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# Psychophysical isolation of a motion-processing deficit in schizophrenics and their relatives and its association with impaired smooth pursuit

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**ABSTRACT** **Schizophrenia patients and many of their relatives show impaired smooth pursuit eye tracking. The brain mechanisms underlying this impairment are not yet known, but because reduced open-loop acceleration and closed-loop gain accompany it, compromised perceptual processing of motion signals is implicated. A previous study showed that motion discrimination is impaired in schizophrenia patients. Motion discrimination can make use of position and contrast as well as velocity cues. Here, we report that the motion discrimination deficit, which occurs in both schizophrenic patients and in their first-degree relatives, involves a failure of velocity detection, which appears when judging intermediate target velocities. At slower and faster velocities, judgments of velocity discrimination seemed normal until we experimentally disentangled velocity cues from nonmotion cues. We further report that compromised velocity discrimination is associated with sluggish initiation of smooth pursuit. These findings point to specific central nervous system correlates of schizophrenic pathophysiology.**

Although schizophrenia is significantly influenced by genetic factors (1, 2), the clinical disorder occurs relatively infrequently; estimates vary from 3.5% to ≈8% in the nuclear families of schizophrenic probands (3). This low intrafamilial prevalence poses difficulties for studies of genetic linkage in schizophrenia. Certain physiological traits, however, although uncommon in the general population, occur more frequently than the clinical syndrome in first-degree relatives and suggest themselves as more penetrant alternative phenotypes for the study of the genetics and pathophysiology of schizophrenia (4). One of the more widely studied of these cofamilial traits is eye tracking dysfunction (5–7).

Eye tracking dysfunction shows itself specifically in smooth pursuit eye movements, a tracking response to moving visual targets. Other kinds of eye movements, such as voluntary saccades (8, 9), vestibularly controlled eye movements (10), and the oculocephalic reflex (11), are normal in both patients and relatives. This set of findings indicates that the eye tracking dysfunction is specific to the smooth pursuit system and that its neuroanatomical substrate is above the brain stem.

Several investigators have characterized the nature of the eye tracking dysfunction in schizophrenia as low closed-loop gain (the ratio of eye velocity to target velocity) with frequent compensatory catch-up saccades and low initial acceleration of the eye, both of which indicate that eye velocity lags behind target velocity (12–15). There may be two explanations for these findings: (*i*) Processing of velocity signals during target movement is deficient (16, 17); and (*ii*) general performance is inefficient when processing external signals (18).

As evidence to support the hypothesis that deficient velocity processing is involved in eye tracking dysfunction, it is necessary to show that velocity discrimination is compromised in schizophrenic patients and that the same specific deficit also occurs in their relatives. A previous study (19) assessed velocity discrimination by measuring the amount of contrast needed to perceive velocity differences between two moving targets. That study showed that schizophrenic patients had raised contrast thresholds when judging velocities of moving gratings (19). On other visual tasks, orientation discrimination and contrast detection, no group differences were observed. We here directly assess motion sensitivity by measuring the precision with which small differences in velocities can be discriminated by schizophrenic patients. Further, we here determine whether schizophrenic patients are able to process velocity information when nonmotion cues are minimized. In addition, we tested a group of first-degree relatives of schizophrenic patients on the same procedures, for two reasons: (*i*) to determine whether a motion discrimination deficit is merely a consequence of having a schizophrenic illness or of being treated for that illness with antipsychotic medications; and (*ii*) to determine the familiality of the deficits. Both issues can be effectively examined by testing first-degree relatives of schizophrenic patients. If one assumes that a schizophrenia disposition is genetically transmitted as a dominant trait, then about half of these individuals, although clinically unaffected by the illness and therefore untreated by antipsychotic medications, would be presumed to share a genetic predisposition for schizophrenia. If the disposition were transmitted as a recessive trait, then 25% of the first-degree relatives would be expected to share the predisposition. Previous studies have shown that from ≈20% to >40% of first-degree relatives show the eye tracking dysfunction associated with schizophrenia (6). We reasoned that, if the velocity discrimination deficit were familial and not a consequence of clinical schizophrenia or its treatment, then a significant proportion of relatives would show the same motion processing deficits seen in the schizophrenic patients.

## EXPERIMENT 1

### Velocity Discrimination in Schizophrenic Patients, Their Relatives, and Normal Subjects

**Methods.** *Subjects.* We tested 20 schizophrenic patients who met criteria set by The American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders* (third edition, revised) (20) for schizophrenia or schizoaffective disorder, based on a standardized interview (21) and a review of all psychiatric hospital records. All patients were medicated on maintenance doses of antipsychotic compounds. We also tested 24 first-degree relatives (siblings and/or parents) of the schizophrenic patients and 20 normal controls. These people, too, were screened by a standardized clinical interview (21), and none were clinically affected with a psychotic disorder. (See Table 1 for demographic information on the subjects.) Diagnostic assignment for all sub-

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Abbreviation: MT, middle temporal.

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Table 1. Subject demographic information

| | Age | Sex* | Verbal IQ† | Education | SES‡ |
|---|---|---|---|---|---|
| Schizophrenic ($n$ = 20) | 37 (7.3) | 11 F, 9 M | 107.7 (12.4) | 13.5 (2.2) | 2.45 (1.1) |
| Relative ($n$ = 24) | 45 (13.5) | 14 F, 10 M | 109.4 (16.1) | 14.7 (1.9) | 2.04 (0.7) |
| Normal Control ($n$ = 20) | 34 (13.6) | 13 F, 7 M | 108.6 (12.9) | 14.3 (2.5) | 1.94 (0.7) |

All numbers in parentheses are ±1 standard deviation.
*M, male, F, female.
†Based on Wechsler Adult Intelligence Scale (Revised).
‡Social–economic status, based on Hollingshead and Redlich Two-Factor Index (36).

jects was accomplished by at least two experienced clinicians blind to the purpose and results of the present study. After written informed consent was obtained, all subjects were instructed orally and were given sufficient practice trials to ensure that they understood the task.

*Procedures.* Subjects viewed two sequentially moving targets that differed in velocity; the task was to decide which target moved faster. A two-alternative, forced-choice procedure, in combination with a standard three-down-one-up staircase, was used to determine the velocity discrimination threshold [the just-noticeable-difference or Weber fraction ($\Delta V/V$)]. The staircase stopped after 12 reversals, thus ensuring that all subjects performed at 79.4% accuracy.

The targets were sinusoidal vertical (90°) gratings with a spatial frequency of 0.5 cycle/degree, displayed on a Macintosh monochrome monitor (frame rate, 70 Hz). The basal velocity of the gratings were 3.8°/s, 6.2°/s, 10°/s, 16.2°/s, and 26.3°/s. The stimuli, presented in a circular window, subtended 19° of visual angle with a space average luminance of 35 cd/m$^2$. For the determination of velocity discrimination thresholds, each target was present for 300 ms. The interval between comparison targets was 500 ms. The grating contrast for the stimuli was 0.15. A central cross facilitated fixation.

**Results.** In Fig. 1, we plot velocity discrimination thresholds ($\Delta V/V$) as a function of base velocity for patients, relatives, and normal control subjects. Normal subjects show a U-shaped curve, with the lowest thresholds obtained at intermediate velocities (10–16.2°/s). This result is in agreement with those of numerous other studies (22). Schizophrenic subjects show a pattern that is different both quantitatively and qualitatively. Overall, thresholds are elevated, but the largest threshold elevations are primarily in the midrange of velocity. At faster velocities, the difference between the schizophrenics and normal controls is diminished; at the slowest velocity tested (3.8°/s), the thresholds for the schizophrenics and the normals do not differ.

Like the schizophrenic patients, the relatives show a significant elevation of the velocity discrimination threshold ($\Delta V/V$) at a midrange of velocities, compared with the normal controls. Their thresholds are comparable with those of the schizophrenic subjects. As was found in the patients, the difference between the relatives and normal controls at target velocities of 10°/s and 16.2°/s are statistically significant ($P < 0.001$) whereas the thresholds of the relatives and the normal controls do not differ at the slower or the faster velocities.

The overall pattern of deficit is more obvious when the data from the groups are considered as a ratio (Fig. 2*a*). Mirroring the results in Fig. 1, Fig. 2*a* shows the greatest deficit for patients at intermediate velocities, much less deficit at the fast end, and no deficit at the slow end of the velocity range. The detailed basis of this comparison becomes more evident from inspection of Fig. 2*b*, showing histograms of schizophrenic performance for three base velocities. In comparison with the mean performance of normal observers, those of the schizophrenics are not statistically different ($P > 0.05$) at the slowest velocity (3.8°/s); the distribution of the schizophrenics' scores straddles the median value of the normals. At the fastest velocity (26.2°/s), the difference between the normal and schizophrenic groups is reduced, but the difference remains significant. This effect is to be contrasted with the Weber threshold scores at intermediate velocities (e.g., 10°/s), where the differences between the groups are much larger ($P < 0.005$). The distribution of scores for the schizophrenic patients at this intermediate velocity is shifted and has a larger variance, with an indication of some extreme values within the schizophrenic population.

The relatives and normal controls, likewise, can be compared by examining the ratio of the relatives' thresholds to that of the normal controls at each velocity (Fig. 3*a*). At the low and high velocities, the ratios are close to unity. At the intermediate velocity of 10°/s, however, the ratio clearly exceeds unity. As was true of the patients, the distribution of the relatives' scores shows a shift of central tendency to the high end of the normals' scores (Fig. 3*b*). The threshold scores of normals and relatives for the slowest and fastest velocities, on the other hand, overlap each other ($P = 0.47$ at 3.8 °/s and $P = 0.22$ at 26.2 °/s) (Fig. 3*b*).

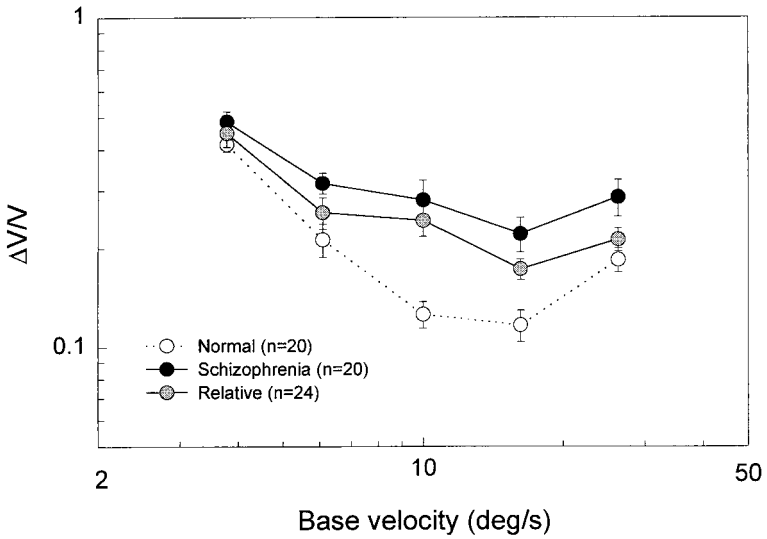


FIG. 1. Velocity discrimination thresholds of schizophrenic patients, their first-degree relatives, and normal controls. The abscissa represents the range of base velocities tested in this experiment. The ordinate, expressed as the Weber fraction ($\Delta V/V$, or the just-noticeable differences between the velocities of the targets to be compared), represents the velocity discrimination threshold values of the three groups. The error bars correspond to ±1 standard error of the mean threshold.

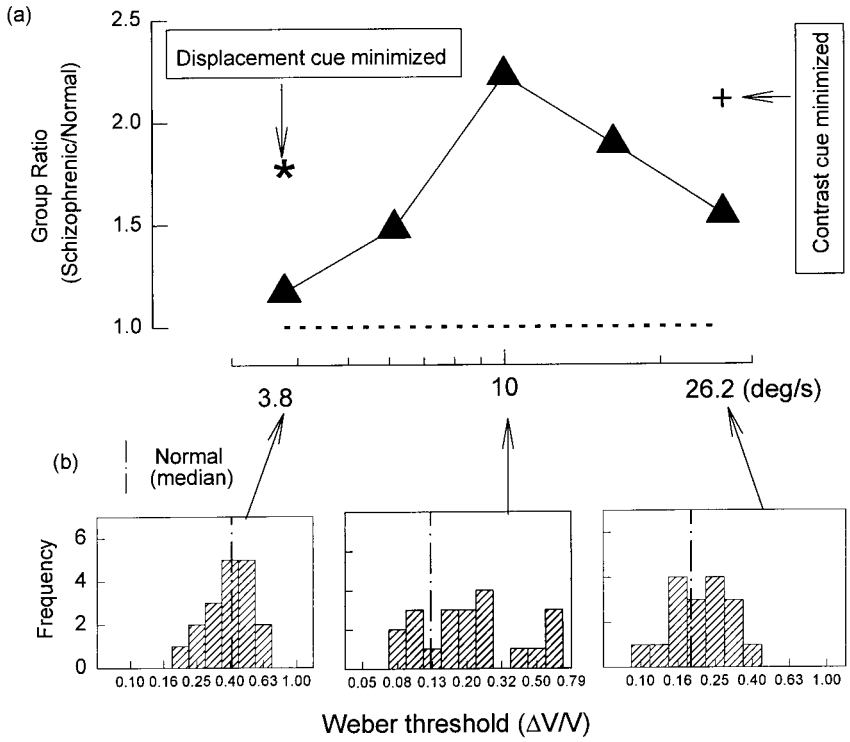


FIG. 2. Comparison of velocity discrimination of schizophrenic and normal control groups. (*a*) Group ratios (schizophrenia/normal control) of Weber thresholds plotted as a function of base velocity. A ratio of unity, shown in the dotted horizontal line, indicates equivalent performance by the two groups. The larger the ratio is, the higher the velocity discrimination threshold of the patients relative to the normal controls. The asterisk and cross sign represent the group ratios after exposure time for the 3.8°/s target (asterisk) and amount of contrast for the 26.2°/s target (cross sign) were randomized. (*b*) Histograms in the three panels (from left to right) represent distributions of individual patients' thresholds at the slowest (3.8°/s), middle (10°/s), and fastest (26.2°/s) base velocities. The vertical line in each panel indicates the median threshold of the normal control group.

**Discussion.** The pattern of results for the patients and the relatives is similar. Inasmuch as the relatives are not clinically psychotic and have never been treated for a psychotic illness, their threshold elevations cannot be attributed to the effects of the schizophrenic illness or its pharmacological treatment. In light of our hypothesis regarding the possible relation of smooth pursuit deficits to motion sensitivity, these results present an interpretive challenge. On the one hand, motion sensitivity deficits in the midrange of velocities might account for a sluggish initiation of pursuit eye movements. On the other hand, normal velocity detection at slow velocities is at odds with the appearance of deficits in the maintenance of pursuit in schizophrenia. That is, to maintain normal smooth pursuit, it is only slow velocities that must be registered because the smooth pursuit task requires only that one adjust the mean velocity of the eye to the small differences between eye and target velocity (23). These results can, however, be more clearly understood after more differentiated experimental analysis of response components, a kind of psychophysical parsing.

When required to discriminate between two target velocities, observers have available other potential sources of information in addition to velocity cues to complete the behavioral task. McKee (24) and Nakayama and Tyler (25) have shown that, at slow velocities, observers can make use of position information: The distance traveled provides cues about the velocity of moving targets. For a fixed duration of presentation, the faster the velocity of the target, the greater the distance it will have moved. On the other hand, Pantle (26) showed that, at fast velocities,

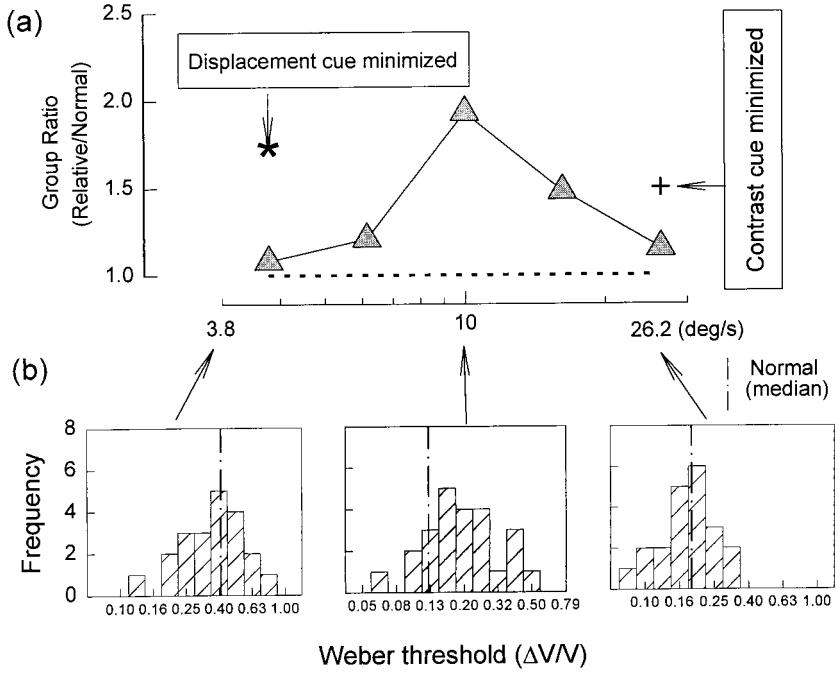


FIG. 3. Comparison of velocity discrimination between first-degree relatives of schizophrenia patients and normal controls. (*a*) Group ratio (as in Fig. 2, but here for relatives/normal controls) of Weber fraction thresholds plotted as a function of base velocity. The asterisk and cross sign represent group ratios after exposure time and amount of contrast of the two velocity comparison targets were randomized. (*b*) Histograms in the three panels represent, from left to right, the distributions of individual relatives' thresholds at the slowest, middle, and fastest velocities. Other details are similar to those in Fig. 2.

diminution of target contrast provides velocity information; faster velocities have lower contrast than slower velocities. It is, therefore, plausible that schizophrenic patients and their relatives can utilize these subtle nonvelocity cues of position displacement and contrast diminution to make velocity discriminations at slow and fast velocities, thereby appearing more normal than they really are. To examine this possibility, we used a psychophysical strategy often used in the testing of color vision, in which the contaminating influence of luminance can be rendered ineffective by varying it from trial to trial. With this strategy, we attempted to minimize position and contrast cues to see how this manipulation affected the velocity discrimination thresholds of schizophrenic patients and their relatives.

## EXPERIMENT 2

### Random Fluctuations of Position (Duration) and Contrast Further Isolate Motion Deficits

**Methods.** *Subjects.* We retested six schizophrenic subjects, six of their relatives, and six normal controls, selected randomly. In this experiment, we restricted our measurements to the slowest (3.8°/s) and fastest velocities (26.2°/s).

*Procedures.* The procedures were the same as those used in Experiment 1 with the following modifications**:** To minimize the use of nonmotion position cues for the slowest base velocity, we randomly varied the presentation time of the targets among five values: 240, 270, 300, 330, and 360 ms, thus altering unpredictably the distance traveled from trial to trial. To minimize the use of nonmotion contrast cues for the fastest velocity, we randomly varied the contrast of the targets among five values: 0.10, 0.125, 0.15, 0.175, and 0.20.

**Results.** Fig. 4 presents the velocity discrimination thresholds before and after nonvelocity cues were minimized. At the slowest velocity (3.8°/s), all but one schizophrenic subject showed elevated thresholds when position-displacement was randomized, compared with the standard presentation (constant exposure time in Experiment 1). In contrast, normal subjects showed no systematic differences between the two conditions (Fig. 4*a*). Although there was no significant group difference at this slow base velocity when position was held constant, the groups now differed significantly ($P < 0.03$) when position was randomized. That is, after eliminating position cues as a source of velocity information, the mean threshold of the schizophrenic patients was significantly higher than that of normal controls, even at this slow velocity. Similarly, at the fast velocity (26.2°/s), in the contrast-randomized condition, all but one schizophrenic patient showed thresholds elevated above those of the standard condition whereas normal subjects showed no significant change (Fig. 4*b*). After eliminating contrast cues as a source of information for judging velocity, the mean threshold of the schizophrenic patients was significantly higher than that of the normal controls ($P < 0.01$) at this fast velocity. The effect of eliminating nonvelocity cues on the group ratio is indicated by the asterisk and plus sign in Fig. 2*a*. The same results were obtained for the group of relatives (Fig. 3*a*). Their velocity sensitivity thresholds also increased significantly at the slowest and fastest velocities ($P < 0.05$) as a result of randomization.

Using the same methods to minimize position displacement and contrast cues, we readministered the velocity discrimination tasks at the intermediate velocity, 10°/s. The randomization manipulations had no significant effects on velocity sensitivity in any of the groups at 10°/s, presumably because velocity had already served as the primary cue. The differences remained statistically significant between the patients and controls ($P < 0.01$) and between relatives and controls ($P < 0.05$) for both manipulations.

**Discussion.** Both Experiment 1 and Experiment 2 indicate that motion processing is impaired in schizophrenic patients and in their relatives. The impairment is specific to velocity-based signals because it occurs only when velocity cues are dominant at intermediate velocities and, at extreme velocities, only when nonvelocity cues are made unavailable (by randomization). In Experiment 1, the seemingly "normal" thresholds of the patients and relatives at the slow and fast velocities resulted from the use of nonvelocity cues, which masked their velocity discrimination deficits. When nonvelocity cues are removed at the slow and fast velocities, the velocity discrimination threshold increases among the patients and relatives but has little effect on the normal controls. We turn now to the relation of these findings of raised velocity sensitivity thresholds to eye tracking dysfunction.

## EXPERIMENT 3

### The Relation Between Velocity Discrimination and Eye Tracking Dysfunction in Schizophrenic Patients and Their Relatives

**Methods.** *Subjects.* We tested all schizophrenia patients ($n = 20$), relatives ($n = 24$), and normal controls ($n = 20$) who participated in Experiment 1.

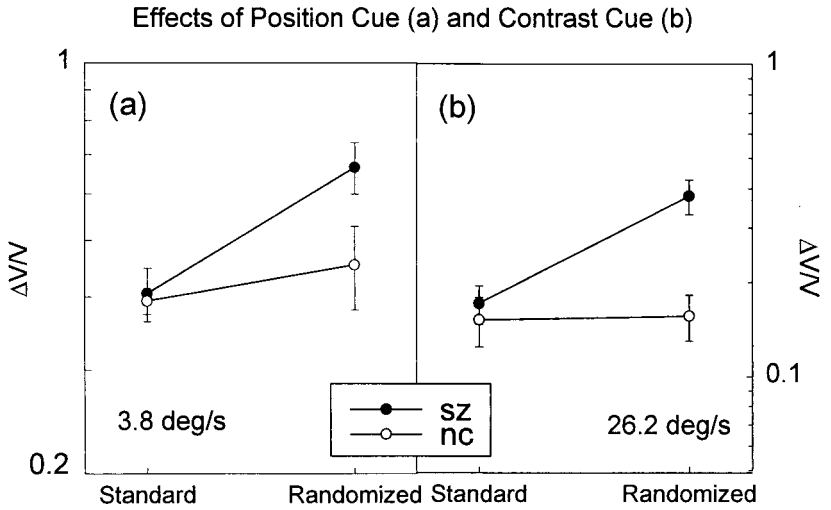


FIG. 4. The effect of minimizing positional displacement and contrast cues on velocity discrimination. (*a*) Threshold values (mean and SE) of schizophrenic patients and normal controls obtained during the standard condition (constant exposure time) and after the exposure times of velocity-comparison targets were randomized. (*b*) Values for the schizophrenic patients and normal controls during the standard condition and after amount of contrast of the targets has been randomized.

*Procedure.* We recorded smooth pursuit eye movements while subjects tracked a step-ramp target, introduced by Rashbass (27). Subjects were asked to follow a small circle of light that subtended a visual angle of 1.25°. The target, located straight ahead, remained stationary for a short period that varied randomly from 1 to 3 s and then jumped either to the right or left of the central fixation point (the "step"). It then began immediately to move smoothly and continuously in a horizontal direction opposite to that of the jump (the "ramp"). The ramp velocities were 5, 10, and 20°/s. Both the directions and velocities were unpredictable from trial to trial to ensure that each eye movement was based on novel motion signals. There were four trials at each of the three velocities and for each direction of movement (24 trials). The initial smooth pursuit response, which is termed "open-loop acceleration," is to the perceived target movement alone and does not yet involve any corrective feedback from target position or from an efference copy of an eye movement (28).

The apparatus for recording eye movements was a fully computerized limbus tracker (Eye and Brain Technologies, Thessolonika, Greece). It consisted of photodiodes, sensors that receive infrared reflections from the eyes, an amplifier, and a digitizer. The sampling rate for eye position was 1,000 Hz. Eye position signals were recorded by a Digital Equipment computer (466D2LP) that also controlled the presentation of the moving targets. Each subject's head was immobilized by use of a custom-fitted bite bar made of dental compound. We computed open-loop acceleration, defined as the mean acceleration of initial pursuit for each of the 24 step-ramp trials (28). Eye acceleration was obtained by computing the second derivative of eye position signals after low-pass filtering; trials containing saccades during this open-loop period were excluded.

Because the velocity discrimination deficit is most apparent at 10°/s in both the schizophrenia patients and relatives, we examined the relation between the Weber fraction at 10°/s and average open-loop acceleration for the 10°/s step-ramp targets. For each subject group, we computed the Pearson product-moment correlation between the Weber fraction and the average open-loop acceleration for eight trials.

**Results.** Initiation of eye tracking (measured by open-loop acceleration) was slower for the schizophrenic subjects than in the normal controls. Fig. 5 illustrates representative responses for a normal control and a schizophrenic subject. After target onset, the normal subject shows a smooth eye acceleration at ≈200 ms. The schizophrenic subject, however, shows no obvious eye acceleration, but at ≈350 ms typically makes an abrupt saccade to refoveate the target. The acceleration during the open-loop period was extremely low for this patient.

The correlation between the Weber fraction and open-loop acceleration was −0.60 ($P < 0.01$) for the schizophrenic patients, −0.34 ($P < 0.10$) for the relatives, and −0.18 (not significant; 90% confidence interval [−0.53, +0.23]) for the normal control group.

**Discussion.** The significant correlation between velocity sensitivity and initial acceleration indicates that, in the schizophrenic group, a functional relation exists between these two variables. There also appears to be a trend toward a similar relation in the sample of relatives. Although the correlation between velocity sensitivity and initial acceleration is not statistically significant in the normal control group, it is not possible to determine from our data whether that low correlation indicates that no functional relation exists between those two variables or that the scores within the normal group are within a restricted range. One may consider the hypothesis that the underlying functional relation is the same for all three groups and that they are sampled from different parts of the distribution. An analysis of the three regression lines is consistent with this hypothesis, although more data are necessary for its validation.

## GENERAL DISCUSSION AND CONCLUSIONS

The experiments reported here show that schizophrenia patients and their relatives have raised velocity sensitivity thresholds at intermediate velocities. At slow and fast velocities, the thresholds for velocity discrimination appeared to be indistinguishable from those of normal control subjects (indicating that the patients understood and could perform the task) until subjects were prevented from relying on nonvelocity cues of position displacement and contrast blur. Minimizing the availability of these cues raised the velocity discrimination thresholds of only the patients and relatives. Thus, the impairments are specific to the velocity domain.

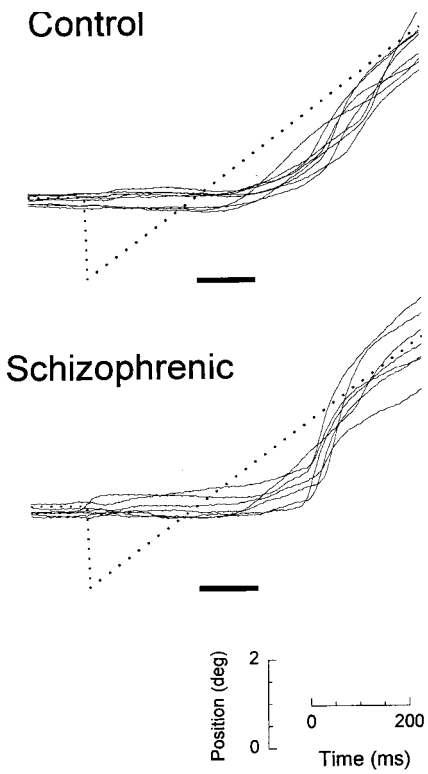


FIG. 5. Representative responses of eye tracking to the step-ramp target by a normal control (seven trials) and a schizophrenic subject (seven trials). The thick bar denotes the time windows for computation of open-loop acceleration.

These results extend those of two previous studies (19, 30) that used different measurements to demonstrate a motion sensitivity impairment in schizophrenia. Stuve *et al.* (30), who studied coherent motion, found that schizophrenic patients were impaired in processing the direction of movement signals. Chen *et al.* (19) reported that contrast sensitivity for velocity discrimination was reduced in schizophrenic patients only when judging the relative velocities of two gratings and not when judging orientation or detecting the presence of a target.

We tested the relation between these discrimination thresholds and one aspect of smooth pursuit eye movements, open loop acceleration, which has been shown to be abnormal in schizophrenic patients (12, 14). The correlation, −0.60, accounts for a significant portion of the variance (≈36%) in the scores for open-loop acceleration and the Weber fraction at a base velocity of 10°/s.

According to our general hypothesis of the transmission of impaired smooth pursuit eye tracking in families of schizophrenia patients (31), this deficit is associated with a nearly dominant autosomal gene with high penetrance (although penetrance for schizophrenia is not high). Therefore, ≈50% of the first-degree relatives of schizophrenics should be gene carriers. Our genetic hypothesis can be examined in light of the observed correlation between the Weber fraction and open-loop acceleration in the relatives. If the group of relatives is assumed to be a mixture of individuals who are expected to perform like schizophrenics (≈50%) and individuals who are expected to perform like

normals (≈50%), the expected correlation between the Weber fraction and open-loop acceleration in such a heterogeneous group of relatives can be derived from the observed correlations in the schizophrenic group and the normal group, together with the means and variances of each of the two measures in each of these groups. The calculation is a straightforward application of the properties of conditional expectation. Based on the observed data in the schizophrenia and normal groups, such a mixture in the relatives yields an expected correlation of −0.42, which is quite close to the observed value of −0.34. The empirical data in this experiment are therefore consistent with our genetic hypothesis.

As shown in other studies, smooth pursuit eye movements rely on functionally intact motion processing areas of the brain. Zihl *et al.* (17) demonstrated that a patient with a posterior parietal lesion that included the middle temporal (MT) area showed both smooth pursuit and motion detection impairments. Wurtz *et al.* (16) and Newsome *et al.* (32) established that there is a linkage between motion processing and smooth pursuit eye movements in monkeys; a lesion to area MT impaired both detection of coherent motion and the initiation of pursuit. The present study presented quantitative data that support this link by showing that schizophrenia patients who have degraded velocity discrimination have difficulty in generating smooth pursuit. Moreover, because the patients are chronically ill, the raised velocity discrimination thresholds appear to represent an enduring characteristic of a schizophrenic disposition. One feature of those deficits that is unlike those seen in most small lesion studies of animals (32) and of humans (33) is that the latter tend to show significant recovery. In this respect, schizophrenic deficits resemble those shown by monkeys with large MT lesions (16). Our findings suggest that a thorough neuropathological study of area MT in schizophrenia would be worthwhile.

The raised thresholds of our patients and their relatives occur in the absence of any obvious structural lesions, yet they point to the possible involvement of a network of brain areas that affects motion processing. One role for such a network is to provide functional redundancy that aids in recovery after a lesion in a small area of the brain. Because there is no recovery of the velocity-processing deficit in our chronic patients and their relatives, the velocity discrimination deficit should be considered in the context of the entire network of brain areas that are involved in motion processing. This network would include the motion-sensitive areas of the MT and medial superior temporal areas (34, 35) of the parietal lobe and would involve frontal and prefrontal areas. Further studies are needed to distinguish between specific defects in area MT and in other motion processing areas.

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1. Gottesman, I. I. & Shields, J. (1972) *Schizophrenia and Genetics: A Twin Study Vantage Point* (Academic, New York).
2. Kety, S. S., Rosenthal, D. & Wender, P. H. (1978) in *Critical Issues in Psychiatric Diagnosis*, eds. Spitzer, R. L. & Klein, D. F. (Raven, New York), pp. 213–223.
3. Tsuang, M. T., Winokur, G. & Crowe, R. R. (1980) *Brit. J. Psychiatry* **137,** 497–504.
4. Holzman, P. S. (1992) *J. Psychiatr. Res.* **26,** 427–445.
5. Holzman, P. S., Proctor, L. R. & Hughes, D. W. (1973) *Science* **181,** 179–181.
6. Levy, D. L., Holzman, P. S., Matthysse, S. & Mendell, N. R. (1993) *Schizophr. Bull.* **19,** 461–536.
7. Clementz, B. A. & Sweeney, J. A. (1990) *Psychol. Bull.* **108,** 77–92.
8. Levin, S., Jones, A., Stark, L., Merrin, E. L. & Holzman, P. S. (1982) *Biol. Psychiatry* **17,** 1277–1287.
9. Iacono, W. G., Tuason, V. B. & Johnson, R. A. (1981) *Arch. Gen. Psychiatry* **38,** 991–996.
10. Levy, D. L., Holzman, P. S. & Proctor, L. R. (1978) *Arch. Gen. Psychiatry* **35,** 972–981.
11. Lipton, R. B., Levin, S. & Holzman, P. S. (1980) *Psychiatry Res.* **3,** 193–203.
12. Levin, S., Luebke, A., Zee, D., Hain, T., Robinson, D. R. & Holzman, P. S. (1988) *J. Psychiatr. Res.* **22,** 195–206.
13. Levin, S., Jones, A., Stark, L., Merrin, E. L. & Holzman, P. S. (1982) *Arch. Gen. Psychiatry* **39,** 1125–1130.
14. Clementz, B. A. & McDowell, J. E. (1994) *Psychophysiology* **31,** 79–86.
15. Friedman, L., Jesberger, J. A. & Meltzer, H. Y. (1991) *Biol. Psychiatry* **30,** 537–556.
16. Wurtz, R. H., Yamasaki, C. J., Duffy, C. J. & Roy, J. P. (1990) in *Cold Spring Harbor Symp. Quant. Biol.* **55,** 717–727.
17. Zihl, J., von Cramon, D. & Mai, N. (1983) *Brain* **106,** 313–340.
18. Chapman, L. & Chapman, J. (1973) *Disordered Thought in Schizophrenia* (Appleton Century Crofts, New York).
19. Chen, Y., Palafox, G., Nakayama, K., Levy, D., Matthysse, S. & Holzman, P. (1999) *Arch. Gen. Psychiatry* **56,** 149–154.
20. American Psychiartric Association (1987) *Diagnostic and Statistical Manual of Mental Disorders* (Am. Psychiatr. Assoc., Washington, DC).
21. Spitzer, R., Williams, J., Gibbon, M. & First, M. (1990) *Structural Clinical Interview for DSMIII-R* (Am. Psychiatr. Assoc., Washington, DC).
22. McKee, S. P., Silverman, G. H. & Nakayama, K. (1986) *Vision Res.* **26,** 609–619.
23. Yasui, S. & Young, L. R. (1975) *Science* **190,** 906.
24. McKee, S. (1981) *Vision Res.* **21,** 491–500.
25. Nakayama, K. & Tyler, C. W. (1981) *Vision Res.* **21,** 427–433.
26. Pantle, A. (1978) *Percept. Psychophys.* **24,** 285–294.
27. Rashbass, C. (1961) *J. Physiol.* **159,** 326–338.
28. Lisberger, S., Evinger, C., Johanson, G. & Fuchs, A. (1981) *J. Neurophysiol.* **46,** 229–249.
29. Chen, Y., Levy, D. L., Nakayama, K., Matthysse, S. W. Palafox, G. & Holzman, P. S. (1999) *Arch. Gen. Psychiatry* **56,** 155–161.
30. Stuve, T. A., Friedman, L., Jesberger, J. A., Gilmore, G. C., Strauss, M. E. & Meltzer, H. Y. (1997) *Psychol. Med.* **27,** 143–152.
31. Holzman, P. S., Kringlen, E., Matthysse, S. W., Flanagan, S., Lipton, R. B., Cramer, G., Levin, S., Lange, K. & Levy, D. L. (1988) *Arch. Gen. Psychiatry* **45,** 641–647.
32. Newsome, W. T. & Pare, E. B. (1988) *J. Neurosci.* **8,** 2201–2211.
33. Plant, G. T. & Nakayama, K. (1993) *Brain* **116,** 1337–1353.
34. Wurtz, R. H., Komatsu, H., Yamasaki, D. S. G. & Dursteler, M. R. (1990) in *Vision and Brain,* eds. Cohen, B. & Bodis-Wollner, I. (Raven, New York), pp. 211–231.
35. Mikami, A., Newsome, W. T. & Wurtz, R. H. (1986) *J. Neurophysiol.* **55,** 1308–1327.
36. Hollingshead, A. B. & Redlich, F. L. (1958) *Social Class and Mental Illness* (Wiley, New York).