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Saccadic Reaction Times in Acute and Remitted Schizophrenics

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Summary. Schizophrenics are known to have various disturbances of the visuomotor system. Whereas smooth pursuit eye movement disorders have been repeatedly confirmed, there are relatively few reports regarding possible disturbances of the saccadic system. In this study, the saccadic reaction times of 47 schizophrenic inpatients were investigated upon admission and later in the remitted state; 28 age- and sex-matched normal volunteers were tested as controls. Psychopathology and outcome were evaluated according to the Brief Psychiatric Rating Scale and the Prognostic Scale. Light stimuli were presented at random direction, location (ranging from 0° to 20°) and duration (800, 1000, and 1200 ms). The eye movements were recorded by electro-oculography. Compared with the control group, schizophrenics revealed prolonged saccadic reaction times, which correlated with pronounced negative symptoms and an unfavourable course of the illness. The saccadic reaction times remained prolonged in schizophrenic patients. These findings suggest attentional deficits in schizophrenics.

Key words: Schizophrenia – Eye movements – Saccadic reaction time – Attentional deficit

Introduction

There are two kinds of essential physiological eye movements: smooth pursuit and saccadic movements. Smooth pursuit enables the foveal stabilization of a moving visual object; saccades are rapid eye movements with a certain programmed behaviour regarding direction and amplitude serving the recognition of novel visual stimuli. Saccades can be described in terms of reaction time, speed and accuracy. Smooth pursuit eye movements and saccades are partially generated and controlled by interrelated cortical-subcortical structures (Baloh et al. 1982; Leigh and Zee 1983). Even though both oculomotor functions, – because of their reciprocal relationship, are of almost equal importance in exploring visual surroundings, in schizophrenics smooth pursuit tracking has received the greater interest.

Based on the studies of Diefendorf and Dodge (1908), Holzman and co-workers have been studying oculomotor responses since the early 1970s. In 50%–85% of schizophrenics they have discovered disruptive smooth pursuit eye movements (Holzman et al. 1973), whereas in a normal population only 8% display this finding. Holzman's results in schizophrenics have been reproduced frequently (Shagass et al. 1974; Brezinova and Kendell 1977; Kuechenmeister et al. 1977; Salzman et al. 1978; Cegalis and Sweeney 1979; Mialet and Pichot 1981; Levin et al. 1982; Iacono and Koenig 1983; Van den Bosch et al. 1987).

There have been few investigations concerning saccadic eye movements in schizophrenics. Early reports showed normal saccadic reaction times (Diefendorf and Dodge 1908; Couch and Fox 1934); these findings were confirmed by Levin et al. (1981).

The saccadic stimulus programmes used were relatively simple in structure, the pre-interval being fairly long (1–6 s). In programmes designed with random presentation and fast changes of visual stimuli, a high level of information processing is necessary. These processes are closely associated with attentional functions. In manual stimulus response tasks, delayed reactions have been observed consistently as a consequence of attentional deficits in schizophrenics (Nuechterlein 1977; Nuechterlein and Dawson 1984). When varying the interval between the warning stimulus and the

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imperative stimulus – the so-called preparatory interval – chronic schizophrenics in particular demonstrate the cross-over phenomenon (Rodnick and Shakow 1940). The conclusion that there is a general attentional deficit and diminished processing capacities in schizophrenics derives also from the results of a variety of attentional tests, such as the forced-choice span of apprehension or the continuous performance test, which are considered to be potential vulnerability indicators for schizophrenia (Nuechterlein et al. 1986). In these tests, attentional deficits were consistently associated with negative symptoms. Therefore, it was our aim to investigate saccadic reaction times in schizophrenics using a more complex stimulus programme with a higher information load than those used in previous studies. In addition, we wanted to study saccadic reaction times in relation to psychopathology, especially negative symptoms, course of illness and prognosis.

Subjects and Methods

Forty-seven inpatients (21 male, 26 female), classified as schizophrenics according to the ICD-9, without neuroleptic medication participated in the study after their informed consent had been obtained. The following subgroups of schizophrenic illness were differentiated: 295.1 ($N=4$), 295.3 ($N=32$), 295.6 ($N=9$), 295.8 ($N=2$). The mean age was 31.8 years (range 16.6–56.9). Patients with alcohol or drug dependency, visual disturbances, neurological dysfunctions and tardive dyskinesia were excluded from the study. The mean age at the first manifestation of the illness was 24.9 ± 8.5 years. On the average, the illness had manifested itself 3.2 ± 3.3 times; 17 of the 47 patients presented with the first manifestation. Testing was performed on the 4th day after admission, no prior psychopharmacological treatment was initiated.

Based on documentations from previous hospitalizations, reports from psychiatrists who had treated these patients as outpatients, as well as the information obtained from the patients themselves, an exact up-to-date history of the neuroleptic medication was determined for each patient. Fifteen patients had never taken any neuroleptics prior to their admission. For the remaining 32 patients, we determined the average cumulative neuroleptic dose at $167{,}382 \pm 209{,}693$ mg chlorpromazine equivalents during the total pre-hospitalization treatment period.

Twenty-six remitted patients were followed up after a mean duration of 11.5 weeks of neuroleptic therapy; the remaining 21 patients had left the clinic before their remittance or had denied consent for a second testing. The 26 inpatients had been treated with a mean daily dose of 376 ± 248 mg chlorpromazine equivalents.

As controls, we tested 28 age- and sex-matched volunteers with no personal or family history of psychiatric disorders, for whom we applied the same exclusion criteria as for the patient group.

Psychopathology. The psychopathological symptoms manifest at the first testing were documented according to the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham 1962; Overall 1976). The Prognostic Scale of Strauss and Carpenter (1977) was performed to determine prognostic relationships.

Apparatus and Testing Procedure. DC recordings of changes in the corneoretinal potentials for horizontal and vertical eye movements were registered using electro-oculography. After preparation of the skin with alcohol six Ag/AgCl electrodes were placed symmetrically and evenly spaced from the centre of the pupil, at the inner and outer canthus as well as above and below the left eye. The ground electrode was placed on the left ear lobe. Vertical eye movements were recorded in order to differentiate eye-blink artefacts. After pre-amplification, the signals were fed into an amplifier (Toennis) and charted on paper with an electroencephalograph (Siemens ELEMA Mingograph) and pulse code modulated. Digitalization was performed by a VAX-11-750 computer with a sampling rate of 500 Hz. The position signal and sudden saccadic movements were projected onto a graphic terminal and the reaction times between presentation of the position signal and the beginning of each eye movement were determined with an electronic crosshair. The sampling rate of 500 Hz allowed a measurement accuracy of 2 ms. Saccades with superimposed artefacts, particularly eye blinks, were excluded.

The subjects sat in a darkened room with their heads fixed. A board with 511 light emitting diodes (LEDs) was placed at eye level at a distance of 122 cm from the eyeballs. Since the board was curved ($r=122$ cm), the distance of each light diode to the eye remained constant. During calibration, the stimulus position varied systematically between 5°, 10° and 20° in both directions. At the beginning of the saccade programme, the middle position was fixated for 6 s; the diodes lit up randomly ranging from 0° to 20° with the lowest possible angular distance at 2.5°. The duration of the stimulus was also chosen at random: 800, 1000 or 1200 ms. A total of 52 saccadic stimuli were presented.

The statistical evaluation was performed with the SAS computer programme. *t*-Values were calculated in order to test significant group differences in saccadic reaction times. Relationships between reaction times, psychopathology and course of the illness were determined with Pearson correlations.

Results

Comparison of Saccadic Reaction Times in Patients and Controls

Table 1 demonstrates that, in agreement with our hypothesis, schizophrenic patients had significantly prolonged saccadic reaction times. There was no evidence of lateralization; the reaction times were equally prolonged for saccadic eye movements to the left and right.

Influence of Age, Sex and Medication

Both groups revealed slower saccadic reaction times with increasing age (schizophrenics: $r=0.50$, $P<0.01$; controls: $r=0.49$, $P<0.01$), whereas sex had no significant influence (schizophrenics: $r=-0.01$, $P>0.05$; controls: $r=0.19$, $P>0.05$).

We observed a slight correlation between the cumulative neuroleptic dose and saccadic reaction

Table 1. Comparison of saccadic reaction times of schizophrenics and normal controls

	Schizophrenics ($N = 47$)	Normal controls ($N = 28$)	t-Test (P)
Saccadic reaction time (ms):			
to the right	200 ± 53	183 ± 17	0.038
to the left	209 ± 57	192 ± 17	0.058

Table 2. Saccadic reaction times in schizophrenic subgroups

	295.1 ($N = 4$)	295.3 ($N = 32$)	295.6 ($N = 9$)	295.8 ($N = 2$)
Saccadic reaction time (ms):				
to the right	174 ± 28	196 ± 56	235 ± 45	182
to the left	191 ± 27	202 ± 57	249 ± 57	185

Table 3. Pearson correlations of saccadic reaction times and psychopathology (BPRS)

Saccadic reaction times	r	P
BPRS items		
– suspiciousness	0.28	0.055
– motor retardation	0.41	0.004
– unusual thought content	0.29	0.044
– blunted affect	0.34	0.020
BPRS factor withdrawal/retardation	0.41	0.004
BPRS total	0.28	0.053

times ($r = 0.26$, $P = 0.07$). Since older patients had a higher cumulative dose of neuroleptics, this correlation might have been influenced by the age factor.

Saccadic Reaction Times in Relation to the Schizophrenic Subgroups

Owing to the small number of patients in three of the four subgroups, statistical comparisons were not performed. The group with chronic schizophrenic patients displayed the longest saccadic reaction times (Table 2).

Correlations Between Saccadic Reaction Times and Psychopathology and Prognosis

Table 3 illustrates the Pearson correlations between BPRS items and the saccadic reaction times. We only considered statistically significant correlations. The factor "withdrawal retardation" is composed of the items "emotional withdrawal (BPRS 3)", "motor retardation (BPRS 13)", and "blunted affect (BPRS 16)", and reflects the extent of negative symptoms. Thus, patients with negative symptoms were particularly characterized by prolonged reaction times.

By computing a multiple regression with the 18 BPRS items as predictor variables and saccadic reaction times as criteria variables, a 49% variance for saccades directed to the right and 43% for those directed to the left was explained. Negative symptoms, expressed by the factor "withdrawal retardation", resulted in a mutual variance percentage of 22.2% for saccades directed to the right and 13.9% for those directed to the left.

Table 4. Pearson correlations between saccadic reaction times and outcome (Prognostic Scale)

Saccadic reaction time	r	P
Prognostic Scale items		
– number of social relations most usual in past year	−0.30	0.037
– previous hospitalization	−0.30	0.041
– length of time since first occurrence of hallucinations or delusions	−0.40	0.005
– longest period psychiatric symptoms ever persisted	−0.29	0.046
– presence of thought disorder, delusions or hallucinations in past year	−0.41	0.004
– most usual ability to meet own basic needs in past year	−0.36	0.013
Prognostic Scale total	−0.30	0.037

As demonstrated in Table 4, there was evidence of a correlation between the extent of an unfavourable prognosis (a lower score means an unfavourable prognosis) and reaction times of saccadic movements. This was true for the complete evaluation and particularly for the single items "length of time since the first occurrence of hallucinations or delusions", "presence of thought disorder, delusions, or hallucinations in the past year", as well as "most usual ability to meet own basic needs in the past year".

Intraindividual Comparison of Saccadic Reaction Times in Acute and Remitted Schizophrenics

In the 26 remitted schizophrenics, the saccadic reaction times did not differ significantly from those at the time of admission (Table 5). There was no signif-

Table 5. Comparison of saccadic reaction times of schizophrenics at the first and second testing

	First testing ($N = 26$)	Second testing ($N = 26$)	t-Test (P)
Saccadic reaction times (ms):			
to the right	198 ± 61	192 ± 48	NS
to the left	210 ± 69	205 ± 52	NS

icant correlation between the reaction times and the doses of neuroleptics determined in chlorpromazine equivalents ($r = 0.08$) administered during the hospitalization.

Discussion

Manual reaction times have been investigated systematically in schizophrenics and have consistently been reported as prolonged (Nuechterlein and Dawson 1984). In contrast, there have been relatively few studies on ocular reaction times, and the results have shown normal values (Diefendorf and Dodge 1908; Levin et al. 1981; Mather and Putchat 1983; Schmid-Burgk et al. 1983). In these studies, testing saccadic reaction times in schizophrenics, visual stimuli were changed slowly and were predictable either in time or location. Nuechterlein and Dawson (1984) emphasized that only tasks with a high processing load will disclose deficits in schizophrenics. Our programme was designed with random presentation and fast stimulus change at 800, 1000 and 1200 ms. The time from a visual command to change the direction of gaze until the beginning of the rapid eye movement response is defined as the saccadic reaction time. It consists of sensory, motor and central processing components. In saccadic tracking, the eyes are attentively fixating a foveal target and the fixation process must be discontinued before a new saccade can be made. A shift of attention to the new stimulus position is needed before the coordinates of the new saccade can be computed. Tsal (1983) concluded that the attentional focus traversed the visual field in an analogue manner at a constant velocity, with attentional processing ceasing during the course of the movement. On the other hand, Remington and Pierce (1984) concluded that the velocity of the change in attentional focus is proportional to the distance to be travelled. Although in our paradigm we could not measure how quickly the attentional focus shifted from one locus to another, prolonged saccadic reaction times in schizophrenics using a complex stimulus programme with a high information load are attributed to reduced attention, while reduced attention itself is conceived as diminished processing resources, which could be concentrated on specific areas in the visual field.

Saccadic reaction times are considered to be sensitive indicators of attentional impairment in patients with central disorders (Leigh and Zee 1983). In our study, we observed prolonged reaction times mainly in patients with negative symptoms and poor prognosis. Whereas McGhie and Chapman (1961) interpret attentional deficits as a core symptom of schizophrenia, other authors describe attentional disturbances predominantly in schizophrenics with negative symptoms (Andreasen and Olsen 1982; Nuechterlein et al. 1986). Negative symptoms are often associated with structural cerebral lesions (Crow 1980, 1985). Visual attention is controlled by a neuronal system involving the posterior parietal lobe and areas of the thalamus and midbrain (Lynch et al. 1977; Mountcastle 1978; Posner et al. 1984). At the present time, we can only speculate about possible relationships between negative symptoms and deficits in these brain structures.

Functional hemispheric imbalances in schizophrenics are well known (Gaebel 1988). Testing of reaction times to stimuli presented separately to the right and left visual field in schizophrenics, in comparison with the control group, disclosed prolonged reaction times for both directions. The left hemisphere is assumed to be responsible for functions related to language and speech, whereas the right hemisphere governs visuospatial processes (Springer and Deutsch 1985; Geschwind and Galaburda 1987). Since the right hemisphere most likely contains the neural apparatus for attending to both the right and left spatial fields (Howes and Boller 1975), delayed reaction times in schizophrenics to stimuli presented to both right and left visual fields suggest that the source of the deficit might lie in the right hemisphere.

Shagass et al. (1974) demonstrated a high consistency in smooth pursuit eye movement disturbances in schizophrenics. Our study revealed a delay in saccadic reactions during the second testing among remitted schizophrenics; this leads one to consider a state-independent trait.

There are some other aspects of prolonged saccadic reaction times in schizophrenics. In the literature, little attention has been given to psychopathology in its relation to oculomotor dysfunctions in schizophrenics. In our study, schizophrenics with delusions and hallucinations predominated. It might be expected that the acoustic hallucinations could cause a delay in the saccadic reaction times because of easy distractability. However, in our study those schizophrenics characterized by hallucinations (ICD 295.3) did not show disproportionally prolonged saccadic reaction

times (Table 2) when compared with the other subgroups.

A decreased level of vigilance due to neuroleptics can be easily excluded, since the results of the first testing were obtained from unmedicated patients (none of them had received medication for 3 days prior to the first testing; most patients had received no medication for an even longer time). Furthermore, the reaction times following treatment with neuroleptics during remittance revealed no additional delay, nor could a correlation be found between the reaction times during the remitted state and the levels of chlorpromazine equivalents administered during hospitalization.

The Prognostic Scale disclosed a relationship between poor outcome and prolonged reaction times, particularly in patients with a long course of illness. In manual stimulus reaction tasks, poor results also correlate with an unfavourable prognosis (Cancro et al. 1971; Zahn and Carpenter 1978). Since patients with long and unfavourable courses of illness have often been receiving neuroleptics for many years, the effects due to their chronic state upon saccadic reaction times cannot be separated completely from those of long-term neuroleptic medication.

The age dependency of saccadic reaction times is in agreement with earlier reports (Abel et al. 1983; Hutton and Palet 1986). Since we used an age-matched control group, the delayed ocular reaction times in schizophrenics cannot be related to age. Accordingly, the correlation of age with saccadic reaction times was the same in both groups.

Clearly, further research will be needed to examine the relationship between oculomotor dysfunctions and attentional deficits in schizophrenics.

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