



Visual motion integration in schizophrenia patients, their first-degree relatives, and patients with bipolar disorder

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We would like to dedicate this paper to Dr. Philip S. Holzman,
whose vision and enthusiasm inspired a series of research studies including the one reported here.

Abstract

Many schizophrenia patients show degraded detection of coherent motion. This visual deficit may (1) be a consequence of having a specifically schizophrenic psychosis, (2) be a non-specific effect of suffering from a severe illness (i.e., “generalized deficit”), or (3) reflect properties of the visual motion processing system that play an antecedent, possibly causal role in the pathophysiology of a disposition to schizophrenia. To distinguish among these possibilities, we measured the accuracy of detecting the direction of coherent motion in 29 schizophrenia patients, 20 first-degree relatives of schizophrenia patients, 19 patients with bipolar disorder and 33 normal controls. The task requires the integration of dynamic signals from stochastic random dot patterns in order to discern the direction of their motion. Schizophrenia patients, as a group, showed significantly elevated thresholds for detecting the direction of coherent motion, but relatives of schizophrenia patients and patients with bipolar disorder did not differ from normal controls on this task. The results indicate that visual motion integration, normally mediated in motion-sensitive brain areas such as the Middle Temporal Area, is impaired in patients with a clinically manifest schizophrenic psychosis, but is intact in patients with a non-schizophrenic psychosis (bipolar disorder) and in the relatives of schizophrenia patients. Our findings suggest that deficiencies in integrating motion signals, while specific for schizophrenia, do not seem to be a co-familial trait.

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1. Introduction

Schizophrenia is associated with a variety of behavioral dysfunctions. Some of these are consequences of having the psychotic disorder. Others may be an intrinsic part of the disease process itself while being quite independent of the presence or absence of the

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psychotic form of the illness. Yet others reflect the decline in general functioning that accompanies most severe illnesses, but do not shed light on the pathophysiology of any specific disease. Here we focus on an aspect of visual processing: the capacity to detect the direction of coherent motion.

Our interest in motion perception in schizophrenia arose from the rediscovery of Diefendorf and Dodge's (1908) finding that smooth pursuit eye movements—the ability to track a moving target—was impaired in schizophrenia patients. We reported that from about 50% to over 80% of schizophrenia patients and from about 25–40% of their first-degree biological relatives had impaired pursuit movements (Holzman et al., 1973, 1974). Many replications of the finding of impaired smooth pursuit in schizophrenia followed (e.g., Cegalis and Sweeney, 1979; Clementz et al., 1990a; Iacono et al., 1981; see Levy et al., 1993 for a review; Thaker et al., 1996).

We parsed this complex eye tracking dysfunction (ETD) into simpler components in order to understand its role in schizophrenia (Holzman, 1994). An essential component of the ETD is impaired velocity appraisal, inferred from the fact that the ratio of eye velocity to target velocity (pursuit gain) is low in those patients with ETD (e.g., Abel et al., 1991; Clementz et al., 1990b; Levy et al., 2000; Sweeney et al., 1994, 1999). Indeed, we found that patients with schizophrenia as well as a proportion of their unaffected biological relatives show significant impairments in judging the comparative velocities of moving gratings, although other aspects of visual processing, such as contrast detection and orientation discrimination are normal (Chen et al., 1999a,b,c; see also Stuve et al., 1997).

We recently reported that the processing of global motion is impaired in schizophrenia (Chen et al., 2003b). Here we ask whether this global motion impairment is specific for schizophrenia, and if so, whether it represents a co-familial trait. In primates, the processing of global motion information involves neural systems that are different from those involved in local motion processing. It is therefore feasible to infer the specific brain mechanisms that are implicated in the global motion deficits in schizophrenia. Such an inference would profit from knowing whether the global motion deficit is simply an expression of the generalized dysfunctions that accompany most serious illnesses, or is specific to schizophrenia, and if it is

specific, whether it is a characteristic of the psychotic condition or of a more general disposition that is independent of the schizophrenic psychotic state.

To address the specificity and generalized deficit issues (Chapman and Chapman, 1973), we compared performance on the detection of coherent motion and on contrast detection in schizophrenia patients, bipolar patients, and normal controls. To address whether the global motion deficit represents a co-familial trait or is characteristic only of those who develop the schizophrenic psychotic condition, we examined the performance of clinically unaffected first-degree relatives of the schizophrenia patients on these same visual tasks.

2. Methods

2.1. Subjects

Four groups of subjects were included in this study: (1) Schizophrenia patients (SCZ, $n=29$); (2) the first-degree relatives of schizophrenia patients (RELSCZ, $n=20$); (3) patients with bipolar disorder with psychotic features (BP, $n=19$); and (4) non-psychiatric controls (NC, $n=33$). About 23 of the 29 SCZ patients and 26 of the 33 NC had participated in a prior study of global motion discrimination (Chen et al., 2003b). Consensus DSM IV diagnoses were made independently of the experimental procedures, and blind to their results, by experienced clinicians based on a review of a standardized interview, the Structured Clinical Interview for the DSM-IV (Spitzer et al., 1994), conducted by experienced interviewers, and an evaluation of all available hospital records. All patients were outpatients at the time of testing. All schizophrenia patients except one were receiving antipsychotic medication (mean daily chlorpromazine dose equivalent: 557 mg; $\sigma=384$ mg). Eight of the SCZ patients were receiving typical antipsychotic medications, and of these, seven were also receiving atypical antipsychotics. Of the seven receiving both atypical and typical medications, two were also receiving anxiolytics, two were also receiving antidepressants, and two were receiving antidepressants and anxiolytics. Twenty of the SCZ patients were receiving atypical antipsychotics, and of these three were also receiving antidepressants, two anxiolytics, five antidepressants and anxiolytics, and four lithium. One SCZ patient was

receiving only antidepressant medication. The average Brief Psychiatric Rating Scale (BPRS) score (Overall and Gorham, 1962) of the SCZ patients was 40.0 ($\sigma = 13.8$).

In the BP group, three patients took no psychotropic medication. Five were taking atypical antipsychotic drugs, three of whom were also on a mood stabilizer and one of whom was receiving both a mood stabilizer and an antidepressant. Three BP were on typical antipsychotic drugs and a mood stabilizer (one of these patients was also on an antidepressant). One BP patient received only an antidepressant. Seven BP patients were receiving mood stabilizers and one of these patients was also taking an antidepressant drug. The average BPRS score was 30.9 ($\sigma = 7.7$) for the BP group.

The average duration of illness was 15.2 years ($\sigma = 7.1$ years) for the SCZ group and 10.0 years ($\sigma = 7.6$) for the BP group. The SCZ group had a significantly higher mean BPRS score than the BP ($t = 2.89$, $p < 0.05$, $df = 45$). The elevated BPRS scores and the lengthy duration of illness indicate that these patients, although outpatients, were chronically ill, in various stages of remission, rather than acutely ill patients.

We excluded from the RELSCZ and the NC groups individuals who met DSM-IV criteria for a psychotic condition (lifetime), bipolar disorder without psychotic features, or for schizotypal, paranoid, or schizoid personality disorder, based on a standardized interview (Kendler, 1989; Kendler et al., 1989). Demographic characteristics of the samples are contained in Table 1. The groups did not differ on demographic characteristics, with the exception of the slightly older mean age

of the RELSCZ group. Written informed consent in accord with the IRB guidelines of McLean Hospital and Harvard University was obtained from all participants prior to testing.

2.2. Procedures

The experimental task was to detect the *direction* of coherent motion. The comparison task was to detect the *presence* of a moving target. The tasks and methods were similar to those used in (Chen et al., 2003b) and are summarized below.

2.2.1. Detection of coherent motion

A random dot pattern was used to test the detection of coherent motion. Displayed on a computer screen, this target contained a signal component—an array of dots moving coherently in one direction (left or right) and a noise component—another array of dots moving in random directions. These two components were intermixed spatially within a rectangular window ($8 \times 20^\circ$). The dots were small (2×2 min arc) and white, and were presented on an otherwise black screen. Target movement, equivalent to $10^\circ/s$, was created by positional displacement of the individual dots.

The task was to indicate the direction (left or right) of motion of the signal component. The percentage of signal dots in the target, called motion coherence, represents the task-difficulty level. The smaller the percentage of signal dots (i.e., the lower the coherence) in a stimulus, the more difficult it is to perceive the direction the dots are moving in. The critical measure is the minimum percentage of signal dots (i.e., the

Table 1
Demographic characteristics of subjects

| | Sex | Age in years (SD) | SES ^a | Verbal IQ ^b (SD) | Education in years (SD) |
|----------------------------------------------------------------------|----------------|-------------------|---------------------------------------------|-----------------------------|-------------------------|
| Schizophrenia/ Schizoaffective ($N = 29$) | M = 14, F = 15 | 39.1 (6.9) | I = 20.7% II = 41.4% III = 31% IV = 6.9% | 106.3 (12.8) | 14.4 (2.1) |
| Bipolar ($N = 19$) | M = 7, F = 12 | 39.3 (9.6) | I = 42.1% II = 31.6% III = 26.3% | 109.7 (9.5) | 16.3 (1.9) |
| Normal controls ($N = 33$) | M = 7, F = 26 | 39.2 (12.6) | I = 21.2% II = 45.5% III = 33.3% | 106.7 (10.0) | 14.7 (2.4) |
| Relatives of Schizophrenia/ Schizoaffective Patients ($N = 20$) | M = 6, F = 14 | 41.1 (10.3) | I = 15% II = 50% III = 30% IV = 5% | 111.5 (12.6) | 15.2 (2.6) |

^a Socio-economic status based on the Hollingshead and Redlich two-factor index (Hollingshead, 1965).

^b Estimated verbal intelligence quotient from vocabulary subtest score of the WAIS (Wechsler, 1981).

minimum coherence level) at which the performance of a subject reaches the criterion of 80% correct in judging the movement direction of the random dot pattern. This percentage level is defined as the threshold (see Fig. 1). We measured the thresholds of all subjects at three dot density conditions—low (50 dots, or 0.31 dots/deg²), medium (100 dots, or 0.62 dots/deg²) and high (200 dots, or 1.24 dots/deg²).

The stimuli were generated on a computer screen (Macintosh Quadra 610). Subjects initiated a testing session by pressing a key. Each session contained 80 trials, which were evenly divided but randomly distributed across five motion coherence levels. The percentage of signal dots in the random dot pattern varied across trials according to the method of constant stimuli (among 3%, 6%, 12%, 24% and 48% coherence). The direction of the signal dots' move-

ment, left or right, was varied randomly from trial to trial. After the dot flow stimulus was presented for 750 ms, subjects indicated their judgment about the direction of motion by pressing one of two designated keys. No feedback for the correctness of the response was provided except in practice sessions (see below). Inter-trial intervals were varied randomly from 500 to 1000 ms. To prevent subjects from focusing on any single dot, rather than on the whole pattern, dot lifetime was limited to 90 ms (6 frames). A small fixation circle was provided continuously at the center of the field.

2.2.2. Detection of the presence of a moving target (contrast detection)

The task, serving as a control condition for the coherent motion task, required the observer to detect the presence of a moving target by indicat-

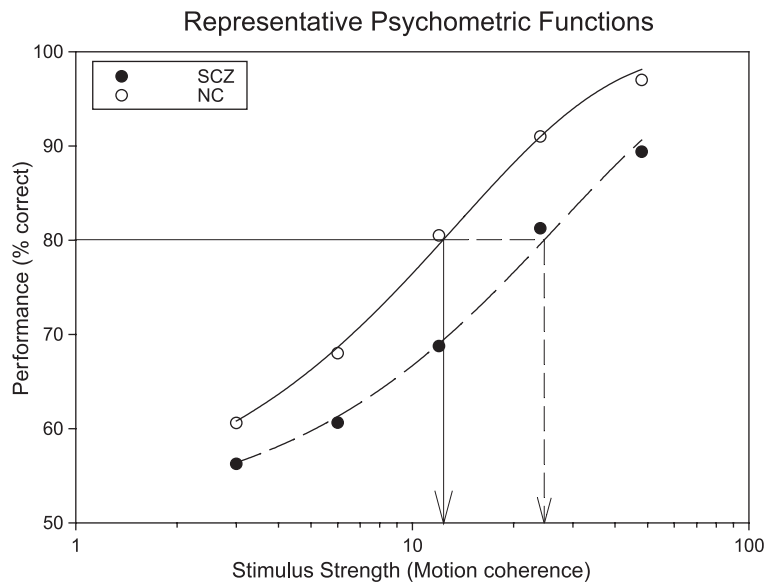


Fig. 1. Representative psychometric functions for determining thresholds for detecting of coherent motion. The data represent the performance at the medium dot density condition (100 dots) of one schizophrenic patient (SCZ) and one normal control (NC) who were randomly selected from each group. The five coherence levels of the random dot presentations (3%, 6%, 12%, 24%, and 48%) are represented on a logarithmic scale along the abscissa; the accuracy with which a subject determines the direction of movement of the signal dots is represented on a linear scale on the ordinate. The five data points for each group represent the percent correct judgments at these five coherence levels. The most difficult coherence level is at 3%, and there the percent correct is near a chance level (50%); the easiest level is at 48% where percent accuracy score is over 90% for the NC. The data are fit by a form of Weibull function, which is expressed in the following equation: $y = 100 - 50 \exp[-(x/\alpha)^\beta]$, where y = the percent correct scores, x = the stimulus coherence level, α and β are two curve-fitting parameters; \exp is the exponential function used in this curve-fitting procedure. From the fitted curve, a threshold can be determined. The thresholds in this illustration, set at a criterion of 80% correct, are at a coherence level of 11.2% for NC, and 22.4% for SCZ.

ing in which of two temporal intervals (first or second) in a trial the moving target was present. In the other interval of a trial, a blank screen was presented. The target was a vertical grating with a sinusoidal spatial luminance distribution of 0.5 cycles/°. The temporal modulation was set at 5 Hz, which yielded target movement of 10°/s either to the right or to the left, with the direction varying randomly from trial to trial. Each interval (target and blank) was presented within a circular window with a diameter of 10° of visual angle for 300 ms. A fixation cross was present at the center of the field.

The critical measure in the contrast detection task was the minimum amount of contrast necessary to achieve a criterion performance of 79% correct. The contrast level of the gratings was set initially at 1.5%, which is adequate to detect the presence of a motion target. The level of contrast varied from trial to trial according to a two alternative forced-choice staircase method (1-up–3-down). Specifically, the contrast level decreased by 5% of the current level if three correct responses were made in a row, and increased by 5% of the current level if one incorrect response was made. Twelve reversals of staircase direction terminated an experimental session. The contrast levels at all reversals, except for the first one, were averaged to produce a threshold.

Detailed instructions and adequate practice to insure that subjects understood the task were administered prior to formal data collection. Short breaks were provided during the session as necessary to minimize fatigue and inattention.

3. Results

3.1. Coherent motion

Fig. 2 presents the average thresholds of all subject groups obtained under the three dot-density conditions. The results, tested in a 4 (groups) \times 3 (dot densities) repeated measures analysis of variance (ANOVA), showed a significant overall effect ($F=2.63$, $p=0.0032$, $df=11$), which was due to a significant effect of groups ($F=7.75$, $p=0.001$, $df=3$). Planned contrasts showed that the SCZ group had global motion detection thresholds significantly elevated over those of all other groups (SCZ vs. NC: $t=4.08$, $p<0.001$, $df=178$; SCZ vs. RELSCZ: $t=3.23$, $p<0.01$, $df=138$; SCZ vs. BP: $t=2.17$, $p<0.05$, $df=137$). There was no significant effect of dot densities and no significant interaction of groups with dot densities, indicating that RELSCZ and BP patients showed thresholds similar to those of the NC at all dot densities. Fig. 3

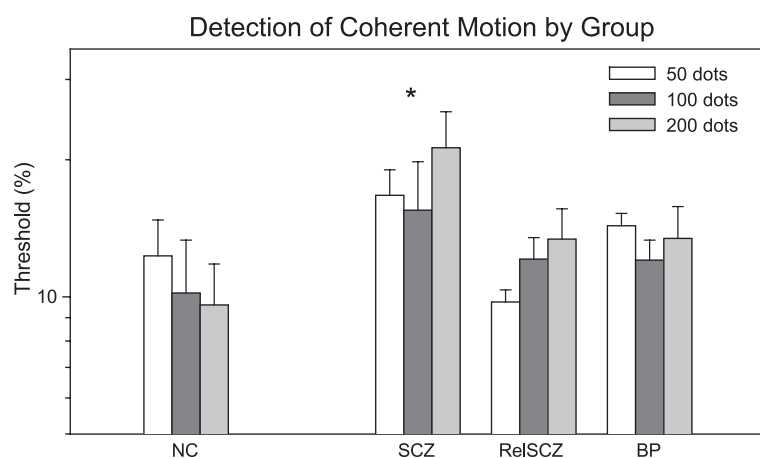


Fig. 2. Coherent motion thresholds for the three dot-density conditions. The ordinate represents the detection thresholds on a logarithmic scale. The abscissa denotes the four subject groups. Error bars indicate 1 standard error. The asterisk (*) denotes that the SCZ group is significantly difference ($p<0.05$) from the other groups.

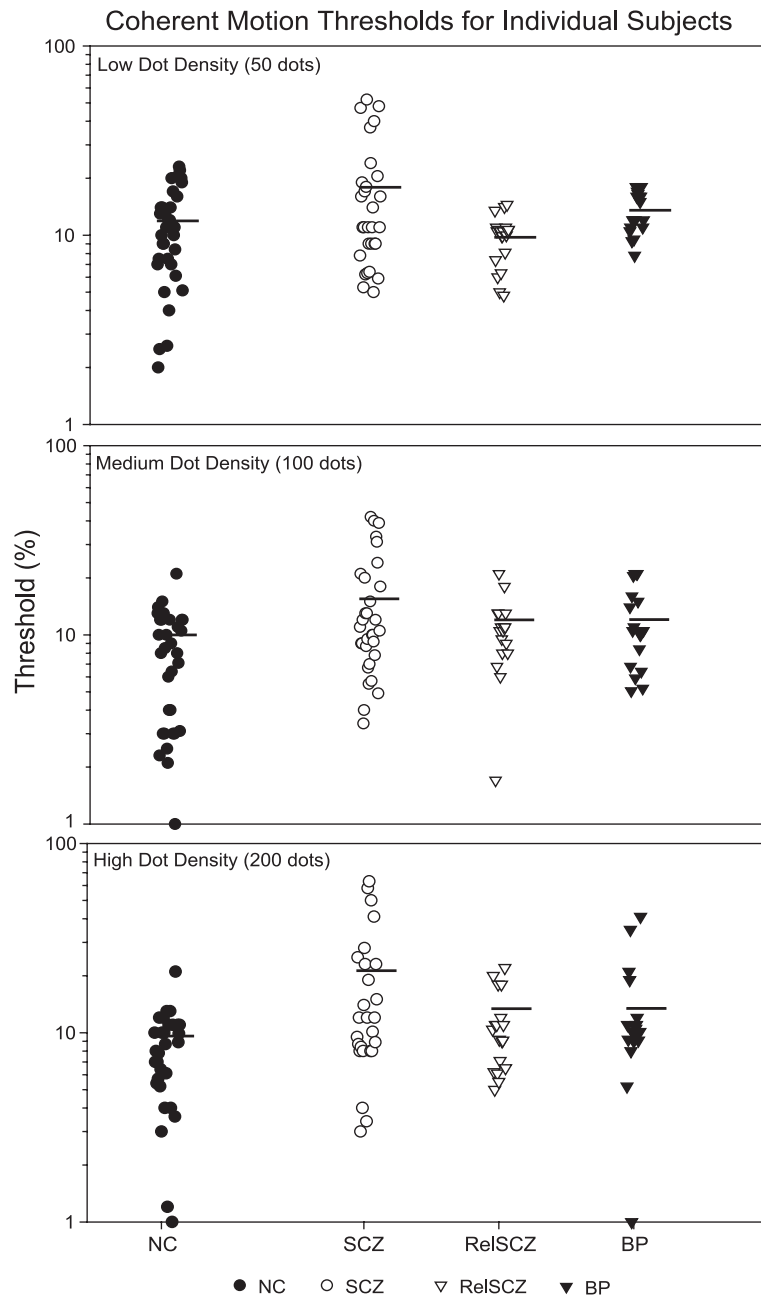


Fig. 3. Scatter diagram of the coherent motion detection thresholds for the four subject groups for each of three dot-density conditions. The dark bars represent the means of each group. The distribution of thresholds is shown on a logarithmic scale on the ordinate.

presents scatter diagrams of the groups in all dot density conditions and illustrates that the higher thresholds of the SCZ patients are not referable to outlier performance.

3.2. Contrast detection

The contrast detection thresholds of the four groups were tested by an ANOVA. The results

showed no significant effect of group ($F=1.21$, $p=0.3123$, $df=3$).

3.3. Effects of other variables (illness severity, symptoms, medication)

There was no significant correlation between duration of illness and task performance in the patients. Nor was there any significant relation between global motion thresholds and severity of illness; the Pearson product–moment correlations between BPRS scores and the coherent motion thresholds for the low, medium, and high dot densities were 0.014, 0.26, and 0.01 for schizophrenia patients and 0.12, 0.25, and -0.04 for bipolar patients, all of which are statistically non-significant. With respect to distinguishing between patients who performed either very poorly or within the range of the NC group on global motion, we were unable to find significant differences in the BPRS scores and CPRS scores of visual and auditory hallucinations (Chapman and Chapman, 1980).

To determine the effect of medication on the performance of the motion tasks, we examined whether the motion thresholds and the dose of antipsychotic drugs (CPZ equivalent) were correlated and did not find significant relations between these variables ($r_{50 \text{ dots, CPZ}}=0.03$, $r_{100 \text{ dots, CPZ}}=0.14$, $r_{200 \text{ dots, CPZ}}=0.03$), suggesting that patients' impaired performance in the motion tasks are not attributable to antipsychotic drugs.

To determine whether the patients who performed poorly at one dot density also performed poorly at other two dot densities, we computed the correlations among the three dot densities. The correlation coefficients ($r_{50 \text{ dots, 100dots}}=0.54$, $r_{50 \text{ dots, 200 dots}}=0.21$, and $r_{100 \text{ dots, 200 dots}}=0.64$), indicate that performance of the patients under different task conditions is significantly correlated between two near dot densities (50 vs. 100 and 100 vs. 200), indicating that the performances of schizophrenic patients are generally consistent.

4. Discussion

Our results showed that schizophrenia patients had significantly higher thresholds for detecting the direction of coherent motion at all three dot densities,

compared with normal participants. That is, the schizophrenia patients require a greater percentage of motion coherence among the random dots to detect the direction of an aggregation of moving dots. This result was reported in a previous study (Chen et al., 2003b), and is confirmed here in a sample of schizophrenia patients that is augmented over that used earlier. This result is also consistent with the findings by Stuve et al. (1997) of impaired motion perception using random dot targets. The present study also showed that neither RELSCZ nor BP have coherent motion detection thresholds that differ from those of NC. A comparison task, contrast detection, showed no differences among the groups.

4.1. The issue of co-familiality

The finding of normal global motion processing in RELSCZ is noteworthy because substantial proportions of these same RELSCZ show deficits on other independently measured schizophrenia-related traits that are co-familial. Fourteen of the 20 RELSCZ (70%) in the present study were tested on a velocity discrimination task in a previous study; five of these 14 (35.7%) had velocity discrimination thresholds that were significantly above the mean of the normal control group. Similarly, 9 of the 20 relatives (45%) had pursuit gain scores below 0.75; 6 of the 20 relatives (30%) had Thought Disorder Index scores that were significantly higher than the mean of the normal population; and 8 of the 20 relatives (40%) had ratings of formal thought disorder that were classified as characteristically schizophrenic. Thus, the present group of RELSCZ contains many individuals who manifest one or more co-familial traits associated with schizophrenia, but as a group they performed normally with respect to the detection of coherent motion employed here. Moreover, the relatives with abnormal and normal Thought Disorder Index scores showed very similar motion thresholds (10% vs. 10% at the low dot density, 13% vs. 11% at the medium dot density, and 11% vs. 11% at the high dot density).

In summary, the processing of global motion, as elicited by the coherent motion task employed here, is compromised specifically in the clinical form of schizophrenia, but is unimpaired both in relatives of schizophrenia patients and in patients who have a

different chronic major psychosis, i.e., bipolar disorder. The global motion-processing deficit appears to be specific to schizophrenia and, although it is associated with schizophrenia, it does not appear to be a co-familial trait.

4.2. Clinical variables

One may raise the question of whether the global processing impairment in SCZ reflects a general performance deficit that accompanies most severe illnesses, referred to as “generalized deficit” by Chapman and Chapman (1973). In rejecting this explanation of our results, we note that the schizophrenia patients performed normally in contrast detection, a task that requires focused attention and discriminating capacity. This difference between normal performance on contrast detection and impaired performance on global motion perception indicates that the impairment on the latter task represents a specific dysfunction rather than a general one, and, therefore, refers to specific neural mechanisms involved in the processing of global motion.

4.3. Detection of coherent motion as motion integration

Detection of coherent motion requires two elementary processes—one for rejecting the noise component embedded in the stimulus and the other for integrating the signal component. Spatial and temporal filtering in the early stage of the motion system is largely responsible for rejecting the noise embedded in visual inputs. On the other hand, integration of complex motion signals such as those in the random dot patterns (RDP) relies on the neural interaction in the late stage of the motion system, which may be tentatively linked to dynamic grouping (Watt and Phillips, 2000). Pre-specified computation does not appear to play a significant role in the neural integration here partly because the receptive field profiles of typical motion-sensitive neural units do not match the unnatural or artificial configurations of visual stimuli such as RDP. Our procedure, using a limited dot lifetime, forced subjects to adopt a global strategy to perform the task; a short dot lifetime of 90 ms makes it virtually impossible for subjects to move their eyes from one dot to

another when judging the directions of RDP, or to follow the position of a single dot. Deficient detection of coherent motion in schizophrenic patients, shown in this and other studies, may be regarded as evidence for impaired motion integration or dynamic grouping in schizophrenia (see, e.g., Phillips and Silverstein, 2003), if an abnormality of the neural mechanisms for rejecting noise can be ruled out, an issue that awaits a separate study.

4.4. The pathophysiology of motion processing in schizophrenia: processes of integration vs. differentiation

Detection of coherent motion requires integration of motion signals in space in order to form a global percept of motion direction whereas velocity discrimination requires differentiation of motion signals in order to discern fine velocity differences. Neural computation for combining distributed visual signals relies on the responses of neuronal units with large receptive fields (see, e.g., Livingstone et al., 2001), whereas neural computation for discriminating between two similar visual signals relies on changing amplitudes in a neuronal response function (see, e.g., Barlow et al., 1987; Chen et al., 1996). It is likely that the pathophysiology of schizophrenia affects these two types of neural computation differently. One possibility is that the disease process of schizophrenia implicates altered response functions of individual neurons in a subtle way that is apparent when the observer must discriminate between two signals that differ subtly, a process that requires a differentiating computation. This alteration may be present independently of the manifestation of obvious clinical symptoms of a schizophrenic disorder, and thus can also be present in a number of biological relatives of patients who are clinically unaffected.

In contrast to the finding that velocity discrimination is impaired in both SCZ and clinically unaffected RELSCZ, we found here that detection of the direction of coherent motion signals is impaired only in SCZ but not in RELSCZ. This divergence suggests a difference in pathophysiology between patients and relatives. Both motion differentiation (velocity discrimination) and integration (detection of coherent motion) involve MT activity, but these two processes implicate different aspects of MT (Born and Tootell,

1992). In the case of motion integration the medial superior temporal (MST) area is implicated as well. As noted above, global motion processing in the presence of a complex field with many units to be integrated—as in targets used in this study—requires that the visual system combine a large amount of information in order to sift the signal from the noise. This processing load may be considerably greater than that required for detecting the movement of either a single point or even an object, which informs the observer about the direction of its movement from any point on its surface.

A phenomenological approach to understanding the motion processing capacities of schizophrenia patients and their relatives might propose that the task of motion integration imposes a high processing load on schizophrenia patients, who are under pressure from a decompensatory process that affects many psychological functions. Relatives, who are not under that decompensatory pressure, may muster auxiliary compensatory resources to respond more adaptively to the global stimuli. Or it may be that the global motion system is spared from dysfunction in relatives, but targeted in patients. Some of these impairments may be present in people who later manifest the psychotic form of the disorder, but are not present in those who never become psychotic. Moreover, some of these impairments may persist after the psychosis has more or less remitted, and thus assume the status of a trait. These ad hoc explanations should be consistent with a recognized pathophysiology of the motion processing system, to which we now turn.

In primates, motion-sensitive areas MT and MST have a modular organization. For example, the lateral area of MT, representing the fovea (referred to as MTf), typically has small receptive fields and responds specifically to small moving targets. Lesions to MTf impair the monkey's ability to use motion cues to pursue an object and to make an accurate initial saccade to the moving target. MTf lesions, however, do not impair the use of either position or contrast detection (Dursteler and Wurtz, 1988; Dursteler et al., 1987; Newsome and Pare, 1988; Newsome et al., 1988) This same pattern of both spared and impaired functions was found in schizophrenia patients and their relatives: impaired smooth pursuit and motion detection, but unimpaired position and contrast detection (Chen et al., 1999a, 2003a).

Area MST also has a modular organization, and two components have been identified: a dorsal (MSTd) and a lateral (MSTl) area. The receptive fields of MSTd are large and extend as much as 40° into the ipsilateral field (Dukelow et al., 2001). MSTd is deployed in the context of optic flow and large moving patterns (Andersen et al., 1990; Duffy and Wurtz, 1991; Saito et al., 1986). MSTl, on the other hand, contains a mixture of large and small visual fields (Komatsu and Wurtz, 1988), responds better to small moving objects, and is deployed for separating the motion of small objects from the background (Eifuku and Wurtz, 1999). Lesions to MSTl impair the maintenance of smooth pursuit, whereas lesions to MSTd do not. This parcellation of MT and MST suggests that one would expect impaired functioning of MSTl in both SCZ and in a significant proportion of RELSCZ. On the other hand, MSTd, where only large visual fields are preferred, would be impaired specifically in schizophrenia patients, an expectation consistent with the results of the current study. It is thus possible that those relatives who are predisposed to schizophrenia by virtue of possessing traits associated with that disorder manifest a specific dysfunction in motion processing that is regulated by MTf and MSTl, and spares MSTd. If the disease develops into the clinical form of schizophrenia, however, other aspects of the pathophysiology are triggered (or may already have been triggered in those destined to become psychotic) as part of a cascade of impairments that characterize the progressive advance of the disorder. These changes, perhaps through a shift in types of neurotransmitters involved in the progression of the disease, can include an alteration within area MT, for example, as well as altered processes in MSTd. Unlike some progressive neurological disorders like Parkinson's or Alzheimer's disease, however, the extent of the progressive decline in schizophrenia appears to be a limited one (Bleuler, 1950 (Original published 1911); Kraepelin, 1919).

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