Exp Brain Res (1998) 120:316–324

RESEARCH ARTICLE

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Target anticipation and impairment of smooth pursuit eye movements in schizophrenia

Received: 27 January 1997 / Accepted: 26 November 1997

Abstract A reduced gain of smooth pursuit eye velocity has frequently been reported in schizophrenic patients. With respect to predictable stimuli, this could be due to a deficit in predicting the target path. To determine this contribution to smooth pursuit eye movement performance, we analyzed the ocular smooth pursuit response to a sinusoidally moving target that was suddenly stopped after some cycles of regular movement. Horizontal eye movements were recorded with infrared reflection oculography in a group of 17 schizophrenic in-patients and 16 age-matched healthy subjects for controls. The patients exhibited a reduced gain of smooth pursuit velocity, but phase lag was not different from the control group. After the unpredictable stop of target movement, predictive sinusoidal smooth pursuit was maintained for 150 to 200 ms in both groups. The resulting maximal position and velocity error was larger in the patient group. In conclusion, schizophrenic patients were able to generate a normal anticipatory component of smooth pursuit and to switch it off in response to external demands. They showed, however, an increased velocity of anticipatory pursuit, which might be used to compensate for the primary deficit of smooth pursuit velocity frequently found in schizophrenics.

Key words Smooth pursuit · Schizophrenia · Prediction · Monitor theory · Human

Introduction

Eighty-eight years after their first description (Diefendorf and Dodge 1908), global smooth pursuit eye movement (SPEM) deficits in schizophrenic patients have been outlined in numerous reports (for review, see Levy et al. 1993). Nevertheless, there is an ongoing debate about the nature and the diagnostic value of this deficit.

Apart from the hope that an identification and precise physiological description of the deficit might help to unveil brain structures involved, considerable impetus for research in this field comes from the use of SPEM impairment as a biological trait marker for genetic liability to schizophrenia in the context of vulnerability theories. Since liability to schizophrenia rather than overt manifestation of the disease is believed to be inherited, possible gene carriers who are not or not yet affected by the disease have to be identified for linkage studies. For this purpose phenotypic markers are needed, one of which could be SPEM impairment (Clementz et al. 1992; Levy et al. 1993; Arolt et al. 1996).

The ability of the SPEM system to approach and maintain target velocity with continuing stimulation by a moving target is denoted as pursuit maintenance and is measured as gain (quotient of eye and target velocity), which was reported to be abnormally low in schizophrenic patients, particularly with higher stimulus velocities (Levin 1988; Moser et al. 1990; Clementz and McDowell 1994; Schoepf et al. 1995).

Three physiological components are important for maintaining SPEM: first, target velocity on the retina (called "retinal slip velocity"); second, after SPEM initiation, an internal feedback about current eye velocity (efference copy) is added, thus creating a continuous internal representation of target motion in space (Robinson et al. 1986). Third, if the target repeats a certain pattern regularly, anticipation of the target path enables the pursuit system to further improve gain by predicting the eye movements necessary for tracking. The presence of prediction can be inferred from the absence of a phase lag between the eye and the stimulus movement or by the amount of gain improvement in comparison with a nonpredictive task. It is assumed that a predictive and a nonpredictive visually guided component add up to a resulting SPEM output, which depends on the amplitude of these components and their phase relation (van den Berg 1988).

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Most studies with schizophrenic patients have been performed with predictive stimuli oscillating horizontally with either constant or sinusoidally modulated velocity. Usually, the gain in a predictive task is lower in schizophrenic patients than in a normal population (reviews: Clementz and Sweeney 1990; Abel et al. 1992; Levy et al. 1993). An interesting result was reported by Levin et al. (1988), who found an increased latency of direction reversal during pursuit of a triangular waveform stimulus in their schizophrenic population. This was interpreted as a deficit in prediction. On the other hand, the gain improvement of schizophrenic patients in a predictive versus a nonpredictive task even exceeded the respective gain improvement in normal controls.

Studying prediction in the pursuit system of schizophrenic patients seems to be particularly important, since it constitutes the internally generated (rather than externally triggered) component of SPEM, and it is a dysfunction of internally generated actions that is believed to be crucial for the interpretation of schizophrenic psychopathology (Liddle 1995). In this respect, Frith and Done (1988) have interpreted the positive symptoms of schizophrenia in their monitor theory. This theory claims that in the human brain a hypothetical monitor registers self-intended and stimulus-evoked acts and thoughts. With a defective monitor, internally generated acts and thoughts will appear to arise from outside, thus giving rise to the phenomena of delusion and thought insertion. Experimental evidence for these ideas is provided by an impaired error correction by schizophrenic patients if the detection of an erroneous response to a stimulus cannot be achieved by external feedback but only by an internally generated copy of the response-related efferent signal (Malenka et al. 1982). Their impaired performance in such a task is explained by defective storage of this copy by the monitor. A complementary challenge for the integrity of the monitor can be constructed by presenting a regular predictable stimulus and then disturbing the regular pattern. In the regular part of the stimulus, an internal representation of target velocity is formed by adding up retinal slip velocity and an internal feedback (efference copy) about eye velocity, according to current models of the SPEM system (Robinson et al. 1986; van den Berg 1988). This internal feedback loop further includes a "lead element" for predictive information (anticipation) about the impending target path which at least in part guides eye movements by predicting the required motor commands (Fig. 1). If the target deviates from the expected path in the nonpredictive part of the stimulus, these internally generated commands give rise to an error (retinal slip velocity) is detected by visual feedback. This must lead to a stop of predictive influences on SPEM output that can only be achieved if prediction is monitored properly via the internal feedback loop, analogous to the monitor proposed by Frith and Done (1988).

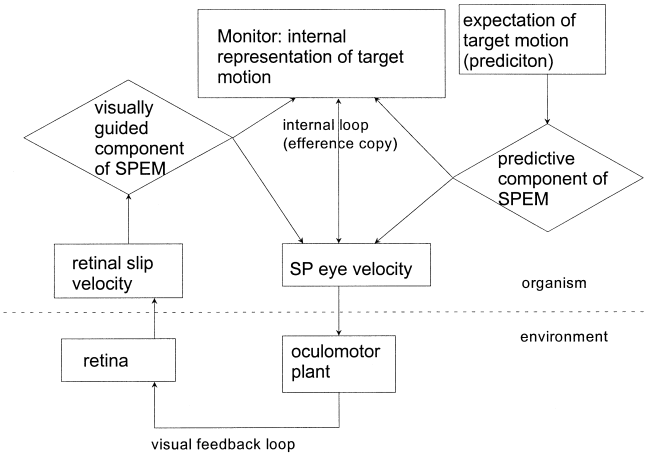

Fig. 1 Scheme of internally generated (predictive) and externally triggered (visually guided) component of smooth pursuit (*SP*) eye velocity by a hypothetical monitor. The elements of the flow chart are taken from Frith and Done (1988). Their hypothetical function has been adapted to the context of SP eye movement (*SPEM*), with the assumption of a visual feedback loop and an internal loop, according to current models of the SPEM system, such as that proposed by van den Berg (1988). The anatomical substrates of the elements in Frith and Done's model and in our proposed SPEM model do not necessarily have to be identical

For our experiment we adapted a stimulus used by van den Berg (1988) in normal subjects and applied it to schizophrenic patients. In the regular sinusoidal interval of the stimulus, measures for predictive performance (SPEM gain and phase) can be established. The nonpredictive part consists of an unexpected stop of the target. After the stop, any movement continuing beyond the delays that are commonly conceded as reaction times can be attributed to target path prediction. These continuing movements were quantified by maximal errors in eye position and eye velocity and by the latency when eye velocity starts to decline in order to match the new target velocity (v=0). With a defective monitor (internal feedback loop) these errors and the latency should be elevated in schizophrenics.

Materials and methods

Subjects

For our study, a normal control group (N; n=16) and a group of schizophrenic patients (S; n=17) were recruited. Informed consent was obtained from all participants of the study, according to the declaration of Helsinki. Diagnosis of schizophrenia was based on DSM-III-R as well as on ICD-10 by an experienced examiner who also applied the rating instruments reported in Table 1. Eight patients were diagnosed to suffer from paranoid, 7 from undifferentiated and 2 from residual schizophrenia. Fourteen patients were on neuroleptic treatment, 2 were on additional anticholinergic medication. No patient received anxiolytic drugs.

Since eye velocities after the unpredictable stop were likely to depend on the eye velocity before this stop, a subgroup "schizophrenic group with high gain" (SHG) was selected from S that was appropriate for comparison with N with respect to smooth pursuit gain. In SHG (n=9), the mean gain ranged between 0.945 and 1.056, which corresponded to the range measured in N. Thus, N and SHG exhibited identical overall predictive pursuit performance. The rationale for the selection of this subgroup is pointed out in greater detail in the Discussion.

Demographic data of the groups are given in Table 2. Group N did not differ significantly in age or distribution of gender from groups S or SHG (*t*-test, χ^2-test).

Recording of eye movements

Horizontal eye movements were recorded using infrared reflection oculography (Eye-Tracker; Amtech), which measures the position of the center of the subject's pupil with a linear output up to 20° deflection from primary position (Katz et al. 1987). Positive eye-position signals corresponded to deflection to the right. The eye-position signal was digitized at a frequency of 200 Hz and stored on hard disk for off-line analysis.

Measurements were performed in a dark and quiet room with the subject's head fixed by a head holder and a chin rest at a distance of 116 cm from a tangent white screen on which the target was marked by a laser spot of 0.5° diameter. The stimulus was presented once to every subject to exclude any anticipation of the unexpected event.

Stimulus

The target was visible during the whole trial and performed horizontal sinusoidal oscillations with an amplitude of ±14.1° and a frequency of 0.30 Hz (corresponding to a period of 3.3 s for one cycle). After 4.25 cycles (predictable part), the target stopped at its extreme position for half a cycle (perturbation of predictable pattern) and then continued with the sinusoidal movement. Hence, the unexpected target stop occurred at zero velocity when the target velocity changed direction. Maximum velocity of the stimulus was 26.2°/s, maximum acceleration was 4.87°/s^2. Target position and velocity as a function of time are shown in Fig. 2.

Analysis of data

The eye position recordings were analyzed if at least for one eye the segment following the unpredictable target stop was free of artifacts. Calibration of the device was performed with saccades of known amplitude. Saccades interrupting pursuit were identified using the commercially available program EYEMAP (version 2.0, Amtech). The program uses a velocity criterion (change of velocity by more than 40°/s in 5 ms) and checks additional criteria (amplitude of an assumed saccade more than 0.2°, saccade peak velocity less than 1000°/s). The identified saccades were checked interactively by visual inspection. In the unsmoothed eye position traces, maximal position error in the unpredictable segment was determined. Then data were smoothed with a sliding average procedure with Gaussian weight function (full width of half-maximum 20 ms) and differentiated.

Velocity gain was determined in time windows of 1400 ms centered at the maxima of the target velocity by dividing the mean eye velocity by the mean target velocity in these intervals. Eye and stim-

Table 1 Psychopathology data (median and range) of patients [*S* schizophrenic patients, *SHG* schizophrenic patients with normal gain, *SANS* scale for the assessment of negative symptoms (Andreasen 1983), *SAPS* scale for the assessment of positive symptoms (Andreasen 1984), *BPRS* brief psychiatric rating scale (Overall and Gorham 1962), *AIMS* abnormal involuntary movement scale (National Institute of Mental Health 1975), *ESE* extrapyramidal side effects (Simpson and Angus 1970)]

Scale	S		SHG	
	Median	Range	Median	Range
SANS	33	24–40.75	35	29–48.5
SAPS	8.5	0.5–22	9	1–25.5
BPRS	31.5	28–41	28	25–45
AIMS	0	0–0	0	0–0
ESE	0	0–14	0	0–14

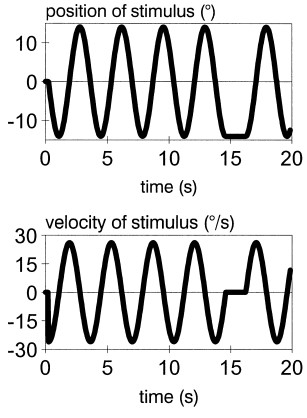

Fig. 2 Stimulus position and velocity. *Positive ordinates* correspond to rightward deflection of the target and to target movement to the right, respectively

Table 2 Demographic data of groups examined (*N* normal controls, *S* schizophrenic patients, *SHG* schizophrenic patients with normal gain)

Subjects (*n*)		N 16	S 17	SHG 9
Age (years)	Mean±SD Range	28.1±4.7 20–39	32.5±10.0 19–64	27.7±7.7 19–47
Sex	M F	12 4	11 6	6 3
Duration of illness	Median Range		7.45 0.25–27	6.5 3–27
Neuroleptic medication in milligrams chlorpromazine equivalent	Median Range		163 0–770	200 0–660
Medication state not reported			1	0
Patients on atypical neuroleptic medication (Clozapine, Zotepine, Risperidone)			6	2
Patients without any treatment			4	3
Patients on additional antiparkinsonian medication (Biperiden)			2	0

ulus velocities during saccades were excluded from this calculation, as well as eye velocity data within the 1st half-cycle of sinusoidal smooth pursuit.

Using a least-square algorithm, a sine function was fitted to the eye velocity data in the 4 predictable cycles to determine the phase relation between eye velocity and target velocity. Phase data will be given in degrees, 360° corresponding to 1 cycle and a positive phase indicating a phase lag. Again, eye velocities and target velocities during saccades were ignored in the fit process.

In the nonpredictable segment, the velocity maximum was characterized by its velocity and its latency with respect to the sudden stop of target motion. Further, the latency of the change of SPEM direction was determined.

Eye velocities were averaged data point by data point across each group in a time window of −100 ms to 900 ms with respect to the unexpected target arrest and compared between the two groups of subjects as well as with the expected stimulus velocity. Data from saccades were excluded from the averaging.

In order to assess the influence of oscillations of the velocity trace, Fourier analysis was performed within a time window of 640 ms after the target stop, and the spectrum was compared between the groups. Further, a low-pass filter with a cut-off frequency at 3.9 Hz was applied. The filter had a length of 397 data points. The attenuation beyond the transition region (2.9–4.8 Hz) was at least 44 dB, the maximal attenuation below 2.9 Hz was 0.054 dB. For the filtering process, eye velocity during saccadic intrusions was interpolated linearly from the velocity immediately prior to and after the saccade.

Statistical analysis

For normally distributed variables, Student's *t*-test was applied and Wilcoxon's *U*-test otherwise. For the analysis of phase data and the comparison of mean eye velocities with expected stimulus velocities, a single-sample *t*-test and Wilcoxon's matched-pairs test were used, respectively. A level of 0.05 was chosen as cutoff for significance; if (as for velocity variables) both S and SHG were compared with N, Bonferroni correction was applied.

Results

Predictable stimulus part

The range of the mean SPEM gain in groups N and S overlapped considerably (Fig. 3). However, eight patients exhibited a gain below the range of normal controls. Accordingly, mean gain was significantly reduced in S as compared with N (means 0.987± 0.033 vs 0.923±0.097; P=0.02, *t*-test). This was associated with a significant increase in the cumulative amplitude of saccades interrupting pursuit (mostly catch-up saccades) in S (6.3±2.2° vs 10.6±5.8° during 1 cycle of target movement; P=0.01, *t*-test). In both N and S there was no significant phase shift with respect to the stimulus (N: −0.1°±1.7°, P=0.81; S: −0.36°±2.4°, P=0.43, P for single-sample *t*-test). In order to exclude a phase shift immediately prior to the unpredictable target stop, we determined the latency when eye velocity crossed zero with respect to the time when the target stopped. This latency did not significantly differ from zero (N: 12±38 ms, P=0.24; S: 7±38 ms, P=0.49, single-sample *t*-test), so there was no phase shift at that moment in either group.

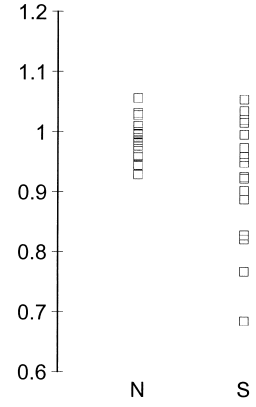

Fig. 3 Scatter of mean smooth pursuit gain in normal controls (*N*) and schizophrenic patients (*S*)

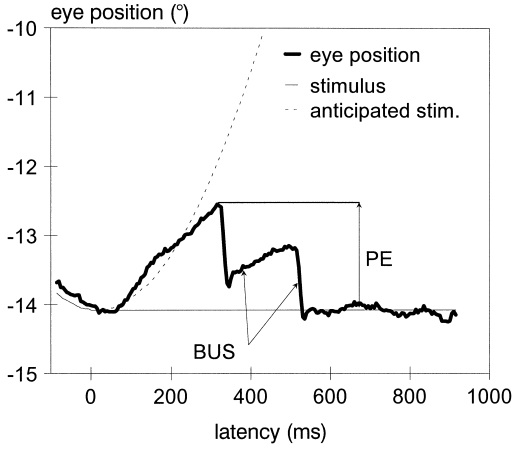

Fig. 4 Eye position trace of a normal subject in response to the unpredictable target stop. Latency is given with respect to the unpredictable target stop. The arising position error is corrected by two back-up saccades (*BUS*). The position error (*PE*) reaches a maximum prior to the first back-up saccade

In summary, in the predictable part of our stimulus, the schizophrenic patients showed a deficit in SPEM gain without any apparent deficit in prediction.

Nonpredictable stimulus part

After the target stopped in its left extreme position, both normals and schizophrenic patients continued to move rightward, thus pursuing the expected target movement. The resulting deviation of eye position from target position was corrected by 2–3 back-up saccades and usually reached its maximum just before the first back-up saccade (an example for an eye position trace is plotted in Fig. 4; the eye velocity for the same subject is plotted in Fig. 5). This maximal position error after the target stop was significantly larger in S than in N (1.83±0.48° vs 1.52±0.27°; P=0.02, *t*-test). The latency of the first back-up saccade after the target stop was not different between the groups [307±111 ms (N) and 329±117 ms (S)]. Therefore, there was a larger position error in the schizophrenic group that

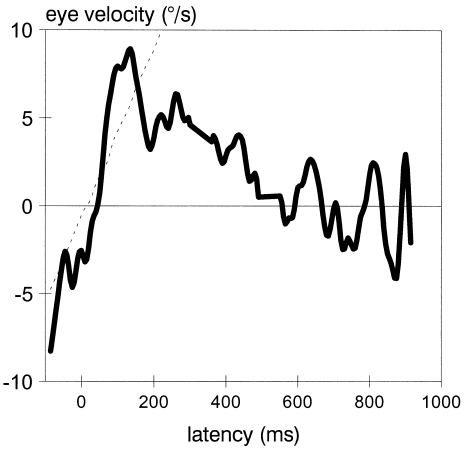

Fig. 5 Eye velocity trace of a normal subject in response to the unpredictable target stop. Latency is given with respect to the unpredictable target stop. Note the onset of oscillations with termination of pursuit

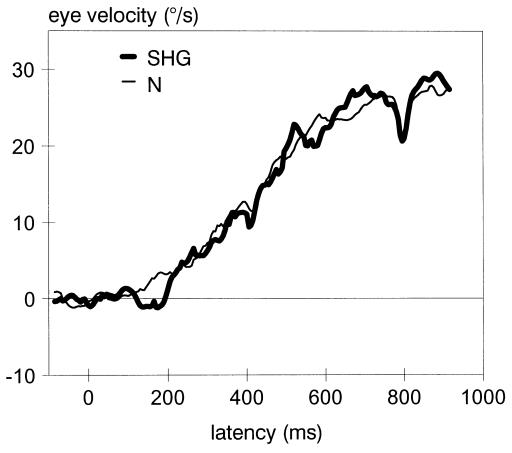

Fig. 7 Deviation of the mean unfiltered eye velocity in groups SHG and N from the velocity of the expected stimulus. Latency is given with respect to the unpredictable target stop. A significant deviation is visible after 210 ms for group SHG and after 150 ms for N

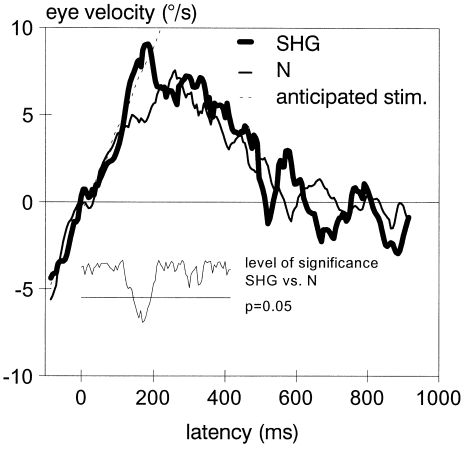

Fig. 6 Mean unfiltered pursuit eye velocity in groups N and schizophrenic patients with normal gain (*SHG*) after the sudden stop of target motion (at 0 ms). The significant difference 145–190 ms after target stop is indicated by the *inserted curve*

was not due to a delay in saccadic reaction, but to an alteration of SPEM before the first back-up saccade.

After the target stop, which occurred when target velocity was expected to increase above zero, eye velocity increased, reached a maximum, and then dropped to zero. The latency of this maximal eye velocity did not differ significantly between the groups [211±62 ms (N), 238±100 ms (S)]. But although schizophrenic patients (S) had reduced eye velocities in the predictive part (as indicated by the reduced gain), their maximal eye velocity after the target stop (denoted as "velocity error") was significantly larger than in the normal control group (11.52±3.04°/s vs 8.91±2.08; $P<0.01$, *t*-test).

For further analysis of this enlarged velocity error, we averaged the eye velocity traces across subjects within each group (Fig. 6). Since a reduced gain in the predictable part reflects a reduced eye velocity, we selected the schizophrenic subgroups SHG whose predictive SPEM gain was comparable with that of the controls, as was explained in the Materials and methods section. Therefore, by comparison of N and SHG, differences in reaction to the target stop can be demonstrated for individuals with identical predictable persuit performance.

There were no differences between the groups during the deceleration phase following the velocity maximum, and significant velocity differences were confined to an interval between 145 and 190 ms after the target stop (Fig. 6). The mean velocity trace of group N starts to deviate significantly from the expected target path; there is a first significant deviation from the expected target path 150 ms after the target stop (assessed by a *U*-test with $P=0.05$ as criterion of significance). This deviation is caused by a reduced increase in the eye velocity, which amounts to approximately 50% of the expected increase. About 260 ms after the target stop a maximum is reached and eye velocity declines to zero. In group SHG, the eye velocity does not deviate from the expected target velocity until 210 ms after the target stop, and the first significant deviation coincides with the beginning of the decline to zero. For illustration, differences between averaged eye velocities and expected target velocity are plotted in Fig. 7.

To exclude the possibility that the velocity differences between the groups were due to oscillations of the eye velocity around the target velocity, which were visible for both patients and controls (Fig. 5), we applied Fourier analysis to the velocity signal for a time window of 0–640 ms with respecto to the target arrest. There were no significant differences between the groups for the spectral power at frequencies above zero. The frequency of the oscillations ranged around 5 Hz.

We further eliminated the oscillations by low-pass filtering with a cuttoff frequency of 3.9 Hz, which still left a significant difference in maximum velocity error between groups N and SHG [7.1±1.2°/s (N) vs 8.8±1.4°/s (SHG);

$P<0.02$ after Bonferroni correction, U-test]. Latencies with respect to onset of perturbation did not differ between the groups (255 ms for N, 278 ms for SHG).

Therefore, schizophrenic patients showed a significantly increased velocity error after a sudden target stop which was more pronounced in patients with a normal overall gain in a predictable tracking task than in those with an abnormally low gain. Since there were no differences in latency, this cannot be attributed to a delayed switch-off of predictive pursuit but rather to an altered tracking behavior before this switch-off.

Discussion

Our experiment was designed to assess the role of predictive mechanisms in the context of SPEM impairment in schizophrenic patients. In the field of SPEM, these mechanisms represent an example of self-generated mental activity. The initiation and monitoring of self-generated mental activity is considered to be affected in schizophrenia, and this deficit seems to be central for the understanding of the psychopathology of this condition.

In the predictable part of our stimulus, we assessed the presence and quality of the predictive component of SPEM. After perturbing the predictable pattern, we determined errors caused by further adherence to this pattern.

We found a weak impairment of predictive SPEM in group S. For sinusoidal tracking tasks, maximal target acceleration is believed to be the critical parameter determining velocity gain (Lisberger et al. 1981). As the maximal acceleration of our stimulus is relatively low (48.7°/s^2), this might explain why gain differences were only moderate. The large variance within group S points to a heterogeneity of our schizophrenic sample, which did not correlate with the dose of their neuroleptic drugs, thus being not due to medication effects. However, we did not include a sufficient number of subjects to perform a mixture analysis as reported by Ross et al. (1996), Sweeney et al. (1993), and others.

The nonpredictive visually guided component of SPEM always exhibits a considerable phase lag with respect to the stimulus (Levin et al. 1988), which is in principle caused by the delay of approximately 150 ms accompanying afferent and efferent conduction and central computational mechanisms necessary for SPEM. Therefore, the absence of any significant phase lag of eye velocity clearly indicates an adequate predictive component of SPEM for both groups. Considering predictive eye movements as a model for the initiation of self-generated mental activity, we conclude that for our schizophrenic group no impairment of this psychological subfunction was detectable.

Note that Ross et al. (1996) reported a significant phase lag in their schizophrenic patients tracking a 0.3-Hz sinusoidal stimulus. However, this phase lag of approximately 1° is in the same order of magnitude as the insignificant phase lead we found and corresponds (at a stimulus frequency of 0.3 Hz) to delays of 0.9 ms, which is still very small compared with the 150 ms mentioned above. For predictable triangular stimuli, the phase relation between stimulus movement and eye movement is commonly determined as latency of the direction reversal of eye velocity with respect to that of stimulus velocity. Levin et al. (1988) reported this latency to be increased in schizophrenic patients and concluded that prediction was deficient in their patient. However, in triangular stimuli, there is no deceleration prior to the inversion of target motion (as in sinusoidal stimuli), and prediction must rely on memorization of the global target pattern, particularly the timing of the turning points. Therefore, prediction of triangular stimuli might be more difficult than prediction of sinusoidal stimuli. There is, however, no doubt that the patients in Levin's study used prediction, since they showed a substantial gain improvement in predictive compared with nonpredictive tasks that even exceeded the gain improvement in normal controls.

To separate visually guided and predictive nonvisually guided components of SPEM, various methods have been proposed: Becker and Fuchs (1985) switched off the target in a predictable constant velocity paradigm. They found eye velocity to decrease 190 ms after blanking, until after 280 ms a stable velocity is reached, corresponding to a gain of 40–55%, which can be maintained for 1 s and longer. Therefore, roughly 50% of smooth pursuit eye velocity can be assumed to be caused by predictive mechanisms.

The influence of target switch-off can be avoided if the target is foveally stabilized by a feedback mechanism that drives target position by the measured eye position signal (van den Berg and Collewijn 1987). Since under this condition there is no retinal slip serving as input for the SPEM system, the isolated contribution of prediction can be analyzed. However, this would require head fixation by a bite bar (which was refused by most patients) or recording with a magnetic search-coil system, in order to provide a sufficient quality and stability of the eye position signal for retinal stabilization.

A simpler approach to identify predictive components of SPEM is to bring predictive and stimulus-guided influences on pursuit output into conflict. This can be achieved by a target that unexpectedly stops. Any movement continuing beyond the delays that are commonly conceded as reaction times will then be due to prediction of the target path.

In our paradigm, both normal controls and schizophrenic patients continued to pursue the expected target trajectory after perturbation of the predictable stimulus pattern, thus generating an increasing deviation of eye position from target position, which reached a maximum that was significantly larger for schizophrenic patients than for normal controls. This was caused by a corresponding difference in eye velocity before this event: After target arrest, eye velocity continued to increase matching the expected target velocity, until a maximum was reached. Inversion of eye acceleration corresponds to the velocity maximum and can be considered as reaction time of the pursuit system to the unpredictable target stop

(van den Berg 1988). It marks the moment when for the first time sensory influences outweight influences of prediction. This switch-off of pursuit is believed to be generated by a fixation system different from the pursuit system (Luebke and Robinson 1988).

In his experiment, van den Berg (1988) found this switch-off after a latency of 180 ms for target frequencies of above 0.4 Hz. Since for decreasing frequencies an increase in latency was observed, this is in reasonable agreement with a mean latency of 210 ms (stimulus frequency 0.3 Hz) in our group N. The maximum velocity error of ca. 7°/s in this study is below our result of 8.9°/s. Note, that this discrepancy is explained by the maximal stimulus velocities in the predictive parts, which were lower in his stimulus (18°/s vs 26.2°/s). This finding supports the assumption that velocity errors in the unpredictable part increase in proportion with the eye velocities achieved in the predictable part. Therefore, the subgroup SHG had to be selected to meet the predictive performance of N.

The maximum velocity error is clearly increased in group S with respect to normal controls, but there was no difference in latency. This is surprising, since the reduced gain in group S should rather imply a reduced velocity maximum. For the subgroup SHG the increased velocity error was significant even after low-pass filtering.

We performed this additional analysis of data with low-pass filtering of the velocity signal, since eye velocity oscillated around target velocity in both groups, which rendered the identification of the maximal velocity error more difficult. Similar oscillations are well known during ongoing pursuit (Goldreich et al. 1992) and seem to be caused by gating of spontaneous instabilities of the pursuit system. However, they are uncommon after pursuit termination by fixation. In fact, their absence proves that fixation is not a pursuit with zero velocity (Luebke and Robinson 1988). Van den Berg (1988) , from whom we adapted our stimulus, did not report any oscillations in his velocity recordings. Since the search coil technique employed by him offers a signal-to-noise ratio superior to ours, the significance of the oscillations in our data remains unclear. However, in the relevant interval of 640 ms following the target arrest, the amplitude of oscillations did not differ between the groups.

We conclude that the increased velocity error of schizophrenic patients is not caused by delayed switch-off of predictive pursuit but rather by an altered tracking behavior before this switch off. A number of effects could contribute to this altered tracking. There could be an impaired perception of stimulus velocity relative to predicted velocity. This is unlikely, since the delection of a serious difference between these two velocities must trigger the switch-off of predictive pursuit, and there is no difference in latency for this switch-off between the groups. For the same reason, improper control of the predictive component by the monitor is unlikely.

In N, the mean eye velocity shows a decreased slope after a latency of 150 ms with respect to target arrest (Fig. 6). This latency corresponds to the known latency

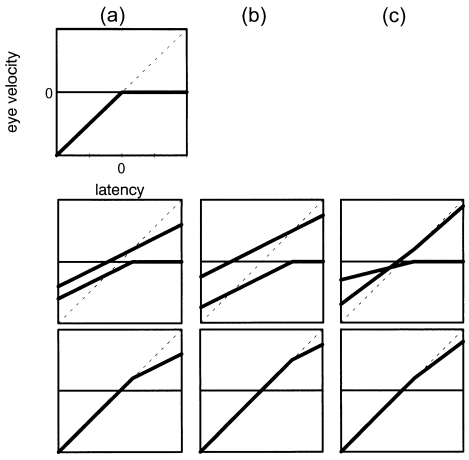

Fig. 8a–c Velocity traces of predictive and nonpredictive components of SPEM around the unpredictable target stop under various conditions. *First row* Stimulus (*solid line*) and expected stimulus (*dashed line*). *Second row* Expected stimulus (*dashed line*) predictive component (*solid straight line*) and visually guided component (*solid curved line*). *Last row* Expected stimulus (*dashed line*) and sum of predictive and nonpredictive components (*solid line*). *First column* **a** Normal situation: the gain of each component is 0.5. *Second column* **b** Increased phase lead of the predictive component to compensate for a delay of the visually guided component. This results in a delayed deviation from the expected path. *Last column* **c** Increased gain of the predictive component resulting in a weak deviation from the expected path after a normal delay. This was the case in group SHG

of the SPEM system to react to a retinal velocity error. The change of slope suggests that pursuit velocity is influenced by visual input resulting in a compromise between prediction and visual input in N until – after a further delay of 110 ms – pursuit velocity declines, indicating its switch-off in favor of fixation. In SHG, no change of slope is observed within a latency of 210 ms after the target arrest, suggesting that in this interval there is no visible interaction of the predictive component and the external, visually guided component (retinal slip) in group SHG.

There are two possible explanations for this finding, which are illustrated by Fig. 8: Consider Fig. 8a showing a stimulus with uniformly increasing velocity and assume that a stable predictive component contributing to SPEM output has been established. Suppose that the visually guided component is characterized by gain g_v and delay Δ_v and denote the corresponding properties of the predictive component by g_p and Δ_p. If tracking velocity is perfectly matched with target velocity, then $g_v\,\Delta_v = g_p\,\Delta_p$ and $g_v + g_p 1$. Note, that a delay Δ_v must be compensated by a lead Δ_p to have no delay in the output. Clearly, a deviation from the predicted path is visible not before Δ_v.

If Δ_v exceeds the reaction time of the fixation system, only the switch-off of pursuit and no superposition of predictive and nonpredictive components is visible (Fig. 8b). However, for pursuit initiation from fixation, Clementz and McDowell (1994) as well as Schoepf et al. (1995) reported mean Δ_v of maximal 170 ms (as compared to ca. 150 ms for normal controls), whereas the switch off of

pursuit occurred at 210 ms in our mean velocity data. Therefore, prolonged reaction times for the visually guided component of pursuit do not seem to account for the observed effect.

A more probable explanation is that the gain of the visually guided component is low as a consequence of the schizophrenic SPEM deficit. Then, the deviation from expected path due to correction by visually guided influences is small (Fig. 8c) or even absent. If the gain of the visually guided component is low and g_p is near 1, tracking is based almost exclusively on prediction, which could be interpreted as a compensatory strategy to overcome the deficit of the visually guided component. This is an attractive hypothesis, because it explains why, particularly, schizophrenic patients with normal SPEM gain adhere to the predictive pattern.

The results presented above as well as those reported by others do not provide an obvious clue to a brain region affected in schizophrenia. In general, involvement of frontal structures is assumed. There is some evidence from deficits in the saccadic system (impaired performance in oculomotor delayed response tasks; increased number of express saccades) pointing to the dorsolateral prefrontal cortex (DLPC; Park and Holzman 1992; Clementz 1996), which is supported by a positron emission tomography (PET) study by Liddle et al. (1992). However, Heide et al. (1996) demonstrated that focal lesions in this brain region do not alter SPEM performance. In contrast supplementary motor area (SMA) lesions did affect prediction of target reversals during pursuit of a triangular stimulus pattern, in accordance with recent primate data (Heinen 1995).

In particular, this is an important result, since hypothetical deficits in prediction as assessed by a reduced number of anticipatory saccades during pursuit have been attributed to the involvement of the DLPC in schizophrenia (Allen et al. 1990). These findings should rather be interpreted as a deficit in generating anticipatory saccades (as reported by Hommer et al. 1991) and not as a deficit of the predictive component of SPEM, which seems to be unimpaired according to our results. In conclusion, if there is involvement of the DLPC in schizophrenia, this involvement is probably not responsible for the SPEM deficit of these patients. Recently, two clinical lesion studies have shown that lesions of the frontal eye field (FEF) predominantly reduce ipsiversive smooth pursuit gain without leading to an excessive phase lag (Heide et al. 1996; Lekwuwa and Barnes 1996). In accordance with this, a PET study in schizophrenics (Ross et al. 1995) revealed decreased glucose utilization in the FEF, associated with abnormal SPEM. However, whether schizophrenia really causes dysfunction of the FEFs needs to be evaluated by future studies.

In summary, schizophrenic patients were able to create an adequate predictive component of pursuit, although their overall pursuit gain was diminished. They were able to switch off this predictive component after the detection of an unexpected stop of the otherwise regular trajectory without any significant difference in latency compared with normal controls. This points to adequate monitoring of the predictive component in the context of the monitor theory. However, there is evidence that schizophrenic patients rely more heavily on prediction than normal controls, thus compensating for their deficient visually guided component of SPEM.

Acknowledgements This research was supported by the Deutsche Forschungsgemeinschaft (grant Ar 234/1-1).

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