Eur Arch Psychiatry Clin Neurosci (1994) 244:153–160

ORIGINAL PAPER

Regine Schlenker · Rudolf Cohen · Patrick Berg
Werner Hubman · Fritz Mohr · Hans Watzl · Petra Werther

Smooth-pursuit eye movement dysfunction in schizophrenia: the role of attention and general psychomotor dysfunctions

Received: 5 August 1993 / Accepted 13 June 1994

Abstract Smooth-pursuit eye-tracking performance was examined in 100 schizophrenic patients and various control groups under both attention-enhancing and attention-distracting conditions. The level of attentional demand was varied by introducing a secondary reaction time task that directed attention either toward or away from the visual-tracking target. Distraction from the target led to a significant deterioration of tracking performance in all subjects, which was most pronounced in the group of schizophrenic patients. Attention-enhancement, on the other hand, did not normalize performance in this group. In schizophrenic patients, mainly in the distraction condition, there was a moderate association between performance in tracking and tests presumably measuring prefrontal functions. Tracking accuracy from both conditions was related to general motor performance as measured by the Neurological Evaluation Scale. It was concluded that in schizophrenic patients attentional factors (distraction) may contribute to eye-tracking impairment, and that the impairment may be viewed as an aspect of general motor dysfunctions.

Key words Schizophrenia · Eye movements · Attention
Psychomotor functions · Neuropsychological tests

Introduction

There has been broad interest in the study of smooth-pursuit-eye-movement (SPEM) abnormalities of schizophrenic patients over the past two decades (Levy et al. 1993, 1994). Eye-movement disorders, particularly abnormalities of SPEM, have repeatedly been suggested as a potential biological (genetic) marker for schizophrenia (Holzman 1987; Clementz and Sweeney 1990; Iacono et al 1992). Not only has a substantial proportion (80%) of schizophrenic patients been found to show such abnormalities, but also approximately 45% of the clinically well first-degree relatives of schizophrenic patients. This is in contrast to only approximately 10% of first-degree relatives of nonschizophrenic psychiatric patients (Holzman et al. 1974). Similar results were reported by Levy et al. (1983), Siegel et al. (1984), Mather (1985), Clementz et al. (1990, 1991), and Iacono et al. (1992). The base rate for SPEM abnormalities in the general population was found to be on the order of 8% (Holzman et al. 1984). The SPEM impairment has been found to be fairly stable over time in schizophrenic patients (Rea et al. 1989; Clementz and Sweeney 1990). It has been observed in patients with remitted schizophrenia, largely independent of medication status (Campion et al. 1992). Several studies have found the probability of the occurrence of these abnormalities in schizophrenic samples to considerably exceed the rates among nonpsychotic psychiatric patients, i.e. patients with psychoneurosis, personality disorders or substance-dependence (Shagass et al. 1974; Holzman et al. 1974; Mialet and Pichot 1981; Radant and Hommer 1992; Feil and Iacono 1993). The high prevalence of SPEM abnormalities in first-degree relatives who are clinically well, and in unmedicated or never medicated schizophrenic patients (Bartfai et al. 1984; Levy et al. 1984; Spohn et al. 1988) suggests that the abnormalities are not caused by neuroleptic medication.

Another area to look for a promising candidate of a "trait" marker of schizophrenia is attentional impairment. There is an extensive literature concerned with deficits in selective attention (e.g. Nuechterlein and Dawson 1984) and in the capacity to attend to a continuous input of information over time. The latter has been studied frequently using the Continuous Performance Test (CPT), where schizophrenic patients have reliably been found to be characterized by lower sensitivity (d′) than controls. This impairment is evident regardless of clinical state, is detectable before illness onset, and is apparently inheri-

Regine Schlenker (✉) · Rudolf Cohen · Patrick Berg
Hans Watzl · Petra Werther
Department of Psychology, University of Konstanz,
Postfach 5560, D-78434 Konstanz, Germany

Werner Hubman · Fritz Mohr
Psychiatric Hospital, Haar, Germany

table (Cornblatt and Keilp 1994). Because eye tracking involves the capacity to attend to the continuously changing target position, the attentional deficits of schizophrenic patients are likely to contribute to difficulties in this task. Accordingly, SPEM performance has been shown to improve when attention is focused on the target, e.g. by reading numbers appearing on the target during tracking (Shagass et al. 1976), and introduction of distractors has a detrimental effect on tracking accuracy (Acker and Toone 1978). In the present experiment SPEM was assessed under conditions where attention-enhancement and distraction were manipulated by using a secondary reaction time task.

The neural network involved in the control of smooth-pursuit eye movements is extremely complex (Wirtschafter and Weingarden 1988) and so far little is known about the neurophysiological bases of SPEM disorder in schizophrenic patients. Furthermore, no precise measure of specific deviation in eye tracking has been established as the most informative indicator of any underlying neurophysiological process (Levy et al. 1993). Schizophrenic patients do not seem to have a general oculomotor deficit: Their saccadic reaction times tend to be in the normal range (Iacono et al. 1981; Ross et al 1988) and their optokinetic nystagmus (Latham et al. 1981) seems to be intact. On the other hand, they appear to have difficulties in the inhibition of task-irrelevant saccades during fixation (Mialet and Pichot 1981; Levin et al. 1982; Paus 1991) as well as in making saccades in the direction opposite to where a stimulus occurs (Fukushima et al. 1988, 1990). During this antisaccade task schizophrenic subjects have been found to make more erroneous saccades towards the stimulus than healthy subjects. The same response pattern has been found in patients with frontal-lobe lesions (Guitton et al. 1985). Although there is evidence for the involvement of prefrontal structures in the inhibition of task-irrelevant saccades, evidence for their role in the poor SPEM performance in schizophrenic patients has gained only indirect support thus far: Studies by Bartfai et al. (1985) and Katsanis and Iacono (1991) have reported significant correlations between a global measure of SPEM impairment and performance in tests sensitive to prefrontal functioning. A number of studies have demonstrated that schizophrenic patients perform poorly in prefrontal tasks such as the Wisconsin Card-Sorting Test (WCST). An association between poor test performance and regional cerebral blood flow (rCBF) has indicated an involvement of the dorsolateral prefrontal cortex (Weinberger et al. 1986). In the present study a series of neuropsychological tests that have been found to be sensitive to prefrontal dysfunctions was administered in order to further examine the relationship between eye-tracking accuracy and prefrontal test performance.

In order to study the association between motor coordination and eye tracking, a battery of tests was administered to measure psychomotor dysfunction and neurological signs (Heinrichs and Buchanan 1988). Although schizophrenic patients have long been known to show a wide range of abnormalities in motor functions (Manschreck 1986), we were interested in the association between oculomotor and more global movement dysfunctions. Data from schizophrenic patients were compared with those of normal controls, healthy siblings of schizophrenic patients, and alcohol-dependent patients.

Subjects and methods

A total of 100 inpatients with a schizophrenic disorder from two psychiatric state hospitals in Germany participated in the study. They were diagnosed according to DSM-III-R criteria on the basis of the Present State Examination (Wing et al. 1973). Patients were excluded from the study if they were older than 35 years, if they had been hospitalized for more than 12 months within the previous 2 years, or if they had not been engaged in some type of regular occupational or occupation-like activity during the previous year. These criteria served to exclude the most chronic deficit states and disabilities arising from prolonged institutionalization or social isolation. Patients with a diagnosed neurological disorder or with mental retardation were also excluded. Patients were tested when acute psychotic symptoms were markedly reduced and discharge from the hospital was being considered.

The mean age of the schizophrenic patients was 27.4 years (SD 4.5 years; 63% were male). They had been ill for an average of 4.8 years (SD 4.3 years) with a mean total duration of hospitalization of 8.2 months (SD 11.3 months). At the time of testing all except two patients were under neuroleptic medication. The mean neuroleptic dose was 326.5 mg CPE (Q1–Q3:200–500 mg CPE). None of the patients received lithium or benzodiazepines. Of the 100 schizophrenic patients, 10 fulfilled criteria for tardive dyskinesia (TD) according to criteria of Schooler and Kane (1982; data not considered in the following analyses). Two of the patiens were unwilling to participate in psychophysiological assessment.

A total of 58 healthy volunteers, comparable to the patients with regard to mean age and gender distribution, served as controls (54% were male; mean age 26.8 years; SD 5.6 years). None of the controls reported any history of psychiatric disorder and/or treatment. Most of the subjects were recruited from the hospital staff.

A total of 80 alcoholic inpatients of psychiatric state hospitals (age 18–50 years) who met DSM-III-R criteria for alcohol dependence also participated in the study. The time interval between detoxification and participation in the study was at least 4 weeks so that no withdrawal symptoms were to be expected. None of the patients were simultaneously taking any psychoactive drugs. The mean age was 34.5 years (SD 6.3 years), which was significantly higher than that of the schizophrenic patients (27.4 years).

Finally, a group of 40 healthy siblings of our schizophrenic patients were examined. Although all siblings of our patients were asked to participate in the study, many refused. When more than one sibling had participated only the sibling that was most comparable with the patient (according to age and gender) was considered for group comparisons. The mean age of these siblings was 26.3 years (SD 5.4 years; 42% were male). None of the siblings had any history of psychiatric disorder or treatment. For technical reasons mainly due to unrecognized failures of the apparatus data from several subjects in each group are missing. The number of subjects included in each analysis is presented in Tables 1 and 2.

Procedures

SPEM measurement

Subjects were seated in front of a CRT monitor. They were asked to place their heads on a head-and-chin rest at a distance of approximately 70 cm from the screen. They were told to keep their eyes on the target stimulus, a small dot with a diameter of 0.8 cm moving sinusoidally on a colored background (a horizontal band 1.8 cm in width across the monitor) at a frequency of 0.4 Hz. The

Table 1 Average root-mean-square-error (RMSE) scores (in degrees of visual angle) of subgroups compared under two experimental conditions and results of ANOVA

Comparison	Attention-enhancing condition		Attention-distracting condition		Groups	Conditions	Groups × conditions
	Mean	SD	Mean	SD			
Schizophrenic patients ($n = 41$) vs	1.05	0.62	2.27	1.20	$F(1,87) = 7.17$**	$F(1,87) = 92.5$***	$F(1,87) = 4.24$*
healthy controls ($n = 47$) (matched)	0.83	0.51	1.64	1.01			
Schizophrenic patients ($n = 81$) vs	1.03	0.55	2.28	1.05	$F(1,134) = 14.97$***	$F(1,134) = 142.5$***	$F(1,129) = 8.65$**
healthy controls ($n = 54$) (unmatched)	0.82	0.49	1.59	0.96			
Schizophrenic patients ($n = 27$) vs	1.09	0.71	2.30	1.10	$F(1,53) = 1.54$	$F(1,53) = 58.2$***	$F(1,53) = 0.16$
healthy siblings ($n = 27$)	0.90	0.55	2.00	1.24			
Schizophrenic patients ($n = 34$) vs	0.92	0.41	2.32	1.23	$F(1,73) = 0.28$	$F(1,73) = 82.4$***	$F(1,73) = 0.00$
alcohol-dependent patients ($n = 39$)	1.02	0.59	2.42	1.49			
Healthy siblings ($n = 33$) vs	0.92	0.56	1.95	1.19	$F(1,86) = 2.14$	$F(1,86) = 89.01$***	$F(1,86) = 1.90$
healthy controls ($n = 54$)	0.82	0.49	1.59	0.95			
Alcohol-dependent patients ($n = 22$) vs	1.08	0.68	2.15	1.43	$F(1,43) = 1.89$	$F(1,43) = 36.09$***	$F(1,43) = 0.32$
healthy controls ($n = 22$)	0.83	0.39	1.72	1.12			

* $P < 0.05$
** $P < 0.01$
*** $P < 0.001$

Table 2 Spearman rank correlation coefficients between RMSE scores and neuropsychological test performance and neurological evaluation scales. AEC attention-enhancing condition; DC distraction condition; RPM Raven progressive matrices; SOPT subject ordered pointing task; Wisconsin card-sorting task; WT Weigl test; TOL Tower of London

	Schizophrenic patients ($n = 81$)		Alcohol-dependent patients ($n = 69$)		Healthy controls ($n = 54$)		Siblings of schizophrenic patients[a] ($n = 33$)	
	AEC	DC	AEC	DC	AEC	DC	AEC	DC
Neuropsychological test scores								
RPM: standard score	−0.09	−0.15	−0.06	−0.30*	0.09	−0.29*	0.08	−0.06
SOPT: number of errors	0.14	0.08	0.21	0.41***	−0.01	0.27*	0.01	0.38*
WCST: perseverations (Milner 1963)	0.22*	0.23*	0.04	0.30*	0.02	0.25	0.17	−0.19
WCST: perseverations (Nelson 1976)	0.12	0.27**	0.17	0.25*	−0.01	−0.03	−0.06	0.06
WT: no. of categories	−0.08	−0.27**	0.00	−0.13	0.25	0.05	−0.10	−0.07
TOL: no. of optimal solutions	−0.15	−0.21	−0.04	−0.36**	−0.11	−0.25	0.06	0.00
Neurological evaluation scale								
Sensory integration	0.23*	0.29*	0.24	0.35**	0.00	0.22		
Motor coordination	0.24*	0.21	−0.15	0.23	0.07	0.18		
Sequencing of complex motor acts	0.17	0.45***	−0.04	0.30*	−0.01	0.35*		
Others	0.23*	0.29*	0.16	0.29*	−0.08	0.25		
NES total scores	0.28**	0.44***	0.09	0.44***	0.02	0.39**		

* $P < 0.05$
** $P < 0.01$
*** $P < 0.001$
[a] Neurological signs were not assessed in siblings

display subtended a visual angel of ± 10 degrees from the center. Two smooth-pursuit tasks, each lasting 60 s, were administered in a fixed order: (1) An attention-enhancing task during which the target stimulus changed color every 5–8 s requiring the subjects to press a button as quickly as possible whenever a change in color accurred and (2) An attention-distraction task during which the background (the horizontal band on which the target was moving) changed its color with the same temporal distribution as in the other task. Again, subjects had to respond to each color change with a fast button press.

Horizontal eye movements were recorded by means of an electrooculogram (EOG) with Picker Ag-AgCl electrodes placed on the outer canthi of the two eyes. For vertical eye movements and blinks electrodes were placed above and below the right eye. Both

EOG signals were filtered at a cut-off frequency of 15 Hz and high-pass filtered at 0.005 Hz. Data were digitized on line at a rate of 500 Hz.

For a quantitative evaluation of tracking accuracy root-mean-square-error scores (RMSE) were calculated as follows: For each cycle the amplitude of the horizontal EOG was calibrated to the target amplitude by minimizing the sum of the squared differences between the EOG and the target. The minimized value is the RMSE score for one cycle. This method is analogous to Iacono and Lykken's (1979) procedure of first setting the mean of the EOG to zero and subsequently adjusting the amplitude to match that of the target, but is probably more conservative, because the RMSE score is by definition the minimum possible. When blinks were detected on the vertical channel the data of the horizontal channel were not evaluated from 200 ms before to 300 ms after the blink maximum.

For technical reasons the 1st, 12th, 13th, and 24th cycle were not correctly recorded and were excluded from evaluation. The RMSE score was computed for each of the remaining 20 cycles in units of degrees of visual angle. The median of these scores was taken to represent performance of the subject in each task. With this measure singular events of extremely poor tracking are not considered, and it is thus a conservative measure of tracking abnormalities. Because RMSE quantifies the deviation between target and eye movement, higher scores represent poorer tracking quality. Although RMSE scores do not give any information about the precise nature of pursuit dysfunction (Abel and Ziegler 1988; Levy et al. 1993), it has been found repeatedly to be a reliable and differentially valid index of eye-tracking performance.

Neuropsychological tests

Four tests were selected as sensitive to prefrontal dysfunctions, measuring to various extents categorization, cognitive flexibility, and planning: the WCST (Milner 1963; Nelson 1976), the Subject Ordered Pointing Task (SOPT; Petrides and Milner 1982), the Weigl Sorting Task (WEIGL; Weigl 1941), and the Tower of London (TOL; Shallice 1982), which was used in the modified version of Röhrenbach et al. (1991). In this version for each task the balls are presented in different starting positions and must be rearranged to one given target position per series. There are two series of ten tasks each with different target patterns. As a test for general cognitive functioning the Raven Standard Progressive Matrices Test (SPM) was administered to all subjects.

Neurological evaluation and extrapyramidal side effects

Neurological signs were assessed using the Neurological Evaluation Scale (NES) by Buchanan and Heinrichs (1989). This instrument comprises four subscales, three of which are assumed to measure dysfunctions of different functional areas: Sensory Integration, Motor Coordination, and Sequencing of Complex Motor Acts. The fourth scale ("Others") comprises heterogeneous items such as reflexes, memory, synkinesis, gaze impersistence, etc. Each item is scored from 0 (normal) to 2 (maximum deviation). Video recordings of the assessments were evaluated by two independent raters. The interrater reliabilities (Spearman rank correlation) varied between $r = 0.88$ and $r = 0.99$ for the four different subscales. Within the same session neuroleptic side effects were assessed and scored on the Simpson-Angus Scale for extrapyramidal side effects (Simpson and Angus 1970) and on the Abnormal Involuntary Movements Scale (AIMS; Research Branch 1975).

Psychopathology and negative symptoms

Semistandardized clinical interviews with a minimum length of 20 min were carried out with all patients. Videotapes of these interviews were rated independently by two trained psychologists or psychiatrists on scales focusing to a large extent on negative symptoms: the Scale for the Assessment of Negative Symptoms (SANS; Andreasen and Olsen 1983), the Positive and Negative Symptom Scale (PANSS; Kay et al. 1989), and the Brief Psychiatric Rating Scale (BPRS; Lukoff et al. 1986).

Results

Quantitative assessment of SPEM

The following analyses compare SPEM performance of schizophrenic patients with the SPEM performance of the other three groups, i.e. healthy controls, healthy siblings of schizophrenic patients, and alcohol-dependent patients. Because these groups differ with regard to age and general intelligence (Raven SPM), and because these two variables correlated with SPEM performance in alcohol-dependent patients and healthy subjects ($-0.29 \leq r \leq 0.34$), separate subsamples of matched pairs corresponding in age and general intelligence were considered for these analyses. Schizophrenic patients included in these comparison of matched groups had significantly higher scores in the SPM than those who could not be matched (Wilcoxon $z = 4.22$; $P < 0.001$), but did not differ with regard to duration of illness, age, age of onset, or total duration of hospitalization (all Wilcoxon z-values < 0.90).

Means and SDs of RMSE scores and number of subjects in all subsamples are presented in Table 1. When 41 schizophrenic patients were compared with a matched group of healthy controls in a two-way ANOVA with repeated measurements on one factor the following results were obtained: (1) SPEM performance of the two groups differed significantly across both tracking conditions (F [1,87] = 7.17; $P < 0.01$), showing a poorer performance in the schizophrenic patients, (2) The difference between conditions was found to be highly significant (F [1.87] = 92.50; $P < 0.001$) with tracking better during the attention-enhancing condition and (3) According to the interaction effect groups × conditions (F[1,87] = 4.24; $P < 0.05$) the performance of schizophrenic patients is more strongly disturbed by the distracting task than the performance of healthy controls.

When the *total* group of schizophrenic patients (all patients with valid RMSE values and excluding patients with TD: $n = 81$) was compared with all normal controls (here the Raven SPM were significantly different (F[1,135] = 9.05; $P < 0.01$), the F-values for both main effects and the interaction were systematically larger (Table 1).

In contrast to these clear-cut differences comparing schizophrenic patients and healthy controls, tracking performance did not differ significantly between schizophrenic patients and matched groups of 39 alcohol-dependent patients (F[1,72] = 0.28) or 27 of their healthy siblings (F[1,53] = 1.54). There were no significant interactions between groups and conditions, indicating that the experimental manipulations had similar effects on the subjects of all groups. In addition, when siblings of schizophrenic patients and the alcohol-dependent patients were compared with healthy controls, no significant group differences emerged, although in both comparisons the performance of the healthy controls was better than

Table 3 Medians (M) and interquartile intervals (Q3–Q1) of neuropsychological tests and the neurological evaluation

	Schizophrenic patients		Alcohol-dependent patients		Healthy controls		Siblings of schizophrenic patients[a]	
	M	Q3–Q1	M	Q3–Q1	M	Q3–Q1	M	Q3–Q1
Neuropsychological test scores								
RPM: standard score	104.5	14.0	103.5	14.0	111.0	14.0	111.0	12.0
SOPT: total errors	5.5	7.0	3.5	4.0	2.0	3.0	2.0	3.0
WCST: perseverations (Milner 1963)	1.0	4.0	1.0	4.0	1.0	2.0	1.0	2.0
WCST: perseverations (Nelson 1976)	1.0	4.0	1.0	2.0	0.0	1.0	0.0	1.0
WT: no. of categories	13.0	4.0	13.0	5.0	14.0	3.0	15.0	2.0
TOL: no. of optimal solutions	13.0	3.5	14.0	2.0	14.0	3.0	15.0	3.0
Neurological evaluation scale								
Sensory integration	3.0	3.0	2.0	3.0	1.0	2.0		
Motor coordination	1.0	2.0	1.0	2.0	0.0	2.0		
Sequencing of complex motor acts	3.0	5.0	2.0	3.0	1.0	2.0		
Others	5.0	4.0	4.5	4.5	3.0	3.0		
NES total scores	11.0	11.0	11.0	9.0	6.5	7.0		

* $P < 0.05$
** $P < 0.01$
*** $P < 0.001$
[a] Neurological signs were not assessed in siblings

that of the comparison group (alcohol-dependent patients vs healthy controls $F[1,43] = 1.89$; $P = 0.18$; healthy siblings vs healthy controls $F[1,86] = 2.14$; $P = 0.15$).

In all groups tracking was found to be significantly better when the secondary task focused attention on the moving-target stimulus than when attention was distracted toward the background of the stimulus.

Correlates of SPEM performance in schizophrenic patients

With the exception of 10 schizophrenic patients with TD all schizophrenic patients who participated in the study were considered for the following analyses, with no regard to their comparability to other groups (i.e. age or performance in the SPM test). Because most variables were not normally distributed Spearman rank correlations were computed.

Demographic and anamnestic variables

Gender and age were not related to eye-tracking performance in either condition, nor were age of onset, duration of illness, or total duration of hospitalization. Correlation coefficients ranged from $r = 0.01$ (duration of hospitalization) to $r = 0.15$ (duration of illness).

Neuropsychological test performance

Correlations between eye-tracking performance and neuropsychological test scores are presented in Table 2. (For medians and ranges of the variables see Table 3.) In the attention-enhancing condition only the number of perseverative errors (Milner 1963) showed a significant positive correlation with RMSE scores from the tracking task ($r = 0.22$; $P < 0.05$). In the distraction condition both perseverative errors scores of the WCST and the number of correct categories in the Weigl Test correlated with eye-tracking performance. There were no significant correlations between eye-tracking in both conditions and performance in the Raven SPM.

Neurological Evaluation Scales

Correlations between SPEM impairment and NESs are presented in Table 2. Both tracking conditions showed positive associations with all subscales, many of which were significant. The more neurological signs found in schizophrenic patients, the poorer their eye-tracking performance.

Medication

No relationship was found in either condition between neuroleptic dosage (chlorpromazine equivalents) and eye-tracking impairment. There was no significant difference between patients receiving medication with considerable anticholinergic effects ($n = 41$) and patients without such medication ($n = 40$; $t \leq 1.59$). Correlations between SPEM impairment and ratings of extrapyramidal side effects (Simpson-Angus Scale [1970]) were positive, but only approached significance in the attention-enhancing condi-

tion ($r = 0.19$; $P = 0.09$). Correlation coefficients between side effects and the subscales of the NES ranged from $r = 0.00$ to $r = 0.15$.

Psychopathology and negative symptoms

No association was found between negative symptoms and SPEM performance: For both the total score of the SANS and PANSS as global measures of negative symptoms, positive but nonsignificant correlations were found with eye-tracking impairment ($0.14 \leq r \leq 0.20$). The total score of the BPRS as a measure of general psychopathology was not associated with eye-tracking in either condition ($r \leq 0.13$).

Correlates of SPEM impairment in other groups

Correlation coefficients (Table 2) between SPEM performance, the scores in the neuropsychological tests, and the NESs across alcohol-dependent patients and healthy controls were similar to those found in the group of schizophrenic patients. Again, SPEM impairment was found to be significantly related to poor performance in the neuropsychological tests as well as to impairments in the NES tasks. The NES performance was not assessed in the siblings of schizophrenic patients. The correlations between SPEM performance and performance in the neuropsychological tests found in this group were generally very low. The only significant correlation was obtained with the number of errors in the SOPT ($r = 0.38$; $P < 0.05$).

Discussion

Our results with a group of 81 schizophrenic patients confirm findings of previous studies that schizophrenic patients are impaired in smooth-pursuit eye-tracking relative to healthy controls. It should be noted that in contrast to many earlier studies patients with severely chronic deficit states were excluded. The difference between schizophrenic and healthy subjects was found not only in the attention-distraction condition but also in an attention-enhancing condition, when attention was focused on the target by means of a dual-task instruction. Such conditions are likely to improve performance and to reduce the differences between groups (Shagass et al. 1976; Amador et al. 1991). The severely impaired tracking performance in schizophrenic patients, during the condition in which changes in the color of the background on which the target was moving required a button press, clearly indicates that distraction can worsen SPEM performance. It is not clear whether attentional factors contributed to the poor performance in the attention-enhancing condition.

Similar to a number of earlier studies the siblings of our schizophrenic patients also showed relatively poor SPEM performance: Their RMSE scores were intermediate between those of the schizophrenic patients and the healthy controls, and did not differ significantly from the scores of either group. The effects of the experimental conditions were similar to those observed in the schizophrenic patients. We cannot exclude the possibility that some of the siblings suffered from some kind of undetected psychiatric disorder or from substance abuse. Their performance in the neuropsychological test battery was significantly better than that of schizophrenic patients and did not differ from that of the normal control group (Table 3). Correlations between RMSE scores and test performance were negligible. Thus, their reduced tracking performance is not merely a function of some generalized deficit.

Similarly, the alcohol-dependent patients in this study did not differ significantly from either schizophrenic patients or normal controls. Although Kobatake et al. (1983) reported impaired SPEM in chronic alcoholics, other studies (Radant and Hommer 1992; Feil and Iacono, 1993) did not find any significant deficit in alcohol- or substance-abusing patients. One might expect that differences between the investigated samples are responsible for these discrepancies: Patients with extensive consumption of alcohol over a period of several years are probably more impaired in SPEM performance than patients with a shorter duration of illness. In our sample of alcohol-dependent patients we found RMSE scores to be significantly associated with duration of illness ($r = 0.26$), supporting this hypothesis. On the other hand, RMSE scores were only modestly and nonsignificantly correlated with other indicators of severity of illnes such as number of former inpatient treatments ($r = 0.20$) or amount of ethanol consumed per day ($r = 0.12$). More than these variables age seems to have an important influence on SPEM performance ($r = 0.33$ in alcohol-dependent patients and $r = 0.24$ in healthy controls), and when the total group of alcohol-dependent (mean age 34.5 years) patients was compared with healthy controls (mean age 26.8 years) the group difference was highly significant ($F[1/120] = 24.68$; $P < 0.0001$). From the present data it seems premature to draw specific conclusions on the SPEM performance in alcohol-dependent patients.

In schizophrenic patients SPEM impairment was not correlated with ratings of negative symptoms and general psychopathology. This result is at variance with the study by Katsanis and Iacono (1991), who reported a substantial positive correlation with their negative symptom index of $r = 0.54$ and a negative correlation of $r = -0.43$ with their positive symptom index. The lack of a correlation in the present study may be explained by the sampling procedure, which excluded both patients with current psychotic symptoms and those with severe deficit states. Zero correlations were also obtained with anamnestic variables such duration of illness, duration of hospitalization, or age of onset. This is consistent with the findings of impaired SPEM in siblings and other first-degree relatives of schizophrenic patients possibly indicating some kind of genetic vulnerability.

In schizophrenic and alcohol-dependent patients, and to a lesser degree also in normal controls, tracking perfor-

mance during the distraction condition was significantly associated with performance in the neuropsychological test battery. Whereas in alcohol-dependent patients the correlations were comparably high for the Raven SPM and most tests purportedly measuring prefrontal functions, significant correlations in schizophrenic patients were limited to the WCST and the Weigl Sorting Task. We have no indication to what extent these correlations really point to deficiencies in prefrontal functions, because no tests were given that rely primarily on other neuropsychological functions. The results are well in line with the findings of Katsanis and Iacono (1991), who reported significant associations between RMSE scores and the WCST as well as the Verbal Fluency Task. In their study eye tracking was measured in a standard tracking task without any additional attention-enhancing or attention-distracting demands. The somewhat higher correlations with most neuropsychological test scores in the attention distraction relative to the attention-enhancing condition may be taken as an indicator that focusing attention on the target may have lessened the impact on prefrontal functions on SPEM performance. It is unclear why it is particularly the WCST (number of perseverative errors as defined by Milner [1963]) that showed the most consistent association with poor SPEM performance in schizophrenics, whereas in the other three groups the Subject Ordered Pointing Task showed the highest correlations.

Consistent associations were found between eye-tracking performance and the NES in all investigated groups. These correlations are somewhat higher in the distraction relative to the attention-enhancing condition. The highest correlation ($r = 0.45$) is found with the subscale Sequencing of Complex Motor Acts in the group of schizophrenic patients. It suggests that eye-tracking dysfunctions may be best understood not as a specific dysfunction of the smooth-pursuit system, but as part of a more general impairment of psychomotor functions – as frequently observed in many schizophrenic patients (Manschreck 1986). The consistent correlations of SPEM performance with all four subscales of the NES suggest a broad but subtle neurological deficit in schizophrenic patients interfering not only with SPEM, but also with a much broader range of psychomotor functioning. this finding corresponds with Meehl's (1990) postulate of a general neurointegrative deficit in schizophrenics. In conclusion, SPEM abnormalities in schizophrenic patients could be shown to be influenced by attentional and general psychomotor dysfunctions. It is correlated with some indicators of poor prefrontal functioning. Our results do not allow differentiation of the relative contributions of these factors.

Acknowledgements The research reported was supported by the Bundesministerium für Forschung und Technologie (BMFT), Germany. Patients were recruited from the Psychiatric State Hospitals Reichenau and Haar, both in Germany. The authors thank Christine Wahlheim, Ellen Buchholz, Christian Dobel, and Ingeborg Link for their help with data collection, inspection of raw data, and statistical evaluation.

References

Aber LA, Ziegler A (1988) Smooth pursuit eye movements in schizophrenics: What constitutes quantitative assessment? Biol Psychiatry 24:747–761

Acker W, Toone B (1978) Attention, eye tracking and schizophrenia. Br J Soc Psychol 17:173–181

Amador XF, Sackeim HA, Mukherjee S, Halperin R, Neeley P, Maclin E, Schnur D (1991) Specificity of smooth pursuit eye movement and visual fixation abnormalities in schizophrenia: comparison to mania and normal controls. Schiz Res 5:135–144

American Psychiatric Association (1987) Diagnostic and statistical, manual of mental disorders (DSM-III-R), 3rd edn, revised. American Psychiatric Association, Washington DC

Andreasen NC, Olson S (1983) Negative v positive schizophrenia. Definition and validation. Arch Gen Psychiatry 39:789–794

Bartfai A, Levander SE, Nybäck H, Berggren B, Schalling D (1985) Smooth pursuit eye tracking, neuropsychological test performance, and computed tomography in schizophrenia. Psychiatry Res 15:49–62

Buchanan RW, Heinrichs DW (1989) The neurological evaluation scale (NES): A structured instrument for the assessment of neurological signs in schizophrenia. Psychiatry Res 27:335–350

Campion D, Thibaut F, Denise P, Pottier M, Levillain D (1992) SPEM impairment in drug-naive schizophrenic patients: evidence for a trait marker. Biol Psychiatry 32:891–902

Clementz BA, Sweeney JA (1990) Is eye movement dysfunction a biological marker for schizophrenia? A methodological review. Psychol Bull 108:77–92

Clementz BA, Sweeney JA, Hirt M, Haas G (1990) Pursuit gain and saccadic intrusions in first-degree relatives of probands with schizophrenia. J Abnorm Psychol 99:327–335

Clementz BA, Sweeney JA, Hirt M, Haas G (1991) Phenotypic correlations between oculomotor functioning and schizophrenia-related characteristics in relatives of schizophrenic probands. Psychophysiology 28:570–578

Cornblatt BA, Keilp JG (1994) Impaired attention, genetics, and the pathophysiology of schizophrenia. Schiz Bull 20:31–46

Feil KJ, Iacono WG (1993) Chronic alcoholism unlikely to affect smooth pursuit eye movements in schizophrenia. Schiz Res 9:155 (abstract)

Fukushima J, Fukushima K, Chiba T, Tanaka S, Yamashita I, Kato M (1988) Disturbances of voluntary control of saccadic eye movements in schizophrenic patients. Biol Psychiatry 23:670–677

Fukushima J, Fukushima K, Morita N, Yamashita I (1990) Further analyses of the control of voluntary saccadic eye movements in schizophrenic patients. Biol Psychiatry 28:943–958

Guitton D, Buchtel HA, Douglas RM (1985) Frontal lobe lesions in man cause difficulties in suppressing reflexive glances and in generating goal-directed saccades. Exp Brain Res 58:455–472

Heinrichs DW, Buchanan RW (1988) Significance and meaning of neurological signs in schizophrenia. Am J Psychiatry 145:11–18

Holzman PS (1987) Recent studies of psychophysiology in schizophrenia. Schiz Bull 13:49–75

Holzman PS, Proctor LR, Levy DL, Yasillo NJ, Meltzer HY, Hurt SW (1974) Eye tracking dysfunction in schizophrenic patients and their relatives. Arch Gen Psychiatry 31:143–151

Holzman PS, Levy DL, Proctor LR (1976) Smooth pursuit eye movements, attention, and schizophrenia. Arch Gen Psychiatry 33:1415–1420

Holzmann PS, Solomon CM, Levin S, Waternaux CS (1984) Smooth pursuit eye movement dysfunctions in schizophrenia: family evidence for specificity. Arch Gen Psychiatry 41:136–139

Iacono WG, Lykken DT (1979) Electro-oculographic recording and scoring of smooth pursuit on saccadic eye tracking: a parametric study using monozygotic twins. Psychophysiology 16: 94–107

Iacono WG, Tuason VB, Johnson RA (1981) Dissociation of smooth-pursuit and saccadic eye tracking in remitted schizophrenics. An ocular reaction time task that schizophrenics perform well. Arch Gen Psychiatry 38: 991–996

Iacono WG, Moreau M, Beiser M, Fleming JAE, and Lin T (1992) Smooth-pursuit eye tracking in first-episode psychotic patients and their relatives. J Abnorm Psychol 101: 104–116

Katsanis J, Iacono WG (1991) Clinical, neuropsychological, and brain structural correlates of smooth-pursuit eye tracking performance in chronic schizophrenia. J Abnorm Psychol 100: 526–534

Kay SR, Fiszbein A, Opler LA (1987) The positive and negative syndrome scale (PANSS) for schizophrenia. Schiz Bull 13: 261–276

Kobatake K, Yoshii F, Shinohara Y, Nomura K, Takagi S (1983) Impairment of smooth pursuit eye movement in chronic alcoholics. Eur Neurol 22: 392–396

Latham C, Holzman PH, Manschreck TC, Tole J (1981) Optokinetic nystagmus and pursuit eye movements in schizophrenia. Arch Gen Psychiatry 38: 997–1001

Levin S, Jones AJ, Stark L, Merrin EL, Holzman PS (1982) Identification of abnormal patterns in eye movements of schizophrenic patients. Arch Gen Psychiatry 39: 1125–1130

Levy DL, Lipton RB, Holzman PS, Davis JM (1983) Eye tracking dysfunction is unrelated to clinical state and treatment with haloperidol. Biol Psychiatry 18: 813–819

Levy DL, Lipton RB, Yasillo NJ, Peterson J, Pandey G, Davis JM (1984) Psychotropic drug effects on smooth pursuit eye movements: a summary of recent findings. In: Gale A, Johnson F (eds) Theoretical and applied aspects of eye movement research. Elsevier, Amsterdam, pp 497–505

Levy DL, Holzman PS, Matthysee S, Mendell NR (1993): Eye tracking Dysfunction and schizophrenia: a critical perspective. Schiz Bull 19: 461–536

Levy DL (1994) Eye tracking and schizophrenia. Schiz Bull 20: 47–62

Lukoff D, Nuechterlein KH, Ventura J (1986) Manual for the expanded brief psychiatric rating scale (BPRS). Schiz Bull 12: 594–602

Mather JA (1985) Eye movements of teenage children of schizophrenics: a possible inherited marker of susceptibility to the disease. J Psychiatr Res 19: 523–532

Manschreck TC (1986) Motor abnormalities in schizophrenia. In: Nasrallah HA, Weinberger DR, (eds) Handbook of schizophrenia, vol 1. The neurology of schizophrenia. Elsevier, Amsterdam

Meehl PE (1990) Toward an integrated theory of schizotaxia, schizotypy, and schizophrenia. J Pers Disord 4: 1–99

Mialet JP, Pichot P (1981) Eye tracking patterns in schizophrenia: an analysis based on incidence of saccades. Arch Gen Psychiatry 38: 183–186

Milner B (1963) Effects of different brain lesions on card sorting. Arch Neurol 9: 100–110

Nelson HE (1976) A modified card sorting test sensitive to frontal lobe defects. Cortex 12: 601–614

Nuechterlein KH, Dawson ME (1984) Information Processing and attentional functioning in the developmental course of schizophrenic disorders. Schiz Bull 10: 160–203

Paus T (1991) Two modes of central gaze fixation maintenance and oculomotor distractibility in schizophrenic patients. Schiz Res 5: 142–152

Petrides M, Milner B (1982) Deficits on subject-ordered tasks after frontal and temporal lobe lesions in man. Neuropsychologia 20: 249–262

Radant AD, Hommer DW (1992) A quantitative analysis of saccades and smooth pursuit during visual pursuit tracking. Schiz Res 6: 225–235

Rea MM, Sweeney JA, Solomon CM Walsh V, Frances A (1989) Changes in eye tracking during clinical stabilization in schizophrenia. Psychiatry Res 28: 31–39

Research Branch (1975) Abnormal involuntary movement scale. Psychopharmacology 44: 907–912

Röhrenbach C, Cohen E, Matthes CG von (1991) Kognitives Planungsdefizit und Negativsymptomatik bei Patienten mit erworbenen Hirnschädigungen. Z Neuropsychologie 2: 83–90

Ross DE, Ochs AL, Hill MR, Goldberg SC, Pandurangi AK, Winfrey CJ (1988) Erratic eye tracking in schizophrenic patients as revealed by high-resolution techniques. Biol Psychiatry 24: 675–688

Schooler NR, Kane JM (1982) Research diagnoses for tardive dyskinesia. Arch Gen Psychiatry 39: 486–487

Shagass C, Amadeo M, Overton DA (1974) Eye tracking performance in psychiatric patients. Biol Psychiatry 9: 245–260

Shagass C, Roemer RA, Amadeo M (1976) Eye tracking performance and engagement of attention. Arch Gen Psychiatry 33: 121–125

Shallice T (1982) Specific impairments on planning. Philos Trans R Soc Lond B298: 199–209

Siegel C, Waldo M, Miznor G, Adler LE, Freedman R (1984) Deficits in sensory gating in schizophrenic patients and their relatives. Arch Gen Psychiatry 41: 607–612

Simpson GH, Angus JWS (1970) A rating scale for extrapyramidal side-effects. Acta Psychiatr Scand 212 (Suppl): 11–19

Spohn HE, Coyne L, Spray J (1988) The effect of neuroloptics and tardive dyskinesia on smooth pursuit eye movements in chronic schizophrenics. Arch Gen Psychiatry 45: 833–840

Weigl E (1941) On the psychology of so-called processes of abstraction. J Abnorm Soc Psychol 36: 3–33

Weinberger DR, Berman KF, Zee RF (1986) Physiologic dysfunction of dorsolateral prefrontal cortex in schizophrenia. I. Regional Cerebral Blood Flow Evidence. Arch Gen Psychiatry 43: 114–124

Wing JL, Cooper JE, Sartorius N (1973) The Present State Examination (PSE). Medical Research Council, Cambridge University Press

Wirtschafter JD, Weingarden AS (1988) Neurophysiology and central pathways in oculomotor control: physiology and anatomy of saccadic and pursuit eye movements. In: Johnston CW, Pirozzolo FJ (eds) Neuropsychology of eye movements. Erlbaum, Hillsdale, NJ pp 5–30