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Smooth Pursuit Eye Movements and Neuropsychological Tests in Schizophrenic Patients: Possible Involvement of Attentional Components

O. Gambini and S. Scarone

Psychiatric Branch, Department of Biomedical and Technological Sciences, University of Milan Medical School and Istituto Scientifico H S Raffaele, Milano, Italy

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Summary. The relationships among different components of frontal lobe dysfunction and voluntary attention were studied. Drug-free schizophrenic patients and matched normal controls were recruited and assessed for smooth pursuit eye movements, voluntary saccadic eye movements and by means of neurophsychological tests (Toluse-Pieron test and Wisconsin Card Sorting Test). No clear-cut relationship was found between eye movement performance and neuropsychological impairment.

Key-words: Schizophrenia – Eye Movements – Neuropsychological Tests

Introduction

The extensive literature on eye tracking impairment in schizophrenic patients consistently reports an increase of saccadic movements in smooth pursuit eye movements (Holzman et al., 1985; Abel, 1988; Siever, 1991). Separate areas of neurons in the cortical frontal eye fields have been identified for both smooth pursuit and saccadic eye movements (Creutzfeld, 1988), and recent experimental evidence (Thaker et al., 1990) suggests that the frontal eye fields have an important role in feedback modulation of the control of visual tracking and particularly in the inhibition of saccades during fixation and smooth pursuit.

Nevertheless, even though a relationship between disrupted eye movements in schizophrenia and some deficit on sustained attention have been postulated, no definitive data have been reported (Abel, 1988).

An attention deficit is relevant in clinical descriptions of schizophrenia and, further, it has been considered as a main manifestation of a general information processing deficit in schizophrenia (Hirst, 1986). Moreover, deficits in selection and integration of an external stimulus in schizophrenia have been related more specifically to frontal lobe dysfunction (Levin, 1984a; Levin, 1984b).

On the other hand, data on frontal lobe dysfunction in schizophrenia have been consistently reported during the last 10 years (Weinberger et al., 1985; Williamson et al., 1989).

The Wisconsin Card Sorting Test (WCST) is one widely recognized as highly accurate in assessing frontal region dysfunctions both in patients with neurological lesions and in psychiatric patients.

The aim of the present study was to evaluate the relationship among different components of frontal lobe dysfunction and voluntary attention components in a sample of drug-free schizophrenic patients and matched normal controls. To this end, both schizophrenics' and controls' Smooth pursuit eye movements (SPEM) and voluntary saccadic eye movements (VSEM) were recorded. During the same testing session, the subjects performed a simple neuropsychological attention test, the Tolouse-Pieron test (TP), and were also evaluated on their frontal functioning by means of the WCST. To assess the possibility of correctly classifying each subject into a group on the basis of his eye movement performances, discriminant analysis (DA) was performed on the total sample (i.e. controls and schizophrenics) for SPEM and VSEM separately. Discriminant analysis also made it possible to identify the patients correctly and incorrectly classified according to their SPEM and VSEM performances. Further, WCST and TP test performances were compared in correctly and incorrectly classified schizophrenic patients. Demographic variables also were checked for accuracy and incorrect classification in order to assess the possible influence of disease subtype, age at onset and duration of illness on neurophysiological performances.

Methods

Subjects

Fifty-seven subjects, 30 schizophrenic out-patients (16 male, 14 female; mean age 30.7, SD 7.5 yrs; mean education 10.7, SD

Correspondence to: Orsola Gambini, M.D., Psychiatric Branch, DSNP, University of Milan Medical School, Via Prinetti 29, 20127, Milano, Italy

3.5 yrs, education range 5 to 18 yrs) and 27 controls (11 male, 16 female; mean age 26.5, SD 2.6 yrs; mean education 17.0, SD 2.5 yrs). Both patients and controls were younger than 45 years so as to exclude aging factors that might affect eye movements.

Schizophrenic patients were classified according to their diagnostic subtype (15 undifferentiated, 10 disorganized and 5 paranoid). The diagnosis of schizophrenia, the subtype classification and the evaluation of chronicity were made on the basis of DSM III-R criteria (APA, 1980) employed by two senior psychiatrists.

At the time the test was administered, the schizophrenic patients had not been taking medication for at least 2 weeks. Patients were off therapy for drug holidays or because they themselves decided to stop taking neuroleptics. Some patients had been taking hypnotics at bedtime at the mean flurazepam dose-equivalent of 15 mg. Only patients who satisfied the following conditions were selected: they could understanding the examiner's instructions and were cooperative study subjects. The control subjects were students of the medical school and/or hospital employees without a history of neurological or psychiatric illness. They were matched for age with the patient group. Before admission to the study, these potential subjects underwent physical and neurological examinations in order to enable us to exclude those with any possible disorders. Additional exclusion criteria included current use of alcohol and drugs for both patients and control. Visual acuity was checked and those with visual defects were excluded. All the subjects were righthanded, handedness having been evaluated by means of a standardized questionnaire (Razkowsky, 1974). All the subjects, gave their informed consent after receiving a full explanation of the study.

Eye Movement Testing Procedure

Eye movements were recorded by means of the Nicolet Nystar TM Plus System. Subjects were seated on a chair in front of the light bar (Nicolet Nystar) 90 cm away from their eyes. Calibration values were performed before the smooth pursuit test and before the voluntary saccadic test. Recommended calibration values between 15 and 30 mmV and 0.1°–0.6° resolution for each test were obtained from all subjects. In the first series of the present study, targets consisted of a horizontal sinusoidally moving target on the light bar. Subjects were instructed to follow the target as carefully as possible. The duration of each test was 40 seconds. One trial was performed for smooth pursuit with 0.4 Hz frequency and 40°/s peak velocity. For smooth pursuit eye movements the following values were considered: Peak Velocity (PV, derived from the discrete Fourier transform analysis), Gain (i.e. ability of the subject to pursue a sinusoidally moving target), CD offset (left/right asymmetry), Total Harmonic Distortion Index (THD index of the integrity of the signal), number of saccades during SPEM test. A second trial consisted of the recording of fixed and random horizontal voluntary saccades. The random horizontal voluntary saccade test (6°–32° jumps and 3°–16° jumps) consists of 28 target jumps (14 each direction) on the light bar in a random amplitude sequence and at random time intervals (duration of the test is 40 s). The fixed horizontal voluntary saccade test consists of 14 jumps (7 in each direction) on the light bar in 3 fixed amplitudes (10°, 20° and 30° jumps) at fixed time intervals (duration of the test is 40 s). For voluntary saccades following values were considered: Delay (reaction time i.e., mean time from the target jump to the start of the subsequent saccade) and Accuracy (amount of overshots or undershots of the targets).

Testing Procedures for the Neuropsychological Tests

The Wisconsin Card Sorting Test (WCST) administration procedure was fully explained in the original work (Milner, 1963). Briefly, four stimulus cards differing in color, form and number are placed in front of the subject, who is given a pack of 128 response cards varying in these same characteristics. The subject is instructed to place each response card in front of one of the four stimulus cards, i.e., wherever he thinks it should go. He is told that the examiner will inform him as to whether he is right or wrong. Upon the examiner's response the subject is requested to get as many "right" cards as he can. After ten consecutive correct responses to the first criterion, the principle shifts to the second one and then to a third final one. This procedure is repeated twice or until all 128 cards have been placed. The indices which have been considered for the test evaluation are as follows: 1. SN: number of stages terminated by the subject. 2. TE: total error score. 3. PE: perseverative error score, defined as a sort which would have been correct in the immediately preceding stage or, in the first stage, or a persistently repeated response in terms of the patient's initial preference.

The Toluse-Pieron test (TP) was used as an easy tool for checking attention. Briefly, the subject has to select the same symbol among other similar symbols as quickly as possible. Correctly selected items (CI), incorrect selected items (II) and time (T) of preformance were computed.

Statistical Analysis

Differences in age and educational level were tested for schizophrenics and controls by means of the t test. One-way Analysis of Variance was performed for WCST and TP variables with diagnosis as the independent variables. Discriminant Analysis (SPSS, 1988) was performed separately on the SPEM variables (Peak velocity, Gain, left/right asymmetry, number of saccades) and the VSEM variables (Delay, Accuracy) with diagnosis as a grouping variable. Patients who were correctly and incorrectly classified by means of discriminant analysis on SPEM and VSEM were examined by means of the ANOVA for differences in WCST and TP performances and clinical variables such as age at onset, duration of illness and subtype.

Results

As shown in Table 1, age and educational level are significantly different between groups. Table 2 shows discriminant analysis results for SPEM and VSEM considered separately. As far as the discriminant analysis is concerned, for SPEM the percentage of correctly classified schizophrenics was 80% and controls 77%, for VSEM 76% of schizophrenics and 85% of controls. By means of the MANOVA, significant differences were found between schizophrenics and controls in WCST and TP performances. No significant difference was found between correctly and incorrectly classified schizophrenic patients by means of ANOVA for performances on WCST items (SN, TE, PE) and TP items (CI, II, T), for clinical variables (age at onset, duration of illness and subtype) between correctly and incorrectly classified schizophrenics.

Discussion

SPEM and VSEM performances discriminate schizophrenics from controls with an accuracy of at least 75%.

Table 1. Age and education in schizophrenic and control subjects

	Age m + sd	Education m + sd
Schizophrenics (27)	26.5 + 2.5	10.8 + 3.6
Controls (30)	30.6 + 7.5	17.8 + 2.6
	$t = 2.71$, $P < 0.01$	$t = 7.57$, $P < 0.001$

Table 2. Classification results

		Actual group	No. of cases	Predicted group 1	Membership 2
TP	Group NOR	1	27	27 100.0%	0 0.0%
	Group SKZ	2	30	10 33.3%	20 66.7%
	Percent of "grouped" cases correctly classified: 82.46%				
WS	Group NOR	1	27	35 92.6%	2 7.4%
	Group SKZ	2	30	11 36.7%	19 63.3%
	Percent of "grouped" cases correctly classified: 77.19%				
SPEM	Group NOR	1	27	21 77.8%	6 22.2%
	Group SKZ	2	30	6 20.0%	24 80.0%
	Percent of "grouped" cases correctly classified: 78.95%				
SACC	Group NOR	1	27	23 85.2%	4 14.8%
	Group SKZ	2	30	7 23.3%	23 76.7%
	Percent of "grouped" cases correctly classified: 80.70%				

This is quite satisfactory. Our results are consistent with previous reports in the literature (Holzman, 1987) on SPEM and VSEM performances showing significant differences between schizophrenics and controls. Our data of altered performances in SPEM show a general impairment for schizophrenics with lower gain values (Gain), lower eye velocity values (DC offset), a higher number of saccadic intrusions than controls. All of these variables were significant in discriminant analysis. These findings confirmed that the global measures of pursuit quality provide an indication that a defect exists. When the smooth pursuit system is unable to maintain an eye velocity equal to target velocity, catch-up saccades act to bring the target back on the fovea. In this case, pursuit gain is less than one. Our sample of schizophrenics shows a range of gain values from 0.32 to 0.98. These data confirm the malfunctioning of the SPEM system also when evaluated by quantitative means.

In the frontal eye field regions, two separate neuronal populations have been found; one saccade-related and one pursuit-related (Bruce, 1985; Bizzi, 1970). The pursuit-related neurons showed a steady activation during fixation of gaze.

Several findings described in the literature (for a review see Levin, 1984a) give rise to the frontal lobe hypothesis in eye movement impairment. Patients with frontal lobe lesions are unable to look away from a central target or to inhibit eye movements toward peripheral distracting targets (Buchtel and Guitton, 1980, Guitton et al. 1982). Levin supports the hypothesis that abnormal smooth pursuit eye movements patterns in schizophrenia are consistent with a dysfunction of inhibitory cortical mechanism that are involved in a dual-mode control of visual tracking and that the dysfunction may be localized in the frontal eye field in the frontal lobes. Nevertheless, failure of the smooth pursuit system can be initiated by dysfunction in any of the cortical areas involved (frontal, posterior parietal and middle temporal areas) (Thaker, 1990).

Similar findings have been obtained for the VSEM trials. Patients show a general impairment on latency time and accuracy, both significantly lower than controls. Van Gelder (Van Gelder et al., 1990) hypothesized that purposive saccaded are inappropriately produced by frontal lobe activity in the unnatural act of attempting to direct smooth pursuit by attention effort in a tracking condition. Recent results in normal subjects show an activation of the anterior mesial frontal cortex by means of scalp potentials recorded prior to saccades in relation to visual targets (Moster et al., 1990). On the other hand, data on VSEM obtained by Thacker (Thacker et al., 1990) in chronic schizophrenics showed increased distractibility and volitional saccade latency. The authors speculated that increased distractability is most probably secondary to basal ganglia and/or frontal eye field dysfunction.

SPEM correctly and incorrectly classified patients do not differ significantly in TP performances. Again, correctly and incorrectly VSEM classified schizophrenics do not show significant differences in TP performances. Therefore, it seems reasonable to exclude a direct involvement of a voluntary attentive mechanism in determining bad SPEM and VSEM performances in schizophrenics. Consequently, the data of the present experiment must be cautiously interpreted. When compared with controls, our sample of schizophrenics shows significantly worse performances on WCST. That is consistent with data reported in the literature (Weinberger, 1985). Nevertheless, correctly and incorrectly classified schizophrenic patients do not show significant differences in WCST performances.

Moreover, clinical variables such as subtype, age at onset and duration of illness are not significant in determining the performances on WCST, and correctly and incorrectly classified patients again do not differ relative to clinical characteristics. One possible hypothesis about our results could be that the complex functional structure of frontal eye movement regulation probably does not seem directly related to frontal regions involved in WCST performances. On the other hand, a frontal lobe dysfunction has been hypothesized as a possible localization for eye movement impairment. The frontal lesioned patient may show diminished capacity to actively direct and sustain attention, whether in relation to sensory-perceptual information or upon the contents of consciousness. However, frontal lesions have been seen to induce certain abnormalities of perception that cannot easily be attributed to an attention deficit (Fuster, 1989). The primary defect seems to be in organizing perception over time with the aid of properly steered and maintained attention (Luria, 1980). Along with frontal areas involved

in eye movement control, posterior parietal lobe lesions have the greatest effect on the ability to disengage from an attention focus to focus on a target.

Further, the neurophysiology of SPEM is related not only to a general frontal lobe dysfunction but also more specifically to parietal lobe dysfunction. If these were the case, our patients could show defective performances in ocular movements and neuropsychological tests, though not simultaneously. In our sample only 9 out of 30 patients were correctly classified on all the tests (SPEM, VSEM, TP and WCST) and therefore can be considered impaired relative to both neuropsychological tests and eye movements. These 9 cases do not show any difference in clinical variables when compared with the other part of the sample. The results of the present investigation therefore do not support a definite relationship between neuropsychological and neurophysiological performances in our schizophrenic sample.

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