A longitudinal analysis of eye tracking dysfunction and attention in recent-onset schizophrenia

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Abstract

The effect of an attentional manipulation on eye tracking dysfunction (ETD) in the early stages of schizophrenia was examined in 34 recent-onset schizophrenic patients and 24 demographically matched normal subjects over a 1-year period. An attentional enhancement manipulation improved eye tracking performance of recent-onset schizophrenic patients more than that of normal subjects. Eye tracking level also was moderately stable for both groups over the course of 1 year. The possible role of attentional allocation in ETD highlights the need for further examination of the interface between attentional and eye tracking measures of vulnerability to schizophrenia.

Descriptors: Smooth pursuit eye tracking, Schizophrenia, Attention, Temporal stability, Recent-onset schizophrenia, Eye tracking dysfunction

Numerous studies have demonstrated that a significant proportion of schizophrenic patients experience eye tracking dysfunction (ETD), as compared with normal subjects (see reviews by Clementz & Sweeney, 1990; Levy, Holzman, Matthysse, & Mendell, 1994). In subsequent research, investigators have attempted to identify and manipulate variables that might affect the poor eye tracking performance observed in schizophrenic patients. For instance, characteristics of the target stimulus have been manipulated (e.g., subjects required to read numbers on the target, color of the target changed) to investigate the possibility that ETD reflects inattention or a lack of motivation to perform the tracking task (e.g., Shagass, Roemer, & Amadeo, 1976). Attention manipulations of this sort resulted in improved smooth-pursuit tracking in schizophrenic and normal control subjects, but schizophrenic patients continued to exhibit clear ETD relative to normal controls (e.g., Holzman, Levy, & Proctor, 1976; Iacono, Tuason, & Johnson, 1981; Shagass et al., 1976). This consistent pattern of results led Holzman (1987, p. 53) to conclude that "if any attentional quality is involved [in disrupted

This research was supported in part by a research grant from the Committee on Research of the Academic Senate of the Los Angeles Division of the University of California (C. M. Yee) and by research grant MH37705 (K. H. Nuechterlein) and Mental Health Clinical Research Center grant MH30911 (R. P. Liberman) from the National Institute of Mental Health. This manuscript was prepared while M. E. Dawson was supported by a Research Scientist Development Award (1 KO2 MH01086) from the National Institute of Mental Health.

We gratefully acknowledge the assistance of Craig Childress, Karen Hemmerling, Don Jensen, Diego Mechoso, Mitchell Stoddard, and Kenneth Zaucha in data collection and scoring, and we thank Jim Mintz and Sun Hwang for statistical support and consultation.

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eye tracking], it is the automatic, nonvoluntary deployment of attention that seems defective." This premise is consistent with the available data, yet it may be premature to dismiss the role of voluntary attention until more extensive investigations are conducted. Although the presence of ETD in schizophrenic patients and their biological relatives is well established (Clementz & Sweeney, 1990; Levy et al., 1994), abnormalities in several aspects of attention in these groups are also well documented (Nuechterlein & Dawson, 1984; Braff, 1993). Thus, the interface between ETD and attentional abnormalities remains of substantial interest.

Despite an extensive literature on ETD in schizophrenia, only a few studies have focused on the initial stages of this disorder. To our knowledge, no published investigation has specifically addressed the effects of attention enhancement on ETD during the early stages of schizophrenia because investigators have largely employed simple moving targets. For instance, Sweeney, Haas, and Li (1992) required subjects to track the letter X as it oscillated across the screen of a computer monitor. First-episode schizophrenic patients were impaired relative to normal controls in pursuit gain, number and size of catchup saccades, and frequency of square wave jerk intrusions during pursuit. In a large-scale study of first-episode psychosis, Iacono, Moreau, Beiser, Fleming, and Lin (1992) found that schizophrenic patients displayed poorer pursuit performance than did normal subjects when instructed to track a luminous spot. Lieberman et al. (1993) included an attentional manipulation that involved counting the number of times the target changed colors, but their report only states that a higher proportion of schizophrenic patients exhibited ETD as compared with controls; no mention was made of possible differential group differences as a function of the attentional condition.

Empirical investigations are needed, therefore, to determine whether voluntary attentional enhancements can differentially re-

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duce or even temporarily eliminate ETD in the initial stages of schizophrenic illness. Perhaps the corrective role of voluntary attention diminishes over the course of schizophrenia, reflecting factors such as a deterioration in attentional functioning in chronic schizophrenia, sustained neuroleptic treatment, or adaptation to a chronic illness. Until such factors are controlled, the possibility remains that the failure to override or eliminate ETD completely with attentional manipulations is a function of chronicity of illness in groups that have been studied and that ETD can be normalized temporarily by attentional manipulations during the early course of schizophrenia. Accordingly, one goal of the present research was to evaluate the extent to which ETD can be improved with an attentional manipulation in patients with a recent onset of schizophrenia. If recent-onset patients exhibit substantial eye tracking improvement with an attentional manipulation and can perform as well as normal controls, it would suggest that voluntary attention may be more critical to ETD than commonly believed, at least during the early course of illness, and that certain aspects of voluntary attentional functioning and eye tracking remain relatively intact after the immediate onset of schizophrenia. This finding would indicate either that ETD has not become so severe that it cannot be altered substantially or that the deficit in voluntary attention has not become so severe that it is not a viable tool for reversing ETD temporarily. However, if schizophrenic patients continue to perform poorly on the eye tracking task as compared with normal controls during the attentional manipulation, it would support the view that involvement of voluntary attention in eye tracking is minimal in schizophrenia or that voluntary attentional functioning is involved but already seriously compromised during the initial period of schizophrenia.

The second purpose of this study was to investigate the longitudinal stability of smooth-pursuit tracking in recent-onset schizophrenia. Gooding, Iacono, and Beiser (1994) compared the smooth-pursuit performance of first-episode schizophrenic, nonschizophrenic psychotic, and normal control subjects over a 9.5month period. Examining root mean square (RMS) error scores, they found stability coefficients of .68 for schizophrenic patients, despite changes in medication and clinical status, and .57 for normal controls. These data suggest that the temporal stability of ETD is moderately high in schizophrenic patients during the initial course of illness. Because temporal stability is critical to the hypothesis that ETD is a biological marker of schizophrenia (see Clementz & Sweeney, 1990; Iacono, 1983), we attempted to extend the evaluation of temporal stability to a 12-month interval with a group of recent-onset schizophrenic patients who were maintained on a longacting injectable neuroleptic medication.

A related issue concerns the temporal stability of improvements in eye tracking performance that are associated with the introduction of an attentional manipulation. There is little doubt that pursuit tracking is enhanced in both normal control and schizophrenic subjects when voluntary attention is directed toward the changing characteristics of the target stimulus. It remains to be determined, however, if the effects of an attentional manipulation can be duplicated over time or if deficits in the regulation of attention follow a pattern of progressive decline over the early course of schizophrenic illness, such that the attentional manipulation has a diminished effect later in the disorder.

In the present study, we examined ETD over a 12-month period by comparing smooth-pursuit performance in a group of recentonset schizophrenic patients with that of demographically matched normal subjects. Comparisons were made between eye tracking performance under conditions with and without an attentional manipulation to assess the stability of pursuit impairment and of attentional functioning as it relates to the oculomotor system. We hypothesized that recent-onset schizophrenic patients would exhibit an overrepresentation of ETD, thereby replicating previous findings. Although the attentional manipulation was expected to improve tracking performance across all subjects, we predicted that eye movement deficits would persist in the schizophrenic patients even in this attentional enhancement condition. In light of the stability coefficients reported by Gooding et al. (1994), we predicted that ETD in our group of schizophrenic patients and normal control subjects also would remain reasonably stable over time.

Method

Subjects

Participants were 34 recent-onset schizophrenic patients (29 men, 5 women) and 24 normal control subjects (18 men, 6 women). Schizophrenic patient and normal control subjects were matched for age ($M=23.6\pm SD=3.5$ years and 24.1 ± 3.4 years, respectively), and level of education (12.4 ± 2.1 years and 13.6 ± 1.6 years, respectively). All subjects were participating in a longitudinal follow-through project that examined schizophrenic patients during the initial years after onset of a schizophrenic disorder (for a complete description of the study design and protocol, see Nuechterlein et al., 1992). Only subjects with eye tracking data collected at the initial outpatient and the 1-year follow-up tests were included. The mean time between onset of the first psychotic episode and the initial outpatient test was 11.3 months for this patient sample.

Upon entry into the study, all patients met Research Diagnostic Criteria (Spitzer, Endicott, & Robins, 1978) for schizophrenia (n =30) or schizoaffective disorder, mainly schizophrenia (n = 4), and DSM-III-R criteria (American Psychiatric Association, 1987) for schizophrenia (n = 23), schizophreniform disorder (n = 8), or schizoaffective disorder (n = 3). Diagnoses were made on the basis of a patient's responses to an expanded version of the Present State Examination (PSE; Wing, Cooper, & Sartorius, 1974) and relevant information provided by family members. All patients were required to have a recent onset of schizophrenia, with their first psychotic episode beginning within 2 years of entry into the study. Subjects were excluded if there was any evidence of a neurological disorder, significant and habitual substance abuse or alcoholism in the 6 months prior to their psychotic episode, a history of substance abuse that obscured the diagnosis, or mental retardation. Following the procedure used by Gooding et al. (1994), patients diagnosed at entry with schizophreniform disorder were included in these analyses only if they met criteria for schizophrenia after their first year of participation. As a result, one additional patient was excluded from this report.

Thirty of the 34 schizophrenic patients were receiving a standardized starting dosage of 12.5 mg of fluphenazine (Prolixin) decanoate every 2 weeks at their initial outpatient test and were on this same dosage at the 1-year follow-up test. One patient was initially stabilized on 12.5 mg of fluphenazine decanoate every 2 weeks for 1-month, received an increase in dosage to 20.0 mg just prior to the initial outpatient test, and was maintained on 12.5 mg by the 1-year follow-up test. Another patient began on 12.5 mg every 2 weeks but became pregnant after the initial test and was free of medication at the time of the 1-year retest. One patient was unable to tolerate side effects from the standardized starting dosage and instead received 6.25 mg of fluphenazine decanoate every

2 weeks. One patient was stabilized initially on 10.0 mg of fluphenazine decanoate every 2 weeks but subsequently required 15.0 mg of the same medication. To assess clinical symptomatology during the 24-hr period prior to testing, an expanded version of the Brief Psychiatric Rating Scale (Expanded BPRS; see Lukoff, Nuechterlein, & Ventura, 1986; Overall & Gorham, 1962; Ventura et al., 1993) was administered at each test occasion to schizophrenic patients and normal control subjects.

Normal comparison subjects were excluded from the project if there was evidence of schizophrenia spectrum disorder (i.e., schizophrenia, schizotypal personality disorder, or paranoid personality disorder) or other major psychopathology (i.e., other psychotic disorders, bipolar disorder, recurrent major depressive disorder, cyclothymia, dysthymia, or enduring anxiety disorders) based on an expanded version of the PSE that was adapted for a lifetime perspective and a Minnesota Multiphasic Personality Inventory (Hathaway & McKinley, 1967) profile. Additional exclusionary criteria included evidence of a neurological disorder, significant and habitual substance abuse or alcoholism, prior treatment for a psychiatric disorder, or presence of a major psychiatric disorder in a first-degree relative.

Apparatus and Eye Movement Recording

The target stimulus consisted of a 2-cm white dot projected on a screen 1 m from the subject. The target was projected by a Kodak Model B-2 carousel slide projector. Target position on the screen was controlled by an Exact Model 119B function generator that drove a servomotor with connected mirror to deflect the light beam to the appropriate location on the screen (Research Oriented Instruments). Movement of the target was sinusoidal with a 0.4-Hz frequency of oscillation, and the target subtended 20 degrees of visual arc.

Pursuit eye movements were recorded using the electrooculogram (EOG), with SensorMedics miniature Ag/AgCl electrodes placed at the outer canthus of each eye. Vertical eye movements were detected with electrodes placed above and below the left eye. EOG signals were amplified with a Princeton Applied Research Model 113 preamplifier, monitored with a SensorMedics Model R511A dynograph, and recorded on frequency modulated (FM) tape. Low- and high-frequency cutoffs were set at 0.1 and 300 Hz, respectively.

Procedure

The procedure we used replicates that of Holzman et al. (1976) in which pursuit eye movements were recorded during four 50-s trials, each separated by a brief rest period. During each trial, subjects were instructed to follow the moving target stimulus only with their eyes; head motion was restrained by the use of a chin rest. An attentional manipulation was used during the third of the four trials by introducing semirandom target color changes (i.e., white to orange to white to blue) and instructing subjects to note these changes. To assist subjects with maintaining their gaze on the target stimulus during each 50-s period, re-alerting instructions ("Continue to follow the dot") were given 30 s into each trial. This same procedure was used at both the initial outpatient and the 1-year follow-up tests.

Data were examined for two occasions. An initial outpatient test was completed about 1 month after a relatively standardized starting outpatient medication level had been achieved and clinical state was stabilized. One year later, a follow-up test battery was administered.

Eye Movement Analysis

Eye tracking was assessed as part of a longitudinal study that was initiated at a time when researchers relied upon global quantitative and qualitative measures of eye tracking performance. Although global scores cannot characterize the precise nature of eye tracking impairment, quantitative and qualitative scores are valuable for indicating the presence of ETD (Levy et al., 1994). As Grove and Iacono (1994) noted, global measures have been undervalued and rejected out of hand by some, but they remain important in the field of schizophrenia research. In particular, global measures allow for a direct comparison with a substantial body of past research on ETD and the influence of attention in chronic schizophrenia.

Quantitative scoring was accomplished following a procedure developed by Lindsey, Holzman, Haberman, and Yasillo (1978). Using an analog version of a fast Fourier transform, the eye tracking signal was passed through bandpass filters with one band set for peak sensitivity at 0.4 Hz, the center of the frequency band of the target, and the second band registering higher frequency distortions of the primary signal from 1.2 to 12 Hz. After power was measured in each of these bands to represent signal and noise, respectively, the ratio of these two measures was transformed into natural logarithmic units and expressed as the log signal-to-noise ratio (ln S/N). Portions of the record containing eye blinks were removed prior to scoring.

Qualitative scoring was completed using a 5-point scale, following the procedure developed by Shagass et al. (1976). In the present study, a score of 5 signified very good tracking and a score of 1 indicated extremely poor tracking. Each record was assessed by one of three independent raters who were blind to group membership. Each rater was required to demonstrate high interrater reliability with an expert judge of eye movement records (P. S. Holzman). Interrater reliability was determined on the basis of 40 records, selected to reflect the range of recordings typically observed in a sample of schizophrenic patients. Interrater reliability was calculated independently for each rater and trial and indicated good reliability (Rater 1: r = .88, .90, .82, and .84 for the three noncolor trials and the color-variation trial, respectively; Rater 2: r = .79, .76, .81, and .77; Rater 3: r = .78, .74, .76, and .78).

For data analysis, scores from the first two noncolor trials were averaged to create single quantitative and qualitative index scores of tracking ability. The third noncolor trial (i.e., the fourth trial overall) was not included in this average because it may have been influenced by the introduction of an attentional manipulation.

As in previous studies of schizophrenic patients (e.g., Holzman, Solomon, Levin, & Waternaux, 1984; Levin, Lipton, & Holzman, 1981), quantitative and qualitative scores were highly related; during the initial outpatient and 1-year follow-up tests, r=.72 and .80 for noncolor trials and r=.72 and .67 for color trials. Prior research has shown that these measures also correlate strongly with another commonly used measure for evaluating eye tracking performance, RMS error (see Iacono & Clementz, 1993).

Subjects were classified as relatively good or poor trackers on the basis of qualitative cutoff scores comparable to those employed in previous research (e.g., Levin et al., 1981; Lipton, Levin, & Holzman, 1980). Qualitative scores ranging from 1.00 to 2.75 were considered to reflect poor tracking. Scores ranging from 2.76 to 5.00 were labeled as instances of good tracking.

Results

Hypotheses were tested using analyses of variance (ANOVAs) for mixed design. Quantitative and qualitative scores were analyzed

using a Group \times Target Type \times Test Occasion design. Simple effects ANOVAs were used to interpret significant interactions.

Because in some ETD studies, schizophrenic patients who present initially with schizophreniform disorder have been grouped with schizophrenic patients (e.g., Gooding et al., 1994) whereas in other studies these groups have been evaluated separately (e.g., Iacono et al., 1992), initial comparisons were made between the two groups in the present sample. Results of these analyses revealed no significant differences; therefore, data from the two groups were examined together.

Attention and Eye Tracking Performance

Significant group effects were obtained for quantitative and qualitative scores, F(1,56) = 4.60, p < .04 and F(1,56) = 15.64, p < .04.001, respectively. As predicted, schizophrenic patients displayed poorer pursuit tracking performance than did normal control subjects. Target type effects also were obtained, with schizophrenic patients and normal control subjects exhibiting improved tracking performance during attentional color manipulation of the target stimulus for quantitative, F(1,56) = 35.56, p < .001, and qualitative, F(1,56) = 50.22, p < .001, scores. These main effects were qualified, however, by a significant Group × Target Type effect for quantitative, F(1,56) = 7.15, p < .01, and qualitative, F(1,56) =6.08, p < .02, scores (Figure 1). In contrast to previous reports using chronic schizophrenic patients for quantitative scores, changing the color of the target stimulus improved pursuit tracking in these schizophrenic patients to such an extent that they were not reliably different from normal controls. Simple-effects ANOVAs confirmed that pursuit tracking was significantly impaired in schizophrenics relative to normal control subjects during noncolor trials, quantitative scores: F(1,56) = 6.97, p < .02; qualitative scores: F(1,56) = 18.82, p < .001, but that tracking performance did not differ between the two groups in the presence of a color target for quantitative scores, F(1,56) = 1.82, n.s. For qualitative scores, the difference between schizophrenic and normal control subjects on the color trial remained significant, F(1,56) = 10.95, p < .01, but the magnitude of the difference was somewhat less than that observed on noncolor trials.

To examine the possibility that enhanced performance on the color trial was due to practice effects because the attentional manipulation always occurred on the third of four trials, eye tracking scores from the fourth trial were compared with those obtained on the first two trials and on the color trial during the initial outpatient test. Across subjects, eye tracking on noncolor trials prior to the color trial was not different from performance obtained after the attentional manipulation was introduced for quantitative, F(1,54)=0.03, ns., or qualitative, F(1,54)=1.93, ns., scores. However, subjects showed significantly better tracking in the color trial than in the subsequent noncolor trial for quantitative, F(1,54)=24.42, p<.001, and qualitative, F(1,54)=20.01, p<.001, scores (Figure 1). Thus, improvement during performance of the color trial appears to be due to the attentional manipulation rather than practice.

Stability of Eye Tracking Performance Over Time

Scatter plots of eye tracking performance during the initial outpatient test and at the 1-year retest are presented in Figure 2. Test-retest correlations for quantitative and qualitative scores were

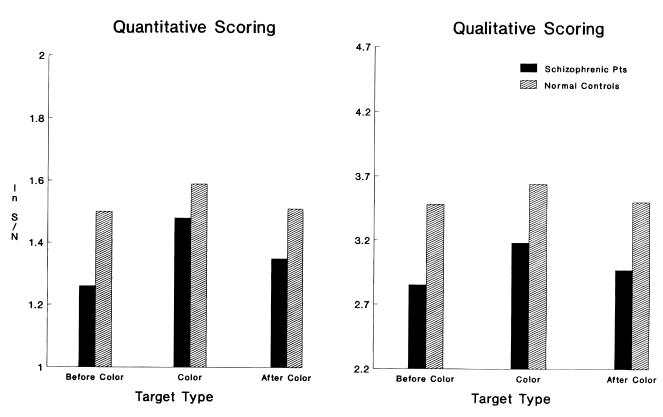
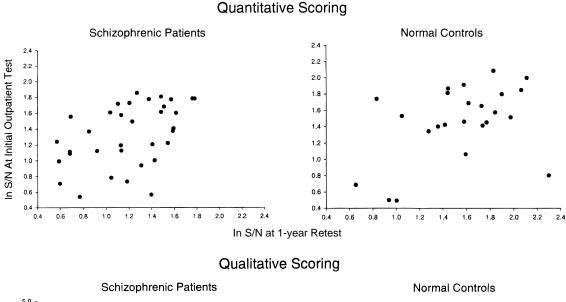


Figure 1. Effect of the attentional color manipulation on eye tracking dysfunction (ETD) in recent-onset schizophrenic patients and normal control subjects, as quantified by the natural logarithm of the signal-to-noise ratio (ln S/N) and qualitative ratings on a dichotomous scale. Higher scores are associated with more accurate tracking.



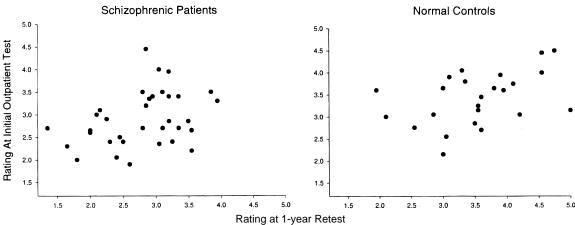


Figure 2. Smooth-pursuit eye tracking during noncolor trials at an initial outpatient test and 1-year retest in recent-onset schizophrenic patients and normal control subjects, as quantified by the natural logarithm of the signal-to-noise ratio (ln S/N) and qualitative ratings on a dichotomous scale. Higher scores are associated with more accurate tracking.

statistically significant, ranged from .35 to .47, and suggest that eye tracking performance was moderately but not highly stable across the 1-year period. Intraclass correlations were computed to provide an index of the extent to which subjects obtained the same

absolute score at the two time points (Table 1). To allow for direct comparisons with data reported by Gooding et al. (1994), the Pearson product–moment correlations also were computed. Comparing the Pearson correlation coefficients obtained for quantitative scor-

Table 1. Correlation Coefficients for Eye Tracking Performance to Two Targets Types on Two Occasions

Target	Quantitative		Qualitative	
	Intraclass correlation	Pearson correlation	Intraclass correlation	Pearson correlation
Schizophrenic patients $(n = 35)$				
Noncolor	.43**	.47**	.36*	.36*
Color	.36*	.40**	.38*	.38*
Normal control subjects $(n = 24)$				
Noncolor	.44*	.44*	.42*	.43*
Color	.40*	.40*	.35*	.35*

^{*}p < .05, one tailed. **p < .01, one tailed.

ing of the noncolor trials in the present study with those reported by Gooding et al. through use of Fisher's *z*, we demonstrated that there was no significant difference in correlations for the schizophrenic samples or for the normal control groups.

A significant Group × Test Occasion effect was obtained for quantitative scores, F(1,56) = 4.68, p < .04 (Figure 3, left). The Group × Target Type × Test Occasion interaction did not approach significance, F(1,56) = 0.00. During the initial outpatient test, schizophrenic patients and normal control subjects demonstrated comparable levels of performance when averaged across target conditions, F(1,56) = 0.49, ns. It was not until the 1-year follow-up test that the two groups diverged; the schizophrenic patients exhibited poorer smooth-pursuit eye tracking averaged across target conditions as compared with the normal controls, F(1,56) = 9.33, p < .01. Figure 3 (left) also suggests that eye tracking performance may be declining over time for schizophrenic patients while improving for normal control subjects. Because a change over time in ETD would be of theoretical significance, comparisons were made between the two time points for each group of subjects. Results indicated that schizophrenic patients were performing more poorly by the 1-year retest, F(1,33) = 4.70, p < .04, whereas normal controls maintained comparable performance over time, F(1,23) =

This Group \times Test Occasion interaction was not significant for the qualitative scores, F(1,56)=0.46, nor was the Group \times Target Type \times Test Occasion interaction, F(1,56)=2.22. In contrast to the quantitative score, when the eye tracking performance of schizophrenic patients and normal controls was compared at the initial outpatient test on the qualitative ratings (Figure 3, right), schizophrenic patients exhibited impaired tracking relative to normal subjects when tested initially as outpatients, F(1,56)=10.61, p<0.01, averaged across task conditions.

Influence of Time and Attentional Enhancement on Eye Tracking Classification

Seventeen schizophrenic patients (50%) but only 3 normal control subjects (12%) were classified as poor trackers based on the non-color trials at the initial outpatient test, $\chi^2=6.41$, df=1, p<.05. At the 1-year follow-up test, 13 (38%) schizophrenic patients and 3 normal controls (12%) were classified as exhibiting abnormal eye tracking, $\chi^2=4.32$, df=1, p<.05. A McNemar test for two correlated proportions showed no significant change in the proportion of schizophrenic patients classified as having poor tracking from the first to the second assessment.

Among schizophrenic patients, 11 of 17 (65%) who were classified as poor trackers at the initial outpatient test could be reclassified as good trackers with the introduction of the attentional color manipulation. At the 1-year followup, only 6 of 13 (46%) of the poor tracking patients exhibited enough substantial improvement in response to the color manipulation to permit reclassification. Although appearing to decline somewhat, the number of individuals who showed improvement from poor to good tracking with attentional enhancement did not change significantly over the two assessments as determined by a McNemar test.

Clinical Status Across Occasions

To document the symptom levels of the patients at the two testing points, a Group \times Test Occasion ANOVA was completed for the 18-item total composite scores from the Expanded BPRS. Schizophrenic patients exhibited very low symptom levels, with mean $(\pm SD)$ BPRS total scores of 25.7 \pm 6.4 and 24.1 \pm 5.5 at the initial outpatient and 1-year test occasions, respectively, where 18 is the

lowest possible score. These scores, nonetheless, were significantly higher than those obtained by the normal control subjects, F(1,56) = 21.57, p < .001. Normal subjects received mean BPRS total scores of 20.6 ± 3.1 and 19.6 ± 1.5 at the initial and 1-year test points, respectively. The main effect for test occasion on symptom levels and the Group \times Test Occasion interaction failed to reach significance, F(1,56) = 2.62, ns, and F(1,56) = 0.09, ns, respectively.

Discussion

The present findings replicate those of prior research by demonstrating that ETD is present more often in recent-onset schizophrenic patients than in normal control subjects (Iacono et al., 1992; Lieberman et al., 1993; Sweeney et al., 1992). This study also represents an extension of prior research because our findings show that the introduction of an attentional manipulation can differentially improve eye tracking accuracy among patients who have recently experienced their first schizophrenic episode. On one of two global performance indices, this improvement was sufficient to eliminate significant differences between recent-onset schizophrenic patients and normal subjects. A similar pattern of differential improvement was obtained with the second measure, suggesting that recent-onset schizophrenic patients benefit more from an attentional manipulation than do normal control subjects. These data contrast with those reported in prior research, such as the study conducted by Levin et al. (1981), in which the introduction of a color target appeared to improve eye tracking to a similar extent in schizophrenic patients and normal control subjects. Thus, our findings indicate that voluntary attention may play a notable role in reducing overall ETD during the early course of schizophrenic illness.

The difference between these results and those obtained in previous investigations examining the effects of voluntary attention on the same quantitative and qualitative measures (e.g., Levin et al., 1981) as those used in the present study is most likely associated with differences in duration of schizophrenic illness. Prior studies investigating the impact of attention on eye tracking relied on groups of chronic schizophrenic patients, whereas the current study was conducted with a group of schizophrenic patients having a very recent onset of illness. In addition, the present group of schizophrenic patients was relatively asymptomatic at the two assessment points. Although factors such as illness chronicity, history of psychotropic medication, and symptom levels clearly have potential bearing on attentional enhancement of eye tracking performance in schizophrenia, it is unclear which of these factors might be the key element.

One possible explanation for differences between recent-onset and chronic schizophrenic patients in the effectiveness of the attentional manipulation is that voluntary attention may be diminished as the illness progresses. That is, perhaps the impairments in attentional functioning that often accompany schizophrenia are relatively subtle during the very early stage of illness. After the first few years of schizophrenic illness, however, any deterioration in attentional functioning might be more apparent. Thus, voluntary attentional processes that are critical to modifying eye tracking may be relatively intact during the early years of schizophrenia represented in these analyses. A pattern of progressive decline in attentional functioning during the first few years of schizophrenia would be consistent with cross-sectional data suggesting that other cognitive declines might occur during this period (e.g., Bilder et al., 1992), although longitudinal data sug-

gesting cognitive recovery during this period also exist (Hoff et al., 1992).

Using the qualitative measure in the present study, results obtained on the basis of classifying schizophrenic patients as good or poor trackers are directionally consistent with this hypothesis. We observed a tendency for the attentional manipulation to be less effective in remediating ETD by the 1-year retest, although this change was not statistically significant. This tendency might be explained by greater intrinsic motivation to perform the eye tracking tasks by the 1-year retest and, therefore, less need for attentional enhancement. Increased motivation, however, would presumably be reflected in improved performance on the noncolor trials during the 1-year retest rather than the observed poorer performance, at least as judged by the quantitative measure.

There is some evidence from research utilizing a cross-sectional design that schizophrenic patients might exhibit a deterioration in smooth-pursuit eye tracking when the illness becomes chronic. Holzman et al. (1974) observed that 52% of recent schizophrenic patients exhibited ETD as compared with 86% of chronic schizophrenics. In a cross-sectional study comparing first-episode and multiple-episode cases of schizophrenic patients, Sweeney et al. (1992) also found less ETD during the early course of schizophrenia. These findings led Sweeney and colleagues to speculate that either (a) disturbances in smooth-pursuit eye tracking deteriorate over the course of schizophrenia or (b) schizophrenic illness involving recurrent episodes is associated with more severe disturbances in eye tracking. Either interpretation is consistent with the present data. It will be necessary to collect data beyond the first year or two of illness to determine if the eye tracking performance

of patients is indeed on a downward trajectory associated with multiple episodes of schizophrenia.

Clementz and Sweeney (1990) proposed that the pathophysiology underlying ETD may be independent of the neural systems invoked by an attentional manipulation. Attention manipulations, therefore, may only mask a tracking abnormality rather than reflect true amelioration of ETD. In contrast, Grove et al. (1991) reported preliminary evidence that a vigilance abnormality and ETD may be part of a common familial component in schizophrenia. Thus, it is possible that at least some aspects of attention and ETD share common variance.

Given that attention appears to be implicated to some degree in poor eye tracking, the separability of ETD and certain attentional abnormalities as biological markers for schizophrenia deserves further clarification. It will be necessary to disentangle these various possibilities and to elucidate potential mechanisms that might account for the differential effectiveness of attentional enhancement in recent-onset and chronic schizophrenic patients. Future analyses also will be able to determine the extent to which more specific measures of oculomotor functioning (e.g., pursuit gain, saccadic intrusions) are influenced by enhanced attention.

Results from the present study regarding the longitudinal stability of eye tracking are consistent with previous findings. Utilizing quantitative and qualitative scores, our data suggest that the temporal stability of smooth-pursuit eye tracking in recent-onset schizophrenic patients and normal controls is moderate. Gooding et al. (1994) reported somewhat higher reliability coefficients (r = .57-.68), but these values were not significantly different from those obtained in the present study. Because the two studies included

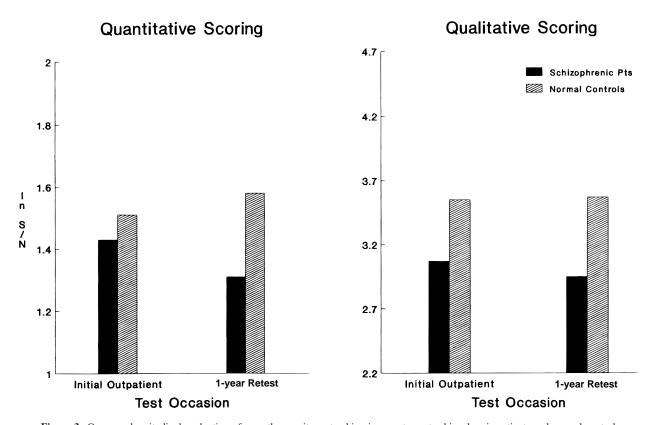


Figure 3. One-year longitudinal evaluation of smooth-pursuit eye tracking in recent-onset schizophrenic patients and normal control subjects, as quantified by the natural logarithm of the signal-to-noise ratio ($\ln S/N$) and qualitative ratings on a dichotomous scale. Higher scores are associated with more accurate tracking.

only 38 and 34 schizophrenic patients, respectively, the statistical power to detect differences between the studies was limited.

It is rather surprising that the degree of concurrence between the two studies is not higher, because the subject populations were generally similar on a number of dimensions. Studies have varied somewhat, however, in defining first-episode and recent-onset schizophrenia (Keshavan & Schooler, 1992). For instance, Gooding et al. (1994) may have excluded schizophrenic patients with a brief prior psychotic episode that warranted contact with a mental health service within the past 2 years whereas the present study would have included such patients. In contrast to the present study, the Gooding et al. investigation may have included schizophrenic patients with prior psychotic episodes that started more than 2 years before entry into the project if treatment was not sought (see Iacono & Beiser, 1989). There also was a small difference in age between the individuals in the present study and those included in Gooding et al.'s study, with average ages of 23.7 years and 21.6 years, respectively. It is possible, therefore, that the group in the current study included patients who were somewhat older and who had been on antipsychotic medications for a slightly longer period than the patients in the Gooding et al. study, but it is not readily apparent how these small sample differences would affect eye-tracking stability.

Gooding et al. (1994) did use a different quantitative measure of overall eye tracking accuracy (RMS error) than we did in the present study (ln S/N). However, these measures are highly correlated (Iacono & Clementz, 1993). We imposed a slightly longer intertest interval of 1 year versus the 9.5 months required by Gooding et al. Nonetheless, test–retest reliability indicated moderate stability over time.

Significant mean differences in ETD quantitative scores, averaged across attentional conditions, between schizophrenic patients

and normal controls were not obtained until the 1-year retest; this was not true of qualitative scores. Results of qualitative scoring indicated a greater likelihood of ETD in schizophrenic patients than in normal controls even at the initial outpatient testing. Although quantitative and qualitative scores were highly correlated in this and previous studies (Holzman et al., 1984; Levin et al., 1981), the two measures are not entirely analogous. For instance, Gooding, Clementz, Iacono, and Sweeney (1990) compared different methods of measuring eye tracking and demonstrated that the measures produced different results depending upon the task. Levy et al. (1994) suggested that, unlike qualitative classification, quantitative scoring can underestimate the extent of an abnormality when many small saccades are present; the authors assert, however, that no single measure or combination of measures has yet been identified as the most informative indicator. Our failure to find a group difference with quantitative scoring at the initial outpatient test, therefore, could be a function of the measure utilized rather than actual lack of ETD at this point.

The present results provide evidence that voluntary attention is implicated in poor eye tracking during the early course of schizophrenia in that attentional enhancement produced differential reduction in ETD in the recent-onset schizophrenia patients relative to normal subjects. Although ETD appears to be reasonably stable across a 1-year period in recent-onset schizophrenic patients, the possibility remains that transient normalization of ETD by an attentional manipulation may be more effective near the onset of illness, even while patients are maintained on medication. Because ETD and attentional deficits have both been implicated as potential vulnerability factors for schizophrenia, the relationship between voluntary attention and eye movement dysfunctions warrants continued investigation.

REFERENCES

- American Psychiatric Association. (1987). *Diagnostic and statistical manual of mental disorders* (3rd ed., revised). Washington, DC: Author.
- Bilder, R. M., Lipschutz-Broch, L., Reiter, G., Geisler, S. H., Mayerhoff, D. I., & Lieberman, J. A. (1992). Intellectual deficits in first-episode schizophrenia: Evidence for progressive deterioration. *Schizophrenia Bulletin*, 18, 437–448.
- Braff, D. L. (1993). Information processing and attention dysfunctions in schizophrenia. Schizophrenia Bulletin, 19, 233–259.
- Clementz, B. A., & Sweeney, J. A. (1990). Is eye movement dysfunction a biological marker for schizophrenia? A methodological review. *Psy*chological Bulletin, 108, 77–92.
- Gooding, D. C., Clementz, B. A., Iacono, W. G., & Sweeney, J. A. (1990). Methods for assessing tracking proficiency: A comparative analysis. *Psychophysiology*, 27, S35.
- Gooding, D. C., Iacono, W. G., & Beiser, M. (1994). Temporal stability of smooth-pursuit eye tracking in first-episode psychosis. *Psychophysiol*ogy, 31, 62–67.
- Grove, W. M., & Iacono, W. G. (1994). Comment on Levy et al. "Eye tracking dysfunction and schizophrenia." Schizophrenia Bulletin, 20, 781–786.
- Grove, W. M., Lebow, B. S., Clementz, B. A., Cerri, A., Medus, C., & Iacono, W. G. (1991). Familial prevalence and coaggregation of schizotypy indicators: A multitrait family study. *Journal of Abnormal Psychology*, 100, 115–121.
- Hathaway, S. R., & McKinley, J. C. (1967). Minnesota Multiphasic Personality Inventory Manual (revised). New York: Psychological Corporation.
- Hoff, A. L., Riordan, H., O'Donnell, D., Stritzke, P., Neale, C., Boccio, A., Anand, A. K., & DeLisi, L. E. (1992). Anomalous lateral sulcus asymmetry and cognitive function in first-episode schizophrenia. *Schizophrenia Bulletin*, 18, 257–272.
- Holzman, P. S. (1987). Recent studies of psychophysiology in schizophrenia. Schizophrenia Bulletin, 13, 49–75.

- Holzman, P. S., Levy, D. L., & Proctor, L. R. (1976). Smooth pursuit eye movements, attention, and schizophrenia. Archives of General Psychiatry, 33, 1415–1420.
- Holzman, P. S., Proctor, L. R., Levy, D. L., Yasillo, N. J., Meltzer, H. Y., & Hurt, S. W. (1974). Eye tracking dysfunctions in schizophrenic patients and their relatives. *Archives of General Psychiatry*, 31, 143–151.
- Holzman, P. S., Solomon, C. M., Levin, S., & Waternaux, C. S. (1984).Pursuit eye movement dysfunctions in schizophrenia: Family evidence for specificity. *Archives of General Psychiatry*, 41, 136–139.
- Iacono, W. G. (1983). Psychophysiology and genetics: A key to psychopathology research. *Psychophysiology*, 20, 371–383.
- Iacono, W. G. & Beiser, M. (1989). Age of onset, temporal stability, and eighteen-month course of first-episode psychosis. In D. Cicchetti (Ed.), The mergence of a discipline: Rochester symposium on developmental psychopathology (Vol. 1, pp. 221–260). Hillsdale, NJ: Erlbaum.
- Iacono, W. G., & Clementz, B. A. (1993). A strategy for elucidating genetic influences on complex psychopathological syndromes (with special reference to ocular motor functioning and schizophrenia). In L. J. Chapman, J. P. Chapman, & D. C. Fowles (Eds.), Progress in experimental personality and psychopathology research (pp. 11–65). New York: Springer.
- Iacono, W. G., Moreau, M., Beiser, M., Fleming, J. A. E., & Lin, T. (1992). Smooth-pursuit eye tracking in first-episode psychotic patients and their relatives. *Journal of Abnormal Psychology*, 101, 104–116.
- Iacono, W. G., Tuason, V. B., & Johnson, R. A. (1981). Dissociation of smooth-pursuit and saccadic eye tracking in remitted schizophrenics. *Archives of General Psychiatry*, 38, 991–996.
- Keshavan, M. S. & Schooler, N. R. (1992). First-episode studies in schizophrenia: Criteria and characterization. Schizophrenia Bulletin, 18, 491– 512
- Levin, S., Lipton, R. B., & Holzman, P. S. (1981). Pursuit eye movements in psychopathology: Effects of target characteristics. *Biological Psychiatry*, 16, 255–267.

- Levy, D. L., Holzman, P. S., Matthysse, S., & Mendell, N. R. (1994). Eye tracking and schizophrenia: A selective review. *Schizophrenia Bulletin*, 20, 47–62
- Lieberman, J. A., Jody, D., Alvir, J. M. J., Ashtari, M., Levy, D. L., Bogerts, B., Degreef, G., Mayerhoff, D. I., & Cooper, T. (1993). Brain morphology, dopamine, and eye-tracking abnormalities in first-episode schizophrenia. Archives of General Psychiatry, 50, 357–368.
- Lindsey, D. T., Holzman, P. S., Haberman, S., & Yasillo, N. J. (1978). Smooth-pursuit eye movements: A comparison of two measurement techniques for studying schizophrenia. *Journal of Abnormal Psychol*ogy, 87, 491–496.
- Lipton, R. B., Levin, S., & Holzman, P. S. (1980). Horizontal and vertical pursuit eye movements, the oculocephalic reflex, and the functional psychoses. *Psychiatry Research*, 3, 193–203.
- Lukoff, D., Nuechterlein, K. H., & Ventura, J. (1986). Appendix A: Manual for expanded Brief Psychiatric Rating Scale (BPRS). Schizophrenia Bulletin, 12, 594–602.
- Nuechterlein, K. H., & Dawson, M. E. (1984). Information processing and attentional functioning in the developmental course of schizophrenic disorders. *Schizophrenia Bulletin*, 10, 160–203.
- Nuechterlein, K. H., Dawson, M. E., Gitlin, M., Ventura, J., Goldstein, M. J., Snyder, K. S., Yee, C. M., & Mintz, J. (1992). Developmental processes in schizophrenic disorders: Longitudinal studies of vulnerability and stress. *Schizophrenia Bulletin*, 18, 387–425.

- Overall, J. E., & Gorham, D. R. (1962). The Brief Psychiatric Rating Scale. *Psychological Reports*, 10, 799–812.
- Shagass, C., Roemer, R. A., & Amadeo, M. (1976). Eye-tracking performance and engagement of attention. Archives of General Psychiatry, 33, 121–125.
- Spitzer, R. L., Endicott, J., & Robins, E. (1978). Research Diagnostic Criteria: Rationale and reliability. Archives of General Psychiatry, 35, 773–782.
- Sweeney, J. A., Haas, G. L., & Li, S. (1992). Neuropsychological and eye movement abnormalities in first-episode and chronic schizophrenia. *Schizophrenia Bulletin*, 18, 283–293.
- Ventura, J., Lukoff, D., Nuechterlein, K. H., Liberman, R. P., Green, M. F., & Shaner, A. (1993). Brief Psychiatric Rating Scale (BPRS), expanded version (4.0): Scales, anchor points, and administration manual. *Inter*national Journal of Methods in Psychiatric Research, 3, 227–243.
- Wing, J. K., Cooper, J. E., & Sartorius, N. (1974). The measurement and classification of psychiatric symptoms: An instruction manual for the PSE and CATEGO programs. London: Cambridge University Press.

(RECEIVED October 29, 1996; ACCEPTED November 24, 1997)