(Accepted 20 September 1984)

Smooth pursuit eye movements in the parents of schizophrenics

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ABSTRACT. Smooth pursuit eye movements and fixation were studied, using quantitative techniques, in eight parents of chronic schizophrenics. Only one subject showed a statistically significant excess of square wave jerks (SWJ) and other saccadic intrusions during fixation. All subjects were capable of normal smooth pursuit gains during ramp pursuit. Six subjects, however, made 'anticipatory saccades' which took the eyes ahead of the target; they spent considerable time fixating off-target. These hitherto undescribed movements, which superficially resemble SWJ, appear to represent an involuntary attentional disturbance in these clinically normal individuals.

Key words: smooth pursuit; schizophrenia; square wave jerks; attention

INTRODUCTION

In the past decade a large body of work has appeared, originating with Holzman and colleagues, examining the smooth pursuit eye movements of schizophrenics and, in some instances, their relatives (Holzman *et al.*, 1973, 1974, 1977; Iacono & Lykken, 1979). Most of this work used electro-oculography to record the eye movements and analyzed the data in ways that met with criticism by those more familiar with accurate ocular motor recording (Troost *et al.*, 1974). Indeed, the 'velocity arrest,' a purported measure of pursuit quality frequently used in this literature, has been held to reflect muscle artifact in the EOG tracing rather than indicate anything about the functioning of the patient's ocular motor pathways (Troost *et al.*, 1974; Iacono & Lykken, 1979). Thus, the nature, etiology and even the existence of smooth pursuit deficits in schizophrenia remained unclear. This was particularly the case when the purported pursuit deficits were being used as evidence for abnormalities in brainstem function in these patients. Given the sensitivity of the pursuit system to lapses in attention, these claims seemed tenuous.

More recently, however, the methodology employed in some of these studies has improved and, as it has, the nature of the abnormalities described has changed. Lindsey *et al.* (1978) compared simultaneous EOG and infrared eye movement recordings of smooth

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pursuit in five psychiatric patients and five controls. They found that while qualitative scores and the signal/noise ratios were highly correlated for the two methods, 'pursuit arrests' were not. This supported the artifactual origin of the latter measure. Using infrared oculography, Levin *et al.* (1982) found frequent square wave jerks (which they referred to as 'saccadic intrusions') during both fixation and smooth pursuit in three of six schizophrenic patients. Since square wave jerks are associated with everything from old age to progressive supranuclear palsy, being possibly the most non-specific eye sign, their localizing value is quite minimal. Levin *et al.* (1982) also found reduced smooth pursuit gain (eye velocity/target velocity) in their patients. This sort of generalized reduction in smooth pursuit function is also quite non-specific in origin, having many possible causes (Troost & Abel, 1982); it is often related to a lack of attention rather than to any structural abnormality in the central nervous system. Indeed, Schmid-Burgk *et al.* (1982) found only mildly defective pursuit in schizophrenics but did observe an increase in hypometric saccades and saccades away from a fixation target; they attributed these to impaired attention.

Even those data recorded using relatively artifact-free techniques generally have not been evaluated in ways which can be related to the existing ocular motor literature. The papers by Levin *et al.* (1982) and Schmid-Burgk *et al.* (1982) are among the very few that quantify the eye movements of schizophrenics sufficiently well to permit identification of those characteristics that make their tracking 'abnormal.' Measures such as qualitative rating scores or signal-to-noise (S/N) ratios are too global and imprecise to provide any information about either the nature or origin of any pursuit impairment. Furthermore, none of the recent papers in this area have applied their improved methodologies to the study of the clinically normal relatives of schizophrenics. Since the techniques used in the older studies (Holzman *et al.*, 1973, 1974, 1976, 1977) left not only the nature but even the existence of pursuit defects in this population unclear, the present study was undertaken.

PATIENTS AND METHODS

Subjects for this study, six women and two men, ranged in age from 54 to 74 (mean 61.9, S.D. = 7.64). All were parents of patients hospitalized at the Wade Park Veterans Administration Medical Center on the psychiatric service during September and October, 1982. The proband patients all were diagnosed as schizophrenic as defined in DSM III. Their pathology was manifest as delusional thought, hallucinations and/or formal thought disorder. All patients met the criteria for paranoid or undifferentiated type schizophrenia. Additionally, in all cases the psychopathology had been present for more than six months. No patient had had his eye movements recorded and it was unknown whether any had any ocular motor abnormalities.

The parents of these patients were contacted and asked to participate in this study. All of the parents who made themselves available for testing denied ever having been hospitalized for psychiatric reasons or having taken neuroleptic drugs. Upon interview, none of them showed any evidence of loose associations or illogical thought; all denied hallucinations and showed no evidence of delusional thought. One of the subjects (No. 1) was taking psychoactive medication at the time of testing (10 mg diazepam 15 hrs before testing).

Eye movements were recorded using the infrared reflection technique. A vertical EOG lead was used to detect blinks. Subjects were seated in a chair with headrest and chin support. Targets were red light-emitting diodes mounted on a 1.5 m radius arc mounted that distance

from the subject. All surfaces in the room were painted black and the room was in near darkness. The experimental protocol was as follows: After calibration, the subjects were instructed to stare straight ahead at the 0 deg fixation light provided. This was continued for two minutes, followed by a one minute rest. The subjects were then told to look at the light and hold their eyes still; this was also carried out for two minutes. Another two minute rest was then given, followed by the smooth pursuit tests. The target for these was a red laser spot projected on the target arc under the control of a mirror galvanometer. It was driven by a triangle wave generator between ± 15 deg at constant velocities of 5, 10, 20, 40 and 80 deg/sec. Ten cycles of each velocity were presented and 30 sec rest periods were provided between each trial. Occasional verbal encouragement was given throughout the test.

Control data were taken from a related study on the effects of distraction on smooth pursuit (Kaufman *et al.*, 1984). Thirteen young (mean age 25.5, S.D. = 3.8) and 13 elderly subjects (mean age 77.6, S.D. = 5.7) tracked the target spot for 6 cycles at 5 deg/sec and 12 cycles at 20 deg/sec. They were told at the beginning of each trial to follow the spot; no further encouragement was given.

All recordings were subsequently analyzed by eye for evidence of specific dysfunction of the smooth pursuit system by measuring the best pursuit gain (eye velocity/target velocity) sustained for at least 0.25 sec in the two directions. We examined the eye movement recordings during both fixation and pursuit for additional ocular motor abnormalities such as square wave jerks and other saccadic intrusions. Evidence of impaired attention was sought by measuring the total amount of time that the subjects took their eyes off the target; for smooth pursuit, this was scored as the total time off target per cycle and was computed for the three lowest target velocities.

RESULTS

The 'hold' and 'stare' fixation tests showed no consistent difference in the incidence of square wave jerks (SWJ) or other saccadic intrusions between the two conditions. The instruction to subjects to 'hold their eyes still' had led to a significant reduction in the frequency of square wave jerk occurrence in normals (Steinman *et al.*, 1967) and amblyopes (Ciuffreda *et al.*, 1979). Results for our subjects are shown in Table 1. SWJ frequencies for young (mean age, 32) and old (mean age, 71) were given by Herishanu & Sharpe (1981). Our oldest (74) subject's SWJ frequency slightly exceeded the mean plus 2 standard deviations for his age group.

TABLE 1

Subject No.	*Age*	*SWJ/min*		*Other S.I./min*	
		Hold	*Stare*	*Hold*	*Stare*
1	54	2	3.5	0	0
2	59	16.5	29	0	0.5
3	59	29.5	18.5	3	1.5
4	63	0	0.5	1	0
5	52	19.5	29.5	2	2.5
6	71	9	9	0	1
7	74	48	46	8.5	3
8	63	1	1.5	0	0

Peak smooth pursuit gains for the two directions and four of the target velocities are given in Table 2 (none of the subjects showed any appreciable pursuit for the 80 deg/sec targets). The values given represent the highest gain over at least a 0.25 sec interval; such a measure indicates the best performance of which the smooth pursuit system is capable. Since the early work on the eye movements of schizophrenics and their relatives claimed an actual abnormality in these brainstem circuits, it was important to assess whether our subjects were ever capable of normal pursuit. An example of good pursuit is shown in Fig. 1. In keeping with the evaluation of tracking made

TABLE 2. Peak pursuit gains

Subj. No.	5 deg/s		10 deg/s		20 deg/s		40 deg/s	
	L	R	L	R	L	R	L	R
1	0.9	1.0	0.9	0.95	0.95	1.0	0.88	0.82
2	1.0	1.0	1.0	1.0	1.0	1.0	0.81	0.94
3	0.9	0.8	0.85	0.85	0.78	0.81	0.76	0.78
4	1.0	1.0	0.8	0.7	0.75	0.75	1.0	0.63
5	1.0	1.0	1.0	1.0	0.94	0.88	0.88	0.80
6	1.0	1.0	1.0	0.95	1.0	1.0	0.78	0.81
7	1.0	1.0	1.0	1.0	0.83	0.93	0.51	0.69
8	1.0	1.0	1.0	1.0	0.95	0.90	0.80	0.70

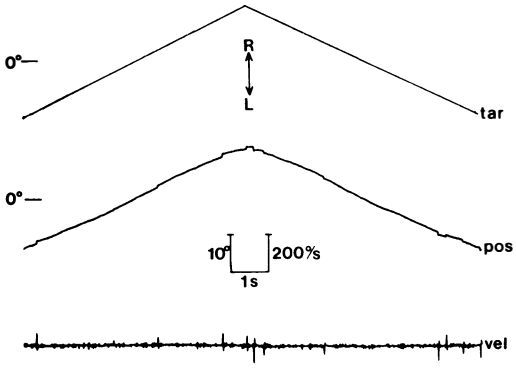

Fig. 1. Pursuit at 5°/s by subject 2, showing only infrequent catch-up saccades and SWJ. In this and the subsequent figure, tar = target, pos = position and vel = velocity.

TABLE 3. Square wave jerks/min during pursuit

Subj. No.	5 deg/s	10 deg/s	20 deg/s
1	8.7	10.6	6.5
2	0.5	4.7	0
3	4.8	6.4	8.0
4	3.0	3.3	0
5	16.1	13.2	0
6	13.0	4.4	0
7	39.0	22.8	3.8
8	6.5	3.0	0
Young controls	7.0		1.0
Old controls	17.1		0.6

in schizophrenic patients by Levin *et al.* (1982) we also counted the number of SWJ that occurred during pursuit. These results are shown in Table 3.

The most striking feature of these subjects' smooth pursuit was that several of them would interrupt their tracking by looking *ahead* of the target and either waiting for it to reach the point at which they were looking or by making a saccade back to the target. While these sometimes superficially resembled SWJ, they were generally of larger amplitude and longer duration. More significantly, when SWJ took

TABLE 4. Total time off target/cycle (sec)

Subj. No.	5 deg/s	10 deg/s	20 deg/s
1	0.57	0.07	0
2	0	0.10	0.20
3	0.95	0.44	0.42
4	0	0	0
5	2.23	1.76	1.15
6	3.84	1.37	0
7	0.84	0.49	0.62
8	2.07	0.72	0
mean	1.31	0.62	0.29
Young controls	0.034		0.015
Old controls	0.292		0.155

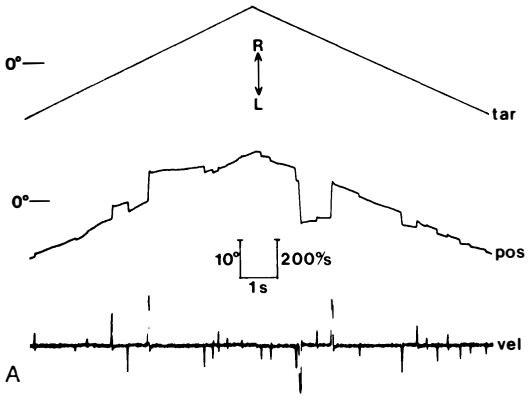

Fig. 2A. Pursuit at 5°/s by subject 3. Note large 'anticipatory saccades' taking the eyes 5-10° ahead of the target, with the subject's gaze being misdirected for 0.5-1.5 s. Also note the reduced or absent pursuit gain seen after these saccades.

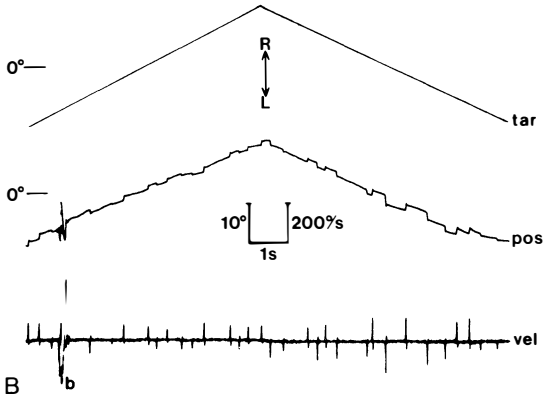

Fig. 2B. Pursuit at 5°/s by subject 7. Frequent SWJ are seen. Compare SWJ with the anticipatory saccades in A with respect to amplitude, intersaccadic latency and pursuit gain. b= blink.

the eyes off target, *pursuit continued* even though the stimulus was not on the fovea. In contrast, during 'anticipatory saccades' (AS) smooth pursuit eye movements were rarely seen. Examples of both these interruptions and of SWJ during pursuit are seen in Fig. 2A and B. Table 4 shows the total amount of time per cycle that the anticipatory saccades took the eyes off target.

DISCUSSION

The past history of the study of the eye movements of schizophrenics has seen gradual improvements in the techniques used to both collect and evaluate data, changes in the results obtained and revisions of the interpretations of these results. The earliest studies (Holzman *et al.*, 1973, 1976, 1977) introduced the concept of the 'velocity arrest,' which was defined as a reduction of eye velocity to zero not followed by a catch-up saccade. Since this would violate the synergistic interaction of the saccadic and pursuit subsystems, it was immediately criticized in the ocular motor literature (Troost *et al.*, 1974). The velocity arrest, as pointed out by the latter authors, was primarily a reflection of recording artifacts of various types. The high-gain differentiators needed to show smooth pursuit velocity excel at differentiating the surface electromyographic potentials which are inevitably included in an EOG recording. This measure has now been abandoned by those who introduced it (Lipton *et al.*, 1983). Another popular measure was the use of panels of raters to subjectively scale the quality of tracking (Iacono & Lykken, 1979; Siever *et al.*, 1982). While such ratings have proven to be reproducible, it is impossible to relate a poor score to a specific type of performance deficit. This has made it difficult to relate claims of impaired pursuit in patients and their relatives to the various forms of pathology known to cause poor tracking in neurologic disease. Thus, while numerous publications over the years have reported abnormal smooth pursuit eye

movements in schizophrenics and their relatives, the nature and origin of such disturbances have remained remarkably elusive. Although claims have often been made for the robustness of this finding, it is difficult to see how a succession of reports whose results are often fundamentally different, albeit abnormal, represent repeated manifestations of one underlying pathological process. Qualitative evaluation methods, *by their nature*, are unable to provide information about what sort of dysfunction might be causing a low score. This is also true of evaluations using S/N ratios or root-mean-square error calculations (Iacono & Lykken, 1979). Quantitative techniques used include measurements of pursuit gain and incidence of square wave jerks (Levin *et al.*, 1982), number of saccades per cycle of tracking (Schmid-Burgk *et al.*, 1982) and the now-discredited velocity arrest (Holzman *et al.*, 1973). An attempt by Lipton *et al.* (1983) to provide a rationale for the latter measure by suggesting that it reflects a zero-velocity period between the saccades of an SWJ fails, since pursuit continues during this time (Fig. 2a) and since the arrests vanish when infrared recordings are made. Thus, out of the copious literature on eye movements in schizophrenics (see Lipton *et al.* (1983) for a review), only a few papers actually provide any hints as to *what* might be abnormal in the tracking of these individuals. Further, the techniques used in the quantitative studies had not been applied in even recent investigations of patients' relatives (Holzman *et al.*, 1984). Since this possible genetic link was one of the potentially most interesting aspects of these studies, we undertook the present short study of the parents of schizophrenics.

One basic finding of our investigation was that the ability to generate normal smooth pursuit eye movements was *unimpaired* in our subjects. Their peak pursuit gains were all quite good for targets up to at least 20 deg/sec. Thus, there is *no* evidence in these individuals for any fundamental deficit in this ocular motor subsystem *per se*. However, this does not mean that we observed nothing but normal tracking. Indeed, there were some points of agreement with previous studies. As Levin *et al.* (1982) found in three of six schizophrenics, we observed a high incidence of square wave jerks in four of our subjects (numbers 2, 3, 5 and 7). Although the absence of published norms for all age groups makes it impossible to determine with certainty whether SWJ frequencies in these subjects were abnormal, the impression was one of unusually high numbers. These SWJ were not reduced by the use of the 'hold' command. Although often mentioned in regard to cerebellar disease, SWJ are perhaps the minimal saccadic ocular motor sign and are highly non-specific (Herishanu & Sharpe, 1981). We therefore found no eye signs in our parents of schizophrenics which were indicative of dysfunction in any ocular motor pathway.

An unanticipated finding in our subjects was occurrence of large anticipatory saccades (AS) seen prominently in six of our subjects. Similar eye movements have not hitherto been described. Although superficially similar to square wave jerks, AS were generally larger, had a longer intersaccadic interval and showed minimal or absent pursuit during the time the eyes were off the target. Also, while the initial saccade of an SWJ could occur in either direction, we never observed a movement like an AS that was initially directed behind the target. Examples of these features are shown in Fig. 2. AS are also unrelated to the large saccades referred to as 'Type I' or 'saccadic substitution' tracking (Holzman & Levy, 1977). This latter pattern consists of the

replacement of smooth pursuit by large saccades between the endpoints of target motion. In contrast, AS were generally seen while the subjects were accurately tracking the target. Since they *do* bear a superficial resemblance to SWJ, it is possible that some of the saccadic intrusions ('Type II' tracking) previously reported (Levin *et al.*, 1982) were actually AS.

Because the AS are not corrective in nature and occurred in spite of frequent verbal encouragement, they suggest an apparent difficulty in maintaining concentration on the pursuit task, particularly at the lower target velocities. The subjects spent far more time off-target than did either control group (Table 4). Such an apparent distractability occurred in the absence of any sensory stimuli competing with the moving target for the subjects' attention. This response was not prominent in the smooth pursuit of normal elderly subjects unless the pursuit stimulus traversed a complex visual background (Kaufman *et al.*, 1984). The anticipatory saccades appear to reflect more than simple lapses in attention, since they are not directionally random; rather, they always *lead* the target. They might instead represent a partial breakdown in the performance of the tracking task; the subjects move their eyes in the proper direction while sporadically neglecting the necessity to do so only while fixating the pursuit target. It is also possible that anxiety induced by the testing process might have contributed to the occurrence of AS, since the subjects knew that they had been recruited because they had a schizophrenic child. However, we have examined many patients over the years for diagnostic purposes and have never observed similar eye movements during these procedures, which might also be expected to produce anxiety. Further study of both schizophrenic patients and their relatives is warranted, using *quantitative* recording and analysis techniques, to determine whether this is, in fact, an ocular motor indicator of an involuntary attentional abnormality in both groups.

ACKNOWLEDGEMENT

This work was supported in part by the Veterans Administration.

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