It has been demonstrated in normal subjects that smooth pursuit latency is reduced in gap pursuit tasks. We have now measured smooth pursuit latency in a group of schizophrenic subjects in both gap and non-gap conditions. In non-gap tasks pursuit latency was longer in the schizophrenic subjects than in controls. While the addition of gaps produced reductions in pursuit latency in the schizophrenic subjects, the effect was more variable than in controls, with a greater asymmetry between rightward and leftward pursuit latencies. Our results are consistent with the hypothesis that pursuit initiation is modified in schizophrenia and that as with the gap effect on saccades, the gap effect on pursuit is also modified. NeuroReport 10:2635–2639 © 1999 Lippincott Williams & Wilkins.

Key words: Gap effect; Oculomotor control; Schizophrenia; Smooth pursuit

Introduction

Deficits in smooth pursuit (SP) are one of the most extensively studied behavioral features of schizophrenia. Diefendorf and Dodge [1] were probably the first to recognize that SP performance was altered in schizophrenia, but the basic observation has been extensively confirmed [2]. Although SP deficits might serve as biological markers for the underlying genetic and neurobiological abnormalities which lead to schizophrenia [3], many early studies relied on qualitative judgements of SP [4] or on global measures of performance [5] rather than clearly segregating out different aspects of SP. Thus basic questions remain about the nature of the SP deficit in schizophrenia.

One important distinction that must be made is between SP initiation and maintenance. SP is initiated in response to real [6] or apparent [7] target motion. Important initiation parameters such as latency are modified by a number of factors such as visual stimulus conditions [8], task type (e.g. ramp vs step–ramp) and task predictability [9]. It has also recently been demonstrated that when a temporal gap is introduced between the extinction of a central fixation target and the illumination of a pursuit target, SP latency is reduced compared to non-gap conditions [10,11]. This gap effect is similar to the gap effect on saccade latency [12,13]. The gap effect on saccade latency has been investigated in schizophrenics and it has been reported that they have a higher frequency of express saccades than control subjects [14], and that this is most marked when targets are presented in the right visual field [14,15].

SP initiation in schizophrenic subjects has been investigated previously and it has been reported that while initial acceleration is lower than in control subjects, latency remains within normal limits [16,17]. We previously found in a single subject both that SP latency was considerably longer and that the gap effect was modified compared with control subjects [18]. It has also recently been reported that motion processing is abnormal in schizophrenia [19,20], a deficit that should affect SP latency. We therefore examined SP initiation in a group of schizophrenic subjects and report here an analysis of SP latency in both normal (i.e. non-gap) and gap conditions.

Materials and Methods

With local ethical approval a group of 10 subjects meeting DSMIV/ICD10 criteria for schizophrenia (nine male, one female; age range 23–40 years of age, mean 32.1 years) were assessed both optometrically and orthoptically. All had normal or corrected to normal visual acuity. One subject had been free of psychotropic medication for >3 months, five were on novel antipsychotic medication, three on conventional neuroleptics (mean chlorpromazine equivalent 550 mg daily), one on both. All but one were able to perform the pursuit tasks. Comparisons were made with four normal control subjects.

Methods were identical to those used in previous
studies [9,10]. Briefly, subjects viewed a visual display monocularly with their left eye. Visual stimuli consisted of small grey squares (0.3 × 0.3°, luminance 32.3 cd/m²) presented on a light background (43 cd/m², contrast 25%). Schizophrenic subjects were presented with two runs of 96 trials in which, after a randomly variable fixation period (0.5–1.5 s), the pursuit target appeared randomly 5° to the right or left of fixation, and moved back through the centre of the display at 14°/s (i.e. a centripetal ramp–step task [9,6]). Sets of four tasks were presented in random order; in each set there were always two leftward and two rightward tasks, one task with no gap and three with gaps of 100, 200 or 400 ms. Between each run there was an opportunity for the subject to rest. Horizontal eye movement was recorded using an infra-red corneal reflection device (IRIS: Skalar), and the eye position signal digitised using a CED μ1401. Data from 100 ms before, to 500 ms after the appearance of the target was stored on disc for analysis off-line. Smooth pursuit latency was measured from the computer screen using an analysis program which displayed the recorded eye position (Fig. 1a), the calculated eye velocity (Fig. 1b) and the time at which the pursuit target appeared (arrow 1 in Fig. 1). SP latency was measured from the velocity traces using a regression technique [11,21] (Fig. 1b). A linear regression of velocity on time was fitted through the data from approximately 50 ms before, to 50 ms after the time of target appearance (Fig. 1b). A second regression was calculated over the initial, acceleration phase of the SP response. The calculated intersection between the two functions was shown, and although it could be overridden by the operator, was usually taken to estimate the time of SP initiation (arrow 2 on traces in Fig. 1). Only responses which were preceded by stable fixation, and were not contaminated by blinks or anticipatory saccades (i.e. saccades with latencies < 80 ms) were analysed.

**Results**

Of the nine schizophrenic subjects whose data was analysed, all performed the pursuit tasks well. The data illustrated in Fig. 1 are typical of their performance. Many of them responded with only a smooth eye movement. A saccade in the direction of the target step was often observed at very long latency, occurring outside the 600 ms window of data which we analysed. We analysed only pre-saccadic pursuit responses.

There was considerable variation in the SP latency in the normal tasks (gap = 0 ms; Fig. 2a). Individual mean latencies for schizophrenic subjects ranged from 205 ± 21 ms (mean ± s.d.) to 327 ± 59 ms for leftward and from 224 ± 28 ms to 340 ± 81 ms for rightward SP. The comparable figures for the control subjects were 173 ± 28 ms to 229 ± 32 ms and 183 ± 33 ms to 225 ± 34 ms, respectively.

For both the schizophrenic and control groups there were statistically significant differences between the mean leftward and rightward SP latencies (Fig. 2b). Mean leftward SP latency was significantly less than rightward SP latency (Fig. 2b, comparison 4: \(t = 3.445, \text{df} = 517, p < 0.001\); comparison 3: \(t = 4.964, \text{df} = 273, p < 0.0001\)). Note that the asymmetry was slightly more marked in the schizophrenic group. There were also clear differences between the groups. The latencies both leftward and rightward SP for the schizophrenic group were significantly longer than for the control group (leftward, comparison 1: \(t = 7.438, \text{df} = 273, p < 0.0001\); rightward, comparison 2: \(t = 10.03, \text{df} = 187, p < 0.0001\)).

The gap effect on SP latency in schizophrenic subjects was both more variable and more asymmetric than in control subjects. Figure 3 shows the reductions in latency observed with gaps of 100 ms (Fig. 3a) and 400 ms (Fig. 3b) as a percentage of the
latency observed in the normal (gap = 0 ms) condition. Within the schizophrenic group, the introduction of a 100 ms gap produced a statistically significant reduction in latency for leftward SP in only one of the nine subjects (SC10, t = 2.52, df = 41, p < 0.05), and for rightward SP in three of the nine (e.g. SC6, t = 2.48, df = 36, p < 0.05). Indeed in three subjects there were small, statistically insignificant increases in latency (SC3, SC7 and SC9). Note that in all four control subjects 100 ms gaps produced a statistically significant reduction in SP latency for SP to left and right.

In the 400 ms gap condition, latency for SP to the right was reduced from the normal condition by a statistically significant amount in two of the nine schizophrenic subjects (SC2 and SC10), although there were small statistically insignificant reductions in a further five subjects (Fig. 3b). In two subjects there were small, statistically insignificant increases in SP latency for SP to the right (SC3 and SC7). For SP to the left however, there were statistically significant reductions in seven of the nine subjects. Thus with 400 ms gaps there was a marked asymmetry in the gap effect. While there were usually significant reductions in latency for leftward SP, for SP to the right the reductions did not reach significance and indeed there were occasional increases in latency (SC3 and SC7) compared with the normal (gap = 0 ms) condition. Note that this is different to the pattern in the control subjects where with 400 ms gaps significant reductions in latency were always observed for both leftward and rightward SP and the reductions were always greater than those observed with the 100 ms gaps.

Pooled means for each gap condition were calculated for the two groups. Given the variability of the gap effect in the schizophrenic group, we tested the normality of the distributions of the group data. For each condition, the data were consistent with the hypothesis that the data were normally distributed (Kolmogorov-Smirnov test, p > 0.1). There was a clear separation between the schizophrenic and the control group data (Fig. 4). All of the latencies for the controls were shorter than those for the schizophrenia group.
phrenic group across all conditions. There was also a larger separation of leftward and rightward latencies in the schizophrenic group across all conditions than in the control group. Overall, the gap effect for leftward SP was more pronounced than that for rightward SP in the schizophrenic group. Thus comparing the normal and 400 ms conditions, while the reduction for leftward SP was 38 ms (statistically significant: $d^*=6.17$, $p<0.001$), it was 26 ms ($d^*=3.53$, $p<0.001$) for rightward SP. The comparable results from the control group were 42 ms ($d^*=11.6$, $p<0.001$) and 37 ms ($d^*=10.3$, $p<0.001$), respectively.

Discussion

We have found that in normal (i.e. non-gap) tasks, SP latency in schizophrenic subjects is consistently longer than that observed in control subjects in the same tasks in similar visual conditions. Previous reports had indicated that there were no significant differences in SP latency in schizophrenic subjects. However, these tended to be based on small numbers of trials per condition per subject (e.g. 5 [16] or 6 [17]). Even so, in one study, while latency differences were not statistically significant, the pattern of results was similar to that reported here. Latencies were longer in schizophrenic than in normal subjects and there was an asymmetry in SP latency in both control and schizophrenic subjects; latency for leftward SP was lower than latency for rightward SP [17]. Our observation in both individual and group data of an enhanced asymmetry in SP latency in schizophrenic subjects, suggests that it is unwise to combine data from leftward and rightward responses [16].

It might be argued that increased latency was simply due to a generalized deficit. However, when subjects are tired or not attending to tasks, responses with early saccades predominate and subsequent SP is broken up by numerous saccades. There was little evidence of this in our data, suggesting sufficient alertness and motivation. Any generalized deficit should also have appeared in earlier work, yet it has been claimed that SP latency is essentially normal in schizophrenic subjects [16,17].

Increased SP latency is consistent with recent results indicating a deficit in processing visual motion information in schizophrenia [19,20]. While deficits in motion processing have been linked to the reduced initial acceleration observed in schizophrenia, a latency effect is not unexpected as increased motion thresholds would increase motion detection time and hence latency.

The gap effect on saccade latency has been investigated on schizophrenic subjects. In general schizophrenics produce more express saccades than controls, particularly when targets are presented in the right visual field. While there does not appear to be any robust phenomenon of express SP, the generalized reduction in SP latency in gap conditions has been shown repeatedly [8–11]; we have shown that it is also present in schizophrenic subjects. However it is more variable and more asymmetric than in controls. In particular, while in control subjects latency continues to decline as gap duration increases, we found that in the schizophrenic group with 400 ms gaps the effect for rightward SP was greatly reduced in half of the subjects, and indeed in two subjects increased. Rightward SP in our experiments is executed in response to targets initially appearing in the left visual field. As pursuit pathways from the cortex to the brain stem are ipsilateral, the longer latencies and the reduced gap effect for rightward SP might be indicative of a modification of left hemisphere processing, similar to that reported for attentional processing [22,23].

As only one of our subjects was drug free at the time of testing and none were drug naive, we cannot definitively rule out antipsychotic medication as explaining the effects we have observed. However, in this respect our subjects were little different from those examined in earlier studies [17,20]. We found no significant differences in performance within our group related to the type of medication being taken.

Conclusion

Our results indicate that, in addition to deficits in initial acceleration and gain, and contrary to a num-

![Figure 4](image-url)
ber of reports in the literature, SP latency is significantly lengthened in schizophrenia. There is an asymmetry in SP latency and in the gap effect on SP latency which is suggestive of alterations in left hemisphere processing. Certainly these results show that the SP deficit in schizophrenia is as much a deficit of initiation as of maintenance.

References


Acknowledgements: We are grateful to the Wellcome Trust for support. G.O.M. is supported by a Vision Science’s Departmental Postgraduate Scholarship.

Received 17 June 1999; accepted 22 June 1999