*Psychological Medicine*, 1997, **27**, 1411–1419. Printed in the United Kingdom
© 1997 Cambridge University Press

# Smooth pursuit eye movements in schizophrenia and affective disorder

K.-M. FLECHTNER,[1] B. STEINACHER, R. SAUER AND A. MACKERT

*From the Psychiatrische Klinik und Poliklinik der Freien Universität Berlin, Germany*

## ABSTRACT

**Background.** Smooth pursuit eye movement (SPEM) dysfunction is considered to be a promising candidate for a biological marker for genetic vulnerability to schizophrenia. There are conflicting findings regarding the question of what is exactly dysfunctional in SPEM dysfunction and what component of eye movements is really specific to schizophrenia. The purpose of the current study was to help to clarify the nature of (SPEM) dysfunction and its specificity to schizophrenia.

**Methods.** Smooth pursuit eye movements of 43 schizophrenic patients, 34 patients with major depression and 42 normal controls were examined using high resolution infrared oculography. These groups were compared on several indices of oculomotor functioning (gain, different saccadic categories).

**Results.** Schizophrenics had a significantly higher catch-up saccade rate than depressed patients and normals. The percentage of subjects with an abnormally high catch-up saccade rate defined as beyond the mean plus 2 S.D. of the normal control group was significantly higher in schizophrenics (27·9%) than in depressed patients (8·8%) and normal controls (0%). Low gain and higher numbers of intrusive saccades tended to be more prevalent in both patient groups but did not distinguish schizophrenics from depressed patients.

**Conclusions.** Low gain and high rates of intrusive saccades contribute to SPEM dysfunction in major depression. Abnormally high rates of catch-up saccades seem to be the oculomotor component in smooth pursuit, that is specific to schizophrenia.

## INTRODUCTION

Since the report of Holzman *et al.* (1973) numerous studies have demonstrated dysfunction of smooth pursuit eye movements (SPEM) in schizophrenic patients (Holzman *et al.* 1974; Mialet & Pichot, 1981; Holzman, 1987; Grove *et al.* 1992; Levy *et al.* 1993). Although SPEM dysfunction is now considered to be one of the most promising candidates for a biological marker of schizophrenia (Iacono & Clementz, 1992), several questions remain unanswered. The exact nature of SPEM dysfunctions has not been established. There is no consensus whether the dysfunction is due to a primary defect in the pursuit system, as measured by pursuit gain (ratio eye velocity/target velocity), or to saccadic intrusions or both. The issue of diagnostic specificity is not entirely resolved. Although rates of eye-tracking abnormality have generally been found to be higher in schizophrenia than in other psychiatric disorders (Iacono *et al.* 1982; Holzman 1984; Yee *et al.* 1987), there are studies that have found some measures of SPEM dysfunctions also in affective disorder patients (Couch & Fox, 1934; Shagass *et al.* 1974; Lipton *et al.* 1980; Levin *et al.* 1981; Iacono *et al.* 1982; Küfferle *et al.* 1990; Abel *et al.* 1991; Friedman *et al.* 1992). It is not well established if, or which, specific indices of oculomotor functioning (gain, different saccadic categories) are indeed specific for schizophrenia. Only a few

[1] Address for correspondence: Dr Klaus-Malte Flechtner, Psychiatrische Klinik und Poliklinik der Freien Universität Berlin, Abteilung für Sozialpsychiatrie, Platanenallee 19, 14050 Berlin, Germany.



https://doi.org/10.1017/S0033291797005709 Published online by Cambridge University Press

studies using quantification of these different parameters of eye movements have addressed this important issue. Radant & Hommer (1992) found lower pursuit gain, a higher frequency of saccades and especially catch-up saccades in schizophrenic patients compared to substance abusing patients and normals. Abel *et al.* (1991) and Friedman *et al.* (1992) reported that only the rate of catch-up saccades during pursuit of fast-moving targets distinguished between schizophrenic and affective disorder patients but neither differed from normals. Sweeney *et al.* (1994) found a higher percentage of schizophrenic patients to have elevated rates of catch-up saccades as opposed to affective disorder patients and normals. For all the other measured oculomotor parameters they did not find any support for the hypothesized specificity for schizophrenia.

After more than 20 years of research the questions of what is deviant about deviant smooth pursuit eye movements (Cegalis *et al.* 1983) and what is specific to schizophrenia remain largely unclear. To help clarify the nature of SPEM dysfunctions and its diagnostic specificity we examined pursuit gain and the different saccadic categories during smooth pursuit in schizophrenic patients, patients with major depression and normals.

## METHOD

### Subjects

The sample included 42 healthy controls (22 females, 20 males), 43 schizophrenic patients (16 females, 27 males) and 34 patients with major depression (25 females, 9 males). Seven of the depressed patients had a bipolar illness, the rest was unipolar. All patients met DSM-III-R criteria for schizophrenia or major depression (American Psychiatric Association, 1987). Exclusion criteria for all subjects were: age under 18 or above 65, history of substance dependence or recent substance abuse, signs of organic brain disease, neurological or ophthalmological illnesses, evidence of mental retardation. Control subjects were also excluded if they or their first-degree relatives had a history of psychiatric disease. After complete description of the study to the subjects, written informed consent was obtained.

Eye-movement testing and clinical assessments in patients were performed within the first days after admission to the Psychiatric Clinic of the Free University Berlin. The following clinical rating scales were used to obtain detailed description of psychopathological status: the Brief Psychiatric Rating Scale (BPRS) (Overall & Gorham, 1962), the Global Assessment Scale (GAS) (Endicott *et al.* 1976), the Schedule for the Assessment of Negative Symptoms (SANS) (Andreasen, 1984), the Schedule for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984), the Hamilton Depression Rating Scale (Hamilton, 1967), the Bech–Rafaelsen Melancholia Scale (BRMS) (Bech & Rafaelsen, 1980), the Strauss–Carpenter Prognostic Scale (Kokes *et al.* 1977), and the Rating Scale for Extrapyramidal Side-Effects (EPS) (Simpson *et al.* 1970). For every patient we obtained as accurate information as possible about previous history of medication, duration of illness, number of exacerbations and hospital admissions. Neuroleptic medication was converted into Chlorpromazine Equivalents (CPZ) (Davis, 1978). Cumulative CPZ dosages for life-time and 3 months prior to hospital admission were then calculated. Information about smoking habits were obtained since cigarette smoking has been shown to have a possible effect on SPEM performance (Thaker *et al.* 1991).

### Procedures

Subjects were seated comfortably in a quiet, darkened room and had their head fixed to a head rest in order to inhibit head movements. To induce smooth pursuit eye movements a red laser light spot moved continuously in a horizontal plane at 0·4 Hz across $\pm 10°$ of visual angle in a pendular manner. To exclude training effects subjects were not given practice trials and the light spot completed 12 pendular cycles. Calibration was done directly before and after the tracking task. Subjects were instructed to watch the target closely at all times. Eye movements were recorded with high-resolution infrared oculography (AMTech, Eye tracker 3). Data were digitized on-line at 250 Hz. Every single recording was visually inspected on the computer monitor and blinks and artefacts were cut out. We also rejected three-quarters of the first sinus because initiation of pursuit is different from maintenance of pursuit. Saccades as small as 0·2° could readily be detected.

https://doi.org/10.1017/S0033291797005709 Published online by Cambridge University Press

Recent studies have recommended the measurement of several oculomotor parameters as an index of oculomotor functioning: pursuit gain, catch-up saccades, anticipatory saccades, square-wave jerks. Pursuit gain is a measure of how accurately the eye can match target velocity during smooth pursuit and is calculated as the ratio of eye velocity to target velocity. In this study we calculated gain using data $\pm$400 ms around the point of highest velocity. This means that we cut off the end-points of the sinus, because at low velocities the variability of gain values and the risk of errors increases. We also eliminated 'pauses' after anticipatory saccades, since reduction of gain is here physiologically due to the previous saccade. For determining gain we used each point of measurement without filtering or smoothing transformation. A gain less than one means that pursuit velocity is slower than target velocity. In that case the eyes fall gradually behind the target and the resulting position error is corrected by catch-up saccades. These are fast eye movements that serve to bring the retinal image back quickly onto the fovea. They are in the direction of the target motion and take the eyes from a position behind the target to one on or near the target. Inappropriate saccades that can occur during pursuit are saccadic intrusions. They are functionally independent of the pursuit system and take the eyes off target during pursuit. The most common ones are square-wave jerks (SWJ), which are small pairs of saccades in opposite directions, separated by a normal saccadic latency of 200–450 msec. During this time, pursuit continues practically uninterrupted. Anticipatory saccades (AS) have larger amplitudes and take the eyes ahead of the stimulus. After an AS, pursuit gain values drop sharply as a result of reduced eye velocity, until the stimulus has caught up. Sometimes a back-up saccade is made after an AS.

Age correlated significantly with eye movement parameters in all three groups. Therefore multivariate and univariate analyses of covariance (MANCOVA, ANCOVA) were conducted with diagnosis and sex as independent factors, eye movement parameters as dependent variables and age as covariate. In order to compare diagnostic groups appropriate contrasts were tested. Additionally, since some of the data are supposed to violate assumptions of parametric procedures, non-parametric tests (Kruskal–Wallis and Mann–Whitney *U*) were performed using age-corrected data. *P* values were not corrected for multiple testing.

## RESULTS

### Demographic and clinical characteristics

The group with major depressive disorder had a higher mean age ($F = 28$, df $= 2$, $P < 0{\cdot}0001$; normals *v.* depressed: $t = -4{\cdot}95$, $P < 0{\cdot}0001$; schizophrenics *v.* depressed: $t = -7{\cdot}8$, $P < 0{\cdot}0001$) and contained significantly more females (Table 1) than the other groups (Pearson $\chi^2 = 10{\cdot}6$, df $= 2$, $P = 0{\cdot}005$). Analyses with the Mann–Whitney *U* test indicated that the patient groups did not differ in number of previous hospitalizations ($U = 565$, $P = 0{\cdot}6$) and number of previous manifestations of disease ($U = 491$, $P = 0{\cdot}2$). They also did not differ in the number of cigarettes smoked per day ($U = 411$, $P = 0{\cdot}3$). Schizophrenics had received a higher cumulative life-time CPZ dose than depressed patients (Mann–Whitney *U* test: $U = 468$, $P < 0{\cdot}05$, one-tailed). The mean washout period for medication for both patient groups was 61·4 days $\pm$ 39·6 (S.D.). There were 10 schizophrenic patients and four depressed patients, who had never received psychotropic medication before.

### Group differences in eye movement measures

Table 2 shows mean values of the oculomotor parameters for the three diagnostic groups.

#### *Multivariate analysis*

In the MANCOVA there was a significant main effect (Wilks' lamda) for diagnosis ($F = 3{\cdot}8$, df $= 10$, $P > F = 0{\cdot}0001$), age ($F = 6{\cdot}4$, df $= 5$, $P > F = 0{\cdot}0001$) and sex ($F = 2{\cdot}8$, df $= 5$, $P > F = 0{\cdot}02$). Schizophrenics differed from normals ($F = 6{\cdot}4$, df $= 5$, $P > F = 0{\cdot}0001$) and depressives ($F = 2{\cdot}5$, df $= 5$, $P > F = 0{\cdot}035$). The difference between normals and depressives did not reach statistical significance ($F = 2{\cdot}1$, df $= 5$, $P > F = 0{\cdot}07$).

#### *Univariate analyses*

*Catch-up saccades*

Schizophrenics had a higher rate of catch-up saccades than normals ($F = 19{\cdot}5$, df $= 1$, $P = 0{\cdot}0001$) and depressed patients ($F = 7{\cdot}8$, df $= 1$, $P = 0{\cdot}006$). The difference between normals and

https://doi.org/10.1017/S0033291797005709 Published online by Cambridge University Press

Table 1. *Demographic characteristics and clinical data*

| | Normal controls ($N = 42$) | Schizophrenia ($N = 43$) | Major depression ($N = 34$) |
|---|---|---|---|
| Age, years, M (S.D.) | 34·3 (10·9) | 30·7 (7·2) | 46·9 (11·0) |
| Females ($N$) | 22 | 16 | 25 |
| Males ($N$) | 20 | 27 | 9 |
| Life-time CPZ, M (S.D.) | | 97056 (164664) | 13182 (36080) |
| Washout period, days, M (S.D.) | | 56·6 (40·2) | 73 (34) |
| Prognostic scale, M (S.D.) | | 47·1 (11·9) | 54·5 (6·2) |
| BPRS, M (S.D.) | | 42·5 (8·7) | |
| GAS, M (S.D.) | | 38·5 (8·7) | |
| SANS, M (S.D.) | | 14·0 (4·2) | |
| SAPS, M (S.D.) | | 8·3 (3·1) | |
| HAMD, M (S.D.) | | | 18·9 (5·9) |
| BRMS, M (S.D.) | | | 18·8 (6·4) |

M, mean; S.D., standard deviation; CPZ, neuroleptic dose in chlorpromazine equivalents; BPRS, Brief Psychiatric Rating Scale; GAS, Global Assessment Scale; SANS, Schedule for the Assessment of Negative Symptoms (total of global scores); SAPS, Schedule for the Assessment of Positive Symptoms (total of global scores); HAMD, Hamilton Depression Rating Scale; BRMS, Bech–Rafaelsen Melancholia Scale.

Table 2. *Gain and frequency of saccades per minute during smooth pursuit by patients with schizophrenia, major depression and normal controls*

| Oculomotor parameter | Schizophrenia ($N = 43$) Mean S.D. | Major depression ($N = 34$) Mean S.D. | Normal control ($N = 42$) Mean S.D. |
|---|---|---|---|
| Pursuit gain | 0·91 ± 0·07 | 0·92 ± 0·08 | 0·96 ± 0·04 |
| Catch-up saccades | 109·1 ± 34·3 | 92·1 ± 27·0 | 82·5 ± 22·7 |
| Anticipatory saccades | 9·3 ± 9·0 | 7·8 ± 11·3 | 3·9 ± 7·0 |
| Back-up saccades | 5·0 ± 6·2 | 4·4 ± 8·6 | 3·1 ± 6·6 |
| Square-wave jerks | 9·6 ± 9·9 | 14·7 ± 18·3 | 9·2 ± 10·3 |

depressed patients was not significant ($F = 0{\cdot}53$, df = 1, $P = 0{\cdot}47$). The Kruskal–Wallis test for the factor diagnosis was significant ($\chi^2 = 13{\cdot}94$, df = 2, $P = 0{\cdot}0009$). The Mann–Whitney $U$ tests showed that schizophrenics made more catch-up saccades than normals ($P = 0{\cdot}0002$) and depressives ($P = 0{\cdot}019$). Depressed patients were not different from normals ($P = 0{\cdot}19$).

*Square-wave jerks*

There was a trend for depressives to make more square-wave jerks than normals ($F = 3{\cdot}67$, df = 1, $P = 0{\cdot}057$). Differences between schizophrenics and depressives and schizophrenics and normals were non-significant. There were no significant differences in the non-parametric tests between diagnostic groups.

*Anticipatory saccades*

Schizophrenics made more anticipatory saccades than normals ($F = 8{\cdot}62$, d = 1, $P = 0{\cdot}004$). Differences between normals and depressives and between depressives and schizophrenics were non-significant. The non-parametric tests yielded equivalent results.

*Back-up saccades*

Differences between groups were non-significant. The Kruskal–Wallis rank-sum test was on the border to statistical significance ($\chi^2 = 5{\cdot}7$, df = 2, $P = 0{\cdot}055$). The Mann–Whitney $U$ test indicated that schizophrenics made more back-up saccades than normals ($P = 0{\cdot}01$). All other group comparisons in non-parametric tests were non-significant.

*Gain*

Gain differentiated between schizophrenics and normals ($F = 19{\cdot}79$, df = 1, $P = 0{\cdot}0001$) and between depressives and normals ($F = 4{\cdot}24$, df = 1, $P = 0{\cdot}042$). The gain of patients was

https://doi.org/10.1017/S0033291797005709 Published online by Cambridge University Press

Table 3. *Prevalence (percentages) of eye movement abnormalities in patients with schizophrenia, major depression and a normal control group. Abnormality for every oculomotor parameter was defined as a value beyond the mean plus* 2 S.D. *of the normal control group*

| Oculomotor parameter | Schizophrenia ($N = 43$) % | Major depression ($N = 34$) % | Normal control ($N = 42$) % |
|---|---|---|---|
| Low-gain pursuit | 37·2 | 23·5 | 4·8 |
| Catch-up saccades | 27·9 | 8·8 | 0 |
| Anticipatory saccades | 11·6 | 23·5 | 7·1 |
| Back-up saccades | 7·0 | 11·8 | 7·1 |
| Square-wave jerks | 7·0 | 20·6 | 4·8 |

lower than that of normals. No significant difference was found between schizophrenics and depressives ($F = 2{\cdot}49$, df $= 1$, $P = 0{\cdot}117$). The non-parametric tests yielded equivalent results. There was a significant negative correlation between gain and catch-up saccade rate ($r = -0{\cdot}46$; $P = 0{\cdot}002$).

## Subgroups

Statistically significant differences between unipolar and bipolar depressed patients were not found for any eye movement parameter. Previously unmedicated and previously medicated patients did not differ significantly in either patient group for any eye movement parameter.

## Prevalence of eye movement abnormalities

To estimate the prevalence of pursuit dysfunction in the three groups we defined a performance of more than 2 S.D.s below (gain) or beyond (saccades) the mean of the normal control group to be abnormal. Among the patient groups prevalence rates of low pursuit gain and abnormally high frequencies of anticipatory saccades and back-up saccades were not significantly different. There was a trend for depressed patients to have an abnormally high frequency of square-wave jerks than expected compared to schizophrenics, (Pearson $\chi^2 = 3{\cdot}1$, df $= 1$, $P = 0{\cdot}077$). The prevalence of an abnormally high catch-up saccade frequency was significantly higher in schizophrenic patients than in depressed patients (Pearson $\chi^2 = 4{\cdot}4$, df $= 1$, $P = 0{\cdot}03$) and normals, see Table 3. In the group of drug-naïve patients (four depressed patients and 10 schizophrenics) no depressed patients and three schizophrenic patients had an abnormally high catch-up saccade frequency.

## Gender

In the univariate analyses the main effect for the factor sex was significant for the variables gain ($F = 5{\cdot}5$, df $= 1$, $P = 0{\cdot}02$), square-wave jerks ($F = 8{\cdot}5$, df $= 1$, $P = 0{\cdot}004$) and anticipatory saccades ($F = 3{\cdot}9$, df $= 1$, $P = 0{\cdot}05$). Females tended to have higher saccade rates and a lower pursuit gain. There was no significant effect for catch-up saccade rate ($F = 0{\cdot}2$, df $= 1$, $P = 0{\cdot}6$) and back-up saccade rate ($F = 2{\cdot}9$, df $= 1$, $P = 0{\cdot}09$). In the non-parametric tests only the difference in square-wave jerks was statistically significant ($P = 0{\cdot}004$).

## Correlation of eye movement measures with demographic and clinical factors

In the schizophrenic patients there were no significant correlations between scores for BPRS, SAPS, SANS and any eye-movement measure. GAS score and square-wave jerks correlated negatively ($r = -0{\cdot}34$; $P = 0{\cdot}03$). No other eye-movement measure correlated significantly with GAS scores. Duration of illness, number of acute manifestations of the illness, and number of previous hospital admissions did not correlate significantly with any eye-movement measure. Scores for the prognostic scale correlated negatively with catch-up saccade rate ($r = -0{\cdot}32$; $P = 0{\cdot}04$). No other eye-movement measure correlated significantly with scores for the prognostic scale. Cumulative neuroleptic dosage 3 months prior to hospital admission did not correlate significantly with oculomotor parameters but life-time neuroleptic dosage correlated with catch-up saccade frequency ($r = 0{\cdot}32$; $P = 0{\cdot}04$) and negatively with pursuit gain ($r = -0{\cdot}34$; $P = 0{\cdot}03$). Eye-movement measures

https://doi.org/10.1017/S0033291797005709 Published online by Cambridge University Press

did not correlate significantly with EPS scores, assessing extrapyramidal side effects.

In the depressed patients there were no significant correlations between scores indicating severity of psychopathology (HAMD, BRMS), duration of illness, number of hospital admissions or manifestations of illness, neuroleptic dosage and any eye-movement measure.

## DISCUSSION

Our results indicate that schizophrenic and depressed patients have a lower mean gain and a higher prevalence of a low-gain pursuit than normals. Low-gain pursuit did not differentiate between the two patient groups, suggesting that dysfunction of the pursuit eye-movement system is not specific to schizophrenia.

Although schizophrenic patients have similar gain values as depressed patients, they have markedly elevated rates of catch-up saccades. Almost 28% of schizophrenics have an abnormally high catch-up saccade frequency compared to 8·8% of depressed patients and none of the normal control group. This result is consistent with other studies (Abel *et al.* 1991; Radant & Hommer, 1992; Sweeney *et al.* 1994) that report increased rates of catch-up saccades in schizophrenia. Our findings suggest that increased rates of catch-up saccades may be more specific to schizophrenia than the other studied oculomotor parameters. Disturbances of smooth pursuit eye movements in schizophrenic patients that have been described in earlier studies using global rating scales, seem, therefore, largely due to elevated rates of catch-up saccades.

There was a trend for depressed patients to have a higher percentage of an abnormally high rate of square-wave jerks compared to schizophrenics and normals. Sweeney *et al.* (1994) found also elevated rates of square-wave jerks in bipolar disorder patients, whereas Friedman *et al.* (1992) found no significant differences between affective disorder patients, schizophrenics and normals. Since high frequencies of square-wave jerks are found in a variety of neuropsychiatric disorders (Leigh & Zee, 1991), the non-elevated rates of schizophrenic patients was unexpected. An explanation could be that the high number of catch-up saccades limits the number of other saccades because in a certain time unit there is an upper limit to the number of overall saccades that can occur (Sweeney *et al.* 1994). We found a much smaller negative correlation between rates of catch-up saccades and square-wave jerks ($r = -0{\cdot}26$; $P = 0{\cdot}09$) to support this hypothesis than previously reported ($r = -0{\cdot}42$; and $r = -0{\cdot}35$) by Friedman *et al.* (1992) and Sweeney *et al.* (1994). Our data suggest that an abnormally high rate of square-wave jerks can occur in major depression and may even be an explanation for studies reporting SPEM dysfunctions in affective disorder patients using global measures of pursuit quality.

Schizophrenics had significantly more anticipatory saccades and more back-up saccades than controls, but the two patient groups were not significantly different from each other. Although depressed patients had a much higher prevalence of an abnormally high rate of anticipatory saccades than schizophrenics, again, the difference did not reach statistical significance. Therefore, it can be concluded that the rate of anticipatory saccades is not a reliable parameter to characterize either one of the patient groups. The same can be said of back-up saccades, which are dependent upon foregoing anticipatory saccades.

Age correlated significantly with oculomotor parameters and there were significant main effects in the multivariate and univariate analyses for age and all eye-movement measures except square-wave jerks. This indicates that with a higher age of the study population lower pursuit gain and a higher saccade frequency including catch-up saccades must be expected.

In the MANCOVA we found a significant main effect for sex. The univariate analyses showed significant effects for sex in eye-movement measures except catch-up saccades and back-up saccades. In the non-parametric tests the difference between females and males was only significant for square-wave jerks. This could be interpreted in that there is a rather small difference – females tending to have a lower pursuit gain and higher saccade frequencies than males – that could become statistically significant in non-parametric tests with a larger sample size.

Other possible confounding variables are psychopathological status and medication. In neither patient group did we find statistically significant correlations across several indices of

https://doi.org/10.1017/S0033291797005709 Published online by Cambridge University Press

severity of acute psychopathology and any eye-movement measure. There was also no significant correlation between acute neuroleptic medication prior to hospital admission and any oculomotor parameter in either patient group. Previously unmedicated and previously medicated patients did not differ significantly in any eye movement parameter. Thirty per cent of schizophrenic patients who were never mediated had an abnormally high catch-up saccade frequency *versus* none of the depressives who were never medicated. This argues against a strong medication effect and underlines that an abnormally high catch-up saccade frequency may be specific to schizophrenia. Although these findings do not completely rule out the possibility that pursuit abnormality may be state-related in affective disorder (Holzman *et al.* 1984) or schizophrenia, they make it unlikely. Rather they suggest that pursuit abnormality may be largely independent of acuteness of psychopathological status and acute effects of neuroleptic medication. Cumulative neuroleptic life-time dose, though, correlated significantly with catch-up saccade rate and gain. This indicates that there could be long-term effects of neuroleptic medication on smooth pursuit eye movements, similar to tardive dyskinesia. We did not find significant correlations between eye-movement measures and scores on the EPS to support this hypothesis. But, there were also only few patients with substantial scores on the EPS, which could explain this statistically non-significant correlation. Patients with a high life-time neuroleptic dose also have a longer duration of illness, tend to have more hospital admissions, more chronic symptoms and a worse prognosis. Therefore, catch-up saccade rate and gain could also be related to 'chronicity' or an unfavourable course of the illness itself and not so much to a sole medication effect.

Although our results seem to be consistent with previous reports (Abel *et al.* 1991; Radant & Hommer, 1992; Sweeney *et al.* 1994), it is important to recognize the limitations of each study. There are only few studies using the same recording techniques, the same stimulus paradigms, the exactly same definitions for saccades and gain, and there are of course confounding variables that are always difficult to control for. One methodological problem seems to us the lack of clear and positive criteria for saccadic classification. Catch-up saccades are by definition corrective saccades that compensate for a temporary reduction in gain. The smooth pursuit system serves to hold the retinal image constantly on the fovea. Therefore, gain reduction results in an accumulating position error of the retinal image and above a certain, but unknown, threshold a corrective catch-up saccade is initiated. If the retinal image is small compared to the fovea, the eye could move without the retinal image leaving the boundaries of the fovea. If the movement of the retinal image out of the fovea is slow, the smooth pursuit system itself could compensate this movement by increasing eye velocity. There is also the possibility of smooth pursuit while the retinal image is extrafoveal. It is conceivable that the threshold for initiating a catch-up saccade may also be influenced by velocity, acceleration and direction of the retinal image movement and may even vary depending on eye velocity, acceleration and direction of eye movement. Gain reduction prior to a saccade may therefore, not always be a sufficient criterion to determine a catch-up saccade. If the retinal image is big compared to the fovea, the fovea could move within the boundaries of the stimulus. The eye movement recording systems now in use do not give absolute position co-ordinates of the eye but depend instead on calibration to determine eye position relative to stimulus position. Even if calibrations are repeated several times, small variations can occur that can let the starting point of a small saccade falsely appear to be behind or in front of the stimulus. All this renders the distinction between corrective saccades and intrusive saccades sometimes difficult and leaves room for a certain amount of subjectivity in classifying small saccades. These problems of saccade definition and assessment are also not solved by computer programs using fixed algorithms to classify saccades. We, therefore, cannot entirely exclude that some saccades that we classified as catch-up could in fact be intrusive saccades. There was a significant negative correlation between gain and catch-up saccade rate ($r = -0{\cdot}46$; $P = 0{\cdot}002$), which can be expected if gain reductions are followed by saccadic corrections. But if intrusive saccades take the eye ahead of the stimulus, this may be followed by low gain as in anticipatory saccades and would also explain such a correlation.

https://doi.org/10.1017/S0033291797005709 Published online by Cambridge University Press

Our two patient groups did not differ in gain values but in catch-up saccade rate. A large amount of falsely classified intrusive go-ahead saccades would, as a consequence, result in low gain and can, therefore, not explain this finding. Instead, the results suggest that schizophrenics have a lower threshold for generating catch-up saccades than depressives or normals. Schizophrenic patients would tolerate only smaller position errors than the other groups. This could be due to a relative failure to adjust or increase eye velocity adequately to stimulus velocity within the velocity range of the smooth pursuit system. Because of the limited ability to increase eye velocity adequately a catch-up saccade would be initiated. If so, the primary problem would be with the neural control of the smooth pursuit system. An alternative explanation could be that the problem lies with saccade generation. Levin (1984) suggested that the increase in saccades is related to a failure of the frontal lobes to inhibit saccades. A general disinhibition of saccades can be expected to result in a high number of intrusive saccades, which we did not find. But there could be a decreased inhibition or facilitation of precalculated corrective saccades in schizophrenics whenever a gain reduction occurs. The primary problem would then be with the neural mechanisms controlling the interaction of the saccadic and smooth pursuit systems.

This study was supported by Deutsche Forschungsgemeinschaft (DFG), MA 1211/2 – 1, 2. The authors thank S. Traversi for recording and processing of eye movement data. We also acknowledge our gratitude to Dipl.-Math. Martin Hellmich for his valuable statistical help.

## REFERENCES

Abel, L. A., Friedman, L., Jesberger, J., Malki, A. & Meltzer, H. Y. (1991). Quantitative assessment of smooth pursuit gain and catch-up saccades in schizophrenia and affective disorder. *Biological Psychiatry* **29**, 1063–1072.

American Psychiatric Association (1987). *Diagnostic and Statistical Manual of Mental Disorders* (*3rd edn – Revised*). American Psychiatric Association: Washington, DC.

Andreasen, N. C. (1984). *Schedules for the Assessment of Positive* (*SAPS*) *and Negative* (*SANS*) *Symptoms*. University of Iowa Press: Iowa City.

Bech, P. & Rafaelsen, O. J. (1980). The use of rating scales exemplified by a comparison of the Hamilton and the Bech–Rafaelsen Melancholia Scale. *Acta Psychiatrica Scandinavica* **62** (suppl 285), 128–132.

Cegalis, J. A., Hafez, H. & Wong, P. S. (1983). What is deviant about deviant smooth pursuit eye movements in schizophrenia? *Psychiatry Research* **10**, 47–58.

Couch, F. H., & Fox, J. C. (1934). Photographic study of ocular movements in mental disease. *Archives of Neurology and Psychiatry* **34**, 556–578.

Davis, J. M. (1978). Comparative doses and costs of antipsychotic medication. *Archives of General Psychiatry* **33**, 858–861.

Endicott, J., Spitzer, R. L., Fleiss, J. L. & Cohen, J. (1976). The Global Assessment Scale. *A procedure for measuring overall severity of psychiatric disturbance. Archives of General Psychiatry* **33**, 766–771.

Friedman, L., Abel, L. A., Jesberger, J. A., Malki, A. & Meltzer, H. Y. (1992). Saccadic intrusions into smooth pursuit in patients with schizophrenia or affective disorder and normal controls. *Biological Psychiatry* **31**, 1110–1118.

Grove, W. M., Clementz, B. A., Iacono, W. G. & Katsanis, J. (1992). Smooth pursuit ocular motor dysfunction in schizophrenia: evidence for a major gene. *American Journal of Psychiatry* **149**, 1362–1368.

Hamilton, M. (1967). Development of a rating scale for primary depressive illness. *British Journal of Social and Clinical Psychology* **6**, 278–296.

Holzman, P. S. (1987). Recent studies of psychophysiology in schizophrenia. *Schizophrenia Bulletin* **13**, 49–75.

Holzman, P. S., Proctor, L. R. & Hughes, D. W. (1993). Eye tracking patterns in schizophrenia. *Science* **181**, 179–181.

Holzman, P. S., Proctor, L. R., Levy, D. L., Yasillo, N. J., Meltzer, H. Y. & Hurt, S. W. (1974). Eye tracking dysfunctions in schizophrenia patients and their relatives. *Archives of General Psychiatry* **31**, 143–151.

Holzman, P. S., Solomon, C. M., Levin, S. & Waternaux, C. S. (1984). Pursuit eye movement dysfunction in schizophrenia: family evidence for specificity. *Archives of General Psychiatry* **41**, 136–139.

Iacono, W. G. & Clementz, B. A. (1992). A strategy for elucidating genetic influences on complex psychopathological syndromes (with special references to ocular motor function and schizophrenia). In *Progress in Experimental Personality and Psychopathology Research: Frontiers of Psychopathology*, *Vol. 16* (ed. L. J. Chapman, J. P. Chapman and D. C. Fowles), pp. 11–65. Springer: New York.

Iacono, W. G., Peloquin, L. J., Lumry, A. E., Valentine, R. H. & Tuason, V. B. (1982). Eye tracking in patients with unipolar and bipolar affective disorder in remission. *Journal of Abnormal Psychology* **91**, 35–44.

Kokes, R. F., Strauss, J. S. & Klorman, R. (1977). Premorbid adjustment in schizophrenia. Part II: measuring premorbid adjustment – the instruments and their development. *Schizophrenia Bulletin* **3**, 186–213.

Küfferle, B., Friedmann, A., Topitz, A., Földes, P., Kutzer, M. & Steinberger, K. (1990). Smooth pursuit eye movements in schizophrenia: influences of neuroleptic treatment and the question of specificity. *Psychopathology* **23**, 106–114.

Leigh, R. J. & Zee, D. S. (1991). *The Neurology of Eye Movements*, *2nd edn*. F. A. Davis: Philadelphia.

Levin, S. (1984). Frontal lobe dysfunction in schizophrenia. I. Eye movement impairments. *Journal of Psychiatric Research* **18**, 27–55.

Levin, S., Lipton, R. B. & Holzman, P. S. (1981). Pursuit eye movements in psychopathology: effects of target characteristics. *Biological Psychiatry* **16**, 255–267.

Levy, D. L., Holzman, P. S., Matthysse, S. & Mendell, N. R. (1993). Eye tracking dysfunction and schizophrenia: a critical perspective. *Schizophrenia Bulletin* **19**, 461–536.

Lipton, R. B., Levin, S. & Holzman, P. S. (1980). Horizontal and vertical pursuit eye movements, the oculocephalic reflect, and the functional psychoses. *Psychiatry Research* **3**, 193–203.

Mialet, J. P. & Pichot, P. (1981). Eye tracking patterns in schizophrenia; an analysis based on incidence of saccades. *Archives of General Psychiatry* **38**: 183–186.

Overall, J. E. & Gorham, D. R. (1962). The Brief Psychiatry Rating Scale. *Psychological Reports* **10**, 799–812.

Radant, A. D. & Hommer, D. W. (1992). A quantitative analysis of

https://doi.org/10.1017/S0033291797005709 Published online by Cambridge University Press

saccades and smooth pursuit during visual pursuit tracking. A comparison of schizophrenics with normals and substance abusing controls. *Schizophrenia Research* **6**, 225–235.

Shagass, C., Amadeo, M. & Overton, D. A. (1974). Eye tracking performance in psychiatric patients. *Biological Psychiatry* **9**, 245–260.

Simpson, G. M., Angus, C. B. & Angus, J. W. S. (1970). A rating scale for extrapyramidal side-effects. *Acta Psychiatrica Scandinavica* **211**, 111–119.

Sweeney, J. A., Clementz, B. A., Haas, G. L., Escobar, M. D., Drake, K. & Frances, A. J. (1994). Eye tracking dysfunction in schizophrenia: characterization of component eye movement abnormalities, diagnostic specificity, and the role of attention. *Journal of Abnormal Psychology* **103**, 222–230.

Thaker, G. K., Ellsberry, R., Moran, M., Lahti, A. & Tamminga, C. A. (1991). Tobacco smoking increases square-wave jerks during pursuit eye movements. *Biological Psychiatry* **29**, 82–88.

Yee, R. D., Balogh, R. W., Marder, S. R., Levy, D. L., Sakala, S. M. & Honrubia, V. (1987). Eye movements in schizophrenia. *Investigative Ophthalmology and Visual Science* **28**, 366–374.

https://doi.org/10.1017/S0033291797005709 Published online by Cambridge University Press