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Asymmetry of eye movement disturbances in schizophrenic patients

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Thirty patients with paranoid schizophrenia were studied during exacerbation of symptoms. Control group consisted of thirty persons, age and sex-matched. Eye trackings were measured during point fixation and smooth pursuit movement. Frequency of intrusive saccades and total duration of square wave jerks were recorded for each eye. Schizophrenic patients had extensive eye tracking disturbances on both tasks, significantly more marked for the right eye than for the left one. In these patients, significant correlation was found between the intensity of the disturbance and the magnitude of right-left eye difference. The results point to the asymmetry of eye tracking disturbances in schizophrenia with greater right eye pathology.

Key words: schizophrenia, eye movements, lateralization, intrusive saccades, asymme-

Introduction

The eye movement disturbances in schizophrenia were first described in 1908 by Diefendorf and Dodge [11]. In 1970s [20] they were considered as a possible neurophysiological marker of vulnerability to schizophrenia. Such disturbances occur in 80% of patients with schizophrenia, in 50 % of their first degree relatives, and only in 10 % of healthy subjects [18]. While a genetic component is postulated [2, 19], the intensity of eye movement disturbances in schizophrenic patients may also be related to the acquired brain impairment [22, 24, 26].

The most frequent eye movement disturbances in schizophrenia include reduction of smooth pursuit gain, an increased number of intrusive saccades during smooth pursuit movement [19,25, 33, 34], abnormalities of antisaccadic task, e.g antisaccade latency and antisaccade errors rate [25, 29, 31, 39]. They also include abnormalities of visual fixation such as a decreased number of fixation points, a longer fixation time and an increased number of intrusive saccades occurring during fixation both in horizontal and vertical components [2, 35].

The data on the neuroanatomy of eye movements suggest that the areas of the brain involve mostly frontal and parietal cortical areas as well as the basal ganglia. Posterior

parietal areas specifically control visually guided eye movements, whereas frontal and parietal areas co-operate in controlling the more internally generated oculomotor functions [23]. Neuroimaging studies in schizophrenia showed that eye movement dysfunctions are connected with a decreased metabolism in the frontal and parietal association cortex [32]. In this study, patients with schizophrenia showing greater eye movement disturbances had significantly decreased metabolism in oculomotor region of frontal cortex. MacAvoy and Bruce [27] found an association between the intensity of eye movement disturbances and frontal impairment measured by neuroimaging and by the performance on Wisconsin Card Sorting Test.

According to the hypothesis of lateralization for cerebral dysfunctions, formulated by Flor-Henry [12], schizophrenic psychopathology is mostly associated with left hemisphere dysfunction. Recent results of neurophysiological and neuroimaging studies brought some confirmation of this concept. Studies with dichotic listening in schizophrenic patients point to abnormal right ear advantage, compatible with left hemisphere dysfunction [4, 21]. In paranoid schizophrenic patients, significantly more rightward conjugate lateral eye movement (CLEM) in response to emotional and spatial stimuli were described [38, 13, 3]. Neuroimaging studies in schizophrenia revealed structural changes of cortical and limbic regions, predominant on the left side [41, 5, 40, 10, 37] as well as disturbances of blood flow and glucose metabolism in left frontal and prefrontal cortex, especially during verbal tasks [14, 36]. Pathology of left cerebral hemisphere in schizophrenia has been accentuated during exacerbation of symptoms [16, 15, 4].

In this study, we put forward a hypothesis postulating that eye movement disturbances in schizophrenia during an acute episode (measured as intrusive saccades) may present an asymmetry, compatible with left hemisphere dysfunction, i.e. being more marked in the contralateral (right) eye. To this end, the eye movement disturbances measured in patients with schizophrenia were calculated separately for each eye and the data were compared with those of healthy control subjects.

Subjects

The experimental group consisted of thirty right-handed patients with paranoid schizophrenia (15 male and 15 female, aged 19-48 years, mean 31±10 years). All subjects were hospitalised at an inpatient unit, Department of Psychiatry, University School of Medical Sciences in Bydgoszcz. None had the history of substance abuse, neurological and serious somatic illness or ophtalmic abnormalities. The diagnoses were made by psychiatric staff of the unit, using ICD-10 and DSM-IV criteria.

The assessments of eye movements were performed during exacerbation of psychotic symptoms, when patients were drug-free for at least 7 days. The mean intensity of schizophrenic symptoms as measured by PANSS scale at this time was 111±20 points.

The control group consisted of thirty healthy right-handed persons, age and sex-matched (15 male and 15 female, aged 19-48 years, mean 33±8 years). All subjects were somatically healthy and without any significant psychiatric history and without

any ophtalmic dysfunctions.

The project was accepted by the Ethical Committee at the University School of Medical Sciences in Bydgoszcz. All patients and control subjects gave the informed consent to the study, after the nature of the procedures had been fully explained to them.

Method

Eye trackings were measured by infrared reflectometry method, using Ober II system and Grenoble 96 computer program. Investigated subjects were seated in a darkened room, in front of the computer screen with goggles (with infrared detectors) on their eyes, the distance between 17-inches computer screen and subject's eye being 60 cm.

The conditions for measurements were sampling rate of 400 Hz and measurement time 20 sec, during two tasks: 1) point fixation on central position on the computer screen and 2) smooth pursuit at the moving point on Lisajou's curves. The reason for choosing the Lisajou curves in Ober II system for the measurement of smooth pursuit movement was that these curves have constant mathematical characteristics but, unlike sinusoidal curve, the subject investigated cannot predict the direction of the moving point.

The subjects were instructed to keep their eyes fixed on the point during point fixation task and to observe the moving point during smooth pursuit task.

The main indexes of eye movement disturbances were the frequency of intrusive saccades (IS) occurring during each task and total duration of square wave jerks (SWJ), regardless of their amplitude. The following assessment criteria were applied: 1) frequency of intrusive saccades (N/sec), 2) mean duration (SWJ) to spend eye away from the course of the observed point.

Blinks were detected and eliminated from the analysis. All results were calculated separately for the left eye and for the right one. For the frequency intrusive saccades and total duration of square wave jerks, the values of cut-off point (mean +1 SD for the results of healthy controls) were defined.

Statistical analysis was performed using Statistica 5.0 program. To evaluate normality distribution of the variables, the Shapiro-Wilk test was applied. Consequently, nonparametric tests were used for comparisons of differences between left and right eye (Wilcoxon test), between schizophrenic and control subjects (Mann-Whitney test) and between fractions of subjects (Chi-square test). Also Spearman correlation coefficients were calculated between the intensity of particular eye movement disturbances and the magnitude of right-left eye difference.

Results

The frequency of intrusive saccades as well as total duration of square wave jerks

Table 1

Frequency of intrusive saccades and total duration of square wave jerks (mean +SD) during point fixation and smooth pursuit calculated separately for left and right eye in patients with schizophrenia and in healthy controls.

			LEFT EYE	RIGHT EYE
POINT FIXATION	Frequency of IS (/sec)	Schizophrenia	0.45±0.25	0.95±0.5*
		Controls	0.14±0.15#	0.16±0.14##
	Duration (msec) SQJJ	Schizophrenia	95±106	238±316**
		Controls	12±15##	14±16##
SMOOTH PURSUIT	Frequency of IS (/sec)	Schizophrenia	1.1±0.5	1.6±0.5*
		Controls	0.32±0.2#	0.35±0.3#
	Duration (msec) SQJJ	Schizophrenia	358±316	634±466**
		Controls	55±53##	73±63##

Difference right vs left eye * $p<0.05$ ** $p<0.01$
Difference controls vs schizophrenia # $p<0.01$ ## $p<0.001$

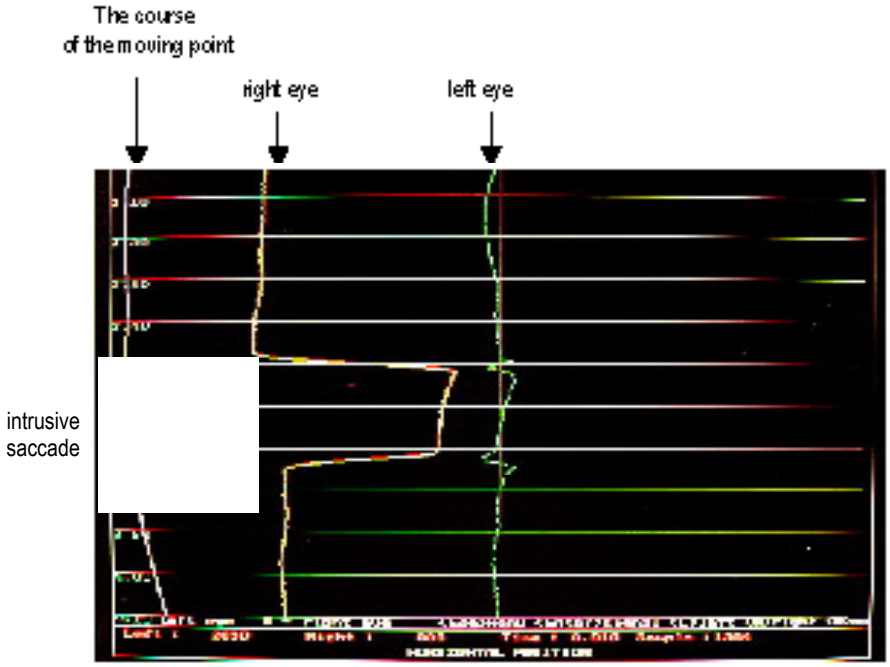
during point fixation and smooth pursuit task, calculated separately for left and right eye in patients with schizophrenia and in healthy controls are shown in table 1.

Schizophrenic patients compared with healthy control subjects had significantly more eye tracking disturbances for all measures: intrusive saccades frequency and square wave jerks duration time, both in point fixation and smooth pursuit task, and for both left and right eye. In schizophrenic patients these disturbances were significantly more marked for the right eye than for the left one, for all measures on both point fixation and smooth pursuit task. In control subjects the values of disturbances were slightly higher for the right eye, however, never reaching significance vs. the left one.

A frequent finding in schizophrenic patients, especially during smooth pursuit task, was an appearance of intrusive saccade in the right eye, while at the same time the recording of the left eye was normal. This was never the case in control subjects. Such phenomenon was illustrated on figure 1.

In table 2, a percentage of schizophrenic patients with abnormal values (>cut-off point) during point fixation and smooth pursuit task in left and right eye is presented. The cut-off point was adopted as mean results + 1 SD for healthy control subjects.

In schizophrenic patients, the percentage of subjects with abnormal values (> cut-off point) for intrusive saccades frequency, and duration of square wave jerks amounted to 33-100 % on fixation task and to 47-100% on smooth pursuit task. These percentages were greater for the right eye on all measures. The difference between fractions of schizophrenic patients with abnormalities of brief intrusive saccades in right and left eye was significant, both during point fixation ($c^2=13.3$ $p<0.001$) and smooth pursuit task ($c^2=4.44$, $p<0.0035$). The most robust abnormalities, measured as values in schizophrenic patients falling outside cut-off point, were those occurring in the right eye. All patients with schizophrenia (100%) fell outside cut-off point for total duration of square wave jerks in the right eye, both during point fixation and smooth pursuit



Legend to figure 1 Recording of the movement of left and right eye during smooth pursuit on Lisajou curve in schizophrenic patient. Intrusive saccade occurs in right eye while at the same time no abnormality is seen in left eye.

Table 2

Values of cut-off point for the duration and frequency of intrusive saccades and the percentage of schizophrenic patients with abnormal values > cut-off point Cut-off point =mean +1 SD healthy control subjects.

		LEFT EYE		RIGHT EYE	
		Values of cut-off point	% of patients > cut-off point	Values of cut-off point	% of patients > cut-off point
Point fixation	Duration SDJJ msec	28.00	70	3 1.00	90
	Frequency IS/ Msec	0.32	53	0.34	80
Smooth pursuit	Duration SDJJ msec	106.05	83	137.32	100
	Frequency IS/ Msec	0.6	77	0.66	93

task, and 93% of schizophrenic patients had abnormal right eye values for frequency of intrusive saccades on smooth pursuit task.

Table 3

Correlation between the intensity of eye movement disturbances and the magnitude of right-left eye difference

		Spearman correlation coefficient	Significance
Point fixation	Duration SWJ msec	0.636	P=0.001
	Frequency IS /sec	0.522	P=0.003
Smooth pursuit	Duration SWJ msec	0.524	P=0.003
	Frequency IS /sec	0.274	ns

Correlation between the intensity of particular eye movement disturbances and the magnitude of right-left eye difference in schizophrenic patients is shown in table 3.

The correlation between the intensity of disturbances and right vs. left eye differences was highly significant for SWJ duration on both point fixation and smooth pursuit task, and for IS frequency on point fixation task.

Discussion

The results of this study confirm the existence of very profound abnormalities of eye tracking in schizophrenic patients during exacerbation of illness compared with control persons, in terms of highly increased frequency of intrusive saccades and duration of square wave jerks. This is in line with the results obtained by other researchers [25, 8, 31, 42]. However, the main finding of our study was the observation that these abnormalities in schizophrenic patients are clearly asymmetric, i.e. they are more marked in the right eye than in the left one. This may confirm our working hypothesis.

The studies on the possible laterality of eye movement disturbances in schizophrenia are scarce. Allen et al.[1] in their study of schizophrenic patients from Pacific population found a significantly higher number of antisaccadic errors for right visual field, pointing to dysfunction of the left hemisphere. Crawford et al. [9] found a correlation between a higher number of errors on antisaccadic task and a decreased blood flow in the anterior cingulate, insula and in the left striatum. Since the point fixation and smooth pursuit tasks used in this study did not involve right or left visual field, the asymmetry of eye movement disturbances found by us should predominantly be due to the differences in motor control of each eye exerted by the contralateral hemisphere.

In right-handed persons, the right eye performs the function of the “leading” eye and thus may be more vulnerable to the disturbances precipitated by external tasks. This was confirmed in our study by showing slight (statistically insignificant) asymmetry in eye movements observed in healthy persons (higher amplitude and higher

frequency of IS in right eye). However, in patients with schizophrenia, such asymmetry was highly significant and right eye movement disturbances in schizophrenic patients had the greater discriminant power versus healthy control subjects than such disturbances in the left eye. Our finding of a higher degree of right eye movement disturbances in schizophrenic patients may thus corroborate the results obtained in various studies, pointing to greater pathogenic involvement of the left hemisphere in schizophrenia 14, 40, 41].

High prevalence of eye movement disturbances in the first degree relatives of schizophrenic patients indicates a substantial genetic component to them. A locus on chromosome 6 has been postulated for these disturbances as a putative genotypic susceptibility marker to schizophrenia (Arolt et al., 1996). However, several lines of evidence point that the intensity of eye movement dysfunctions in schizophrenic patients, besides of genetic vulnerability, may be connected with acquired brain impairment. Kinney et al., [22] among subjects with eye movement disturbances found more common occurrence of obstetric complications in schizophrenic patients as compared to their first-degree relatives. In line with this, Malaspina et al. [26] found that the disturbances of smooth pursuit eye movement were more marked in non-familial schizophrenic patients that in patients with family history. Finally, Litman et al. [24] found a lower intensity of eye movement disturbances in monozygotic twin discordant for schizophrenia. To answer the question whether asymmetry of eye movement disturbances is connected with genetic or neurodevelopmental component one may speculate on the basis of our results concerning correlations between the intensity of particular eye movement disturbances and the magnitude of right-left eye asymmetry. Since highly significant correlations were obtained for all parameters measured on point fixation task and for total duration of square wave jerks on smooth pursuit task, it seems that the asymmetry of eye movement disturbances in schizophrenia may be mainly due to the brain impairment occurring in the course of neurodevelopmental process.

It would be of interest to know whether the asymmetries of eye movement disturbances found during exacerbation of symptoms in schizophrenia may persist into the period of clinical improvement and whether they also occur in 1st degree relatives of schizophrenic patients. Also, the possible effect of neuroleptic treatment on these dysfunctions may be worth studying. Finally, the research on this issue performed in other psychiatric illnesses (e.g. bipolar and unipolar mood disorders) where the opposite lateralization than in schizophrenia is reported [28, 6, 30, 3] may throw more light on this interesting phenomenon.

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