

Antisaccades and Smooth Pursuit Eye Tracking and Schizotypy

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Background: Eye tracking deficits are one of a few widely validated behavioral markers of risk for schizophrenia. Recently, it has been proposed that antisaccade performance may also constitute a marker of schizophrenia risk. This study investigated whether eye tracking and antisaccade deficits could be found in another population with putative liability to schizophrenia—nonclinical subjects with elevated scores on a psychometric index of perceptual aberrations.

Methods: Subjects were 55 university students who received either high or normal scores on the Perceptual Aberration Scale, a measure of schizotypy indexing body image and perceptual distortions. Subjects completed a smooth pursuit eye tracking task and an antisaccade task. Eye movements were monitored using an infrared limbus tracker.

Results: Subjects with high Perceptual Aberration Scale scores (putative “schizotypes”) had lower pursuit qual-

ity and a lower percentage correct on the antisaccade task than the controls. The 2 groups did not differ in antisaccade or error latencies. The increase in antisaccade errors in the schizotypes was accounted for almost entirely by an increase in perseverative errors, but virtually no difference between groups on random errors. Antisaccade performance was significantly related to pursuit quality.

Conclusions: Subjects with elevated Perceptual Aberration Scale scores have performance deficits on oculomotor tasks that have been linked to latent liability to schizophrenia, namely, smooth pursuit and antisaccade performance. The antisaccade errors in the schizotype group were primarily perseverations, a behavioral pattern often associated with frontal lobe dysfunction and observed in the performance of schizophrenic patients.

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IN POPULATIONS at increased risk for schizophrenia, a notable proportion of individuals show abnormalities on cognitive, perceptual, or motor tasks—abnormalities that are similar to those found in schizophrenic patients. At-risk populations also have elevated scores on subclinical symptoms related to schizophrenia, such as thought disorder, abnormal perceptual experiences, and social withdrawal.^{1,2} The behavioral and perceptual anomalies that occur at higher rates in populations at risk for schizophrenia have been called “behavioral markers” of latent liability to the disorder.³ These markers are the subject of extensive study, both because they may enhance the power of genetic studies of schizophrenia, and because an understanding of their neural basis may elucidate the nature of brain abnormalities relevant to schizophrenia.

Eye tracking dysfunctions (ETD) are one of the most widely validated of the be-

havioral markers.⁴ Eye tracking dysfunctions are found at elevated rates in schizophrenic patients; relatives of schizophrenic patients have elevated rates of ETD, but relatives of bipolar patients do not. Patients with schizotypal personality, but not patients with nonspectrum personality disorders, have poorer pursuit quality than normal controls (NCs).⁵

Recently, deficits on the antisaccade task have been proposed as another marker of latent liability.^{6,7} In the antisaccade task (**Figure 1**), the subject fixates a central dot that steps at random to the left or right. When the target steps into the periphery, the subject's task is to look away from the target to the opposite hemifield. Numerous reports⁸⁻¹⁰ have been published of elevated rates of antisaccade errors in schizophrenic patients. Recently a robust increase in error rates^{6,7} and an increase in antisaccade latencies¹⁰ have been reported in healthy first-degree relatives of schizophrenic patients. These findings in a high-

SUBJECTS AND METHODS

SUBJECTS

Subjects were undergraduates at Cornell University, Ithaca, NY, recruited from an entering class using an epidemiological survey method. We have described these procedures extensively elsewhere.¹⁴ Of the 2000 students approached, 1684 subjects completed the 250-item questionnaire, which included the 35 items from the Perceptual Aberration Scale. The 84.2% response rate was consistent with representative sampling.¹⁵ Two percent of the subjects were excluded for having elevated scores on an infrequency scale used to detect random responding.¹⁶ Subjects were assigned to the high Perceptual Aberration Scale (HPA) group, also referred to as "schizotypic," if they scored more than 2 SD above the mean of their sex, and to the NC group if they scored within 0.5 SD of their sex.^{11,17} Of the 1646 students, 76 students met criteria for inclusion in the HPA group, and 1332 subjects met criteria for the NC group. Fifty cases were selected randomly from those eligible for each group as possible participants. The consent rate did not differ between HPA and NC subjects. Thirty-one HPA and 24 NC subjects yielded scoreable data on the eye tracking and antisaccade tasks (described in the "Eye Movement Measurement" section). The mean (\pm SD) Perceptual Aberration Scale score for the HPA group was 19.77 ± 6.34 ; for the NC group the mean was 0.77 ± 0.99 . Demographic characteristics are given in the **Table**.

CLINICAL MEASURES

Schizotypy Measure

The Perceptual Aberration Scale is a 35-item, true-false, self-report inventory of body image and perceptual disturbances conceptually related to schizophrenia-related psychopathology.¹² It includes items like "Now and then when I look in the mirror, my face seems quite different than usual" (keyed true).¹² Internal consistency analyses typically yield α coefficients around 0.90 and high test-retest reliability ($r = 0.75$). In nonclinical university samples, individuals with high Perceptual Aberration Scale scores exhibit many of the neurocognitive abnormalities observed in schizophrenic patients and high-risk populations.¹⁸⁻²² Subjects with high Perceptual Aberration Scale scores also have increased levels of clinically significant schizotypal symptoms²³ and elevated risk for treated schizophrenia among first-degree relatives.²⁴

Psychological State Measures

The Beck Depression Inventory²⁵ was used to measure depressive and dysphoric symptoms. The State Trait Anxiety Inventory²⁶ measured state and trait anxiety. The self-

administered computerized version of the Diagnostic Interview Schedule was used to screen for lifetime history of schizophrenia, schizophreniform illness, mania, and dysthymia.²⁷ The Diagnostic Interview Schedule demonstrates excellent sensitivity for these disorders.²⁸ Each subject provided written consent to obtain access to his or her official Scholastic Aptitude Test (SAT) verbal and quantitative scores. These were used as indexes of the subjects' general level of intellectual functioning.

Eye Movement Measurement

Oculomotor recordings were obtained in a darkened room. Eye movements were monitored using a commercially available software package (Optokinetograph System, Eye and Brain Technology Inc, Thessalonika, Greece). Each subject sat 57cm in front of a computer monitor; the subject's head was stabilized in a custom-made chin rest. Infrared light-emitting diodes and sensors, mounted in ophthalmologic eyeglass frames, were positioned at the level of the limbus in each eye. Subjects completed a 6-point calibration across 24° , repeated before each trial of data collection. After calibration, eye position data were represented linearly across a visual angle of $\pm 12^\circ$. Eye movement recordings were digitized at 250 Hz. Saccades were defined as eye movements with a velocity 100% greater than target velocity. This criterion is sensitive to corrective saccades superimposed on smooth pursuit with amplitudes as small as 0.5° . For the antisaccade task, saccades were defined as having a minimum velocity of 8 degrees per second and a minimum duration of 18 milliseconds. The minimum amplitude was 3° and the minimum latency was 100 milliseconds. Saccades were automatically identified by our software (Optokinetograph System) and traces were visually inspected to confirm correct categorization. Testing was done blind to group membership.

SMOOTH PURSUIT STIMULI AND DATA COLLECTION

The target, a 0.5° square, moved with a triangle wave velocity profile at 8 degrees per second across a visual angle of 20° . Eight cycles were collected.

ANTISACCADE STIMULI AND DATA COLLECTION

Subjects fixated a square subtending $1^\circ \times 1^\circ$ in visual angle at the center of the screen (Figure 1). After a random interval, the target stepped horizontally to a position 12° to the left or right of the fixation point. The direction of the target step was pseudorandom. The screen then went blank for 1000 milliseconds during which the subject's task was not to look toward the target, but to look in the opposite direction. Subjects were instructed that although they were to respond quickly, it was more important to be correct in the direction of the saccade than to be fast. Each subject was given 15 practice trials with the experimenter

risk population suggest that antisaccade deficits are unrelated to the disease process but may be related to latent liability for the disorder.

Three strategies are used to define populations at risk for schizophrenia: (1) a biological relationship to an affected person (eg, first-degree relative); (2) an Axis II

diagnosis of cluster A personality disorders (eg, schizotypal personality disorder); and (3) deviance on an established laboratory measure or psychometric marker of schizotypy (eg, indexes of schizotypic phenomena).¹¹ We undertook this study to determine if at-risk subjects ascertained by the third strategy would show the same pat-

providing feedback. Subjects then performed 45 trials of the antisaccade task. No feedback was given during testing.

DATA REDUCTION, SCORING AND STATISTICAL ANALYSES

Smooth Pursuit

The pursuit traces were evaluated independently by 2 raters (G.O'D. and P.S.H.) blind to subject identity and group membership. Traces were assigned a score of normal (3), mixed (2), or abnormal (1). (Mixed was defined as a pursuit trace in which several normal cycles were found, along with clearly abnormal cycles.) After interrater reliability was determined, the scores assigned by the 2 raters were averaged to create a mean pursuit quality score for each subject. Global ratings of pursuit quality, such as qualitative ratings, have been reported to be better than specific pursuit measures, such as pursuit gain, at discriminating schizophrenic patients and their first-degree relatives from NCs.^{29,30} Qualitative ratings of pursuit are reliable across laboratories,³⁰ and are highly correlated with other global measures such as root mean square error and log signal-to-noise ratio.²⁹ The distribution of the pursuit quality scores was, as expected, significantly nonnormal (SPSS, Chicago, Ill, Kolmogorov-Smirnov procedure $z = 1.4, P = .04$). Therefore nonparametric statistics were used.

Antisaccade

Dependent variables were percent correct, latency to antisaccades and to errors, and percent of perseverative errors (PEs) and nonperseverative errors (NPEs). Antisaccade errors were corrected by the subjects, indicating that they understood the task. The percent correct score was calculated as follows: (number of correct antisaccades)/(number of correct antisaccades+number of reflexive saccades [errors]).

We were interested to determine whether subjects' errors reflected a tendency to perseverate, a response pattern associated with frontal dysfunction.³¹ Perseverative errors were operationalized as errors that represented a continuation of a motor set that was established in the trials immediately preceding the error. The motor pattern had to have been executed consecutively twice immediately prior to the error. This definition yielded 2 types of PEs, as follows: (1) a reflexive saccade (error) in the same direction as the saccades made on the previous 2 trials (ie, left-left-left [error] or right-right-right [error]); and (2) an inappropriate continuation of a pattern of alternation that had been executed consecutively twice in the preceding trials (ie, left-right-left-right-left [error], or right-left-right-left-right [error]). If the error represented a change from, rather than a continuation of, the established motor set, or if no motor set had been established in the previous trials, the errors were classified as NPE. Of the 45 trials, 15 required that the subject abandon an established motor set to make

a correct response, while 30 trials required responses that were consistent with the established motor set or were trials in which no momentary motor set had been established. The percent PE score was calculated as follows: (number of PEs)/(15, ie, number of trials in which a PE could be made).

The percent NPE score was calculated as follows: (number of NPEs)/(30, ie, number of trials in which an NPE could be made).

The trials that contributed to PE and NPE scores were classified a priori, assuming a correct pattern of responses in the trials immediately preceding. Because this classification would be incorrect if the subject also made an error in the immediately preceding trials, a second analysis was conducted for each subject using only the direction of the saccades in the previous trials (and not target direction) to define PEs and NPEs. The results were almost identical, and all findings that were significant using one method were significant using the other.

Of 2475 trials collected, 77 (3%) could not be scored for blinks, misfixations, anticipations (latency <100 milliseconds) and failures to respond (saccade <3°). More trials were unscorable in the HPA group (62) than in the NC group (15) (Mann-Whitney *U* test, $z = -2.45, P = .01$). This was attributable to more misfixations and blinks in the HPA group. There was no difference between groups ($P > .8$) on the number of anticipatory saccades or the number of failures to respond. Between-groups analyses using raw data (number of errors) rather than percent correct were also calculated. All significant between-group results remained significant. Therefore, only the percent correct data are reported below.

The percent correct variable and the percentage of PEs and NPEs were significantly nonnormal in their distribution (Kolmogorov-Smirnov statistic, all $P < .01$). The usual transformations were attempted but these did not normalize the distributions. Therefore the original data were analyzed using nonparametric statistics. The latency to antisaccades and saccades were calculated separately, with outliers excluded using box-and-whisker plots. Because all latency outliers were made within the time allotted to subjects, they were retained in the error analyses. Antisaccade and error latencies were normally distributed.

The correlation between pursuit quality and percent correct on the antisaccade task was evaluated using the Spearman rank correlation coefficient. Correlations of smooth pursuit and antisaccade indexes with the mental state (anxiety and depression) measures were evaluated using both Spearman and Pearson product-moment correlation coefficients. Partial correlation analysis was used to control for the effects of mental state variables. Between group differences in eye movement performance were evaluated using directional (1-tailed) tests based on our a priori hypotheses and based on published results using these tasks in other high-risk populations, with an α level of .05.^{4,6,10} All other tests were two tailed.

tern of eye movement deficits seen in schizophrenic patients and their first-degree relatives. We used a well-established measure of schizotypy, the Perceptual Aberration Scale,¹² to select nonpsychotic schizotypic individuals for study. We hypothesized that the group with elevated Perceptual Aberration Scale scores would have

poorer smooth pursuit quality and worse performance on the antisaccade task than nonschizotypic controls. Because it has been proposed that both ETD and poor antisaccade performance may reflect deficient inhibitory control of saccades,¹³ we evaluated the relationship between smooth pursuit quality and antisaccade performance.

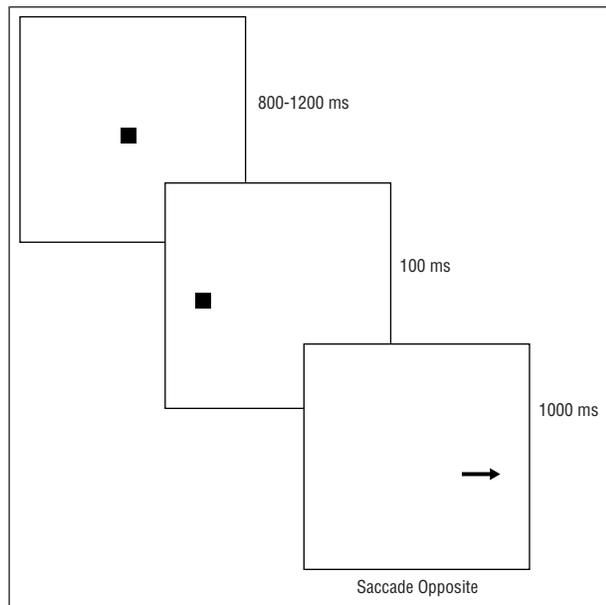


Figure 1. Antisaccade Task. Trial begins with a central fixation point of duration 800 to 1200 milliseconds. When the fixation point is extinguished, a cue simultaneously appears for 100 milliseconds 12° to left or right of central fixation. Subjects are instructed to look in the opposite direction of the flash, ie, to the mirror position on the opposite side of the screen.

RESULTS

SUBJECT CLINICAL CHARACTERISTICS

State and Trait Anxiety Scores

State and trait anxiety scores for HPA subjects exceeded those of NC subjects (State Anxiety: HPA, 39.23 ± 10.19 ; NC, 31.5 ± 6.12 ; $t_{53} = 3.17$, $P = .002$; Trait Anxiety: HPA, 45.26 ± 10.61 ; NC, 35.13 ± 7.74 ; $t_{53} = 3.94$, $P < .001$). Higher levels of depression (Beck Depression Inventory) were found in the HPA group than in the NC group (HPA, 10.39 ± 5.89 ; NC, 2.38 ± 2.57 ; $t_{53} = 6.78$, $P < .001$). No subject screened positive for a definite lifetime diagnosis of schizophreniform disorder, schizophrenia, bipolar disorder or dysthymia on the Diagnostic Inventory Schedule.

General Intellectual Level

The 2 subject groups did not differ in either quantitative or verbal domains of the SAT (Table 1).

Smooth Pursuit Performance

The interrater reliability (intraclass correlation coefficient [ICC]) for the rating of pursuit quality was high (0.93). The HPA group had significantly lower pursuit quality than the NC group (1.99 ± 0.73 vs 2.42 ± 0.79 , $n = 51$, Mann-Whitney test, $z = 2.2$, $P = .01$). The modal pursuit score for the HPA group was 1 (abnormal), and the median was 2 (mixed); for the NC group, both the mode and the median pursuit scores were 3 (normal).

Subject Demographic Characteristics*

Characteristic	Normal Controls (n = 24)	HPA Subjects (n = 31)	Statistical Test	P
M/F	10/14	15/16	$\chi^2_1 = 0.25$.68
Age, y	$19.04 \pm .36$	$19.0 \pm .05$	$t_{53} = 0.34$.74
Subjects who were right-handed, %	71	80.6	$\chi^2_1 = 0.89$.35
SAT				
Verbal	575.50 ± 67.39	594.26 ± 84.67	$t_{53} = 0.89$.39
Quantitative	648.46 ± 67.46	658.32 ± 95.04	$t_{53} = 0.45$.65

*HPA indicates High Perceptual Aberration Scale score; SAT, Scholastic Aptitude Test. Values are expressed as mean \pm SD unless otherwise indicated.

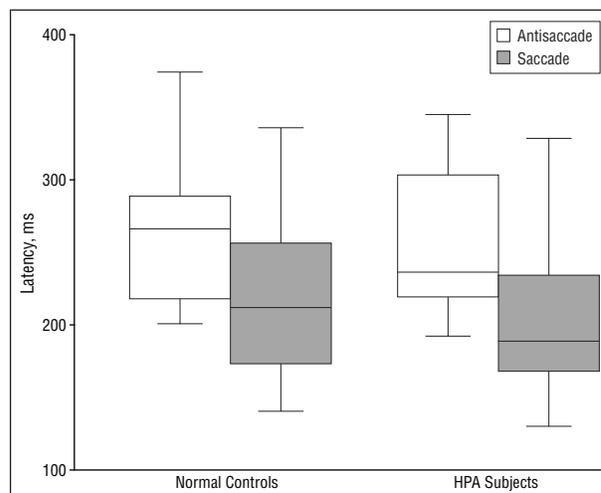


Figure 2. Boxplot of antisaccade and saccade latencies of normal controls and High Perceptual Aberration Scale (HPA) score subjects. There were no between-groups differences on latency to antisaccades ($t_{53} = 0.38$, $P = .35$) or latency to saccades ($t_{34} = 0.95$, $P = .17$). Latency to antisaccades were significantly longer than latency to saccades for both groups (matched-pair t_{35} , $P < .001$).

Antisaccade

Visual field had no effect on percent correct or latency ($P > .2$). Therefore, results for all trials were combined. The HPA group had significantly lower percent correct on the antisaccade task (0.94 ± 0.06 vs 0.98 ± 0.02 , Mann-Whitney test, $z = -2.12$, $P = .02$). One quarter of the HPA group made 4 or more errors; no NC subject did.

The groups did not differ in latency to an antisaccade (NC, 266.3 ± 40.4 ; HPA, 261.8 ± 45.3 ; $t_{53} = 0.38$, $P = .35$) or latency to a reflexive error (NC, 225.3 ± 59.7 ; HPA, 206.5 ± 57.3 ; $t_{34} = 0.95$, $P = .17$) (Figure 2). The latency to an antisaccade was, as expected, significantly longer than the latency to a reflexive error (antisaccade, 259.46 ± 48.4 ; saccade latency, 213.79 ± 58.15 ; matched-pair $t_{35} = 4.1$, $P < .001$).

High Perceptual Aberrational Scale subjects made significantly more PEs than did NCs ($9.5\% \pm 10.2\%$ vs $2.2\% \pm 3.8\%$, Mann-Whitney test, $z = 2.89$, $n = 55$, $P = .002$). This corresponds to an effect size (ϕ) of 0.39. The 2 groups did not differ on NPEs (HPA, $3.3\% \pm 4.4\%$ vs NC, $2.1\% \pm 3.1\%$, Mann-Whitney test, $z = 0.99$, $n = 55$, $P = .16$).

Only subjects in the HPA group were more likely to make an error when a correct response required that they change motor set (PE, $9.5\% \pm 10.2\%$ vs NPE, $3.3\% \pm 4.3\%$, matched-pair $t_{30} = 4.16$, $P < .001$ (effect size d of .78 [Cohen's d for matched pair t test]); for NC group, error rate was unaffected by the requirement to change motor set (PE, $2.2\% \pm 3.8\%$ vs NPE, $2.1\% \pm 3.1\%$, $t_{23} = 0.13$, $P = .45$ [effect size d of .03]). There was no difference in latency to the 2 types of errors (PE, 194.89 ± 53.19 ; NPE, 191.64 ± 7.8 , matched-pair $t_{13} = 0.51$, $P = .62$).

Correlational Analyses for Antisaccade Performance and Pursuit Quality

Pursuit quality was significantly correlated with percent correct on the antisaccade task (Spearman rank $\rho = 0.33$, $n = 51$, $P = .02$), and with PE ($\rho = -0.32$, $n = 51$, $P = .01$) and NPE ($\rho = -0.27$, $n = 51$, $P = .03$).

Correlations of Anxiety, Depression, and SAT Scores With Oculomotor Performance

The Spearman and Pearson correlations between oculomotor scores, the clinical measures and general intellectual functioning were essentially identical. We therefore report only the Pearson correlations along with the relevant partial correlation analyses. Smooth pursuit quality was not significantly correlated with any of the mental state variables, nor was it related to the SAT scores. The antisaccade percent correct, PE and NPE indexes were uncorrelated with anxiety measures and the SAT scores. The scores on the Beck Depression Inventory were significantly correlated ($P = .04$) with antisaccade percent correct ($r = -0.29$) and with antisaccade PE and NPE (both correlations = 0.29). To examine whether the relationship between antisaccade performance and group membership would remain if the effect of depression were controlled for, we conducted partial correlation analyses. Controlling for depression, the associations between group status and antisaccade PE (partial $r = 0.31$, $P = .01$) and antisaccade percent correct (partial $r = -0.22$, $P = .06$) remained; the association between group membership and NPE did not (partial $r = -.03$, $P = .41$). The partial correlations suggest that the association between group membership (ie, schizotypy status) and PE particularly, but also antisaccade percent correct, are not solely a function of depression.

COMMENT

Our results demonstrate that subjects identified as schizotypic (or "hypothetically psychosis prone") by the Perceptual Aberration Scale have a pattern of smooth pursuit and saccadic deficits similar to that observed in schizophrenic patients and their first-degree relatives. Furthermore, the smooth pursuit and antisaccade performance deficits do not seem to be the result of third-variable confounds such as anxiety, depression, or general intellectual ability differences between the groups. A relationship between schizotypal symptoms and antisaccade error rate has been reported in 2 other at-risk popu-

lations, first-degree relatives ($N = 29$, $r = 0.33$, $P < .08$) and clinically diagnosed schizotypal patients.¹⁰ To our knowledge, this is the first study to report on antisaccade performance in subjects selected using the psychometric approach to schizotypy.

In our study, the difference in the percent correct scores between HPA and NC groups is accounted for almost exclusively by an increase in the number of PEs in the HPA group. When a correct response required a change in motor set established in the previous trials, HPA subjects showed a 187% increase in error rates over the trials in which no change was required; NC subjects showed only a 4.5% increase in errors. This pattern of errors, in which the subject is unusually vulnerable to proactive interference from previous trials and has difficulty changing sets when momentary, irrelevant response tendencies have been established, is characteristic of monkeys with prefrontal lesions.³¹ Previous studies of schizophrenic patients have linked antisaccade errors and perseverative tendencies on the Wisconsin Card Sort.^{32,33} To our knowledge, however, this has not previously been shown in schizotypal or other at-risk populations.

Other studies of university students with elevated Perceptual Aberration Scale scores have also reported performance deficits consistent with a possible frontal impairment, eg, deficits in sustained attention,¹⁹ executive functioning,²¹ and spatial working memory.²⁰ These tasks, like the antisaccade task,^{34,35} have been shown to activate frontal-striatal-thalamic circuitry in positive emission tomography studies.³⁶⁻³⁸ Although our study was specifically interested in prefrontal dysfunction, dysfunction elsewhere in the oculomotor circuit may yield similar deficits.^{39,40} Clarification of the substrates of ETD and antisaccade deficits in vulnerable populations await in vivo imaging investigations. We are conducting such an investigation in first-degree relatives.⁴¹

No differences in reaction times were observed between the HPA and NC groups. Schizophrenic patients generally have longer reaction times than NCs.⁴² This has been demonstrated in one study of first-degree relatives as well.¹⁰ However, in that study, the relatives were significantly older than NCs. Two other studies found no difference in antisaccade latency in first-degree relatives of schizophrenic patients compared with NCs, and one study found no difference in predictive saccade latencies.^{6,7} Thus, latency differences on voluntary tasks are not as robust in populations at risk for schizophrenia as they are in the patients themselves; they may be related to the disease process or its treatment rather than liability.

Our study found a higher percent correct in the antisaccade task than reported in some other studies.^{6,10} This is likely due to small differences in the paradigm used. Studies that use, as we did, both a practice session with feedback and a single amplitude stimulus report error rates in the NC group consistent with those reported here.^{9,43,44} The antisaccade paradigm used in this study was shown in a previous positive emission tomography study³⁴ to significantly activate frontal eye fields relative to saccades, and to yield antisaccades with significantly longer latencies than saccades; thus, even at low error rates, the task makes significant demands on the voluntary control of eye movements.

Our study also demonstrates that schizotypic subjects identified with the Perceptual Aberration Scale have reliable deficits in pursuit quality. Our findings are consistent with prior studies that have found that university students with ETD have elevated scores on a variety of measures of schizotypal symptoms.⁴⁵ Siever et al,^{5,46} studying clinically identified schizotypal subjects, found that ETD were significantly more common in schizotypal subjects than in NCs, but that the symptom that best predicted pursuit quality was social withdrawal. The association between deficitlike symptoms and ETD has been noted by other investigators.⁴⁷⁻⁵⁰ Nevertheless, several studies have reported a significant relationship between ETD and "psychotic-like" symptoms and/or perceptual abnormalities in clinical and normal populations.⁵¹⁻⁵⁴ For example, scores on the Perceptual Aberration Scale are significantly associated with pursuit quality among schizophrenic patients⁵⁵ and with pursuit variability among undergraduates.⁵⁶

One limitation of our study is that we selected our groups using an imperfect measure of schizotypy: the Perceptual Aberration Scale is thought to generate an admixture of schizotypes and an unknown proportion of individuals who experience perceptual anomalies for reasons unrelated to schizophrenia risk. Although the Perceptual Aberration Scale is a fallible marker of schizophrenia liability, as yet there is no marker in any domain of schizophrenia, including genetics, neurobiology, psychophysiology, and psychometrics, that is capable of specifically detecting liability for schizophrenia with complete fidelity. Nevertheless, we believe this instrument detects a significant number of individuals liable to schizophrenia. The body of data that support this position, reviewed at length elsewhere,⁵⁷ are not yet as robust for other psychometric measures of schizotypy.

On 10-year clinical follow-up, individuals initially selected for high Perceptual Aberration Scale scores revealed a variety of psychiatric outcomes, with most, but not all, of a schizophrenia-related nature.¹ Clearly, not all those scoring high on the Perceptual Aberration Scale go on to develop schizophrenia or related illnesses. However, such heterogeneity of outcomes is also seen in the clinical follow-up of children at risk for schizophrenia. Nevertheless, the inclusion of valid but fallible quantitative markers can greatly improve the power of genetically oriented investigations.⁵⁸

A few studies^{59,60} have failed to document elevated Perceptual Aberration Scale scores among first-degree relatives of schizophrenic patients, and another study⁶¹ has reported significantly lower scores on the Perceptual Aberration Scale in relatives than in NCs. In agreement with some of the authors of these studies, we believe that the findings of lower Perceptual Aberration Scale scores in relatives may be attributable to a defensive response set. Since each of these studies recruited relatives who knew they were being recruited on the basis of their relationship to a schizophrenic proband, it is possible that they interpreted the intent of the questions differently than NCs. However, in a more direct test of the relevance of high Perceptual Aberration Scale scores for genetic risk for schizophrenia, it was found that nonpsychotic individuals with elevated Perceptual Aberration Scale scores

had significantly elevated risk of schizophrenia in their first-degree relatives, but no increase in rates of bipolar or unipolar affective illness.²⁴

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