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Smooth pursuit eye tracking over a structured background in first-episode schizophrenic patients

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Abstract Whilst most laboratory smooth pursuit tasks are performed in the dark, in everyday life pursuit commonly occurs over a structured background. This background provides a powerful stimulus to the optokinetic reflex (OKR), inducing a background "drag" on pursuit eye movements. An inability to inhibit the influence of the OKR may be a contributing factor to the dysfunctional pursuit performance observed in many schizophrenic patients. Smooth pursuit performance was measured in 23 first-episode schizophrenic patients and 23 healthy controls matched for age and estimated IQ, both in the dark and over a structured background (a random checkerboard of black and white squares). Velocity gain was measured, as well as the number and size of corrective saccades (catch-up saccades) and intrusive saccades (anticipatory saccades and square wave jerks). Overall, schizophrenic patients had lower velocity gain and made more catch-up saccades than controls. The effect of the background was to lower velocity gain and increase the number of catch-up saccades to the same extent in schizophrenic patients and controls. There were no significant interactions between group and background effect. These results suggest that, although their overall level of performance was worse, the schizophrenic patients were as able as controls to inhibit the effect of the OKR. Since lesion studies show that inhibition of the OKR requires intact inferior parietal regions in man (Lawden et al., 1995), one hypothesis is that the parietal component of smooth pursuit may be intact in schizophrenia.

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Introduction

Eye movements can be broadly categorised as either fast saccadic movements, which serve to foveate an object of interest, or slower smooth pursuit movements, which allow the object to remain foveated should it begin to move. Abnormal smooth pursuit eye tracking has emerged as a consistent finding in schizophrenia (see Hutton and Kennard 1998 for a review) and has been observed in drug naïve first-episode patients, chronically medicated patients and the first degree relatives of schizophrenic patients (Hutton et al. 1998; Friedman et al. 1995; Grove et al. 1992).

However, the neurobiological basis of smooth pursuit abnormalities in schizophrenia has not been fully elucidated. Early research tended to rate smooth pursuit performance qualitatively, and consequently researchers were unable to distinguish between abnormalities *of* pursuit and abnormalities *during* pursuit (Abel & Ziegler 1988). The smooth pursuit and saccadic systems operate together interactively during pursuit. If the eye lags behind, or moves ahead of the target, corrective catch up (CUS) or backup (BUS) saccades are initiated which serve to bring the target back onto the fovea. However, other saccades occur during smooth pursuit which are intrusive, rather than corrective. The most common are square wave jerks (SWJ) and anticipatory saccades (AS).

It has been suggested smooth pursuit dysfunction might reflect an underlying "saccadic disinhibition" due to dysfunctional prefrontal cortex (Levin 1984; Matsue et al. 1986), the argument being that otherwise normal pursuit is interrupted by a series of intrusive saccades.

In order to address this hypothesis, recent studies have quantified the number and type of intrusive and corrective saccades which occur during pursuit. In addition, the ratio of the eye velocity to the target velocity (velocity gain) is taken. This measure provides a sensitive index of the pursuit system's ability to perform its primary function, matching eye velocity to target velocity. These studies have failed to observe an increase in intrusive saccades during smooth pursuit in schizophrenic patients (Clementz et al. 1994; Radant and Hommer 1992; Friedman et al. 1995). In fact, the most consistent finding is that smooth pursuit in schizophrenic patients is characterized by a reduction in velocity gain accompanied by an increased number of corrective CUS rather than intrusive saccades (AS and SWJ).

An alternative hypothesis is that smooth pursuit deficits in schizophrenic patients reflect an inability to inhibit the influence of the optokinetic reflex (OKR). In everyday life, pursuit of a moving target generally occurs over a structured background. Under these conditions, most of the flow of visual information across the retina is in the direction opposite to the target's motion. This background effect provides a powerful stimulus to the OKR and thus may impose a "drag" on pursuit eye movements. Indeed, smooth pursuit velocity gain is reduced by between 10–20% in healthy controls when the target moves over a structured background compared to performance in the dark, and this has been attributed to incomplete inhibition of the OKR (Barnes and Crombie 1985; Collewijn and Tamminga 1984).

There is only one study which has addressed this effect in schizophrenic patients. Yee et al. (1988) compared the smooth pursuit velocity gain of schizophrenic patients and controls tracking a sinusoidally moving target against a striped background. A measure of the background effect which combined the inhibitory effect of the background moving away from the target with the facilitatory effect of the background moving with the target differentiated schizophrenic patients from controls, at a fast, but not slow target speed. Further indirect support is provided by Pivik et al. (1988), who found impaired smooth pursuit in schizophrenic patients under light conditions, but not when pursuit was performed in total darkness. One explanation is that in the light conditions patients were less able to inhibit the OKR than controls.

In order to explore further the influence of the OKR on smooth pursuit tracking we report an experiment in which smooth pursuit performance is measured in first-episode schizophrenic patients and matched controls in two conditions: complete darkness, and over a structured background. We hypothesized that if schizophrenic patients are less able than controls to inhibit the input of the OKR then they will suffer a greater reduction in velocity gain than controls when smooth pursuit is performed over a structured background. As Yee et al. (1987) only observed a background effect at a fast target speed, we explored this possible interaction by using four different target speeds.

Method

Subjects

The patient sample consisted of 23 patients experiencing their first psychotic episode and who subsequently received a diagnosis of DSM-IV schizophrenia. These patients were recruited during the first 2 years of an ongoing longitudinal study of the neurobiology of schizophrenia (the West London first-episode schizophrenia study). Eight of the patients were completely drug naïve at the time of testing. The remaining 15 patients had been receiving antipsychotic medication for between 2 and 60 days. Patients were assessed with the Scale for the Assessment of Negative Symptoms (SANS; Andreason 1984a) and the Scale for the Assessment of Positive Symptoms (SAPS; Andreason 1984b), and at presentation the mean total global scores were 23.7 (sd = 16.10) and 34.8 (sd = 17.70) respectively.

These subjects were compared with 23 healthy controls, recruited from the community and matched with respect to age (Mean (SD) Controls = 24.95(7.94), Patients = 24.73(4.1); $t(43) = -0.126$, $p = 0.99$), gender (M/F Controls = 15/8, Patients = 18/5; chi-square = 1.928, $p = 0.165$) and IQ as estimated by the National Adult Reading Test (NART, Nelson 1976; Mean(SD) Controls = 105.04(10.1), Patients = 99.22(9.01); $t(38) = 1.87$, $p = 0.07$). The controls were screened for a family history of schizophrenia and substance use. The data from one control was excluded because the subject failed to adequately follow the instructions.

Procedures

In both paradigms the subjects were seated 1.5 meters from the screen upon which the targets were displayed. Eye movements were recorded using a Skalar IRIS infrared limbus reflection device. Stimulus display and data sampling (500 Hz) were controlled by a PDP 11/73 computer. Recordings were preceded by calibration trials during which nine LED targets with known horizontal positions were illuminated sequentially. Subjects were asked to fixate each target in turn.

Smooth pursuit

The smooth pursuit stimulus was a bright red laser spot, back-projected onto a translucent screen. The target oscillated horizontally with a triangular waveform of amplitude 22.5 degs. Four velocities: 10, 20, 30 and 36.5 degs per second were used, and 6 full cycles recorded at each velocity. Subjects performed the task twice: once in the dark, and once over a high-contrast structured background consisting of random black and white squares (overall luminance 5.9 lux, each square subtending 2 x 2 degs of visual angle) front projected onto the translucent screen. In the structured background condition, in order that the target should remain clearly visible and of constant contrast it moved within a dark stripe which divided the background pattern horizontally.

Data analysis

Smooth pursuit analysis was conducted off-line using a specialised smooth pursuit data analysis program (EYEMAP, AMTech GmbH, Heidelberg, Germany). The software is capable of detecting saccades of 0.25 degs. In each half cycle, based on visual inspection, a 50 ms portion of smooth pursuit eye movement was identified and expressed as peak velocity gain (eye velocity / target velocity). This portion always occurred between saccades and was collected from the middle third of each half cycle, to avoid acceleration and deceleration transients which occur at the beginning and the end of each ramp. Saccadic eye movements were identified, and, based on the criteria of Abel et al. (1991) and Friedman et al. (1992), were classified as either catch-up saccades (CUS), back up saccades (BUS), anticipatory saccades (AS) or square wave jerks (SWJ). Briefly, CUS were defined as saccades which occur in the direction of target motion during smooth pursuit, and which take the eye from a position behind the target to a position on or near the target. BUS were defined as saccades which occur in a direction opposite to the target motion and serve to bring the eyes from a position ahead of the target to a position on or near the target. SWJ were defined as intrusions into smooth pursuit consisting of an initial small saccade in either direction, followed by a short period of continued pursuit and terminated by another small saccade, similar in size to the first, in the opposite direction. Finally, AS were defined as large intrusive saccades which take the eye to a position ahead of the target, and are followed by a short period of low, or zero velocity gain, and/or a BUS.

Statistical analyses were conducted with SPSS for Windows. For the smooth pursuit task group differences in velocity gain were examined with a mixed 3-way ANOVA, with Target Speed (10, 20, 30 & 36 degs/s) and Condition (No background, BG- vs. Background, BG+) as within subject factors and Group (Schizophrenic vs. Control) as a between subject factor. Group differences in CUS rate were explored using mixed 2-way ANOVAs with Group as the between subject variable and Condition as the within subject variable. The relatively low number of intrusive saccades (AS and SWJ) made these variables unsuitable for analysis by repeated measures ANOVA. The total number of AS and SWJ in the two conditions were compared with Wilcoxon tests, and group differences with Mann-Whitney tests. Finally, for each subject a "background effect" measure was calculated by subtracting the mean velocity gain in the BG+ condition from the mean velocity gain in the BG- condition. This measure was then entered into a correlational analysis with global SAPS and SANS scores.

Results

Velocity Gain

The mean velocity gains at the four target speeds for controls and schizophrenic patients, performing smooth pursuit in the dark and over a structured background, are displayed in Fig. 1. The ANOVA revealed a significant main effect of Speed, with both patients and controls having lower gains at the faster target speeds ($F(3,129) = 110.85$, $p < 0.001$). In addition there was also a significant main effect of Group with schizophrenic patients having lower gains than controls in both conditions ($F(1,43) = 4.36$, $p < 0.05$). Both schizophrenic patients and controls had lower velocity gains when performing pursuit over a structured background (BG+) compared to the dark (BG-) (main effect of Background, $F(1,43)=30.39$, $p< 0.001$). The predicted interaction between Background and Group was not significant ($F(1,43) = 0.77$, $p = 0.38$), indicating that the structured background lowered velocity gain to the same extent in both groups. The Speed by Condition interaction approached significance ($F(3,129) = 2.57$, $p = 0.057$) indicating that across both groups the structured background lowered gain more at the higher target speeds. The Group by Speed and three-way Group by Speed by Condition interactions were not significant ($F(3,129) = 1.61$, $p = 0.19$ and $F(3(,129) = 0.29$, $p = 0.83$ respectively).

Saccades

The average total number of corrective (CUS) and intrusive (SWJ and AS) saccades made by schizophrenic patients and controls during the smooth pursuit tracking task are displayed in Fig. 2. Schizophrenic patients made more CUS overall than controls ($F(1,43) = 4.15$, $p < 0.05$), and all subjects made more CUS in the background condition compared to the dark ($F(1,43) = 37.70$, $p < 0.001$). Again, the Group by Background interaction effect was not significant ($F(1,43) = 0.01$, $p = 0.99$), indicating that the effect of the structured background was to increase CUS equally in both schizophrenic and control subjects. In the BG- condition, AS rate did not differ between patients and controls (Mann-Whitney $U = 249.5$, $p = 0.94$) but controls made significantly more SWJ than schizophrenic patients (Mann-Whitney $U = 147.5$, $p = 0.02$). Across patients and controls, AS rates increased significantly in the BG+ condition (Wilcoxon, $Z = -3.411$, $p = 0.01$) but SWJ rates were significantly reduced (Wilcoxon, $Z = 3.358$, $p < 0.01$). Despite these changes, there were no significant differences in the BG+ condition between the two groups in the rates of either AS (Mann-Whitney $U = 240$, $p = 0.78$) or SWJ (Mann-Whitney $U = 187$, $p = 0.14$).

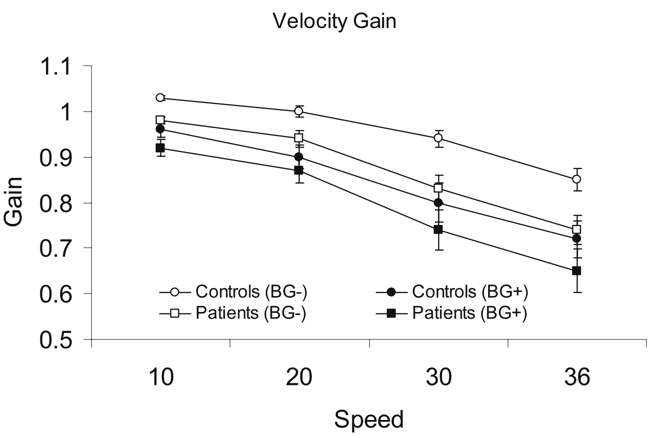

Fig. 1 Mean smooth pursuit velocity gain for schizophrenic patients and controls when performed in the dark (BG-) and over a structured background (BG+).

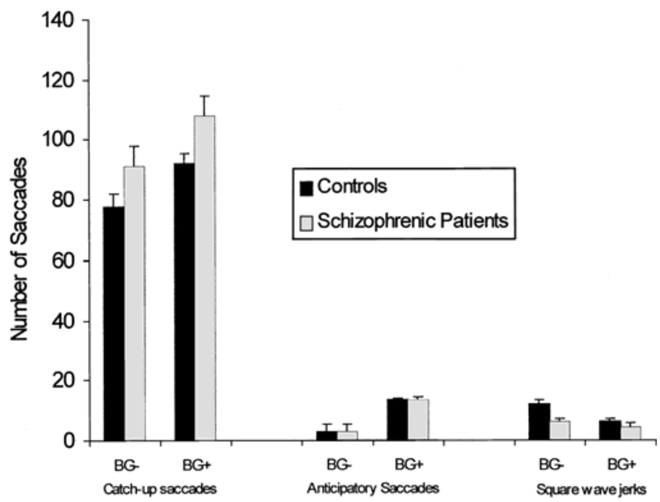

Fig. 2 Average total number of catch-up saccades, anticipatory saccades and square wave jerks made by schizophrenic patients and controls during the tracking task.

Correlations between measures in the patient group.

The background effect did not correlate with negative nor positive symptomology as measured by global SANS (r = 0.035, p = 0.87) and SAPS scores (r = –.182 p = 0.41). There was also no difference in the magnitude of the background effect between the drug-naïve (N = 8) and the drug-treated (N= 15) schizophrenic patients (t(21) = 0.45, p = 0.66). In the treated patients, there was no correlation between mean chlorpromazine equivalent units and magnitude of the background effect (r = 0.08, p = 0.82).

Discussion

The main finding of this study is that first-episode patients with schizophrenia are as able as controls to inhibit the effect of the optokinetic reflex (OKR) when tracking a smoothly moving target over a structured background. Velocity gain in the presence of the structured background was reduced on average by 11.2 % in control subjects. This value is consistent with other studies in control subjects (Barnes and Crombie 1985; Collewijn and Tamminga 1984). Although schizophrenic subjects had lower velocity gains overall, they suffered a virtually identical decrement (11.3 %) to the control subjects. This decrement did not increase with increasing target speeds.

Our findings differ from those of Yee et al. (1987) who reported a greater background effect for schizophrenic patients than controls at a target speed of 0.4 Hz but not at 0.2 Hz. There are, however, several differences between the studies which may account for these contradictory results. Most obviously, the measure of background effect used by Yee et al. reflects both the facilitatory effect of the background moving in the same direction as the target as well as the inhibitory effect of the background moving in the opposite direction to the target.

The saccadic analysis revealed that both schizophrenic subjects and controls compensated for the reduction in velocity gain induced by the presence of a structured background by increasing the number of corrective catch-up saccades (CUS). In addition, both patients and controls made more intrusive anticipatory saccades (AS). However, as before, these effects were of the same magnitude for schizophrenic patients and controls. Together these findings argue against an interpretation of smooth pursuit dysfunction in schizophrenia in terms of an inability of the smooth pursuit system to inhibit the influence of the OKR.

The results of the present experiment may have implications for our understanding of the neurological basis of oculomotor abnormalities in schizophrenia. The current study demonstrates that while the velocity of smooth pursuit eye tracking is reduced in patients with first-episode schizophrenia, the neural pathways responsible for suppressing the effects of a structured background are spared. The neural pathways subserving smooth pursuit in non-human primates and man involve temporo-parietal, parietal and frontal cortical areas as well as several subcortical areas (e. g. Tusa and Zee 1989; Heide et al. 1996). The neural systems mediating the OKR are less clearly understood, although they appear to include the neural systems which mediate smooth pursuit itself (Tusa and Zee 1989). In man, Lawden et al. (1995) compared smooth pursuit in the dark and over a structured background in 26 patients with hemispheric lesions of cortex or white matter. They found that patients least able to inhibit the OKR had lesions confined either to the posterior parietal lobule or to an area of white matter thought to consist of parieto-frontal cortico-cortical fibres. One patient with a lesion confined to the frontal cortex did not demonstrate an abnormal background effect. These results suggest that in man the parietal cortex and its projection to frontal cortex are important for inhibiting the OKR in these circumstances. By inference, this might suggest that the posterior hemispheric component of the smooth pursuit system is intact in patients with schizophrenia, at least relatively early in the course of the illness. However, more direct studies are required to test this hypothesis.

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