

**Social Perception in Schizophrenia:  
Evidence of Occipital and Prefrontal Dysfunction**

BY

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THESIS

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## TABLE OF CONTENTS

<u>Chapter</u>	<u>PAGE</u>
I. INTRODUCTION .....	1
A. Social Cognition in Schizophrenia .....	1
B. Neural Correlates of Social Cognition in Schizophrenia .....	4
1. Early visual processing .....	4
2. The social brain .....	5
3. Social cognition in schizophrenia: functional MRI findings .....	8
4. Social cognition in schizophrenia: structural MRI findings .....	9
C. The Current Study .....	10
1. Goals .....	10
2. Hypotheses .....	11
II. METHOD .....	11
A. Participants .....	11
B. Procedure .....	13
C. Data Acquisition .....	14
D. Data Analysis .....	14
1. Behavioral ratings .....	14
2. Functional MRI images .....	15
a. Whole-brain analyses .....	15
b. Region-of-interest analyses .....	16
III. RESULTS .....	16
A. Behavioral Ratings .....	16
B. Whole-Brain Analyses .....	17
C. Region-of-Interest Analyses .....	18
IV. DISCUSSION .....	19
CITED LITERATURE .....	29
IRB APPROVAL NOTICE .....	37
VITA .....	41

## LIST OF TABLES

<u>TABLE</u>		<u>PAGE</u>
I.	SAMPLE DEMOGRAPHICS FOR SCHIZOPHRENIA (SZ) AND HEALTHY CONTROL (HC) PARTICIPANTS .....	26

## LIST OF FIGURES

<u>FIGURE</u>		<u>PAGE</u>
1.	Average image arousal ratings for SZ and HC participants .....	27
2.	Brain response to affective (left) and neutral (right) social images, in healthy controls compared to schizophrenia patients .....	28

## **SUMMARY**

Individuals with schizophrenia evidence deficits in social functioning such as difficulties in communication, maintaining employment, and functioning as a member of the community. Impairment in functions such as these has been linked with higher order social cognitive deficits, which, in turn, have been associated with abnormalities in brain structure and function. However, it is unclear whether brain abnormalities are found specifically for higher order social cognitive functioning, or whether “lower order” social processing, such as perceiving social stimuli, might demonstrate abnormalities at the neural level. The current study used functional magnetic resonance imaging to explore the neural correlates of social perception in schizophrenia. Individuals with schizophrenia and healthy comparison participants were presented with social (i.e., faces, people) and nonsocial (i.e., scenes, objects) images that varied in affective content (emotional, neutral). Schizophrenia patients showed increased brain activation, compared to controls, in occipital lobe regions associated with early visual processing in response to emotional and neutral social images. They also failed to show prefrontal deactivation that was present in controls in response to neutral social images, which may reflect abnormal default mode activity. Results indicate aberrant neural response during early stages of visual processing of social information, which may contribute to higher order social cognitive deficits characteristic of this population.

## **I. INTRODUCTION**

Schizophrenia is a severe and chronic psychiatric disorder characterized by distinct positive (e.g., hallucinations, delusions) and negative (e.g., flat affect, poor motivation) symptoms as well as significant social and occupational dysfunction. Impaired social functioning has long been considered a core feature of the illness and is required for a diagnosis (American Psychiatric Association, 1994). Specifically, social impairment is defined by the Handbook of Social Functioning in Schizophrenia as “the inability of individuals to meet societal defined roles such as homemaker, worker, student, spouse, family member or friend. In addition, individuals’ satisfaction with their ability to meet these roles, their ability to care for themselves and the extent of their leisure and recreational activities are often subsumed under the rubric of social functioning” (Mueser & Tarrier, 1998; p. xi). Accordingly, individuals with schizophrenia often withdraw from social contact, and when they do interact with others, tend to have less effective social interactions and poorer social skills, particularly in terms of conversational ability and self-assertion (Mueser & Bellack, 1998); in addition, schizophrenia patients show lower levels of employment (Marwaha & Johnson, 2004) and reduced quality of life (Pinikahana, Happell, Hope, & Keks, 2002). Social dysfunction is evident prior to the onset of psychosis (Davidson, Reichenberg, Rabinowitz, Weiser, Kaplan, & Mark, 1999), persists throughout the course of the disorder (Addington & Addington, 2000), and predicts inpatient status (Perlick, Stastny, Mattis, & Teresi, 1992).

### **A. Social Cognition in Schizophrenia**

To investigate possible factors contributing to social dysfunction in schizophrenia, research has examined social cognition, specifically focusing on the mental processes underlying social perception, interpretation and response to the intentions and dispositions of others

(Brothers, 1990; Fiske & Taylor, 1991; Kunda, 1999). Results indicate widespread social cognitive deficits associated with schizophrenia that have been broadly categorized into five domains: theory of mind, attribution bias, emotion processing, social knowledge, and social perception (Green, Penn, Bentall, Carpenter, Gaebel, & Gur, et al., 2008).

First, individuals with schizophrenia show impaired ability to infer other people's intentions, dispositions, and beliefs, as assessed with Theory of Mind (ToM) tasks. Studies report significant ToM deficits despite absence of acute psychosis, suggesting ToM impairment may be a trait rather than state characteristic of the illness (Bora, Yucel, & Pantelis, 2009). Second, some schizophrenia patients exhibit abnormal attribution styles, and thus make errors in inferring the causes of positive or negative behaviors. Paranoid patients have been shown to make more external personal attributions for negative events than healthy controls (Craig, Hatton, Craig, & Bentall, 2004; Kaney & Bentall, 1989; Kinderman & Bentall, 1997), depressed (Candido & Romney, 1990; Kaney & Bentall, 1989; Kinderman & Bentall, 1997), or Asperger's (Craig et al., 2004) patients, though attribution bias also appears to vary based on delusion content (Jolley, Garety, Bebbington, Dunn, Freeman, & Kuipers, et al., 2006; Sharp, Fear, & Healy, 1997; Silverman & Peterson, 1993).

The third domain of social cognitive deficits, emotion processing, refers to perceiving, using, and expressing emotions, and is also impaired in schizophrenia. Accurate emotion recognition is necessary for successful social interactions, and misinterpretation of facial emotional expression has been hypothesized to be a key contributor to delusions of persecution and social withdrawal in schizophrenia (Frith, 1992). Individuals with schizophrenia have difficulty accurately perceiving and recognizing facial expressions of emotion (for review, see Tremeau, 2006). They also exhibit impaired processing of faces in general, specifically in



discriminating between or matching faces and recognizing faces as familiar (for review, see Marwick & Hall, 2008). However, it remains to be clarified whether such deficits reflect faulty early visual processing in general or whether there are more specific deficits in visual processing of faces.

Fourth, people with schizophrenia exhibit deficits in understanding the roles, rules, and goals of social situations, abilities collectively referred to as social knowledge (Addington, Saeedi, & Addington, 2006; Cutting & Murphy, 1988, 1990). Impaired social knowledge has been associated with neuropsychological deficits (McEvoy, Hartman, Gottlieb, Godwin, Apperson, & Wilson, 1996) as well as poor quality of life and decreased social initiation in this population (Matsui, Sumiyoshi, Arai, Higuchi, & Kurachi, 2008). Lastly, schizophrenia patients have difficulties with social perception, or the ability to use social cues to infer situational events and identify social roles, societal rules, and social context (e.g., Addington et al., 2006; Monti & Fingeret, 1987; Toomey, Schuldberg, Corrigan, & Green, 2002). Social perception appears to be influenced by abnormalities in early aspects of visual processing in individuals with schizophrenia (Corrigan, Green, & Toomey, 1994; Sergi & Green, 2002; Sergi, Rassovsky, Nuechterlein, & Green, 2006), and one prior study found that social perception mediated the relationship between impaired early visual processing and social functioning in schizophrenia patients (Sergi et al., 2006).

Extant research indicates deficits in social functions requiring goal-oriented, effortful cognitive processing, such as reasoning, judging, and making inferences. Despite this body of research demonstrating higher order social cognitive impairment in schizophrenia, it is unclear whether lower order social processing (i.e., viewing social stimuli) might also be abnormal, and account for impaired functioning in this population. A biological approach could clarify this

important question by identifying the neural correlates of social perception and examining whether they differ from those of healthy individuals. The current study employed functional neuroimaging techniques to assess differences in activity in brain regions engaged during early visual processing, which are expected, in turn, to contribute to abnormalities in perception of social (i.e., faces, people) in contrast to nonsocial (i.e., scenes, objects) images.

## **B. Neural Correlates of Social Cognition in Schizophrenia**

To better understand the biological bases of impaired social cognition, recent research has turned to neuroimaging techniques. Studies have employed functional magnetic resonance imaging (fMRI) to evaluate whether neural activity associated with social cognition differs between schizophrenia patients and healthy individuals, and structural MRI to examine regional volumes in brain structures that support social cognition. Such neuroimaging studies have revealed an array of differences in both brain structure and function in individuals with schizophrenia compared to healthy controls. Before detailing brain abnormalities that may contribute to social cognitive dysfunction in schizophrenia, it is first necessary to review brain structures involved in early visual processing and social information processing.

### **1. Early visual processing.**

Visual information first enters the brain from the optic nerve via the lateral geniculate nucleus in the thalamus, then is sent to visual cortical area V1, in the occipital lobe. Processing concerning object spatial location proceeds via the dorsal “where” pathway, while information about object and form representation is sent to the ventral “what” pathway, moving ventrally and anteriorly through the occipital and temporal lobes (Ungerleider & Haxby, 1994). In the context of social perception, visual social information proceeds through the ventral stream during early visual processing, and then is sent to regions such as the prefrontal cortex when higher order

cognitive processing is necessary. Research has shown that face processing occurs in the ventral stream, and location of activation depends on task, suggesting a hierarchical organization of the ventral stream (Ungerleider & Haxby, 1994). Specifically, faces may activate the thalamus, fusiform, temporooccipital cortex, lingual gyrus and paracingulate gyrus (e.g., Dicther et al., 2009), while face and body stimuli additionally activate the superior temporal sulcus and middle occipital gyrus (Morris, Pelphrey, & McCarthy, 2006). The ventral stream may also be involved in perception of emotional stimuli, via significant connectivity with the amygdala (Murty, Richtey, Adcock, & LaBar, 2010). Thus, in the context of early visual processing, social and emotional information are processed in the ventral stream, including the thalamus, occipital, and temporal lobes.

## **2. The social brain.**

Following initial visual perception, social information is processed in what is known as “the social brain” for higher order cognitive processing. A network of interconnected and related, but specialized, brain structures is implicated in social cognition: the medial prefrontal cortex, anterior cingulate, fusiform gyrus, superior temporal sulcus, temporo-parietal junction, middle occipital gyrus, parahippocampal gyrus, amygdala, and thalamus. Medial regions of the PFC (mPFC) are thought to subserve high-level social cognitive processes such as inferring others’ beliefs and emotions (Van Overwalle, 2009). The mPFC has also been associated with encoding emotional (Phan, Wager, Taylor, & Liberzon, 2002) and social (Adolphs, 1999; Harvey, Fossati, & Lepage, 2007) stimuli as well as social reasoning and decision-making (Adolphs, 1999). Within the mPFC, the anterior cingulate has been identified as a specific structure implicated in social cognition, particularly in acquiring and using social information to guide decisions

(Rushworth, Buckley, Behrens, Walton, & Bannerman, 2007). Thus, the mPFC appears to be involved in a variety of higher order social cognitive processes.

In addition to frontal lobe structures, temporal regions are also associated with social cognitive functions. The fusiform gyrus is activated during perception of human beings (e.g., Harvey et al., 2007) and may also be sensitive to emotional influences, as one study reported greater fusiform activation to emotional than neutral visual stimuli (Geday, Gjedde, Boldsen, & Kupers, 2003). The superior temporal sulcus (STS) also has a specialized role in social processing; specifically, the STS detects biological motion, a function relevant to understanding intentions of others (Grossman & Blake, 2002; Puce & Perrett, 2003). It is also activated while viewing images of people (Harvey et al., 2007). Temporal lobe boundaries with the parietal and occipital lobes also appear to be strongly involved in processing social information. The temporo-parietal junction (TPJ) is consistently activated in higher order mentalizing tasks. In addition to theory of mind (e.g., Aichhorn, Perner, Weiss, Kronbichler, Staffen, & Ladurner, 2009; Gobbini, Koralek, Bryan, Montgomery, & Haxby, 2007), studies have reported TPJ response to spatial orientation between people (Abraham, Werning, Rakoczy, von Cramon, & Schubotz, 2008), moral judgment (Young & Saxe, 2008) and social inference (Van Overwalle & Baetens, 2009).

Regions of the occipital lobe, commonly activated by emotional stimuli, may also respond to social stimuli. Because of its involvement in early stages of visual processing, the occipital lobe may be sensitive to lower order social information processing involved in social perception. In support of this notion, studies have found occipital activation during gaze monitoring (Kuzmanovic, Georgescu, Eickhoff, Shah, Bente, & Fink, et al., 2009), detection of faces (Dichter, Felder, Bodfish, Sikich, & Belger, 2009), and orienting to social cues (Greene,

Mooshagian, Kaplan, Zaidel, & Iacoboni, 2009). Furthermore, one study found increased middle occipito-temporal blood-oxygen-level-dependent (BOLD) response to social compared to nonsocial images, particularly for emotional images (Norris, Chen, Zhu, Small, & Cacioppo, 2004).

In addition to cortical regions, subcortical structures have also been implicated in social processing. The amygdala has long been recognized as a core structure involved in processing emotional information, particularly negative affect, and has more recently been implicated in social cognition. Studies typically find greater amygdala activation to negative than neutral or positive stimuli (e.g., Lane, Reiman, Bradley, Lang, Ahern, & Davidson, et al., 1997; Straube, Pohlack, Mentzel, & Miltner, 2008; Zald & Pardo, 1997). The amygdala is also activated during detection of eye gaze (Kawashima, Sugiura, Kato, Nakamura, Hatano, & Ito, et al., 1999), social judgment of faces (Adolphs, 1999), and evaluation of trustworthiness in faces of unknown people (Winston, Strange, O'Doherty, & Rolan, 2002). These findings suggest that the amygdala may extract emotional meaning from social information. The basal ganglia and thalamus have also been found to be active during facial emotion processing (for review, see Adolphs, 2002). In addition, one study reported thalamic activation in response to perceiving faces compared to shapes (Dichter et al., 2009). Due to its role in early visual processing, thalamic activation during social processing suggests that social stimuli are perceived differently than nonsocial stimuli during initial sensory perception.

There is also some direct evidence of overlap between social and emotional processing. Some have argued that social stimuli are inherently emotional, so processing social information necessarily involves regions of emotion networks; to test this hypothesis, one study presented images varying in social and emotional content to healthy individuals, and found increased brain

activation in the amygdala, medial prefrontal cortex, inferior frontal gyrus, superior temporal sulcus, and middle occipito-temporal cortex in response to social compared to nonsocial images, though superior temporal and middle occipito-temporal clusters were qualified by interactions with emotional content (Norris et al., 2004). The authors suggested interactions between social and emotional displays occur in early stages of visual processing, and function to increase attentional resources and enhance processing. Another study presented images varying in emotional and social complexity and found interactive effects in the fusiform, inferior occipital, and medial frontal gyri (Geday et al., 2003). Thus, it appears that emotional content affects processing of visual social stimuli, so it is important to consider the influence of emotion on social factors in the current study.

### **3. Social cognition in schizophrenia: functional MRI findings.**

Neuroimaging studies have begun to elucidate the neural correlates of impaired social cognition in schizophrenia. Studies assessing brain activation during ToM tasks have found differences in BOLD response between healthy and schizophrenia participants in frontal and temporal lobe regions; however, the direction of activation differences are mixed (Benedetti, Bernasconi, Bosia, Cavallaro, Dallaspezia, & Falini, et al., 2009; Brune, Lissek, Fuchs, Witthaus, Peters, & Nicolas, et al., 2008; Russell, Rubia, Bullmore, Soni, Suckling, & Brammer, et al., 2000; Walter, Ciaramidaro, Adenzio, Vasic, Ardito, & Erk, et al., 2009), suggesting a complex relationship between brain activation and social deficits that may vary with task and patient characteristics. One recent study of attribution bias reported decreased patient BOLD response, compared to controls, in the amygdala and frontal lobe regions while participants inferred the situational causes of happy avatars, but increased patient BOLD response in cerebellar and posterior cingulate/precuneus regions during situation inference of angry avatars (Park, Kim, Ku,

Kim, Lee, & Kim, et al., 2009), suggesting differences in the way patients interpret emotional behaviors of others. The neural basis of abnormalities in identification of facial emotional expressions has received significant attention. Studies of facial expression processing largely implicate the amygdala as a region of dysfunction in schizophrenia, with mixed findings regarding direction of activation differences between groups (Gur, McGrath, Chan, Schroeder, Turner, & Turetsky, et al., 2002; Hempel, Hempel, Schonknecht, Stippich, & Schroder, 2003; Holt, Kunkel, Weiss, Goff, Wright, & Shin, et al., 2006; Kosaka, Omori, Murata, Iidaka, Yamada, & Okada, et al., 2002; Phillips, Williams, Senior, Bullmore, Brammer, & Andrew, et al., 1999). Taken together, these findings suggest dysfunction broadly in amygdala, frontal and temporal lobe regions, in a variety of social cognitive tasks and argue for the importance of examining these regions in the current study.

#### **4. Social cognition in schizophrenia: Structural MRI findings.**

In addition to the previously discussed functional abnormalities, structural brain alterations exist in schizophrenia patients that may contribute to impaired social cognition. In addition to decreased whole brain volume, schizophrenia patients show volumetric reductions in the prefrontal cortex (Shenton, Dickey, Frumin, & McCarley, 2001), thalamus (Konick & Freidman, 2001), anterior cingulate (Baiano, David, Versace, Churchill, Balestrieri, & Brambilla, 2007), and temporal regions including the hippocampus, amygdala, and superior temporal gyri (Lawrie & Abukmeil, 1998; Nelson, Saykin, Flashman, & Riordan, 1998). Voxel-based morphometry studies support region-of-interest findings, reporting reduced gray matter density in prefrontal and temporal regions, anterior cingulate, thalamus and fusiform gyrus (Honea, Crow, Passingham, & Mackay, 2005). Of note, these regions that show structural differences overlap with those that show functional aberrance, providing further support for neural

abnormalities underlying social cognitive processes. Given that volumetric reductions and functional abnormalities have been reported in virtually every brain structure described in the social brain, it is not surprising that schizophrenia patients exhibit profound deficits in social functioning.

### **C. The Current Study**

Though several studies have examined higher order social cognition and its neural correlates, the brain basis of simple social perception (i.e., neural response to viewing images with human content) in this population remains underinvestigated. Studies have examined neural response to perception of faces, but not to complex social scenes that include both affective and contextual information that would influence interpretation of affective displays. In addition, studies of face perception have typically focused on identification of affective expression, rather than emotional or social responses to such stimuli. Therefore, a next step in the field is to determine brain response during perception of social information, and further, to assess how this is influenced by emotional factors. Abnormal perception of social stimuli in early stages of sensory processing would necessarily influence information available for higher order aspects of social cognition and other later social processes. Therefore, understanding the neural correlates of social perception (i.e., viewing images with social content) in schizophrenia is an important research goal.

#### **1. Goals.**

In the current study, we used images from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2005) to assess the ability of individuals with schizophrenia to encode social stimuli. The IAPS is a widely-used library of images that includes emotionally-valenced and neutral pictures that vary on human content. The IAPS has typically been used in



research on emotion but more recently has also been used to explore social perception and cognition. The current study aimed to identify neural correlates of early aspects of social perception in schizophrenia patients. Specifically, we compared brain response to viewing social versus nonsocial IAPS images in schizophrenia compared to control participants. Furthermore, images varied in affective content, enabling us to examine whether the effects of social content on brain response differ in affectively valenced or neutral images. The study employed both a whole-brain and region-of-interest approach to examine brain response in regions associated with social processing.

## **2. Hypotheses.**

We predicted between-group differences in BOLD response to initial perception of social compared to nonsocial images in regions of the social brain previously outlined. Our main hypothesis predicted reduced BOLD response in schizophrenia participants in brain regions associated with early visual processing, including the occipital lobe and the thalamus, in response to social compared to nonsocial images. Because effects in early processing regions may contribute to higher order processing abnormalities, and participants rated emotional response to images online, we also expected patient hypoactivation in regions implicated in higher order social cognition and face processing, including the medial prefrontal cortex, anterior cingulate, temporo-parietal junction, superior temporal sulcus. Given the literature indicating patient medial temporal hyperactivation in response to neutral images, we believed affective valence would moderate effects in the amygdala, fusiform, and parahippocampal gyrus.

## **Method**

### **Participants**

Study participants included individuals meeting *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV*; American Psychiatric Association, 1994) criteria for schizophrenia or schizoaffective disorders (n=14) and healthy controls (n=14). Schizophrenia participants were recruited from ads in the community, special interest web sites (National Alliance on Mental Illness, National Institutes of Health), and physician referral. Healthy controls were recruited via ads in the community and were matched to schizophrenia participants on the basis of age, sex, ethnicity, years of education, and intelligence. Exclusionary criteria included history of head trauma with loss of consciousness longer than 15 minutes, substance abuse or dependence within the past 6 months, or neurological or systemic disease. Diagnoses for all participants were established with the Structured Clinical Interview for *DSM-IV* diagnosis (First, Spitzer, Gibbon, & Williams, 1997). Severity of symptoms was rated by a clinician blind to individuals' task performance with the Positive and Negative Syndrome Scale (Kay, Fiszbein, & Opler, 1987). Schizophrenia participants were clinically stable outpatients and had been on a stable medication regimen for a minimum of 4 weeks prior to testing. Participants were asked to avoid caffeine and tobacco for at least two hours prior to the neuroimaging session. All participants completed the Wide Range Achievement Test, 3<sup>rd</sup> ed. (WRAT; Wilkinson, 1993), a measure of estimated premorbid intelligence, and the Wechsler Abbreviated Scale of Intelligence, 3<sup>rd</sup> ed. (WASI; Wechsler, 1999), a measure of current intelligence. See Table 1 for participant demographics.

Written informed consent was obtained via protocols approved by the University of Illinois at Chicago Institutional Review Board. Participants received financial compensation for their time participating in the research. General exclusionary criteria included a history of head trauma with loss of consciousness greater than 15 minutes, contraindication for MRI scanning

(e.g., metallic implants in the body), claustrophobia, or serious medical conditions that could influence brain activity or blood flow (e.g., epilepsy).

## **Procedure**

To acclimate participants to the MRI scanner and prevent gross movement, participants completed a mock scan session prior to the neuroimaging session. During the scan, participants viewed and rated the intensity of their emotional responses to emotional and neutral images. Positive, negative, and neutral images were selected from the IAPS library (Lang et al., 2005). Positive and negative images were equated on arousal, and were rated as more arousing than neutral images, based on the IAPS normative data. Positive, negative, and neutral images also differed by valence ratings (Lang et al., 2005). Images were equated on human content such that half of the images in each valence contained human content. Social images were defined as pictures that contained at least one human being, while nonsocial images were void of any human content. Emotional images were collapsed across valence, including positive and negative images. Extreme images were excluded so the task would be less disturbing to participants and because they would threaten the ecological validity of the study as they are not representative of daily functioning. Across the four conditions (emotional/social, neutral/social, emotional/nonsocial, neutral/nonsocial), images did not differ in average valence, hue, or saturation. Neutral social images were significantly lower in luminance, complexity, and red, blue, and green intensity than the other three conditions ( $p$ 's < .05), which were not different from each other.

During the task, participants viewed 108 IAPS images (24 positive/social, 12 positive/nonsocial, 24 negative/social, 12 negative/nonsocial, 24 neutral/social, 12 neutral/nonsocial). Images were presented in blocks of 12 of each condition, for a total of 9

blocks. Each image was presented for 4 seconds, and 10 second rest periods were included between blocks to allow brain activation to return to baseline before the subsequent block. During the presentation of each image, subjects rated the intensity of their emotional response to the image, either low (none to low) or high (moderate to strong), via button press.

### **Data Acquisition**

Structural and functional scans were acquired on a 3 Tesla scanner (Signa, General Electric Medical System, Milwaukee, Wisconsin) at the University of Illinois at Chicago Medical Center. The acquisition protocol for the encoding functional scan was a gradient-echo echo-planar imaging (EPI) series with TR = 2000ms, TE = 25ms, flip angle = 90 degrees, field of view = 200mm, matrix = 64mm x 64mm, slice thickness = 3mm, gap = 1mm, for 33 axial slices. High-resolution anatomical brain scans were collected for co-registration with functional images. The acquisition protocol for the structural data was a spoiled gradient recalled (SPGR) series with TR = 9.87ms, TE = 2.88ms, flip angle = 25 degrees, field of view = 240mm, matrix = 256mm x 256mm, slice thickness = 1.5mm, no gap, for 120 slices.

### **Data Analysis**

#### **Behavioral ratings.**

Between-group differences in ratings of emotional response to the stimuli were examined using repeated measures ANOVA, with social (social, nonsocial) and emotional content (emotional, neutral) as within-subject factors, and group (SZ, HC) as the between-subjects factor. We specifically examined main effects of group and social content, as well as social x emotion, social x group, and social x emotion x group interactions. Two subjects were excluded from behavioral analyses: one SZ patient, due to difficulty using the button box, and one HC participant, due to poor understanding of the task instructions.

### **Functional MRI images.**

fMRI data were processed using public domain Analysis of Functional Neuroimages (AFNI) software (<http://afni.nimh.nih.gov/afni/>). AFNI's 3D volume registration program was used to detect and correct for motion across individual participants' time series. Individual data were spatially smoothed using a 5mm full-width half-maximum Gaussian filter, and then were deconvolved to obtain per-voxel fit coefficients corresponding to BOLD response for each condition (social/emotional, social/neutral, nonsocial/emotional, nonsocial/neutral). Next, images were normalized to stereotaxic space (Talairach & Tournoux, 1988) to correct for individual neuroanatomical variation and resampled to the original acquisition size of  $3 \times 3 \times 3 \text{ mm}^3$  voxels.

For the whole brain analysis, a combined voxel contiguity-significance level threshold was used to detect brain-wise activity at the  $p < .05$  level. AFNI's AlphaSim was used to determine the size of the cluster threshold, using a 5.98mm connectivity radius to define areas of contiguous activation. We required  $1296 \text{ mm}^3$  contiguous voxels significant at the  $p < .01$  level for whole-brain significance of  $p < .05$ . Neuroanatomical locations of activation surviving threshold were identified using Talairach Daemon software (Lancaster, Woldorff, Parsons, Liotti, Freitas, & Rainey, et al., 2000).

### *Whole-brain analyses.*

Our initial analyses focused on assessing whether emotional salience and social content differentially engaged brain activity in SZ and HC participants. Specifically, we tested between-group differences in BOLD response in social versus nonsocial conditions. We used mixed-effects analysis of variance (ANOVA), with group (SZ, HC) and social content (social, nonsocial) as fixed factors and subject as a random factor, separately for affective and neutral images. Between-group contrasts compared brain response between groups within each of the

four conditions (emotional/social, emotional/nonsocial, neutral/social, neutral/nonsocial). Next, to explore the hypothesis that social and emotional factors may have an interactive effect, a mixed-effects ANOVA was conducted within each group, with social content (social, nonsocial) and emotional content (emotional, neutral) as fixed factors and subject as a random factor.

#### *Region-of-interest analyses.*

Region-of-interest (ROI) analyses examined brain activity in regions of the social brain: medial prefrontal cortex, anterior cingulate, temporo-parietal junction, superior temporal sulcus, middle occipital gyrus, thalamus, amygdala, fusiform gyrus, and parahippocampal gyrus. ROIs based on anatomical structures are available on AFNI and were applied to individual subject data. Average intensity values in each ROI were calculated using AFNI's 3dROIstats and entered into the previously described ANOVAs, with the addition of brain hemisphere as a within-subject factor to probe possible hemisphere effects. In order to constrain type one error, contrasts of interest relating to between-group and social content effects were specified *a priori*, whereas effects of hemisphere or emotion, collapsed across group or social content, were not of theoretical interest and thus were not examined.

## **Results**

### **Behavioral Ratings**

Two interactions at trend level were observed. We found an Emotion x Group trend ( $p = .055$ ; partial  $\eta^2 = 0.145$ ), indicating that SZ subjects tended to report more arousal in response to neutral images than HC subjects. Second, we observed an Emotion x Social trend ( $p = .073$ ; partial  $\eta^2 = 0.128$ ), suggesting that emotional social images were rated as more arousing than emotional nonsocial images, while neutral social were rated similarly to neutral nonsocial images. See Figure 1.

## Whole-Brain Analyses

A whole-brain approach was taken to investigate regions of BOLD response differences between group, emotion, and social content. Specifically, we used analysis of variance to probe Group x Social interactions within affective valence, and Emotion x Social interactions within group, and these interactions were not significant. Between-group contrasts were written to determine whether brain activation differed between groups in any of the four conditions. Results indicated differences between SZ and HC participants during perception of emotional social and neutral social images, but not emotional or neutral nonsocial images, consistent with our hypothesis of altered patient brain response to social images. In the contrast comparing HC and SZ BOLD response to emotional social images, two clusters were found: 1) one with peak activation in the right lingual gyrus, spanning right posterior cingulate, cuneus, cerebellum, and parahippocampal gyrus, and 2) one with peak activation in the left lingual gyrus, spanning left posterior cingulate, cuneus, cerebellum, and middle occipital gyrus. In both clusters, patients showed greater brain activation than controls. In the contrast comparing HC and SZ BOLD response to neutral social images, two clusters were found: 1) one with peak activation in the right precuneus, extending to the right cuneus, and 2) one with peak activation in the right superior frontal gyrus, extending to the left superior frontal gyrus, bilateral medial frontal gyri, and bilateral anterior cingulate. In both clusters, BOLD response was greater in patients than controls. Results were confirmed with t-tests comparing emotional social and neutral social conditions to fixation, in patients compared to controls. See Figure 2.

Next, to determine the nature of the observed between-group effects, within-group t-tests were computed comparing emotional social and neutral social conditions to fixation, e.g., schizophrenia emotional social - fixation. Results indicated that both between-group clusters in

the emotional social condition were driven by higher patient than control activation compared to fixation. In the neutral social condition, the posterior cluster was driven by higher patient than control activation compared to fixation, while the frontal cluster was driven by greater control deactivation than patient deactivation compared to fixation.

### **Region-of-Interest Analyses**

Because the whole-brain approach requires areas of large contiguous activation, region-of-interest analyses were also performed to better examine smaller brain regions, and to allow for inclusion of effects of group, brain hemisphere, social content, and affective content in the statistical model. To limit the possibility of type one error, only effects concerning social content and group were examined. Significant effects of social content and/or group were noted in the medial frontal, fusiform, and middle occipital gyri. First, in the medial frontal gyrus, a Group x Hemisphere interaction ( $p = 0.016$ ; partial  $\eta^2 = 0.202$ ) revealed significant group effects in the left but not right hemisphere. Follow-up comparisons indicated that SZ patients showed higher activation (or less deactivation) than HC participants in response to neutral images in the left medial frontal gyrus ( $p = 0.017$ ; partial  $\eta^2 = 0.199$ ), though both groups showed deactivation compared to baseline. Second, in the fusiform gyrus, a main effect of social content was present ( $p = 0.004$ ; partial  $\eta^2 = 0.283$ ), that was qualified by a Social x Emotion x Hemisphere interaction ( $p = 0.014$ ; partial  $\eta^2 = 0.211$ ). As with the medial frontal gyrus, activation within each condition was lower than baseline, indicating task-related deactivation. Follow-up comparisons showed greater deactivation to nonsocial than social images in both the emotional ( $p = 0.019$ ; partial  $\eta^2 = 0.195$ ) and neutral conditions, though only in the right hemisphere of the neutral condition ( $p = 0.002$ ; partial  $\eta^2 = 0.308$ ). Third, a Group x Social x Emotion x Hemisphere interaction was revealed in the middle occipital gyrus ( $p = 0.028$ ; partial  $\eta^2 =$



0.172). Follow-up comparisons indicated an effect of emotion on perception of social images in the left hemisphere, such that brain activity was greater to emotional than neutral social images ( $p = 0.044$ ; partial  $\eta^2 = 0.147$ ). There were no significant main or interaction effects of social content or group in the thalamus, amygdala, superior temporal gyrus, parahippocampal gyrus, or temporo-parietal junction ( $p$ 's  $> 0.05$ ).

## **Discussion**

The current study aimed to identify the neural correlates of social perception in schizophrenia and determine whether regions of activation associated with social perception differ from those of healthy individuals. Furthermore, we investigated whether affective valence moderated BOLD response to social perception. We hypothesized that schizophrenia patients would show decreased brain activation in response to social versus nonsocial images, compared to healthy controls, in the thalamus and occipital regions associated with early visual processing. We also expected differences in other higher order social and face processing regions: medial prefrontal cortex, anterior cingulate, temporo-parietal junction, superior temporal sulcus, amygdala, fusiform gyrus, and parahippocampal gyrus. Whole-brain and region-of-interest (ROI) approaches were both used in order to allow for examination of the entire brain as well as smaller regions that may not be detected in whole-brain analyses.

Results of the study indicate differences in brain activation between schizophrenia patients and healthy individuals during the perception of social, but not nonsocial, visual stimuli. Furthermore, affective salience moderated this effect. In contrast to our predictions of lower levels of brain activity in schizophrenia than control subjects in response to social stimuli, we found patient hyperactivation in posterior cortical regions, including the lingual, parahippocampal and middle occipital gyri, precuneus, and cuneus, that was more widespread

for affective than neutral images. These between-group differences were driven by patient increased BOLD response compared to baseline. ROI analyses corroborated increased middle occipital activation in response to affective versus neutral social images, though between-group differences failed to reach significance.

Past research on healthy populations indicates higher middle occipito-temporal cortical activation to social compared to nonsocial images (Norris et al., 2004), as well as higher and more widely distributed visual cortex activation in response to emotional versus neutral images (Lane et al., 1997; Lang, Bradley, Fitzsimmons, Cuthbert, Scott, & Moulder, et al., 1998). Of note, these occipital regions are involved in early stages of processing and may function to garner increased attention to salient information. Norris et al. (2004) suggested increased visual cortical response to emotional social images may reflect natural selective attention, or increased allocation of neural resources to stimuli with survival significance. That patients show more activation than controls may suggest increased assignment of social relevance early in the processing stream, particularly for affectively valenced information. However, the neutral social images in our study had lower ratings of visual qualities such as image complexity and color intensity, which may have contributed to the findings of smaller regions of activation, compared to the affective social condition. Our pattern of results of patient occipital hyperactivation may also relate to findings of increased patient medial temporal activation to neutral faces (Hall, Whalley, McKirdy, Romaniuk, McGonigle, & McIntosh, et al., 2008; Holt et al., 2006; Surguladze, Russell, Kucharska-Pietura, Travis, Giampietro, & David, et al., 2006), that are interpreted to reflect abnormal attributions of motivational salience of neutral stimuli (Kapur, 2003).

We also found differences in brain response between patients and controls during social perception in prefrontal regions, including the bilateral superior frontal and medial frontal gyri and anterior cingulate, but only for neutral and not affective images. Results were driven by deactivation in controls, and this deactivation was not present in patient participants. That is, controls showed significantly greater BOLD response at baseline than during perception of neutral social images. We believe this task-induced deactivation reflects default-mode activity. The default mode network (DMN), proposed by Raichle and colleagues (2001), is a network of brain regions that is active when an individual is alert but not engaged in attention-demanding tasks—for example, when an individual engages in passive visual fixation. When an individual engages in a task requiring focus, DMN activity decreases, resulting in “deactivation” of the DMN during task performance. The DMN includes two main major midline regions: the posterior cingulate/precuneus, responsible for gathering visual information, and the medial PFC, which monitors the interaction between cognitive and emotional processes. The cluster of deactivation noted in controls is consistent with the PFC DMN region.

Interestingly, both patients and controls showed similar midline PFC deactivation in response to affective social images, though this cluster was more superior than the HC cluster of deactivation in the neutral social condition. ROI results of the medial frontal gyrus were consistent with abnormal DMN activity in patients, with controls showing greater deactivation than patients across conditions. Research on the DMN in schizophrenia indicates aberrant DMN activity in this population (e.g., Garrity, Pearlson, McKiernan, Lloyd, Kiehl, & Calhoun, 2007; Harrison, Yucel, Pujol, & Pantelis, 2007; Mannell, Franco, Calhoun, Canive, Thoma, & Mayer, 2010; Whitfield-Gabrieli, Thermenos, Milanovic, Tsuang, Faraone, & McCarley, et al., 2009), though findings are mixed regarding the nature of DMN differences in schizophrenia. Our results

suggest an absence of prefrontal DMN suppression in patients while rating their responses to neutral social stimuli, but similar activity to controls when the stimuli are affectively valenced or nonsocial in nature. These findings suggest that SZ patients differed from HC in showing less inhibition of their DMN activity specifically in response to neutral social images. Alternatively, the lack of difference in midline PFC activity between the neutral social condition and fixation could reflect SZ recruitment of PFC for interpretation of neutrally social stimuli. For example, prefrontal regions may be engaged more when schizophrenia subjects attempt to make sense of emotionally ambiguous human stimuli, in contrast to human stimuli in which emotion is more directly expressed. This hypothesis is consistent with our findings that SZ patients tended to rate neutral images as more emotionally arousing than controls, and past research suggesting patient medial temporal hyperactivation in response to neutral stimuli (Hall et al., 2008; Holt et al., 2006; Surguladze et al., 2006).

Though we found differences between groups as predicted in the medial PFC, anterior cingulate, parahippocampal gyrus, and middle occipital gyrus associated with perceiving social stimuli, our findings failed to support our hypothesis of patient hypoactivation in perceiving social compared to nonsocial stimuli. A lack of significant interactions between group and social content may be due to low power to detect differences, especially considering our modest sample size. We did find between-group differences in social but not nonsocial contrasts in the whole-brain analyses, so it is possible that with a greater sample size, significant interactions would emerge. Examination of effect sizes suggested that failure to find the neutral Social x Group interaction was likely due to low power, as the effect sizes for these interactions ranged from .25 to .29, which are in the small to medium range. In contrast, the effect sizes for the emotional

Social x Group interactions ranged from .08 to .11, which are in the very small to small range according to Cohen's criteria.

We also failed to find Social x Group interactions in the fusiform gyrus, superior temporal gyrus, temporo-parietal junction (TPJ), amygdala, and thalamus. These regions may be intact in patients during perception of social images, or may not have been recruited by our task. Given the small Social x Group interaction effect sizes in the ROI analyses of these regions, it is not likely that null findings are due to low power. Past findings regarding the fusiform gyrus are mixed, and our results are consistent with Yoon et al. (2006), who observed intact fusiform function in patients during facial perception. While the superior temporal sulcus may respond to images of people (e.g., Harvey et al., 2007), its role is largely in detecting biological motion (e.g., Puce & Perrett, 2003); in our study, neither patients nor controls showed STS activation, which may be due to our stimuli being still images. Similarly, neither group showed amygdala or TPJ activity during social perception, which may be due to the simplicity of our task; amygdala involvement in social cognition has been noted in higher order social evaluative functions, such as judgment of trustworthiness (Winston et al., 2002), while TPJ activity is largely implicated in theory of mind. Lastly, we failed to find group differences in the thalamus, though healthy controls showed thalamic deactivation during social perception while patients did not; furthermore, a trend-level 4-way interaction was observed in the thalamus in our ROI analysis, so lack of between-group differences in the thalamus may be due to low power.

Although these findings contribute to our understanding of social perception in schizophrenia, the following limitations must be considered. First, we used a block design, which has inherent limitations due to reliance on the subtraction method. This method compares one task condition to another, but does not allow for determination of absolute baseline or absolute

task-related brain activity; that is, results indicate a *difference* in activity between task conditions and fixation, which does not necessarily reflect a *presence* of activity during the task. Next, we combined blocks of negative and positive images for our affective conditions. As such, we did not consider whether differences exist between perceiving positive social and negative social stimuli, for example. There is some evidence of valence-specific differences in emotional processing, as striatal deactivation in schizophrenia patients has been observed during perception of positive but not negative images, which is thought to be related to reward processing (Dowd & Barch, 2010). Future studies might examine specific valence effects. Also, in contrast to many studies using IAPS stimuli, our affective conditions excluded extreme images such as mutilated bodies or pornographic images in order to not upset our participants or decrease ecological validity; thus, our range of affective valence was restricted. More extreme images would likely elicit increased limbic brain response and perhaps lead to different results in the affective condition. Further, our patient sample was largely medicated and was heterogeneous in medication usage. It is possible that our results were influenced by psychotropic medication usage, both between groups and within the patient group. However, given that most schizophrenia patients in psychiatric care are treated with antipsychotic medication, this data provides important information about brain functioning in this group of individuals.

In sum, our findings provide evidence of occipital lobe dysfunction in schizophrenia patients during perception of social stimuli, suggesting aberrance in early stages of visual processing. Abnormalities early in the processing stream would likely influence information available for later social cognitive processes, such as attribution or social evaluation. A recent study found schizophrenia-related differences in brain activation during an emotion recognition task but not during an affective theory of mind task despite behavioral differences, supporting

the notion that lower order deficits affect higher order social cognitive processing; furthermore, the pattern of differences was consistent with our findings of patient hyperactivation, although in the medial temporal lobe (Mier, Sauer, Lis, Esslinger, Wilhelm, & Gallhofer, et al., 2010). We have identified brain functional abnormalities during initial social perception in schizophrenia that vary based on affective content. A next step is to determine the higher order cognitive or clinical effects of such dysfunction. Future studies should examine the relationship between abnormalities in brain activity in response to social stimuli in early visual processing areas and clinical symptoms and social functioning.

**TABLE 1****SAMPLE DEMOGRAPHICS FOR SCHIZOPHRENIA (SZ) AND HEALTHY CONTROL (HC) PARTICIPANTS**

	<i>SZ [M±SD]</i>	<i>HC [M±SD]</i>	<i>p</i>
<i>N</i>	14	14	
Age (years)	31.57±7.52	31.36±11.38	n.s.*
Sex (% female)	29	36	n.s.
Race (% African American)	50	71	n.s.
Years of Education	13.89±3.00	13.64±1.65	n.s.
Handedness (% right)	100	100	n.s.
WRAT	102.57±12.47	94.57±10.79	n.s.
WASI	104.43±12.74	99.50±14.87	n.s.
PANSS Positive	17.93±4.75		
PANSS Negative	17.36±5.81		
PANSS General	38.79±9.24		
<b>Medication</b>			
Number on Medication	11	0	
Typical Antipsychotics (N)	3	0	
Atypical Antipsychotics (N)	9	0	
Antidepressants (N)	4	0	
Stimulants (N)	0	0	
Mood Stabilizers (N)	1	0	
Sedative/Hypnotics (N)	2	0	

\*n.s.: nonsignificant,  $p > .05$

*Note.* WRAT: Wide Range of Achievement Test; WASI: Wechsler Abbreviated Scale of Intelligence; PANSS: Positive and Negative Syndrome Scale.



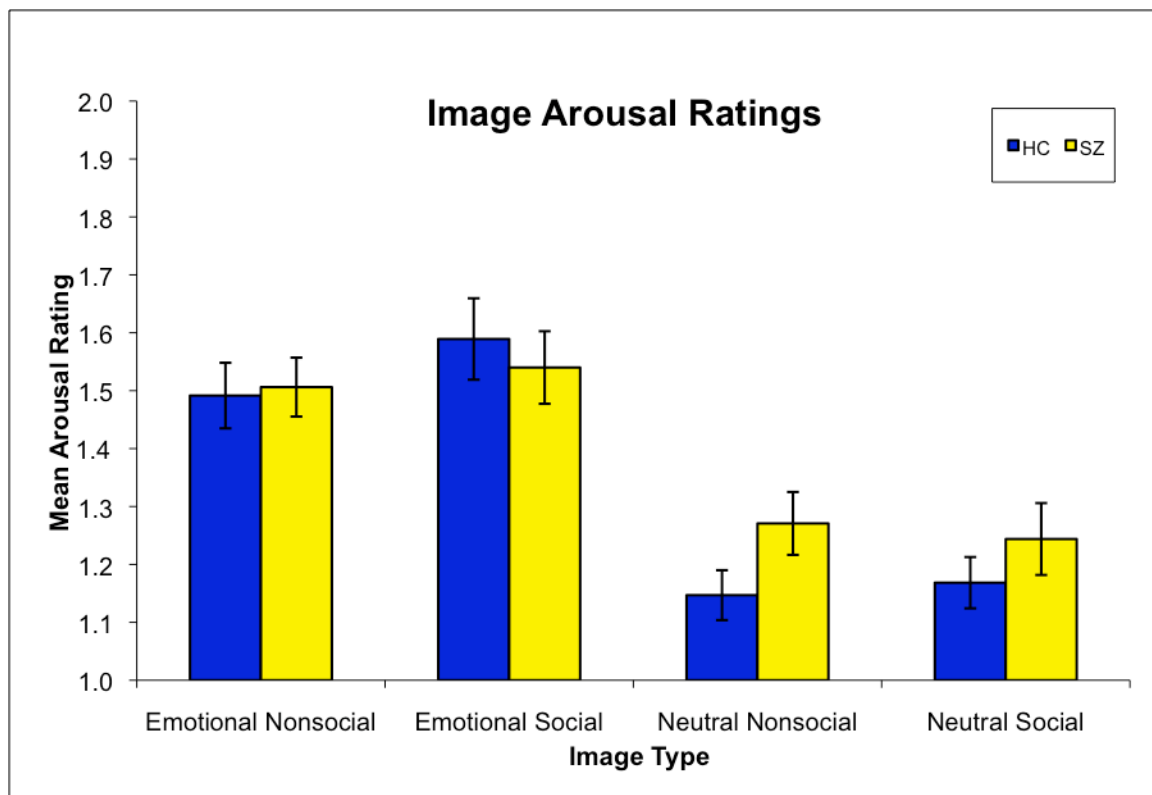


Figure 1. Average image arousal ratings for SZ and HC participants.

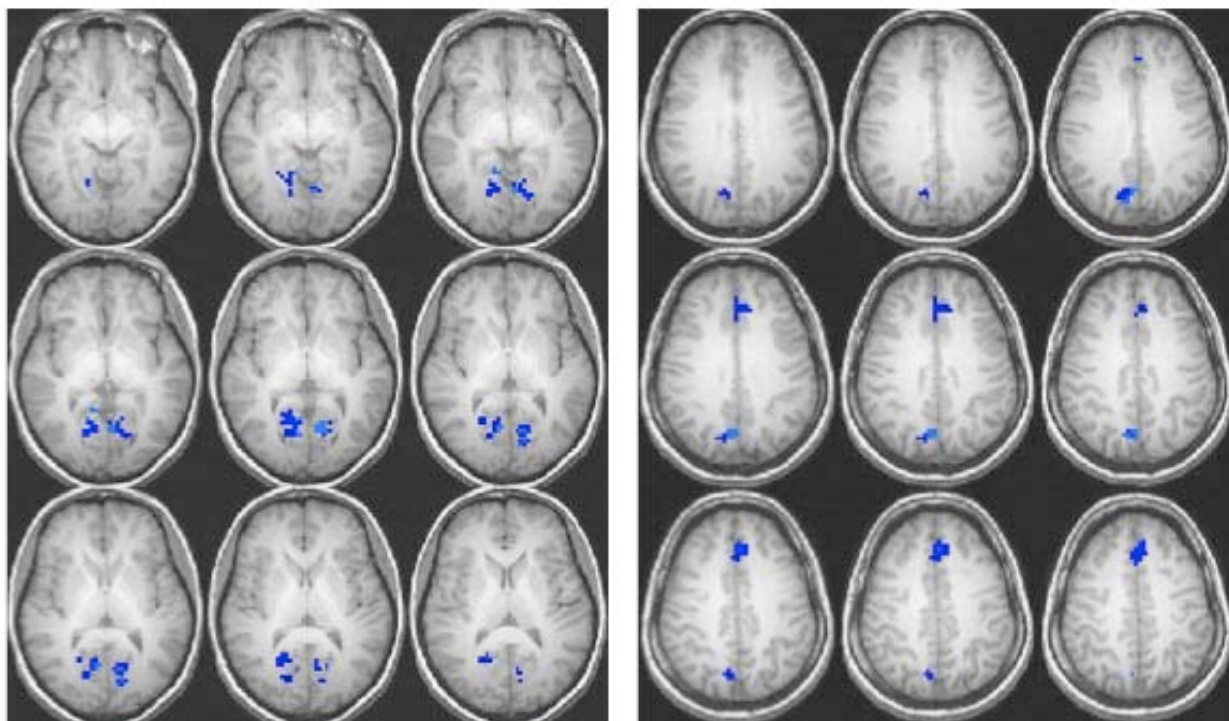


Figure 2. Brain response to affective (left) and neutral (right) social images, in healthy controls compared to schizophrenia patients. Blue indicates greater patient response. Z values range from -7 (top left) to 11 (bottom right), for affective (left panel) images; and from 30 (top left) to 44 (bottom right) for neutral (right panel) images.

## CITED LITERATURE

- Abraham, A., Werning, M., Rakoczy, H., von Cramon, D. Y., & Schubotz, R. I. (2008). Minds, persons, and space: An fMRI investigation into the relational complexity of higher-order intentionality. *Consciousness and Cognition*, 17(2), 438-450.
- Addington, J., & Addington, D. (2000). Neurocognitive and social functioning in schizophrenia: A 2.5 year follow-up study. *Schizophrenia Research*, 44, 47-56.
- Addington, J., Saeedi, H., & Addington, D. (2006). Influence of social perception and social knowledge on cognitive and social functioning in early psychosis. *The British Journal of Psychiatry*, 189, 373-378.
- Adolphs, R. (1999). Social cognition and the human brain. *Trends in Cognitive Sciences*, 3(12), 469-479.
- Adolphs, R. (2002). Recognizing emotion from facial expressions: Psychological and neurological mechanisms. *Behavioral and Cognitive Neuroscience Reviews*, 1(1), 21-62.
- Aichhorn, M., Perner, J., Weiss, B., Kronbichler, M., Staffen, W., & Ladurner, G. (2009). Temporo-parietal junction activity in theory-of-mind tasks: Falseness, beliefs, or attention. *Journal of Cognitive Neuroscience*, 21(6), 1179-1192.
- American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders* (4<sup>th</sup> ed.). Washington, DC: Author.
- Baiano, M., David, A., Versace, A., Churchill, R., Balestrieri, M., & Brambilla, P. (2007). Anterior cingulate volumes in schizophrenia: A systematic review and a meta-analysis of MRI studies. *Schizophrenia Research*, 93, 1-12.
- Benedetti, F., Bernasconi, A., Bosia, M., Cavallaro, R., Dallaspezia, S., Falini, A., Poletti, S., Radaelli, D., Riccaboni, R., Scotti, G., & Smeraldi, E. (2009). Functional and structural brain correlates of theory of mind and empathy deficits in schizophrenia. *Schizophrenia Research*, 114(1-3), 154-160.
- Bora, E., Yucel, M., & Pantelis, C. (2009). Theory of mind impairment in schizophrenia: Meta-analysis. *Schizophrenia Research*, 109, 1-9.
- Brothers, L. (1990). The social brain: A project for integrating primate behavior and neurophysiology in the new domain. *Concepts in Neuroscience*, 1, 27-51.
- Brune, M., Lissek, S., Fuchs, N., Witthaus, H., Peters, S., Nicolas, V., Juckett, G., & Tegenthoff, M. (2008). An fMRI study of theory of mind in schizophrenic patients with "passivity" symptoms. *Neuropsychologia*, 46(7), 1992-2001.

- Candido, C. L., & Romney, D. M. (1990). Attributional style in paranoid vs. depressed patients. *The British Journal of Medical Psychology*, 63(4), 355-363.
- Corrigan, P. W., Green, M. F., & Toomey, R. (1994). Cognitive correlates to social cue perception in schizophrenia. *Psychiatry Research*, 53, 141-151.
- Craig, J. S., Hatton, C., Craig, F. B., & Bentall, R. P. (2004). Persecutory beliefs, attributions and theory of mind: Comparison of patients with paranoid delusions, Asperger's syndrome and healthy controls. *Schizophrenia Research*, 69, 29-33.
- Cutting, J., & Murphy, D. (1988). Schizophrenic thought disorder. A psychological and organic interpretation. *The British Journal of Psychiatry*, 152, 310-319.
- Cutting, J., & Murphy, D. (1990). Impaired ability of schizophrenics, relative to manics or depressives, to appreciate social knowledge about their culture. *The British Journal of Psychiatry*, 157, 355-358.
- Davidson, M., Reichenberg, A., Rabinowitz, J., Weiser, M., Kaplan, Z., & Mark, M. (1999). Behavioral and intellectual markers for schizophrenia in apparently healthy male adolescents. *American Journal of Psychiatry*, 156(9), 1328-1335.
- Dichter, G. S., Felder, J. N., Bodfish, J. W., Sikich, L., & Belger, A. (2009). Mapping social target detection with functional magnetic resonance imaging. *Social Cognitive and Affective Neuroscience* 4(1), 59-69.
- Dowd, E. C., & Barch, D. M. (2010). Anhedonia and emotional experience in schizophrenia: Neural and behavioral indicators. *Biological Psychiatry*, 67(10), 902-911.
- First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. W. (1997). *Structured Clinical Interview for DSM-IV Axis I Disorders*. Arlington, VA: American Psychiatric Publishing.
- Fiske, S. T., & Taylor, S. E. (1991). *Social cognition* (2<sup>nd</sup> ed.). New York, NY: McGraw-Hill Book Company.
- Frith, C. D. (1992). *The cognitive neuropsychology of schizophrenia*. Hillsdale: Lawrence Erlbaum Associates.
- Garrity, A. G., Pearlson, G. D., McKiernan, K., Lloyd, D., Kiehl, K. A., & Calhoun, V. D. (2007). Aberrant "default mode" functional connectivity in schizophrenia. *American Journal of Psychiatry*, 164(3), 450-457.
- Geday, J., Gjedde, A., Boldsen, A.- S., & Kupers, R. (2003). Emotional valence modulates activity in the posterior fusiform gyrus and inferior medial prefrontal cortex in social perception. *NeuroImage*, 18, 675-684.

- Gobbini, M. I., Koralek, A. C., Bryan, R. E., Montgomery, K. J., & Haxby, J. V. (2007). Two takes on the social brain: A comparison of theory of mind tasks. *Journal of Cognitive Neuroscience*, 19(11), 1803-1814.
- Green, M. F., Penn, D. L., Bentall, R., Carpenter, W. T., Gaebel, W., Gur, R. C., Kring, A. M., Park, S., Silverstein, S. M., & Heinssen, R. (2008). Social cognition in schizophrenia: An NIMH workshop on definitions, assessment, and research opportunities. *Schizophrenia Bulletin*, 34(6), 1211-1220.
- Greene, D. J., Mooshagian, E., Kaplan, J. T., Zaidel, E., & Iacoboni, M. (2009). The neural correlates of social attention: Automatic orienting to social and nonsocial cues. *Psychological Research*, 73, 499-511.
- Grossman, E. D., & Blake, R. (2002). Brain areas active during visual perception of biological motion. *Neuron*, 35, 1167-1175.
- Gur, R. E., McGrath, C., Chan, R. M., Schroeder, L., Turner, T., Turetsky, B. I., Kohler, C., Alsop, D., Maldjian, J., Ragland, J. D., & Gur, R. C. (2002). An fMRI study of facial emotion processing in patients with schizophrenia. *American Journal of Psychiatry*, 159(12), 1992-1999.
- Hall, J., Whalley, H. C., McKirdy, J. W., Romaniuk, L., McGonigle, D., McIntosh, A. M., Baig, B. J., Gountouna, V.-E., Job, D. E., Donaldson, D. I., Sprengelmeyer, R., Young, A. W., Johnstone, E. C., & Lawrie, S. M. (2008). Overactivation of fear systems to neutral faces in schizophrenia. *Biological Psychiatry*, 64, 70-73.
- Harrison, B. J., Yucel, M., Pujol, J., & Pantelis, C. (2007). Task-induced deactivation of midline cortical regions in schizophrenia assessed with fMRI. *Schizophrenia Research*, 91, 82-86.
- Harvey, P.-O., Fossati, P., & Lepage, M. (2007). Modulation of memory formation by stimulus content: Specific role of the medial prefrontal cortex in successful encoding of social pictures. *Journal of Cognitive Neuroscience*, 19(2), 351-362.
- Hempel, A., Hempel, E., Schonknecht, P., Stippich, C., & Schroder, J. (2003). Impairment in basal limbic function in schizophrenia during affect recognition. *Psychiatry Research: Neuroimaging*, 122, 115-124.
- Holt, D. J., Kunkel, L., Weiss, A. P., Goff, D. C., Wright, W. I., Shin, L. M., Rauch, S. L., Hootnick, J., & Heckers, S. (2006). Increased medial temporal lobe activation during the passive viewing of emotional and neutral facial expressions in schizophrenia. *Schizophrenia Research*, 82, 153-162.
- Honea, R., Crow, T. J., Passingham, D., & Mackay, C. E. (2005). Regional deficits in brain volume in schizophrenia: A meta-analysis of voxel-based morphometry studies. *American Journal of Psychiatry*, 162, 2233-2245.

- Jolley, S., Garety, P., Bebbington, P., Dunn, G., Freeman, D., Kuipers, E., Fowler, D., & Hemsley, D. (2006). Attributional style in psychosis-The role of affect and belief type. *Behaviour Research and Therapy*, 44, 1597-1607.
- Kaney, S., & Bentall, R. P. (1989). Persecutory delusions and attributional style. *The British Journal of Medical Psychology*, 62(2), 191-198.
- Kapur, S. (2003). Psychosis as a state of aberrant salience: a framework linking biology, phenomenology, and pharmacology in schizophrenia. *American Journal of Psychiatry*, 160(1), 13-23.
- Kawashima, R., Sugiura, M., Kato, T., Nakamura, A., Hatano, K., Ito, K., Fukuda, H., Kojima, S., & Nakamura, K. (1999). The human amygdala plays an important role in gaze monitoring. A PET study. *Brain*, 122(4), 779-783.
- Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. *Schizophrenia Bulletin*, 13, 261-276.
- Kinderman, P., & Bentall, R. P. (1997). Causal attributions in paranoid and depression: Internal, personal, and situational attributions for negative events. *Journal of Abnormal Psychology*, 106(2), 341-345.
- Konick, L. C., & Friedman, L. (2001). Meta-analysis of thalamic size in schizophrenia. *Biological Psychiatry*, 49 28-38.
- Kosaka, H., Omori, M., Murata, T., Iidaka, T., Yamada, H., Okada, T., Takahashi, T., Sadato, N., Itoh, H., Yonekura, Y., & Wada, Y. (2002). Differential amygdala response during facial recognition in patients with schizophrenia: An fMRI study. *Schizophrenia Research*, 57, 87-95.
- Kunda, Z. (1999). *Social cognition: Making sense of people*. Cambridge, MA: MIT Press.
- Kuzmanovic, B., Georgescu, A. L., Eickhoff, S. B., Shah, N., Bente, B., Fink, G. R., & Vogeley, K. (2009). Duration matters: Dissociating neural correlates of detection and evaluation of social gaze. *NeuroImage*, 46, 1154-1163.
- Lancaster, J. L., Woldorff, M. G., Parsons, L. M., Liotti, M., Freitas, C. S., Rainey, L., Kochunov, P. V., Nickerson, D., Mikiten, S. A., & Fox, P. T. (2000). Automated Talairach atlas labels for functional brain mapping. *Human Brain Mapping*, 10, 120-131.
- Lane, R. D., Reiman, E. M., Bradley, M. M., Lang, P. J., Ahern, G. L., Davidson, R. J., & Schwartz, G. E. (1997). Neuroanatomical correlates of pleasant and unpleasant emotion. *Neuropsychologia*, 35(11), 1437-1444.

- Lang, P. J., Bradley, M. M., Fitzsimmons, J. R., Cuthbert, B. N., Scott, J. D., Moulder, B., & Nangia, V. (1998). Emotional arousal and activation of the visual cortex: An fMRI analysis. *Psychophysiology*, 35, 199-210.
- Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (2005). *International Affective Picture System (IAPS): Digitized photographs, instruction manual, and affective ratings* (Tech. Rep. No. A-6). New York: Wiley.
- Lawrie, S. M., & Abukmeil, S. S. (1998). Brain abnormality in schizophrenia. A systematic and quantitative review of volumetric magnetic resonance imaging studies. *The British Journal of Psychiatry*, 172(2), 110-120.
- Mannell, M. V., Franco, A. R., Calhoun, V. D., Canive, J. M., Thoma, R. J., & Mayer, A. R. (2010). Resting state and task-induced deactivation: A methodological comparison in patients with schizophrenia and healthy controls. *Human Brain Mapping*, 31(3), 424-437.
- Marwaha, S., & Johnson, S. (2004). Schizophrenia and employment: A review. *Social Psychiatry and Psychiatric Epidemiology*, 39, 337-349.
- Marwick, K., & Hall, J. (2008). Social cognition in schizophrenia: A review of face processing. *British Medical Bulletin*, 88, 43-58.
- Matsui, M., Sumiyoshi, T., Arai, H., Higuchi, Y., & Kurachi, M. (2008). Cognitive functioning related to quality of life in schizophrenia. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, 32, 280-287.
- McEvoy, J. P., Hartman, M., Gottlieb, D., Godwin, S., Apperson, L. J., & Wilson, W. (1996). Common sense, insight, and neuropsychological test performance in schizophrenia patients. *Schizophrenia Bulletin*, 22(4), 635-640.
- Mier, D., Sauer, C., Lis, S., Esslinger, C., Wilhelm, J., Gallhofer, B., & Kirsch, P. (2010). Neuronal correlates of affective theory of mind in schizophrenia out-patients: evidence for a baseline deficit. *Psychological Medicine*, 40, 1607-1617.
- Monti, P. M., & Fingeret, A. L. (1987). Social perception and communication skills among schizophrenics and nonschizophrenics. *Journal of Clinical Psychology*, 43(2), 197-205.
- Morris, J. P., Pelfrey, K. A., & McCarthy, G. (2006). Occipitotemporal activation evoked by the perception of human bodies is modulated by the presence or absence of faces. *Neuropsychologia*, 44(10), 1919-1927.
- Mueser, K. T., & Tarrier, N. (Eds.). (1998). *Handbook of social functioning in schizophrenia*. Needham Heights, MA: Allyn & Bacon.

- Mueser, K. T., & Bellack, A. S. (1998). Social skills and social functioning. In K. T. Mueser & N. Tarrier (Eds.), *Handbook of social functioning in schizophrenia* (p. 79-96). Needham Heights, MA: Allyn & Bacon.
- Murty, V. P., Ritchey, M., Adcock, R. A., & LaBar, K. S. (2010). fMRI studies of successful emotional memory encoding: A quantitative meta-analysis. *Neuropsychologia*, 48, 3459-3469.
- Nelson, M. D., Saykin, A. J., Flashman, L. A., & Riordan, J. W. (1998). Hippocampal volume reduction in schizophrenia as assessed by magnetic resonance imaging: A meta-analytic study. *Archives of General Psychiatry*, 55, 433-440.
- Norris, C. J., Chen, E. E., Zhu, D. C., Small, S. L., & Cacioppo, J. T. (2004). The interaction of social and emotional processes in the brain. *Journal of Cognitive Neuroscience*, 16(10), 1818-1829.
- Park, K. -M., Kim, J. -J., Ku, J., Kim, S. O., Lee, H. R. Kim, S. I., & Yoon, K. -J. (2009). Neural basis of attributional style in schizophrenia. *Neuroscience Letters*, 459, 35-40.
- Perlick, D., Stastny, P., Mattis, S., & Teresi, J. (1992). Contribution of family, cognitive and clinical dimensions to long-term outcome in schizophrenia. *Schizophrenia Research*, 6, 257-265.
- Phan, K. L., Wager, T., Taylor, S. F., & Liberzon, I. (2002). Functional neuroanatomy of emotion: A meta-analysis of emotion activation studies in PET and fMRI. *NeuroImage*, 16, 331-348.
- Phillips, M. L., Williams, L., Senior, C., Bullmore, E. T., Brammer, M. J., Andrew, C., Williams, S. C. R., & David, A. S. (1999). A differential neural response to threatening and non-threatening negative facial expressions in paranoid and non-paranoid schizophrenics. *Psychiatry Research: Neuroimaging*, 92, 11-31.
- Pinikahana, J., Happell, B., Hope, J., & Keks, N. A. (2002). Quality of life in schizophrenia: A review of the literature from 1995 to 2000. *International Journal of Mental Health Nursing*, 11, 103-111.
- Puce, A., & Perrett, D. (2003). Electrophysiology and brain imaging of biological motion. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, 358, 435-445.
- Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences of the USA*, 98(2), 676-682.



- Rushworth, M. F. S., Buckley, M. J., Behrens, T., Walton, M. E., & Bannerman, D. M. (2007). Functional organization of the medial frontal cortex. *Current Opinion in Neurobiology*, 17, 220-227.
- Russell, T. A., Rubia, K., Bullmore, E. T., Soni, W., Suckling, J., Brammer, M. J., Simmons, A., Williams, S. C., & Sharma, T. (2000). Exploring the social brain in schizophrenia: Left prefrontal underactivation during mental state attribution. *American Journal of Psychiatry*, 157(12), 2040-2042.
- Sergi, M. J., & Green, M. F. (2002). Social perception and early visual processing in schizophrenia. *Schizophrenia Research*, 59, 233-241.
- Sergi, M. J., Rassovsky, Y., Nuechterlein, K. H., & Green, M. F. (2006). Social perception as a mediator of the influence of early visual processing on functional status in schizophrenia. *American Journal of Psychiatry*, 163(3), 448-454.
- Sharp, H. M., Fear, C. F., & Healy, D. (1997). Attributional style and delusions: An investigation based on delusional content. *European Psychiatry*, 12, 1-7.
- Shenton, M. E., Dickey, C. C., Frumin, M., & McCarley, R. W. (2001). A review of MRI findings in schizophrenia. *Schizophrenia Research*, 49, 1-52.
- Silverman, R. J., & Peterson, C. (1993). Explanatory style of schizophrenic and depressed outpatients. *Cognitive Therapy and Research*, 17(5), 457-470.
- Straube, T., Pohlack, S., Mentzel, H. J., & Miltner, W. H. R. (2008). Differential amygdala activation to negative and positive emotional pictures during an indirect task. *Behavioural Brain Research*, 191(2), 283-288.
- Surguladze, S., Russell, T., Kucharska-Pietura, K., Travis, M. J., Giampietro, V., David, A. S., & Phillips, M. L. (2006). A reversal of the normal pattern of parahippocampal response to neutral and fearful faces is associated with reality distortion in schizophrenia. *Biological Psychiatry*, 60, 423-431.
- Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain: 3-dimensional proportional system: An approach to cerebral imaging*. Thieme: Stuttgart.
- Toomey, R., Schuldberg, D., Corrigan, P., & Green, M. F. (2002). Nonverbal social perception and symptomatology in schizophrenia. *Schizophrenia Research*, 53, 83-91.
- Treméau, F. (2006). A review of emotion deficits in schizophrenia. *Dialogues in Clinical Neuroscience*, 8(1), 59-70.
- Ungerleider, L. G., & Haxby, J. V. (1994). 'What' and 'where' in the human brain. *Current Opinion in Neurobiology*, 4, 157-165.

- Van Overwalle, F. (2009). Social cognition and the brain: A meta-analysis. *Human Brain Mapping, 30*, 829-858.
- Van Overwalle, F., & Baetens, K. (2009). Understanding others' actions and goals by mirror and mentalizing systems: A meta-analysis. *NeuroImage, 48*(3), 564-584.
- Walter, H., Ciaramidaro, A., Adenzto, M., Vasic, N., Ardito, R. B., Erk, S., & Bara, B. G. (2009). Dysfunction of the social brain in schizophrenia is modulated by intention type: An fMRI study. *Social, Cognitive, and Affective Neuroscience, 4*(2), 166-176.
- Weschler, D. (1999). *Wechsler Abbreviated Scale of Intelligence*. San Antonio, TX: The Psychological Corporation.
- Whitfield-Gabrieli, S. W., Thermenos, H. W., Milanovic, S., Tsuang, M. T., Faraone, S. V., McCarley, R. W., Shenton, M. E., Green, A. I., Nieto-Castanon, A., LaViolette, P., Wojcik, J., Gabrieli, J. D., & Seidman, L. J. (2009). Hyperactivity and hyperconnectivity of the default network in schizophrenia and in first-degree relatives of persons with schizophrenia. *Proceedings of the National Academy of Sciences, 106*(4), 1279-1284.
- Wilkinson, G. S. (1993). *Wide Range Achievement Test* (3rd ed.). Austin, TX: Pro-Ed.
- Winston, J. S., Strange, B. A., O'Doherty, J., & Rolan, R. J. (2002). Automatic and intentional brain responses during evaluation of trustworthiness of faces. *Nature Neuroscience, 5*(3), 277-283.
- Yoon, J. H., D'Esposito, M., & Carter, C. S. (2006). Preserved function of the fusiform face area in schizophrenia as revealed by fMRI. *Psychiatry Research: Neuroimaging, 148*, 205-216.
- Young, L., & Saxe, R. (2008). The neural basis of belief encoding and integration in moral judgment. *NeuroImage, 40*(4), 1219-1920.
- Zald, D. H., & Pardo, J. V. (1997). Emotion, olfaction, and the human amygdala: Amygdala activation during aversive olfactory stimulation. *Proceedings of the National Academy of Sciences of the USA, 44*, 4119-4124.

UNIVERSITY OF ILLINOIS  
AT CHICAGO

Office for the Protection of Research Subjects (OPRS)  
Office of the Vice Chancellor for Research (MC 672)  
203 Administrative Office Building  
1737 West Polk Street  
Chicago, Illinois 60612-7227

**Approval Notice  
Continuing Review**

June 7, 2010

Ellen S. Herbener, PhD  
Psychiatry  
912 S. Wood St.  
136 N.P.L.-S, M/C 913  
Chicago, IL 60612  
Phone: (312) 413-2638 / Fax: (312) 413-4122

RE: Protocol # 2003-0622  
"Emotional Functioning in Schizophrenia Spectrum Disorders and Depression"

Dear Dr. Herbener:

Your Continuing Review was reviewed and approved by the Convened review process on May 25, 2010. You may now continue your research.

Please note the following information about your approved research protocol:

**Protocol Approval Period:** May 27, 2010 - May 26, 2011

**Approved Subject Enrollment #:** 300

**Additional Determinations for Research Involving Minors:** The Board determined that this research satisfies 45CFR46.406; research involving greater than minimal risk (representing a minor increase over minimal risk) and having no direct benefit to the individual subjects, but likely to yield generalizable knowledge about the subjects condition. In accordance with 45CFR46.408, both parent's permission/signature (two signature lines needed) is required unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. Wards of the State may not be enrolled unless the IRB grants specific approval and assures inclusion of additional protections in the research required under 45CFR46.409. If you wish to enroll Wards of the State contact OPRS and refer to the tip sheet.

**Performance Sites:** UIC

**Sponsor:** National Institutes of Health

**PAF#:** 2003-04409

**Grant/Contract No:** 1 K23 MH067223

**Grant/Contract Title:** Affective Deficits in Schizophrenia

**Research Protocol:**

- a) "Emotional Functioning in Schizophrenia Spectrum Disorders and Depression," Version #7, 05/05/2008

Phone: 312-996-1711

<http://www.uic.edu/depts/ovcr/oprs/>

FAX: 312-413-2929

**Recruitment Materials:**

- a) Web Ad, "Emotional Functioning in Schizophrenia Spectrum Disorders and Depression," Version #9, 05/10/2010
- b) "Emotional Functioning in Schizophrenia Spectrum Disorders and Depression," Web/Newsletter Ad, Version #7, 05/10/2010
- c) Board Ad, "Healthy Subjects Needed for Research Study Investigating Psychiatric Disorders," Version 5, 05/10/2010
- d) Information Sheet, Version 5, 05/10/2010
- e) Brochure, Patient Participants Needed for Medical Research Study - "Emotional Functioning in Schizophrenia Spectrum Disorders and Depression," Version #7, 05/10/2010
- f) Telephone Screening Script, Version #4, 05/10/2010

**Informed Consents:**

- a) "Emotional Functioning in Schizophrenia Spectrum Disorders and Depression," Subject with Psychiatric Disorder, Version #21, 05/10/2010
- b) "Emotional Functioning in Schizophrenia Spectrum Disorders and Depression," Healthy Control, Version #16, 05/10/2010

**Assents:**

- a) 15-17yo Patient assent: Emotional Functioning in Schizophrenia Spectrum Disorders and Depression, Version #3, 05/10/2010
- b) 15-17yo Healthy assent: Emotional Functioning in Schizophrenia Spectrum Disorders and Depression, Version #3, 05/10/2010

**Parental Permissions:**

- a) Parent/Legal Guardian Patient: Emotional Functioning in Schizophrenia Spectrum Disorders and Depression, Version #6, 05/10/2010
- b) Parent/Legal Healthy Control: Emotional Functioning in Schizophrenia Spectrum Disorders and Depression, Version #6, 05/10/2010

**HIPAA Authorizations (Continue to use the previously approved, stamped documents):**

- a) "Emotional Functioning in Schizophrenia Spectrum Disorders and Depression," Authorization, Version #4, 06/08/2006
- b) Parental Authorization: Emotional Functioning in Schizophrenia Spectrum Disorders and Depression, Version 1, 09/02/2008

**Please note the Review History of this submission:**

Receipt Date	Submission Type	Review Process	Review Date	Review Action
05/12/2010	Continuing Review	Convened	05/25/2010	Approved

Please remember to:

→ Use your **research protocol number** (2003-0622) on any documents or correspondence with the IRB concerning your research protocol.

→ Review and comply with all requirements on the enclosure,

**"UIC Investigator Responsibilities, Protection of Human Research Subjects"**

**Please note that the UIC IRB has the right to seek additional information, require further modifications, or monitor the conduct of your research and the consent process.**

**Please be aware that if the scope of work in the grant/project changes, the protocol must be amended and approved by the UIC IRB before the initiation of the change.**

We wish you the best as you conduct your research. If you have any questions or need further help, please contact OPRS at (312) 996-1711 or me at (312) 413-3788. Please send any correspondence about this protocol to OPRS at 203 AOB, M/C 672.

Sincerely,



Rachel Olech, B.A., CIP  
Assistant Director, IRB # 3  
Office for the Protection of Research Subjects

Enclosures:

1. **UIC Investigator Responsibilities, Protection of Human Research Subjects**
2. **Informed Consent Documents:**
  - a) "Emotional Functioning in Schizophrenia Spectrum Disorders and Depression," Subject with Psychiatric Disorder, Version #21, 05/10/2010
  - b) "Emotional Functioning in Schizophrenia Spectrum Disorders and Depression," Healthy Control, Version #16, 05/10/2010
3. **Assent Documents:**
  - a) 15-17yo Patient assent: Emotional Functioning in Schizophrenia Spectrum Disorders and Depression, Version #3, 05/10/2010
  - b) 15-17yo Healthy assent: Emotional Functioning in Schizophrenia Spectrum Disorders and Depression, Version #3, 05/10/2010
4. **Parental Permissions:**
  - a) Parent/Legal Guardian Patient: Emotional Functioning in Schizophrenia Spectrum Disorders and Depression, Version #6, 05/10/2010
  - b) Parent/Legal Healthy Control: Emotional Functioning in Schizophrenia Spectrum Disorders and Depression, Version #6, 05/10/2010
5. **Recruiting Materials:**
  - a) Web Ad, "Emotional Functioning in Schizophrenia Spectrum Disorders and Depression," Version #9, 05/10/2010
  - b) "Emotional Functioning in Schizophrenia Spectrum Disorders and Depression," Web/Newsletter Ad, Version #7, 05/10/2010
  - c) Board Ad, "Healthy Subjects Needed for Research Study Investigating Psychiatric Disorders," Version 5, 05/10/2010
  - d) Information Sheet, Version 5, 05/10/2010
  - e) Brochure, Patient Participants Needed for Medical Research Study - "Emotional Functioning in Schizophrenia Spectrum Disorders and Depression," Version #7, 05/10/2010
  - f) Telephone Screening Script, Version #4, 05/10/2010
6. **Optional Form 310 - Protection of Human Subjects, Assurance Identification/Certification/Declaration**

cc: Anand Kumar, Psychiatry, M/C 912  
OVCR Administration, M/C 672



**Protection of Human Subjects**  
**Assurance Identification/IRB Certification/Declaration of Exemption**  
**(Common Rule)**

Policy: Research activities involving human subjects may not be conducted or supported by the Departments and Agencies adopting the Common Rule (56FR28003, June 18, 1991) unless the activities are exempt from or approved in accordance with the common rule. See section 101(b) the common rule for exemptions. Institutions submitting applications or proposals for support must submit certification of appropriate Institutional Review Board (IRB) review and approval to the Department or Agency in accordance with the common rule.

Institutions must have an assurance of compliance that applies to the research to be conducted and should submit certification of IRB review and approval with each application or proposal unless otherwise advised by the Department or Agency.

1. Request Type <input type="checkbox"/> ORIGINAL <input checked="" type="checkbox"/> CONTINUATION <input type="checkbox"/> EXEMPTION	2. Type of Mechanism <input checked="" type="checkbox"/> GRANT <input type="checkbox"/> CONTRACT <input type="checkbox"/> FELLOWSHIP <input type="checkbox"/> COOPERATIVE AGREEMENT <input type="checkbox"/> OTHER:	3. Name of Federal Department or Agency and, if known, Application or Proposal Identification No. National Institutes of Health Grant #: 1 K23 MH067223 PAF#: 2003-04409
4. Title of Application or Activity Emotional Functioning in Schizophrenia Spectrum Disorders and Depression, UIC Protocol #2003-0622		5. Name of Principal Investigator, Program Director, Fellow, or Other Ellen S. Herbener, PhD

6. Assurance Status of this Project (Respond to one of the following)

- ☒ This Assurance, on file with Department of Health and Human Services, covers this activity:  
Assurance identification no. FWA00000083, the expiration date January 18, 2011, IRB Registration no. IRB00000117
- ☐ This Assurance, on file with (agency/dept) \_\_\_\_\_, covers this activity.  
Assurance No. \_\_\_\_\_, the expiration date \_\_\_\_\_, IRB Registration/Identification no. \_\_\_\_\_ (if applicable)
- ☐ No assurance has been filed for this institution. This institution declares that it will provide an Assurance and Certification of IRB review and approval upon request.
- ☐ Exemption Status: Human subjects are involved, but this activity qualifies for exemption under Section 101(b), paragraph \_\_\_\_\_

7. Certification of IRB Review (Respond to one of the following IF you have an Assurance on file)

- ☒ This activity has been reviewed and approved by the IRB in accordance with the Common Rule and any other governing regulations.  
by: ☒ Full IRB Review on (date or IRB meeting) May 25, 2010 or ☐ Expedited Review on (date) \_\_\_\_\_  
☐ If less than one year approval, provide expiration date \_\_\_\_\_
- ☐ This activity contains multiple projects, some of which have not been reviewed. The IRB has granted approval on condition that all projects covered by the Common Rule will be reviewed and approved before they are initiated and that appropriate further certification will be submitted.

8. Comments

Approval Period: May 27, 2010 - May 26, 2011

9. The official signing below certifies that the information provided above is correct and that, as required, future reviews will be performed until study closure and certification will be provided.	10. Name and Address of Institution University Of Illinois At Chicago Institutional Review Board Room 203 AOB, M/C 672 1737 W. Polk Street Chicago, IL 60612
11. Phone No. (with area code) (312)-996-1711	15. Title  Associate Director
12. Fax No. (with area code) (312)-413-2929	
13. Email: <u>uicirb@uic.edu</u>	
14. Name of Official  Cynthia Tom Klebba	

16. Signature  


17. Date  
June 7, 2010  
Sponsored by HHS

Public reporting burden for this collection of information is estimated to average less than an hour per response. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to: OS Reports Clearance Officer, Room 503 200 Independence Avenue, SW., Washington DC 20201. Do not return the completed form to this address.

## VITA

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### Education

**University of Illinois at Chicago** 2008-present  
Doctoral Program in Clinical Psychology  
GPA: 4.0

**University of California, Los Angeles** 2001-2005  
Bachelor of Science, Psychobiology  
GPA: Cumulative 3.7, Psychology 3.9

### Honors and Awards

Graduate Student Council Presenter's Award 2009, 2010  
Psychology Department Presenter's Award 2009, 2010  
Graduate College Student Presenter's Award 2009, 2010  
National Society of Collegiate Scholars 2002-2005  
UCLA Alumni Scholar 2001-2005  
College Latin Honors, Cum Laude 2005

### Publications

**Bjorkquist, O.A.**, Fryer, S.L., Reiss, A.L., Mattson, S.N., & Riley, E.P. (2010). Cingulate gyrus morphology in children and adolescents with prenatal alcohol exposure. *Psychiatry Research: Neuroimaging*, 181(2), 101-107.

Fryer, S.L., Schweinsburg, B.C., **Bjorkquist, O.A.**, Frank, L.R., Mattson, S.N., Spadoni, A.D., & Riley, E.P. (2009). Characterization of white matter microstructure in fetal alcohol spectrum disorders. *Alcoholism: Clinical and Experimental Research*, 33(3), 514-521.

McGee, C.L., **Bjorkquist, O.A.**, Price, J.M., Mattson, S.N., & Riley, E.P. (2009). Social information processing skills in children with histories of heavy prenatal alcohol exposure. *Journal of Abnormal Child Psychology*, 37(6), 817-830.

McGee, C.L., **Bjorkquist, O.A.**, Riley, E.P., & Mattson, S.N. (2009). Impaired language performance in young children with heavy prenatal alcohol exposure. *Neurotoxicology and Teratology*, 31(2), 71-75.

McGee, C.L., Fryer, S.L., **Bjorkquist, O.A.**, Riley, E.P., & Mattson, S.N. (2008). Deficits in social problem solving in adolescents with prenatal exposure to alcohol. *The American Journal of Drug and Alcohol Abuse*, 34(4), 423-441.

*In preparation:*

**Bjorkquist, O. A.**, & Herbener, E. S. (in preparation). Social perception in schizophrenia: Evidence of prefrontal and occipital dysfunction. *Manuscript to be submitted to Social, Cognitive, and Affective Neuroscience*.

Behar, E., McGowan, S. K., McLaughlin, K. A., Borkovec, T. D., Goldwin, M., & **Bjorkquist, O.** (under review). Concreteness of positive, negative, and neutral repetitive thinking about the future. *Manuscript submitted to Behavior Therapy*.

## **Posters**

**Bjorkquist, O. A., & Herbener, E. S.** Social perception in schizophrenia: Evidence of occipital and prefrontal dysfunction. Presented at the annual meeting of the Society for Research in Psychopathology, Seattle, WA, October 7-10, 2010.

Nelson, B. D., Herbener, E. S., & **Bjorkquist, O. A.** Is there an association between trait anhedonia and neural activity in response to emotional pictures in schizophrenia? An fMRI investigation. Presented at the 4th Annual Meeting of the Social & Affective Neuroscience Society, Chicago, IL, October 28-31, 2010.

Behar, E., Kerns, G., Zachrel, E., **Bjorkquist, O.**, Goldwin, M., McGowan, S. K., & Bohacz, B. Validity of a coding system for abstractness and concreteness of thoughts. Presented at the annual meeting of the Association of Behavioral and Cognitive Therapy, San Francisco, CA, November 18-21, 2010.

McGowan, S. K., Goldwin, M. A., **Bjorkquist, O.**, Bohacz, B., McLaughlin, K. A., & Behar, E. B. The effects of positive, negative, and neutral preservative thinking on abstractness and concreteness of thought content. Presented at the annual meeting of the Association of Behavioral and Cognitive Therapy, New York, NY, November 19-22, 2009.

**Bjorkquist, O. A., & Herbener, E. S.** Arousal and anhedonia predict emotional memory in schizophrenia. Presented at the annual meeting of the Society for Research in Psychopathology, Minneapolis, MN, September 10-13, 2009.

Herbener, E. S., **Bjorkquist, O. A.**, & Palmer, M. A. Impairment in long-term retention of preference conditioning in schizophrenia. Presented at the annual meeting of the International Congress of Schizophrenia, San Diego, CA, March 28-April 1, 2009.

Wagner, A.E., McGee, C.L., **Bjorkquist, O.A.**, & Mattson, S.N. Alterations in perceived organization of hierarchical figures in children with heavy prenatal alcohol exposure. Presented at the annual meeting of the Research Society on Alcoholism, Washington, DC, June 28-July 2, 2008.

McGee, C.L., **Bjorkquist, O.A.**, Price, J.M., Mattson, S.N., & Riley, E.P. Social information processing skills in children with histories of heavy prenatal alcohol exposure. Presented at the fetal alcohol spectrum disorders study group at the annual meeting of the Research Society on Alcoholism, Washington, DC, June 28-July 2, 2008.

Riley, E.P., & **Bjorkquist, O.** Could alterations in brain and behavior in children with FASD be related to stress? Presented at the first international meeting "Alcoholism and Stress: A Framework for Future Treatment Strategies," Volterra, Italy, May 6-8, 2008.

Fryer, S.L., Schweinsburg, B.C., **Bjorkquist, O.A.**, Frank, L.R., Mattson, S.N., Spadoni, A.D., & Riley, E.P. Evidence of global white matter microstructural damage in fetal alcohol spectrum disorders. Presented at the 37<sup>th</sup> annual meeting of the Society for Neuroscience, San Diego, CA, November 3-7, 2007.

McGee, C.L., **Bjorkquist, O.A.**, Riley, E.P., & Mattson, S.N. Impaired language performance in young children with heavy prenatal alcohol exposure. Presented at the 35<sup>th</sup> annual meeting of the International Neuropsychological Society, Portland, OR, February 7-10, 2007.



## **Research Experience**

### **Center for Cognitive Medicine, University of Illinois at Chicago**

Aug 2008-Present

*Research Assistant*, Supervisor: Ellen S. Herbener, Ph.D., Departments of Psychology/Psychiatry

- Assist in fMRI projects examining emotional memory in individuals with schizophrenia including scan acquisition, data preparation, management, and analysis.
- Administer behavioral test batteries including WRAT, WASI, and computerized tasks measuring emotion processing and social cognition in individuals with schizophrenia.
- Assist in subject recruitment and coordination of studies.
- Create tasks targeting social cognitive functioning in schizophrenia.
- Author scholarly publications, present at conferences, and conduct literature reviews.

*Research Assistant*, Supervisor: Scot Hill, Ph.D., Department of Psychiatry Jan 2010-Aug 2010

- Perform data analysis for an fMRI project examining cognition in individuals with schizophrenia, including scan acquisition, image preprocessing, and group analyses.
- Manage and analyze fMRI behavioral data.
- Administer neuropsychological test batteries including MATRICS, WRAT, WASI, and computerized tasks.

### **Center for Behavioral Teratology, San Diego State University**

Jan 2006-Jun 2008

*Research Assistant*, Supervisor: Edward P. Riley, Ph.D., Department of Psychology

- Assist in MRI, fMRI, and DTI neuroimaging projects on children with Fetal Alcohol Spectrum Disorder (FASD) including scan acquisition, data preparation, and image analysis.
- Administer and score neuropsychological test battery measuring social information processing in children with FASD.
- Author scholarly publications, edit grants and presentations, and conduct literature reviews.
- Assist with data quality assurance procedures and administrative tasks.

## **Clinical Experience**

### **Office of Applied Psychological Services, University of Illinois at Chicago**

Aug 2008-Present

*Clinician*, Supervisors: Gloria Balague, Ph.D., Nancy Dasso, Ph.D., Audrey Ruderman, Ph.D.

- Administer intake interviews and write intake reports for individuals seeking psychotherapy.
- Provide psychotherapy services with a focus in Cognitive Behavioral Therapy.
  - Individual therapy addressing issues such as depression, anxiety, assertiveness, anger, and stress management.
  - Manualized group therapy addressing social anxiety disorder.
- Provide neuropsychological assessment services, including test administration, scoring, interpretation, report writing, and feedback to clients.
  - Trained in the Beery VMI Developmental Test, Brief Visuospatial Memory Test-Revised (BVRT-R), California Verbal Learning Test (CVLT), Child Behavior Checklist (CBCL), Comprehensive Test of Phonological Processing (CTOPP), Conners ADHD Index, Conners Continuous Performance Test II (CPT-II), Delis-Kaplan Executive Function System (DKEFS), Key Math 3, Learning and Study Strategies Inventory (LASSI), MATRICS Consensus Cognitive Battery (MCCB), Minnesota Multiphasic Personality Inventory (MMPI), Nelson Denny Reading Test, Oral and Written Language Scales (OWLS), Structured Clinical Interview for DSM-IV (SCID-IV), Victoria Symptom Validity Test (VSVT), Wechsler Adult Intelligence

Scale-IV (WAIS-IV), Wechsler Intelligence Scale for Children-IV (WISC-IV),  
Wender Utah Rating Scale (WURS), Wisconsin Card Sorting Test (WCST),  
Woodcock Johnson Test of Achievement, Woodcock Johnson Test of Cognitive  
Abilities

### **Teaching Experience**

**Department of Psychology, University of Illinois at Chicago**

Aug 2008-Present

*Teaching Assistant*

- Courses include Introduction to Psychology, Research Methods, Theories of Personality, and Fieldwork in Psychology
- Conduct weekly discussion sections, including reviewing lecture material and leading classroom activities.
- Supervise advanced undergraduate students in fieldwork, providing individual instruction in development of research ideas, conducting research, and writing research papers.
- Grade papers and proctor examinations.

*Guest Lecturer*

Mar, Oct 2010

- Create and implement lecture designed to teach advanced psychology undergraduate students how to write an introduction section of a research paper, including idea development, literature review, study goals and hypotheses.

### **Invited Talks**

**Department of Psychology, University of Illinois at Chicago**

Nov 2010

- Presented Masters thesis entitled “Social perception in schizophrenia: Evidence of prefrontal and occipital dysfunction” at weekly Brown Bag seminar

### **Ad Hoc Student Editorial Experience**

- Wrote critical reviews for empirical research articles submitted to *Biological Psychiatry* and *Journal of Abnormal Psychology*, under advisor supervision.

### **References**

Ellen S. Herbener, Ph.D.  
Assistant Professor of Psychology  
University of Illinois at Chicago  
1007 W Harrison St., Chicago, IL 60607  
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