Dependence of Impaired Eye Tracking on Deficient Velocity Discrimination in Schizophrenia

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Background: Abnormal smooth pursuit eye movements have been found in many schizophrenic patients and in about 40% of their first-degree biological relatives. A velocity-discrimination deficit has also been demonstrated in schizophrenic patients. In this study, we address the relationship between deficient velocity discrimination in impaired smooth pursuit eye movements, assessed in brain regions responsible for processing eye movements signals in generating and maintaining smooth pursuit.

Methods: Horizontal eye movements of 15 schizophrenic patients and 8 normal controls were recorded in response to sine wave (predictable) and step ramp (non-predictable) targets. Smooth pursuit eye movements were assessed during both the initiation and maintenance periods. Correlations were computed between measures of smooth pursuit (i.e., peak gain, saccade frequency, and initial acceleration) and contrast sensitivity for velocity discrimination.

Results: Contrast sensitivity for velocity discrimination was significantly correlated with initial acceleration and peak gain, but was not significantly correlated with saccade frequency and qualitative ratings of pursuit integrity. No significant correlations were found within the normal control group.

Conclusion: Deficient processing of velocity information seems to be one component that contributes to a dysfunction in the initiation and maintenance of smooth pursuit in schizophrenia.

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Previously, we reported that about 40% of schizophrenic patients had significantly raised thresholds for velocity discrimination compared with normal controls. Here we address the relationship between raised thresholds in motion perception and abnormal smooth pursuit eye movements (SPEM) or eye tracking dysfunction (ETD), which has been stable in a significant proportion of schizophrenic patients and their first-degree biological relatives. This study was undertaken to explore the processes that underlie ETD.

See also page 149

Eye-tracking dysfunction in schizophrenia comprises irregularities in tracking that reflect at least two major factors: slow-to-reactive gain, low open-loop acceleration (OLA) (eye acceleration after the first 120 milliseconds following target movement), and increased frequency of saccades during eye movements. A comprehensive review may be found in Levy et al.

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SUBJECTS AND METHODS

SUBJECTS

Fifteen patients with chronic schizophrenia and 8 normal control subjects who had participated in the motion perception tasks took part in the current study. Diagnostic procedures are described in Chen et al. All patients met DSM-III-R criteria for schizophrenia (N=5) or schizoaffective disorder (N=10). Based on the Structured Clinical Interview for DSM-III-R administered by trained interviewers and reviewed, together with all hospital records, by a team of experienced clinicians, all of whom were blind to the experimental data, subjects had no concurrent substance abuse or dependence for at least 6 months and no diagnosed central nervous system abnormalities. Eleven patients were receiving antipsychotic pharmacologic treatment. All participants gave written informed consent and were paid modest honorariums. Normal controls were also clinically screened with the Structured Clinical Interview for DSM-III-R, none met criteria for any DSM-III-R Axis I psychotic condition.

PROCEDURES

Previous Motion Perception Experiments

A full description of the procedures used to obtain thresholds for velocity discrimination is contained in Chen et al. In brief, we obtained contrast sensitivities for velocidiscrimination (which of 2 targets moves faster), contrast detection, and orientation discrimination. We used the standard psychophysical "staircase" method, which increases the task difficulty by 1 step after 3 consecutive correct responses, and decreases the task difficulty by 1 step after 1 incorrect response. This procedure identifies for each individual the threshold of a psychometric function at which all subjects, patients and controls alike, perform at 79.4% accuracy. Thus, the dependent variable in all of these threshold measurements was the amount of target contrast necessary to achieve an accurate perceptual judgment of 79.4% correct.

SPEM Tasks

All subjects were asked to follow a small circle of light that subtended a visual angle of 1.25°, presented on a computer screen 56 cm in front of the subject. There were 2 eye movement tasks. In the first, the target moved horizontally and simultaneously at a temporal frequency of 0.4 Hz. The amplitude of the excursion was 28° peak to peak, maximal velocity was 35° per second. The color of the circle changed unpredictably and the subject was asked to count silently the number of times the color changed. This manipulation enhances attention to the task and minimizes anticipatory saccades.

The second target presentation employed a subset of the step-ramp introduced by Rabbah. The target, located straight ahead, remained stationary for a short period that varied quasi-randomly from 1 to 3 seconds, and then jumped either right or left of the central fixation point (the "jump"). After a jump (200 milliseconds), the target began to move slowly in a horizontal direction opposite to that of the jump (the "ramp"), running the entire 200 milliseconds later. The ramp velocity was 5°, 10°, and 20° per second. Both the directions and velocities were unpredictable from trial to trial. There were 4 trials at each of the 3 velocities and, for each direction of movement, for a total of 24 trials. Because the normal initial smooth pursuit response, which occurs within about the first 100 milliseconds, is to the perceived target movement alone and does not yet involve any corrective feedback from target position or from an absence copy of an eye movement, it is termed "open-loop." Sustained smooth pursuit then follows. This phase of eye tracking, during which corrections are based on the feedback of retinal slip, is usually measured by closed-loop gain.

deficit seemed plausible because SPEM is impaired when the motion-sensitive areas of the brain—the middle temporal (MT) area and the medial superior temporal (MST) area—suffer lesions, either experimentally produced in monkeys or naturally occurring in humans. We demonstrated that schizophrenic patients have impaired motion perception, as measured by the contrast required to detect small differences in velocity, but that they did not show impairments in motion tasks. These features of motion perception were stable over time in both normal controls and schizophrenic patients, and thus represent trait characteristics.

In this article, we examine whether and how performance on smooth pursuit and on velocity discrimination tasks are related in schizophrenic patients. We hypothesized that relative insensitivity in velocity discrimination is associated with both low OLA and closed-loop gain in SPEM.

RESULTS

VELOCITY DISCRIMINATION

The previous study of motion perception established that the contrasts sensitivities for velocity discrimina-
tion were significantly lower in schizophrenic patients, as compared with normal controls, when the velocities to be compared differed by 20% (11° per second vs 9° per second). This suggests that contrast sensitivity for contrast detection and orientation discrimination and for judging velocities thus differs by 100% (13° per second vs 5° per second), however, were similar for both groups.

SMOOTH PURSUIT

Figure 1 shows representative responses of a normal control and a schizophrenic subject to the sine wave target. Compared with the normal control, the patient's sustained eye tracking appears to have lower gain and is consistently accompanied by saccades. Figure 2 shows representative responses of a normal control and a schizophrenic patient to the 20° per second step-ramp target. The normal control exhibits a smooth, high-speed, pursuing eye movement about 150 milliseconds after the target begins to move in its ramp trajectory. In contrast, the patient's eye movement shows a very low ini-

ARCH GEN PSYCHIATRY/VOL 56, FEB 1999

738
Eye Movement Apparatus and Recording
The apparatus for recording eye movements was a fully com-
puterized limbos tracker (Eye and Brain Technologies Inc.,
Thessaloniki, Greece). It consisted of photodiodes, sensors that
record infrared reflections from the eyes, an amplifier, and
digitizer. The sensors were placed on spectacle frames that
the subject wore during the eye movement recordings.
The sampling rate for eye position was 1000 Hz. Eye posi-
tion was calibrated to ±2°. Eye position signals were re-
corded by a computer that also controlled the presentation of
the moving targets. Each subject’s head was immobilized
by use of a custom-fitted bar made of dental compound.

Principal Measures
The data were analyzed both qualitatively and quantita-
tively using custom-designed software. For data obtained
from sinusoidal tracking, a 5-point qualitative rating sys-
tem, modified from the scale of Bisiach,22 was used to char-
acterize the integrity of the eye tracking. A score of 1 in-
dicated very good eye tracking, and a score of 5 indicated
very impaired eye tracking. The qualitative ratings mainly
take account of the frequency of intrusive and corrective
saccades as well as the peak gain.22 Two judges, highly ex-
perienced in rating STEM, independently rated each sinus-
oidal recording; interrater agreement was more than 95%.

Data from the pursuit records were also analyzed quan-
titatively. For the sinusoidal targets, we computed peak
gain and frequency of saccades. After excluding saccades (de-
dined as eye movements faster than 60° per second, or 1.7
times the maximum velocity of the target), blocks, and square
wave jerks,22 we calculated peak gain, defined as the ratio
of eye velocity to target velocity, both averaged across a range
of ±200 milliseconds around the maximum velocity of the
target for every cycle of target movement. The number of saccadic
events during 30 seconds of tracking was an-
other quantitative index of eye tracking performance. For

the step-ramp target we computed OLA, defined as the
mean acceleration of initial pursuit, beginning 130 milliseconds
after the onset of the ramp component of each of the 24
step-ramp trials and lasting 100 milliseconds.22 Eye acceler-
cation was obtained by computing the second derivative
of eye position signals after filtering by a second-order But-
terworth low-pass filter (cutoff frequency, 50 Hz); trials con-
taining saccades during this open-loop period were ex-
cluded.

In summary, 4 eye movement measures were used to
evaluate smooth pursuit: a qualitative rating, peak gain, sac-
cade frequency (all for the sinusoidal target), and OLA (for
the step-ramp target).

Data Analysis
Using Pearson product-moment correlations separately within
the schizophrenic group and the 8 normal controls, we ex-
amined the association between velocity discrimination and
each of the 4 measures of smooth pursuit. We also analyzed
the differences between the patients and normal controls with
respect to OLA at the 3 ramp velocities by repeated-measures
analysis of variance. To determine whether our version of the
step-ramp procedure was equivalent to the standard Bub-
haus presentation (no delay between step and ramp),22 we
tested 20 additional subjects (approximately equal numbers of
patients and controls) on both paradigms; the correlation
between OLA on both procedures was 0.99 (P<.005), with
no outliers. The 2 paradigms thus give similar OLA data. The
effects of medication status and the differences between schizo-
phrenic and schizoaffective patients on each of the mea-
sures were assessed by t tests, with significance fixed at an
level of .05, tailed. There were no significant differences be-
tween these 2 patient groups on any of the measures used in
this study. The 11 patients receiving antipsychotic medic-
tions did not differ from the 4 patients receiving no antipsy-
chotic medications with respect to open-loop and peak gain,
saccade frequency, qualitative score, and motion sensitivity.

RELATION OF VELOCITY DISCRIMINATION TO INITIATION OF SMOOTH PURSUIT

We calculated the mean initial acceleration for all subjects
during the open-loop period for the step-ramp targets. These
values are plotted as a function of the 3 ramp velocities in
Figure 3. In both the schizophrenic patients and the nor-
mal controls, initial acceleration progressively increased as
ramp velocity increased. However, the initial acceleration
of the schizophrenic patients was significantly lower than
that of the normal controls for all 3 ramp velocities (F1,22=5.45,
P=.03 as 5° per second; F1,22=4.78, P=.04 as 10°
per second; F1,22=4.39, P=.06 as 20° per second). These
data agree with previous reports of low initial acceleration in
schizophrenic patients.21,22

The Pearson correlation coefficient between OLA for the
ramp at 10° per second and velocity discrimination is
0.70 (P<.01), which indicates that about 30% of the
variance in OLA can be accounted for by contrast sen-
sitivity for velocity discrimination. The observed corre-
lation suggests a strong relationship between velocity dis-

## Table: Velocity Discrimination and Eye Tracking Measurements

<table>
<thead>
<tr>
<th>Measure</th>
<th>Schizophrenic Patients</th>
<th>Normal Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Velocity discrimination</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(contrast sensitivities)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5° vs 10° per second</td>
<td>439 (181)</td>
<td>417 (174)</td>
</tr>
<tr>
<td>11° vs 15° per second</td>
<td>173 (106)</td>
<td>71 (39)</td>
</tr>
<tr>
<td>Eye tracking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Qualitative rating (1-6)*</td>
<td>2.87 (1.3)</td>
<td>1.44 (0.77)</td>
</tr>
<tr>
<td>Initial accelerations, degrees per second²</td>
<td>49.5 (26.7)</td>
<td>75.0 (25.8)</td>
</tr>
<tr>
<td>Peak gain</td>
<td>0.75 (0.1)</td>
<td>0.80 (0.44)</td>
</tr>
<tr>
<td>Saccade frequency</td>
<td>12.9 (3.0)</td>
<td>10.7 (3.4)</td>
</tr>
</tbody>
</table>

* indicates normal eye tracking; 5: abnormal eye tracking.
² indicates normal eye tracking; 5: abnormal eye tracking.

are necessarily wide because of the limited sample size
(90% CI, 0.38-0.87). Therefore, a weaker but still a non-
zero effect cannot be definitely ruled out. Both measure-
ments (velocity discrimination and OLA) were ob-
teined with the target moving at or around 10° per second,
presumably within the optimal range for motion processing. Correlation coefficients with similar magnitudes were obtained between velocity discrimination and OLA for ramp targets of 5° per second (r=0.39, P<.05) and 20° per second (r=0.63, P<.01). Those schizophrenic patients with low contrast sensitivity for velocity discrimination show low initial acceleration, as seen in the scatter diagram of that relationship (Figure 4). For the 8 normal controls, none of the correlations between OLA and velocity discrimination were statistically significant.

We also tested motion discrimination around a base velocity of 20° per second. These faster-moving targets resulted in higher thresholds for both groups of partici-

pants. Schizophrenic patients, however, were again significantly less sensitive than the normal controls. The correlations between OLA and velocity discrimination between velocities of 18° per second and 22° per second followed the same pattern, with the same regression slopes as those around the 10° per second base.

RELATION OF VELOCITY DISCRIMINATION TO MAINTENANCE OF PURSUIT

Qualitative Rating

Five (33%) of the 15 patients had qualitative ratings of 4 or 5, indicating ETI. The correlation between the qualitative ratings of SPEM and the contrast sensitivities for discrimination of the 20° velocity differences was 0.23 (P<.27; 90% CI, +0.2 to 0.63). Thus, overall sustained eye tracking, as measured by global qualitative ratings,
seems not to be significantly related to sensitivity in detecting small velocity changes.

**Peak Gain**

For the schizophrenia group and the normal control group, the mean (±SD) peak gain for the 0.4 Hz sine wave target was 0.75 (±0.10) and 0.80 (±0.04), respectively. The 5 patients with qualitative ratings of 4 or 5 had a mean peak gain score of 0.73 (±0.07), which was significantly lower than that of the normal controls (n=26,2, P<.05). The scatter diagram (Figure 5) of the relationship between mean peak gain and contrast sensitivities for velocity discrimination shows that patients with low contrast sensitivities for velocity discrimination tended to have low peak gain. The correlation between velocity discrimination and peak gain for the sine wave was 0.53 (P<.05; 90% CI, 0.12-0.79).

**Saccade Frequency**

The correlation between saccade frequency and velocity discrimination in the schizophrenic patients was -0.39 (P=0.15; 90% CI, -0.71 to 0.66). Although not reaching a statistically significant level, the negativity of the correlation is consistent with the relation described above between peak gain and velocity discrimination. That is, patients with low contrast sensitivity for velocity discrimination tended to make more saccades to compensate for low gain pursuit.

**COMMENT**

We report that velocity discrimination, previously shown to be impaired in schizophrenic patients, is associated with lowered OLA and closed-loop gain. This association contributes to our understanding of the origin of ETD in schizophrenia.

**MOTION DISCRIMINATION DEFICIT: A COMPONENT OF ETD**

Both OLA and closed-loop gain involve detection of motion signals. To initiate a normal pursuit movement in response to a visual stimulus that has begun to move, the viewer must first be aware that the target is moving. Open-loop acceleration, which appears to be a pure response to motion signals from the sensory system, is reduced when motion detection is impaired. During this period of open loop, no feedback is available from the effects of a previous eye movement response to the target, since none has yet been made. Cognitive factors such as anticipation of target movement may also influence pursuit initiation, a factor that merits separate study. Steady state or peak gain, which is involved in maintaining smooth pursuit, is also associated with impairments in velocity discrimination, and is affected by previous eye movements, such as the feedback when retinal slip occurs. It has been suggested that the position of a moving target drives sustained eye tracking. It is, therefore, possible that schizophrenic patients with impaired velocity discrimination partially compensate for their motion perception deficit by reliance on position cues to keep the focus on a moving target, particularly when target velocity is relatively slow and when target movement is predictable. This interpretation may partially explain why the qualitative ratings of sustained tracking target are poorly related to velocity discrimination, whereas measures of OLA and closed-loop gain are significantly related to velocity discrimination. The qualitative rating reflects more than the velocity match between eye and target movement. It no doubt includes position match and some extraretinal events (such as predictive tracking), which appear as irregularities in the record and which have not been taken into account in the accelerometer and gain measurements. We note here that correlations between OLA and orientation discrimination (r=0.17, P=0.50 and contrast sensitivity (r=0.40, P=0.08) are not significant, indicating that the results of this study do not reflect impaired motivation and generalized deficit performance frequently found in schizophrenia.

**ARE MOTION-SENSITIVE AREAS OF THE BRAIN IMPLICATED IN ETD?**

The processing of visual signals in the brain is carried out in many different areas of the visual system. These areas respond to different attributes of a visual stimulus, such as color, form, slant, and motion. It is now known that the MT and MST areas have a large population of cells devoted to precise and rapid tracking of target movement, including detection of changes in velocity. Moreover, these same areas play a principal role in the adaptive control of eye movements, including SPM. 12 For example, reported that a punctate chemical lesion in monkey MT produced a deficit in motion perception tasks and in the onset of smooth pursuit. These deficits are quite similar to those seen in the present experiment in the initial eye tracking responses of schizophrenic patients with compromised motion discrimination. Studies also show that the lateral dorsal area of MST is involved in the regulation of the maintenance of pursuit.2 The cells in this region respond to both retinal and extraretinal signals, the latter perhaps representing a proprioceptive input that is relevant to pursuit maintenance.

Because MT and MST are involved in both motion perception and smooth pursuit, any irregularity in the neural responses of these 2 areas should affect performance on both types of tasks. This indeed was the out-
One of the present experiment, which showed that schizophrenic patients whose velocity discrimination was poor had lowered open-loop and peak gains.13 Steve et al.14 had earlier reported that responses to the direction of motion in a coherent motion task and performance on a smooth pursuit task are significantly correlated to schizo-
phrenic patients. Consequently, it was found that sensitivity to perception of velocity is implicated. Both stud-
ies suggest that impaired functioning of motion-sensitive areas such as MT and MST may be causally implicated in the ETD found in schizophrenic patients.

**INVOLVEMENT OF OTHER BRAIN AREAS IN ETD**

Smooth pursuit eye movements, including planning and executing them, are complex processes. They involve many brain areas, as has been shown in numerous physi-
ological and brain-lesion studies. Those areas involved in the generation of smooth pursuit include both corti-
cal regions—such as MT and MST and frontal eye fields (FEF)—and subcortical regions such as the basol pallid and cerebellum. It is conceivable, however, that after the motion signals are processed and relayed, other brain ar-
eas, such as those in the frontal lobes, play important roles in executing and maintaining smooth pursuit based on the current eye movements and on target movement. In-
formation from eye velocity and eye position are also used adaptively to control on-line smooth pursuit, which may not solely be registered in MT and MST. Information about target movement may be conveyed not only from up-
dated sensory signals but also from memory of, or ex-
trapolation from, previously retained knowledge about the target motion; the latter would implicate neuronal activity in the frontal lobes. Indeed, Bruce et al.15 found so-called ‘pursuit neurons’ in FEF. Other reports16,17 showed clear activity of neurons in several areas of the frontal lobes while monkeys tracked a small target. Smooth pursuit to a target with predictable movement is usually paralysed when lesions occur in other brain areas but im-
pairments were observed in a patient with damage to the FEF.18

With respect to schizophrenia, it has been shown that the behavioral impairment in at least 2 independ-
ent tasks is related to functional integrity in the frontal lobe. First, spatial working memory, which is associ-
ated with neural responses of area 46 in the frontal lobe,19 was found to be impaired in schizophrenic pa-
tients.20 Second, endogenous (sustained), but not exog-
genous (transient), attention engagement, in which pre-
frontal cortex may be involved, was compromised in schizophrenia.21 These considerations suggest that smooth pursuit impairment in schizophrenia may reflect contri-
butions from non-pursuit components, particularly dur-
ing pursuit maintenance.

Many of the brain areas mentioned are, of course, interconnected with each other. Area MT is located within the occipito-parietal cortex of the rhesus monkey. Maun-
sell and Van Essen22 traced projections from the striate cortex to MT via the striate areas V2 and V3, and from there to the superior temporal sulcus and parietal cor-
tex, which includes MST and the inferior parietal lob-
ule. These areas contain neurons that project to the FEF,23 which also discharge during SPM. Lesions to FEF and MT and MST all cause very profound impairment of SPM.24 Similarly, after comprehensively reviewing the effects on SPM of various diseases and specific lesions, Sharpe and Morrow25 conclude that MT, MST, inferior parietal lobule, and the FEF are critically implicated in specific abnormalities of SPM, including lowered gain. The existence of the network linking these brain areas makes it difficult to be certain, when one brain area (such as MT) is damaged, whether the resulting SPM impair-
ments is caused by damage to this area or by the effects of such damage on other connected areas of the net-
work, such as the MST or FEF.

In the case of schizophrenia, several previous eye tracking studies attribute the dysfunction to prefrontal involvement.26 The neural activities of the frontal and pre-
frontal lobes in SPM of schizophrenic patients should be considered in the context that these brain areas also receive inputs from, or provide feedback to, the poste-
erior parietal lobe, where motion information is prima-
arily processed (but also see Nawroz and Rizzo27 for a role of the cerebellum in visual motion processing). Two stud-
ies of schizophrenic patients28,29 reported that patients’ initial saccades to a step-ramp target were similar to those of the normal controls. The authors concluded that the patients’ generation of unimpaired saccades to a moving target indicated that motion processing was intact, be-
cause an earlier study of monkeys with lesions in the mo-
tion-sensitive MT area showed impaired saccades to moving targets. However, we must point out that gen-
erating saccades to moving or stationary visual targets may rely on position as well as motion information. There-
fore a direct assessment of motion discrimination, as was done in our earlier study,1 is required to decide the is-
Sue of whether motion processing is impaired in schizo-
phrenia. It is noteworthy, moreover, that Newsome et al.30 reported that a decrease in initial eye velocity in smooth pursuit accompanied damage to area MT, and Clem-
ens,31 in a study of saccades to moving targets in schizo-
phrenia, also reported low OLA. In this article, we show that low OLA is significantly related to raised motion dis-
crimination thresholds. We therefore suggest that whereas MT and MST are functionally involved in abnormal gen-
eration of smooth pursuit, the impairment in the main-
tenance of smooth pursuit in schizophrenia probably also implicates frontal and prefrontal areas.32,33. Our finding of a significant functional relation between impaired ve-
locity discrimination and reduced OLA and closed-loop gain in schizophrenic patients represents only the be-
ginning phase of unraveling these complex processes.

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