Eye Gaze Processing in Schizophrenia

by

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ANOVA	Analysis of variance
BACS	Brief Assessment of Cognition in Schizophrenia
CNTRICS	Cognitive Neuroscience Treatment Research to Improve Cognition in Schizophrenia consortium
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th Edition
ERP	Event-related brain potentials
HC	Healthy controls
MATRICS	Measurement and Treatment Research to Improve Cognition in Schizophrenia committee
MSCEIT	Mayer-Salovey-Caruso Emotional Intelligence Test
PCA	Principal component analysis
RT	Reaction time
SANS	Scale of Assessment of Negative Symptoms
SAPS	Scale of Assessment of Positive Symptoms
SCID-I	Structured Clinical Interview for DSM-IV Axis-I Disorders
SCZ	Schizophrenia

CHAPTER I

Overview

Schizophrenia is a severe mental disorder that often runs a chronic course and affects 1% of the population (i.e., 3.5 million Americans). The overall cost incurred by schizophrenia in the U.S. was estimated to be $62.7 billion in 2002 (Wu et al., 2005). Unemployment and disabilities caused by the disorder, rather than excessive health care, accounted for the largest component ($32.4 billion). Much of the difficulty people with schizophrenia have with employment and community functioning is related to their deficits in social cognition (Couture, Penn, & Robert, 2006). Therefore, if treatment and rehabilitation programs would focus on social cognition in schizophrenia, there would be the potential for much reduced suffering and increased productivity and quality of life in individuals with schizophrenia. The development of effective interventions to address social cognition in schizophrenia would require more knowledge of the nature of social cognitive dysfunction in the disorder.

This dissertation focuses on self-referential social information processing in schizophrenia. Accurately perceiving and interpreting self-referential social cues constitute a critical component of social cognition and is crucial to social adaption. Deficits in processing self-referential social information may be particularly relevant to the psychopathologies of schizophrenia symptoms. For example, misinterpreting benign, irrelevant social signals as threatening and self-relevant (e.g., "They are watching me,") may result in paranoid delusions. Patients who have difficulty interpreting self-referential social signals may as a result withdraw from social interactions. Given the important role of self-referential information processing in social adaptation and its potential relationship with clinical symptoms of schizophrenia, insight into self-referential information processing in schizophrenia may inform the disease process and direct future diagnostic, treatment, and prevention strategies.

Among all forms of self-referential social signals, gaze direction is a powerful way to convey attention and intention in primates and human (Emery, 2000). Few studies have examined gaze perception in schizophrenia and the findings have been inconsistent. Hooker and Park (2005) and Rosse et al. (1994) found that schizophrenia patients are more likely than healthy controls to perceive averted gaze as looking at them, whereas Franck et al. (1998, 2002) and Kohler et al. (2008) have found no group differences in gaze discrimination. These conflicting results are likely due to the wide methodological variations across studies, and some of these studies are limited by the small number of trials and non-optimal statistical procedure. It remains unclear whether individuals with schizophrenia have abnormal gaze perception. Data on the relationship between gaze perception and clinical and functional variables are also lacking.

Study 1 (Chapter II) of this dissertation clarified whether individuals with schizophrenia have abnormal gaze perception, and how abnormal gaze processing is related to clinical symptoms and socio-emotional functioning in the disorder. Face stimuli that cover a full range of gaze directions (from direct to averted gaze with gradual increments) were used. This allowed better understanding of the nature of gaze perception via the use of psychophysics method to estimate the strength of signal needed to perceive eye contact and if perception of self-referential vs. non-self-referential is a clear-cut dichotomy in schizophrenia. Two factors with documented effects on normal gaze perception, head orientation and emotion, were also manipulated and examined. Specially, head orientation is the "default" cue of direction of attention (Emery, 2000) and it interferes with gaze discrimination when presented as incongruent direction of gaze (Langton, 2000; Seyama & Nagayama, 2005). Inclusion of both forward and averted head orientations would enable the examination of how the context of head orientation influences gaze perception in schizophrenia. Facial emotion reveals information about one's mental state, and has been shown to display a motivational congruency effect on gaze perception, such that approach-oriented expressions (e.g., angry) facilitate the perception of direct gaze while avoidance-oriented emotions (e.g., fearful) facilitates the perception of averted gaze, and vice versa (Adams & Kleck, 2005; Graham & LaBar, 2007; Tipples, 2006). Individuals with schizophrenia have been shown to have heightened sensitivity to threat-related emotions (Kring & Neale, 1996), and such sensitivity may be related to core schizophrenic symptoms such as paranoid delusions, thus the effect of a threat-related emotion on gaze perception was examined. Due to the consideration of participant fatigue, only one threat-related emotion was included in addition to neutral faces in order to limit the number of trials in the experiment to a reasonable amount. From clinical observations, patients often describe feelings of threat or hostile intentions from the environment rather than from specific individuals. Because seeing fearful emotion with averted gaze in others is an important signal of danger in the environment, fearful faces were selected in favor of angry faces as the threat-related emotion.

Kohler et al. (2008) reported altered brain activation patterns in patients with schizophrenia even though they were as accurate as healthy controls, highlighting the possibility that same behavioral responses may be produced through different neural mechanisms. Likewise, more errors and slower reaction time (which are often observed in schizophrenia) may be due to a number of psychological processes (e.g., difficulty encoding stimuli, paying attention, selecting responses). Study 2 (Chapter III) of this dissertation sought to further understand the characteristics of gaze perception in schizophrenia at the neural level. Neural activity during gaze discrimination was measured using event-related brain potentials (ERP), which reveal the multiple psychological processes manifested within a very brief period of time. Attention was focused on two psychological processes of particular relevance to gaze perception: face structural encoding (indexed by N170) and assignment of significance (indexed by P300).

Finally, given that basic visual perceptual functions are frequently disrupted in schizophrenia (Butler, Silverstein, & Dakin, 2008), it is reasonable to ask whether abnormal gaze perception in schizophrenia may be adequately explained by basic perceptual difficulties. There is limited work conducted on the relationship between basic visual perception and social cognition in schizophrenia. Study 3 (Chapter IV) of this dissertation attempted to address this issue by assessing a basic visual perceptual function: *integration* (i.e., the ability to integrate individually coded local attributes of a scene into a global complex structure) and its role in gaze perception and broader socio-emotional functioning in schizophrenia.

The specific aims of this dissertation are as follows:

Study 1). To determine whether patients with schizophrenia (SCZ) have abnormal eye-contact perception using a gaze perception task. It was hypothesized that SCZ would overperceive eye contact and show decreased dichotomous gaze (i.e., more ambiguity) compared with healthy controls (HC). These abnormalities were expected to be correlated with severity of clinical symptoms and broader socio-emotional functioning.

Study 2). To delineate the neural correlates of gaze perception in schizophrenia by measuring event-related brain potentials (ERP) during a gaze discrimination task. It was hypothesized that SCZ would show deficits in facial stimulus encoding (as indexed by the N170 wave) and aberrant enhancement of self-referential perception (as indexed by the P300 wave).

Study 3). To examine the role of basic visual perception in gaze perception in schizophrenia. SCZ participants were hypothesized to show poorer performance than HC on two basic visual perception tasks measuring visual integration, and the group differences in gaze perception and socio-emotional functioning were expected to diminish after controlling for visual integration function, thus supporting the role of basic visual perception in higher-level social cognition in schizophrenia.

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CHAPTER II

Study 1. Eye-Contact Perception in Schizophrenia: Relationship with Symptoms and Socio-emotional Functioning[1]

Schizophrenia is a severe mental disorder often accompanied by marked deficits in social cognition that significantly compromise social functioning (see Couture, Penn, & Robert, 2006 for a review). Accurately perceiving and interpreting social cues, particularly self-referential ones, constitute a critical component of social cognition and is crucial to social adaption. Deficits in processing self-referential social information may be particularly relevant to schizophrenic symptoms. For example, misinterpreting benign, irrelevant social signals as threatening and self-relevant (e.g., "They are watching me") may be related to paranoid delusions. Patients who have difficulty interpreting self-referential social signals may withdraw from social interactions. Given the important role of self-referential information processing in social adaptation and its potential relationship with clinical symptoms in schizophrenia, insight into self-referential information processing in schizophrenia may inform the disease process and direct future diagnostic, treatment, and prevention strategies.

Among all forms of self-referential social signals, gaze direction is one of the most powerful ways to convey attention and intention in humans (Emery, 2000). It remains unclear whether gaze perception is impaired in schizophrenia. The present study aimed to clarify whether individuals with schizophrenia exhibit abnormal gaze perception and to elucidate the relationships between gaze perception and clinical variables.

Gaze Perception in Schizophrenia

To the best of our knowledge, only five studies have directly addressed the question whether gaze direction discrimination is impaired in schizophrenia and the findings have been conflicting. Two studies (Hooker & Park, 2006; Rosse, Kendrick, Wyatt, & Isaac, 1994) found that individuals with schizophrenia (SCZ) are more likely than healthy controls (HC) to perceive averted gaze as looking at them. However, others (Franck et al., 1998, 2002; Kohler et al., 2008) have reported no group differences in gaze discrimination. These inconsistent findings are likely due to the wide methodological variations across studies, summarized in Table 2.1. It appears that SCZ's difficulty with gaze processing relates to making self-referential judgments rather than directional judgments. When asked to determine whether gaze was looking left or right, SCZ performed comparably to HC (Franck et al., 1998, 2002), suggesting that the basic perceptual function of discriminating gaze direction is preserved in schizophrenia. However, when the task was put in a self-referential context ("Is this person looking at you?"), SCZ were slower to respond (Franck et al., 2002; Hooker & Park, 2005). In addition, SCZ appeared to show a self-referential bias when faced with ambiguous signals. Studies using mostly averted faces (Rosse et al., 1994) or briefly presented backward-masked faces (Hooker & Parker, 2005) tended to find over-perception of eye contact in SCZ, likely due to the amplified level of ambiguity. When examining group difference at each gaze angle, Hooker and Park (2005) found that SCZ endorsed more eye contact for ambiguous gaze but not clearly direct and averted gaze. As we can see in Table 2.1, the question as to whether gaze perception is related to clinical symptoms remains unclear. The generally assumed that gaze perception is an important determinant of social cognition has also remained unexamined. These together suggest that it would be informative to examine self-referential gaze perception along the whole spectrum of gaze angles and its relationship with clinical and functional outcomes in schizophrenia.

Factors Influencing Normal Gaze Perception

Head Orientation. There is evidence that gaze judgment in healthy individuals is not solely based on gaze direction. Head orientation has been shown to be a particularly influential factor of gaze perception. In primates, including humans, head orientation is helpful in determining the direction of others' attention when gaze direction is obscured (Emery, 2000). However, head orientation also affects perception of *seen* gaze. In particular, congruent gaze-head directions facilitate and incongruent ones interfere with the judgments of both gaze and head directions (Langton, 2000; Seyama & Nagayama, 2005). The effect of averted head orientation is likely due to its being a robust cue of head turn, a strong suggestion of directed-away social attention (Todorović, 2006, 2009). In fact, healthy individuals are more likely to reject direct gaze as looking at them when the head is averted compared to facing forward (Itier et al., 2007).

The effects of gaze direction and head orientation on eye-contact perception in schizophrenia have not been differentiated. However, the finding that SCZ were more likely than HC to make eye-contact judgment when presented with backward-masked ambiguous stimuli (i.e., face outline with no internal facial features) suggests a tendency to accept ambiguous social information as directed to self in schizophrenia (Hooker & Park, 2005). Therefore, when the face is averted, SCZ would be expected to endorse even more eye contact than HC. Since gaze direction and head orientation do not always line up in real life when eye-contact judgments need to be made, examining the interaction between gaze and head direction on eye-contact perception would provide an ecologically valid understanding of gaze perception in schizophrenia.

Emotion. Facial emotion is another powerful modulator of gaze perception, as it reveals information about one's mental state. Experimental studies have demonstrated that facial expression interferes with gaze judgment (Graham & LaBar, 2007; Lobmaier, Tiddeman, & Perrett, 2008). In particular, compared to neutral faces, fearful faces bias people to perceiving averted gaze (Tipples, 2006) and, likewise, averted gaze enhances the perception of fear, likely because averted gaze matches the avoidance-oriented behavioral intent underlying fearful emotion (Adams & Kleck, 2005).

Threat-related emotions are of particular relevance to the study of schizophrenia. Since paranoid delusions involve the false perception of danger in one's environment, gaze information may be processed in a distinctive way when coupled with threat-related emotions. Because seeing fearful emotion with averted gaze in others is an important signal of danger in the environment, studying eye-contact perception in schizophrenia using fearful in addition to neutral face stimuli would allow more comprehensive understanding of perception of self-referential social information in the disorder. On the one hand, an elevated emotion effect in eye-contact perception may be expected in SCZ for their special sensitivity to negative emotions, as suggested by their heightened emotional response to daily stressors and negative life events (Myin-Germeys et al., 2003) and elevated neural response to threat-related images (Taylor, Phan, Britton, & Liberzon, 2005). This entails an expectation that SCZ show a stronger bias than HC to perceive gaze as averted (i.e., endorse eye contact less frequently) for fearful faces relative to neutral faces. On the other hand, a reduced emotion effect may be expected as SCZ have been shown to experience increased aversion to neutral stimuli (Cohen & Minor, 2010) and exhibit reduced emotion modulation of face encoding (Lynn & Salisbury, 2008) compared to HC. Empirical data are needed to demonstrate what effect threat-related emotions have on eye-contact perception in schizophrenia.

The Present Study

To address whether individuals with schizophrenia show abnormal eye-contact perception, this study used a psychophysical approach to examine eye-contact perception as a function of eye-contact signal strength. Face stimuli that cover the full range of gaze directions, from averted to direct gaze, with gradual increments, were used. A relatively large number of trials (12) for each gaze direction were used to ensure reliable measures. Gaze at these different averted angles then represents a full spectrum of "eye-contact signal strength" that ranged from 0 (averted gaze) to 1.0 (direct gaze). Participants made yes-no responses to the question "Looking at me?" for each face. The faces were presented in a pseudo-random order, so that the chance of direct or averted gaze in each trial was unpredictable, avoiding bias due to anticipation. Although the majority of the responses would be "no," this bias to respond "no" induced by the experiment structure was equal across individuals, thus not affecting the comparisons between individuals or diagnosis groups.

Since the self-referential nature of gaze is putatively dichotomous, the percentage of "yes" responses along the continuum of eye-contact signal strength was theorized to resemble a logistic function. Two particular psychophysical properties were estimated using this logistic response function: thresholds and rate of change of categorical shift. In psychophysics, "threshold" refers to the signal strength corresponding to "yes" responses at a certain frequency. For example, sensory threshold and absolute threshold, two frequently used thresholds, are the signal strength where "yes" responses are given 75% and 50% of the time, respectively. Response cutoff values other than 50% and 75% may also be used. For instance, Hooker and Park (2005) chose a response cutoff of 30% because it was the base rate of "yes" responses in their study. In this study, multiple response cutoffs (ranging from 10% to 90%) were used to obtain multiple thresholds, in order to compare with results of previous studies (Franck et al., 2002; Hooker & Park, 2005) and explore the threshold that most effectively discriminates between SCZ and HC. It is important to note that for this eye-contact perception paradigm, unlike sensory detection paradigms, "yes" is not necessarily the correct response. Therefore, lower thresholds (i.e., perceiving eye contact with weaker signal) are not necessarily better than higher thresholds and, in fact, likely to be problematic. Further, rapid changes from non-self-referential to self-referential gaze perception indicates more clearly dichotomous perception (i.e., from "no" to "yes") whereas gradual changes indicate more uncertainty in deciding the self-referential nature of gaze. Therefore, the rate of change of categorical shift, defined as the slope of the response function where "yes" responses are given 50% of the time, was measured. In addition to varying gaze direction, the face stimuli in this study also varied in head orientation and facial emotion so that their effects on eye-contact perception in schizophrenia could be examined.

Hypotheses

1) SCZ would show a positive bias and experience more uncertainty than HC in eye-contact perception. This entails predictions that: a) SCZ would endorse eye contact more often than HC, especially for ambiguous gaze (i.e., medium eye-contact signal strengths); b) SCZ would show lower eye-contact perception thresholds than HC; c) SCZ would show decreased rate of change of categorical shift relative to HC; d) SCZ's positive bias would be accentuated for averted relative to forward head orientation.
2) Abnormalities in gaze perception (over-perception of eye contact, decreased categorical perception) in SCZ would be associated with higher symptom severity and poorer socio-emotional functioning.

Method

Participants

SCZ were volunteers aged 18 to 60 meeting DSM-IV criteria for schizophrenia or schizoaffective disorder. They were recruited through advertisements in the community and referrals by clinicians of local community mental health clinics or clinical researchers of the University of Michigan. Exclusion criteria for SCZ included: unable to give informed consent, have other active Axis-I disorders (except anxiety and depressive disorders), and a history of alcohol or substance abuse/dependence in the past 6 months. HC were recruited from advertisements in the community and referrals by other researchers. Exclusion criteria for HC included: lifetime Axis-I disorders, and history of psychosis and bipolar disorder among first-degree relatives. Each participant had at least 20/30 vision according to a Snelling chart. Written informed consent was obtained from each participant after complete description of the study was given.

The participants of this study also participated in another experiment examining basic visual perception; 22 SCZ and 22 HC of this study participated in an event-related potential (ERP) experiment on gaze discrimination. Since these experiments are out of the scope of this paper, the results are not included in this report and will be reported elsewhere.

Assessments

Clinical diagnoses were established or ruled out using the Structured Clinical Interview for DSM-IV (SCID; First et al., 1995) by a trained graduate student in clinical psychology, with 80% of the cases confirmed by consensus of another trained graduate student. SCZ were assessed for positive symptoms using the Scale for Assessment of Positive Symptoms (SAPS; Andreasen, 1984) and negative symptoms with the Scale for Assessment of Negative Symptoms (SANS; Andreasen, 1983). Inter-rater reliability as indexed by concordance correlation for these clinical ratings is displayed in Table 3.

All participants completed the Brief Assessment of Cognition for Schizophrenia (BACS; Keefe et al., 2004) and the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT; Mayer, Salovey, & Caruso, 1999). The BACS and the MSCEIT are the performance-based measures of neurocognition and emotion-related social cognitive skills, respectively, recommended by the National Institute of Mental Health (NIMH)

Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) committee (Green, Olivier, Crawley, Penn, & Silverstein, 2005).

Experimental Material and Task

Face materials for the Eye-Contact Perception Task were adopted from Gur et al. (2002). Black-and-white pictures of six actors in forward and 30º averted head orientation in neutral and evoked-fearful emotion were extracted from the original pool of 3-dimensional images for editing. Since all original faces were looking straight ahead, Photoshop was used to edit the iris area to create direct gaze for faces in averted head orientation and averted gaze for faces in forward head orientation. Then, morphing software was used to create varying gaze direction, from averted (0 eye-contact signal strength) to direct (1.0 eye-contact signal strength) with ten 10% increments (see Figure 2.1 for illustration). A total of 528 faces were produced and used for the experiment: 12 trials (6 actors × 2 mirror images) for each of the 11 eye-contact signal strengths in each of the four combinations of head orientation (forward, averted) and emotion (neutral, fearful).

The Eye-Contact Perception Task was presented using the software E-prime 1.0. The faces were presented in a pseudo-randomized order such that no consecutive trials were faces of the same actor (in order to avoid potential illusory eye motion). Participants were required to press a button to indicate if they feel that the person is "looking at me" and another button to indicate "looking away." To reduce variance introduced by time pressure in SCZ, a population known to have slower reactions and more vulnerable to psychological stress (Docherty & Hebert, 1997; Tso, Grove, & Taylor, in press), the task imposed no time constraint for response. The task typically took 10-15 minutes to complete. Button pressing was counter-balanced across participants.

Statistical Analyses

The data were first analyzed using a psychophysical approach (see Figure 2.2 for illustration). For each participant, his/her data (percentage of “yes, looking at me” responses against eye-contact signal strength) were fitted in a logistic function:

$$P = 1/(1 + c \cdot b^{x}) \, . \qquad (1)$$

where P is the percentage of “looking at me” responses, x is eye-contact signal strength, and c and b are constant parameters provided by the PASW Statistics 18 Curve Estimation (logistic) function. Nine thresholds of eye-contact perception were obtained using response cutoffs from 10% to 90%, calculated by finding the expected x values for P = 10%, 20%, …, 90%. The rate of change of the categorical shift was defined as the slope of *Equation 1* at P = 50%. This was estimated using the first derivative of *Equation 1*:

$$\mathrm{d}P/\mathrm{d}x = \{-\ln(\mathrm{b}) \cdot e^{[-\ln(\mathrm{c}) - \ln(\mathrm{b}) \cdot x]}\}/\{1 + e^{[-\ln(\mathrm{c}) - \ln(\mathrm{b}) \cdot x]}\}^{2} \, . \qquad (2)$$

where e is exponential function. Since $x = -\ln(c)/\ln(b)$ when P = 50%, *Equation 2* becomes: $\mathrm{d}P/\mathrm{d}x = -\ln(b)/4$. Note that while most of the participants’ data for forward faces fit well into a logistic function and fitting in terms of R^2 did not differ between SCZ (M = 0.80, SD = 0.08) and HC (M = 0.82, SD = 0.08), $F(1, 47) = 1.11$, $p = .298$, responses to averted faces did not approach logistic functions. As a result, this part of analyses was performed for forward faces only. Threshold of eye-contact perception was subject to a 9 (response cutoffs) × 2 (emotions) × 2 (groups) mixed model ANOVA;

slope of categorical shift was analyzed using a 2 (emotions) × 2 (groups) mixed model ANOVA.

In order to include the data on averted faces in the analysis, a mixed model 4-way ANOVA was performed, with eye-contact signal strength (Gaze: 0, 0.1, …, 1.0), head orientation, and emotion as within-subjects variables, group as between-subjects factor, and percentage of "looking at me" responses as dependent variable. Huynh-Feldt adjustment was used for all ANOVAs in case of violation of the sphericity assumption.

Relationships between eye-contact perception measures and clinical/functional variables were examined using Pearson's correlations and multiple regressions. Due to the very limited variance on the SAPS Bizzare Behavior and Inappropriate Affect subscales, these two subscores were excluded from the correlation analyses. Pairwise correlations were visually inspected for violations of assumptions and outliers, and cases with Cook's Distance > 4/*n* (Bollen & Jackman, 1990) were subject to further investigations. All statistical analyses were performed using PASW Statistics 18.

Results

Participant Characteristics

Twenty-eight SCZ and 24 HC completed the task. Data of one SCZ and one HC were discarded as their responses approached chance level and were therefore deemed unreliable. Data of another SCZ participant were loss due to corruption of the electronic data file. The remaining 26 SCZ and 23 HC participants, whose data were used in subsequent analyses, were well matched for age, sex, and parental education. As expected, SCZ had poorer socio-emotional functioning than HC as suggested by their lower MSCEIT scores. See Table 2.2 for details of participant characteristics.

Abnormal Eye-Contact Perception in Schizophrenia

Over-perception of eye contact. Eye-contact perception thresholds of SCZ and HC obtained using different response cutoffs are presented in Figure 2.3. SCZ's mean threshold across response cutoffs ($M = 0.63$, $SD = 0.18$) was only marginally lower than HC's ($M = 0.73$, $SD = 0.18$), $F(1, 47) = 3.73$, $p = .059$. However, the Cutoff Value × Group interaction, $F(1.02, 48.02) = 5.49$, $p = .023$, indicated that SCZ showed significantly lower threshold than HC when threshold was obtained using a response cutoff of 60% or lower. This Cutoff Value × Group interaction did not vary by emotion, $F(1.02, 48.03) = 0.92$, $p = .345$. These together suggested that SCZ began endorsing eye contact earlier along the continuum of eye-contact signal strength.

Response patterns of SCZ and HC in each of the four head/emotion conditions are presented in Figure 2.4. Overall, SCZ ($M = 33\%$, $SD = 12\%$) were more likely than HC ($M = 23\%$, $SD = 12\%$) to perceive gaze as looking at them, $F(1, 47) = 7.93$, $p = .007$. Further, group differences along the signal strength spectrum varied by head orientation and emotion, as indicated by the significant Gaze × Head × Group interaction, $F(4.73, 222.29) = 4.36$, $p = .001$ (Figure 2.5 a) and Gaze × Emotion × Group interaction, $F(4.73, 222.29) = 2.08$, $p = .040$ (Figure 2.5 b).

Decreased categorical perception. SCZ ($M = 2.48$, $SD = 0.63$) showed reduced slope of categorical shift compared to HC ($M = 2.87$, $SD = 0.63$), $F(1, 47) = 4.64$, $p = .036$. The group difference was constant across emotions, $F(1, 47) = 0.05$, $p = .830$, although categorical shift occurred more rapidly for neutral (M = 2.79, SD = 0.75) than fearful faces (M = 2.56, SD = 0.62), $F(1, 47) = 8.71$, $p = .005$.

Relationship with Clinical and Functional Variables

Correlations between eye-contact perception measures and clinical and functional variables among SCZ participants are summarized in Table 2.3. In general, eye-contact perception was not associated with antipsychotic dose and SAPS. SANS was associated with higher percentages of "yes" responses and lower thresholds. Over-perception of eye contact (i.e., increased percentage of "yes" response for low/medium but not high signal strengths, and decreased thresholds obtained using low/medium but not high response cutoffs) was significantly correlated with lower BACS and MSCEIT scores. Higher slope of categorical shift was correlated with better MSCEIT.

To make sure that the relationship between eye-contact perception and MSCEIT was not solely driven by general deficits in schizophrenia, regression analyses using a model comparison approach were performed to isolate the effects of eye-contact perception variables from that of BACS on MSCEIT. The slope of categorical shift was the only eye-contact perception variable that explained significantly more variance of MSCEIT *in addition to* BACS (Table 2.4).

Among HC, slope of categorical shift, but not other eye-contact perception variables, was also correlated with MSCEIT ($r = .51$, $p = .026$). Group membership (SCZ, HC) significantly predicted MSCEIT ($r = .40$, $p = .013$), but this correlation became non-significant after the effect of slope of categorical shift was partialled out ($r_p = .20$, $p = .229$), suggesting that lower MSCEIT scores in SCZ could be largely accounted for by their reduced categorical function in eye-contact perception. Figure 2.6 illustrates that the linear relationship between MSCEIT and slope of categorical shift was comparable between SCZ and HC.

Discussion

This study examined whether individuals with schizophrenia have abnormal perception of self-referential gaze, what factors influence this perception, and its relationship with clinical symptoms and socio-emotional functioning. The results supported our hypotheses that SCZ are more likely than HC to perceive gaze as directed to them and experience more ambiguity as operationalized by reduced categorical perception compared to HC. In addition to gaze direction, both head orientation and emotion of the face stimuli were shown to be influential factors of eye-contact perception in schizophrenia. Furthermore, abnormalities in eye-contact perception (over-perception of eye contact and reduced categorical perception) were significantly associated with more severe negative symptoms, poorer neurocognition, and lower emotional intelligence in schizophrenia, supporting the relevance of gaze perception to clinical and functional outcomes in the disorder.

Nature of Abnormalities in Eye-contact Perception in Schizophrenia

A positive bias in eye-contact perception in schizophrenia was shown by the results of lower thresholds and higher rate of eye-contact endorsement in SCZ compared to HC. The eye-contact threshold gap between SCZ and HC was maximal at the lowest response cutoffs and gradually disappeared as response cutoff went up, suggesting that eye-contact perception in schizophrenia is characterized by an earlier readiness (in the gaze direction spectrum) to contemplate that gaze may be directed to self. This finding helps explain the discrepancy between the findings from Hooker & Park (2005) and Franck et al. (2002), where the former found a significant difference in eye-contact perception threshold between SCZ and HC using a lower response cutoff and the latter found no group difference using a higher cutoff. Examination of the group differences in percentage of "yes" responses along the continuum of gaze directions revealed that SCZ's difficulty is most prominent when gaze direction is ambiguous. For forward faces, SCZ showed the strongest positive bias when the eye-contact signal strength was medium (i.e., gaze direction was ambiguous), consistent with Hooker and Park's (2005) finding. It should be emphasized that SCZ's performance was indistinguishable from HC's when signal strength was strong (i.e., direct gaze), suggesting that their difficulty with eye-contact perception was specific to ambiguous gaze and is unlikely due to a general deficit problem. For averted faces, however, SCZ showed most elevated eye-contact perception for strongest eye-contact signal strengths. This was due to HC's low eye-contact endorsement rate (< 50% of the time) for direct gaze in averted head orientation. While this low endorsement rate may be reflecting a combined effect of people's general poorer ability to detect direct gaze from averted faces (Itier et al., 2007; Rosse et al., 1994) and the imperfect face stimuli used in this study (see below for further discussion), at the same time this suggests that HC perceived the presumably direct gaze as ambiguous. Then, the results for averted faced once again showed that over-perception of eye contact in SCZ is most prominent when gaze direction is ambiguous.

Together with the finding that SCZ's eye-contact perception was less dichotomous than HC's, this study showed that individuals with schizophrenia experience more uncertainty when determining the self-referential nature of gaze and a self-directed bias is activated when gaze is ambiguous. Previous studies have shown that SCZ have a tendency to blame others for negative events (Janssen et al., 2006). This study further showed that this externalizing bias applies to the perception of ambiguous social signals without direct consequences. This attributional bias and the observed uncertainty in gaze perception may be reflecting the failure to recruit critical brain regions (e.g., paracingulate cortex, temporo-parietal junctions) in tasks involving theory of mind (i.e., attribution of intention to others) in schizophrenia (Walter et al., 2009). While neurobiological interventions targeting these brain functions are yet to be developed and tested (Green & Horan, 2010), results of studies using psychosocial interventions to improve social cognition in schizophrenia have been encouraging (Horan et al., 2009; Horan, Kern, Green, & Penn, 2008; Roberts & Penn, 2009). The modifiability of social cognition in the disorder through psychosocial methods lends support to the development of training targeting at perception and interpretation of ambiguous social signals.

Modulation of eye-contact perception by fearful emotion was reduced in schizophrenia. The largest group difference in eye contact endorsement rate for neutral faces occurred when eye-contact signal was medium, whereas the largest group difference for fearful faces occurred later in the spectrum of signal strength. This was because HC endorsed eye contact less frequently for direct gaze shown in fearful compared to neutral faces (consistent with previous reports of a bias to perceive averted gaze from fearful faces: Adam & Kleck, 2005; Tipples, 2006), while SCZ's eye-contact perception was affected in the same direction but to a lesser extent. The reduced modulation by fearful emotion among SCZ may be related to the tendency to experience elevated negative emotional responses to neutral faces in schizophrenia as discussed earlier (Cohen & Minor, 2010). Examining the interaction between subjective emotional response and processing of self-referential social information in future studies would inform the underpinning of this reduced emotion (at least fearful) modulation. Moreover, given that disruptions in basic visual perception have been frequently reported in schizophrenia, it is reasonable to ask and address in future studies the question as to whether abnormal gaze perception in schizophrenia is related to deficits in basic visual perception (*cf.* Sergi & Green, 2003).

Relationships with Symptoms and Socio-emotional Functioning

The present study showed that negative symptoms, particularly avolition/amotivation, were associated with a self-referential bias in gaze perception (more "yes' responses and lower thresholds). This finding was unlikely caused by artifacts such as slower response and lower motivation. The task had no time limit and thus the observed positive bias could not be attributed to mistakes due to time out. More importantly, those who are less motivated to do well on the task would make equally more mistakes along the continuum of eye-contact signal strength (i.e., endorse eye contact more frequently for low and medium signal strengths but less frequently for high signal strengths), but this was not the case. The connection between negative symptoms and a self-referential bias may seem counter-intuitive, but as noted in qualitative work exploring the subjective dimension of negative symptoms, patients with schizophrenia describe an increased self-awareness and constant perplexity about the relations between self and the external world, which often result in motor slowing and social withdrawal (Sass & Parnas, 2003). As such, the self-referential bias observed in negative symptoms may be reflecting one of the aspects of self-disturbances as described in the schizophrenia literature. This is consistent with research data showing deficits in brain regions that are responsible for self-referential processing (e.g., medial prefrontal cortex, anterior cingulated cortex) in schizophrenia (Brunet-Gouet & Decety, 2006) and a common factor underlying negative symptoms and theory-of-mind deficits (Woodward, Mizrahi, Menon, & Christensen, 2009).

The lack of association between positive symptoms, especially paranoid delusions, and self-referential bias in gaze perception deserves some comments. Patients with these symptoms often complain that they *know* that their experiences/thoughts are false, yet they *feel* real to them. Given that research has generally found modest or no correlations between positive symptoms and functional impairment (Harvey et al., 1998; Kurtz, Wexler, Fujimoto, Shagan, & Seltzer, 2008) and that most of the self-referential positive symptoms observed in our sample were mild to moderate, it is plausible that many participants with these symptoms were able to respond to the gaze task intellectually, despite their inconsistent internal feelings. Nevertheless, without substantiating data, this remains a speculation and needs further investigation to verify.

The present study confirmed the widely accepted assumption that eye-contact perception is critical to broader socio-emotional functioning in schizophrenia. Over-perception of eye contact and reduced categorical perception were significant associated with MSCEIT in schizophrenia. Notably, the relationship between reduced categorical eye-contact perception and MSCEIT in SCZ persisted after controlling for basic neurocognition (BACS), suggesting that the relationship could not be completely attributed to a general deficit problem. Also noteworthy was that this relationship was present in comparable strength among HC, suggesting that the importance of clear-cut categorical gaze perception to broader socio-emotional functioning applies to both individuals with and without schizophrenia. In fact, MSCEIT difference between SCZ and HC disappeared after controlling for slope of categorical shift, suggesting that the observed compromised socio-emotional deficits in schizophrenia may lie in the ambiguity in discriminating the self-referential nature of social signals. This is an intriguing finding in that a measure of supposedly high-level socio-emotional reasoning was correlated with a lower-level social cognition (gaze perception). However, if we consider a core ability tapped by the MSCEIT—the ability to efficiently put boundaries between categories of major socio-emotional entities, including perceptual ones such as facial expressions and more abstract ones such as labels of complex emotions, the connection between MSCEIT and categorical gaze perception becomes illuminated. In addition, the MSCEIT Managing Emotion branch, which requires higher reasoning in complex socio-emotional contexts, showed lower correlations with categorical gaze perception compared to other MSCEIT branches, further supporting that efficient mental categorization of socio-emotional concepts is an underlying factor of the connection between MSCEIT and gaze perception. Therefore, it appears that categorical gaze perception may involve processing at the perceptual level as well as, to some degree, the interpretation level.

Limitations

As discussed before, response patterns for forward and averted head orientations were significantly different. Although people are generally less able to detect direct gaze from averted faces (Itier et al., 2007; Rosse et al., 1994), the eye-contact endorsement rate found in this study (~50%) was substantially lower than the commonly observed range (70% - 90%), pointing to the possibility that the editing of the gaze of the original averted faces was not perfectly convincing even though an prior informal in-house validation was performed. Ideally, images should be generated by taking pictures of actors instructed to look at different pre-marked directions in front of a camera. However, it would have been extremely challenging to have actors pose fearful repeatedly for all gaze angles. Whether or not the lack of fit of participants' responses into a logistic function reflects the true nature of eye-contact perception for averted faces remains a topic to be addressed.

Participants with schizophrenia of this study were mostly chronic, medicated patients. Since schizophrenia tends to run a chronic course and most patients with schizophrenia in North America are treated with medications, the results of this study inform eye-contact perception in the typical person with the disorder. Replications in the early and prodromal phases of illness would help evaluate the effects of medications and illness chronicity on eye-contact perception. Comparisons with other psychiatric disorders (e.g., bipolar disorder, autism) would also provide information about the specificity of eye-contact perception deficits to schizophrenia.

Conclusions

The present study showed that individuals with schizophrenia exhibited abnormal eye-contact perception characterized by over-attribution of self-directed intention to ambiguous gaze and more uncertainty when determining the self-referential nature of gaze. These abnormalities are related to more severe negative symptoms and deficits in broader socio-emotional functioning in schizophrenia and warrant further investigations.

Table 2.1

Summary of Methodological Differences and Major Findings of Previous Gaze Perception Studies in Schizophrenia

Study	N	Head angles	Gaze angles	Task(s)	Stimulus presentation	# of trials	Statistical analysis strategy	Major findings	Relationship with symptoms
Franck et al. (1998)	22 SCZ 36 HC	0°	0°, ±15°, ±30°	Looking left/right?	Stimulus: no time limit, until response given	30 trials (6 trials per gaze angle)	Mann-Whitney U-tests to compare group medians of percentage of "left" responses	No group difference for each gaze angle	No group differences between paranoid (*n* = 11) and non-paranoid (*n* = 11) SCZ
Franck et al. (2002)	32 SCZ 32 HC	0°	7 angles from 0° to ±30°	Task 1: Looking left/right Task 2: Looking at me/elsewhere	Stimulus: no time limit, until response given	130 trials per task (10 trials per gaze angle)	Kruskal-Wallis tests to compare group medians of absolute threshold (AT)	No group differences in AT	No group differences in AT between paranoid (*n* = 20) and non-paranoid (*n* = 12) SCZ
Hooker & Park (2005)	15 SCZ 19 HC	0°	0°, ±20°, ±30°, ±40°, ±50°, ±55°	Task 1: Direct gaze? y/n Task 2: Black square centered to white rectangle? y/n	Stimulus: 30 ms Backward mask: 75 ms ISI: 30 ms, 60 ms, 180ms	For each task, 96 trials for gaze angle of 0° and 48 trials for each other gaze angle	ANOVA to test effects of task, gaze angle, ISI, and group on rate of "yes" responses	SCZ endorsed direct gaze more often than HC for gaze angle of ±20°	Performance uncorrelated with demographic and clinical variables
Kohler et al. (2008)	13 SCZ 12 HC	0°, ±4°, ±8°	0°	Looking at me/away?	Stimulus: 1 s ISI: 16 s	8 trials for head angle of 0° and 4 trials for each other head angle	ANOVA to test effects of head angle and group on rate of correct responses	No group differences for each head angle	Not examined
Rosse et al. (1994)	24 SCZ 25 HC	0°, ±2.5°, ±5°, ±10°, ±20°	9 angles for each head angle	Looking directly at me? y/n	Stimulus: no time limit, until response given	40 trials in total	MANCOVA to test group differences in gaze discrimination specificity, sensitivity, and positive bias, controlling for age and education	SCZ showed lower specificity, higher sensitivity and positive bias than HC	Paranoid SCZ (*n* = 12) higher on sensitivity and positive bias than non-paranoid SCZ (*n* = 12)

Note. Gaze angle of 0° means looking straight ahead; Head angle of 0° means facing forward to the viewer.

Table 2.2

Participant Characteristics

Variable	SCZ (n = 26) Range	SCZ (n = 26) Mean ± *SD*	HC (n = 23) Range	HC (n = 23) Mean ± *SD*	t / χ^2	p
Age	19 – 60	43.9 ± 12.5	19 – 59	43.5 ± 13.1	0.11	.913
Sex (male/female)	--	19/7	--	18/5	0.18	.674
Education	10 – 18	13.6 ± 2.0	12 – 21	16.4 ± 2.6	-4.17	< .001
Parental education	4 – 21	14.9 ± 3.8	9 – 20	15.0 ± 2.8	-0.12	.905
BACS	-2.46 – 2.07	-0.96 ± 1.12	- 2.65 – 1.85	0.39 ± 1.02	-4.22	< .001
Duration of illness	1 – 41	24.4 ± 12.8	--	--	--	--
CPZeq (mg daily)	0 – 2000	453 ± 511	--	--	--	--
SAPS	0 – 12	5.4 ± 3.6	--	--	--	--
Hallucinations	0 – 4	1.6 ± 1.6	--	--	--	--
Delusions	0 – 4	2.0 ± 1.6	--	--	--	--
Bizzare Behavior	0 – 2	0.4 ± 0.6	--	--	--	--
Thought Disorder	0 – 3	1.1 ± 1.3	--	--	--	--
Inappropriate Affect	0 – 2	0.4 ± 0.7	--	--	--	--
SANS	0 – 12	4.2 ± 3.1	--	--	--	--
Flat Affect	0 – 4	1.4 ± 1.2	--	--	--	--
Alogia	0 – 3	0.4 ± 0.7	--	--	--	--
Avolition	0 – 3	0.7 ± 0.9	--	--	--	--
Anhedonia	0 – 4	1.8 ± 1.4	--	--	--	--
MSCEIT overall[a]	60.8 – 136.3	91.1 ± 19.3	80.2 – 140.8	106.5 ± 17.4	-2.62	.013
Perceiving Emotions[a]	67.0 – 129.4	93.8 ± 13.6	86.6 – 146.2	109.3 ± 18.5	-3.09	.004
Using Emotions[a]	65.8 – 127.2	96.0 ± 16.5	78.5 – 162.2	110.8 ± 20.3	-2.63	.012
Understanding Emotions[a]	70.5 – 130.5	95.1 ± 17.2	72.4 – 130.8	106.0 ± 15.4	-2.23	.031
Managing Emotions[a]	66.4 – 149.5	89.7 ± 18.9	71.6 – 149.2	102.3 ± 17.6	-2.34	.024

a. Due to missing data, the number of subjects for the MSCEIT scores varied: overall score (20 SCZ, 19 HC); Perceiving Emotions branch (22 SCZ, 19 HC); Using Emotions branch (22 SCZ, 21 HC); Understanding Emotions branch (24 SCZ, 21 HC); and Managing Emotions branch (25 SCZ, 21 HC).
Note. BACS = Brief Assessment of Cognition for Schizophrenia composite score, with reference to normal data of 83 healthy controls (30% female; age = 40.5 ± 11.7; parental education = 16.2 ± 2.6 years) from multiple studies by our research team; CPZeq = Antipsychotic dose in chlorpromazine equivalent; SAPS = Scale for the Assessment of Positive Symptoms; SANS = Scale for the Assessment of Negative Symptoms; MSCEIT = Age- and gender-adjusted scores on the Mayer-Salovey-Caruso Emotional Intelligence Test.

Table 2.3

Correlations between Eye-contact Perception, Clinical and Functional Variables among SCZ

Variable	1.	2.	3.	3a.	3b.	3c.	4.	4a.	4b.	4c.	4d.	5.	6.	6a.	6b.	6c.	6d.
1. CPZeq	--																
2. Duration of illness	.17	--															
3. SAPS total	.00	-.08	(.81)														
3a. SAPS Hallucinations	.10	-.23	.61**	(.89)													
3b. SAPS Delusions	-.15	.11	.79***	.32	(.89)												
3c. SAPS Thought Disorder	.13	.05	.70**	.06	.51**	(.54)											
4. SANS total	-.04	.20	.20	-.08	.26	.27	(.83)										
4a. SANS Flat Affect	.01	.40*	.13	-.24	.21	.30	.75***	(.75)									
4b. SANS Alogia	-.02	.28	.33†	-.01	.36†	.55**	.59**	.41*	(.69)								
4c. SANS Avolition	-.10	.18	.20	-.05	.27	.09	.70***	.27	-.31	(.81)							
4d. SANS Anhedonia	-.01	-.01	.02	.05	.04	-.01	.81***	.42*	-.22	.49*	(.64)						
5. BACS	.07	-.45*	-.02	.30	-.02	-.08	-.07	-.12	-.17	-.31	.24	--					
6. MSCEIT overall	-.11	-.51*	-.10	.34	-.09	-.33	-.15	-.44†	-.01	-.15	.16	.57**	--				
6a. Perceiving Emot	.06	-.28	-.01	.20	.11	-.18	.11	-.21	.17	.05	.32	.39†	.83***	--			
6b. Using Emot	-.12	-.50*	.07	.41†	.11	-.21	-.13	-.46*	.11	-.09	.12	.54**	.78***	.69***	--		
6c. Understanding Emot	.08	-.46*	-.07	.41*	-.16	-.23	-.00	-.19	-.11	-.28	.39†	.68***	.90***	.71***	.60**	--	
6d. Managing Emot	-.30	-.40*	-.34	.22	-.38†	-.45*	-.24	-.43*	-.14	-.25	.07	.52**	.71***	.29	.45*	.64***	--
P("looking at me")																	
At low signal strengths[a]	.06	.34†	-.01	-.17†	-.09	.04	.43*	.19	.12	.58***	.35†	-.51**	-.60**	-.46*	-.55**	-.49*	-.31
At medium signal strengths[a]	-.13	.44*	-.00	-.21*	.09	-.21	.49*	.26	.22	.61***	.34†	-.51**	-.56*	-.40†	-.48*	-.52**	-.27
At high signal strengths[a]	-.28	.33	-.19	-.12	-.02	-.25	.33†	.13	.14	.42*	.28	-.22	-.21	-.30	-.15	-.24	.15
Threshold																	
Using low response cutoffs[b]	.14	-.35†	-.05	.12	-.04	-.05	-.36†	-.16	-.27	-.44*	-.23	.57**	.52*	.44*	.50*	.50*	.20
Using medium response cutoffs[b]	.27	-.36†	-.04	.08	-.11	.01	-.42*	-.20	-.31	-.45*	-.31	.47*	.37	.34	.38†	.40†	.09
Using high response cutoffs[b]	.36†	-.32	-.01	.03	-.16	.07	-.42*	-.20	-.30	-.39†	-.35†	.28	.12	.14	.17	.22	-.06
Slope of categorical shift	-.28	-.09	-.05	.16	.07	-.10	-.04	.01	.14	-.17	.11	.40*	.58**	.36†	.52*	.39†	.50*

a. Low signal strengths: 0 – 0.3; Medium signal strengths: 0.4 – 0.6; High signal strengths: 0.7 – 1.0.
b. Low response cutoffs: 10% - 30%; Medium response cutoffs: 40% – 60%; High response cutoffs: 70% - 90%.
Note. Numbers in parentheses are inter-rater reliability indexes (concordance correlations) for the corresponding clinical scales.
† $p < .10$. * $p < .05$. ** $p < .01$. *** $p < .001$.

Table 2.4

Hierarchical Regression on MSCEIT among SCZ

	Model statistics				Variable statistics		
Model/Predictor	r^2	Δr^2	ΔF	p	β[a]	t	p
Reduced model	.32	.32	8.48	.009			
BACS					.57	2.91	.009
Full model	.48	.16	5.18	.036			
BACS					.28	1.31	.208
Slope of categorical shift					.49	3.34	.036

a. Standardized beta.

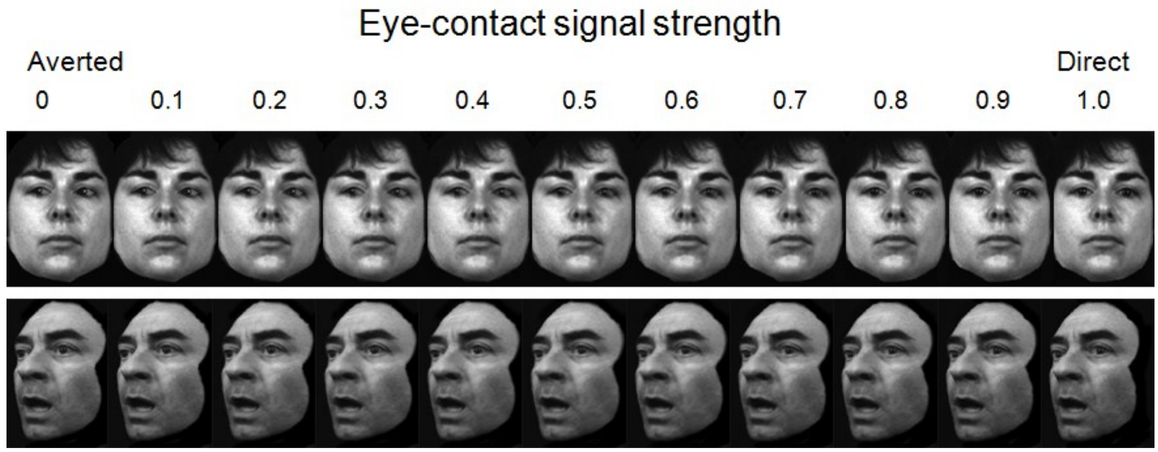

Figure 2.1. Sample face stimuli used in the Eye-Contact Perception Task. Eye-contact signal strength varied from 0 (averted) to 1.0 (direct) in ten 10% increments. The upper panel illustrates face stimuli with forward head orientation and neutral emotion; the lower panel illustrates face stimuli with averted head orientation and fearful emotion.

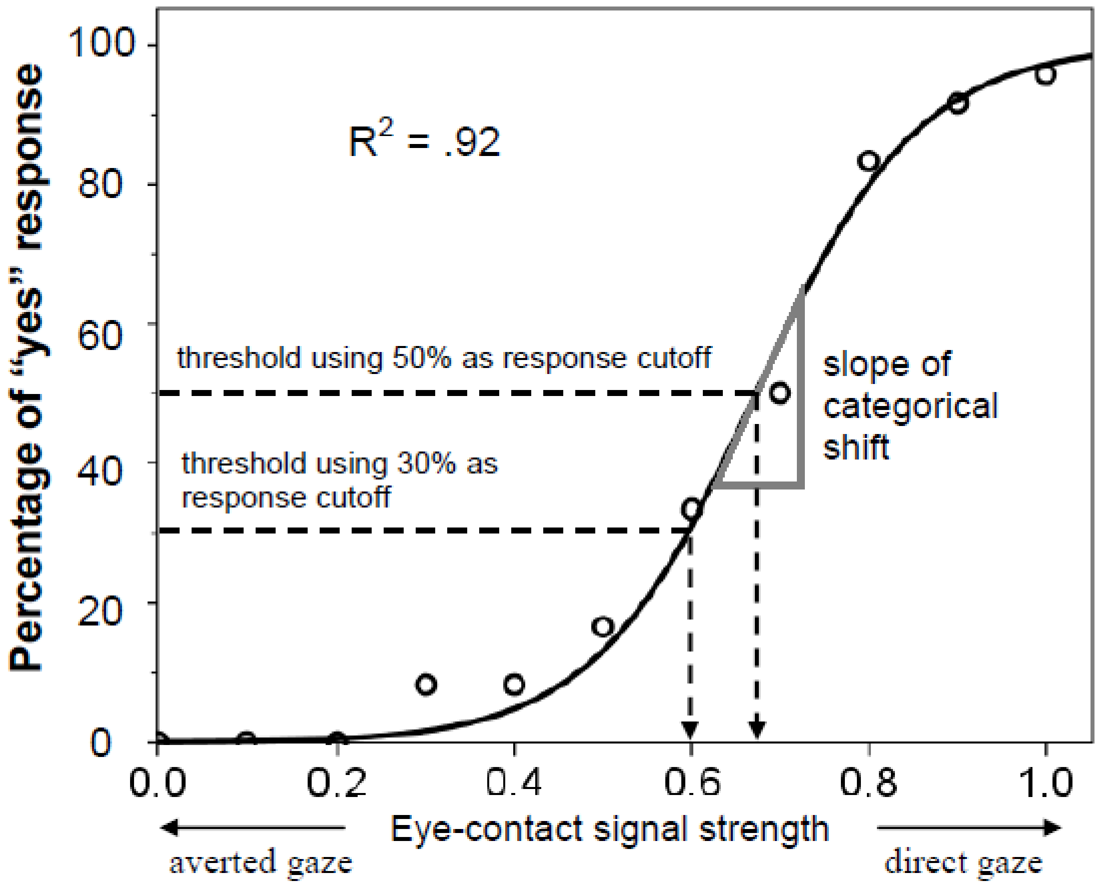

Figure 2.2. An example of the estimation of psychophysical properties of a participant's eye-contact perception. Nine thresholds of eye-contact perception were obtained using response cutoffs from 10% to 90% (shown in graph only thresholds obtained using 30% and 50% response cutoffs). Note that the unit of threshold is the same as eye-contact signal strength, as "threshold" is defined as the signal strength corresponding to certain frequency of "yes" responses. The rate of change of the categorical shift from non-self-referential to self-referential gaze was defined as the slope of the logistic function when percentage of "yes, looking at me" responses = 50% (i.e., when the predominant response changes from "no" to "yes").

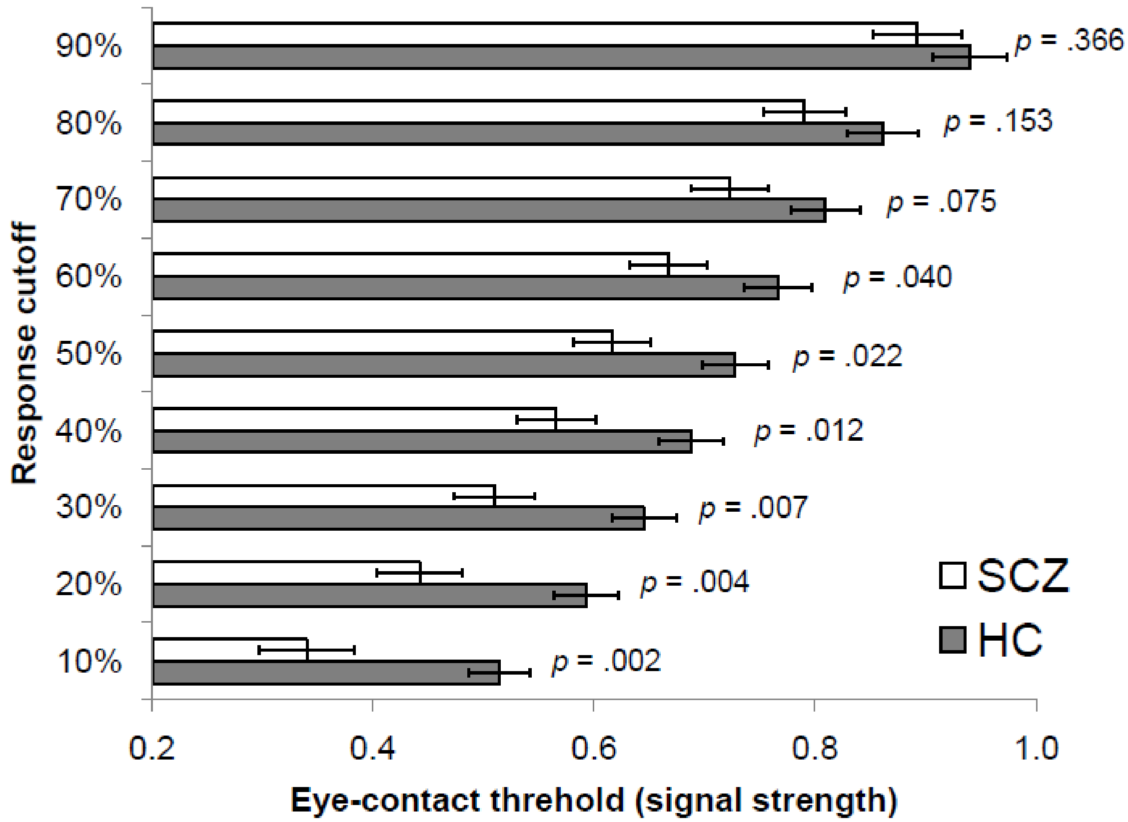

Figure 2.3. Group difference in eye-contact perception threshold for forward faces (collapsed across neutral and fearful) varied by response cutoff (criterion used to obtain threshold).

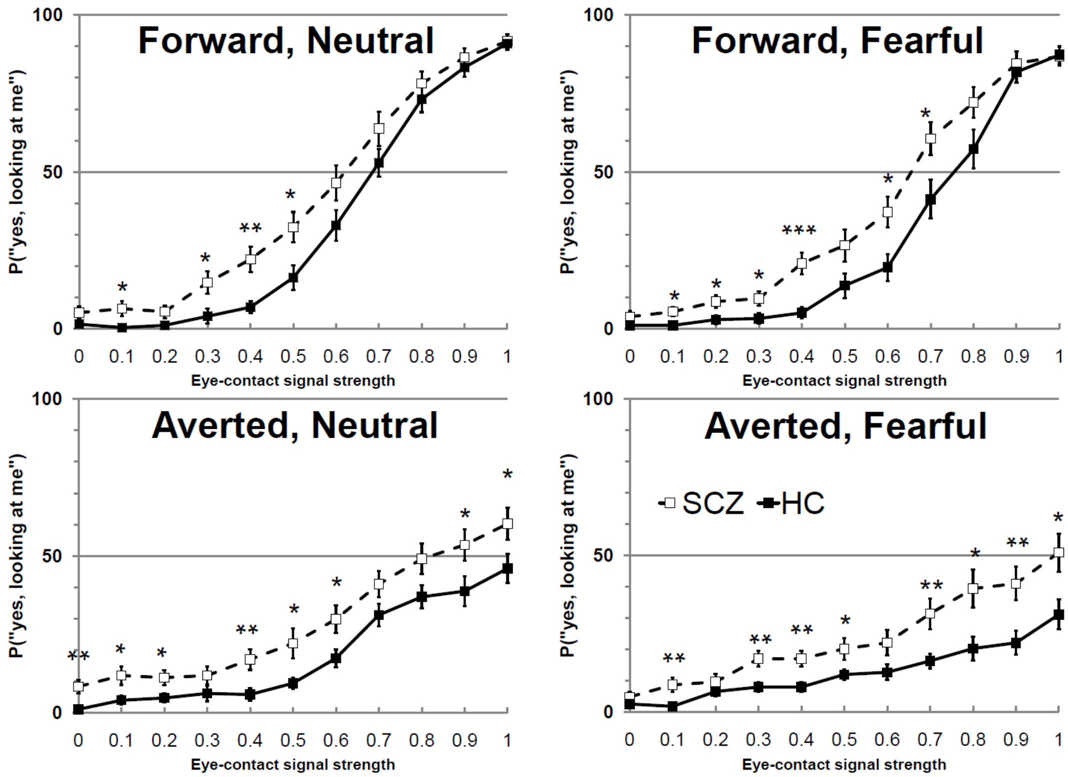

Figure 2.4. Percentage of "yes, looking at me" responses by group (SCZ: dashed line; HC: solid line) along the gaze continuum in each of the face conditions. Upper left: Face stimuli in forward head orientation and neutral emotion. Upper right: Face stimuli in forward head orientation and fearful emotion. Lower left: Face stimuli in 30º averted head orientation and neutral emotion. Lower right: Face stimuli in 30º averted head orientation and fearful emotion.
* $p < .05$. ** $p < .01$. *** $p < .001$.

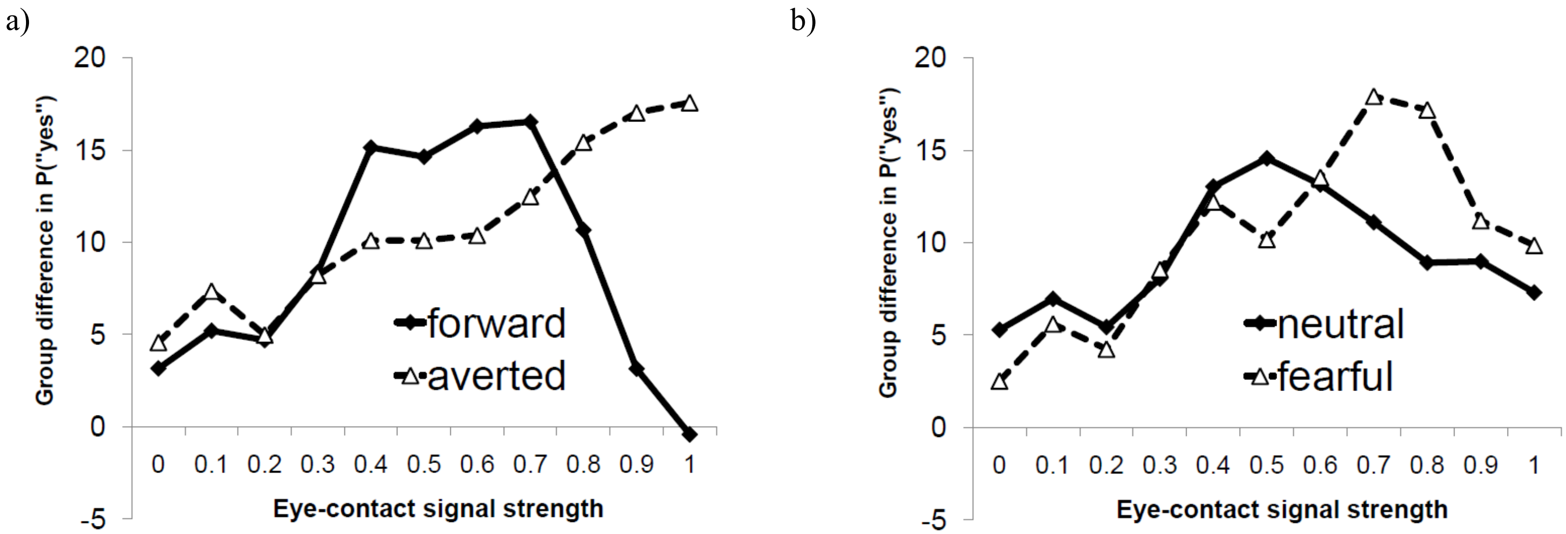

Figure 2.5. Group differences along the eye-contact signal strength continuum varied by head orientation and emotion. a) Gaze × Head × Group interaction: The lines depict group differences (SCZ – HC) in percentage of "yes, looking at me" responses for faces in forward and averted head orientations, respectively. Group difference along the continuum of signal strength for forward head orientation resembled a quadratic function, $F(1, 47) = 9.74$, $p = .003$, where SCZ over-perceived eye contact most at medium signal strengths. However, for averted head orientation, the group difference resembled a linear function, $F(1, 47) = 4.12$, $p = .048$, where SCZ over-perceived eye contact most at high signal strengths. b) Gaze × Emotion × Group interaction: The lines depict group differences (SCZ – HC) for neutral and fearful faces, respectively. For neutral faces, SCZ over-perceived eye contact most at medium signal strengths, whereas for fearful faces the group difference was amplified and the peak occurred later in the signal strength continuum.

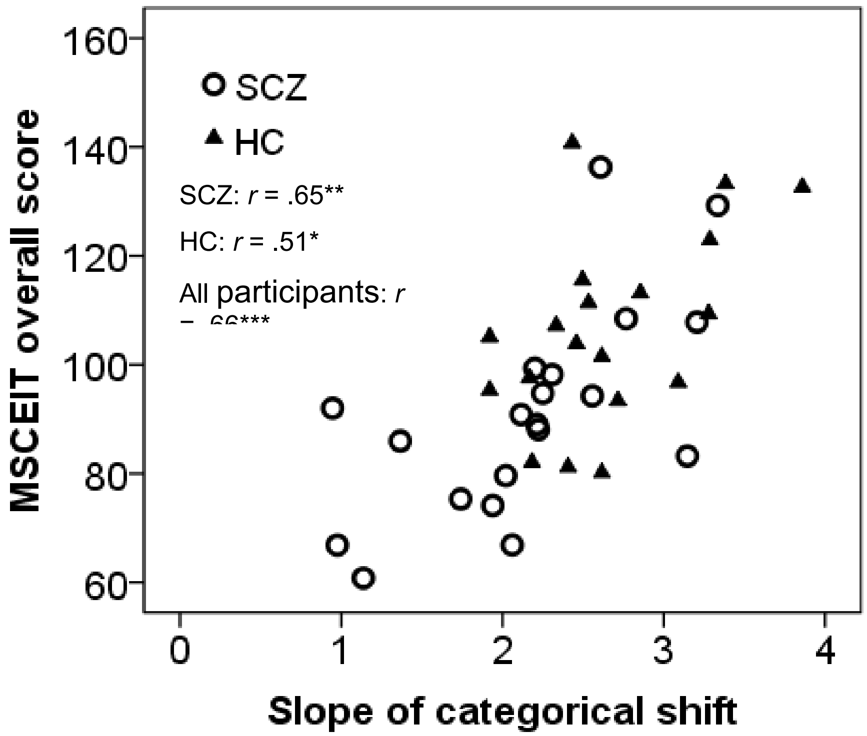

Figure 2.6. SCZ and HC showed comparable relationship between slope of categorical shift and MSCEIT overall score. * $p < .05$. ** $p < .01$. *** $p < .001$.

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CHAPTER III

Study 2. Simultaneous Processing of Gaze Direction and Emotion in Schizophrenia

Using self-directed gaze to orient attention and guide behavior is critical to survival and social adaptation (Emery, 2000). Schizophrenia has been associated with deficits across a wide range of social cognitive processes that adversely affect functional outcomes (Green, Olivier, Crawley, Penn, & Silverstein, 2005), but few studies have examined gaze perception and its link to clinical and functional presentations in schizophrenia. There is some evidence that individuals with schizophrenia (SCZ) over perceive eye contact (Hooker & Park, 2005; Rosse, Kendrick, Wyatt, Isaac, 1994). However, we have recently shown that misperception of eye contact is limited to ambiguous gaze direction only (Tso, Mui, Taylor, & Deldin, in press). Further, SCZ participants' eye-contact perception was less dichotomous compared to healthy controls (HC), suggesting decreased efficiency in mental categorization of gaze information. Such decreased dichotomy in gaze perception explained deficits in broader socio-emotional functioning beyond a general deficit. Given the functional implications of gaze perception in schizophrenia, understanding the specific psychological processes involved in gaze perception in schizophrenia may help direct future research and treatment.

A comprehensive understanding of gaze processing must consider factors other than gaze direction that also influence gaze perception. Head orientation and facial expression have been shown to be two particularly influential factors. Head orientation is the “default” cue used to infer the direction of attention of others when gaze information is not available (Emery, 2000). If presented as an incongruent compared with gaze, head orientation interferes with gaze direction judgment (Langton, 2000; Seyama & Nagayama, 2005). In particular, healthy individuals are less able to detect direct gaze from averted faces compared to forward faces (Itier, Alain, Kovacevic, & McIntosh, 2007; Rosse et al., 1994; Tso et al., in press), suggesting that averted head orientation adds ambiguity to the self-referential nature of gaze direction.

Electrophysiological findings support that forward and averted faces are processed differentially. N170, the “face-specific” event-related brain potential (ERP) component thought to reflect early attention for encoding of face structure (Doi, Sawada, & Masataka, 2007; Eimer, 2000; Itier, Taylor, & Lobaugh, 2004; Letourneau & Mitchell, 2008), has been shown to be larger and delayed to averted compared to forward faces (Itier, Alain, Kovacevic, & McIntosh, 2007), suggesting increased encoding effort and processing time for faces not presented in the conventional, front view. Behavioral data have shown that SCZ’s eye-contact perception is affected by averted head orientation to a lesser degree compared with HC (Tso et al., in press). Demonstration of decreased N170 difference between averted and forward faces, especially if in the absence of overall N170 impairment, during gaze discrimination in SCZ relative to HC would provide further support that SCZ’s eye-contact perception is characterized by a tendency to encode gaze direction out of the context of head orientation.

In addition to head orientation, facial emotion also interacts with gaze direction in face and gaze processing. In healthy individuals, direct gaze facilitates the perception of approach-oriented expressions (e.g., angry) while averted gaze facilitates the perception of avoidance-oriented emotions (e.g., fearful) (Adams & Kleck, 2005). Likewise, fearful emotion biases people to perceiving averted gaze (Tipples, 2006; Tso et al., in press). These suggest that the motivational congruency between gaze direction and facial emotion is automatically evaluated during face processing. Fearful faces provoke exaggerated N170 responses compared to neutral faces (Blau, Maurer, Tottenham, & McCandliss, 2007; Batty & Taylor, 2003; Leppanen, Moulson, Vogel-Farley, & Nelson, 2007; Rigato, Farroni, & Johnson, 2010), suggesting that more attention is allocated to encoding threat-related faces. The interaction between gaze direction and emotion may be particularly relevant in schizophrenia. SCZ participants are abnormally sensitive to gaze direction when orienting their reflexive attention (Langdon, Corner, McLaren, Coltheart, & Ward, 2006). Further, there appears to be a special sensitivity to threat-related stimuli in schizophrenia as evident by heightened emotional reactivity to daily stressors and negative life events (Myin-Germeys et al., 2003; Tso, Grove, & Taylor, 2012) and increased autonomic response to threat-related images (Kring & Neale, 1996). This is particularly true in paranoid SCZ participants (Williams et al., 2004). Given these sensitivities to gaze direction and threat-related signals in schizophrenia, SCZ participants may show particular sensitivity to gaze-emotion combinations that signify external threat (e.g., fearful faces with averted gaze), and N170 would be a promising index of this process in schizophrenia.

Accurately perceiving gaze direction requires mental resources to constantly update the stream of information in order to evaluate and mentally categorize the stimuli ("looking at me?"). This process is best indexed by the P300 wave—a broad positivity over the midline parietal sites, maximal between 300 ms and 500 ms after the onset of a stimulus, generally thought to index memory update for stimulus evaluation and mental categorization (Polich, 2007). P300 has been shown to be larger to direct than averted gaze (Conty, N'Diaye, Tijus, & George, 2007; Itier, Alain, Kovacevic, & McIntosh, 2007) and affective than neutral images (Schupp et al., 2004; Williams, Kemp, et al., 2007; Williams, Palmer, Liddell, Song, & Gordon, 2006), suggesting that increased mental resources are recruited to evaluate salient stimuli. Both neuropsychological (Nuechterlein et al., 2004) and P300 data (Ford, 1999) have consistently shown working memory deficits in schizophrenia, and such deficits are significantly correlated with social problem solving and skill acquisition (Green, 1996). It is likely that working memory deficits as indexed by P300 also occur in and impact gaze perception and higher-level social cognition in SCZ participants.

Previous ERP studies have consistently shown decreased N170 and P300 amplitudes during facial emotion discrimination in schizophrenia (Caharel et al., 2007; Campanella, Montedoro, Streel, Verbanck, & Rosier, 2006; Herrmann, Ellgring, & Fallgatter, 2004; Johnston, Stojanov, Devir, & Schall, 2005; Lee, Kim, Kim, & Bae, 2010; Lynn & Salisbury, 2008; Turetsky et al., 2007), indicating decreased early attention for face encoding and reduced working memory for mental categorization, respectively. However, eye gaze discrimination is significantly different from facial emotion discrimination in several ways. First, accurate emotion identification entails efficient scanning of critical regions of the face, whereas in gaze discrimination one can focus on the eye region, requiring less visual scanning and integration. It is well documented that SCZ participants' compromised performance in emotion identification is related to less efficient visual scanning (Green, Williams, & Davidson, 2003; Loughland, Williams, & Gordon, 2002; Manor et al., 1999; Phillips & David, 1998). Together with a recent finding that SCZ participants demonstrate deficits in visual search tasks only when broad monitoring is involved (Hahn et al., 2011), the previously observed N170 deficits in facial emotion identification in SCZ may not occur to the same degree in gaze discrimination in SCZ. Second, discriminating between emotions is putatively more challenging than discriminating between self-directed and non-self-directed gaze, because facial emotions involve more categories—thus the deficits in response selection in SCZ (Luck et al., 2009) are more relevant—and higher variability across individuals. The findings that SCZ participants showed poorer performance on recognizing prototypical facial emotions (see for a meta-analytic review Kohler, Walker, Martin, Healey, & Moberg, 2010) but equal ability to perceive clearly direct and clearly averted gaze (Franck et al., 1998; Hooker & Park, 2005; Tso et al., in press) compared with HC, support the conclusion that gaze discrimination is easier than emotion identification for individuals with schizophrenia. Taken together, although there is a large body of evidence demonstrating that deficits in emotion identification in SCZ are related to abnormal N170 and P300 processes, the neural correlates of gaze processing in SCZ are poorly understood. Since a gaze discrimination task consisting of faces with only direct and averted gaze would equalize the performance between SCZ and HC, it could serve as a good probe for any differential neuropsychological processes involved in gaze perception in schizophrenia that are not accountable by performance difference and related processes such as response selection.

This study examined gaze perception in schizophrenia by measuring ERP during a gaze discrimination task ("Looking at me?" Yes/no) consisting of faces varying in gaze direction (direct, averted), head orientation (forward, averted), and emotion (neutral, fearful). We hypothesized that: (1) SCZ participants would show equal accuracy but slower reaction time as compared with HC; (2) SCZ participants would show less N170 difference between forward and averted faces than HC; (3a) relative to HC, SCZ participants would show larger N170 amplitudes to fearful faces with averted gaze than to other faces, and (3b) increased N170 in this condition would be correlated with positive symptoms including paranoid delusions; and (4) SCZ participants would show decreased P300 amplitudes, indicating decreased mental categorization, and this would be correlated with poorer socio-emotional functioning.

Method

Participants

Twenty-eight SCZ and 32 HC matched for age, sex, and parental education completed the study. Three SCZ and six HC participants were excluded for not having enough correct trials for one or more of the experimental conditions[2], the sample included in this report consisted of 25 SCZ and 26 HC.

SCZ participants were volunteers aged 18 to 60 recruited through advertisements in the community or referrals by clinicians of local community mental health clinics and

[2] The experimental conditions for which these three SCZ and six HC participants did not have enough correct trials were either or both of the conditions with neutral/fearful faces with averted head orientation and direct gaze (see Figure 3.1). This was likely due to the fact that people are generally less able to detect direct gaze from averted faces (Itier et al, 2007; Rosse et al., 1994; Tso et al., in press).

clinical researchers of the University of Michigan. All SCZ participants met criteria for schizophrenia (*n* = 19) or schizoaffective disorder (*n* = 6) established using the Structured Clinical Interview for DSM-IV Axis-I Disorders (SCID-I) (First, Spitzer, Gibbon, & Williams, 1995). Those who were unable to give informed consent, had a history of substance abuse/dependence in the past 12 months, or a history of close head injury or medical conditions that affect brain functions were excluded. Five SCZ participants were treated with conventional antipsychotics and 19 with atypical; one was medication-free.

HC participants were recruited from advertisements in the community and referrals by other researchers. They could not have, according to an initial phone screening followed by a SCID-I interview, lifetime Axis-I disorders, substance abuse in the past five years, lifetime substance dependence, a history of close head injury or medical conditions that affect brain functions, and history of psychosis and bipolar disorders among first-degree relatives.

The study was conducted in accordance with the protocol approved by the Institutional Review Board of the University of Michigan Medical School. Following full explanation of the study, written informed consent was obtained from each participant. All participants had at least 20/30 vision according to a Snellen chart. Participant characteristics are summarized in Table 3.1.

Task and Procedure

Stimuli of the Gaze Discrimination Task were faces adopted from Gur et al. (2002). A subset of 16 actors (8 female, 8 male) was selected from the original pool of 3-dimensional images for editing. Black-and-white pictures of each selected actor, in forward and 30º averted head orientation and in neutral and evoked-fearful emotion, were used. Photoshop was used to edit the iris area to create direct gaze (“looking at me”) for faces in averted head orientation and averted gaze (“looking away”) for faces in forward head orientation. See Figure 3.1 for an example of the eight (2 gaze directions × 2 head orientations × 2 emotions) experimental conditions.

The Gaze Discrimination Task was presented using the software E-prime 1.0. In each trial, a face was presented briefly and participants were instructed to press a button to indicate that the person was “looking at me” or another button if they felt the person was “looking away from me” (see Figure 3.2). Each trial lasted 1800 ms to 3600 ms, depending on the reaction time. There were 64 trials (16 actors × 2 mirror images × 2 repeats) in each of the eight within-subject conditions, totaling 512 trials. These trials were presented in a randomized order in four blocks. A brief break was enforced between blocks. The task typically took approximately 25 minutes to complete.

Electrophysiological Data Acquisition and Reduction

Participants’ electroencephalographic (EEG) activity was recorded using BrainVision Recorder (Brain Products, GmbH, Munchen, *Germany*) and a Lycra stretchable cap of 32 Ag/AgCl electrodes positioned according to the International 10-20 system. Vertical electro-oculogram (VEOG) was measured with an electrode placed below the right eye. Electrode impedances were kept below 5 kΩ. EEG was referenced to FCz during recording and digitally sampled at the rate of 5000 Hz. Using BrainVision Analyzer (BrainProducts, GmbH, Munchen, *Germany*), EEG data were re-sampled offline at 250 Hz, re-referenced to average mastoids ([TP9 + TP10] / 2), segmented into 1.2-second epochs (200 ms pre-stimulus, 1000 ms post-stimulus), filtered with a 0.01-Hz high-pass filter and a 30-Hz low-pass filter (zero-phase shift and 24 dB/octave roll-off), corrected for eye blinks using regression algorithm (Gratton, Coles, & Donchin, 1983), and then baseline adjusted. Data exceeding +/- 80 μV were automatically rejected. Subsequently, data were subjected to visual inspection and manually scored to remove remaining artifact. Data were then averaged across trials for each of the 8 experimental conditions. N170 was extracted from the data later re-referenced to the common average (Joyce & Rossion, 2005), while P300 was obtained from the data referenced to the average mastoids as typically done in ERP studies. ERP components were isolated based on the typical time windows reported in the literature, inspection of the waveforms, and principal component analysis (PCA) with an extraction criterion of eigenvalue > 1 and Varimax rotation. ERP amplitudes were represented by mean PCA scores (i.e., product of potential amplitude and PCA component loading) in the statistical analyses. Latency of N170 peaks, defined as local maxima within the time window between 120 and 210 ms, was also examined.

Statistical Analyses

Accuracy and reaction time (RT) on gaze discrimination were analyzed with separate 4-way mixed model ANOVAs, with gaze direction, head orientation, and emotion as within-subjects variables and group (SCZ, HC) as between-subjects variable. N170 and P300 were analyzed with separate 5-way mixed model ANOVA based on all trials, with gaze direction, head orientation, emotion, scalp site as within-subjects variables and group as between-subjects variable. Scalp sites for N170 were P7 and P8 and those for P300 were P3, Pz, and P4. All trials (correct and incorrect) were used in the ERP analyses to ensure unbiased ANOVA results, as two of the experimental conditions (averted neutral/fearful faces with direct gaze) had significantly fewer correct responses than the other conditions. Since the SCZ and HC groups showed equal accuracy across conditions (see below for more details), and previous studies showed that implicit gaze processing produced statistically equivalent ERP as explicit gaze processing (Itier, Alain, Kovacevic, & McIntosh, 2007), the use of all trials was deemed to be justified. Hyunh-Feldt adjustment was used in case of violation of the assumption of equal sphericity. Relationships between ERP measures and clinical and functional variables were examined with Pearson's correlations.

Results

Behavioral Data

Accuracy and RT results of the two groups are presented in Figure 3.3. SCZ participants (0.807 ± 0.062) were as accurate as HC participants (0.831 ± 0.074) on the task [$F(1, 49) = 1.66$, $p = .203$]. As expected, SCZ participants (838 ± 191 ms) responded more slowly than HC (696 ± 82 ms) [$F(1, 49) = 12.04$, $p = .001$]. SCZ and HC showed equivalent accuracy and RT modulations by gaze, head orientation, emotion, and interactions between these factors.

Participants were overall highly accurate on all conditions except for averted faces with direct gaze, and this reduced accuracy was more pronounced for fearful than neutral faces [Gaze × Head × Emotion interaction: $F(1, 49) = 4.70$, $p = .035$]. Participants took longer to respond to averted than forward faces [$F(1, 49) = 109.22$, $p < .001$]. RT was not different by gaze direction, although gaze effect depended on head orientation [Gaze × Head interaction: $F(1, 49) = 214.10$, $p < .001$], such that participants took longer to respond to gaze in incongruent head orientation (i.e., averted gaze in forward head, and direct gaze in averted head) than gaze in congruent head direction.

ERP Data

The participants' N170 responses were consistent with patterns observed in previous studies: N170 was lateralized to the right [$F(1, 49) = 4.04$, $p = .050$], larger [$F(1, 49) = 49.13$, $p < .001$] and delayed [$F(1, 49) = 59.67$, $p < .001$] for averted than forward faces, and larger for fearful than neutral faces [$F(1, 49) = 25.28$, $p < .001$]. The delayed latency effect by averted head orientation was more prominent over the right hemisphere [Head × Laterality interaction: $F(1, 49) = 4.94$, $p = .031$]. Gaze direction had no overall effects on N170 amplitude and latency [amplitude: $F(1, 49) = 1.03$, *ns*; latency: $F(1, 49) = 0.46$, *ns*], but it showed significant interactions with head orientation, such that faces with incongruent gaze-head directions elicited larger and delayed N170 compared with those with congruent gaze-head directions [amplitude: $F(1, 49) = 7.89$, $p = .007$; latency: $F(1, 49) = 11.36$, $p = .001$]. Gaze direction also interacted with emotion, such that faces with motivationally congruent gaze-emotion (i.e., neutral faces with direct gaze, and fearful faces with averted gaze) elicited delayed and marginally larger N170 compared to faces with motivationally incongruent gaze-emotion [amplitude: $F(1, 49) = 3.65$, $p = .062$; latency: $F(1, 49) = 5.07$, $p = .029$].

SCZ participants' overall N170 responses were comparable to HC's [amplitude: $F(1, 49) = 0.11$, *ns*; latency: $F(1, 49) = 0.90$, *ns*]. SCZ showed marginally decreased head orientation effect compared with HC [Head × Group interaction: $F(1, 49) = 3.27$, $p = .077$] (see Figure 3.4). As hypothesized, SCZ participants showed an elevated N170 response specifically to averted gaze in fearful emotion, as suggested by the Gaze × Emotion ×

Group interaction [$F(1, 49) = 5.89$, $p = .019$] (see Figure 3.5). Post-hoc analyses showed that among SCZ, N170 magnitude exhibited a Gaze × Emotion interaction [$F(1, 24) = 6.36$, $p = .019$], such that gaze direction had a significant effect on fearful faces (with averted gaze evoking larger N170 than direct gaze) [$t(24) = 2.73$, $p = .012$] but not on neutral faces [$t(24) = -1.65$, $p = .111$]. This Gaze × Emotion interaction was absent among HC [$F(1, 25) = 0.47$, *ns*]. Latency analyses showed that the elevated N170 response for fearful faces with averted gaze in SCZ participants was not accompanied by differential latency in this condition [Gaze × Emotion × Group interaction: $F(1, 49) = 0.36$, *ns*].

As expected, SCZ participants showed substantially reduced P300 as compared with HC [$F(1, 49) = 7.30$, $p = .009$] (Figure 3.6). However, all other main effects and interactions for P300 were statistically equivalent across the two groups. Consistent with the literature, P300 was larger to direct than averted gaze [$F(1, 49) = 13.57$, $p < .001$], larger to forward than averted faces [$F(1, 49) = 37.58$, $p < .001$], and marginally larger to fearful than neutral faces [$F(1, 49) = 4.02$, $p = .051$].

ERP Correlates of Symptoms and Socio-emotional Functioning in SCZ

Contrary to our hypothesis, increment of N170 response to fearful faces with averted gaze relative to other conditions was not significantly correlated with severity of paranoid delusions and positive symptoms in general. However, as hypothesized, decreased P300 amplitudes were associated with poorer scores on the MSCEIT, but this was limited to the Experiencing Emotion module (P3: $r = .65$, $p = .002$; Pz: $r = .45$, $p = .049$; P4: $r = .51$, $p = .022$).

Discussion

The results of this study revealed several differences in gaze perception between SCZ and HC participants despite comparable group performances. First of all, SCZ participants showed abnormally accentuated N170 in response to fearful faces with averted gaze. This is the first study to document aberrant simultaneous processing of gaze direction and facial emotion in an early cognitive stage in schizophrenia. This N170 sensitivity to fearful faces with averted gaze observed in SCZ participant is unlikely related to increased difficulty as suggested by the lack of a latency delay that is usually observed when faces are more difficult to encode (e.g., inverted vs. upright faces, Doi et al., 2007; Eimer, 2000; Itier et al., 2004; Letourneau & Mitchell, 2008). Since averted gaze in fearful faces suggests threat in the environment (Adams & Kleck, 2005; Tipples, 2006), this finding supports a special encoding sensitivity to external threat in schizophrenia. Previous studies showed that increased threat sensitivity is paired with reductions in medial prefrontal cortex activity in paranoid schizophrenia, suggesting that a failure to appropriately appraise the situation and regulate arousals may be related to paranoid delusions (Williams et al., 2007). However, this N170 sensitivity to fearful faces with averted gaze was not significantly correlated with severity of paranoid symptoms in this study, which may indicate that this rapid detection of external threat reflects a trait phenomenon, or that it is simply not related to persecutory delusions. Future work could examine if deficits in slow wave, a late ERP component thought to index elaborative cognitive processes such as appraisal, mental rehearsal and rumination (Hajcak, Moser, & Simons, 2006; Ruchkin, Johnson, Grafman, Canoune, & Ritter, 1992), show closer relationships with paranoid symptoms. Future demonstration of N170 sensitivity to angry faces with direct gaze would also provide further support of the notion of a special encoding sensitivity to external threat in schizophrenia.

Another key psychophysiological difference during gaze perception in SCZ was a reduction, though trend-level, of the normally observed N170 modulation by head orientation (with averted faces eliciting larger N170 than forward faces). As discussed above, previous behavioral data also showed that SCZ participants' gaze perception is less influenced by head orientation compared with HC. Taken together, individuals with schizophrenia appear to integrate the surrounding context (i.e., head orientation) in gaze perception to a lesser degree. This is consistent with the notion of abnormal visual perceptual organization in schizophrenia (Silverstein & Keane, 2011). SCZ participants consistently perform better than HC on tasks in which global integration would normally decrease the accuracy of perception of individual elements (Place & Gilmore, 1980; Rief, 1991; Uhlhaas, Phillips, Schenkel, & Silverstein, 2006), supporting a compromised ability to integrate contextual information in visual perception in schizophrenia. Interestingly, Horton and Silverstein (2001) found that deaf SCZ participants (who conceivably rely more on visual contexts) show normalized contextual perception compared with their hearing counterparts, suggesting that this cognitive process is learned and modifiable in schizophrenia. Future study may test if coaching of gaze discrimination with an emphasis on the consideration of head orientation would normalize the N170 modulation by head orientation in schizophrenia.

It is noteworthy that this study was the first to our knowledge to demonstrate equivalent overall N170 amplitudes in SCZ and HC participants, contrary to previous N170 findings in schizophrenia using emotion identification paradigms (Campanella, et al., 2006; Herrmann et al., 2004; Johnston et al., 2005; Lee et al., 2010; Lynn & Salisbury, 2008; Turetsky et al., 2007). As discussed earlier, eye gaze processing is distinguished from facial emotion processing in several ways, including the involvement of efficient visual scanning and integration, and the degree of ambiguity. While future studies directly comparing gaze vs. emotion discrimination for N170 effect are needed to confirm the speculation that the intact N170 amplitudes in SCZ was due to the task difference, this finding points to the possibility that N170 deficits in schizophrenia may be task-dependent and changeable with instructions relating to focus of attention (*cf.* Russell, Green, Simpson, & Coltheart, 2008), supporting targeted rehabilitative training and using N170 as an outcome measure.

SCZ participants exhibited reduced overall P300 compared to HC participants as expected, consistent with previous work showing reduction in the visual P300, although visual P300 deficits have not been as reliable as auditory P300 deficits (Jeon & Polich, 2003). The reduction we found was significantly correlated with poorer scores on the experiential aspect of emotional intelligence (MSCEIT), suggesting that an overall reduction in mental resources for stimulus evaluation and categorization may be a common factor of abnormal gaze perception and emotion perception. The observed P300 reduction in SCZ did not manifest as lower accuracy in gaze discrimination in this study, likely because the task was relatively easy and did not require sophisticated stimulus discrimination. Previous studies have shown that SCZ participants displayed deficits in eye-contact judgment only when the gaze direction was ambiguous (Hooker & Park, 2005; Tso et al., in press). Therefore, it is possible that the P300 deficits in SCZ participants would manifest in poorer performance in situations where the task is more demanding (e.g., using lowered size/quality images of gaze, increased working memory load, and anxiety induction).

Caution is needed when interpreting the results of this study due to the limitations of sampling and the sample characteristics. Patients who completed the study were relatively stable and motivated individuals as they responded to the advertisements or clinicians' referrals and were able to follow through the instructions. As such, positive and negative symptoms presented by this sample had a relatively limited range, which might have restricted the correlational findings. The sample also contained mostly chronic and medicated patients. While the results of this study inform gaze processing in schizophrenia as most individuals with the illness are treated with medications in North America, the extent to which the observed behavioral and psychophysiological deviations were due to medication and illness chronicity remains to be further explored in future studies. Finally, only averted and direct gaze were included in this experiment. Psychophysiological deviations in schizophrenia while processing ambiguous gaze remain to be addressed.

To conclude, psychophysiological processes during gaze discrimination in schizophrenia were characterized by a heightened encoding sensitivity to faces signaling external threat, a tendency to integrate less the contextual cue of head orientation, and reduced mental resources for stimulus evaluation and categorization despite equivalent performance. These abnormalities were associated with important functional outcomes and warrant further investigations.

Table 3.1. Participant Characteristics

Variable	SCZ (n = 25) (Mean ± *SD*)	HC (n = 26) (Mean ± *SD*)	t / χ^2	p
Age (years)	42.9 ± 13.1	44.2 ± 13.0	-0.36	.721
Sex	17 M / 8 F	17 M / 9 F	0.04	.843
Education (years)	13.6 ± 2.1	16.0 ± 2.4	-3.76	< .001
Parental education (years)	14.6 ± 3.8	14.5 ± 2.8	0.15	.882
Handedness (left/right/mixed)	1 / 20 / 4	0 / 22 / 4	1.08	.584
Age of onset (years)	20.7 ± 7.2	--	--	--
Duration of illness (years)	22.2 ± 12.8	--	--	--
SAPS	4.4 ± 3.3	--	--	--
SANS	3.9 ± 2.7	--	--	--
BACS	-1.0 ± 1.2	0.4 ± 1.0	-4.26	< .001
MSCEIT[a] overall score	90.5 ± 19.3	108.8 ± 18.2	-3.05	.004
Experiencing Emotion	92.7 ± 16.6	112.5 ± 19.7	-3.41	.002
Reasoning Emotion	92.6 ± 19.8	103.5 ± 18.1	-1.95	.058

Note. SAPS = Sum of global subscores on the Scale for the Assessment of Positive Symptoms (Andreasen, 1994); SANS = Sum of global scores of the Flat Affect, Alogia, Apathy, and Anhedonia subscales of the Scale for the Assessment of Negative Symptoms (Andreasen, 1993); BACS = Z-score on the Brief Assessment of Cognition for Schizophrenia (Keefe et al., 2004) standardized using test scores of 83 healthy individuals (30% female; age = 40.5 ± 11.7 years; parental education = 14.9 ± 2.8 years); MSCEIT = Age- and gender-adjusted total score on the Mayer-Salovey-Caruso Emotional Intelligence Test (Mayer, Salovey, & Caruso, 1999).

a. Due to missing data, MSCEIT overall score was available for only 20 SCZ and 19 HC; score on the Experiencing Emotion module was available for 20 SCZ and 19 HC; and score on the Reasoning Emotion module was available for 23 SCZ and 23 HC.

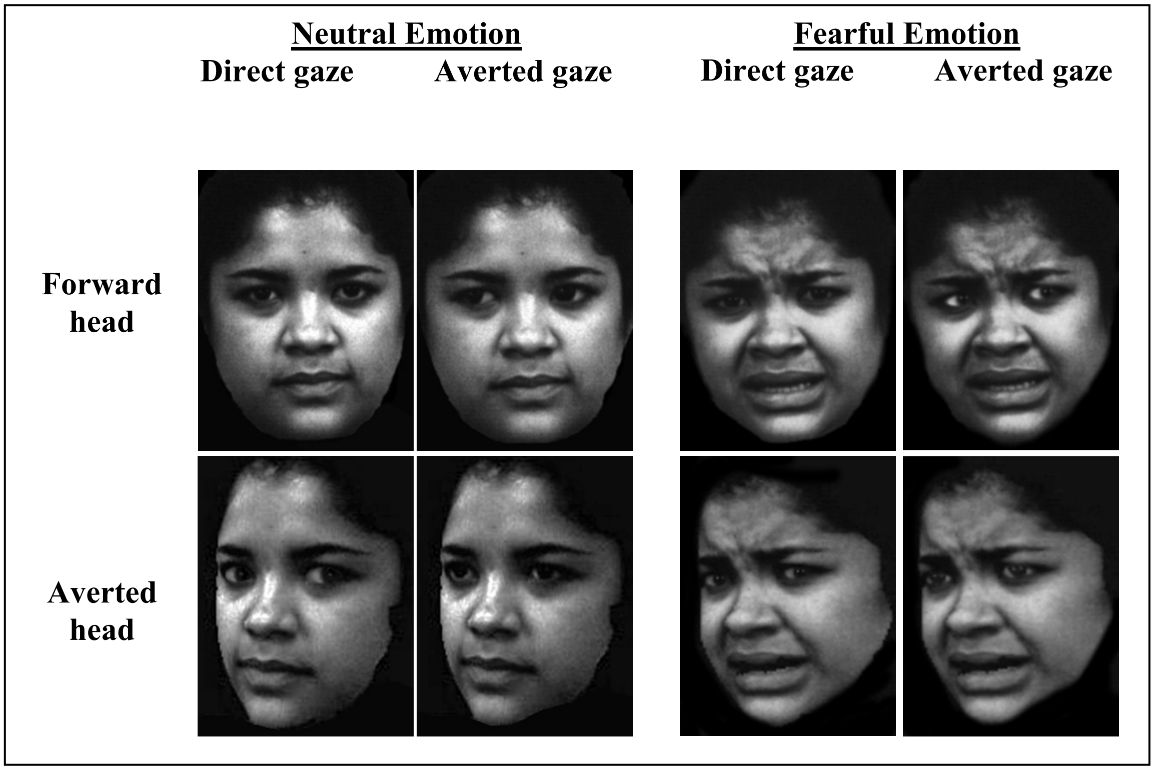

Figure 3.1. Face stimuli in the Gaze Discrimination Task varying in eye gaze direction (direct, averted), head orientation (forward, averted), and facial emotion (neutral, fearful).

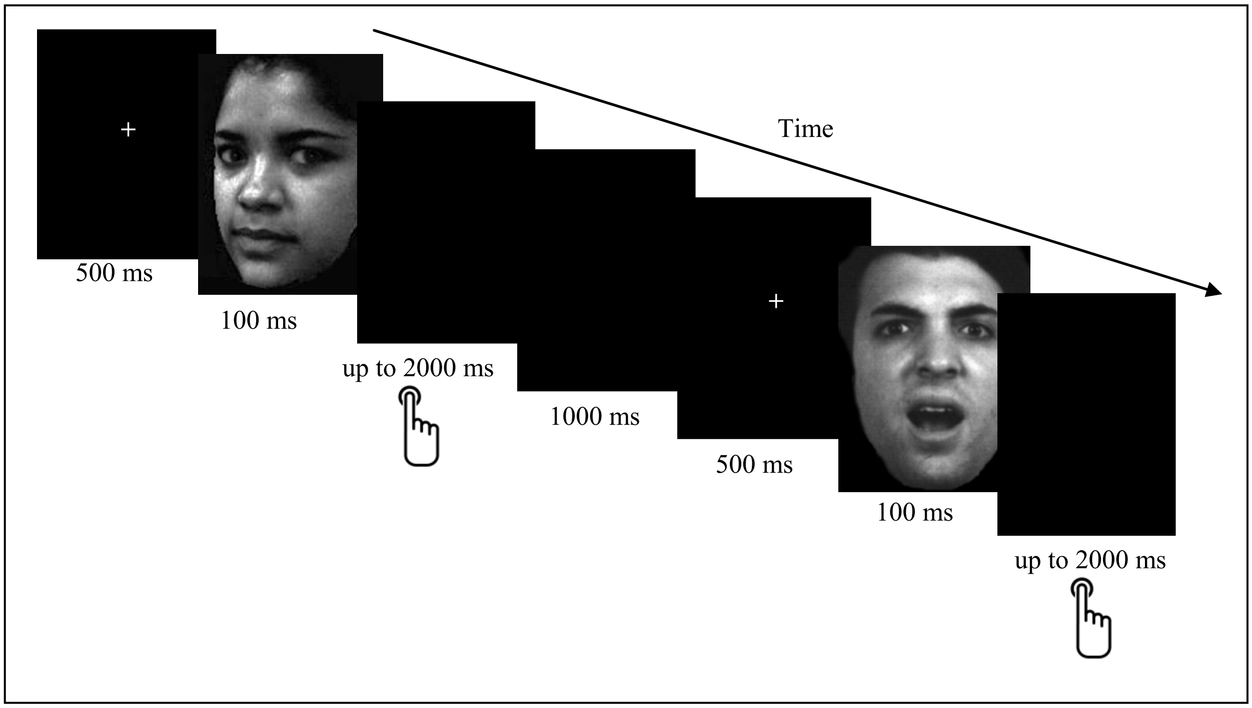

Figure 3.2. Procedure of the Gaze Discrimination Task. Each trial consisted of a fixation cross (500 ms), followed by the target face (100 ms) to which participants were allowed up to 2,000 ms to press a button to indicate whether the face was "looking at me" or "looking away from me," and then a blank screen (1,000 ms).

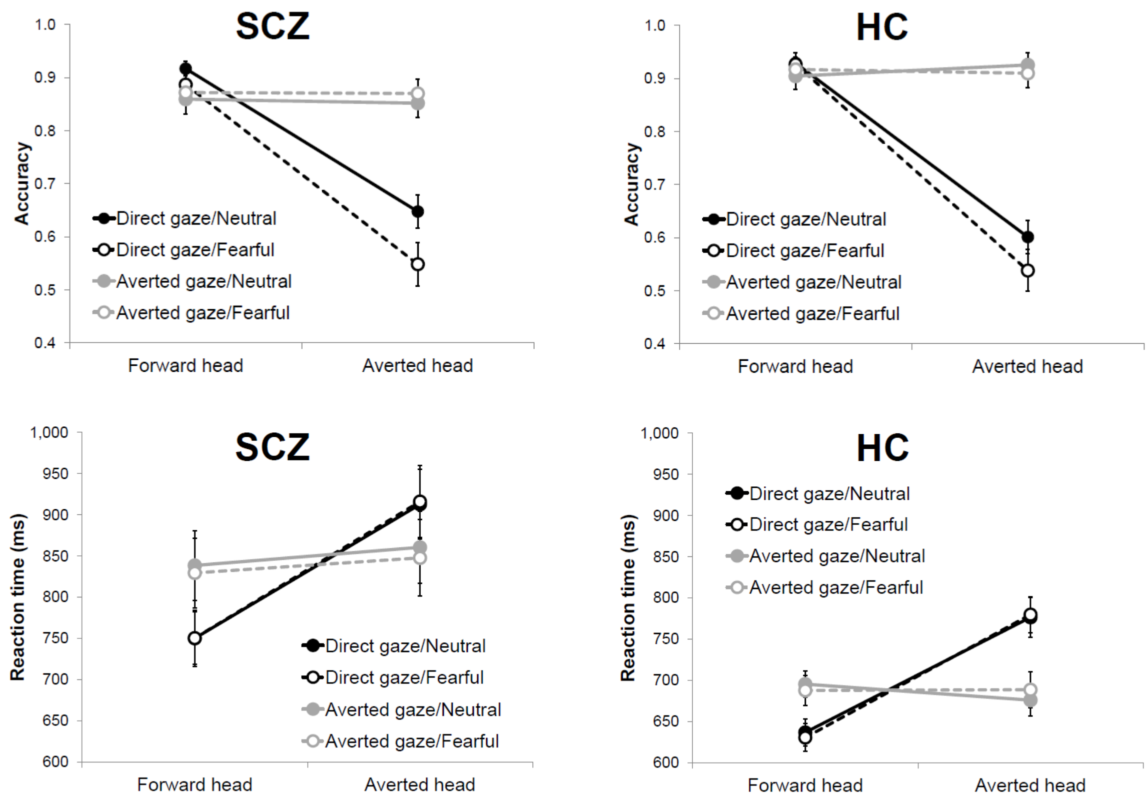

Figure 3.3. Behavioral results based on all trials for the 8 experimental conditions. Upper panels: Accuracy in SCZ (left) and HC (right) participants. Bottom panels: RT in SCZ (left) and HC (right) participants.

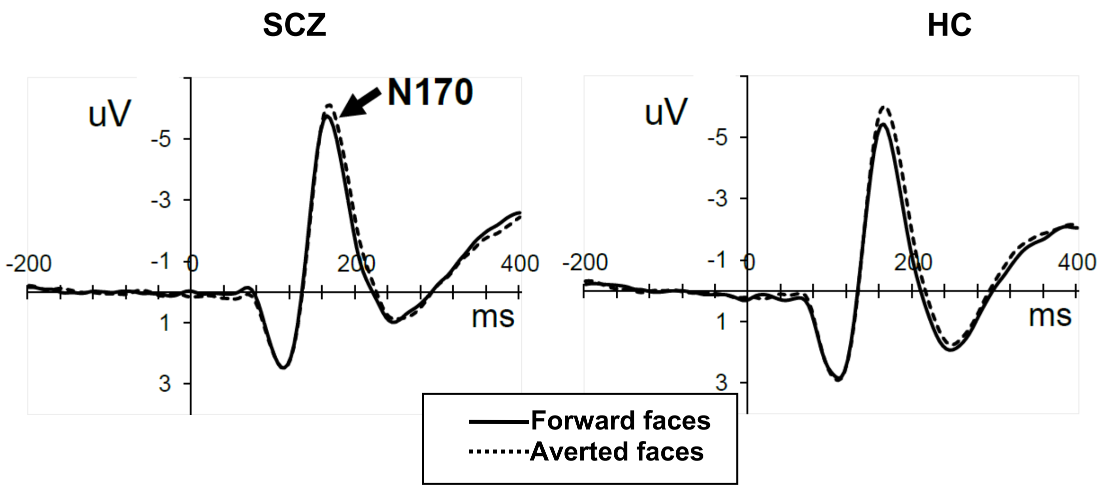

Figure 3.4. SCZ participants showed a trend-level reduction of head orientation effect on N170 compared with HC. Each waveform represents averaged ERP at scalp sites P7 and P8.

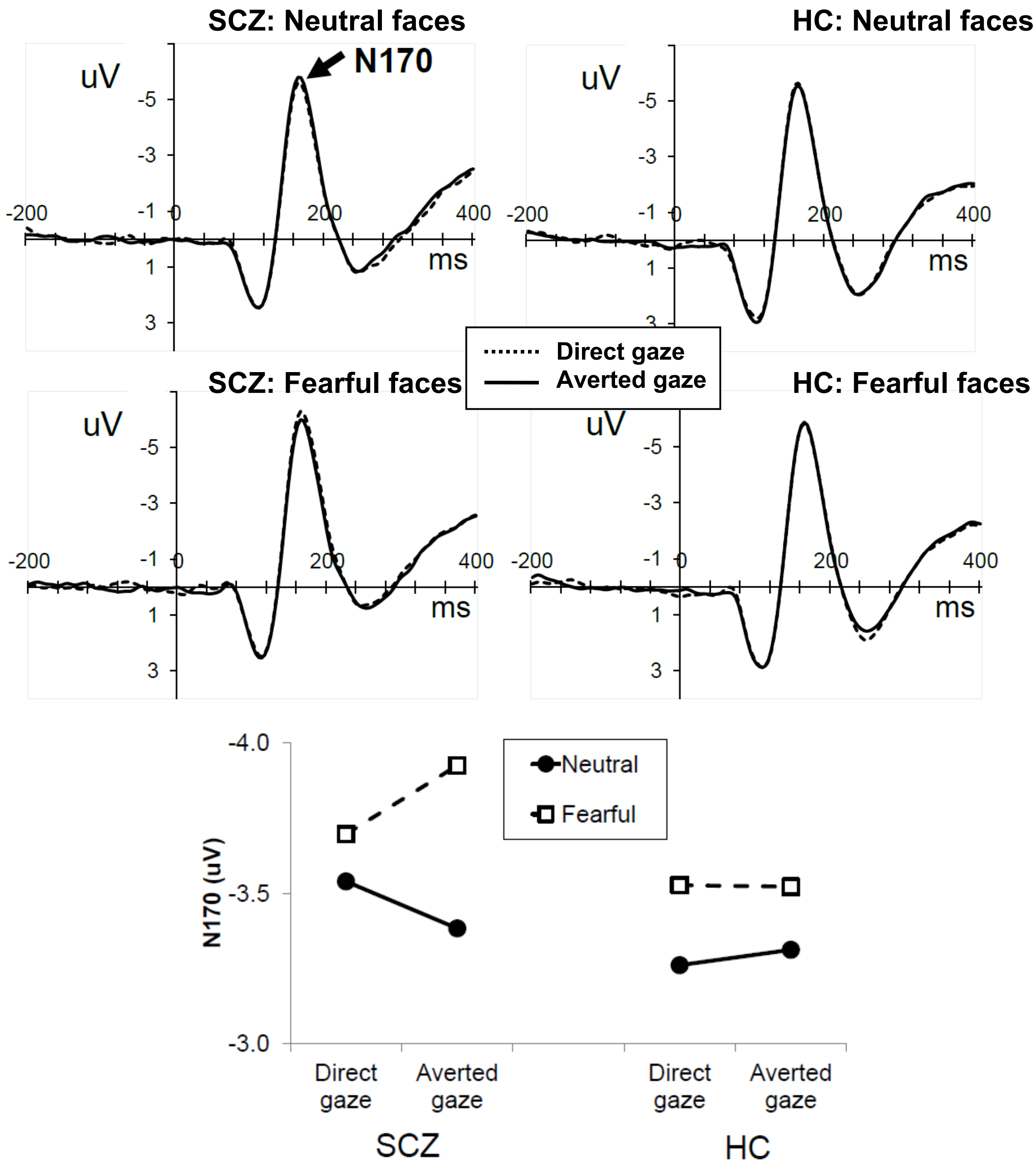

Figure 3.5. Accentuated N170 response to fearful faces with averted gaze in SCZ participants. Each waveform represents averaged ERP at scalp sites P7 and P8.

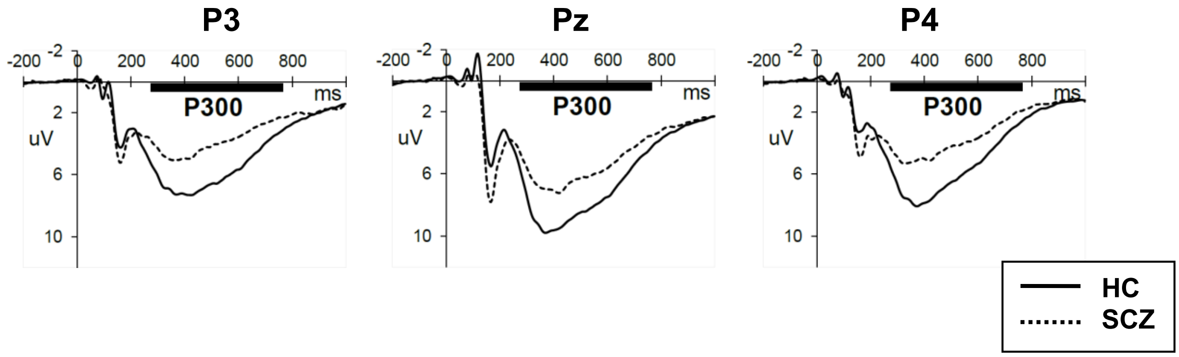

Figure 3.6. SCZ participants showed consistently lower P300 amplitudes than HC. The waveforms represent averaged ERP across the eight experimental conditions.

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CHAPTER IV

Study 3. The Role of Visual Integration in Gaze Perception and Emotional Intelligence in Schizophrenia

Schizophrenia (SCZ) is a severe mental disorder that often runs a chronic course and significantly impacts one's social functioning. Recent research has shown that SCZ is associated with deficits in a wide range of social cognitive processes, from perception-based functions (e.g., emotion recognition, eye-contact perception; Hooker and Park, 2005; Kohler et al., 2010; Rosse et al., 1996; Tso et al., in press) to higher-level reasoning and metacognition (e.g., theory of mind, empathy, social reasoning; see for reviews Bora et al., 2009; Brüne, 2005). Since social cognition has been shown to be critical to social and functional outcomes in SCZ (Couture et al., 2006), a great deal of research efforts has been devoted to understanding the nature of these processes.

Given that many social cognitive processes involve information processing in the visual modality and there are numerous reports of disruptions in basic visual perceptual functions in SCZ (Butler, Silverstein, & Dakin, 2008), it is reasonable to ask whether deficits in basic visual perception may significantly account for abnormal social cognitive processes in SCZ. Surprisingly, relatively little work has been done to examine the role of basic visual perception in socio-emotional functioning in the disorder. This study aims to elucidate the relationship between visual integration and social cognitive processes in schizophrenia.

Visual processing involves a series of complex neuronal responses to visual stimuli and neural interactions including lateral excitatory facilitation, inhibition, and top-down feedback. One functional concept in visual processing that is thought to be of particular relevance to the symptoms and deficits observed in schizophrenia is *integration* (Butler, Silverstein, & Dakin, 2008). Accordingly, visual integration refers to the ability to integrate individual local attributes of a scene into a larger, global complex structure in order to guide behavior (Butler et al., 2008). Examples of integration function include Gestalt grouping phenomena and object recognition.

There is strong evidence that visual integration is compromised in SCZ. Individuals with SCZ have shown poorer performance than healthy controls (HC) in object recognition from fragmented images (Doniger, Foxe, Murray, Higgins, & Javitt, 2002), perceptual grouping by proximity and color similarity (Kurylo, Pasternak, Silipo, Javitt, & Bulter, 2007), and contour integration (Silverstein, Kovacs, Corry, & Valone, 2000; Silverstein et al., 2012; Uhlhaas, Phillips, Mitchell, & Silverstein, 2006; Uhlhaas, Phillips, & Silverstein, 2005; but see also Chey & Holzman, 1997 for intact use of the Gestalt principles). Additionally, individuals with SCZ perform better than HC on tasks in which global integration would normally decrease the accuracy of perception of individual elements (Place & Gilmore, 1980; Rief, 1991; Uhlhaas, Phillips, Schenkel, & Silverstein, 2006), further supporting visual integration deficits in the disorder. In a recent review of perceptual organization in SCZ, a vast majority of the 61 studies reviewed reported some kind of visual integration impairment and SCZ’s difficulty is most pronounced when sophisticated mechanisms and top-down processing are required to process novel, noisy, or highly fragmented forms (Silverstein and Keane, 2011).

Visual integration impairment may contribute to clinical symptoms and functional outcomes in SCZ. There is some evidence linking deficits in visual integration to disorganized symptoms (Silverstein, Kovacs, Corry, & Valone, 2000) and premorbid social dysfunctions in the disorder (Schenkel, Spaulding, & Silverstein, 2005). However, a recent large-sample study found no significant correlation between visual integration and community skills in SCZ (Gold et al., 2012). Silverstein and Keane (2011) asserted that visual integration impairment may affect more specific social cognitive processes in SCZ. For example, the well-documented deficits in face identification and emotion recognition observed in schizophrenia may be due to unsuccessful configural processing of facial features. In fact, event-related brain potentials (ERP) studies have shown that emotion recognition deficits in schizophrenia is associated with reduction of the N170 wave, an index of holistic structural encoding of facial features (Caharel et al., 2007; Turetsky et al., 2007). Further, during gaze discrimination, when compared with HC, SCZ participants' behavioral (Tso et al., in press) and N170 responses (Tso et al., submitted) are less affected by head orientation, indicating a tendency to integrate less the contextual cue of head orientation in gaze processing. Taken together, visual integration likely plays a role in the processing of important social signals and further investigations are needed to elucidate the relationship.

To understand the bottom-up impact of visual integration on socio-emotional information processing in schizophrenia, it is necessary to examine the effect of visual integration on different levels of socio-emotional functions—from perceptual-based ones to higher-level ones. Gaze perception and emotional intelligence are two good candidate constructs because they represent different levels of processing and they each have documented relevance to schizophrenia. Specifically, effective use of gaze direction to guide behavior is critical to social adaptation (Emery, 2000). The determination of the self-referential nature of gaze represents a process that intersects the perceptual and interpretation levels (Tso et al., in press), and SCZ participants have demonstrated abnormalities including overperception of eye contact when gaze direction is ambiguous and reduced dichotomousness of eye-contact perception (Rosse et al., 1996; Hooker & Park, 2005; Tso et al., in press). Emotional intelligence captures broader socio-emotional functioning ranging from the perception of facial emotions to higher-level processes including understanding, inferring, and regulating effectively self's and others' emotional states (Mayer, Salovey, & Caruso, 1999), and SCZ participants have shown consistent deficits in emotional intelligence (Eack et al., 2010; Kee et al., 2009; Tso et al., 2010, in press).

This study aims to examine the relationship between visual integration and social cognition in schizophrenia. Visual integration was measured using a coherent motion task and a contour integration task, as recommended by the Cognitive Neuroscience Treatment Research to Improve Cognition in Schizophrenia (CNTRICS) consortium (Butler et al., 2012). As for social cognition, gaze perception and emotional intelligence were selected for they represent a range of levels of socio-emotional information processing and their documented relevance to schizophrenia.

We hypothesized that: 1) SCZ participants would show poorer visual integration than HC; 2) Visual integration would be associated with social cognition (including and gaze perception and emotional intelligence) in SCZ; and 3) Differences in the social cognitive measures between SCZ and HC would significantly diminish after taking the group difference in visual integration into account.

Method

Participants

Thirty-one SCZ and 23 HC completed the study. However, visual inspection of the data revealed that two SCZ participants' performance approached chance level and thus were excluded from the analyses. The remaining 29 SCZ and 23 HC participants were well matched for age, sex, and parental education (see Table 1 for participant characteristics).

SCZ participants were volunteers aged 18 to 60 recruited through advertisements in the community or referrals by clinicians of local community mental health clinics and clinical researchers of the University of Michigan. They met criteria for schizophrenia (*n* = 21) or schizoaffective disorder (*n* = 8) using the Structured Clinical Interview for DSM-IV Axis-I Disorders (SCID-I) (First et al., 1995). Those who were unable to give informed consent or had a history of substance abuse/dependence in the past 12 months were excluded. Nine SCZ participants were treated with conventional antipsychotics and 19 with atypical; 1 was medication-free.

HC participants were recruited from advertisements in the community and referrals by other researchers. Using an initial phone screening followed by a SCID-I interview, those with lifetime Axis-I disorders, substance abuse in the past 5 years, lifetime substance dependence, a history of close head injury or medical conditions that affect brain functions, or history of psychosis and bipolar disorder among first-degree relatives were excluded.

The study was conducted in accordance with the protocol approved by the Institutional Review Board of the University of Michigan Medical School. Written informed consent was obtained from each participant after full explanation of the study was given. All participants had at least 20/30 vision according to a Snellen chart.

Task and Procedure

Visual integration. Integration was measured using two psychophysics tasks, the Coherent Motion Task and the Contour Integration Task, respectively. The tasks were presented using the software MATLAB 2008 (MathWorks Inc., Natick, MA) in an adaptive approach with a 3-up-1-down staircase method. Tasks were terminated after 12 reversals. Participants' thresholds (the higest difficulty level one reliably responds correctly) on each of the tasks were estimated by obtaining the mean difficulty level of the last 8 reversals. For each task, participants did a practice (consisting of 10 trials with feedback) and then completed the full-length task twice; the mean of the threshold estimates obtained from the two full-length blocks was used as the threshold on the corresponding task. The distance between the stimuli and the viewer was controlled by using a chin rest placed at a fixed position relative to the computer screen.

> *Coherent Motion Task.* Participants were asked to identify the direction (up, down, left, or right) of a group of coherently moving dots against a background of randomly moving noise dots. Difficulty increases as fewer dots move coherently (see Figure 1 for illustration). The density of the dots was 0.5 dots per square

degree, and the dots moved at three degrees per second. In each trial, the moving dots were presented for 1000 ms, and participants were allowed 5 s to respond.

Contour Integration Task. Participants were to locate a contour formed by Gabor elements (left/right on the screen) against a background of noise Gabor elements. Gabor elements were used for their better match with the spatial frequency processing characteristics of orientation-selective simple cells in primary visual cortex (V1) as compared with lines or dots, thus are more able to tap into visual integration (Uhlhaas, Phillips, Mitchell, & Silverstein, 2006). Since two versions (density version and jitter version) have been used in the schizophrenia literature and it is unclear which version is a better measure of visual integration in terms of reliability and ability to discriminate patients from controls, both versions were used in this study. For the density version, difficulty increases as the number of noise Gabor elements increases. For the jitter version, difficulty increases as the degree of jitter of the contour-defining Gabor elements increases. In each trial, the stimulus was presented for 5 s, and participants were required to make a response within this duration. See Figure 2 for illustration.

Eye-contact perception. Twenty-six SCZ and 23 HC participants among those who completed the visual integration tasks also completed the eye-contact perception task. Details of this task and the results are reported in Tso et al. (in press). Briefly, participants made eye-contact judgments (“Looking at me?” yes/no) for faces with varying gaze direction (from averted to direct in ten 10%-increments). For each participant, their response (i.e., percentage of “yes, looking at me” responses) was plotted against the continuum of gaze angles, and a logistic function was fitted into the data.

Using this method, a key gaze perception measure, namely, dichotomous eye-contact perception, was obtained by measuring the slope of the logistic function when eye contact was endorsed 50% of the time (i.e., where response changed from mostly “no” to mostly “yes”), with steeper slopes indicating more dichotomous perception. Dichotomous eye-contact perception was found to be a significant predictor of emotional intelligence even after taking basic neurocognition into consideration. Thus, this measure was used in the analyses in this report.

Emotional intelligence. The Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT; Mayer, Salovey, & Caruso, 1999) is a performance-based measure of emotion-related social cognitive skills recommended by the National Institute of Mental Health (NIMH) Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) committee (Green, Olivier, Crawley, Penn, & Silverstein, 2005). Participants completed all four branches of the test (i.e., Perceiving Emotion, Using Emotion, Understanding Emotion, Managing Emotion). Age- and gender-adjusted scores were used in the analyses.

Statistical Analyses

Since the thresholds of the visual tasks were in different units and directions (i.e., higher magnitudes may indicate better or worse performance depending on the unit used), threshold estimates for each task were transformed into z-scores using HC’s mean and standard deviation and with the sign changed when necessary, so that higher z-scores indicating better performance. Outliers (scores that exceeded 3 SDs from the mean of the participant’s diagnosis group) were excluded, resulting in the exclusion of one SCZ and one HC participants from the Coherent Motion Task, one HC participant from the

Contour Integration Task – density version, and one SCZ participant from the Contour Integration Task – jitter version; these were all different individuals. The two groups were then compared for performance on the three tasks using t-tests. The relationships between visual integration and the social cognition measures were examined using Pearson's correlations and regression analyses.

Results

Visual Integration

Thresholds in z-scores on the visual integration tasks in SCZ are presented in Figure 3. SCZ participants showed intact thresholds on the Coherent Motion Task as compared with HC participants, $t(50) = -0.41$, $p = .68$. However, they showed poorer performance than HC on both versions of the Contour Integration Task [density version: $t(49) = -2.10$, $p = .041$; jitter version: $t(49) = -3.23$, $p = .002$].

Relationship with Eye-Contact Perception and Emotional Intelligence

The correlations between measures of visual integration, social cognition, and clinical symptoms among SCZ participants are shown in Table 3. Briefly, performance on the Coherent Motor Task was not significantly correlated with social cognition measures. The Contour Integration Task – density version showed trend-level correlations with the reasoning domain of the MSCEIT, while the jitter version was significantly correlated with dichotomous eye-contact perception and several domains and the overall score of the MSCEIT.

Since visual integration as measured with the jitter version of the Contour Integration Task appeared to better discriminate SCZ from HC participants and showed significant relationships with other social cognition measures, it was used as the visual perception variable in the regression analyses. Among SCZ participants, visual integration explained 19.9% of variance of dichotomous eye-contact perception, $F(1, 23) = 5.73$, $p = .025$. Visual integration explained 19.2% of variance of emotional intelligence (MSCEIT overall score), $F(1, 19) = 4.50$, $p = .047$. Dichotomous eye-contact perception explained 42.6% of variance of emotional intelligence, $F(1, 18) = 13.38$, $p = .002$. Visual integration and dichotomous eye-contact perception together explained 43.5% of variance of emotional intelligence, $F(2, 16) = 6.15$, $p = .01$.

As expected, diagnosis group was a significant predictor of both dichotomous eye-contact perception [$F(1, 47) = 6.10$, $p = .017$, $R^2 = 11.5\%$] and emotional intelligence [$F(1, 39) = 7.84$, $p = .008$, $R^2 = 16.7\%$]. However, diagnosis group could explain only marginally additional amounts of variance of dichotomous eye-contact perception [$\Delta F(1, 45) = 2.87$, $p = .097$, $\Delta R^2 = 5.3\%$] and emotional intelligence [$\Delta F(1, 37) = 4.06$, $p = .051$, $\Delta R^2 = 8.1\%$] when the effect of visual integration was taken into account. This suggested that group differences in dichotomous eye-contact perception and emotional intelligence could be significantly accounted for by SCZ's compromised visual integration function.

Discussion

This study examined visual integration and its relationship with social cognitive functions in schizophrenia. Consistent with our hypothesis and previous findings (Silverstein, Kovacs, Corry, & Valone, 2000; Silverstein et al., 2012; Uhlhaas, Phillips, Mitchell, & Silverstein, 2006; Uhlhaas, Phillips, & Silverstein, 2005), SCZ participants demonstrated significantly poorer performance than HC on the Contour Integration Task, indicating a reduced ability to integrate individual, local elements to form a larger, holistic structure. As hypothesized, this perceptual function was significantly correlated with both dichotomous eye-contact perception and the MSCEIT. Additionally, the differences between SCZ and HC in both social cognitive measures significantly diminished after visual integration was taken into account. Taken together, the results strongly support that deficits in visual integration play a significant role in the impairment in different levels of social information processing in schizophrenia.

The relationship between visual integration and dichotomous eye-contact perception suggests that the compromised ability to efficiently discriminate self-referential vs. non-self-referential gaze in schizophrenia may be related to a reduced ability to consider the inter-relations of local elements (i.e., facial features) when forming judgment of the direction of the eyes. This is consistent with the recent findings that SCZ participants' eye-contact perception is less affected by contextual factors including head orientation and facial emotion (Tso et al., in press). Although holistic perception of faces does not always result in more "accurate" perception of gaze direction per se—people are less able to detect direct gaze from averted than forward faces (Itier et al., 2007; Rosse et al., 1994; Tso et al., in press) and are biased to perceiving averted gaze from fearful faces (Tipple, 2006; Tso et al., in press), it enables the person to process social information in a more functionally adaptive way.

The relationship between visual integration and MSCEIT supported that disruptions in visual integration may have significant implications to higher-level socio-emotional functioning in schizophrenia. Given this functional implication and its potential sensitivity to treatment effects (Silverstein & Keane, 2009), future research should explore and evaluate treatment modalities that can effectively improve visual integration. It is important to note that visual integration (as measured with the Contour Integration Task) accounted for significant but modest amounts of the differences between SCZ and HC in dichotomous eye-contact perception and MSCEIT, suggesting that disrupted data-driven visual perception may explain only partially the observed social cognitive deficits in schizophrenia. Together with the lack of a zero-degree correlation between visual integration and community skills (Gold et al., 2012), the pathways from visual perceptual dysfunctions to broader functional impairment in schizophrenia remain to be further illustrated, perhaps by considering other mediating and moderating factors (e.g., top-down processes).

This study demonstrated that both of the density and jitter versions of the Contour Integration Task could significantly discriminate SCZ from HC. However, the two versions showed only moderate correlation with each other (r = .54), suggesting that perceiving a contour against a noisy background reflects a somewhat different ability than perceiving a contour made of elements that do not line up perfectly. A recent study showed that compared with other manipulations, the jitter manipulation of the Contour Integration Task corresponds better to activity in visual cortical areas known to be involved in contour processing (i.e., V1, V2/V3, and V4; Silverstein et al., 2009). Our finding that the jitter version appeared to show stronger correlations with the social cognitive measures in SCZ, than did the density version, further suggests that the jitter manipulation may be a more effective way to tap into the construct of visual integration. However, it should be noted that the clinical and functional correlates of the density version were the same direction and of similar magnitudes as those of the jitter version, providing converging evidence that visual integration as measured with the Contour Integration Task has important functional implications.

Contrary to a previous study (Chen et al., 2003), SCZ participants showed intact performance on the Coherent Motion Task. This is possibly due to the methodological differences, including the exclusion of outliers in this study and the use of different paradigm parameters (e.g., dot density, degrees of coherence), which have been shown to be critical in drawing conclusions as to whether individuals with schizophrenia have deficient ability to detect coherent motion (Slaghuis et al., 2007). Although speculative because of the null results, the finding of limited overlap between the Coherent Motion Task and both versions of the Contour Integration Task in this study raises the question whether the Coherent Motion Task is an effective measure of visual integration.

This study was limited by the use of relatively chronic and stable and medicated outpatients. The limited range of clinical symptoms in this sample may have limited the power to detect potential correlations between symptoms and the key variables. Medication effects were also difficult to isolate, though antipsychotic dose was not associated with performance on the visual perception tasks. Since schizophrenia frequently runs a chronic course and individuals with the illness are more often than not treated with medications in North America, the results of this study nevertheless inform basic visual perception and its role in social dysfunctions among many presented with schizophrenia in the health care system.

To conclude, individuals with schizophrenia showed compromised abilities to effectively integrate individual local visual elements into a holistic picture. This perceptual deficit was related to deficits in social cognitive deficits in the disorder, calling for further investigations of the role of visual integration in higher-level information processing in the disorder.

Table 4.1. *Participant Characteristics*

Variable	SCZ (n = 29) (Mean ± SD)	HC (n = 23) (Mean ± SD)	t / χ^2	p
Age (years)	43.6 ± 12.6	43.5 ± 13.1	0.03	.978
Sex (male/female)	20 / 9	18 / 5	0.56	.453
Education (years)	13.6 ± 1.9	16.4 ± 2.6	-4.41	< .001
Parental education (years)	14.7 ± 3.7	15.0 ± 2.8	-0.37	.715
Age of onset (years)	19.8 ± 7.0	--	--	--
Duration of illness (years)	23.8 ± 13.1	--	--	--
SAPS	5.6 ± 3.6	--	--	--
SANS	4.5 ± 3.1	--	--	--
BACS[a]	-1.1 ± 1.2	0.4 ± 1.0	-4.62	< .001
MSCEIT[b]	90.8 ± 18.4	106.5 ± 17.4	-2.80	.008

SAPS = Sum of global subscores on the Scale for the Assessment of Positive Symptoms (Andreasen, 1984); SANS = Sum of global scores of the Flat Affect, Alogia, Apathy, and Anhedonia subscales of the Scale for the Assessment of Negative Symptoms (Andreasen, 1983); BACS = Z-score on the Brief Assessment of Cognition for Schizophrenia (Keefe et al., 2004) standardized using test scores of 83 healthy individuals (30% female; age = 40.5 ± 11.7 years; parental education = 14.9 ± 2.8 years); MSCEIT = Age- and gender-adjusted total score on the Mayer-Salovey-Caruso Emotional Intelligence Test (Mayer, Salovey, & Caruso, 1999).

a. Due to missing data, BACS score was available for all but 3 HC.

b. Due to missing data, MSCEIT overall score was available for only 22 SCZ and 19 HC.

Table 4.2. *Correlations between Visual Integration, Clinical Symptoms, and Social Cognition.*

Variable	1.	2.	3.	4	5.	6.	7.	8.	8a.	8b.	8c.
1. Coherent Motion	--										
2. Contour Integration-density	.06	--									
3. Contour Integration-jitter	-.00	.54**	--								
4. SAPS	.29	-.10	-.00	--							
5. SANS	-.04	.08	-.05	.27	--						
6. BACS	-.11	.18	.35†	-.02	-.16	--					
7. Dichotomous eye-contact perception	.08	.27	.45*	-.05	.04	.41*	--				
8. MSCEIT overall	-.01	.36	.44*	-.11	-.16	.55**	.65**	--			
8a. Perceiving Emot	.02	.28	.09	.03	.14	.37†	.45*	.82***	--		
8b. Using Emot	.22	.33	.43*	.12	-.05	.47*	.47*	.76***	.70***	--	
8c. Understanding Emot	-.15	.38†	.48*	-.12	-.09	.68***	.42*	.88***	.66**	.53**	--
8d. Managing Emot	-.15	.32†	.55**	.34†	-.23	.46*	.45*	.70**	.25	.42*	.62**

†*p* < .10. **p* < .05. ***p* < .01. ****p* < .001.

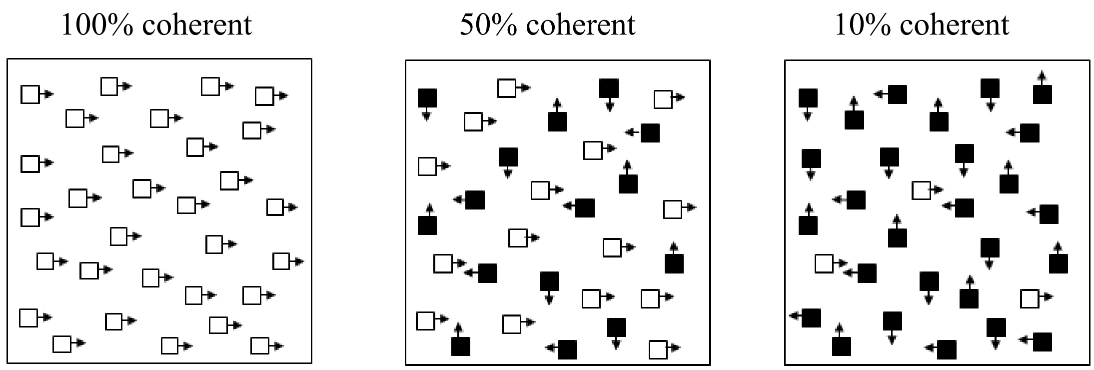

Figure 4.1. Coherent Motion Task. Participants were asked to push a button to indicate the direction to which the coherent dots are moving (either upward, downward, to the left, or to the right). Difficulty level increases as the percentage of coherently moving dots decreases. This figure shows only sample trials with 100%, 50%, and 10% coherence.

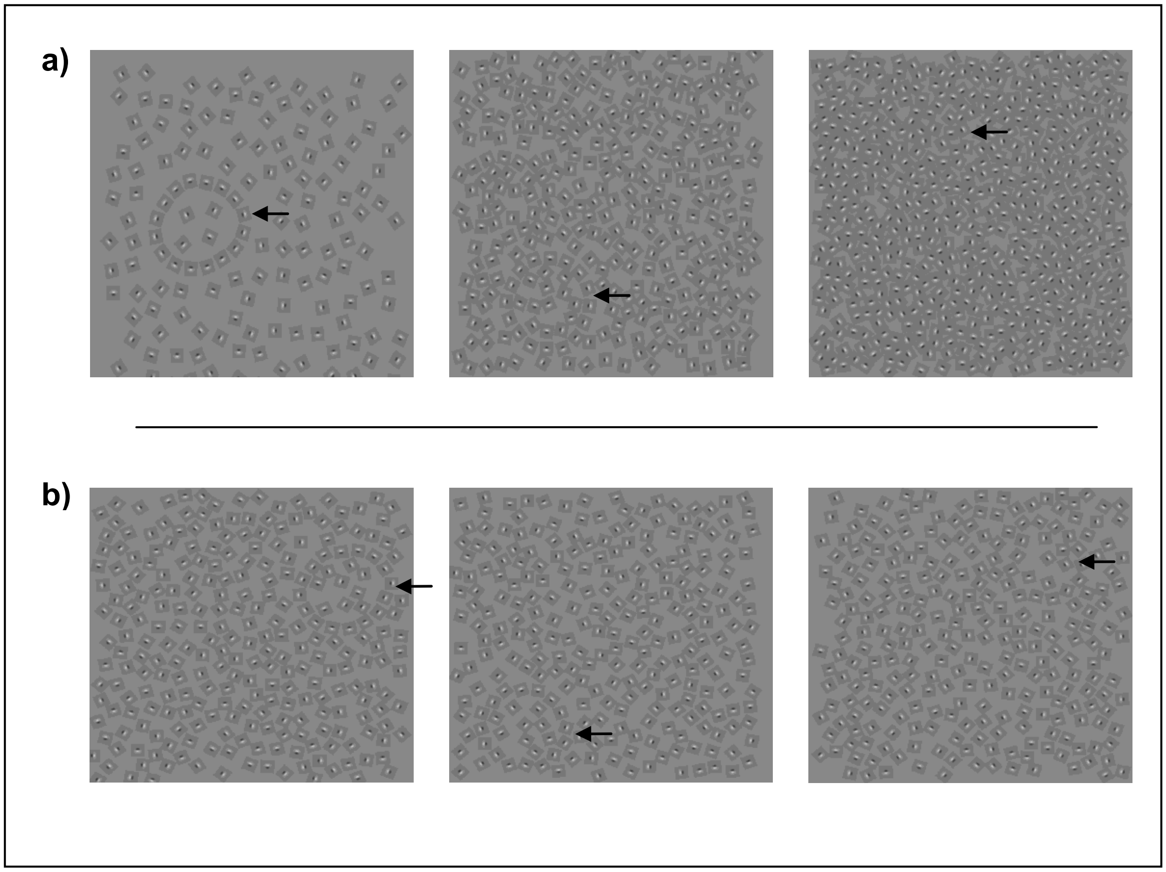

Figure 4.2. Contour Integration Task: a) Density version, and b) Jitter version. Participants were asked to push a button to indicate the location of the contour formed by lined-up Gabor elements (either on the left or right side of the screen). For the density version, difficulty level increases as the number of noise Gabor elements increases. For the jitter version, difficulty level increases as the jitter angle of the contour-forming Gabor elements increases. Arrows indicate the location of the contours.

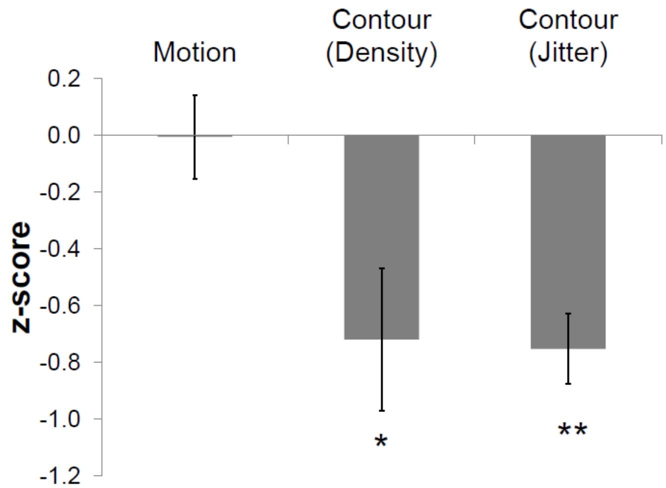

Figure 4.3. Estimated thresholds (in z-scores) on the visual perception tasks in SCZ participants. Lower scores indicate worse perception. *$P < .05$ and **$P < .01$, as compared to HC.

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CHAPTER V

Summary and Conclusions

This dissertation aimed to further our understanding of the distressing and debilitating condition of schizophrenia by examining gaze perception, abnormalities in which process may impair one through distorted and/or diminished relations to the social world. The multi-method approach (behavioral, neural, psychophysics) and manipulation of factors that influence normal gaze perception allowed us to gain a fuller understanding of whether and how eye gaze information is processed differently in schizophrenia and if abnormal gaze perception and higher-level socio-emotional functioning may be adequately explained by deficits in basic visual perception in the disorder. The methods and findings of each of the three studies are summarized below.

Study 1

Participants made eye-contact judgments for faces in varying gaze direction (from averted to direct in ten 10%-increments), head orientation (forward, 30-degree averted), and emotion (neutral, fearful). Psychophysical analyses for forward faces showed that SCZ began endorsing eye contact with weaker eye-contact signal and their eye-contact perception was less of a dichotomous function compared with HC. SCZ were more likely than HC to endorse eye contact when gaze was ambiguous, and this over-perception of eye contact was modulated by head orientation and emotion. Over-perception of eye contact was associated with more severe negative symptoms. Decreased categorical gaze perception explained variance of socio-emotional deficits in schizophrenia after taking basic neurocognition into consideration, suggesting the relationship was not solely due to a general deficit problem.

Study 2

Participants completed a gaze discrimination task with face stimuli varying in gaze direction (direct, averted), head orientation (forward, averted) and emotion (neutral, fearful). ERPs were recorded during the task. SCZ participants were as accurate as, though slower than, HC participants on the task. SCZ participants displayed accentuated N170 responses to fearful faces with averted gaze, indicating a heightened encoding sensitivity to faces signaling external threat. This also suggested that facial emotion and gaze direction are processed simultaneously at an early cognitive stage in schizophrenia. SCZ participants also showed a trend-level reduction of N170 modulation by head orientation, suggesting less integration of context information in gaze perception. They showed significantly lower P300 amplitudes than HC participants, indicating reduced mental resources for stimulus evaluation and categorization. This reduction was significantly correlated with poorer performance on the experiential aspect of an emotional intelligence test.

Study 3

Participants completed a Coherent Motion Task and a Contour Integration Task that measured visual integration in an adaptive psychophysics approach. SCZ participants' performance on the visual integration tasks was compared with HC's, and was examined in relation to their performance on an eye-contact perception task and a measure of emotional intelligence. SCZ participants showed equivalent performance on the Coherent Motion Task as HC, but they performed significantly worse on the Contour Integration Task. Among SCZ participants, visual integration (as measured with the contour integration task) was a significant predictor of eye-contact perception and emotional intelligence. Hierarchical regression analyses showed that visual integration significantly accounted for the group differences in eye-contact perception and emotional intelligence.

Taken together, this dissertation research showed that individuals with schizophrenia exhibited abnormal eye-contact perception characterized by over-attribution of self-directed intention to ambiguous gaze and more uncertainty when determining the self-referential nature of gaze. These abnormalities are related to more severe negative symptoms and deficits in broader socio-emotional functioning in schizophrenia. They also displayed psychophysiological deviations during gaze discrimination that cannot be accounted for by differential performance, including a heightened encoding sensitivity to faces signaling external threat, a tendency to integrate less the contextual cue of head orientation, and reduced mental resources for stimulus categorization. Individuals with schizophrenia showed compromised abilities to effectively integrate individual local visual elements into a holistic picture, and this basic visual perceptual deficit significantly explained the observed deficits in gaze perception and higher-level processing of social information in the disorder. This is consistent with cascade models that visual processing deficits contribute to compromised social cognition, which in turn influences functional outcome in schizophrenia (Rassovsky, Horan, Lee, Sergi, & Green, 2011; Sergi, Rassovsky, Nuechterlein, & Green, 2006). However, the amounts of variance of social functional outcomes explained by visual processing deficits in this dissertation as well as previous studies using structural equation modeling (Rassovsky et al., 2011; Sergi et al., 2006) were far less than perfect (< 50%). This suggests that although visual processing deficits appear to have significant bottom-up effects on higher-level functioning in schizophrenia, other mediating/moderating factors as well as top-down mechanisms—for example, modulation of input processing in sensory regions by the anterior attention system (Sarter, Gehring, & Kozac, 2006; Sarter, Lustig, & Taylor, 2012; Taylor, Chen, Tso, Liberzon, & Welsh, 2011)—must also be considered in order to gain a full understanding of the complex nature of socio-emotional deficits in the disorder.

To conclude, the results of this dissertation informed the nature and functional relevance of self-referential information processing in schizophrenia, and provide directions for future research on the complex dynamics between sensory processing, basic cognition, and social functioning in the disorder, which may eventually help developing treatment options (e.g., cognitive training, transcranial magnetic stimulation, medications) targeting at specific brain areas/functions for persons with or at risk for schizophrenia in the future.

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