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Bipolar and schizophrenic patients differ in patterns of visual motion discrimination

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Abstract

Background—Since Kraepelin's early distinction between bipolar disorder and schizophrenia, it has been assumed that these disorders represent two different pathophysiological processes, although they share many clinical symptoms. Previous studies showed that velocity discrimination, a sensitive psychophysiological measure of the visual motion system, is deficient in schizophrenia. Here we examined whether the motion processing impairment found in schizophrenia also occurs in bipolar disorder.

Methods—We compared 16 bipolar patients, 25 schizophrenic patients, and 25 normal controls on a velocity discrimination task. We measured the psychophysical threshold for velocity discrimination and contrast detection (as a control task) in all subjects.

Results—Bipolar patients showed normal velocity discrimination thresholds at intermediate velocities, the range in which velocity cues dominate velocity discrimination, and at low velocities. Schizophrenic patients, however, showed elevated velocity discrimination thresholds at intermediate and low velocities. At higher velocities, both bipolar and schizophrenic patients showed elevated thresholds. All subjects showed normal contrast detection thresholds.

Conclusions—Normal velocity discrimination in the intermediate range of velocity indicates unimpaired motion processing in bipolar disorder. The abnormal velocity discrimination of both schizophrenic and bipolar patients at higher velocities may reflect impaired temporal processing rather than impaired motion processing *per se*. These results suggest that the pathophysiological processes of bipolar disorder and schizophrenia diverge at the stage of visual motion processing, a sensory component mediated primarily in the extrastriate cortex.

Keywords

Schizophrenia; Vision; Psychiatric disorders; Eye tracking; Temporal processing

Previous studies found that the perceptual capability to discriminate similar velocities, or velocity discrimination, was significantly degraded in schizophrenic patients and in a proportion of their first-degree relatives (Chen et al., 1999a,c, 2004). These studies were prompted by efforts to find the sources of eye tracking dysfunctions (ETD), which occur in many schizophrenic patients and in about 30% to 40% of their first-degree relatives (Holzman et al., 1973, 1974; Shagass et al., 1974; Sweeney et al., 1994; Thaker et al., 1998; for a review, see Levy et al., 1993). One explanation of ETD is based on the finding that both smooth pursuit and motion discrimination are impaired after lesions to the middle temporal area (MT) of the extra-striate cortex (Zihl et al., 1983; Wurtz et al., 1990; Pasternak and Merrigan, 1994), an

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area that processes motion signals. We hypothesized that those patients with schizophrenia who show ETD process velocity signals poorly during target movement, leading to impairments in both smooth pursuit and velocity discrimination. In one of our earlier studies (Chen et al., 1999c), we showed that velocity discrimination thresholds were elevated in schizophrenic patients at intermediate target speeds of 10 to 16.2°/s, where velocity cues predominate. At slower and faster speeds, differences between normal participants and schizophrenic patients (and their relatives) were not significant. We also showed that velocity discrimination performance in schizophrenic patients was significantly correlated with eye tracking — about 58% of the variance in initial eye tracking (pursuit acceleration) was explained by velocity discrimination performance. Similar correlations between motion perception and smooth pursuit eye movements in schizophrenia were found in two other studies (Stuve et al., 1997; Chen et al., 1999b).

It is possible that raised velocity discrimination thresholds occur in psychotic conditions other than schizophrenia, for example, in bipolar affective disorders. Some studies have reported impaired smooth pursuit eye movements in bipolar patients (Shagass et al., 1974; Levin et al., 1981; Iacono et al., 1982; Holzman et al., 1984), whereas other studies showed no difference between affective disorder patients and controls (Holzman et al., 1974; Iacono et al., 1992; Friedman et al., 1995). Several studies found that relatives of affective disorder patients and controls did not differ in eye tracking performance (Levy et al., 1983, 1993; Rosenberg et al., 1997; but see Kathmann et al., 2003). Treatment with lithium carbonate has been associated with poor eye tracking in individuals with bipolar disorder (Levy et al., 1985; Holzman et al., 1991) and in relatives who themselves were being treated for bipolar disorder (Levy et al., 1983, 1985), although one study failed to show this effect (Gooding et al., 1993).

In other visual tasks, bipolar patients show impaired performance when processing of dynamic signals is required, for example, perception of temporally modulated stimuli (Green et al., 1994) and switching from one perceptual state to another (Pettigrew and Miller, 1998). Whether and how processing of motion signals, which requires both spatial and temporal signals, is affected in bipolar disorder is unknown, however. To understand whether the velocity discrimination deficit is specific for schizophrenia or whether motion processing is also compromised in bipolar disorder, we examined velocity discrimination performance in bipolar disorder and in schizophrenia. Since velocity discrimination is one sensory component mediated primarily in the extra-striate cortex, the results can provide independent information on whether the pathophysiological processes of bipolar disorder and schizophrenia overlap at the stage of visual motion processing.

1. Materials and methods

1.1. Subjects

Sixteen bipolar disorder patients, 25 schizophrenic patients, and 25 non-psychiatric controls participated in this study. The patients were chronically ill outpatients and in varying degrees of remission; average duration of illness was 12 years (SD=10 years) for bipolar patients and 15 years (SD=9 years) for patients with schizophrenia. The patients had been discharged from a private psychiatric hospital during the previous year. None of the subjects had participated in any of our previous studies of velocity discrimination. All patients met DSM-IV criteria for bipolar disorder with psychotic features (most recent episode) or for schizophrenia/schizoaffective disorder. In nine of the bipolar patients, the most recent episode was manic; in three it was depressed and in five it was mixed. Consensus diagnoses were made by experienced clinicians based on a review of the Structured Clinical Interview for the DSM-IV (Spitzer et al., 1994) conducted by trained interviewers and an evaluation of all available hospital records. All of the bipolar patients were receiving antimanic medication (anticonvulsant mood stabilizers: $n=9$; lithium: $n=7$); thirteen were on low doses of atypical antipsychotic medication

[mean daily dose in chlorpromazine (CPZ) equivalents=114 mg (SD=94 mg)] (Woods, 2003), five were taking an antidepressant, and one was on no psychotropic medication. Eighteen of 25 schizophrenic patients were receiving atypical antipsychotic medication, three were on typical antipsychotics, three were on both typical and atypical antipsychotic medications [mean daily dose in CPZ equivalents: 388 mg (SD=442 mg)], one was on an antidepressant only, and one was unmedicated. The average BPRS scores of the bipolar and schizophrenic patients were 33 (SD=10) and 43 (SD=13), respectively.

Normal control participants were recruited from a large medical outpatient clinic. None of them met DSM-IV criteria for a psychotic condition (lifetime) or bipolar disorder without psychotic features based on a SCID interview, or for schizotypal, paranoid, or schizoid personality disorder based on a standardized interview (Kendler, 1989). Table 1 displays the demographic characteristics of the subject groups. The three groups of subjects did not differ in average age, sex, education and socioeconomic status. Written informed consent was obtained from all participants prior to testing.

1.2. Stimuli

The visual target was a vertical sinusoidal grating displayed on a Macintosh computer screen. The grating was presented through a circular window of 19° of visual angle and moved horizontally either to the left or to the right; direction of movement was randomized from trial to trial. The base velocities of the grating were 3.8, 6.2, 10, 16.2 and 26.6°/s. The spatial frequency of the grating was 0.5 cycles/° and had a spatial average luminance of 35 cd/m². For the velocity discrimination task, a small cross was provided for central fixation.

1.3. Procedure

We administered two psychophysical tasks, velocity discrimination and contrast detection.

1.3.1. Velocity discrimination—Subjects were shown two moving gratings sequentially that differed in velocity, and were required to decide which one, the first or the second, moved faster (top portion of Fig. 1). Within a trial, each target was presented for 300 ms; the time interval between the two target presentations was 500 ms. The target contrast was fixed at 15%. After viewing the two gratings, subjects indicated their judgments by pressing one of two designated buttons on the keyboard. The initial velocity difference between the two comparison targets was set at 100%. For example, if target one moved at a base velocity of 10°/s and target two moved at 20°/s, the velocity difference is 100% [(20–10)/10=1 or 100%]. We used a two-alternative, forced-choice procedure to determine each subject's velocity discrimination threshold. This procedure was combined with a standard three-down-one-up staircase. In this procedure, the velocity difference in successive trials was adjusted according to the correctness of a subject's responses. Specifically, the velocity difference between successive stimuli was decreased by 5% of the current level if a subject made three consecutive correct responses and increased by 5% of the current level if the subject made one incorrect response. The experimental session terminated after twelve reversals of staircase directions. The velocity difference levels of all reversals, except for the first, were averaged to produce a threshold, which is the just-noticeable-difference (ΔV), or the Weber fraction ($\Delta V/V$), and corresponds to an accuracy level equivalent to 79% correct for each subject (Levitt, 1972). The staircase procedure minimizes the experience of failure, an important consideration when testing psychotic patients.

1.3.2. Contrast detection—This control task uses visual stimuli and psychophysical procedures similar to those used in the velocity discrimination task, but does not require the processing of velocity signals. The target, a grating moving at 10°/s, was presented alternately with a blank interval either at the first or the second interval in a trial. The average luminance

level of the grating was the same as that of the blank interval. Subjects were asked to indicate which of the two intervals (first or second) in a trial contained the target grating (bottom portion of Fig. 1). The initial target contrast was set at 1.5%. Contrast level of the target was adjusted using the same staircase procedure described above.

All experimental conditions were completed in a single one-hour session. Prior to data collection, subjects received detailed instructions and were given a number of practice trials to insure that the task requirements were understood.

2. Results

Fig. 2 presents the mean velocity discrimination thresholds for the three subject groups (see also Table 2). Fig. 3 presents the distribution of threshold scores for the three groups at the slowest, fastest and intermediate velocities. An overall comparison by ANOVA showed that: 1) the group differences were significant ($F(2,113)=10.21, p<0.001$), 2) the velocity differences were significant ($F(4,113)=13.69, p<0.001$), and (3) the interaction between group and velocity was significant ($F(8,113)=2.71, p<0.01$). This analysis indicates that the differences of velocity discrimination thresholds among the three subject groups depend on the velocities in which the threshold measurement was made.

In order to clarify the nature of the group $\times$ velocity interaction, we compared the velocity discrimination thresholds of bipolar patients and normal controls, schizophrenic patients and normal controls, and bipolar and schizophrenic patients at each of five individual velocities. A Bonferroni/Dunn post hoc test was used to correct for multiple comparisons.

- a. Bipolar patients vs. normal controls: The groups did not differ at the three slowest velocities (3.8°/s: $t(1, 39)=0.55, p=0.59$; 6.2°/s: $t(1, 34)=1.41, p=0.915$; 10°/s: $t(1, 39)=2.29, p=0.985$). However, bipolar patients had significantly higher velocity discrimination thresholds than controls at the two fastest velocities (16.2°/s: $t(1, 33)=2.1, p<0.04$, effect size (ES): 0.82; 26.6°/s: $t(1, 39)=2.21, p<0.03$, effect size: 1.15).
- b. Schizophrenic patients vs. normal controls: Schizophrenic patients had significantly higher mean velocity discrimination threshold than controls at each of the five velocities (3.8°/s: $t(1, 42)=3.53, p<0.01$; ES: 1.75; 6.2°/s: $t(1, 35)=2.73, p<0.01$; ES: 3.61; 10°/s: $t(1, 47)=2.69, p<0.01$; ES: 1.30; 16.2°/s: $t(1, 34)=1.80, p=0.08$; ES: 1.51; 26.6°/s: $t(1, 41)=3.86, p<0.01$; ES: 1.94).
- c. Bipolar vs. Schizophrenic patients: Schizophrenic patients had significantly higher thresholds than bipolar patients at the slow and intermediate velocities (3.8°/s: $t(1, 35)=2.35, p<0.02$; ES: 0.78; 6.2°/s: $t(1, 29)=3.39, p<0.01$; ES: 1.24; 10°/s: $t(1, 40)=3.59, p<0.01$; ES: 0.81), but not at the two fastest velocities (16.2°/s: $t(1, 29)=0.72, p=0.48$; 26.6°/s: $t(1, 34)=0.09, p=0.93$).
- d. Contrast detection thresholds did not differ between the bipolar and the normal control groups ($t(1, 37)=1.5, p=0.143$), between the schizophrenic and normal control groups ($t(1, 44)=0.49, p=0.627$) or between the bipolar and the schizophrenic groups ($t(1, 38)=1.4, p=0.108$). Contrast detection thresholds were not significantly correlated with velocity discrimination thresholds at 10.0°/s in any group ($r_{bp}=0.07, p>0.1$; $r_{sz}=0.28, p>0.05$; $r_{nc}=0.009, p>0.1$).
- e. Medication and clinical state effects: In bipolar patients neither dose of antipsychotic medication (in CPZ equivalents) nor BPRS score was significantly correlated with velocity discrimination thresholds for the two fast velocities ($p>0.1$), those on which bipolar patients showed a significant elevation compared with controls. Bipolar patients who were ($n=7$) and were not receiving lithium treatment ($n=9$) did not differ significantly in velocity discrimination thresholds at 16.2°/s ($p=0.99$) and 26.6°/s

($p=0.18$). Similarly, dose of antipsychotic medication was not significantly correlated with velocity discrimination thresholds at any of the five velocities on which schizophrenic patients showed elevated thresholds (all p 's > 0.1). BPRS score was modestly but significantly correlated with velocity discrimination threshold ($r=0.43$, $n=21$, $p<0.05$) for the 3.8°/s target only (all other p 's > 0.05).

3. Discussion

Bipolar patients showed normal velocity discrimination at slow and intermediate velocities compared with normal controls. At the two fastest velocities, velocity discrimination of the bipolar patients was significantly degraded compared with the normal controls, and was similar to that of the schizophrenic patients. Schizophrenic patients showed significantly degraded velocity discrimination along the entire range of base velocities tested in this study. There are two major implications of these findings: 1) visual motion processing is deficient in schizophrenia, but not in bipolar disorder, and 2) poor velocity discrimination only at higher velocities in the bipolar sample implicates a primary disruption in temporal, but not in motion, processing of visual information.

3.1. Motion processing in schizophrenia and in bipolar disorder

In the primate visual system, several aspects of stimulus information, such as velocity, change in spatial location (position) and rate of change over time (temporal frequency) can be used in motion perception. Which aspect of these signals dominates a visual percept depends largely on the velocity of the target. At intermediate velocities (for example, 10°/s), the velocity signal dominates other signals associated with moving targets, such as position, contrast, and temporal frequency (Maunsell and van Essen, 1983; McKee et al., 1986; Chen et al., 1998). At slow velocities, on the other hand, position displacement becomes the dominant signal, and at high velocities, contrast or temporal frequency becomes dominant (McKee, 1981; McKee et al., 1986; Smith, 1987). Therefore, velocity discrimination in the intermediate range of velocities provides a more direct measure of the integrity of motion processing than performance in the slow and fast ranges of velocities, where multiple aspects of visual signals, including velocity and position or contrast, are involved. At the intermediate velocity, where velocity signals dominate other signals, bipolar patients showed normal velocity discrimination, indicating that velocity processing is intact. Schizophrenic patients, on the other hand, showed poor velocity discrimination performance at the same intermediate velocity. This result is consistent with the findings on schizophrenic patients reported in previous studies (Stuve et al., 1997; Chen et al., 1999a,c). The clearly intact motion discrimination performance in bipolar patients at the intermediate velocity suggests that impaired velocity discrimination is a characteristic specifically of schizophrenia and not of bipolar disorder.

The current study and our previous one (Chen et al., 1999c) yielded consistent results in showing that velocity discrimination is impaired when schizophrenia patients have to rely on motion signals at intermediate velocities. Schizophrenia patients in our earlier study showed normal velocity discrimination thresholds at low and high base velocities, whereas schizophrenic patients in the present sample showed elevated mean thresholds not only at the intermediate but also at the lowest and highest velocities. The different velocity discrimination performance at the low and high velocities in the two samples seems to be related to the extent to which patients relied on non-motion cues. When non-motion cues were made unavailable in the earlier study, schizophrenia patients showed deficient velocity discrimination at slow and fast velocities, consistent with the results reported here. In the present study, the standard deviation of the velocity discrimination thresholds of the schizophrenic patient group at the lowest velocity was 29% larger than that of the bipolar group and 113% larger than that of the normal group, suggesting that while a subgroup of some schizophrenic patients may have used

non-motion cues to perform normally, many others did not, resulting in an elevated mean threshold. Note that the effect sizes for the differences in mean thresholds between the schizophrenia and control groups were large across the range of velocities tested (Fig. 2). This finding indicates that an impaired ability to use information from a non-velocity dominant signal, such as position or contrast, also has a deleterious effect on processing of velocity signals.

3.2. Velocity discrimination at fast velocities

During fast motion, temporal changes in visual contrast (or temporal frequency, a non-velocity visual cue) are dominant signals for neural and behavioral processes (Pantle, 1978; Mikami et al., 1986; Smith, 1987). The selectively poor performance of bipolar patients only at fast velocities implicates impaired temporal processing of visual information rather than a primary dysfunction in motion processing. Consistent with this interpretation, Perris (1966) reported significantly lower flicker fusion frequencies in bipolar patients than in normal controls, whether or not the patients were in remission. The lower flicker fusion frequencies suggest that slowed temporal dynamics and poor resolving power of temporally presented signals are associated with bipolar disorder. Miller et al. (2000) showed that bipolar patients are slow to switch from one perceptual state to another during different visual presentations between the two eyes. These studies, combined with our findings, suggest that the processing of dynamic signals is sluggish in patients with bipolar disorder.

A dysfunction in transient mechanisms for handling fast-changing visual information may be a decisive factor in our finding of deficient velocity discrimination of fast motion signals in both bipolar and schizophrenic patients. A related set of findings emerges from studies of backward masking (Green et al., 1994; Butler et al., 2001). Green et al. (1994) showed that the backward mask was effective for a significantly longer period in both schizophrenic and manic patients than in normal control subjects. Butler et al. (2001) reported that the amplitudes of the visual evoked potential responses in schizophrenia were reduced to a greater extent in the presence of stimuli biased toward the magnocellular pathway, which processes transient visual information. These studies support the view that the transient channel at the early stage of visual processing is impaired in schizophrenia and bipolar disorder. Our finding of impaired visual discrimination of fast motion stimuli in bipolar and schizophrenia patients is consistent with the growing evidence implicating deficient temporal processing of visual information in the two disorders.

The roles of temporal and motion processes in velocity discrimination are only partially separable because the velocity range in which the two processes operate may overlap to some extent. Thus, a velocity discrimination deficit at intermediate velocities reflects primarily, but not exclusively, motion processing, whereas a velocity discrimination deficit at fast velocities reflects primarily, but not exclusively, temporal processing. One way to distinguish between the contributions of motion and temporal processing to elevated velocity discrimination thresholds at fast velocities would be to examine temporal frequency discrimination and velocity discrimination in the same individuals. If temporal processing is deficient, temporal frequency discrimination thresholds at fast velocities should be increased. On the other hand, if motion processing is deficient but temporal processing is intact, temporal frequency discrimination thresholds at fast velocities should be normal.

3.3. Contrast detection

We chose contrast detection as a control task for two reasons. First, processing of contrast signals in visual stimuli is a precursor for most visual tasks. If contrast detection is compromised, performance of other visual tasks that rely on upstream mechanisms, such as velocity discrimination, is likely to be affected also. On the other hand, if contrast detection is

normal, any abnormality identified in other visual tasks could not be attributed to early stages of visual processing. Second, the contrast detection and the velocity discrimination tasks used very similar psychophysical paradigms. As a result, the cognitive, motor and attentional requirements were comparable for the two tasks. Performance differences between patients and normal controls in velocity discrimination can therefore be attributed primarily to the perceptual processes associated with velocity discrimination and not to other features of the task.

Contrast detection is modulated by the dopamine system (e.g., Mangel and Dowling, 1985) and typical and atypical antipsychotic drugs have, respectively, strong and moderate antagonistic effects on the dopamine system (Seeman, 2002). In previous studies reporting deficient contrast detection in schizophrenia, many patients were receiving typical antipsychotic drugs, which are likely to reduce contrast sensitivity significantly (e.g., Slaghuis, 1998). Most of the schizophrenic patients in this study (72%) were receiving atypical antipsychotic drugs, however, and their contrast detection performance did not differ from that of the normal controls. We recently showed that schizophrenic patients can have worse-than-normal, normal or even better-than-normal contrast detection, depending on the type of antipsychotic drug treatment or whether they are free of antipsychotic medication (Chen et al., 2003).

3.4. Clinical variables

The bipolar and schizophrenic patients differed in the types and the amounts of medication received and in severity of clinical symptoms. The bipolar patients were taking a lower dose of antipsychotic drugs and had significantly lower BPRS scores than the schizophrenic patients. Medication effects and clinical state are unlikely explanations for the increased velocity discrimination thresholds of the bipolar patients at the fast velocities in that these thresholds were not significantly correlated with dose of antipsychotic drugs or BPRS scores. Velocity discrimination thresholds were also not significantly correlated with dose of antipsychotic drugs in the schizophrenic group, results similar to those we reported in an independent sample (Chen et al., 1999c). Further underscoring the independence of deficient performance from medication effects or symptom severity, velocity discrimination is deficient in a significant proportion of clinically unaffected and never-medicated relatives of schizophrenic patients (Chen et al., 1999c). The isolated finding of a modest but significant correlation between severity of clinical symptoms and velocity discrimination threshold at the slowest target velocity only is difficult to interpret in that clinical state did not have a generalized effect on performance in the schizophrenic group.

The present study shows that the motion-processing deficit seen in schizophrenia is not associated with bipolar disorder. It remains unclear whether and how the impaired visual processing of fast velocities seen in bipolar and schizophrenic patients is related to smooth pursuit performance. One way to delineate the nature and effect of the visual deficit would be to examine smooth pursuit eye movements as a function of target velocities that include a range of fast motion, where temporal processing of visual information is required.

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Fig. 1.
Schematic illustration of velocity discrimination and contrast detection tasks.

Fig. 2.

Mean velocity discrimination thresholds of bipolar patients (BP, gray circles), schizophrenic patients (SZ, black circles) and normal controls (NC, open circles). The abscissa presents the range of base velocities. The ordinate, a logarithmic scale, is expressed as the Weber fraction ($\Delta V/V$, or the just-noticeable difference between the velocities of the targets to be compared) and represents the mean velocity discrimination threshold values of the groups. The error bars correspond to ± 1 standard error of the mean threshold. Sample sizes per target velocity are as follows: BP: $n=16$ for 3.8, 10.0, and 26.6°/s; $n=14$ for 6.2 and 16.2°/s; SZ: $n=21$ for 3.8°/s; $n=17$ for 6.2°/s, $n=25$ for 10.0°/s; $n=16$ for 16.2°/s, and $n=20$ for 26.6°/s; NC: $n=24$ for 3.8, 10, and 26.6°/s; $n=21$ for 6.2 and 16.2°/s.

Fig. 3. Scatter plot of individual subjects' thresholds at the slowest (3.8°/s), the middle (10.0°/s) and the fastest (26.6°/s) velocities. Data from bipolar patients, normal controls and schizophrenic patients are represented by gray, white and black symbols, respectively.

Table 1

Demographic information on participants

Group	Age(year) ¹	Sex ²	SES ³	Education(year) ¹
Bipolar patients(n=16)	37.3 (10.6)	9 f, 7 m	I — 38.9% II — 44.4% III — 16.7%	15.5(2.2)
Schizophrenic patient (n=25)	38.2 (8.3)	13 f, 12 m	I — 7.7% II — 34.6% III — 38.5%	14.0(1.5)
Normal controls(n=25)	40.7 (12.4)	19 f, 6 m	IV — 11.5% V — 7.7% I — 25.9% II — 59.3% III — 14.8%	14.6(2.3)

¹ mean (SD).² f=female, m=male.³ SES — socio-economic status, based on the Hollingshead Two-factor Index (Hollingshead, 1965).

Table 2
Perceptual thresholds: group mean (standard deviation)

Task	Velocity discrimination					Contrast detection
Velocity (°/s) Subject group	3.8	6.2	10.0	16.2	26.6	10.0
Bipolar (<i>n</i> =16)	0.368 (0.212)	0.222 (0.082)	0.157 (0.081)	0.214 (0.007)	0.240 (0.257)	0.0027 (0.0017)
Schizophrenic (<i>n</i> =25)	0.559 (0.273)	0.679 (0.204)	0.397 (0.267)	0.267 (0.275)	0.291 (0.143)	0.0036 (0.0020)
Normal (<i>n</i> =25)	0.339 (0.126)	0.271 (0.113)	0.236 (0.124)	0.152 (0.076)	0.165 (0.065)	0.0039 (0.0027)