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The relationship between smooth pursuit performance, motion perception and sustained visual attention in patients with schizophrenia and normal controls

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ABSTRACT

Background. In this study, we tested the hypothesis that low smooth pursuit gain in schizophrenia is related to an abnormality in motion perception.

Methods. The subjects were 19 schizophrenics treated with clozapine and 19 controls. In addition to smooth pursuit and motion perception paradigms, sustained attention was also assessed using a continuous performance task (CPT).

Results. In the patient group, there was a statistically significant negative correlation between smooth pursuit gain and motion perception threshold ($r = -0{\cdot}60$, $P < 0{\cdot}01$). This relationship was not secondary to attention deficits as assessed by the CPT.

Conclusions. Our results are consistent with the notion that the smooth pursuit gain deficit is related to a deficit in motion perception rather than in attention. Brain area V5 (also referred to as 'MT' in macaque), located in the parieto-occipital region, is known to be critically important both for motion perception and gain. Thus, our results point to an abnormality in this area in schizophrenia.

INTRODUCTION

Smooth pursuit eye movement performance is impaired in patients with schizophrenia (Holzman, 1987; Clementz & Sweeney, 1990; Abel *et al.* 1992; Levy *et al.* 1993). This impairment may reflect cognitive or information processing deficits such as deficits in attention (Bartfai *et al.* 1985; Katsanis & Iacono, 1991; Litman *et al.* 1991; Friedman *et al.* 1995*a*). However, another possibility is that the pursuit impairment is secondary to an impairment of motion perception, since the motion of the target must be detected prior to, and during, smooth pursuit.

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Neuroscientists have focused on the perception of motion as a link between visual perception and ocular motor programming. Neurophysiological studies have determined that a cortical area in the parieto-occipital region is selectively involved in motion processing. This area has been termed area MT in monkeys and corresponds to area V5 in humans. Newsome *et al.* (1985) demonstrated that unilateral damage to area MT results in dramatically elevated motion perception thresholds in the contralateral hemifield, whereas a 'non-motion' related visual discrimination task (contrast sensitivity) was relatively unaffected. A number of further neurophysiological investigations have confirmed and extended the evidence linking area MT to motion perception (Wurtz *et al.* 1990; Schiller & Lee, 1994).

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Area MT is also critically important for smooth pursuit performance, particularly smooth pursuit gain (Wurtz *et al.* 1990; Newsome *et al.* 1985). For example, unilateral lesions of area MT result in a marked decrement in gain when targets move toward the side of the lesion. However, lesions in nearby regions not including MT do not affect gain (Newsome *et al.* 1985). Thus, area MT may be a critical common anatomical/neurophysiological link between the perception of motion and pursuit gain. Therefore, it seemed important to test the hypothesis that the smooth pursuit impairment in schizophrenia is related to an impairment in motion perception.

Students of motion perception make a distinction between two types of motion stimuli: (1) an inferred motion that is deduced when a form changes position over time; and (2) a 'pure' motion signal, with no form content. The latter is achieved with the use of the correlated motion paradigm, based on a series of random dot cinematograms, as described by Newsome & Pare (1988). With this method, described in detail below, there are no form or position cues sufficient to stimulate inferred, or apparent motion.

The issue of smooth pursuit assessment in schizophrenia is a subject of substantial controversy and has been the point of several recent papers (Abel & Ziegler, 1988; Clementz & Sweeney, 1990), including a recent paper from our laboratory (Friedman *et al.* 1995*b*). The purpose of the smooth pursuit system is to match eye-velocity to target-velocity and this ability is, in our view, best assessed by gain, which is the ratio of eye-velocity to target velocity. However, when patients perform such tracking tasks, there are periods when the smooth pursuit system is not engaged. The effect of a failure to engage completely the smooth pursuit system in a tracking study is most sensitively assessed with RMS error, which essentially computes the degree of global match between the target signal and the eye movement signal. Both steady-state smooth pursuit gain and RMS error were assessed in the present study.

The central aim of the present study was to evaluate the correlation between abnormal smooth pursuit performance (low gain and increased RMS error) and the threshold for motion perception. Smooth pursuit performance has been linked to measures of attention (Holzman *et al.* 1976; Shagass *et al.* 1976; Bartfai *et al.* 1985; Coursey *et al.* 1989; Katsanis & Iacono, 1991; Litman *et al.* 1991; Friedman *et al.* 1995*a*) and, since the correlated motion paradigm may require sustained visual attention, it is possible that any correlation between motion perception and smooth pursuit performance could be secondary to attention. In order to assess the role of attention in our study, two tests of sustained visual attention were included.

METHOD

Subjects

The study included 19 patients who met Research Diagnostic Criteria (RDC; Spitzer *et al.* 1978) for schizophrenia ($N = 18$) or schizoaffective disorder, mainly schizophrenia ($N = 1$) and 19 age and gender matched normal controls. Patients were recruited from the in-patient and out-patient wards of a university-based hospital. All subjects were free of neurological disorder and ophthalmological disease.

Diagnosis

Details regarding diagnosis and exclusion criteria for patients have been previously described (Friedman *et al.* 1995*b*). Briefly, patients were evaluated via structured interviews, and diagnosis was achieved during a consensus conference.

Patients had been hospitalized a mean of 9·0 times (S.D. = 7·54) and had been ill for a mean of 14·6 years (S.D. = 7·4). Subjects were periodically assessed with the Brief Psychiatric Rating Scale (BPRS, Overall & Gorham, 1962). The positive symptom score was the sum of items 4, 11, 12, and 15; and the negative symptom score was the sum of items 3, 13, 16, and 18. Mean BPRS was 18·1 (S.D. = 10·9) total; 7·16 (S.D. = 5·5) for positive symptoms; and 2·8 (S.D. = 2·24) for negative symptoms.

Medication status

The patients were all clinically stabilized on clozapine for a minimum of 21 days (maximum = 5·5 years, median = 170 days), with no change in clozapine dose (mean = 426 mg, S.D. = 192 mg) for at least 7 days. The mean age of the patients was 33·4 years (S.D. = 8·01, range = 16

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to 52). At least 24 h had elapsed since the last dose of lorazapam or chloral hydrate.

Exclusion criteria for controls

Controls reported no familial or personal history of mental illness. No control exhibited abnormal psychopathology as measured by the MMPI-168 (Overall & Gomez-Mont, 1974). Mean age of the control group was 32·4 years (S.D. = 7·99, range = 17 to 51). Each patient was matched with a control to within ± 4 years of age. There were 18 males and one female in each group.

General procedures

Uncorrected visual acuity at 6.1 m and corrected visual acuity at 79 cm was evaluated. No group differences in acuity were noted ($P = 0{\cdot}839$, $P = 0{\cdot}188$, respectively).

Four tasks were employed: (1) smooth pursuit; (2) correlated motion perception; (3) Degraded Stimulus CPT; and (4) Array Stimulus CPT. The tasks were organized as sets, with task 1 and task 2 in set A, and task 3 and task 4 in set B. Set A was always presented first, with the order of presentation of tasks 1 and 2 randomized. Tasks 3 and 4 were randomized within set B.

There were seven performance measures of interest in this study, two from the smooth pursuit task (gain and RMS error), one from the motion perception task (threshold) and two each from two different CPT tasks (d′ and log β (natural log)).

Smooth pursuit

Eye movement recording

Recording instrumentation parameters are described in Friedman *et al.* (1995*b*). Ambient light was dim and subjects were dark adapted for 5 min prior to test initiation. Corrective lenses were not in place during the test due to the use of the infra-red oculography spectacles. Prior to digitization, the eye movement signal was passed through a 60 Hz notch filter in cascade with a low-pass filter (5-pole Butterworth, 125 Hz 3 db).

Tracking target

The target was a bright red laser spot moving across an arc-shaped (1·5 m radius) surface positioned 1·5 m directly in front of the iris of the subject's dominant eye. The laser spot was projected onto the arc surface after reflection upon a mirrored galvanometer. The movement of the stimulus was controlled via a computer signal to the galvanometer.

Target waveform

The target waveform was 'trapezoidal', and consisted of a series of constant velocity ramps from 15° left to 15° right and vice versa. Target speed was 5°/s.[1] At the target extremes the target paused for 2·5 s. Data were collected for four cycles, each cycle consisting of two ramps (left and right) and two pauses. The target was moving for a total of 48 s.

Assessment of eye-tracking performance

Two measures of smooth pursuit performance were obtained: (1) steady-state smooth pursuit gain; and (2) RMS error.

Steady-state smooth pursuit gain

Smooth pursuit gain was computed using a recently developed automated procedure described elsewhere (Jesberger & Friedman, 1997). Briefly, the calibrated digitized eye position signals were digitally filtered for noise reduction. Velocities were calculated with a digital differentiator (Usui & Amidror, 1982). Velocity signals were normalized to gain units using the target velocity. An automatic algorithm removed saccades, blinks, large position error and periods during which the subject was not tracking. For each subject, a distribution of gain values was constructed and the mode of each distribution was taken as the best index of gain for a subject.

RMS error

For RMS error calculation, all portions of the signal where the target was in motion were included except portions with blinks. Blinks were identified and removed prior to calculation of RMS error. To calculate RMS error, the difference between the eye position and the target position was calculated for each included

[1] The choice of target speed for eye-tracking was linked to the choice of stimulus speed in the correlated motion paradigm. Speeds above 4°/s are known to optimally stimulate brain area MT, whereas speeds slower than 4°/s probably stimulate other visual areas as well (Newsome *et al.* 1986). We chose a stimulus speed for motion perception of 5°/s, since we have greatest experience with the evaluation of motion perception at this speed. Also, several of our previous eye-tracking studies have documented abnormal smooth pursuit in patients with schizophrenia at this target speed (Friedman *et al.* 1991).

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time sample (400 samples/s, 'raw difference'). The raw differences were then squared, and the squared values were averaged over the tracking interval. The square root of this average was the RMS error.

Motion perception test

Each subject was seated 79 cm away from a cathode ray tube (CRT) monitor with his head secured in a chinrest. Dynamic random dot cinematograms (RDCs) were employed for psychophysical measurement of motion perception thresholds (Newsome & Pare, 1988). The RDC stimulus was comprised of 400 moving white dots (each one pixel in size) presented for 4 s on a dark background. For each stimulus trial, a fixed portion of the moving dots was correlated with respect to velocity and direction, while the motion of the remaining dots was random and uncorrelated. The velocity of the correlated motion was 5°/s.

The motion paradigm was a two-alternative-forced-choice design with the direction of the correlated motion always either left or right. Subjects were instructed to identify the direction of the motion, and if uncertain, to make their best guess. The task began after a 5 min dark adaptation period and several practice trials. The task was presented in two portions with approximately 30 s pause.

A double staircase parameter estimation procedure was used to determine the threshold for detecting motion (Pentland, 1980; Lieberman & Pentland, 1982). The procedure began with a strong signal (98% correlation). Correct responses were followed by a decrease in correlation; errors were followed by an increase in correlation. This double staircase continued until the correlation was identified where the subject responded correctly in 75% of trials given a statistical confidence level of 75%. This correlation was used as the subject's motion perception threshold.

Visual sustained attention (CPT) tasks

General

Two tasks of sustained visual attention were employed in this study: a Degraded Stimulus CPT and an Array Stimulus CPT. Subjects were seated approximately 1 m from the CRT. Room illumination was normal. Subjects were instructed to hold a response button in their dominant hand and press the button as quickly as possible whenever they saw the target stimulus appear on the screen.

Degraded stimulus CPT

This version of Nuechterlein *et al.*'s Degraded Stimulus CPT (Nuechterlein *et al.* 1983; Nuechterlein, 1991) involved the presentation of a randomized series of the numerals 0 through 9. Each number was briefly flashed on the CRT for 50 ms with an interstimulus interval of 1·2 s. The stimuli were degraded by reversing the colour of a random set of 37% of the pixels in the display (white to black and black to white). Subjects were instructed to press a button every time they saw the number '0'. Formal trials were preceded by practice sessions. The formal session consisted of 324 trials and took approximately 7 min.

Array stimulus CPT

The second task was the array scanning test, which was similar to Neale *et al.*'s (1969) Span of Apprehension task. In the present study, a single-target-present design was employed. The display consisted of white letters on a dark background. Subjects were to press a button when the target letter 'T' was present in an array of 'distractor' letters. The number of distractor letters in the target-present condition ranged from 3 to 7, with the target present in 31 of the 144 total trials. Each trial was presented for a duration of 50 ms with an interstimulus interval of 2·5 s. Responses delayed by more than 900 ms from stimulus onset were classified as non-response.

When a target was present and the subject responded, a hit was scored. When the target was present and the subject did not respond, a miss was scored. If the subject responded when there was no target, a false alarm was scored. Typically, CPT performance is not assessed in terms of these raw hits, misses and false alarms, but rather in terms of d′ and β, which are derived from the raw scores (Green & Swets, 1966; Nuechterlein, 1983). In the present case, however, which included a young, healthy normal control group, the number of false alarms during the Degraded Stimulus CPT was frequently 0, and thus d′ and β could not be calculated. Also, there was very little variability in the control group, with most subjects (13 of 19) scoring 0 or 1 false alarms. Therefore,

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analysis of control performance on the Degraded Stimulus CPT could not be meaningfully conducted. A statistical test comparing normal subjects and patients on this test would not be informative. The patients were obviously significantly impaired relative to controls in terms of sensitivity in the Degraded Stimulus CPT. On the other hand, CPT performance on the Array Stimulus test in the controls was sufficiently variable, and was compared to that in patients. Furthermore, variability in patients on both tests was sufficient, and therefore within-group correlations in the patients were assessed. Finally, the convention for transforming β to natural log β prior to data analysis was followed (Green & Swets, 1966; Nuechterlein, 1983).

Statistical analyses

The main measures in the study were: (1) steady-state smooth pursuit gain; (2) RMS error of smooth pursuit; (3) threshold for correlated motion perception; (4) perceptual sensitivity as measured by d′ in the Degraded Stimulus CPT in patients; (5) criteria for responding as measured with Log β in the Degraded Stimulus CPT in patients; (6) d′ value in the Array Stimulus CPT; (7) log β in the Array Stimulus CPT. All measures were available for all subjects.

Group comparisons

The first step in the analysis was to examine the within-group frequency distributions for each measure to evaluate the presence of outliers as well as the shape and spread of the distributions. Since departures from the assumptions of standard parametric statistics (normality and homogeneity of variance) were noted, group comparisons were performed using the resampling method of Pollack *et al.* (1994). Briefly, this method involves the direct, empirical computation of the sampling distribution of group mean differences from which a probability estimate is obtained. Comparisons of the results using the resampling method and conventional *t* tests revealed no substantive differences in the probability values. All tests were one-tailed, since directional hypotheses were obvious *a priori*. Effect sizes (g = mean difference/pooled standard deviation) were also computed. The variability in the controls was compared to the variability in the patients using standard tests (Norušis, 1992).

Within-group correlations

All correlations between the main measures were computed within a diagnostic group to prevent contamination of the correlations with diagnostic group differences in average performance. Pearson correlation coefficients were employed, but significance testing was also based on the resampling approach (Pollack *et al.* 1994). All tests were one-tailed since directional hypotheses were obvious *a priori*.

Comparisons between related correlations within a group

There was a particular interest to determine if smooth pursuit gain was more highly correlated with motion perception than with measures of attention, within each subject group. A special statistical test is required to test if, within each group, the correlation between measure j (gain) and k (motion threshold) is significantly different from the correlation between j and h (measures of attention) (Steiger, 1980). This test involves the computation of the Z_1^* statistic (equation 14, Steiger, 1980). Since differences between these within-group correlations were of interest regardless of direction, two-tailed tests were employed.

Partial correlation analysis

There was a particular interest to determine the magnitude of the correlation between smooth pursuit gain and motion perception threshold after controlling for measures of attention (d′ from the array and the Degraded Stimulus CPTs). For this analysis, a partial correlation procedure was employed.

Comparisons of correlations across diagnostic groups

Differences between correlations across diagnostic groups were tested with the Fisher Z transformation test as outlined by Cohen & Cohen (1983).

RESULTS

Group differences

The two groups were compared on the key measures as shown in Table 1. The following statistically significant findings were noted: patients had poorer attention (as measured by

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Table 1. *Test of group differences on measures of attention, motion perception and smooth pursuit performance*

Domain	Test	Measure	Controls Mean (S.D.) ($N = 19$)	Patients Mean (S.D.) ($N = 19$)	Variance homogeneity P value	Group mean difference resampling P (one-tailed)	Effect size g
Attention	Degraded stimulus CPT	d′	—	3·60 (0·91)	—	—	—
		ln β	—	0·92 (1·49)	—	—	—
Attention	Array stimulus CPT	d′	2·71 (0·60)	2·20 (0·75)	0·546	0·012	0·75
		ln β	1·38 (1·07)	1·31 (1·13)	0·677	0·415	0·07
Motion perception	Correlated motion	Threshold	5·16 (1·83)	7·32 (4·50)	0·017	0·029	−0·63
Smooth pursuit	Steady state 5 °/s	Gain	0·95 (0·07)	0·89 (0·05)	0·076	0·003	0·97
		RMS error	1·13 (0·41)	1·14 (0·81)	0·295	0·470	−0·02

"—" Data not provided because low variability in the control group precluded meaningful interpretation (see text).

d′) in the Array Stimulus CPT, elevated motion thresholds, and low gain. No statistically significant group differences were noted for the other measures. The effect sizes for the array stimulus d′, motion threshold and gain were either moderate-to-large or large.

Patients demonstrated statistically significant increased variability on the motion threshold measure (Table 1). There was a trend for gain to be more variable in controls than in patients. No other differences in variability between groups were noted.[2]

Within-group correlations among the measures of attention

Controls

On the Array Stimulus CPT there was a statistically significant correlation between d′ and the Log β (Table 2).[2]

Patients

For patients, there were two statistically significant correlations among the attention measures. There was a positive correlation between the d′ measure on the Array Stimulus CPT and d′ on the Degraded Stimulus CPT. Also, d′ and Log β from the Array Stimulus CPT were significantly positively correlated (Table 2).

Within-group correlations among the measures of smooth pursuit performance

RMS error and gain were not significantly correlated in either group.

[2] The Degraded Stimulus CPT was not tested for reasons stated in the Method section.

Within-group correlations between measures of attention and motion perception threshold

Motion perception threshold was unrelated to all of the attention measures in both subject groups. In fact, four of the six correlations were less than 0·1 in magnitude.

Within-group correlations between measures of smooth pursuit performance and either motion perception threshold or measures of attention

Controls

Neither gain nor RMS error were significantly correlated with either motion perception threshold or with array CPT performance (Table 2).

Patients

The strongest interrelationship noted in the present study was a statistically significant negative correlation between gain and motion perception threshold in patients (Table 2 and Fig. 1*a*). The negative direction is consistent with our hypothesis that patients with low gain have elevated motion perception thresholds. Two subjects with markedly elevated motion thresholds were clearly influential observations for this correlation (Fig. 1*a*). One way to minimize the influence of these two influential observations is to rescale the variables with rank transformations (Fig. 1*b*). The correlation between the rank on motion threshold and the rank on modal gain was of comparable magnitude to the correlation in the original scale ($r_s = -0{\cdot}55$ *v.* $r = -0{\cdot}60$) and was statistically significant ($P = 0{\cdot}008$). Thus, even when the

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Table 2. *Correlation between measures of attention, motion perception and smooth pursuit*

	Degraded CPT d′	Degraded CPT ln β	Array CPT d′	Array CPT ln β	Motion threshold	Mode gain
(*a*) Pearson *r* correlation coefficients – Controls						
Degraded CPT ln β	—					
Array CPT d′	—	—				
Array CPT ln β	—	—	**0·48***			
Motion threshold	—	—	0·06	−0·29		
Mode gain	—	—	−0·02	0·05	0·10	
RMS error	—	—	−0·25	−0·01	−0·23	0·27
(*b*) Pearson *r* correlation coefficients – Patients						
Degraded CPT ln β	−0·22					
Array CPT d′	**0·51***	−0·02				
Array CPT ln β	0·26	0·29	**0·48***			
Motion threshold	0·03	0·15	−0·09	−0·07		
Mode gain	−0·05	0·12	0·23	0·24	**−0·60****	
RMS error	−0·18	0·26	0·12	0·21	−0·08	0·28

* $P < 0{\cdot}05$, one-tailed; ** $P < 0{\cdot}01$, one-tailed.

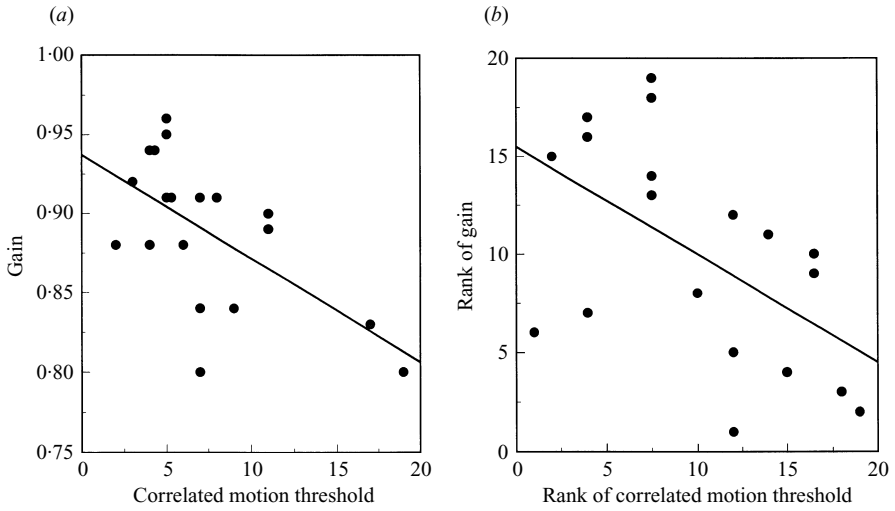


FIG. 1. The relationship between gain and correlated motion threshold in patients. (*a*) Pearson correlation between smooth pursuit gain and motion perception threshold in patients with schizophrenia ($r = -0{\cdot}60$, $P = 0{\cdot}0052$). (*b*) Spearman correlation between smooth pursuit gain and motion perception thresholds in terms of rank order in patients with schizophrenia ($r = -0{\cdot}55$, $P = 0{\cdot}008$).

data are expressed as ranks and are evenly distributed, a strong, negative statistically significant correlation is observed.

Gain was not significantly correlated with any attention measure and RMS error was not correlated with either motion perception threshold or any attention measure.

Is smooth pursuit gain more highly correlated with motion perception than measures of attention?

Controls

The magnitude of correlation between smooth pursuit gain and motion perception threshold was statistically compared to the magnitude of correlation between smooth pursuit gain and the two CPT-based measures of attention in the controls using the method of Steiger (1980) as outlined above. No statistically significant differences were noted.

Patients

The correlation between smooth pursuit gain and motion perception threshold ($r = -0{\cdot}60$) was significantly greater than the correlation between gain and three of the four attention

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related CPT measures (*versus* d′ from the Array Stimulus CPT: $P < 0{\cdot}02$, two-tailed; *versus* log β from Array Stimulus CPT: $P < 0{\cdot}02$, two-tailed; *versus* log β from Degraded Stimulus CPT: $P < 0{\cdot}02$, two-tailed). For the fourth attention-related measure (d′ from the Degraded Stimulus CPT), this test yielded a statistical trend ($P < 0{\cdot}10$, two-tailed).

What is the magnitude of the correlation between smooth pursuit gain and motion perception in patients after controlling for measures of attention?

The magnitude (and direction) of the correlation between smooth pursuit gain and motion perception threshold ($r = -0{\cdot}6018$) was essentially and remarkably unchanged after controlling for either the d′ from the Array Stimulus CPT (partial $r = -0{\cdot}5995$) or the d′ from Degraded Stimulus CPT (partial $r = -0{\cdot}6013$).

Comparisons of correlations across diagnostic groups

Significant differences between correlations across diagnostic groups were tested with a Fisher Z transformation, as outlined above. There was only one statistically significant difference in the correlations across diagnostic groups. The correlation between gain and motion perception threshold was significantly larger in the patient group than in the control group ($P < 0{\cdot}05$, 2-tailed).

DISCUSSION

As noted previously, schizophrenics had low gain (Holzman, 1987; Clementz & Sweeney, 1990; Friedman *et al.* 1991) and decreased sensitivity in a visual sustained attention task (see Nuechterlein, 1991). Also, the patients had elevated motion perception thresholds. Although Wertheim *et al.* (1985) also reported elevated motion perception thresholds in schizophrenics, the stimulus they employed was not a pure motion stimulus. Thus, this is the first report of elevated motion perception thresholds in patients with schizophrenia based on a pure motion stimulus. That schizophrenic patients are impaired on a motion perception task is not surprising given that they are impaired on many tasks (Holzman, 1987). Since the central hypothesis of the present study was that poor smooth pursuit performance in patients with schizophrenia was related to impaired motion perception, the result of greatest interest was the statistically significant negative correlation between gain and motion perception threshold in the patient sample.

On an *a priori* basis, we had hypothesized that motion perception and smooth pursuit gain might both be related to sustained visual attention within either subject group. However, the observed correlations between the CPT sensitivity measures and either motion perception or gain were small and did not approach statistical significance. In the patient group, which showed a statistically significant correlation between motion perception threshold and smooth pursuit gain, partialling out the d′ scores from either CPT had no effect. Therefore, the relationship between motion perception and gain is not secondary to visual sustained attention, and does not reflect a dimension of generalized deficit.

Although we found motion perception to be related to smooth pursuit gain, it was not related to RMS error. In a recent paper by Friedman *et al.* (1995*b*), these two measures of smooth pursuit performance were compared in detail. To summarize, RMS error measures the extent to which the smooth pursuit system is engaged, whereas gain measures the performance of the smooth pursuit system once engaged (Friedman *et al.* 1995*b*). The present results would suggest that the perception of motion is not related to the extent of engagement of the smooth pursuit system. Rather, the results indicate that the perception of motion is related to the ability to match eye and target velocity. This finding is consistent with other evidence, discussed above, linking motion perception and smooth pursuit gain (Newsome *et al.* 1985; Wurtz *et al.* 1990).

An important caveat concerns medication status of the patients. We previously reported in a small sample that a low dose of clozapine for approximately 6 weeks does not lead to a statistically significant decrease in smooth pursuit gain (Friedman *et al.* 1992). However, Litman *et al.* (1994) reported a statistically significant decrease in smooth pursuit gain in a larger sample treated with a larger dose for approximately 10 weeks. The patients in the present study had been medicated for a much longer time period than either previous study (median 24·3 weeks = 170 days) and the mean

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dose was comparable to that reported by Litman *et al*. (1994). It is difficult to know if clozapine was having a depressing effect on gain in our patients. First, the published studies with clozapine are inconclusive, since taken together, these studies only report data from 23 patients. Furthermore, no study has evaluated the effect of chronic treatment with clozapine on smooth pursuit at approximately 6 months. It is unlikely that clozapine was having a marked effect on gain in the present study since the gain of the clozapine treated patients was relatively high (0·89), even though it was statistically lower than that of controls.

Also, little is known regarding the effect of prolonged (6 months) treatment with clozapine on measures of attention or motion perception in patients with schizophrenia. Indeed, we are not aware of any study that has evaluated the effect of chronic clozapine treatment on CPT measures or motion perception per se. Zahn *et al*. (1994) found no effect of approximately 9 weeks of clozapine on reaction-time measures of attention in schizophrenics. Nonetheless, one cannot dismiss the possibility that the correlations between motion perception and smooth pursuit gain may be due either to clozapine, or some characteristic of patients likely to be treated with it (e.g. treatment resistance). Such a possibility will simply have to await further research on unmedicated or never medicated patients.

There are a number of considerations which complicate comparing the present results with the neurophysiologic investigations of Wurtz *et al*. (1990) and Newsome *et al*. (1985). An obvious difference is that those studies were based on data from non-human primates. Also, the stimulus for smooth pursuit in the neurophysiological studies were brief, transient 'step-ramp' stimuli (Rashbass, 1961), whereas the stimulus for pursuit in the present study was a continuous, predictable 'trapezoidal' waveform. It is possible that the perception of motion is more tightly linked to pursuit function at the initial onset of pursuit, before the target becomes predictable. However, it is also possible that the perception of motion continues to influence pursuit performance even after the target becomes more or less predictable. Also, target speed in the Newsome *et al*. (1985) and Wurtz *et al*. (1990) studies was 16°/s, whereas ours was 5°/s. A faster target would tend to activate MT somewhat more selectively than our target, and future studies at faster target speeds are certainly warranted.

Although smooth pursuit gain and motion perception were correlated within the patient group, in the control group the correlation between these two variables was quite small and not statistically significant. Three possible explanations occur to us for the absence of a relationship between motion perception and gain in control subjects. First, the controls had a reduced range (2 to 8) of correlated motion thresholds compared to the patients (2 to 19). Correlation coefficients are reduced in absolute magnitude in the presence of a restriction of range (Cohen & Cohen, 1983). Also, the patients had low gain compared to controls, and it is possible that the relationship between motion perception threshold and gain depends on the range of gain values observed. Finally, it is possible that the diagnosis of schizophrenia is associated with a distinct correlation between gain and motion perception.

In conclusion, the results of the present study suggest that smooth pursuit gain is related to motion perception in patients with schizophrenia, and that this relationship is not secondary to impairment in sustained visual attention. This finding is consistent with the notion that impaired smooth pursuit eye movement performance in schizophrenia is related to a dysfunction in area V5 (or MT).

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