and a maximal velocity of 47.1°/s. Ss viewed the pendulum against three different backgrounds: (1) a black board, (2) an emotionally exciting poster and (3) a luminous point jumping randomly among different positions on the black board. With each background the pendulum was presented for approximately 40 s.

(II) Step Tracking Task. Saccadic eye movements were elicited by a luminous target stepping randomly within a horizontal array of 13 lamps spaced 5° and extending from 30° right to 30° left. The frequency of occurrence decreased linearly from large to small steps, imitating the natural frequency distribution of saccadic amplitudes. The Ss had to track a total of 107 steps in a time period of 10 min. In between steps they were to accurately fixate the target, the mean duration periods lasting 6 s.

Recording Procedures

Recordings were made either with Ag-AgCl-skin electrodes mounted horizontally and vertically, or with infrared detectors, or with both methods simultaneously. Ss sat approximately 2 m in front of the target in a darkened room with the head resting on a chin support and immobilized by a forehead holder. Before each task they were instructed to accurately follow the movements of the target. The whole experiment lasted approximately 30 min. The eye position and the target position signals were recorded on paper and on magnetic tape for further processing.

Data Processing

The eye position signal was electronically differentiated to yield eye velocity. Starting with the third segment of pendulum oscillation a 20 s segment of the eye position and the eye velocity and target position signals were digitized and filtered by computer software (upper cut-off

frequency 20 Hz) on a PDP-11 computer. A sine wave having the frequency of the pendulum was adapted to the velocity trace such as to fit the smooth pursuit epoques of the trace. Deviations of the eye velocity signal from the fitted sine wave exceeding a level of twice the noise level were considered to be either saccades, counter-saccades, velocity arrests or blink artefacts. The deviations were classified as saccades, if the instantaneous velocity v exceeded 2 v_s, v_s being the momentary smooth velocity indicated by the sinusoidal fit. Deviations with $v < -v_s$ for positive v_s, and $v > |v_s|$ for negative v_s were considered to be counter-saccades, and $|v| < 1/2 |v_s|$ was the criterion for velocity arrests. Blinks were obvious from the vertical eye movement trace. Saccades, counter-saccades, velocity arrests and blink aretefacts detected by these criteria were removed from the position signal and replaced by the corresponding segments of the integrated sinusoidal fit. The resulting smooth position signal was compared to the original signal. The ratio of pure pursuit smooth movement to total tracking movement was taken as the gain of the pursuit system, assuming that the total angle of the tracking movement corresponded to the maximum pendulum excursions.

The saccadic eye movements were written out on a strip-chart recorder. They were analyzed manually as to their reaction time and to the occurrence of "dysmetria" and "non-fixation". The reaction time was countered from the target step to the beginning of the next saccade directed toward the new target position. Dysmetria was assumed if the first saccadic reaction had less than 75% of the required total amplitude; non-fixation was defined as the occurrence of saccades leading the gaze by more than 3° away from the target during the fixation period in between target steps (Fig. 2).

Subjects

Fifty-eight psychiatric patients and 20 controls served as subjects. The psychiatric patients consisted of four groups: schizophrenic outpatients ($n=15$), schizophrenic inpatients ($n=19$), manic-depressive inpatients ($n=10$), and alcoholic inpatients ($n=14$). The criteria for the diagnosis followed the guidelines of the ICD 9th revision and diagnosis was based upon consensus of at least two psychiatrists. Of the 19 schizophrenic inpatients 14 were diagnosed as the paranoid type (ICD-295.3), 3 as residual states (ICD-295.6) and 2 as hebephrenic schizophrenia (ICD-295.1). The schizophrenic outpatients all belonged to the paranoid type. The group of manic-depressive patients included only patients with a history of bipolar affective disorder. Depending upon the actual phase, they were either classified as manic (ICD-296.2, 3 patients) or depressive (ICD-296.3, 7 patients). Patients with alcoholism (ICD-303) suffered from chronic alcohol dependence for at least 6 months. Patients who had had a delirium tremens in the past or showed clinical signs of neurological complications at the time of recording were excluded.

The mean age within the groups was 32.6 years with a range of 18 to 48 for schizophrenic outpatients, 46.7 years (21 to 60) for schizophrenic inpatients, 48.5 years (20 to 75) for manic-depressives, 37.4 years (25 to 50) for alcoholics and 31.3 years (19 to 60) for controls. All groups were matched for sex, except the manic-depressives, where women predominated. All schizophrenics, except 4, received neuroleptics. The manic patients were also treated with neuroleptics at a comparable dosage. All depressive patients received thymoleptic treatment. The control subjects were 20 healthy volunteers without any history of psychiatric illness.

All Ss participated in the step tracking task; the pendulum tracking task was performed by 9 schizophrenic inpatients, 14 schizophrenic outpatients and 12 controls.

Effect of Neuroleptics on Saccadic Eye Movements

In order to determine the effect of neuroleptics on saccadic eye movements, 3 healthy paid volunteers received Haloperidol at a dose of 6 mg/day orally for a period of 5 days. The volunteers were fully informed and under daily medical control. Because of marked extrapyramidal side effects, one volunteer received in addition Biperiden at a dose of 8 mg/day after the third day. Before, during and 14 days after drug intake these Ss performed the step tracking task; during the period of drug intake recordings were made on the first, fourth and fifth day of treatment. The saccades of these Ss were stored on computer tape and analyzed by means of a semi-automatic program (Jürgens and Becker 1978) that computed the regression of saccade

amplitude on saccade duration. The slope of this regression has the dimension °/s and is a measure for the average saccadic velocity of the Ss which is independent of the actual size of the individual saccades.

Results

Smooth Pursuit Eye Movements

The different backgrounds against which the Ss viewed the pendulum had no obvious effect on the parameters of the SPEM neither in patients nor in controls. The data presented below are based on tracking against a dark background. The gain (ratio of smooth pursuit amplitude to total tracking amplitude) was lower in schizophrenic patients than in controls (Table 1). However, there is a large overlap between the three populations formed by controls, schizophrenic inpatients and outpatients. As exemplified in Fig. 1, both the individual control and the individual schizophrenic patient may have either "good" SPEM (control 2, patient 2) or distorted and saccadized movements (control 1, patient 1). Correspondingly a comparison of the three populations (by means of the Kruskal-Wallis one way analysis of variance) does not indicate significant differences. Only a bilateral comparison between schizophrenic inpatients and controls would suggest a difference at the 0.05 level (Mann-Whitney *U*-test). In schizophrenic outpatients there was only an insignificant reduction of the gain.

The frequencies of saccades, counter-saccades and velocity arrests interspersed in the SPEM were not significantly different between the three groups.

	Schizophrenic inpatients	Schizophrenic outpatients	Controls
G			
$\bar{x}$	0.84	0.88	0.92
SD	0.10	0.08	0.05
n	9	14	12
S			
$\bar{x}$	30	32	29.5
SD	12.7	17.3	8.3
CS			
$\bar{x}$	3.6	3.1	1.9
SD	5.9	3.5	1.5
VA			
$\bar{x}$	8.2	12.0	9.9
SD	5.8	8.3	5.7
n	9	14	10

Table 1. Pendulum tracking in schizophrenic patients and controls. G = gain (ratio of smooth pursuit amplitude to total tracking amplitude). S, CS, VA number of saccades, counter-saccades and velocity arrests respectively. $\bar{x}$ = mean, SD = standard deviation, *n* = sample size

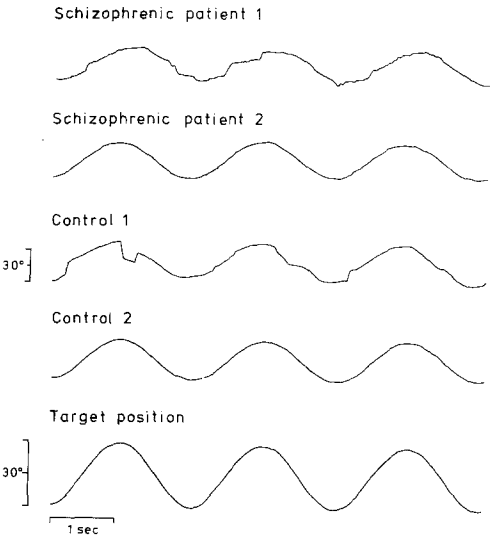


Fig. 1. Examples of pendulum tracking in 4 subjects (2 schizophrenic patients, 2 controls). In the individual patient like in the individual control smooth pursuit tracking may be "good" (high gain, small saccades; patient 2 and control 2) or "bad" (low gain, large saccades; patient 1 and control 1)

Thus the reduced smooth pursuit gain is compensated by larger rather than by more frequent saccades.

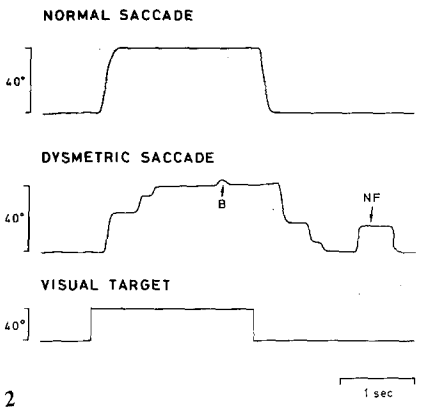
By combining the frequency of saccades and of velocity arrests with the gain no better differentiation between patients and controls could be achieved than by considering only the gain. The reduced gain of the schizophrenic inpatients appears not to be caused by their mean age being higher than that of the controls (46.7 years vs. 31.3 years) since age and gain correlated neither in controls (r= 0.17) nor in patients (r=–0.17).

Saccadic Eye Movements

The results of the step tracking task are summarized in Table 2 and Fig. 3. The most conspicuous result concerns the accuracy of saccadic eye movements. On

Table 2. Step tracking task. Frequency of non-fixation (NF) in between steps and saccadic reaction time (RT, in ms). $\bar{x}$ = mean, SD = standard deviation, n = sample size

	Schizophrenic inpatients	Schizophrenic outpatients	Controls	Alcoholics	Manic-depressives
n	19	15	20	14	10
NF					
$\bar{x}$	21.3	17.3	9.2	8.7	26.1
SD	15.4	19.6	13.3	8.5	20.1
RT					
$\bar{x}$	343	323	278	301	342
SD	60	107	69	32	62



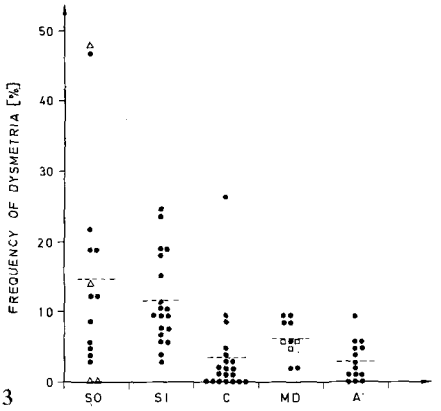


Fig. 2. Examples of normal and of dysmetric tracking saccades. Arrow at B shows eye blink artefact, arrow at NF shows a case of non-fixation

Fig. 3. Frequency of occurrence of dysmetric saccades. *SO* = schizophrenic outpatients, *SI* = schizophrenic inpatients, *C* = controls, *MD* = manic-depressives, *A* = alcoholics. Each symbol represents 1 subject. *Open triangles* in the group SO show patients who were not treated with neuroleptics; *open squares* in group MD show patients who were under treatment with neuroleptics. *Dashed lines* give average frequencies within groups.

average, dysmetria was more frequent in schizophrenic inpatients and outpatients than in controls. However, several schizophrenic patients were within the range of normals; and one normal control was among the three subjects who most often made dysmetric saccades.

Examples of dysmetric saccades and of saccades with normal accuracy are shown in Fig. 2. Between inpatients and outpatients there was no significant difference in the frequency of dysmetria. The manic-depressives investigated made dysmetric saccades more often than controls but not to the extent of the schizophrenics. With the exception of one of the controls neither the controls nor the manic-depressives nor the alcoholics had more than ten dysmetric saccades, while half of the schizophrenics, whether hospitalized or not, were above this score. The higher incidence of dysmetric saccades in the latter patients appears not to be caused by their being older, since no significant correlation between dysmetria and age could be detected within subject groups. Non-fixation of the visual target also occurred more frequently in schizophrenic patients. However, in manic-depressive patients the non-fixation score was even higher than in hospitalized schizophrenic patients. Similarly the saccadic reaction time of schizophrenic and manic-depressive patients was longer than that of controls and alcoholics. Both parameters non-fixation and saccadic reaction time exhibited significant differences only between schizophrenic inpatients and manic-depressives on one side and controls on the other side ($P < 0.05$, multiple comparison of Scheffé after square root transformation of the non-fixation score and logarithmic transformation of the reaction times). No correlation could be found between reaction time and age.

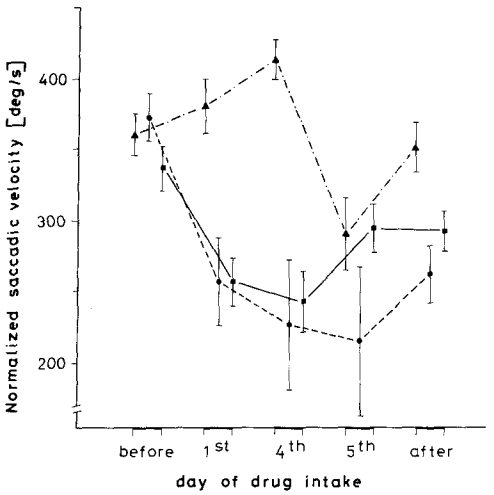


Fig. 4. Effect of neuroleptics upon saccadic velocity in 3 normal subjects. The normalized saccadic velocity shown on the ordinate corresponds to the slope of the regression of amplitude on duration of all saccadic reactions of a subject. Vertical bars give 95% confidence intervals

The frequencies of occurrence of dysmetria and of non-fixation as well as the saccadic reaction time appear to be independent of each other. No significant correlation could be detected between these parameters. There was also no correlation between the pursuit gain and the saccade parameters.

Effect of Neuroleptic Drugs on Saccadic Eye Movements

Our data suggest that the treatment of schizophrenic patients with neuroleptics is not responsible for their increased dysmetria. There were four untreated outpatients. The distribution of the dysmetria score was very similar in these untreated patients as compared to the treated patients (Fig. 3). Furthermore, there were three manic-depressive patients who were treated with neuroleptics; none of them had a pathological score of dysmetria.

In order to investigate more precisely the effect of neuroleptics on saccadic eye movements, 3 healthy volunteers were given Haloperidol for 5 days. There was a slight tendency towards an increase of dysmetria, non-fixation and reaction time during these 5 days, but these changes were not consistent. However, the saccadic velocity of all 3 Ss reached a minimum in the course of the test period (Fig. 4); the day on which this minimum occurred differed between Ss.

In order to test whether, in schizophrenic patients, the increased occurrence of dysmetria was also concomitant to a reduction of saccadic velocity—and therefore possibly of vigilance—the average saccadic velocity of the patients' 40° saccades was estimated by measuring the duration of these saccades from the paper-recordings. The average saccadic velocity was found to be in the normal range (300°/s to 380°/s).

Discussion

Our results confirm the tendency of schizophrenic inpatients to have a disturbed smooth pursuit response in a pendulum tracking task. On average the gain of their SPEM is slightly lower than the gain of controls and consequently the

relative contribution of saccades to the total tracking amplitude is larger in schizophrenics. The increase of the saccadic contribution is achieved by making larger "catch-up"-saccades while the frequency of such saccades is not significantly different from that in controls. This observation seemingly is at variance with the report of Mialet and Pichot (1981) who found an increased frequency of saccades in schizophrenic patients during sinusoidal tracking. However, since these authors used a relatively high threshold for saccade detection (100°/s), their figures may simply reflect the fact that schizophrenic patients need larger catch-up-saccades, which are more likely to exceed a given threshold. The frequency of "velocity arrests" (defined as a sudden drop of the instantaneous eye velocity below 50% of the pursuit velocity) or of the counter-saccades was approximately the same as in controls. In agreement with prior reports (Pivik 1979; Salzman et al. 1978), we found no significant disturbance of SPEM in schizophrenic outpatients. Taken together, our results on SPEM in schizophrenic patients are in keeping with other investigations (Levin et al. 1981; Shagass et al. 1974), which found roughly the same disorders of SPEM in both schizophrenia patients and other psychiatric patients. We do not consider the slight impairment of SPEM in schizophrenic inpatients to be a deficiency specific for schizophrenic but rather a phenomenon which is more frequent in hospitalized psychiatric inpatients than in healthy controls.

Saccadic eye movements were evaluated as to their reaction time and the occurrence of non-fixation and dysmetria. In schizophrenic inpatients the reaction time, on average was longer and non-fixation more frequent than in controls. The increased score of non-fixation is in good agreement with the report of Mialet and Pichot (1981) who found that schizophrenics make more saccades than controls when required to fixate upon a stationary target. However, both the reaction time and the non-fixation score are also increased in manic-depressive patients. Furthermore in schizophrenic outpatients these parameters are not significantly different from controls or alcoholics. Therefore, we feel that the saccadic reaction time and the non-fixation score can be added to the list of unspecific psychomotor signs common to psychotic patients.

The situation appears to be different for dysmetria. Only the population of schizophrenic patients, whether hospitalized or not, had a significantly increased score of dysmetria, though for the individual patient the probability of making an unusual number of dysmetric saccades appears to be only approximately 50%. It is of particular interest that in our admittedly small group of manic-depressive none had more than 10% dysmetric saccades. This is in contrast to the criteria non-fixation and reaction time, where manic-depressives showed even worse scores than schizophrenic patients.

Administration of neuroleptics to volunteers led to a slight trend toward an increase of dysmetric saccades and of non-fixation. This trend was accompanied by a reduction of the saccadic velocity and by a subjective feeling of fatigue. Since the saccadic velocity is sensitive to changes of vigilance, the slight increase of dysmetria and non-fixation in the healthy volunteers could be due to reduced vigilance. Since the average saccadic velocity in schizophrenic patients was found to be in the normal range, the increase of dysmetria in these patients does not seem

to be due to a reduced vigilance as a consequence of chronic treatment with neuroleptic drugs.

In schizophrenics the dysmetric saccades occur irregularly and interspersed between normal saccades, while patients with brain stem or cerebellar lesions, who do show dysmetric saccades, always have dysmetric saccades. This suggests that the site of the disorder is at a higher level, and not a consequence of cerebellar or brain stem lesions affecting the neural circuitry of the saccadic system, although cerebellar atrophy has been observed in schizophrenic patients (Weinberger et al. 1980).

In our view there are two possible explanations for the increase of dysmetria in schizophrenics: i) either it is a long-term effect of chronic treatment with neuroleptics, or ii) it is the expression of impaired attention and increased distractibility. Since manic patients treated with neuroleptic drugs appear to have normal saccades, and untreated schizophrenic patients may show dysmetric saccades, we are inclined to consider the second hypothesis more likely. This impairment of attention does not seem to be voluntary and the proposed term "involuntary inattention" appears to be quite appropriate (Holzman et al. 1976).

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