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Emotion Recognition and Psychosis-Proneness: Neural and Behavioral Perspectives

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Laura Germine

Emotion Recognition and Psychosis-Proneness:
Neural and Behavioral Perspectives

Abstract

Schizophrenia is associated with deficits in social cognition and emotion processing, but it is not known how these deficits relate to other domains of neurocognition and whether they might contribute to psychosis development. The current dissertation approaches this question by looking at the relationship between psychosis proneness and face emotion recognition ability, a core domain of social-emotional processing.

Psychosis proneness was inferred by the presence of psychosis-like characteristics in otherwise healthy individuals, using self-report measures. Face emotion recognition ability was found to be associated with psychosis-proneness across four large web-based samples and one lab sample. These associations were relatively specific, and could not be explained by differences in face processing or IQ. Using functional magnetic resonance imaging (fMRI), psychosis-proneness was linked with reduced neural activity in brain regions that underlie normal face emotion recognition, including regions that are implicated in self-representation. Additional experiments were conducted to explore psychosis-proneness related differences in self-representation, and a relationship was revealed between cognitive-perceptual (positive) dimensions of psychosis-proneness and (1) flexibility in the body representation (as measured by the rubber hand illusion), and (2) self-referential source memory (but not self-referential

recognition memory). Neither of these relationships, however, explained the association between psychosis-proneness and face emotion recognition ability.

These findings indicate that psychosis vulnerability is related to neural and behavioral differences in face emotion processing, and that these differences are not a secondary characteristic of psychotic illness. Moreover, poorer emotion recognition ability in psychosis-prone individuals is not explained by generalized performance, IQ, or face processing deficits. Although some dimensions of psychosis-proneness were related to differences in measures of self-representation, no evidence was found that these abnormalities contribute to psychosis-proneness related differences in emotion recognition ability.

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Background and Introduction

Schizophrenia and Social-emotional Processing

Among the most pervasive and disabling deficits in schizophrenia are difficulties with social interaction and emotional processing (APA, 2000; Bleuler, 1950; Kraepelin & Gosline, 1918). These deficits have been observed across schizophrenia spectrum disorders and include poor social cognitive abilities (Pinkham, Hopfinger, Ruparel, & Penn, 2008) and poor social functioning (Hooley, 2010; Hooker & Park, 2002). Social functioning has a tremendous impact on an individual's mental and physical health. The degree to which an individual seeks and successfully obtains social support predicts risk for developing mental disorders (Dalgard, Bjork, & Tambs, 1995), symptom severity (Norman et al., 2005), likelihood of remission (Corrigan & Phelan, 2005), and chance of relapse after remission (Hooley, 2010). Number and quality of social relationships predicts mortality and a wide range of health-related conditions including vulnerability for infection, metabolic illness, and cancer (Miller, Chen, & Cole, 2009), comparable to the relationship between smoking and risk of mortality from all causes (Cohen et al., 1997; House, Landis, & Umberson, 1998). It is perhaps not surprising then that greater deficits in social cognition in schizophrenia predict poorer outcomes and greater functional disability (Green & Horan, 2010; Hooker & Park, 2002). Schizophrenia-related deficits in social, cognitive, and emotional processing include difficulty recognizing and understanding social stimuli, acquiring appropriate social and emotional responses, low-level mental state inference, and context-sensitive mental state inference (Ochsner, 2008). The term "social-emotional" will be used to refer to this range of processes, with the observation that social and emotional functions are difficult to separate and often contribute to the same overall adaptive capabilities (Keltner & Kring, 1998).

Symptoms of schizophrenia have traditionally been divided into positive and negative symptom clusters thought to represent distinct domains of pathology (Crow, 1985). Positive symptoms represent an excess of functions (Hugblings & Jackson, 1931) and comprise the so-called psychotic symptoms: delusions, thought disorder, and hallucinations in visual, auditory, somatosensory, olfactory, and gustatory domains (APA, 2000). Negative symptoms reflect a deficit of functions (Andreasen, 1982) or social/cognitive withdrawal (Thiemann et al., 1987) and include blunted expression of emotion and reduced feelings of pleasure (also known as affective flattening and anhedonia; APA, 2000). Prominent negative symptoms tend to be indicative of greater illness severity and poorer outcome (Addington, Addington, & Maticka-Tyndale, 1991; Davidson & McGlashan, 1997; Ho et al., 1998) and respond less or not at all to traditional antipsychotic treatment (Johnstone, Crow, & Ferrier, 1983; Kane & Mayerhoff, 1989). Social-emotional deficits are more closely linked with negative symptoms than positive symptoms, in terms of classification (that is, social-emotional deficits are themselves negative symptoms) but also in associations between specific social-emotional processes and symptom severity (Lincoln, Mehl, Kesting, & Rief, 2011).

Deficits in social-emotional processing can be observed from the earliest stages of psychotic disorders, many years before an individual's first psychotic episode (Walker, Grimes, Davis, & Smith, 1993). As mentioned, abnormalities in social-emotional functions are among the negative symptoms of schizophrenia and include affective flattening and anhedonia. Affective flattening is the reduced tendency among individuals with schizophrenia to display or express emotion (APA, 2000). Importantly, affective flattening seems to be present even when an individual's experience of emotions and emotional intensity appears to be normal and thus

may reflect a failure to outwardly express felt emotions rather than a failure of emotion generation (Keltner & Kring, 1998; Kring, Kerr, Smith, & Neale, 1993; Kring & Neale, 1996).

Although emotional experiences seem to be generally intact, schizophrenia spectrum disorders are consistently linked to deficits in the experience of pleasure, or anhedonia. Anhedonia has been noted particularly in the social domain, where patients report reduced pleasure from social interactions and a reduced drive for social affiliation (Bleuler 1911/1950; Kwapil, 1998). Early investigators, such as Rado (1953), described anhedonia as a chronic and ubiquitous feature of psychotic disorders representing a primary abnormality in emotion processing.

Positive symptoms can also be linked with social-emotional processing, as delusions and hallucinations are frequently centered around social content. Some of the most common delusions, for example, involve interpersonal threat, persecution, and/or social evaluation (APA, 2000). Auditory hallucinations of a human voice/voices are present in 50-70% of individuals with schizophrenia (Hoffman et al., 2000). Delusions and cognitive distortions are also typically grounded in socially or culturally salient themes, suggesting a relationship between social conventions, social learning, and the content of delusional thought processes (Tateyama et al., 1998). Social-emotional processing *deficits*, however, are less consistently linked with positive symptoms (Sergi et al., 2007).

In the last two decades, translational research in cognitive neuroscience and psychology has indicated that schizophrenia and related psychotic disorders are linked to measurable differences in social-emotional aspects of neurocognition. These deficits have been measured across a wide range of functions and include deficits in theory of mind (Frith & Corcoran, 1996), source monitoring (Vinogradov et al., 1997), self-referential processing (Fisher et al., 2008), and

emotion perception (Kohler et al., 2010). Deficits in the ability to identify vocal and facial expression of emotion, in particular, are a robust and highly replicated finding (Edwards, Jackson, & Pattison, 2002; Edwards, Pattison, Jackson, & Wales, 2001; Habel et al., 2000; Kohler, Bilker, Hagendoorn, Gur, & Gur, 2000; Kohler & Brennan, 2004; Mandal, Pandey, & Prasad, 1998; Mueser, Penn, Blanchard, & Bellack, 1997; Penn et al., 2000).

Emotion Recognition in Schizophrenia

Emotion recognition is a widely studied neurocognitive ability that is a fundamental component of social understanding and social functioning. Emotion recognition is a source of rich moment-by-moment knowledge of another person's changing mental states that shares universal characteristics across cultures (Ekman, 1992), can occur automatically (Ohman, 2002), and does not necessarily require conscious perception (Adolphs, 2002). Accurate and efficient emotion recognition across modalities enables a person to understand and respond to the changing beliefs, feelings, and intentions of another person. At the same time, it allows us to judge whether our own beliefs, feelings and intentions are being understood and flexibly navigate social interactions. Moreover, emotion recognition is a building block for other areas of social and emotional processing (Adolphs, 2003), supporting the development of higher-level social behavior by providing rich and instant feedback as social skills are refined through development (Keltner & Kring, 1998). Specialized systems in the brain have been identified for emotion recognition whose functions are dissociable from higher-order reasoning systems (Adolphs, 2003) and from perceptual systems that process related types of information, such as person identity (Haxby, Hoffmann, & Gobbini, 2000). Many studies of the neural substrates of face emotion recognition (FER) have identified a network of regions involved in face emotion

processing, including the amygdala, superior temporal cortex, medial prefrontal cortex, and somatosensory cortices (Adolphs et al., 2000; Adolphs, 2003; Allison, Puce, & McCarthy, 2000; Haxby et al., 2000). Looking at variations in FER ability provides a specific and tractable starting point for studying social-emotional processing in psychosis.

Evidence that FER is impaired in schizophrenia is robust and observed across a range of measures (Edwards et al., 2001; Edwards et al., 2002; Habel et al., 2000; Kohler et al. 2000; Kohler & Brennan, 2004; Mandal et al., 1998; Mueser et al. 1997; Penn, et al., 2000). FER ability also predicts social functioning more so than other related neurocognitive and social cognitive variables (Hooker & Park, 2002). Many studies have found schizophrenia-related abnormalities in emotion recognition brain networks. Functional neuroimaging studies of emotion recognition in schizophrenia have repeatedly identified abnormal responses in the amygdala (Das et al., 2007; Gur et al., 2007a; Gur et al., 2002; Hall et al., 2004; Hempel et al., 2003; Holt et al., 2006; Kosaka et al., 2002; Phillips et al., 1999; Pinkham et al., 2008; Schneider et al., 1998; Taylor, Liberzon, Decker, & Koeppe, 2002; Williams et al., 2004) as well as abnormalities in the medial prefrontal cortex (Brüne et al., 2008; Brunet, Sarfati, Hardy-Baylé, & Decety, 2003; Das et al., 2007; Vinogradov, Luks, Schulman, & Simpson, 2008; Whitfield-Gabrieli et al., 2009; Williams et al., 2004), superior temporal cortex (Brüne et al., 2008; Leitman et al., 2008; Pinkham et al., 2008), and somatosensory-related cortices (Farrer et al., 2004; Spence et al., 1997; Waberski et al., 2004). Structural measures suggest reduced volume and/or gray matter volume in schizophrenia in temporal cortices (Davidson & Heinrichs, 2003; Siever & Davis, 2004; Wright et al., 2000) and the amygdala-hippocampal complex (Exner et al., 2004; Lawrie & Abukmeil, 1998; Nelson, Saykin, Flashman, & Riordan, 1998; Wright et al., 2000).

Given the consistent associations between FER and schizophrenia, it has been suggested that FER may serve as a useful neurocognitive endophenotype (Gur et al., 2007b). An endophenotype is an observable characteristic that lies intermediate between a mental disorder and the underlying genetic and/or neurobiological substrates of that disorder (Gottesman & Gould, 2005). The concept was developed to provide a way for researchers to deal with problems arising from diagnostic overlap, heterogeneity, and complexity in investigations of high-level mental disorders (Insel & Cuthbert, 2009). Characteristics of a useful psychiatric endophenotype include an association with illness, state-independence, heritability, cosegregation with illness within families, and presence in unaffected relatives of a person with the illness at higher rates than in the general population (Gottesman & Gould, 2005). FER abnormalities are consistently associated with schizophrenia and appear to be state independent, as they are measurable before psychosis-onset (Häfner et al., 2003; Walker et al., 1993; Yung & McGorry, 1996), in first-episode psychosis (Edwards et al., 2001), and in individuals not experiencing an active psychotic episode (Wolwer, Streit, Polzer, & Gaebel, 1996). FER ability is also heritable (Greenwood et al., 2007), and impaired in individuals at familial risk of developing schizophrenia but not themselves mentally ill, with FER performance intermediate between patients and healthy control participants (Kee, Horan, Mintz, Green 2004; Bediou et al., 2007). Based on the endophenotype approach, understanding FER deficits may provide a means of linking high-level impairments with differences in underlying genetics and biological pathways.

The High-risk Approach

The current literature has demonstrated that schizophrenia is associated with abnormalities in FER behaviorally and neurally. Interpreting findings in schizophrenia research can be challenging, however, due to the many secondary and/or confounding factors associated with having a severe mental disorder. Schizophrenia and related psychotic disorders are associated with significant psychosocial stress, long-term deterioration of function, chronic drug treatment, and other secondary characteristics that significantly impact functioning and neurocognition, but are not part of the core pathophysiology of the disease (Lenzenweger, 2006). Social deficits could arise or be exacerbated, for example, by the widespread social stigma associated with having a severe mental disorder in our society. Moreover, severe deficits in sustained attention and information processing (Heinrichs, 2001) tend to impact performance across a wide range of tasks, making it more difficult to distinguish specific impairments from the background of generalized impairments in schizophrenia patients (Kerr & Neale, 1993). These confounds make it difficult to interpret findings in schizophrenia, which may arise from any of these factors.

One way of addressing the problem of secondary confounds is by investigating emotion processing abnormalities in individuals who are at high-risk of developing schizophrenia or other psychotic disorders, but are not psychotic. High-risk groups that have been used in this type of investigation include individuals who show early clinical signs of psychosis (clinical high-risk and/or schizophrenia prodromes), relatives of people with schizophrenia or related disorder (genetic high-risk), individuals with schizotypal personality disorder, and nonpsychotic individuals who are high in *schizotypy* – a latent dimension of psychosis vulnerability thought to be expressed as subthreshold psychosis-like characteristics (Lenzenweger 2006; Meehl 1962,

1990). In the current set of studies, the focus will be on this latter form of psychometrically-defined psychosis risk, as inferred by the presence of self-reported psychosis-like characteristics. As the term *schizotypy* has come to be associated with the latent genetic predisposition to developing schizophrenia (Meehl 1962/1990), the more etiologically-neutral term *psychosis-proneness* will be used to refer to this form of psychosis vulnerability.

Individuals who are high in psychosis-proneness show similar symptoms and characteristics as those with schizophrenia, but in a subthreshold or attenuated form. These characteristics can include social isolation, social and physical anhedonia, magical thinking, suspiciousness, and perceptual aberrations (Chapman & Chapman, 1980; Kwapil, 1998; Lenzenweger et al., 2006; Rado, 1953; Raine, 1991). These can be assessed via interview, but also by self-report / questionnaire measures. High scores on self-report measures are thought to indicate an underlying genetic or biological predisposition to developing psychosis, as individuals with high psychosis-proneness scores are more likely to develop a schizophrenia spectrum disorder (Kendler, Thacker, & Walsh, 1996; Kwapil, 1998; Kwapil, Miller, Zinser, Chapman, & Chapman, 1997). Along the same lines, psychosis-proneness scores are higher in the relatives of schizophrenia patients than control participants (Faraone, Green, Seidman, & Tsuang, 2001; Kendler & Walsh, 1995).

Many individuals high in psychosis-proneness qualify for a diagnosis of schizotypal personality disorder, so that these two groups overlap (high psychometric psychosis-proneness and schizotypal personality). Some measures of psychosis-proneness are specifically designed to identify people with schizotypal personality traits, as schizotypal personality disorder is a diagnosis defined by the presence of a certain number and type of schizophrenia-like symptoms (Raine, 1991). Those with schizotypal personality disorder will almost invariably score high on

measures of psychosis-proneness. Schizotypal personality disorder is best conceptualized as a particular phenotype associated with high levels of psychosis-proneness. Indeed, findings from samples of individuals high in psychosis-proneness and schizotypal personality disorder often converge (Raine, 1991; 2006).

As a means of identifying high-risk participants, self report measures of psychosis-proneness have the advantage of yielding participant groups that are both phenotypically homogeneous (unlike samples of genetic high-risk participants) and nontreatment-seeking (unlike clinically identified individuals with schizotypal personality disorder). Importantly, research has indicated that scoring high in self-reported measures of psychosis-proneness is related to a 10-fold or greater increased risk of developing psychosis relative to the baseline risk in the normal population (Blanchard et al., 2011; Kwapil, 1998).

Studying dimensions of psychosis-proneness rather than diagnostic categories also maps well onto recent theoretical shifts away from diagnostic categories and towards symptom dimensions (Cuthbert & Insel, 2010). There is an increasing realization among mental health researchers that mental disorders may not respect the diagnostic boundaries defined by the DSM and that behavioral and neural *dimensions* may have more biological reality than specific diagnoses (Cuthbert & Insel, 2010, Hyman, 2007; Smoller et al., 2008). Studying mental disorders through a dimensional rather than categorical framework also increases phenotype homogeneity, a major obstacle thusfar in mental health research, and facilitates a translational approach (Hyman, 2010). Dimensional frameworks also provide clearer connections between research on mental disorders and research on individual differences. This is especially relevant as recent large-scale investigations in psychiatric genetics have revealed that a large proportion of the genetic vulnerability to developing schizophrenia is based on variations in commonly

occurring alleles (Purcell et al., 2009). This means that genetic risk for schizophrenia is, in large part, based on common alleles of small effect and thus may manifest itself in terms of individual differences in neural and neurocognitive endophenotypes (Braff et al., 2007; Gottesman & Gould, 2003; Ivleva et al., 2009; Meyer-Lindenberg & Weinberger, 2006).

Investigations of FER and psychosis vulnerability, from the perspective of individual differences, are thus both timely and potentially informative given shifting approaches to studying mental disorders and recent advances in our understanding of the way genetic vulnerability is related to psychosis development.

Psychosis-proneness and Emotion Recognition: Previous Findings

FER deficits have been observed in individuals with schizotypal personality disorder (Mikhailova et al., 1996; Waldeck & Miller, 2000), individuals at clinical high-risk of developing schizophrenia (Addington et al., 2008), and relatives of individuals with schizophrenia (Bediou et al., 2007; Loughland, Williams, & Harris, 2004; Toomey et al., 1999). Previous studies have indicated that high levels of psychometric psychosis-proneness are related to reduced social functioning (Henry, Bailey, & Rendell, 2008; Jahshan & Sergi, 2007) and social cognitive abilities (Langdon & Coltheart, 2001; Langdon & Coltheart, 2004). Research on the relationship between psychometric psychosis-proneness and FER has been less clear. Some studies have reported reduced FER performance among psychosis-prone individuals (Brown & Cohen, 2010; Poreh, Whitman, Weber, & Ross, 1994; van 't Wout et al., 2004; Williams, Henry, & Green, 2007). Other studies have not found significant differences in FER related to psychosis-proneness (Jahshan & Sergi, 2007; Toomey & Schuldberg, 1995; Toomey et al.,

1999). Mixed findings may be due to lack of sensitivity in FER measures, symptom specific relationships, or small sample sizes (Brown & Cohen, 2010).

Neuroimaging studies of social-emotional processing and psychosis-proneness (including schizotypal personality disorder) are limited, and hence it is difficult to know how and to what extent differences in social or emotional measures are related to differences in underlying neural circuitry. Two studies that focus on emotion processing and psychosis-proneness both used tasks engaging cognitive control systems. A study using an emotional stroop task found that individuals high vs. low in psychosis-proneness (based on positive psychosis-like characteristics) show different patterns of activity in right dorsolateral prefrontal cortex, hippocampus, and amygdala when viewing negative emotion words (Mohanty et al., 2005). A study using an emotion reappraisal task found reduced functional connectivity in frontal and limbic areas in individuals high in psychosis-proneness when compared to a control sample (Modinos, Ormel, & Aleman, 2010). These studies suggest abnormalities in fronto-limbic circuits during emotion processing, which is consistent with findings in schizophrenia samples (Li, Chan, McAlonan, & Gong, 2010).

Studies of structural brain abnormalities in regions implicated in FER have been more plentiful, although these studies are mostly conducted with individuals diagnosed with schizotypal personality disorder and it is not clear how structural differences might relate to FER ability. One of the most consistent structural abnormalities in chronic schizophrenia is reduced volume of the superior temporal gyrus (Davidson & Heinrichs, 2003; Downhill et al., 2001; Siever & Davis, 2004; Wright, et al., 2000). Reduced superior temporal gyrus volume is also a robust finding in schizotypal personality disorder (Dickey, McCarley, & Shenton, 2002; Dickey et al., 2002; Dickey et al., 2003; Downhill et al., 2001; Siever & Davis, 2004). Reduced frontal

lobe volume is less widespread (Hazlett et al., 2008; Kawasaki et al., 2004; Siever et al., 2002; Suzuki et al., 2005). Medial temporal lobe abnormalities (amygdala, hippocampus, parahippocampal gyrus), although robustly identified in schizophrenia samples (Honea, Crow, Passingham, & MacKay, 2005), are inconsistently identified in schizotypal personality disorder (Siever & Davis, 2004). It has been suggested that reduced medial temporal lobe volume may be more prevalent among familial or genetic high-risk individuals (Seidman et al., 2003; van Rijn, Aleman, Swaab, & Kahn, 2005) than in nonfamilial high-risk phenotypes like schizotypal personality disorder (Velakoulis et al., 2006). Altogether, these findings led Siever & Davis (2004) to hypothesize that normal or compensatory frontal lobe function and/or subcortical stability may protect psychosis-prone individuals from primary temporal lobe abnormalities that could otherwise develop into full-blown psychosis. Along the same lines, Nakamura et al. (2005) used diffusion tensor imaging to show that while schizophrenia patients have abnormalities in both frontal-temporal and cortical-limbic connections, schizotypal personality disorder was associated with reduced connectivity in frontal-temporal tracts only. Notably, progressive gray matter loss in the medial temporal lobes and orbital prefrontal cortex has been observed at the transition to psychosis (Pantelis et al., 2007; Velakoulis et al., 2006). Altogether, structural brain measures suggest that temporal cortical abnormalities are related to psychosis-proneness or vulnerability, with other (e.g. frontal and medial temporal) abnormalities emerging and/or progressing with psychosis development.

Volumetric studies focusing on parietal cortex also reveal reduced volume in widespread regions among schizophrenia patients. Reduced parietal lobe volume in schizotypal personality disorder, however, appears to be limited to the postcentral gyrus / somatosensory cortex (Zhou et al., 2007). This is consistent with behavioral evidence that basic aspects of somatosensory

processing are impaired in psychosis-prone participants (Chang & Lenzenweger, 2005; Lenzenweger, 2000) and the relatives of schizophrenia patients (Chang & Lenzenweger, 2001, 2004, 2005; Hooley & Delgado, 2001; Lenzenweger, Nakayama, Chang, & Hooley, 2003). Abnormalities in somatosensory representation may be related to the higher-level deficits in emotion and self-other processing characteristic of psychosis, as would be predicted by action-perception models of social cognition (Brunet-Gouet & Decety, 2006).

Emotion Recognition Deficits: Generalized or Specific Impairment?

Abnormalities in multiple systems could contribute to schizophrenia or psychosis-proneness related deficits in FER. FER deficits could, for example, reflect generalized performance deficits (Mohamed et al., 1999; Whittaker, Deakin, & Tomenson, 2001). Schizophrenia is related to abnormalities in attention, motivation, and disorganized behavior (Docherty, 2005) all of which could impact FER performance in the lab and in everyday life, but do not reflect a specific social-emotional deficit. A generalized impairment explanation would not reduce the importance of social-emotional processing deficits (e.g. deficits in attention that drive FER deficits could still negatively impact social functioning), but it does suggest mechanisms for impairment outside of specialized social-emotional processing networks.

Another possibility is that FER deficits reflect broader deficits in social perception or face processing. Some studies have, for example, found similar deficits in emotional and nonemotional aspects of face processing among patients with schizophrenia (Addington & Addington, 1998) whereas other studies have found greater or selective impairments in emotional face processing (Bediou et al., 2005). Behavioral, neuropsychological, and neuroimaging studies indicate that FER relies on dissociable systems from face identity

recognition (Bruce & Young, 1986; Haxby et al., 2000), and that aspects of FER can be selectively disrupted (Calder, 1996). Among schizophrenia patients, some studies have found abnormal activity in inferior temporal face processing areas during recognition of non-emotional face information (Gur et al., 2002a; Herrmann, Ellgring, & Fallgatter, 2004; Quintana et al., 2003), whereas others have found that there are no differences between patients and control participants in these regions (Foxe, Murray, & Javitt, 2005; Yoon, D'Esposito, & Carter, 2006). Together with mixed behavioral findings, these studies suggest that psychosis may be related to greater or more consistent impairment in FER than for other forms of face processing.

FER and social-emotional processing deficits may also be caused by impairments in self-representation. Some researchers have suggested that abnormalities in self-processing are fundamental to psychotic illness (Sass & Parnas, 2003). Early conceptualizations of schizophrenia reflected this abnormality (e.g. the “orchestra without a conductor”: Kraepelin, 1896). Recent theories of social cognition and perception have proposed that understanding the emotions of others involves the same mechanisms as expressing those emotions ourselves – that is, we use our own somato-motor representations to simulate the observed actions (here, facial expressions) of another individual and use the output of that simulation to understand what another person is feeling (Adolphs, 2002; Gallese, Keysers, Rizzolatti, 2004). Evidence for simulation theories of emotion understanding comes from literature showing contributions of somatosensory, motor, and cognitive self-representation mechanisms to emotion recognition (Adolphs et al., 2000; Adolphs, 2002; Heberlein & Atkinson, 2009; Oberman & Ramachandran, 2007). A large lesion-based study found that damage to brain areas involved in producing and integrating somatosensory information about one’s own body impaired FER ability (primary and secondary somatosensory cortices, insular cortex, and the anterior supramarginal gyrus: Adolphs

et al., 2000). A simulation-based framework of FER, where schizophrenia is related to abnormalities in somato-motor systems, would explain the parallel deficits in emotion expression and emotion recognition that have been found in patients with schizophrenia (Kring et al., 1993). More broadly, abnormalities in the shared neural and neurocognitive mechanisms for representing the self (including somatosensory and motor systems) may underlie the ubiquitous deficits in self processing, emotional expression, and emotion understanding that are associated with schizophrenia spectrum disorders (Brunet-Guoet & Decety, 2006). Abnormalities in this action-perception coupling system have been identified in individuals with autistic spectrum disorder, who exhibit consistent deficits in emotion recognition and social cognitive processing (Dapretto et al., 2006; Oberman et al., 2005; Williams, Whiten, Suddendorf, & Perrett, 2001) that share some features with deficits observed among patients with schizophrenia (Frith, 2004). Differences in cognitive and somatic representations of the self may underlie deficits in FER and social-emotional processing in schizophrenia.

The high-risk approach becomes particularly useful in understanding the contributions of specific vs. generalized impairments in FER ability. Severe generalized impairments in attention and/or perception make emotion specific deficits, if such exist, difficult or impossible to measure. Although psychosis-proneness is also associated with deficits in attention and perception that could affect performance across a range of tasks, these deficits tend to be less marked than those of schizophrenia patients (Chen et al., 1998). Thus, investigations of psychosis-proneness provide a potentially more sensitive approach for looking at specificity of FER deficits and the contribution of deficits in other functions.

Research Questions

The current dissertation consists of a systematic investigation of the relationship between emotion recognition and psychosis-proneness, at behavioral and neural levels, including specificity and contributing processes. As FER deficits represent an important and highly replicated finding in schizophrenia research, understanding the way these deficits relate to psychosis-proneness provides a potentially informative approach for understanding the mechanisms that underlie psychosis vulnerability and psychosis-related social-emotional deficits. If FER differences are explained by deficits in more general functions (e.g. visual perception or self-representation) this provides possible routes for understanding these deficits and targets of interventions to ameliorate them, and ultimately address social functioning abnormalities that contribute to disability and morbidity in schizophrenia patients.

In this dissertation, I provide data to address the following questions:

Experiment #1. *Is psychosis-proneness related to reduced FER ability? Do FER impairments reflect more generalized impairments in visual perception or face processing?*

Paper #1: Germine, L., & Hooker, C.I. (2011). Face emotion recognition is related to individual differences in psychosis-proneness. *Psychological Medicine*, 41(5), 937-948.

Experiment #2. *Is psychosis-proneness related to neural response differences in FER-related brain networks?*

Paper #2: Germine, L., Garrido, L., Bruce, L., & Hooker, C.I. (2011). Social anhedonia is associated with neural abnormalities during face emotion processing. *Neuroimage*, 58(3), 935-945.

Experiment #3a. *Is psychosis-proneness related to differences in bodily self-representation?*

More specifically, is psychosis-proneness related to susceptibility of an individual's body representation to distortion?

Paper #3: Germine, L., Benson, T., Cohen, F., & Hooker, C.I. (under review). Psychosis-proneness and the rubber hand illusion of body ownership.

Experiment #3b. *Do differences in body representation flexibility explain the relationship between psychosis-proneness and FER ability?*

In Additional Findings, p.69

Experiment #3c. *Which dimensions/measures of psychosis-proneness predict differences in FER ability, after accounting for the relationship between psychosis-proneness and IQ?*

In Additional Findings, p.71

Experiment #4. *Is psychosis-proneness related to differences in self-referential processing?*

Specifically, is psychosis-proneness related to biases in (4a) self-referential source memory (remembering the source of information as arising from oneself) or (4b) self-referential recognition memory (recognizing information that has been processed with respect to oneself)?

In Additional Findings, p.75

Experiment #5. *Is psychosis-proneness related to emotion recognition ability in other modalities, besides vision? Specifically, is psychosis-proneness related to voice emotion recognition ability?*

In Additional Findings, p.84

The goal of these experiments is to understand how FER relates to psychosis vulnerability, and, ultimately, how social-emotional impairments contribute to the development of severe mental disorders, like schizophrenia.

Paper #1: Face emotion recognition is related to individual differences in psychosis-proneness

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Abstract

Deficits in face emotion recognition (FER) in schizophrenia are well-documented, and have been proposed as a potential intermediate phenotype for schizophrenia liability. However, research on the relationship between psychosis vulnerability and FER has mixed findings and methodological limitations. Moreover, no study has yet characterized the relationship between FER ability and level of psychosis-proneness. If FER ability varies continuously with psychosis-proneness, this suggests a relationship between FER and polygenic risk factors. We tested two large internet samples to see whether psychometric psychosis-proneness, as measured by the Schizotypal Personality Questionnaire-Brief (SPQ-B) is related to differences in face emotion identification and discrimination or other face processing abilities. Experiment 1 (n = 2332), showed that psychosis-proneness predicts face emotion identification ability, but not face gender identification ability. Experiment 2 (n = 1514) demonstrated that psychosis-proneness also predicts performance on face emotion but not face identity discrimination. The tasks in Experiment 2 used identical stimuli and task parameters, differing only in emotion/identity

judgment. . Notably, the relationships demonstrated in Experiments 1&2 persisted even when individuals with the highest psychosis-proneness levels (the putative high-risk group) were excluded from analysis. Our data suggest that FER ability is related to individual differences in psychosis-like characteristics in the normal population, and that these differences cannot be accounted for by differences in face processing and/or visual perception. Our results suggest that FER may provide a useful candidate intermediate phenotype.

Introduction

Advances in the molecular genetics of schizophrenia increasingly support polygenic risk models based on many genes of small effect (Gottesman & Shields, 1967, Purcell et al., 2009, Shi et al., 2009, Stefansson et al., 2009). For example, in a recent large scale genome-wide association study, Purcell and colleagues of the International Schizophrenia Consortium (2009) reported that at least 1/3 of the variance in schizophrenia liability could be explained by a polygenic model involving thousands of commonly occurring alleles. Polygenic models suggest that the genetic liability may manifest as individual differences in specific neural circuits, producing observable neurocognitive intermediate phenotypes (Braff et al., 2007, Gottesman & Gould, 2003, Ivleva et al., 2009, Meyer-Lindenberg & Weinberger, 2006) .

Based on the criteria proposed by Gottesman and Gould (2003), deficits in face emotion recognition (FER) provide a potential intermediate phenotype for schizophrenia and related disorders (Gur et al., 2007a, 2007b). FER deficits are consistently related to schizophrenia (Kohler and Brennan, 2004, Hooker and Park, 2002, Mandal et al., 1998, Mueser et al., 1997) are observable in early (Edwards et al., 2001) and late psychosis (Mueser et al., 1997), remain after

treatment (Herbener et al., 2005), and are related to familial risk (Bediou et al., 2007, Kee et al., 2004). Evidence suggests that FER ability is also highly heritable (Gur et al., 2007a, 2007b). FER provides the advantage of implicating a well-studied neural network, including the amygdala, superior temporal sulcus, and inferior parietal lobe (Adolphs, 2002), whose function can be dissociated from the function of neural networks concerned with static face features (Haxby et al., 2000). Notably, people with schizophrenia spectrum disorders have structural and functional abnormalities in neural regions that support FER processing (Aleman & Kahn, 2005, Brunet-Gouet & Decety, 2006), but relatively normal function of neural regions such as the fusiform gyrus that support face identity processing (Foxy et al., 2005, Yoon et al., 2006).

Recent evidence suggests that FER deficits are not limited to individuals with schizophrenia, but are more broadly related to psychosis vulnerability (Phillips & Seidman, 2008). FER deficits have been reported in the first-degree relatives of schizophrenia patients (Bediou et al., 2007, Kee et al., 2004), even where other face processing abilities are unimpaired (Bediou et al., 2007). If FER deficits contribute to the development of psychosis by influencing the development of psychosis-like characteristics, they may also be observable in healthy, high-risk individuals with psychosis-like or subthreshold characteristics (schizotypy or psychosis-proneness). Individuals with high familial risk vary widely in how much they express schizotypal or psychosis-like traits (Kremen et al., 1998, Tsuang et al., 1999, Vollema et al., 2002), so studies of psychometric psychosis-proneness provide a critical means of addressing the relationship between FER, phenotype, and psychosis vulnerability.

Results from studies looking at the relationship between psychometric psychosis-proneness and FER have thus far been mixed or unclear. Some studies have shown FER deficits in individuals high (versus low) in schizotypy or psychosis-proneness (Aguirre et al., 2008,

Mikhailova et al., 1996, Poreh et al., 1994, Waldeck & Miller, 2000, Williams et al., 2007) whereas other studies have not (Jahshan & Sergi, 2007, Toomey & Schuldberg, 1995, van 't Wout et al., 2004). Ceiling effects may have contributed to negative results however (e.g. Jahshan & Sergi, 2007, Toomey & Schuldberg, 1995), by reducing the ability to detect between-group differences. Sensitive FER tests are needed to detect individual differences in healthy populations.

Furthermore, general cognitive impairment is associated with schizophrenia patients as well as those at risk; therefore FER deficits could be part of more generalized deficits in face processing or in visual perception rather than emotion processing (Addington & Addington, 1998). Of the studies that have employed face processing related control tasks, Poreh et al. (2004) found evidence of general face processing impairment in psychosis-prone individuals, whereas Williams et al. (2007) reported that high psychosis-proneness was related to face emotion recognition impairments, but not face identity recognition impairments, based on the Benton Face Recognition Test (although the Benton Face Recognition test may be a suboptimal measure of face discrimination ability; see Duchaine & Nakayama, 2004). Moreover, differences in procedure or face stimuli between tasks can contribute to misleading or artefactual results. Hence, it is not clear from current research whether the relationship between psychosis-proneness and FER, where observed, is related to more generic processes. Given the possible role of FER as an intermediate phenotype, good behavioral assays in schizophrenia and schizophrenia risk are an important tool, and more research is needed to determine how best to test, characterize and quantify the extent and specificity of ER deficits in individuals with schizophrenia or at risk for schizophrenia.

In addition, as evidence for polygenic models accumulates, it is increasingly important to characterize the relationship between psychosis liability and neurocognition across the continuum. FER differences may, for example, vary linearly with psychosis-proneness or only be observable in individuals with the highest levels of psychosis-proneness. Clarifying the nature of this relationship is needed for deciding whether a continuous individual differences model (Claridge, 1997) or a discrete, discontinuous model (e.g. Meehl, 1962, 1990) is most appropriate for characterizing FER as an intermediate phenotype. Thus far, no study has examined the relationship between FER and psychosis liability at intermediate levels of psychosis-proneness.

In two experiments using very large, psychometrically-defined samples, we tested the hypothesis that variations across the continuum of psychosis-proneness are related to FER ability but not to other face processing abilities. In Experiment 1, we administered tests of face emotion and face gender identification to extend Bediou et al.'s (2007) finding of selective FER impairments in familial high-risk participants to a sample of participants with varying levels of psychometric risk. In Experiment 2, we replicated our results from Experiment 1 using a test of face emotion and face identity discrimination. These discrimination tasks were designed to be sensitive to individual differences in face processing, closely matched to minimize difficulty or task-related artifacts, and have been shown to rely on specific and dissociable neural subsystems (Garrido et al., 2009, Pitcher et al., 2008).

Experiment 1: Emotion Identification vs. Gender Identification

In order to determine whether individual differences in face emotion processing

performance is related to psychosis-proneness, we administered a face emotion and a face gender identification task to individuals in the normal population with varying levels of psychosis-proneness based on scores from the brief version of the Schizotypal Personality Questionnaire (Raine & Benishay, 1995).

Methods.

Participants. Subjects were individuals who navigated to the website, <http://www.testmybrain.org> and clicked on a link labeled “Recognizing Emotion and Gender from Faces”. Data collected from face processing tests offered on testmybrain.org (different from the ones described here) has been included in a previously published study (Wilmer et al., 2010). There was no specific advertising conducted for the study or the website. Most users arrived at the site through self-generated internet searches and by following links posted by other volunteers on social networking websites and blogs. Subjects were given feedback on their performance at the conclusion of the test as incentive for participating. There were no limitations on who could participate in the experiment, but subjects in the reported sample had to meet several criteria. After filling out an online consent form, participants completed a questionnaire assessing demographics, psychiatric, neurological and medical history. Participants were excluded if they endorsed any of the following: younger than 16 or older than 65 years old, neurological problems, psychological problems, vision problems, a physical disability that might impact their performance, Asperger’s disorder or other autistic spectrum disorder (ASD). At the end of the experiment, subjects who indicated they had had technical problems were also excluded, as were those who may have participated in the experiment before (as indicated by self-report and/or checking the individual’s web browser for a “cookie” that indicated previous participation).

Our final group was comprised of 2332 subjects. Age, gender, and SPQ information for this sample is shown in Table 1.

Table 1. Mean performance and participant information

	Range	Mean	s.d.
Experiment 1 (<i>n</i> = 2332)			
Age (years)	16–65	29.1	11.5
SPQ-B total (all factors)	0–22	9.2 ^a	5.1
Interpersonal factor	0–8	3.8	2.6
Cognitive-perceptual factor	0–8	3.1	2.1
Disorganized factor	0–6	2.3	1.9
% female	68		
Emotion identification (proportion correct)			
All emotions ^b	0.17–0.92	0.67	0.1
Happiness ^c	0.07–1	0.86	0.12
Anger ^c	0–1	0.61	0.17
Disgust ^c	0–1	0.53	0.19
Fear ^c	0–1	0.68	0.17
Gender identification ^d	0.43–1	0.81	0.08
Experiment 2 (<i>n</i> = 1514)			
Age (years)	16–65	29.3	10.6
SPQ-B total (all factors)	0–22	9.5	4.9
Interpersonal factor	0–8	3.9	2.6
Cognitive-perceptual factor	0–8	3	2.1
Disorganized factor	0–6	2.6	1.8
% female	62		
Emotion discrimination ^d	0.4–1	0.81	0.08
Identity discrimination ^d	0.23–1	0.77	0.09

SPQ-B, Schizotypal Personality Questionnaire – Brief version; s.d., standard deviation.

^a Mean SPQ-B score from this sample was approximately equal to the mean obtained from a sample of adults with a similar gender distribution (Irwin, 2001: mean = 9.25, where 63% were female).

^b Proportion correct out of 60.

^c Proportion correct out of 15.

^d Proportion correct out of 40.

Procedure. All subjects began by completing a test of face gender identification and then a test of face emotion identification, both using morphed face stimuli and adapted from tests previously administered to schizophrenia patients and their relatives (Bediou et al., 2007).

In the face gender identification task, faces were created by morphing a gender neutral face with each of four male and four female faces. Each face stimulus contained 20%, 30%, 40%, 50% or 60% of the target gender (male or female), yielding 40 face stimuli (8 identities x 5 percentage categories). In the face emotion identification task, stimuli were faces morphed

between a neutral expression and an emotional expression. There were 4 different emotional expressions: happy, disgusted, angry, and fearful. Faces were created from one male and two female face identities. The faces contained 20%, 30%, 40%, 50%, and 60% of the emotional expression for each identity and each type of facial expression. This yielded 60 face trials (4 emotion types x 3 identities x 5 percentage categories). The original tasks used by Bediou et al. (2007) each contained 10 percentage categories, with trials containing 10% to 100% of the target gender or expression. Based on the control data reported by Bediou et al. (2007), the range 20% to 60% was chosen for the current experiment to maximize the range of difficulty levels in a minimal number of trials. The different increments of emotion and gender intensities created varying levels of difficulty, and therefore increased the sensitivity of the task to reveal individual differences in performance. See Figure 1 for example stimuli.

In both tasks, each trial began with a fixation cross for 250ms, then the face was presented on screen for 1000ms, followed by the list of answer choices. Participants made a choice between “male or female” in the face gender test, and “angry, disgusted, fearful, or happy” in the face emotion test. The answer choices remained on screen for seven seconds or until the participant responded. Participants indicated their response by pressing a key (‘m’ or ‘f’; ‘a’, ‘d’, ‘f’, or ‘h’). For each task, participants who failed to respond within the time limit on more than ten percent of trials were excluded from analysis.

After completing both tests, subjects responded to items from the brief version of the Schizotypal Personality Questionnaire (SPQ-B) (Raine & Benishay, 1995), a measure of psychosis-proneness. The SPQ-B is a 22 item self-report questionnaire that indexes the degree to which an individual has schizophrenia-like cognitive-perceptual (e.g. “Have you ever noticed a common event or object that seemed to be a special sign for you?”), interpersonal (e.g. “I feel I

have to be on my guard even with my friends.”), and disorganized features (e.g. “I sometimes use words in unusual words.”).

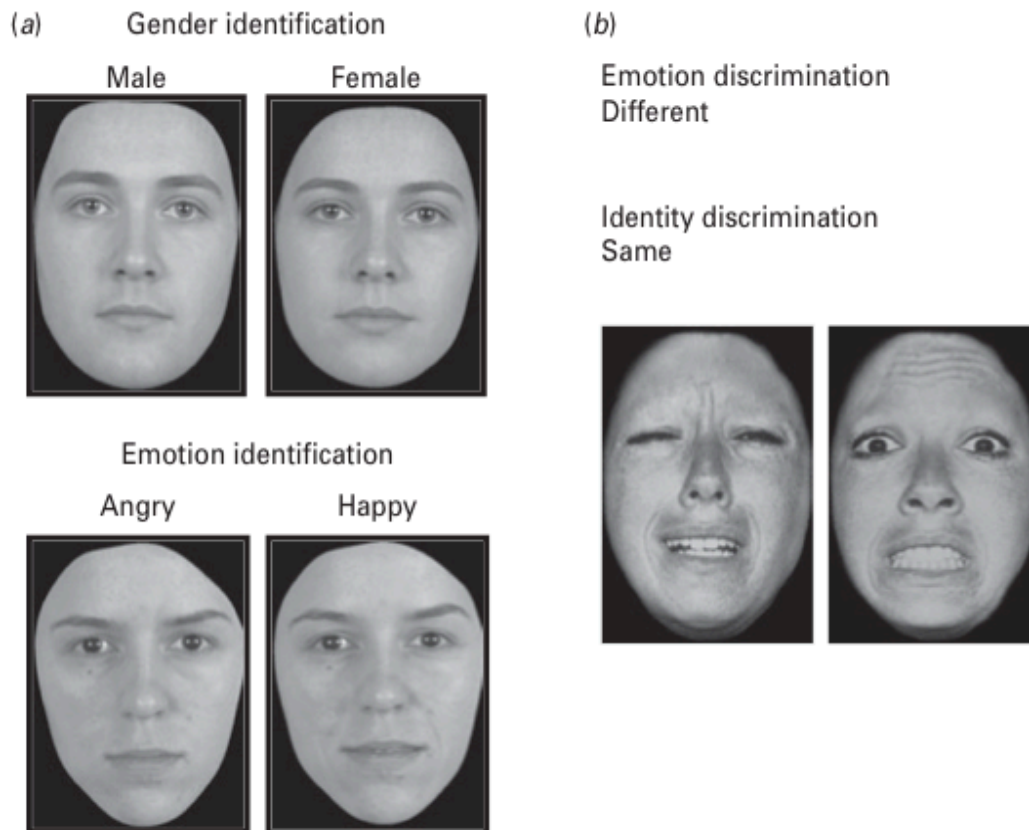


Figure 1. Stimuli from Experiments 1 and 2

(a) Images are shown from Experiment 1 (Bediou et al., 2007). In the gender identification task, participants had to label each morphed face as male or female. In the emotion identification task, participants had to label each emotion as fearful, angry, disgusted, or happy. Correct responses for each image/trial are shown in italics. (b) Images from Experiment 2 are shown (Garrido et al., 2009). Participants had to judge whether two sequentially presented faces had the same or different emotion (emotion discrimination task) or the same or different identity (identity discrimination task). Correct responses for this image pair in each task are shown in italics.

Results. A summary of mean performance for this sample is given in Table 1. Paired sample t-test results showed that participants were more accurate on gender identification as compared with emotion identification ($t(2331) = 59.4, p < 0.001$).

Multiple regression was conducted (SPSS version 16.0, 2007) to test the hypothesis that individual differences in psychosis-proneness were related to emotion identification, but not to gender identification performance, by using age, participant sex, and SPQ-B scores as predictors of face emotion identification. Previous research has indicated that face processing ability is related to both participant sex and age (Bowles et al., 2010, McClure et al., 2000) so we controlled for these effects in our analysis. Since both SPQ-B scores and age ($r = -0.21$) and SPQ-B scores and sex ($r = 0.06$) were significantly related in this sample, controlling for age and sex also allowed us to focus on variations in face processing with psychosis-proneness that were not due to variations in age and sex. As expected, SPQ-B score significantly predicted emotion identification performance ($\beta = -0.09, p < 0.001$), controlling for the effects of sex ($\beta = -0.18, p < 0.001$) and age ($\beta = -0.07, p < 0.01$). The relationship between psychosis-proneness and emotion identification did not change when gender identification performance was added as a predictor ($\beta = -0.09, p < 0.001$).

Two subgroups were defined by total SPQ-B score such that they roughly represented the bottom and top 10% of the sample. The top 10% is traditionally defined as high-risk in studies of psychometric schizotypy and individuals with schizophrenia spectrum disorders such as schizotypal personality disorder are likely to be in the top 10% of scorers (Raine & Benishay, 1995) whereas the bottom 10% is unlikely to contain individual with schizophrenia spectrum diagnoses (Raine, 1991). Individuals with the lowest SPQ-B scores (SPQ-B scores from 0 to 2, bottom 10%) were significantly more accurate than those with the highest SPQ-B scores (SPQ-B

scores 17 and above, top 9%) [mean for low SPQ-B scorers: 0.66 (0.1); mean for high SPQ-B scorers = 0.69 (0.1); independent samples t-test: $t(430) = 2.7, p < 0.01$] and corresponded to a Cohen's d effect size of 0.24. This relationship was not driven entirely by high SPQ-B scorers (those with possible schizophrenia spectrum disorders): SPQ-B scores predicted emotion identification performance even when individuals with high SPQ-B scores (scores of 16 / 22 or higher) were excluded (2023 participants remaining; $\beta = -0.11, p < 0.001$).

To see whether the observed relationship between psychosis-proneness and face perception was specific to emotion processing, we conducted multiple regression of face gender performance on age, sex, and SPQ-B score. Results indicated that although age and sex significantly predicted gender identification performance (age: $\beta = 0.06, p < 0.01$; sex: $\beta = -0.002, p = 0.99$), SPQ-B score did not ($\beta = -0.02, p = 0.43$). Accordingly, high and low SPQ-B scorers did not significantly differ in gender identification performance [mean for low SPQ-B scorers = 0.80 (0.08); mean for high SPQ-B scorers = 0.81 (0.08); independent samples t-test: $t(430) = 1.0, p = 0.3$].

Scores on the SPQ-B can be divided into three subscales: an interpersonal factor, a cognitive-perceptual factor, and a disorganized factor. These three factors are analogous to the three symptom clusters observed in schizophrenia (Arndt et al., 1991). After controlling for the effects of age and sex, multiple regression analysis revealed that each of the factors predicted emotion performance (interpersonal: $\beta = -0.09, p < 0.001$; cognitive-perceptual: $\beta = -0.06, p < 0.01$; disorganized: $\beta = -0.04, p < 0.05$), but not gender performance (interpersonal: $\beta = -0.03, p = 0.23$; cognitive-perceptual: $\beta = 0.01, p = 0.66$; disorganized: $\beta = -0.02, p = 0.27$).

To identify whether the relationship between SPQ-B score and emotion identification was significantly greater than the relationship between SPQ-B score and gender identification,

we used Steiger's $Z1^*$ statistic for comparing two correlation coefficients from the same sample (Steiger, 1980). This analysis showed that the partial correlation between SPQ-B score and emotion identification and SPQ-B score was significantly greater than the partial correlation between SPQ-B score and gender identification ($Z = 2.8, p < 0.01$).

Finally, to explore the relationship between SPQ-B scores and identification of specific emotions, we conducted multiple regression with SPQ-B score, age, and participant sex as predictors of proportion correct for happy, angry, disgusted, and fearful faces separately. Mean performance for individual emotions is shown in Table 1. SPQ-B scores significantly predicted identification of happy faces ($\beta = -0.07, p < 0.001$), angry faces ($\beta = -0.07, p < 0.001$), and fearful faces ($\beta = -0.05, p < 0.05$), but predicted disgusted faces only at the trend level ($\beta = -0.04, p = 0.08$). These results should be interpreted cautiously, however, as we did not have any a priori predictions about the relationship between psychosis-proneness and specific emotions, and the current task was not designed to reveal emotion-specific dissociations.

Figure 2 shows performance on face emotion and gender identification across the range of SPQ-B scores, illustrating that differences in emotion identification begin to emerge at moderate levels of psychosis-proneness.

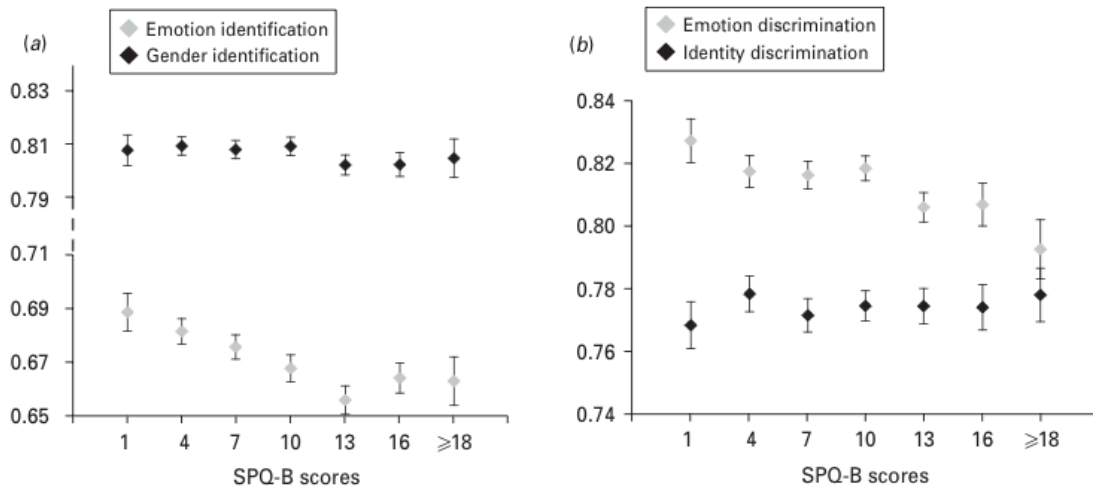


Figure 2. Task performance and psychosis-proneness

Average proportion correct is shown for individuals at different levels of psychosis-proneness in (a) Experiment 1 and (b) Experiment 2. Although performance on both emotion tasks varied with psychosis-proneness, performance on identity and gender tasks did not. Psychosis-proneness was measured using the brief version of the Schizotypal Personality Questionnaire (SPQ-B; Raine & Benishay, 1995). For each experiment, proportion correct was binned by SPQ-B score. The median score for each bin is shown, with the exception of the highest bin, which reflects the high end of the SPQ-B scorers (scores were positively skewed). Bars reflect ± 1 standard error. Bins range in size from $n = 93$ to $n = 495$.

Experiment 2: Emotion Discrimination vs. Identity Discrimination

There was a significant difference in overall accuracy between the two tasks in Experiment 1, so it is possible that our findings were the result of differences in task difficulty or differences in task parameters (e.g. there were four response options for the emotion task and only two for the gender task). Differences in difficulty, in particular, pose a significant problem as more difficult tasks are often more sensitive to group differences. Thus, to replicate our findings from Experiment 1, exclude difficulty-related confounds, and investigate whether or not psychosis-proneness is related to another dimension of face perception (identity processing), we conducted a second experiment using a test of face emotion discrimination and a difficulty-matched test of face identity discrimination. These tests of identity and emotion discrimination

have been used in two prior studies and were shown to tap into dissociable subsystems of face perception, behaviorally and neurally (Garrido et al., 2009, Pitcher et al., 2008). Using a test of emotion discrimination would also allow us to generalize our results from Experiment 1 to face emotion processing more broadly. Whereas emotion discrimination is more purely perceptual, emotion identification relies on other cognitive abilities, such as verbal labeling, that make impairments difficult to interpret (Mandal et al., 1998).

Methods.

Participants. Subjects were individuals who navigated to the website, <http://www.testmybrain.org> and clicked on a link labeled “Recognizing Emotion and Identity from Faces”. Experiments 1 and 2 were never available on our website at the same time, so participant overlap between the two experiments was unlikely to be significant. Exclusion criteria were the same as for Experiment 1, except that we included two additional question prompts to serve as validity checks. Participants were excluded if they responded ‘No’ to the question “I am paying attention to my responses on this questionnaire.” or ‘Yes’ to the question “I responded to most of the last 47 questions without reading them.” Our final group was comprised of 1514 participants. Details of this sample are given in Table 1. All subjects first completed a test of face identity discrimination followed by a test of face emotion discrimination.

Procedure. Stimuli were the same for both emotion and identity discrimination tests, and were comprised of six female models taken from the Ekman and Friesen’s (1976) facial affect series expressing either happiness, sadness, surprise, fear, anger or disgust. Pictures were grayscale and cropped using the same contour to hide the hair and neck. For both tasks, face

pairs were presented sequentially for 500 ms per face with 500ms fixation between images. Participants then had up to seven seconds to indicate whether the two faces had the same or different identity (identity discrimination test) or were expressing the same or different emotion (emotion discrimination test). Half the trials on each test showed pairs with the same identity/emotion, whereas half the trials showed pairs with different identities/emotions. In the emotion test, identity always varied between the face pairs. In the identity test, emotion always varied between the face pairs. Each test contained 40 trials. See Figure 1.

After finishing both tests, subjects again completed items from the brief version of the Schizotypal Personality Questionnaire (SPQ-B) (Raine & Benishay, 1995), the same measure of psychosis-proneness used in Experiment 1.

Results. Mean performance for this sample is given in Table 1. Participants were more accurate on emotion discrimination as compared with identity discrimination (paired samples t-test; $t(1513) = 14.5, p < 0.001$).

To test the hypothesis that psychosis-proneness was significantly related to emotion discrimination performance, multiple regression was conducted in SPSS (version 16.0; 2007) with age, participant sex, and total SPQ-B score as predictors of face emotion discrimination performance. SPQ-B scores in this sample were significantly related to participant age ($r = -0.21$), but not to sex. Participant sex significantly predicted emotion discrimination performance ($\beta = -0.10, p < 0.001$) whereas age did not ($\beta = -0.014, p=0.6$). Psychosis-proneness, as measured by the SPQ-B, significantly predicted emotion discrimination performance ($\beta = -0.11, p < 0.001$), even when controlling for identity discrimination performance ($\beta = -0.10, p < 0.001$). Performance was again significantly different between the participants lowest in psychosis-

proneness (SPQ-B scores from 0 to 2, bottom 8%) and those highest in psychosis-proneness (SPQ-B scores 17 and above, top 9%) [mean for low SPQ-B scorers: 0.83 (0.8); mean for high SPQ-B scorers = 0.79 (0.1); independent samples t-test: $t(261) = 3.3$, $p < 0.001$] corresponding to a Cohen's d effect size of 0.38. As in experiment 1, the relationship between SPQ-B score and emotion recognition performance was not being driven entirely by individuals with the highest levels of psychosis-proneness and possible schizophrenia spectrum diagnoses. When individuals with scores of 16 (out of 22) or greater were excluded from analysis, multiple regression again showed that SPQ-B score significantly predicted emotion discrimination (1322 participants remaining; $\beta = -0.07$, $p < 0.05$).

To see whether psychosis-proneness related differences were limited to emotion discrimination, we conducted multiple regression of face identity discrimination on age, sex, and SPQ-B score. Age and sex predicted identity discrimination performance (age: $\beta = -0.17$, $p < 0.001$; sex: $\beta = -0.14$, $p < 0.001$) whereas psychosis-proneness did not ($\beta = -0.03$, $p = 0.22$). This was despite the fact that overall performance on the identity discrimination task was significantly lower than on the emotion discrimination task, in contrast with Experiment 1 where the emotion task was more difficult. Hence, the observed relationship between psychosis-proneness and emotion processing cannot be explained by difficulty-related confounds.

Multiple regression of emotion discrimination performance on age, sex, and the three factors of the SPQ-B again demonstrated a significant relationship between emotion performance and all three factors (interpersonal: $\beta = -0.07$, $p < 0.05$; cognitive-perceptual: $\beta = -0.10$, $p < 0.001$; disorganized: $\beta = -0.08$, $p < 0.01$). Only the interpersonal factor of psychosis-proneness predicted identity discrimination performance (interpersonal: $\beta = -0.05$, $p < 0.05$; cognitive-perceptual: $\beta = 0.01$, $p = 0.82$; disorganized: $\beta = -0.02$, $p = 0.54$).

In addition, the correlations between SPQ-B score and emotion discrimination and SPQ-B score and identity discrimination were significantly different, based on Steiger's $Z1^*$ statistic (1980) for comparing two correlation coefficients from the same sample ($Z = 2.3, p < 0.01$).

We did not conduct analyses looking at the relationship between psychosis-proneness and specific emotions for this experiment, as the design (same/different; 6 emotion categories) was not conducive to this type of analysis.

Figure 2 illustrates the relationship between psychosis-proneness based on SPQ-B scores and discrimination performance. Consistent with our previous result in Experiment 1, differences in emotion discrimination related to psychosis-proneness are visible at moderate SPQ-B scores.

Discussion

We have demonstrated in two large samples that increasing psychosis-proneness, as indicated by scores on the brief version of the Schizotypal Personality Questionnaire (Raine and Benishay, 1995), is related to reductions in the ability to identify and discriminate facial expressions of emotion. Further, this relationship cannot be accounted for by differences in face processing, visual perception, or a general performance-related factor, as performance on a face gender test (Experiment 1) and a face identity discrimination task (Experiment 2) did not show reductions related to increasing psychosis-proneness. Finally, the relationship between face emotion recognition and psychosis-proneness was significantly predicted by all three factors of our psychosis-proneness measure (interpersonal, cognitive-perceptual, and disorganized). This suggests that face emotion recognition (FER) ability is broadly related to psychosis-like

characteristics and not restricted to a single dimension of psychosis-proneness, such as positive or negative symptoms.

Our data indicate that the phenotypic expression of subthreshold or psychosis-like features is associated with small, but consistent differences in the ability to decode facial expressions of emotion in the normal population. These differences are not likely to be clinically significant, but indicate that FER ability varies with individual differences in psychosis-proneness in the normal population. Schizotypal or psychosis-like features are related to genetic vulnerability to schizophrenia (Kendler & Walsh, 1995, Vollema et al., 2002) and elevated schizophrenia risk (Claridge, 1997, Kwapil, 1998, Kwapil et al., 1997, Vollema et al., 2002). Our results suggest that FER deficits observed in schizophrenia and related disorders do not solely emerge as a result disease-related confounds or secondary characteristics, but instead may be a preexisting or even predisposing neurocognitive feature that vary broadly in the normal population.

We have also shown that FER differences associated with psychosis vulnerability are not associated with more general differences in visual or face processing. Our results are consistent with the results of Bediou et al. (2007) who showed that schizophrenia patients and their relatives have face emotion recognition impairments that are not related to deficits in another type of face processing. This specificity suggests that differences in the neural systems responsible for face emotion recognition may be related to psychosis vulnerability and the expression of psychosis-like characteristics.

A polygenic model of vulnerability to schizophrenia (Gottesman & Shields, 1967) suggests that vulnerability-related features may emerge in a continuous fashion across the spectrum of psychosis-proneness (Chapman & Chapman, 1980, Eysenck, 1960, Raine, 2006) .

Differences in FER may, for example, reflect the expression of differing numbers of risk-conferring genes and hence were present even at moderate levels of psychosis-proneness in our samples (see Figure 2). Differences in performance at moderate levels of psychosis-proneness also imply that reductions in FER ability are not solely attributable to early or subthreshold pathology in at-risk participants.

Our study was conducted using a sample recruited entirely on the internet. An increasingly large body of research demonstrates that results from populations tested over the internet are reliable and empirically valid (Birnbaum, 2004, Gosling et al., 2004, Haworth et al., 2007, Kraut et al., 2004, McGraw et al., 2000, Wilmer et al., 2010) and of broad theoretical interest (Wilmer et al., 2010, Owen et al., 2010). A recent analysis of data collected from our website (www.testmybrain.org) on a test of face recognition memory found that performance and reliability from the internet-based sample was the same as a traditional lab-based sample (Wilmer et al., 2010). Our average psychosis-proneness scores were also almost identical to those reported in a community sample with a similar gender distribution (Irwin, 2001). However, despite many precautions taken here to ensure valid data, it was not possible to monitor the performance of each participant in real time, control for biases in self-selection, and verify the accuracy of information provided by participants. These factors most likely added noise to the data and may have interacted with our results in ways that cannot be ascertained based on available data. Ultimately, testing over the internet allowed us to sample a large and diverse population that would not have been practically feasible if this study were conducted in a traditional lab setting. This large sample increased our ability to detect small but potentially meaningful effects on both our FER and face processing control tasks.

Variations in face emotion processing have been documented for several psychiatric

disorders, including mood disorders (see Lappanen, 2006 for a review) and anxiety disorders (e.g. McClure et al., 2003). Thus, it is possible that our results were partially driven by the overlap between psychosis-like characteristics indexed by the interpersonal factor of the SPQ-B and social anxiety. FER ability was related to multiple subscales of the SPQ-B, however, including scores on the cognitive-perceptual factor, indicating that our results cannot be fully explained by overlap between mood/anxiety symptoms and psychosis-proneness.

Our results recommend an individual differences approach to psychosis-proneness. An individual differences approach has the advantage of complementing the increasing appreciation that schizophrenia and other psychotic disorders are likely to arise from the influence of many common genes of very small effect (Gottesman & Shields, 1967, Purcell et al., 2009, Shi et al., 2009, Stefansson et al., 2009). The potential relationship between increasing vulnerability to developing psychosis and FER ability suggests that differences in social-emotional processing might contribute to the expression of psychosis like traits and, ultimately, to psychosis development.

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Paper #2: Social anhedonia is associated with neural abnormalities during face emotion processing

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Abstract

Human beings are social organisms with an intrinsic desire to seek and participate in social interactions. Social anhedonia is a personality trait characterized by a reduced desire for social affiliation and reduced pleasure derived from interpersonal interactions. Abnormally high levels of social anhedonia prospectively predict the development of schizophrenia and contribute to poorer outcomes for schizophrenia patients. Despite the strong association between social anhedonia and schizophrenia, the neural mechanisms that underlie individual differences in social anhedonia have not been studied and are thus poorly understood. Deficits in face emotion recognition are related to poorer social outcomes in schizophrenia, and it has been suggested that face emotion recognition deficits may be a behavioral marker for schizophrenia liability. In the current study, we used functional magnetic resonance imaging (fMRI) to see whether there are differences in the brain networks underlying basic face emotion processing in a community sample of individuals low vs. high in social anhedonia. We isolated the neural mechanisms related to face emotion processing by comparing face emotion discrimination with four other

baseline conditions (identity discrimination of emotional faces, identity discrimination of neutral faces, object discrimination, and pattern discrimination). Results showed a group (high/low social anhedonia) x condition (emotion discrimination/control condition) interaction in the anterior portion of the rostral medial prefrontal cortex, right superior temporal gyrus, and left somatosensory cortex. As predicted, high (relative to low) social anhedonia participants showed less neural activity in face emotion processing regions during emotion discrimination as compared to each control condition. The findings suggest that social anhedonia is associated with abnormalities in networks responsible for basic processes associated with social cognition, and provide a starting point for understanding the neural basis of social motivation and our drive to seek social affiliation.

Introduction

As fundamentally social creatures, humans are driven by the desire for meaningful and frequent social interaction (Baumeister & Leary, 1995). There are individual differences in the strength of this desire, however, and some individuals exhibit a significantly reduced drive for social affiliation known as social anhedonia (Brown et al., 2007; Kwapil, 1998; Kwapil et al., 2009). Social anhedonia (SA) has been characterized as a deficiency in the need to belong to a social group and is distinct from other constructs that might also predict abnormalities in social interaction such as social anxiety (Brown et al., 2007; Kwapil et al., 2009). Individuals high in SA exhibit a genuine preference for solitude, disengagement during social interactions (Brown et al., 2007), and reduced negative affect when alone (Kwapil et al., 2009). Higher levels of SA are related to lower levels of social support and social functioning (Blanchard et al., 2009). Reduced

social support and smaller social networks are associated with differences in immune functioning and other clinically significant health outcomes (Miller et al., 2009). Furthermore, high SA has been identified as one of the single most predictive traits for future onset of schizophrenia spectrum disorders (Kwapil, 1998) and has long been recognized as a core attribute of psychosis vulnerability (Bleuler, 1950; Horan et al., 2007; Kraepelin & Gosline, 1919; Meehl, 1962; Rado, 1953; Stone et al., 2005). Altogether, existing evidence indicates that SA is a deviation in a psychologically and clinically important social and emotional process that has broad implications for our understanding of normal and abnormal functioning.

Despite evidence for serious physical and mental health difficulties associated with reduced desire for social affiliation, no research to our knowledge has been done exploring the neural basis of SA in nonclinical populations. In schizophrenia, SA is considered a negative symptom that is stable (Blanchard et al., 2001) and can be reliably assessed (Horan et al., 2006). Studies of SA in schizophrenia have indicated that a number of neural systems may be involved in reduced desire for social affiliation, including the amygdala (Becerril & Barch, 2010), caudate nucleus (Dowd & Barch, 2010), dorsolateral prefrontal cortex (Becerril & Barch, 2010), and somatosensory areas (Arnfred & Chen, 2004). However, disease-related confounds and secondary characteristics of schizophrenia illness, such as psychosocial stress and neurodegenerative processes, make it difficult to generalize these findings to SA among healthy individuals or to identify whether neural abnormalities associated with SA are associated with the vulnerability to psychosis (Lenzenweger, 2006).

Differences in the neural processing of face emotion provide a potential starting point for identifying abnormalities associated with high SA. Accurate face emotion recognition is critical for recognizing and responding to other's mental states and is a building block to more complex

social behaviors (Adolphs, 2002). Importantly, face emotion recognition ability (but not face identity processing ability) predicts social functioning in schizophrenia participants (Hooker & Park, 2002) and varies with psychometric psychosis-proneness in nonclinical populations (Germiné & Hooker, 2011). Previous work has also shown that face emotion perception is abnormal in individuals high in social anhedonia (Luh & Gooding, 1999). Thus, individual differences in social anhedonia may be related to deficits in the neural mechanisms supporting face emotion recognition.

The neural substrates of face emotion recognition are well characterized in healthy and clinical populations. Previous work indicates that effective emotion recognition involves the recruitment of a network of regions, including the amygdala (Adolphs, 2002; Adolphs et al., 1994; Anderson & Phelps, 2001), superior temporal sulcus (Allison et al., 2000; Haxby et al., 2000), medial prefrontal cortex (Amodio & Frith, 2006; Blair et al., 1999; Dolan et al., 1996; Gorno-Tempini et al., 2001; Gur et al., 2002a; Phillips et al., 1998; Sprengelmeyer et al., 1998; Wright et al., 2002), and somatosensory-related cortices (including insula, S1, S2, and anterior supramarginal gyrus) (Adolphs, 2002; Adolphs et al., 2000). Using functional neuroimaging, researchers have consistently found abnormalities in these regions during emotion recognition in individuals with schizophrenia (Das et al., 2007; Farrer et al., 2004; Gur et al., 2007; Gur et al., 2002b; Hall et al., 2004; Hempel et al., 2003; Holt et al., 2006; Kosaka et al., 2002; Phillips et al., 1999; Pinkham et al., 2008; Schneider et al., 1998; Spence et al., 1997; Taylor et al., 2002; Waberski et al., 2004; Williams et al., 2004).

Deficits in emotion recognition have been associated with lesions to the amygdala (Adolphs et al., 1994), somatosensory and related cortices (Adolphs et al., 2000) and medial prefrontal cortex (Heberlein et al., 2008). The medial prefrontal cortex, in particular, likely plays

a broad role in many social-cognitive processes and has been implicated in lower-level emotion perception as well as higher-level processes including theory of mind attributions (Gallagher et al., 2000), self-referential processing (Mitchell et al., 2005), and distinguishing between self and other (Heatherton et al., 2006; Ochsner et al., 2004). In terms of functional divisions, the anterior portion of rostral medial prefrontal cortex (arMFC) has been consistently identified in measures of social cognition and emotion processing (Amodio & Frith, 2006) and in social cognition in schizophrenia (Brunet-Gouet & Decety, 2006).

In the present study, we used functional magnetic resonance imaging (fMRI) to examine differences in the neural circuitry underlying face emotion discrimination in otherwise normal individuals who were high versus low in SA. As our face emotion recognition task, we used the Queen Square Face Discrimination Test (QFDT; Garrido et al., 2009). Our primary hypothesis was that high SA would have specific deficits in face emotion processing even when controlling for broader, but equally complex aspects of face perception. The QFDT was chosen because it can dissociate face emotion processing and face identity processing (Banissy et al., 2011; Garrido et al., 2009; Germine & Hooker, 2011; Pitcher et al., 2008). In the QFDT, participants view sequentially presented emotional faces; in one condition they judge whether the two faces are expressing the same emotion, and in another condition they judge whether the two faces have the same identity. Importantly, the two conditions have identical stimuli and are equally difficult for healthy participants. As a result, any differences found between emotion discrimination and identity discrimination can be attributed to differences in specific cognitive processes related to emotion perception and cannot be attributed to differences in the stimuli, number of response options, or difficulty level of the two conditions. This feature of the task is an improvement over face processing studies where the experimental and control tasks differ along these dimensions

(e.g. labeling emotional faces using four options vs. same/different identity of paired neutral faces). In the QFDT, the emotion recognition and identity recognition conditions use the same task structure (both are a forced choice same/different judgment) and the same stimuli. Therefore the comparison of emotion recognition and identity recognition of emotional faces isolates the specific cognitive processes for attending to, processing, and judging face emotions. Using a behavioral version of this task, we found that higher levels of psychosis risk (based on self-report of cognitive-perceptual, interpersonal, and disorganized psychosis-prone characteristics) are associated with reduced emotion discrimination performance, but normal identity discrimination performance (Germine and Hooker, 2011). The QFDT was also used by Pitcher et al. (2008), who found that applying transcranial magnetic stimulation (TMS) to the face area of somatosensory cortex impaired performance in the emotion discrimination condition, but not the identity discrimination condition. Thus, we have good reason to believe that the QFDT emotion discrimination condition depends on one or more processes specific to emotion processing that also vary with psychosis vulnerability. The current fMRI study included three additional control conditions designed to reveal potential group differences in the broader face emotion processing neural network. These conditions included identity discrimination of neutral faces, visual discrimination of objects, and visual discrimination of patterns. Given the putative relationship between SA and vulnerability for psychosis (Kwapil, 1998), we predicted that individuals high in SA would exhibit reduced recruitment of cortical regions involved in face emotion recognition, particularly superior temporal sulcus/gyrus, medial prefrontal cortex and somatosensory-related parietal regions, as well as reduced responses in the amygdala. Between group differences in one or more of these regions would indicate that higher levels of SA are associated with neural

abnormalities during emotion perception, and help us better understand the neural basis of differences in the desire for social affiliation as well as psychosis vulnerability.

Material and Methods

Participants. We recruited a community-based sample comprised of thirty participants who were high or low in social anhedonia based on their scores on the Revised Chapman Social Anhedonia Scale (RSAS; Chapman & Chapman, 1980). Fifteen high social anhedonia participants (high SA) were selected based on scoring in the top 10% on this measure (RSAS score > 16 for females, > 19 for males). Fifteen low social anhedonia participants (low SA) were selected based on having scores at or below the mean (RSAS score < 7 for females and < 9 for males). Participants were recruited from a combination of community advertisements and the community-wide university study pool. Community advertisements were posted on sites like Craigslist and targeted individuals with difficulties in interpersonal functioning associated with social anhedonia and psychosis risk (e.g. “People sometimes find me aloof and distant.”). In addition, items from the RSAS were used to pre-select individuals with high social anhedonia from the community-wide university study pool. Anyone who had a score of 16 or greater on the RSAS was invited to come into the lab for further screening. All participants took the full RSAS after completing MR screening and demographic questionnaires. In total, 12/15 high SA individuals were recruited through community advertisements and 3/15 high SA participants came from prescreening of the community-wide university study pool using the RSAS. Participants in the low SA groups were recruited from prescreening of the community-wide university study pool for low-to-average levels of social anhedonia (based on the RSAS) and

demographic characteristics similar to our high SA group. Altogether, 4/15 participants in our high SA group and 5/15 in our low SA group were university students. All participants were administered the Structured Clinical Interview for DSM-IV (SCID; First et al., 2002) and were excluded if they had any Axis I diagnosis, a history of alcohol or drug dependence, alcohol or drug abuse within the last six months, a past major head injury involving a loss of consciousness lasting more than 2-3 minutes, or did not speak English as a primary language. Socioeconomic status was assessed using the Hollingshead Index (Hollingshead, 1957). One participant in the high SA group and two participants in the low SA group were unable to give parental information, and so the average parental education/ socioeconomic status from that individual's SA group was used to replace the missing values (e.g. the mean parental socioeconomic status from the other 14 members of the high SA group was used in place of the final high SA participant's missing value). Groups did not differ significantly in terms of sex, age, education, parental education, socioeconomic status, or parental socioeconomic status (see Table 2).

Informed written consent was obtained from all participants after the nature of the study and procedures had been fully explained. The study was approved by the Institutional Review Boards at Harvard University and Massachusetts General Hospital (MGH) (Partners health care system).

Table 2: Participant characteristics for low social anhedonia (low SA) and high social anhedonia (high SA) groups

Where applicable, values represent mean and standard deviation (in parentheses) for each group. All p values based on two-tailed independent samples t-tests with $df = 28$. Socioeconomic status was based on the Hollingshead Index (Hollingshead, 1957), where numbers 1 to 7 were assigned to each occupational category with 1 for unskilled employees and 7 for higher executives, major professionals and proprietors. Levels of social anhedonia were determined by scores from the Revised Social Anhedonia Scale (RSAS; Chapman & Chapman, 1980).

	<u>LOW SA</u>	<u>HIGH SA</u>	<u>p</u>
sex	7 / 15 male	7 / 15 male	--
age	32.5 (12.5)	31.5 (10.7)	0.8
education (participant; years)	14.7 (2.4)	15.5 (2.4)	0.4
education (parental; years)	13.6 (2.1)	15.1 (1.9)	0.08
socioeconomic status (participant)	4.3 (1.8)	4.7 (2.0)	0.8
socioeconomic status (parental)	3.9 (1.0)	4.4 (1.3)	0.26
RSAS score	3.7 (2.9)	26.3 (6.6)	< 0.001
handedness	14 / 15 right-handed	14 / 15 right-handed	--

Stimuli and experimental paradigm. In the scanner, participants were asked to judge whether two sequentially presented stimuli were the same or different on a specified characteristic. There were five different conditions presented in a block design. In the main condition of interest, participants were asked to discriminate the emotions of sequentially presented emotional faces (Emotional faces: Emotion discrimination – EE). In a comparison

condition, participants were asked to discriminate the identities of the same set of sequentially presented emotional faces (Emotional faces: Identity discrimination – EI). These two conditions (EE and EI) were taken from the Queen Square Face Discrimination Task (QFDT; Garrido et al., 2009). Using this task, Pitcher et al. (2008) found specific deficits in face emotion discrimination but not face identity discrimination after transcranial magnetic stimulation (TMS) of the face area of somatosensory cortex, one of our regions of interest. Face stimuli were adapted from the images of six female models from Ekman and Friesen's (Ekman & Friesen, 1976) facial affect series, expressing one of six emotions: happy, sad, surprise, fear, disgust, and anger. An example trial is shown in Figure 3. The six facial expressions appeared an equal number of times in the EE task and the six models appeared an equal number of times in the EI task. The same images were used for both tasks, with identity varying between sample and target faces in all EE trials and expression varying between sample and target faces in all EI trials. The order of conditions was counterbalanced across runs. Out of four runs, two started with EE blocks whereas the other two started with EI blocks. We also included three additional baseline/control conditions: identity discrimination of sequentially presented neutral faces (Neutral faces: Identity discrimination - NI), visual discrimination of sequentially presented grayscale cars (Object discrimination - OD), and visual discrimination of sequentially presented patterns (Pattern discrimination - PD). The models used in the NI task were the same as those included in the EE and EI tasks. Objects used in the OD task were all side views of similar-looking sedans. Finally, the PD task used scrambled face images.

The structure of a single trial is shown in Figure 3. Participants had to indicate whether the sample and target image depicted the same face emotion or different face emotion (EE), the

same identity or a different identity (EI, NI tasks), or the same image or a different image (OD, PD tasks). There were 72 trials of each task, with half requiring “same” judgments.

All participants were administered a brief practice including all conditions and correct/incorrect feedback before placement in the scanner. The practice and scanning experiments were administered using E-Prime software.

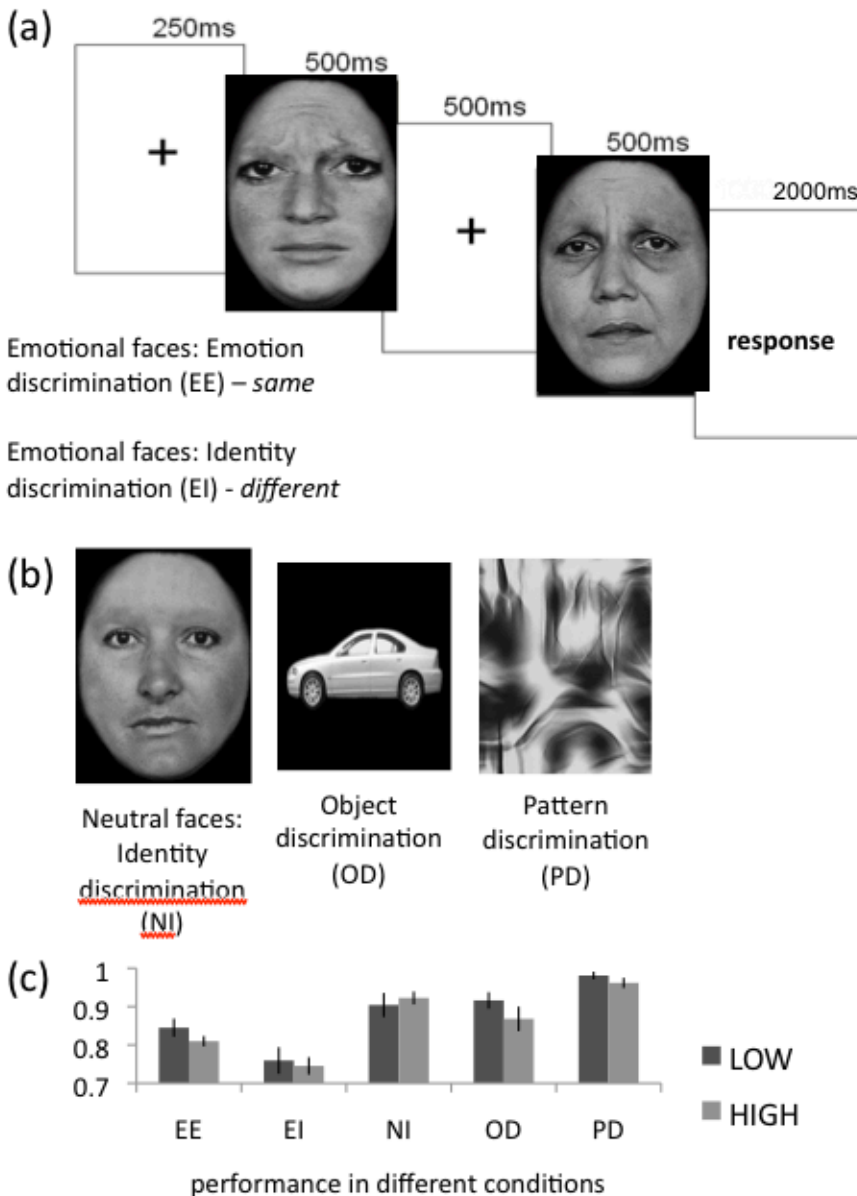


Figure 3. Task stimuli and behavioral performance

(a) A single trial of the Emotional faces: Emotion discrimination (EE) condition. Stimuli were the same for EE and EI (Emotional faces: Identity discrimination) conditions. (b) Example stimuli from the three other comparison conditions. (c) Behavioral performance in terms of proportion correct for each condition. The darker bar represents performance for low social anhedonia participants, whereas the lighter bar represents performance for high social anhedonia participants. There were no between group differences in performance in any condition.

fMRI protocol. Scanning sessions lasted for 40 minutes, and consisted of 4 runs with 3 blocks of each task per run. Across the 4 runs, there were 72 trials of each task. Each block consisted of 6 trials of the same task and lasted 22.5 seconds, preceded by a task cue for 2.5 seconds and followed by a 12.5 second fixation period. While in the scanner, participants wore earplugs to muffle noise, and head fixation was ensured through foam padding in the head coil.

fMRI image acquisition. Brain imaging data were acquired using a 3.0 T Siemens Trio scanner employing a 12 channel whole-head coil. For functional scans, data were acquired in an oblique-axial plane using gradient echo planar imaging (EPI) with an echo time of 30 ms and repetition time of 2500ms. Each volume was comprised of 41 slices with a 2.5mm slice thickness and a gap of 0.8mm giving coverage of the whole brain, except for the most superior portion of the posterior parietal lobe. Voxel size was 3.1 x 3.1 x 2.5 mm and volumes were continuously acquired every 2.5 s in an interleaved fashion. Each run was preceded by 5 ‘dummy’ scans to allow T1 equilibration. A structural scan sequence (MPRAGE) was conducted to obtain a T1-weighted anatomical image (128 sagittal slices, voxel size 1.3 x 1.0 x 1.3 mm, flip angle = 7 degrees, TR = 2530 ms, TE = 3.39 ms).

fMRI: Functional activation analyses. We analyzed the data using SPM8 (Wellcome Department of Cognitive Neurology, London, United Kingdom; <http://www.fil.ion.ucl.ac.uk/spm/software/spm8>). Preprocessing included realignment to the first volume acquired, coregistration of the structural to functional scans, normalization to a structural template (re-sampled voxel size after normalization was 2 x 2 x 2mm), and smoothing with a 6mm Gaussian kernel. Analyses were

conducted with a general linear model framework. Vectors of onset times with durations of 22.5s were defined for all five tasks: EE, EI, NI, OD, and PD. These onset vectors were convolved with the SPM8 canonical hemodynamic response function (HRF) using a box-car function. Additionally, regressors were created using an artifact detection tool (ART; Whitfield-Gabrieli, 2009) to exclude scans with gross motion (>0.6mm relative to previous time frame) or spiking artifacts (global mean image intensity greater than 2.5 SD from mean of the entire time series within a scan) from analysis. Where this procedure resulted in omission of more than 10% of time frames, filters were adjusted to bring the number of excluded scans to approximately 10%. There were no between group differences in number of outliers identified (high SA max = 83; low SA max = 92) or filter parameters. A high-pass frequency filter (200s) was also applied to the time series. For each subject, contrast images were calculated for each of the five tasks (EE, EI, NI, OD, and PD) relative to baseline (blocks of fixation).

Second-level analysis. To verify that our task was activating our regions of interest, we conducted a one sample t-test of EE vs. baseline (fixation) across all participants. To assess whether our EE task was isolating regions for face emotion processing relative to face identity processing, we also conducted a one sample t-test of the contrast of EE versus EI across participants. To look at between group differences, we implemented a flexible factorial design in SPM8. Our hypothesis was a group (high/low SA) x condition (EE/control) interaction, such that high SA would show less activity for EE as compared to each control condition. Four group x condition analyses were conducted: EE vs. EI, EE vs. NI, EE vs. OD, & EE vs. PD. All group maps were thresholded at $p < 0.001$ uncorrected with an extent threshold of 5 voxels. For regions of interest where suprathreshold clusters were identified in our flexible factorial analysis, small volume corrections were performed using Family Wise Error correction (FWE, $p < 0.05$).

The WFU Pickatlas (Maldjian et al., 2003; Maldjian et al., 2004) was used to create anatomically defined masks of the right superior temporal gyrus, bilateral postcentral gyri (somatosensory cortices), and bilateral supramarginal gyri (somatosensory-related or somatosensory association cortices). A mask of the anterior portion of rostral medial prefrontal cortex (arMFC) was defined based on Amodio and Frith (2006). This mask was drawn to include all voxels in prefrontal cortex with MNI coordinates of $x < 20$ and $x > -20$, $y > 20$, and $z > 0$ (4013 voxels total). Any voxel in the left or right hemisphere that fell within these coordinate boundaries was included in a single, bilateral arMFC mask. For regions of interest showing a significant interaction, contrast estimates were extracted from the peak of primary clusters in order to conduct post hoc comparisons.

Results

Behavioral. No significant between group differences were found in performance on any condition (EE, EI, NI, OD, and PD) (all $p > 0.2$). Details of performance in each condition for each group are shown in Figure 3.

Effects of task across all participants. We conducted one sample t-tests on EE (vs. baseline) contrasts across all participants to verify that the EE task was inducing BOLD signal changes in the expected face emotion and face processing regions. This analysis verified task-related activity in a network of regions that included the right superior temporal sulcus, left postcentral gyrus (left primary somatosensory cortex), bilateral supramarginal gyri

(somatosensory-related or somatosensory association cortices), bilateral fusiform gyri, and bilateral medial prefrontal cortex, including the anterior rostral medial prefrontal cortex (arMFC) (see Table 3). No suprathreshold voxels were detected in the amygdala.

To verify that the EE task was uniquely associated with activity in our emotion perception regions of interest relative to other tasks, we also conducted a one sample t-test on the EE vs. EI contrast across all participants. This analysis revealed a network of activation for the EE task (relative to EI) that included the right superior temporal sulcus, bilateral postcentral gyri (primary somatosensory cortices), left supramarginal gyrus (somatosensory-related cortex), and bilateral medial prefrontal cortices, including anterior rostral medial prefrontal cortex (arMFC) (see Table 3). As in our EE vs. baseline contrast, no suprathreshold voxels were detected in the amygdala. With the exception of the amygdala, these results demonstrate that the EE task was associated with activation across all of our regions of interest in the distributed emotion perception network, above and beyond the most closely matched control condition (EI). Given that this is the first time this task has been used in the scanner, our EE vs. EI contrast serves as validation that the EE task is suited to tapping into neural networks associated with emotion perception.

Table 3: Emotional faces: Emotion discrimination (EE) related fMRI BOLD responses across all participants

Neural activity clusters are based on one sample t-tests across all participants with a significance threshold of $p < 0.001$ uncorrected and an extent threshold of 5 voxels. Neuroanatomical labels, MNI coordinates, and t-values are provided for the peak voxel of each cluster. Clusters that include a priori regions of interest are italicized. Superscripts denote clusters containing areas of activation that survive small volume correction based on regions of interest: (1) Includes voxels in anterior rostral medial frontal cortex (arMFC) that survive small volume correction over a bilateral region defined by voxels with MNI coordinates of $|x| < 20$, $y > 20$, and $z > 0$ (Amodio & Frith, 2006); (2) Includes voxels in postcentral gyrus / somatosensory cortex that survive small volume correction over anatomically defined bilateral postcentral gyri; (3) Includes voxels in right superior temporal gyrus that survive small volume correction over anatomically defined right superior temporal gyrus; (4) Includes voxels in supramarginal gyrus / somatosensory-related / somatosensory-association cortex that survive small volume correction over anatomically defined bilateral supramarginal gyri.

Table 3 (continued)

Brain Region	Brodmann Areas	MNI coordinates X Y Z	t value	cluster size in voxels
<u>Emotional Faces : Emotion Discrimination (EE) vs. Baseline – All Participants</u>				
L middle occipital gyrus	19	-22 -98 0	17.21	13,498
<i>L medial frontal gyrus</i> ¹	8	-6 14 48	12.33	2,042
<i>L superior parietal lobule</i> ²	7	-28 -58 48	11.36	10,028
R inferior frontal gyrus	9	42 10 26	10.58	6,471
<i>R inferior parietal lobule</i> ⁴	40	36 -52 48	10.17	1,306
<i>R superior temporal gyrus</i> ³	42	50 -38 10	5.25	128
L cuneus	18	-20 -70 8	4.16	43
pons	NA	0 -30 -34	3.98	54
<u>Emotional Faces : Emotion Discrimination (EE) vs. Emotional Faces: Identity Discrimination (EI) – All Participants</u>				
L inferior frontal gyrus	45	-54 30 4	8.37	2,877
<i>L superior frontal gyrus / arMFC</i> ¹	6	-10 8 60	7.06	1,877
<i>L superior temporal sulcus</i> ⁴	22	-42 -40 2	6.35	1,538
R cerebellum	NA	30 -70 -36	5.84	402
L caudate	NA	-8 14 8	5.18	150
R cerebellum	NA	12 -38 -48	4.67	57
R middle frontal gyrus	47	52 38 -2	4.6	189
<i>R superior temporal sulcus / gyrus</i> ³	22	50 -34 0	4.5	283
<i>R superior temporal gyrus</i> ³	38	40 6 -22	4.39	22
<i>R postcentral gyrus / somatosensory cortex</i> ²	3	20 -40 54	4.37	147
L cingulate gyrus	24	-4 -12 36	4.24	54
<i>L postcentral gyrus / somatosensory cortex</i> ²	4	-18 -28 70	4.24	52
L cingulate gyrus	31	-16 -22 44	4.13	11
L cerebellum	NA	-26 -76 -38	3.84	14
L superior temporal gyrus	38	-48 8 -24	3.64	5
L medial frontal gyrus	6	-8 -30 62	3.63	10
L middle frontal gyrus	10	-38 60 -2	3.6	8
<i>L superior frontal gyrus / arMFC</i>	9	-12 54 28	3.54	6

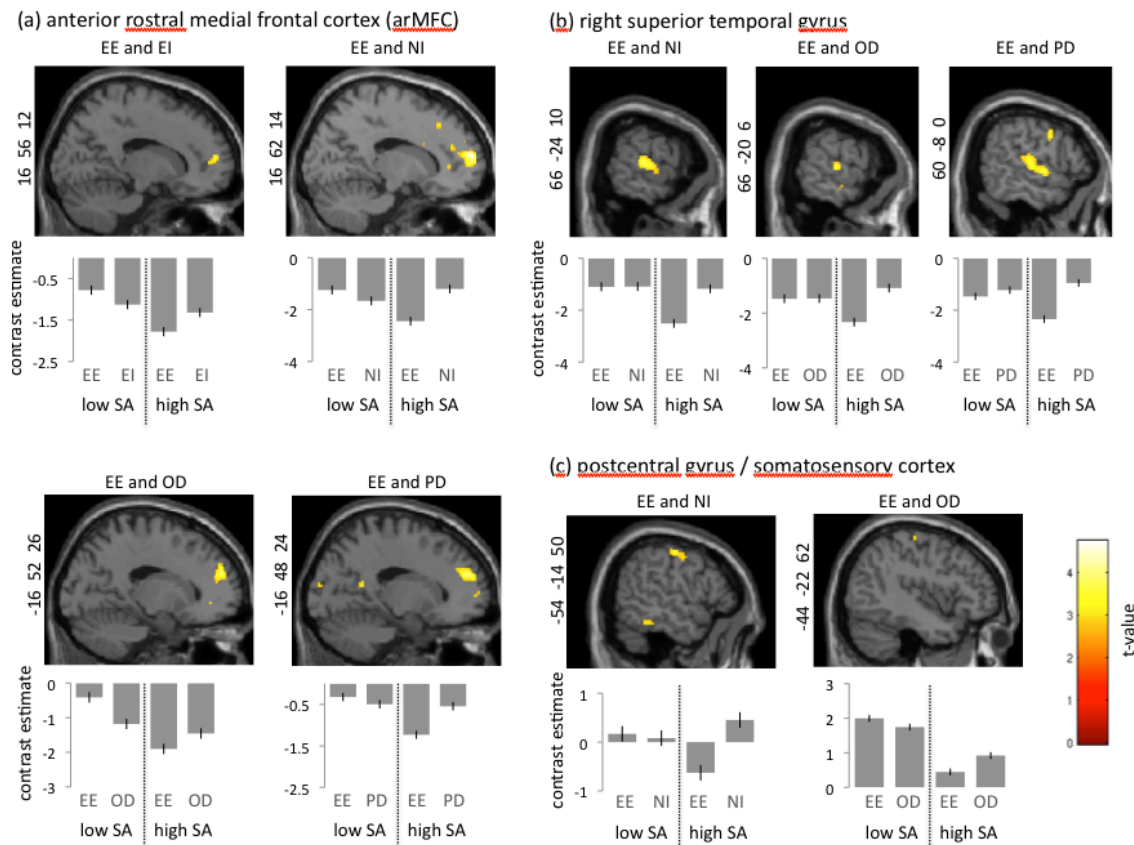


Figure 4. fMRI BOLD responses associated with Emotional faces: Emotion discrimination (EE) in low vs. high social anhedonia (SA) groups

Activation patterns and contrast estimates associated with group x condition interaction effects in our regions of interest are shown. The Emotional faces: Emotion discrimination (EE) condition was compared with Emotional faces: Identity discrimination (EI), Neutral faces: Identity discrimination (NI), Object discrimination (OD), and Pattern discrimination (PD), for low social anhedonia (low SA) and high social anhedonia (high SA) participants. Significant interactions were observed in: (a) anterior rostral medial frontal cortex (arMFC) when comparing Emotion discrimination (EE) with EI, NI, OD, and PD; (b) right superior temporal gyrus when comparing EE with NI, OD, and PD; and (c) left postcentral gyrus / somatosensory cortex when comparing EE with NI and OD. MNI coordinates (x y z) of peak voxels for each cluster are shown to the left of each image. Contrast estimates were extracted from the peak voxel of the cluster and plotted for each group and condition. All results shown above are based on a full flexible factorial model implemented in SPM 8, with a significance threshold of $p < 0.001$ uncorrected. Clusters are displayed at $p < 0.005$ to show activation extent.

Group comparisons. The main hypothesis of the study was that participants with high social anhedonia would show reduced activity in emotion processing regions during emotion discrimination. Regions showing a significant interaction in the expected direction, i.e. where low SA had greater activity than high SA participants for emotion discrimination (Emotional faces – Emotion discrimination condition: EE) versus the control condition, are listed in Table 4. Regions where there was a significant group x condition interaction but with the opposite pattern (i.e. where high SA had more activity than low SA for EE > control) are shown in Table 5. None of these regions (where high SA > low SA during EE) occurred in our regions of interest. Clusters within a priori regions of interest were investigated by extracting contrast estimates from the peak of the cluster. Primary clusters showing significant group x condition interactions are shown together with contrast estimates in Figure 4, organized by region of interest. Finally, Table 5 shows results of post hoc comparisons applied to the contrast estimates in primary clusters located in our regions of interest.

Table 4: Group x condition interactions: Regions where low social anhedonia > high social anhedonia during Emotional faces: Emotion discrimination (EE)

Neural activity clusters are areas where significant group (low social anhedonia vs. high social anhedonia) x condition (emotion discrimination vs. control) interactions were detected at $p < 0.001$ (uncorrected) with an extent threshold of 5 voxels. Neuroanatomical labels, MNI coordinates, and t-values are provided for the peak voxel of each cluster. Regions indicated with a ^ only showed significant interactions when the extent threshold was removed. Small volume correction was applied to the regions corresponding to (1) the anterior portion of rostral medial prefrontal cortex (arMFC) bilaterally as defined by Amodio & Frith (2006) (region defined as all voxels with MNI coordinates: $|x| < 20, y > 20, z > 0$), (2) right superior temporal gyrus and (3) bilateral postcentral gyri (somatosensory cortices). Regions indicated with an asterisk * survived small volume corrections (family-wise error corrected, $p < 0.05$). Clusters that occur in *a priori* regions of interest are italicized.

Brain Region	Brodmann Areas	MNI coordinates X Y Z	t value	cluster size in voxels
<u>Emotional Faces : Emotion Discrimination (EE) vs. Emotional Faces : Identity Discrimination (EI)</u>				
<i>R medial frontal gyrus</i>	10	16 56 12	3.75	6
<u>Emotional Faces : Emotion Discrimination (EE) vs. Neutral Faces : Identity Discrimination (NI)</u>				
<i>R superior frontal gyrus (arMFC)*</i>	10	16 62 14	4.99	112
R caudate	8	24 18 18	4.24	52
<i>R superior temporal gyrus*</i>	42	66 -24 10	3.98	50
R fusiform gyrus	18	38 -72 -12	3.85	22
<i>L medial superior frontal (arMFC)</i>	10	-14 56 2	3.77	9
<i>L superior frontal gyrus (arMFC)</i>	10	-16 50 26	3.75	23
<i>R superior temporal gyrus</i>	41	42 -30 8	3.69	5
<i>R superior temporal gyrus</i>	22	60 -8 0	3.67	5
L precentral gyrus	6	-40 -10 38	3.65	7
<i>L postcentral gyrus (somatosensory cortex)^</i>	3	-54 -14 50	3.64	4
<u>Emotional Faces : Emotion Discrimination (EE) vs. Object Discrimination (OD)</u>				
R anterior cingulate / subgenual cortex	25	2 16 -12	4.58	85
<i>L superior frontal gyrus (arMFC)*</i>	10	-16 52 26	4.11	32
<i>R superior temporal gyrus</i>	22	66 -20 6	3.84	16
L middle frontal gyrus	8	-28 30 48	3.74	8
<i>L postcentral gyrus (somatosensory cortex)^</i>	3	-44 -22 62	3.5	1
<u>Emotional Faces: Emotion Discrimination (EE) vs. Pattern Discrimination (PD)</u>				
<i>R superior temporal gyrus*</i>	22	66 -18 4	4.93	115
<i>L superior frontal gyrus (arMFC)*</i>	10	-16 48 24	4.16	52
L posterior cingulate	30	-10 -54 16	4.1	45
R anterior cingulate / subgenual cortex	25	2 10 -8	4.02	36
<i>R superior temporal gyrus</i>	22	60 -8 0	3.98	29
R precentral gyrus	6	62 0 36	3.67	5
L anterior cingulate	32	-10 42 -4	3.61	6
<i>R medial frontal gyrus (arMFC)</i>	10	18 54 16	3.52	5

Table 5: Group x condition interactions: Regions where high social anhedonia > low social anhedonia during Emotional faces: Emotion discrimination (EE)

Neural activity clusters are areas where significant group (high social anhedonia > low social anhedonia) x condition (emotion discrimination vs. control) were detected at $p < 0.001$ (uncorrected) with an extent threshold of 5 voxels. Neuroanatomical labels, MNI coordinates, and t-values are provided for the peak voxel of each cluster. No clusters showing high social anhedonia > low social anhedonia occurred in any of our regions of interest.

Brain Region	Brodmann Areas	MNI coordinates X Y Z	t value	cluster size in voxels
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Emotional Faces: Emotion Discrimination (EE) vs. Emotional Faces: Identity Discrimination (EI)

L precuneus	7	-18 -56 50	4.12	16
L fusiform gyrus	37	-38 -50 -8	3.93	11
R cingulate gyrus	31	22 -34 32	3.81	9
L cerebellum	NA	-12 -66 -26	3.79	11
L cerebellum	NA	-22 -64 -28	3.65	5

Emotional Faces: Emotion Discrimination (EE) vs. Neutral Faces: Identity Discrimination (NI)

NONE

Emotional Faces: Emotion Discrimination (EE) vs. Object Discrimination (OD)

R precentral gyrus	44	56 10 10	3.5	5
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Emotional Faces: Emotion Discrimination (EE) vs. Pattern Discrimination (PD)

R middle frontal gyrus	9	38 10 34	4.4	49
L middle frontal gyrus	10	-28 52 -8	4.3	22
R inferior frontal gyrus	44	50 6 18	4.18	61
R precentral gyrus	44	46 18 10	3.77	12
R middle frontal gyrus	10	44 48 24	3.75	10
L fusiform gyrus	37	-38 -60 -10	3.66	5

Table 6. Post hoc comparisons for group x condition interactions

Four post hoc comparisons were performed for each cluster showing a group x condition interaction effect shown in Figure 2. The five conditions examined were Emotional faces: Emotion discrimination (EE), Emotional faces: Identity discrimination (EI), Neutral faces: Identity discrimination (NI), Object discrimination (OD), and Pattern discrimination (PD). Low SA signifies the low social anhedonia group, whereas high SA signifies the high social anhedonia group. Where the comparison was within the same group (e.g. low SA : EE vs. low SA : EI), paired t-tests were used (two-tailed; $df = 14$). Where the comparison was between groups (e.g. low SA : EE vs. high SA : EE), independent sample t-tests (two-tailed; $df = 28$) were used.

Brain Region	MNI coordinates X Y Z	Contrast	t value	p value
(1) anterior rostral medial frontal cortex ($ x < 20, y > 20, z > 0$)	16 56 12	low SA : EE – low SA : EI	3.23	0.006
		high SA : EE – high SA : EI	-4.27	0.0008
		low SA : EE – high SA : EE	6.56	<0.0001
		low SA : EI – high SA : EI	0.26	0.23
	16 62 14	low SA : EE – low SA : NI	2.46	0.03
		high SA : EE – high SA : NI	-7.3	<0.0001
		low SA : EE - high SA : EE	5	0.0002
		low SA : NI - high SA : NI	-1.9	0.08
	-16 52 26	low SA : EE - low SA : OD	5.12	0.0002
		high SA : EE - high SA : OD	-3	0.01
		low SA : EE - high SA : EE	7.02	<0.0001
		low SA : OD - high SA : OD	1.29	0.22
	-16 48 24	low SA : EE - low SA : PD	1.7	0.11
		high SA : EE - high SA : PD	-6.7	<0.0001
		low SA : EE - high SA : EE	6.2	<0.0001
		low SA : PD - high SA : PD	0.34	0.74
(2) right superior temporal gyrus	66 -24 10	low SA: EE - low SA : NI	-0.05	0.96
		high SA : EE - high SA : NI	-7.8	<0.0001
		low SA : EE – high SA : EE	5.86	<0.0001
		low SA : NI - high SA : NI	0.36	0.72
	66 -20 6	low SA : EE - low SA : OD	-0.06	0.95
		high SA : EE - high SA : OD	-7.8	<0.0001
		low SA : EE - high SA : EE	4.76	0.002
		low SA : OD - high SA : OD	-1.7	0.11
	60 -8 0	low SA : EE - low SA : PD	-1.7	0.11
		high SA : EE - high SA : PD	-9.7	<0.0001
		low SA : EE - high SA : EE	4.3	<0.0001
		low SA : PD - high SA : PD	-1.3	0.2
(3) postcentral gyrus / somatosensory cortex	-54 -14 50	low SA : EE - low SA : NI	0.55	0.59
		high SA : EE - high SA : NI	-6.76	<0.0001
		low SA : EE - high SA : EE	3.53	0.003
		low SA : NI - high SA : NI	-1.65	0.12
	-44 -22 62	low SA : EE - low SA : OD	2.43	0.03
		high SA : EE – high SA : OD	-4.56	0.0004
		low SA : EE - high SA : EE	10.54	<0.0001
		low SA : OD - high SA : OD	5.6	<0.0001

Emotional Faces: Emotion Discrimination (EE) vs. Emotional Faces: Identity

Discrimination (EI). For the comparison of EE and EI, there was a significant group x condition interaction (where low SA > high SA) in arMFC (see Figure 4), but not other regions of interest. Post hoc comparisons were conducted to investigate the interaction. Statistics for each comparison are in Table 5. As predicted, the results showed that high SA participants had reduced arMFC activity during emotion discrimination. In addition, low SA participants had greater arMFC activity for emotion discrimination as compared to identity discrimination of emotional faces (i.e. among low SA: EE > EI). However, high SA participants deactivated the arMFC during EE, such that high SA had significantly less activity for emotion discrimination as compared to identity discrimination of emotional faces (i.e. among high SA: EE < EI). Moreover, the direct comparison of emotion discrimination between the groups showed that low SA participants had significantly greater arMFC activity than high SA participants (i.e. low SA EE > high SA EE). There was no significant difference between low SA and high SA participants for arMFC activity during identity discrimination of emotional faces (EI condition) (see Table 5).

Activation in arMFC did not survive small volume correction (over bilateral arMFC; see Section 3.3.) in this contrast ($p = 0.15$).

Emotional Faces: Emotion Discrimination (EE) vs. Neutral Faces: Identity

Discrimination (NI). When comparing EE with NI, there was a significant group x condition interaction (where low SA > high SA) in arMFC and right superior temporal gyrus (see Figure 4). Removing the extent threshold ($p < 0.001$ uncorrected, $k = 0$) revealed an additional suprathreshold cluster in left somatosensory cortex (left postcentral gyrus). Post hoc

comparisons (see Table 5) revealed the same overall pattern in arMFC as was observed in the EE vs. EI analysis (see Section 3.3.1.). In right superior temporal gyrus and left somatosensory cortex, high SA participants deactivated regions of both right superior temporal gyrus and left somatosensory cortex during EE relative to NI (i.e. among high SA: $EE < NI$) whereas low SA participants did not show differences between these two conditions (i.e. among low SA: $EE = NI$). As predicted, low SA was associated with greater activity in right superior temporal gyrus and left somatosensory cortex during EE (i.e. low SA $EE >$ high SA EE), but not differences during NI (i.e. low SA $NI =$ high SA NI).

Both arMFC and right superior temporal gyrus clusters survived small volume correction in this comparison ($p < 0.05$).

Emotional Faces: Emotion Discrimination (EE) vs. Object Discrimination (OD).

When comparing EE with OD, there was again a significant group x condition interaction (where low SA $>$ high SA) in arMFC and right superior temporal gyrus (see Figure 4). As in the comparison of EE and NI, removing the extent threshold ($p < 0.001$ uncorrected, $k = 0$) also revealed an additional suprathreshold cluster in left somatosensory cortex (left postcentral gyrus). Post hoc comparisons (see Table 5) revealed the same overall pattern in arMFC and right superior temporal gyrus as was observed in the comparison of EE and NI (Section 3.3.2). In left somatosensory cortex, significant differences were observed in all post hoc comparisons. High SA participants deactivated this region during EE relative to OD (i.e. among high SA: $EE < OD$) whereas low SA participants showed greater activation of this region during EE relative to OD (i.e. among low SA: $EE > OD$). As predicted, low SA showed greater activity in somatosensory cortex during EE than high SA (i.e. low SA $EE >$ high SA EE), but also during OD (i.e. low SA $OD >$ high SA OD).

Differences in arMFC in the comparison of EE and OD survived small volume correction at the trend level ($p = 0.06$), whereas differences in right superior temporal gyrus did not ($p = 0.25$).

Emotional Faces: Emotion Discrimination (EE) vs. Pattern Discrimination (PD).

When comparing EE with PD, there was again a significant group x condition interaction (where low SA > high SA) in arMFC and right superior temporal gyrus (see Figure 4).

Removing the extent threshold did not reveal any additional suprathreshold clusters in other regions of interest. Post hoc comparisons (see Table 5) revealed that, as predicted, low SA had greater activation during EE than high SA in arMFC and right superior temporal gyrus (i.e. low SA EE > high SA EE). High SA also showed deactivation during EE as compared with PD (i.e. among high SA: EE < PD). Among low SA, there was no difference between EE and PD in these regions (i.e. among low SA: EE = PD) and no differences in PD between low and high SA (i.e. low SA PD = high SA PD).

Differences in right superior temporal gyrus survived small volume correction ($p < 0.05$) in this comparison. Differences in arMFC survived small volume correction at the trend level ($p = 0.06$).

Further Analyses.

Amygdala. Although the amygdala was one of our a priori regions of interest, we found no within-subjects differences in this region when comparing EE with any of our control conditions (EI, NI, OD and PD) across all participants. We also failed to detect any significant group x condition interactions in the amygdala.

As the amygdala is considered a central part of the extended face emotion perception network, we conducted further analyses to explore whether the combination of all conditions using faces (EE, EI, and NI) would show suprathreshold amygdala activation when compared with baseline. Using a within-subjects one sample t-test across all participants, we again found no significant differences in the amygdala ($p < 0.001$). An analysis of signal-to-noise in the right amygdala as compared with right superior temporal gyrus in our sample suggested significantly lower signal-to-noise in the amygdala (paired samples t-test: $t(29) = 11.8$; $p < 0.0001$). Previous research has indicated that the amygdala habituates rapidly to emotional information (Brieter et al., 1996) and may show decreased activity during emotion labeling as compared with other forms of encoding (Lieberman et al., 2007). Low signal-to-noise combined with our use of a block design, continuous presentation of faces, and possible emotion labeling demands may have interfered with our ability to detect amygdala differences.

Fusiform gyrus. Given its role in face processing more generally, we also looked at differences in the degree to which emotion modulated BOLD responses in the fusiform gyrus (Vuilleumier et al., 2001) in high vs. low SA participants. We observed a group x condition interaction in both left and right fusiform gyri. In the right fusiform gyrus, the low SA group showed greater BOLD response for EE > NI as compared to the high SA group. These results are consistent with our hypothesis that high SA (vs. low SA) would be associated with reduced neural responses during emotion discrimination. We also found, though, that high SA was associated with greater BOLD response in the left fusiform gyrus for EE > NI and EE > PD as compared to the low SA group. Since face processing is associated more strongly with right fusiform responses in most individuals (Kanwisher et al., 1997; McCarthy et al., 1997), our observation of fusiform gyrus response differences suggests variations in lateralization that may

relate to level of SA. These results are difficult to interpret, however, and warrant further investigation.

Correlations with behavioral performance during emotion discrimination (EE). To explore whether any of our task-related regions showed significant correlations with performance, we extracted contrast estimates from clusters in our regions of interest that were significantly associated with EE vs. EI across all participants (right superior temporal sulcus, somatosensory cortices, and arMFC). None of these regions showed a significant or trend relationship with EE performance across participants.

Discussion

Although social anhedonia has long been recognized as a key feature of schizophrenia illness and liability, there is surprisingly little known about its underlying neural substrates. In this study we investigated whether otherwise healthy individuals with high social anhedonia (SA) had deficient neural activity during face emotion discrimination – a social cognitive process associated with robust behavioral and neural deficits in schizophrenia. The results show that people with high SA have reduced neural response in emotion perception regions during discrimination of emotional faces. Compared to low SA, high SA was associated with reduced neural activity in the anterior portion of the rostral medial prefrontal cortex (arMFC), right superior temporal gyrus, and left somatosensory cortex during emotion discrimination relative to control conditions. Deficient activity for emotion discrimination in the high SA group was most consistent in arMFC. High SA participants showed reduced recruitment of this region when emotion discrimination was compared to each control condition, including identity

discrimination of emotional faces – a condition that is comparable in difficulty and uses the exact same emotional stimuli as the emotion discrimination condition.

Detailed examination of neural activity in the regions that showed a group x condition interaction (arMFC, right superior temporal gyrus, and somatosensory cortex) revealed a few consistent patterns. First, as predicted, there were significant between group differences during emotion discrimination, such that low SA participants had more neural activity than high SA in these regions. Second, the high SA group showed significantly *less* neural activity of these same regions during emotion discrimination compared to the control conditions. In the arMFC, low SA group showed greater neural activity for the emotion discrimination as compared to the control conditions. There were no consistent differences between low SA and high SA in the control conditions. Interestingly, these findings suggest that high SA participants were *deactivating* these regions during emotion perception. It is unclear based on the current work whether these differences were related to differences in strategy during emotion discrimination (e.g. attending to low-level features to perform the task and thus down-regulating activity in emotion processing regions) or other differences in emotional information processing. For example, previous studies have shown that patients with schizophrenia exhibit abnormal visual scanpaths of emotional faces (Loughland et al., 2002) and show greater interference from face identity information during emotion matching compared to healthy control participants (Baudouin et al., 2002).

These findings have important implications for our understanding of the mechanisms underlying individual differences in SA, as well as the clinical and functional consequences of these differences. The medial prefrontal cortex, superior temporal gyrus, and somatosensory cortices are part of a network of brain regions that process face emotions. The medial prefrontal

cortex plays a role in emotion recognition (Heberlein et al., 2008), emotion experience (Heberlein et al., 2008), mentalizing (Gallagher et al., 2000), and self-other processing (Heatherton et al., 2006; Ochsner et al., 2004). The arMFC region, in particular, has been found in previous studies to be consistently associated with mentalizing and other aspects of social cognition (Amodio & Frith, 2006). This region has also been associated with abnormalities during social-cognitive processing in schizophrenia samples (Brunet-Gouet & Decety, 2006). Lesions to ventral (but not lateral or dorsal) regions of the medial prefrontal cortex are also associated with impairments in emotion recognition (Heberlein et al., 2008). The superior temporal gyrus and sulcus are involved in perceptual processing of dynamic social stimuli including facial expressions of emotion and eye gaze (Haxby et al., 2000; Hooker et al., 2003; Hooker et al., 2008; Hooker et al., 2010). Finally, somatosensory cortex and related areas are thought to contribute to emotion processing by allowing facial expressions to be understood using an internal representation of a facial expression maintained in one's own somatosensory cortex (Adolphs et al., 2000; Heberlein et al., 2008; Hooker et al., 2008). Disruption of activity in somatosensory cortex leads to impairments in emotion discrimination of the same emotional face stimuli used in the present study (the Queen Square Face Discrimination Task, QFDT; Pitcher et al., 2008) and lesions to somatosensory and somatosensory-related areas are likewise associated with emotion recognition deficits (Adolphs et al., 2000). As somatosensory cortex and medial prefrontal cortex are involved in both emotion experience and emotion recognition, researchers have suggested that these regions are involved in understanding other's mental states through simulation mechanisms (Adolphs, 2002; Adolphs et al., 2000; Heberlein et al., 2008; Hooker et al., 2008). Given these previous findings, our results suggest that social anhedonia is

related to differences in the neural substrates responsible for self/other representation and social perception, perhaps through their common relationship with simulation mechanisms.

As a personality trait, SA is specifically related with schizophrenia and not to other disorders with anhedonic symptoms (Blanchard et al., 2001). Given this relationship, our findings can also be interpreted in the context of schizophrenia vulnerability. Individuals with schizophrenia have abnormalities in medial prefrontal cortex responses during emotion perception (Hempel et al., 2003) and intention attribution (Brunet et al., 2003). Structural abnormalities have also been consistently identified in superior temporal regions in individuals with schizophrenia and schizophrenia spectrum disorders (Davidson & Heinrichs, 2003; Dickey et al., 2002a; Dickey et al., 2002b; Dickey et al., 2003; Downhill et al., 2001; Siever & Davis, 2004; Wright et al., 2000). Superior temporal gyrus abnormalities may be related to deficits in both emotion perception (Edwards et al., 2002; Hooker & Park, 2002; Mandal et al., 1998; Mueser et al., 1996) and gaze perception (Hooker & Park, 2005; Hooker et al., 2003) observed in individuals with schizophrenia. In addition, deficits in somatosensory processing (e.g. differences in two point discrimination) are often associated with schizophrenia and schizophrenia vulnerability (Chang & Lenzenweger, 2001, 2004, 2005; Hooley & Delgado, 2001; Lenzenweger et al., 2003).

Our neural findings from individuals with high levels of SA are consistent with a relationship between SA and schizophrenia vulnerability (Kwapil, 1998; Stone et al., 2005). High SA in young adults prospectively predicts schizophrenia diagnosis ten years later (Kwapil, 1998). In addition, first-degree relatives of schizophrenia patients have abnormally high anhedonia levels (Stone et al., 2005). Understanding the neural basis of individual differences in SA may thus contribute to our understanding of schizophrenia liability and development.

Although our results indicate a relationship between SA and differences in neural networks related to basic emotion recognition, it is unclear whether these neural response differences are a cause or a consequence of varying levels of SA. High SA is identified by self-report of reduced approach motivation in social situations. If emotion recognition and social approach motivation rely on shared neural substrates, lack of approach motivation may be intrinsically related to reduced recruitment of social cognitive networks. For example, a reduced tendency or ability to simulate the mental states of others might result in both reduced social approach motivation as well as reduced emotion processing / recognition through the same basic mechanisms. Alternatively, over the course of development, social isolation associated with high SA may contribute to reduced engagement of social cognition systems during social interaction. The result of this could then be a reduced tendency of these systems to respond to even straightforward emotion recognition demands. Finally, it is also possible that abnormalities in the neural networks responsible for processing social and emotional stimuli lead to high-level trait differences in SA. That is, reduced responses in social perception networks may create a predisposition to experience lower levels of pleasure from social interaction and thus reduced drive for social affiliation. It is not possible to distinguish between these possibilities based on the current study. Future work might address these questions by looking at how differences in brain function predict differences in social pleasure over hours, days, or years.

The present study has several limitations. First, our use of a block design did not permit us to look at the relationship between brain activation and accuracy on individual trials. Using a block design also meant that we were unable to investigate emotion-specific effects (e.g. positive vs. negative valence) from emotion processing more generally. As social anhedonia is defined

by lack of pleasure from social interactions rather than increased negative affect during social interactions, it is possible that our results were driven by abnormalities in neural responses to positive emotional faces rather than emotional faces more generally. Due to the limited number of trials per emotion and the use of same/different responses, we were not able to look at emotion-specific brain responses and between-group differences in these responses. It is thus unclear whether our results were driven by differences associated with a specific emotion.

Another limitation was that our task failed to produce suprathreshold activity in the amygdala in either low or high SA groups. In addition to possible habituation effects from our use of a block design and continuous face presentation, possible emotion labeling demands (Lieberman et al., 2007) and reduced signal-to-noise in this region may have compromised our ability to detect amygdala differences. Thus it is difficult to interpret our lack of between group differences in medial temporal lobe areas.

Finally, although we assessed Axis I disorders in all participants, we did not conduct a comprehensive assessment of Axis II personality disorders. One of the symptoms of Schizoid Personality Disorder, in particular, is high levels of social anhedonia. It is possible that some of our participants met criteria for this disorder. Although not a form of psychosis, Schizoid Personality Disorder is considered a schizophrenia spectrum disorder and this diagnostic information would have been useful for exploring differences between disordered and nondisordered forms of SA in our sample.

Conclusion

The wide range of physical and mental health outcomes arising from differences in social affiliation and social support argue that the experience of pleasure that accompanies social interaction is a vital component of a functioning social cognitive system (Brown et al., 2007; Kwapil et al., 2009) with broad and meaningful health consequences. Social impairments and low levels of social affiliation are related to increased risk of mental illness (Hooley, 2010), as well as differences in immune functioning and mortality (Miller et al., 2009). Understanding the neural basis of differences in SA is thus both psychologically and clinically important. Our results indicate that individual differences in SA are related to observable differences in neural responses to social-emotional stimuli, especially in systems responsible for emotion perception and higher-level social cognitive functions. Future work elucidating the neural mechanisms underlying SA will have critical implications for our understanding of normal and abnormal social functioning, and the basic processes that fuel our fundamental drive to be social beings.

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Paper #3: Psychosis-proneness and the rubber hand illusion of body ownership

Submitted for publication.

Authors

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Abstract

Psychosis and psychosis-proneness are associated with abnormalities in subjective experience of the self, including distortions in bodily experience that are difficult to study experimentally due to lack of structured methods. In 55 healthy adults, we assessed the relationship between self-reported psychosis-like characteristics and susceptibility to the rubber hand illusion of body ownership. In this illusion, a participant sees a rubber hand being stroked by a brush at the same time that they feel a brush stroking their own hand. In some individuals, this creates the bodily sense that the rubber hand is their own hand. Individual differences in positive (but not negative) psychosis-like characteristics predicted differences in susceptibility to experiencing the rubber hand illusion. This relationship was specific to the subjective experience of rubber hand ownership, and not other unusual experiences or sensations, and absent when a small delay was introduced between seeing and feeling the brush stroke. This indicates that individual differences in susceptibility are related to visual-tactile integration and cannot be explained by differences in the tendency to endorse unusual experiences. Our findings suggest that susceptibility to body representation distortion by sensory information may be related or

contribute to the development of psychosis and positive psychosis-like characteristics

Introduction

Before the rise of symptom-based classifications of mental illness, schizophrenia was described as an abnormality in self-representation by both Kraepelin (the “orchestra without a conductor”; 1913) and Bleuler (the loss of the “individual self”; 1916) (Parnas, 2011). Viewing schizophrenia from a phenomenological perspective, Sass and Parnas more recently suggested that a key factor in the pathogenesis of psychosis is a deficit in “ipseity” or the basic sense of inhabiting the self (Sass & Parnas, 2003). Research in cognitive neuroscience supports the idea that schizophrenia is related to basic deficits in self-processing, such as source monitoring (Frith, 1992; Ditman & Kuperberg, 2005) and self-referential processing (Vinogradov et al., 2008). Deficits in self processing may underly the deficits in social cognitive processing characteristic of schizophrenia (Fisher et al., 2008) and deficits in emotion perception in psychosis-prone individuals (Germine & Hooker, 2011).

Individuals at high risk for developing psychosis report disruptions to the bodily self (Lenzenweger, 2006), including abnormalities in the experience of inhabiting the body (Sass & Parnas, 2003; Nelson et al., 2008) or the perception that the body has undergone some morphological change (Nelson et al., 2008). The perception of one’s body is a basic dimension of subjective experience, and is unique in its stability and consistency relative to external percepts (James, 1890; Merleau-Ponty, 1962). Understanding how body representation stability differs in individuals with varying levels of psychosis-proneness (i.e. with varying levels of

vulnerability to developing psychosis) may offer key insights into the disturbances of self-identity and processing that may contribute to psychosis development (Nelson et al., 2008).

Despite the stability of the body in our perceptual experience, illusions of body ownership are readily inducible in healthy, normal individuals under certain conditions (Botvinick & Cohen, 1998; Tsakiris & Haggard, 2005). The rubber hand illusion, in particular, has been used to investigate the structure of body representations (Tsakiris, 2010) and the phenomenology of the bodily self (Longo et al., 2008). In this illusion, the participant feels the touch of a brush on their own hand, hidden from view, at the same time that they see a brush touching a rubber hand. After a brief period of simultaneous stimulation of the participant's own hand and the rubber hand, approximately 40% of healthy participants will experience the bodily sense that the rubber hand is their own hand despite being fully aware that the rubber hand is not their hand (Botvinick & Cohen, 1998). This distortion in the experience of the body is associated with biases in judgment of the body's location in space (proprioceptive drift; Botvinick & Cohen, 1998), illusory sensations on the rubber hand (Durgin et al., 2007), and cooling of the participant's own hand (Moseley et al., 2008),

Susceptibility to the rubber hand illusion varies across individuals and experimental conditions (Botvinick & Cohen, 1998; Tsakiris & Haggard, 2005). The tendency to experience the illusion can be reduced or eliminated by disrupting perceptual cues that drive visual-tactile integration through asynchronous stimulation (i.e. by stroking the rubber hand and the participant's hand asynchronously, such that the brush is seen to touch the rubber hand at a different time than the touch is felt on the participant's own hand; Tsakiris & Haggard, 2005) or by violating constraints related to knowledge about the body (e.g. by stroking an object that is

structurally dissimilar from a hand, such as a wooden block; Tsakiris, 2010; Tsakiris et al., 2010).

The relationship between the rubber hand illusion and individual differences in illusion susceptibility has been less well-studied. To date, illusion susceptibility has been found to be greater in individuals with low interoceptive sensitivity (Tsakiris et al., 2011) and those with a malleable or distorted body image (Mussap & Salton, 2006; Eshkevari et al., 2011).

Two previous studies have attempted to link psychosis with susceptibility to the rubber hand illusion. Peled et al. (2000) showed that participants with schizophrenia are more prone to experiencing the rubber hand illusion than healthy control participants, and that this relationship was related to degree of positive symptoms. Morgan et al. (2011) found that administration of ketamine, a hallucinogenic drug that induces schizophrenia-like symptoms in healthy adults, is also associated with greater susceptibility to the rubber hand illusion. Together, these studies suggest a link between the positive symptoms of psychosis and illusion susceptibility.

Unfortunately, Peled et al. (2000) lacked a comparison condition in their study, and thus could not control for the general tendency to endorse unusual experiences among schizophrenia patients. Morgan et al. (2011) included an asynchronous stimulation control condition, but found no difference in measures of the rubber hand illusion between the two conditions after ketamine administration. Thus, it is unclear from these previous experiments whether rubber hand illusion susceptibility differences could be explained by a tendency to endorse unusual experiences. It is also unclear whether illusion susceptibility differences are related to psychosis vulnerability or are secondary to the experience of positive symptoms.

The rubber hand illusion provides an experimentally tractable way of tapping into the subjective experience of the body and investigating how individual differences in psychiatric

vulnerability relate to the bodily self. Psychosis and psychosis-proneness are associated with deficits in somatosensory processing (Lenzenweger et al., 2003; Chang & Lenzenweger, 2005) and abnormalities in the experience of the body are evident in the prodromal stages of psychosis, representing a basic aspect of disturbed phenomenology (Sass & Parnas, 2003; Lenzenweger, 2006; Nelson et al., 2008). Given these previous findings, susceptibility to distortions of body representations may be related to individual differences in psychosis-like characteristics (psychosis-proneness) even in the absence of psychotic symptoms. If this is the case, body representation abnormalities may be part of the fundamental vulnerability to developing psychosis or psychosis-like experiences.

The goal of the current study was to identify whether there is a specific relationship between experimentally-induced illusions of body ownership and psychosis-proneness. We hypothesized that greater psychosis-proneness, as measured by self-reported psychosis-like characteristics, would be related to a greater tendency to experience the rubber hand illusion after synchronous stimulation (stroking the rubber hand and the participant's own hand at the same time). We predicted that the tendency to experience the rubber hand illusion, and its relationship with psychosis-proneness, would be reduced or absent after asynchronous stimulation (stroking the rubber hand and the participant's own hand with a small temporal offset), as temporal synchrony is needed for multisensory integration (Tsakiris & Haggard, 2005). In other words, we predicted that the relationship between psychosis-proneness and the rubber hand illusion would be driven by differences in the tendency to alter the body representation in response to visual-tactile cues that lead to illusion formation in healthy adults. We further predicted that the experience of the rubber hand illusion would be more closely associated with positive psychosis-like characteristics (e.g. cognitive and perceptual distortions) than negative psychosis-like

characteristics (e.g. anhedonia), as positive symptoms often include abnormalities in bodily experience. Finally, we predicted that psychosis-proneness would be specifically related to subjective feelings of body ownership/agency and not a general tendency to have or endorse unusual experiences. For example, the experimental procedure can induce feelings of diminished or abnormal sensory perception in the participant's own hand (which we refer to as "reduced afference", e.g. feelings of tingling or numbness; Longo et al., 2008). We expected that variations in psychosis-proneness would not predict variations in feelings of reduced afference. Confirmation of a link between individual differences in psychosis-like characteristics and susceptibility to illusions of body ownership would provide an avenue for further exploration into how the phenomenology of self, body, and psychosis are related.

Methods

Participants. Participants were 55 healthy volunteers (20/55 male) with a mean age of 28 (SD = 11) recruited through the community-wide Harvard University study pool. All participants spoke English as a first or native language, were neurologically healthy, and had no DSM-IV Axis I psychiatric disorders based on administration of the MINI clinical interview before the experiment (Sheehan et al., 1998). All participants gave informed consent before participating and the protocol was approved by the Committee for the Use of Human Subjects at Harvard University.

Psychosis-proneness measures. We assessed psychosis-proneness with several widely used self-report questionnaires that measure positive and negative psychosis-like characteristics. These characteristics are analogous to the positive and negative symptoms of psychosis (Liddle,

1987). Our measure of positive psychosis-like characteristics (positive psychosis-proneness) included 132 items taken from the cognitive-perceptual subscale of the Schizotypal Personality Questionnaire (33 items; Raine, 1991), the Chapman Magical Ideation Scale (30 items; Eckblad & Chapman, 1983), the Chapman Perceptual Aberration Scale (35 items; Chapman et al., 1978), and the Referential Thinking Scale (34 items; Lenzenweger et al., 1997). Our measure of negative psychosis-like characteristics (negative psychosis-proneness) included 73 items taken from the interpersonal subscale of the Schizotypal Personality Questionnaire (33 items; Raine, 1991) and the Chapman Revised Social Anhedonia Scale (40 items; Eckblad et al., 1982; Mishlove & Chapman, 1985). As previous work has indicated that illusions of body ownership in schizophrenia are linked with positive symptoms (Peled et al., 2000), we hypothesized that positive psychosis-proneness would be more strongly related to the rubber hand illusion than negative psychosis-proneness.

Rubber Hand Illusion Procedure. After completing the questionnaires, participants sat at a table and placed their nondominant hand inside of a large opaque box. An opening at the top of the box allowed the participant to see a lifelike rubber hand, located at the participant's midline (Tsakiris & Haggard, 2005). The distance between the middle finger of the rubber hand and of the participant's hand was always 20cm (Lloyd, 2007). Participants wore a smock that fastened to the front of the box, hiding both their arms. An opening on the other side of the box allowed the experimenter to see the participant's hand and the rubber hand. Two paintbrush heads were attached to a rod that passed through the box lengthwise. The paintbrush heads were 20 cm apart, so that rotating the rod caused the paintbrushes to brush the participant's hand and the rubber hand in the same location. Figure 5 provides an illustration of the experimental set-up.

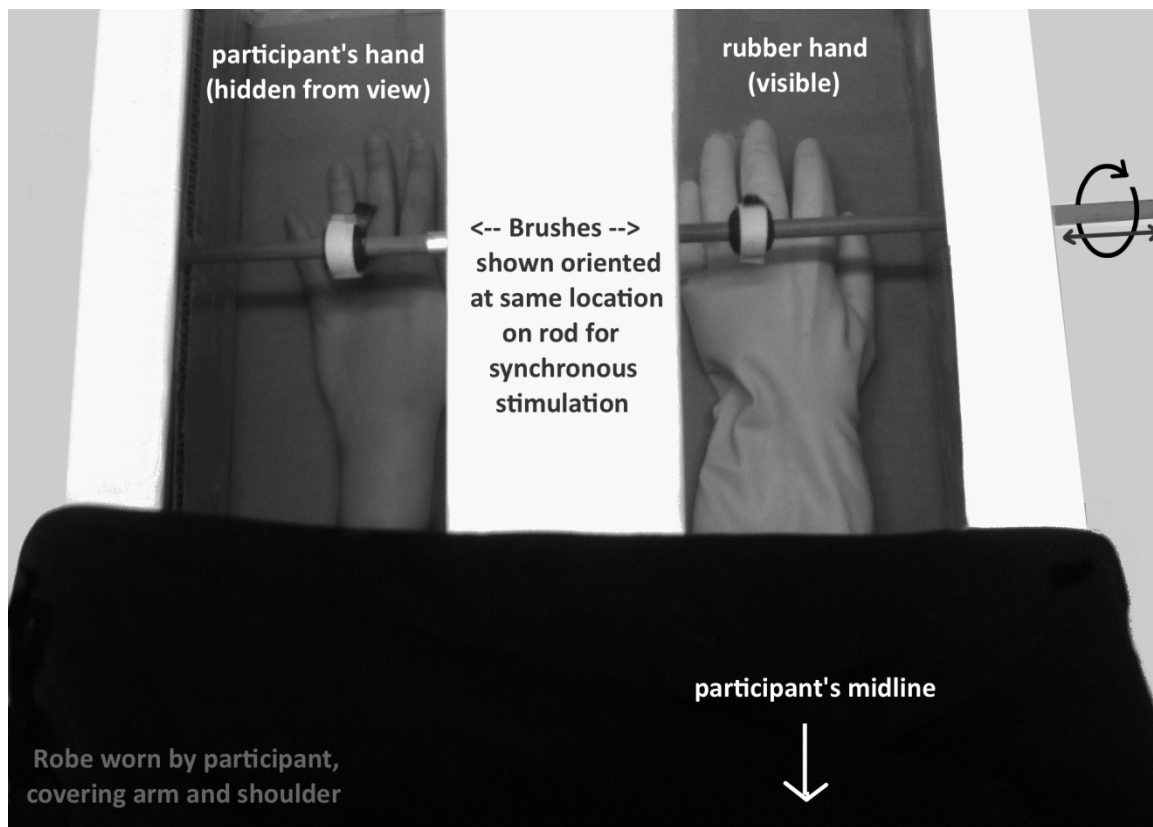


Figure 5. Experiment set-up for inducing the rubber hand illusion

During synchronous stimulation (shown), brushes were oriented on the rod so that a brush was observed touching the rubber hand at the same time and in the same location as the participant felt the brush touching their own hand. During asynchronous stimulation, brushes were misaligned by 90 degrees around the rod, so that the brush touched the participant's hand at a different time than the brush was observed touching the rubber hand.

There were two stimulation phases (Botvinick & Cohen, 1998). During the synchronous phase, the paintbrush heads were aligned so that the participant saw the rubber hand being touched by the paintbrush at the same time as the paintbrush was touching their own hand. During the asynchronous phase, the paintbrush heads were misaligned by 90 degrees along the rod, so that the brush touched the rubber hand a quarter of a second before or after touching the participant's hand (based on a 1 rotation/second frequency of brushing). Each stimulation phase lasted 10 minutes.

Before and after each stimulation phase, the participant indicated the perceived location of the middle finger of their hidden hand by reading off a meter stick that was held just above the box and randomly translated left or right. Proprioceptive drift was estimated as the difference between pre and post-stimulation hand location judgments (Botvinick & Cohen, 1998; Tsakiris & Haggard, 2005). The participant was then asked a series of questions to assess their experience of the illusion (see Table 7; taken from Longo et al., 2008 and Botvinick & Cohen, 1998) and any nonspecific feelings of reduced afference (Longo et al., 2008).

Table 7. Self report items used to measure subjective experiences after synchronous and asynchronous brushing of the participant's hand and the rubber hand

Question	Category	Source
1. It seemed as if I were feeling the touch of the paintbrush in the location where I saw the rubber hand touched.	Ownership	Botvinick and Cohen (1998)
2. It seemed as though the touch I felt was caused by the paintbrush touching the rubber hand.	Ownership	Botvinick and Cohen (1998)
3. I felt as if the rubber hand were my hand.	Ownership	Botvinick and Cohen (1998)
4. It seemed like I was looking directly at my own hand, rather than at a rubber hand.	Ownership	Longo <i>et al.</i> (2008)
5. It seemed like my hand was in the location where the rubber hand was.	Ownership	Longo <i>et al.</i> (2008)
6. It seemed like I could have moved the rubber hand if I wanted.	Agency	Longo <i>et al.</i> (2008)
7. It seemed like I was in control of the rubber hand.	Agency	Longo <i>et al.</i> (2008)
8. I had the sensation of pins and needles in my hand.	Reduced afference	Longo <i>et al.</i> (2008)
9. I had the sensation that my hand was numb.	Reduced afference	Longo <i>et al.</i> (2008)
10. It seemed like the experience of my hands was less vivid than normal.	Reduced afference	Longo <i>et al.</i> (2008)

Subjective experience of rubber hand ownership was measured using five items rated from -3 (strongly disagree) to 3 (strongly agree) (see Table 7; Botvinick & Cohen, 1998; Longo *et al.*, 2008). These questions distinguish between experiences after synchronous versus asynchronous stimulation and are specifically related to the rubber hand illusion (Longo *et al.*, 2008). Feelings of agency over the rubber hand were measured with two questions (Longo *et al.*, 2008). We measured agency and ownership separately based on dissociations in the literature (Gallagher, 2000), particularly in schizophrenia (Frith, 2005) and in the rubber hand illusion

(Longo et al., 2008). Finally, three questions assessed feelings of reduced afference in the participant's own hand (e.g. numbness or tingling) (Longo et al., 2008). Feelings of reduced afference are not directly related to the rubber hand illusion, but rather are more prominent during asynchronous stimulation (Longo et al., 2008). Our prediction was that psychosis-proneness would be associated with feelings of rubber hand agency and ownership, but not reduced afference.

Due to our concern about the possible confound of individual differences in suggestibility, the asynchronous stimulation condition always followed the synchronous stimulation condition. Participants were naïve about the expected effect during synchronous stimulation, but generally knew what to expect (either because of their experiences or post-stimulation assessment) during the asynchronous stimulation condition.

Results

Average scores on measures of psychosis-proneness are shown in Table 8. Average proprioceptive drift and question ratings after synchronous and asynchronous stimulation conditions are shown in Table 8.

Due to positive skew, distributions of scores in our measures of psychosis-proneness and subjective ratings of the rubber hand illusion were significantly nonnormal (Kolmogorov-Smirnov test for normality; all $P < 0.05$). Thus, we report all effects in terms of both parametric and nonparametric statistics.

Table 8. Summary of independent and dependent measures

Shown are mean, standard deviation (SD), and range of psychosis-proneness scores across the sample of 55 individuals. Also shown are mean, SD, and range of dependent measures of the rubber hand illusion after synchronous and asynchronous brushing of the participant's hand and a rubber hand.

	Mean	SD	Range
Positive psychosis-proneness scales			
Referential Thinking	2.6	4.2	0 to 17
Magical Ideation	3.3	2.8	0 to 12
Perceptual Aberration	1.4	2.1	0 to 10
SPQ: Cognitive-Perceptual Factor	4.7	5.7	0 to 23
<i>Total Positive Score</i>	<i>12</i>	<i>13</i>	<i>0 to 60</i>
Negative psychosis-proneness scales			
Social Anhedonia	9.5	8.4	0 to 34
SPQ: Interpersonal Factor	6.9	7.6	0 to 30
<i>Total Negative Score</i>	<i>16</i>	<i>15</i>	<i>0 to 54</i>
Synchronous Stimulation			
Baseline Position (cm) [^]	-0.2	3.4	-9 to 10
Proprioceptive Drift (cm) [^]	1.3	3.4	-9 to 10
Ownership Ratings (average of Q1-5)	-0.23	1.9	-3 to 3
Agency Ratings (average of Q6,7)	-1.5	2	-3 to 3
Deafference Ratings (average of Q8-10)	-1.3	1.7	-3 to 3
Asynchronous Stimulation			
Baseline Position (cm) [^]	1.1	3.6	-8 to 19
Proprioceptive Drift (cm) [^]	0.24	2.7	-6 to 6
Ownership Ratings (average of Q1-5)	-1.6	1.7	-3 to 2.4
Agency Ratings (average of Q6,7)	-2	1.6	-3 to 3
Deafference Ratings (average of Q8-10)	-1.3	1.8	-3 to 2.7

[^]Positive numbers represent distances from the participant's hand towards the rubber hand

To verify our experimental procedure, we compared measures of the rubber hand illusion after each stimulation phase. Based on previous findings, the illusion should be significantly stronger after synchronous stimulation than asynchronous stimulation (Tsakiris & Haggard, 2005; Longo et al., 2008). Compared with asynchronous stimulation, synchronous stimulation

produced higher rubber hand ownership ratings (Wilcoxon Signed-Rank Test, one-tailed, $z = -5.0$, $P < 0.001$; paired samples t-test, one-tailed, $t(54) = 6.0$, $P < 0.001$), higher agency ratings ($z = -2.4$, $P < 0.05$; $t(54) = 2.6$, $P < 0.01$) and greater proprioceptive drift ($z = -1.7$, $P = 0.07$; $t(54) = 1.9$, $P < 0.05$). Although feelings of reduced afference were present in both conditions ($z = -4.4$ for both, $P < 0.001$; $t(54) = -0.56$, $P < 0.001$), there was no difference between conditions ($z = -0.21$, $P = 0.83$; $t(54) = 0.16$, $P = 0.43$). Based on these data, we confirm that our manipulation induced experiences associated with the rubber hand illusion in the synchronous condition compared with the asynchronous (control) condition.

We predicted that positive psychosis-proneness would be associated with greater susceptibility to the rubber hand illusion, as measured by feelings of rubber hand ownership and agency after synchronous stimulation. We examined ownership and agency separately because of ownership/agency dissociations in the schizophrenia literature (Frith, 2005).

Rubber hand ownership and psychosis-proneness. Ownership is the degree to which the participant experiences the bodily sense that the rubber hand is their own hand. Consistent with our hypothesis, positive psychosis-proneness was significantly associated with subjective experiences of rubber hand ownership after synchronous stimulation (Spearman rank correlation, $\rho = 0.32$, $P < 0.05$; Pearson correlation, $r = 0.42$, $P < 0.01$), even when controlling for rubber hand ownership after asynchronous stimulation (Spearman rank partial correlation, $\rho = 0.28$, $P < 0.05$; Pearson partial correlation, $r = 0.35$, $P < 0.05$). There was no significant association between rubber hand ownership and positive psychosis-proneness after asynchronous stimulation ($\rho = 0.17$, $P = 0.2$; $r = 0.26$, $P = 0.06$). The absence of a relationship between positive psychosis-proneness and experiences of rubber hand ownership after asynchronous stimulation indicates that the relationship after synchronous stimulation cannot be explained by an increased

tendency to endorse unusual experiences among psychosis-prone participants.

Negative psychosis-proneness was not associated with the subjective experience of rubber hand ownership ($\rho = -0.08, P = 0.58; r = -0.1, P = 0.48$), despite the strong relationship between positive and negative psychosis-like characteristics in our sample ($\rho = 0.59, P < 0.001; r = 0.60, P < 0.001$).

Figure 6 shows the relationship between ratings of rubber hand ownership after synchronous stimulation, as related to positive and negative psychosis-proneness.

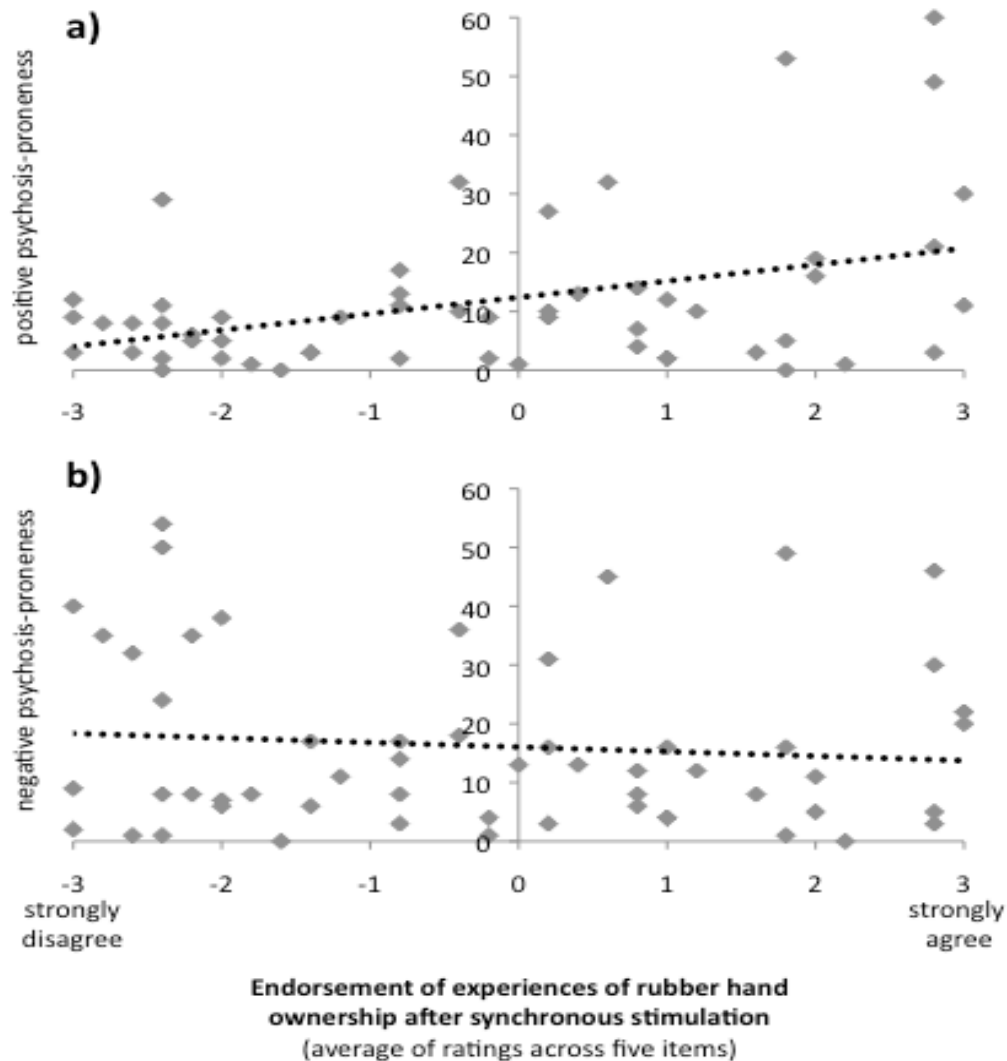


Figure 6. Psychosis-proneness and the subjective experience of the rubber hand illusion after synchronous stimulation

The y-axis shows the number of psychosis-like characteristics a participant endorsed based on questionnaire measures. The x-axis shows how much the participant tended to agree or disagree with statements regarding feelings of body ownership over the rubber hand, after a period of synchronous brush strokes on the rubber hand and the participant's own hand. (a) Endorsement of positive psychosis-like characteristics (e.g. cognitive-perceptual distortions, referential thinking) was associated with a greater tendency to experience feelings of rubber hand ownership. (b) Endorsement of negative psychosis-like characteristics (e.g. social anhedonia) was not associated with feelings of rubber hand ownership.

Agency and psychosis-proneness. Another component of the rubber hand illusion is the subjective experience of agency, or the feeling that one can control the rubber hand. Positive psychosis-proneness was significantly associated with the subjective experience of agency after synchronous stimulation ($\rho = 0.28, P < 0.05; r = 0.3, P < 0.05$), but also after asynchronous stimulation ($\rho = 0.24, P = 0.08; r = 0.33, P < 0.05$). Controlling for agency after asynchronous stimulation abolished the relationship between positive psychosis-proneness and agency after synchronous stimulation ($\rho = 0.14, P = 0.3; r = 0.09, P = 0.52$). It is possible that order effects (asynchronous stimulation always followed synchronous stimulation) created a residual sense of agency after asynchronous stimulation among psychosis-prone individuals. Alternatively, differences in the experience of agency that vary with psychosis-proneness may be less closely related to visual-tactile integration than differences in the experience of rubber hand ownership.

Negative psychosis-proneness was not associated with agency after either synchronous ($\rho = -0.05, P = 0.7; r = -0.04, P = 0.8$) or asynchronous stimulation ($\rho = -0.05, P = 0.7; r = 0.02, P = 0.9$).

Reduced afference and psychosis-proneness. To understand the specificity of the relationship between subjective experiences and psychosis-proneness, we assessed whether positive psychosis-proneness was associated with bodily experiences related to the manipulation, but not to the rubber hand illusion. We measured experiences of reduced afference after illusion induction (Longo et al., 2008) to explore this possibility.

Positive psychosis-proneness was not associated with feelings of reduced afference after synchronous ($\rho = 0.06, P = 0.67; r = 0.08, P = 0.58$) or asynchronous stimulation ($\rho = 0.11, P = 0.41; r = 0.13, P = 0.35$). Differences in negative psychosis-proneness, similarly, showed no association with feelings of reduced afference (synchronous: $\rho = 0.09, P = 0.51; r = 0.13, P =$

0.35; asynchronous: $\rho = -0.04$, $P = 0.8$; $r = -0.1$, $P = 0.46$).

Proprioceptive drift and psychosis-proneness. The rubber hand illusion is often associated with biases in proprioception, where the participant judges their actual (hidden) hand as being closer to the rubber hand after synchronous stimulation. Proprioceptive drift is often used as an objective measure of the rubber hand illusion (Botvinick & Cohen, 1998; Tsakiris & Haggard, 2005; Longo et al., 2008). We predicted that psychosis-proneness would be associated with greater proprioceptive drift towards the rubber hand after synchronous stimulation.

Contrary to our hypothesis, proprioceptive drift after synchronous stimulation was not associated with positive psychosis-proneness ($\rho = 0.03$, $P = 0.85$; $r = 0.07$, $P = 0.62$) or negative psychosis-proneness ($\rho = 0.01$, $P = 0.96$; $r = 0.06$, $P = 0.64$), despite the relationship between positive psychosis-proneness and subjective experiences of rubber hand ownership.

Dissociations between drift and subjective experience of the rubber hand illusion have been documented in previous studies (Holmes et al., 2006), suggesting that these two measures may map onto dissociable aspects of the illusion.

Discussion

We have shown that positive psychosis-like characteristics in otherwise healthy individuals are associated with a greater susceptibility to the rubber hand illusion, an illusion of body ownership. These positive psychosis-like characteristics include a tendency towards referential thinking (Lenzenweger et al., 1997), magical ideation (Eckblad & Chapman, 1983), cognitive-perceptual distortions (Raine, 1991), and perceptual aberrations (Chapman et al., 1978). Our data suggest that susceptibility to body representation distortion may be a

vulnerability factor for developing psychosis, consistent with abnormalities in bodily experience among individuals at high risk of developing psychosis (Sass & Parnas, 2003; Nelson et al., 2008). A tendency to experience distortions in body representations may be linked to the development of positive psychosis-like experiences and to broader deficits in self-processing related to psychosis risk.

The relationship between positive psychosis-proneness and the experience of ownership in the rubber hand illusion was only found when the participant saw a brush stroking a rubber hand at the same time as feeling a brush stroking their own hand (synchronous stimulation). When a small delay was introduced between these two events (asynchronous stimulation), there was no longer a relationship between positive psychosis-proneness and illusion strength. Thus, the relationship between positive psychosis-proneness and rubber hand illusion strength was not being driven by a tendency to endorse unusual experiences, as these should impact both synchronous and asynchronous stimulation conditions. Along similar lines, psychosis-proneness was specifically related to feelings of rubber hand ownership, and not to feelings of reduced afference that were also induced by the experimental procedure (Longo et al., 2008). The specificity of the relationship between positive psychosis-proneness and the experience of rubber hand ownership after synchronous stimulation rules out alternative explanations that previous experiments looking at body ownership and psychosis have failed to exclude.

Rubber hand illusion susceptibility was specifically linked to positive (and not negative) psychosis-like characteristics, suggesting possible mechanisms relating positive psychosis-like characteristics to abnormalities in the subjective experience of the body. Perception involves the integration of internal representations, acquired through previous experience, with incoming sensory information. Perception is thus constrained by prior knowledge and context information

(Frith & Dolan, 1997; Gilbert & Sigman, 2007). Schizophrenia-related cognitive and perceptual abnormalities may result from a failure to adequately couple sensory information with context and previous experience (Fleminger, 1992; Fletcher & Frith, 2009; Gilbert & Sigman, 2007; Hemsley, 1987; Hemsley, 2005)

For example, schizophrenia patients are less likely than control participants to experience the hollow mask illusion, whereby a hollow mask viewed from behind is perceived as if being viewed from the front (i.e. not depth-inverted). This has been interpreted as a reduced tendency to incorporate previous experience in guiding perception towards the more familiar stimulus – a normal face (Schneider et al., 2002).

A reliance on sensory information over previous experience may also increase susceptibility to the rubber hand illusion. The rubber hand illusion is thought to be a consequence of multisensory (visual-tactile) information overriding previous representations of the body (Tsakiris, 2010). Greater susceptibility to the rubber hand could result from a reduced tendency to use previous experience as a constraint on perception. Reduced constraints on perception, across modalities, could give rise to the cognitive and perceptual distortions that we think of as positive psychosis-like characteristics (Raine, 1991). The specific impact of this tendency on the bodily sense, that is having body representations that are susceptible to distortion, may further contribute to positive psychosis-like characteristics by disrupting the stability of self experience (Sass & Parnas, 2003; Nelson et al., 2008; James, 1890).

To our knowledge, only one previous study has looked at the relationship between psychosis-related personality variables and the rubber hand illusion (Asai et al., 2011). The findings of this study are difficult to interpret, however, as a significant relationship was only found between positive psychosis-like characteristics and self-report items not specifically

related to the experience of the rubber hand illusion (e.g. the sensation that the participant's own hand is moving; Asai et al., 2011, supplementary materials).

One limitation of our study is the absence of any relationship between psychosis-proneness and proprioceptive drift after synchronous stimulation. Although self-reported experiences of the rubber hand illusion and proprioceptive drift are generally highly associated (Longo et al., 2008), dissociations between these two measures have been noted in several studies (Holmes et al., 2006; Kammers et al., 2011; Kammers et al., 2009; Morgan et al., 2011; Tsakiris et al., 2011). Positive psychosis-proneness may be related specifically to distortions in the subjective experience of the body and not to differences in proprioceptive localization of the body in space.

Another unexpected finding in our study was a relationship between psychosis-proneness and the experience of rubber hand agency (but not ownership) after both synchronous and asynchronous stimulation conditions. Previous evidence indicates that body ownership and agency are dissociable aspects of subjective experience (Frith, 2005; Gallagher, 2000; Longo et al., 2008). For example, a patient with schizophrenia-related delusions of control may recognize that their hand is moving, but believe that some other agent is controlling that movement (Frith, 2005). Positive psychosis-proneness may be related to a tendency to feel a sense of agency over a rubber hand based on visual similarity alone. Alternatively, the sense of agency induced by synchronous stimulation (always occurring first) may have carried over to the asynchronous stimulation condition, suggesting that the experience of agency might be more durable and/or less dependent on visual-tactile integration than the experience of ownership. We cannot distinguish between these possibilities based on the current study.

Our data suggest a provocative relationship between psychosis vulnerability and illusions

of body ownership. We do not mean to suggest, however, that individuals who are susceptible to illusions of body ownership are therefore also vulnerable to developing psychosis. Those individual differences that underly susceptibility to the rubber hand illusion are poorly understood, and many other individually varying characteristics may increase susceptibility. Previous literature has found, for example, that greater illusion susceptibility is related to low interoceptive sensitivity (Tsakiris et al., 2011), a malleable body image (Mussap & Salton, 2006; Eshkevari et al., 2011), and greater empathic concern (Asai et al., 2011).

In conclusion, our findings indicate that psychosis vulnerability and positive psychosis-like characteristics are related to the tendency to experience illusions of body ownership, even in otherwise healthy individuals. Our findings also demonstrate that susceptibility to body representation distortion is a measurable phenomenon that varies with psychosis risk. Future research might look at how rubber hand illusion susceptibility varies with other measures of self processing that are disturbed in psychosis (e.g. self monitoring), increasing our understanding of the way body representation relates to other forms of self-representation. One might also look at experimental manipulations that interact with psychosis-proneness to alter illusion susceptibility, to provide information about the mechanisms that underlie abnormalities of body experience among psychosis-prone individuals. For example, if the relationship between psychosis-proneness and the rubber hand illusion represents a failure of knowledge to constrain body representation distortions, one might expect substitution of a rubber hand for another type of object (e.g. a wooden block; Tsakiris, 2010) to disrupt illusion formation less for psychosis-prone individuals. An increased understanding of the way body ownership illusions are related to other forms of self-representation and psychosis-proneness can shed light on the distortions in bodily experience that accompany positive symptoms and psychosis-like characteristics, and

ultimately the factors that might lead to psychosis development.

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Additional Findings

Here, experimental findings are presented that were not included in Papers #1-3, but are relevant to the current dissertation. These findings are organized by experiment number, with a brief introduction, method, results, and discussion section for each experiment.

Experiment #3b: Psychosis-proneness, Flexibility in Body Representations, and Face Emotion Recognition (FER)

Introduction. A significant motivation for Experiment #3 was to see whether differences in flexibility of the body representation (as measured by susceptibility to the rubber hand illusion) mediate the relationship between psychosis-proneness and FER, based on simulation theories of FER that posit contributions from somatosensory and motor processing to emotion understanding (Adolphs et al., 2000). The fact that there was no relationship between negative psychosis-proneness and indices of the rubber hand illusion indicates that the latter could not function as a mediator of the relationship between negative psychosis-proneness and FER ability. Nevertheless, this hypothesis was tested for positive psychosis-proneness, which was significantly related to rubber hand illusion susceptibility.

If differences in body representation flexibility account for differences in FER that vary with positive psychosis-proneness, this would suggest that body representation abnormalities may underly reduced FER ability in high psychosis-prone individuals (based on positive psychosis-like characteristics). It was predicted that susceptibility to the rubber hand illusion would be related to reduced FER ability, and mediate the relationship between positive psychosis-proneness and FER performance.

Method. The rubber hand illusion and psychosis-proneness were measured as described in Paper #3. Subjective experiences of ownership and subjective experiences of agency were used as measures of the rubber hand illusion, as relationships between these measures and positive psychosis-proneness were found in Experiment #3. No relationship was found between the rubber hand illusion and negative psychosis-proneness, so negative psychosis-proneness was not included in this analysis.

As a test of FER, the Reading the Mind in the Eyes test (hereafter referred to as the “Eyes Test”) was administered. The Eyes Test is a test of complex emotion perception that has been used to test individual differences in emotion perception and theory of mind (Baron-Cohen et al., 2001). In this test, the participant sees an image of the eye region of a face and must choose which of four complex emotion words (e.g. “arrogant”, “annoyed”, “cautious”) best fits the emotion being expressed in that image.

Results. Positive psychosis-proneness predicted experiences of rubber hand ownership ($\rho = 0.32$, $p < 0.05$, two-tailed) and rubber hand agency ($\rho = 0.28$, $p < 0.05$) (See Paper #3). Positive psychosis-proneness also predicted Eyes Test performance ($\rho = -0.28$, $p < 0.05$).

Rubber hand ownership predicted Eyes Test performance, but in the opposite direction ($\rho = 0.35$, $p < 0.01$). Agency predicted Eyes Test performance at trend level ($\rho = 0.23$, $p = 0.1$), also in the opposite direction. This was contrary to prediction, and suggests that susceptibility to the rubber hand illusion is related to better FER ability and thus cannot account for psychosis-proneness related FER differences.

Discussion. The hypothesis was that variations in rubber hand illusion susceptibility might mediate the relationship between psychosis-proneness and FER. This hypothesis was not confirmed. If differences in somato-motor processing underlie differences in FER in psychosis-

prone individuals, these somato-motor differences do not appear to be measured by susceptibility to the rubber hand illusion.

Another unexpected finding was the positive correlation between Eyes Test performance and rubber hand illusion susceptibility. Previous literature has suggested that greater rubber hand illusion susceptibility may arise from higher levels of empathy (Durgin et al., 2007). Insofar as Eyes Test performance is related to empathy (Rodrigues et al., 2009), this could explain why higher Eyes Test scores were associated with stronger illusions. On the other hand, positive psychosis-proneness was related to rubber hand illusion susceptibility despite being associated with reduced empathy (Henry, Bailey, & Rendell, 2008). Empathy and positive psychosis-proneness may impact illusion susceptibility through different routes. Further investigation would be needed to understand the complex relationship between psychosis-proneness, FER, and illusions of body ownership.

Experiment #3c: Dimensions of Psychosis-proneness and FER

Introduction. Paper #1 (“Face emotion recognition is related to individual differences in psychosis-proneness.”) reported findings from one self-report measure of psychosis-proneness, the Schizotypal Personality Questionnaire (Brief; Raine & Benishay, 1995) and two different tests of FER. Significant associations were found between positive psychosis-proneness and FER as well negative psychosis-proneness and FER, even when controlling for variations in face gender or face identity processing. Although not reported in Paper #3, Experiment #3 included a measure of FER (complex emotion perception: Reading the Mind in the Eyes, Baron-Cohen et al., 2001), a measure of verbal IQ, and a measure of performance IQ. These data thus allowed an investigation of whether the relationship between FER and psychosis-proneness observed in

Experiment #1 replicates across measures of psychosis-proneness, with an FER paradigm that relies on recognition of more complex emotional states, and while controlling for differences in verbal and performance IQ.

Method. A set of widely used self-report questionnaires measuring positive and negative psychosis-like characteristics was administered to 55 individuals, tested in the lab. These included the Schizotypal Personality Questionnaire (cognitive-perceptual and interpersonal subscales; Raine, 1991), the Chapman Magical Ideation Scale (Eckblad and Chapman, 1983), the Chapman Perceptual Aberration Scale (Chapman et al., 1978), the Referential Thinking Scale (Lenzenweger et al., 1997), and the Chapman Revised Social Anhedonia Scale (Eckblad et al., 1982; Mishlove and Chapman, 1985). The brief version of the Schizotypal Personality Questionnaire was also used in Experiment #1. The Revised Social Anhedonia Scale was also used in Experiment #2. All measures were used in Experiment #3a. The sample of 55 individuals was the same as the sample described in Paper #3.

The test of FER was the Reading the Mind in the Eyes test (Eyes Test), described earlier. The Vocabulary subtest of the Wechsler Abbreviated Scale of Intelligence was administered as a measure of verbal IQ and the Matrix Reasoning subtest as a measure of performance IQ (WASI; Wechsler, 1999).

Results are reported in terms of Spearman correlations between each measure of psychosis-proneness (six measures in total) and scores on the Eyes Test. Spearman correlations were chosen due to the nonnormal distributions in questionnaires scores (significant positive skew).

Results. Table 9 shows zero-order correlations between Eyes Test scores and each measure of psychosis-proneness, as well as partial correlations controlling for verbal IQ (based on Vocabulary scores) and performance IQ (based on Matrix Reasoning scores).

Table 9. Psychosis-proneness and Reading the Mind in the Eyes scores: Spearman simple correlation coefficients and partial correlation coefficients

<u>Positive psychosis-proneness</u>	zero order correlation	controlling for verbal IQ	controlling for performance IQ
Cognitive-Perceptual distortions (SPQ subscale)	-0.27*	-0.24	-0.22
Magical Ideation	-0.21	-0.2	-0.09
Perceptual Aberrations	-0.34*	-0.29*	-0.25
Referential Thinking	-0.3*	-0.26	-0.21
<i>Sum of all positive scales</i>	-0.28*	-0.26	-0.19
 <u>Negative psychosis-proneness</u>			
Interpersonal difficulties (SPQ subscale)	-0.33*	-0.32*	-0.29*
Social Anhedonia	-0.41**	-0.33*	-0.33*
<i>Sum of all negative scales</i>	-0.4**	-0.34*	-0.33*

* $p < 0.05$, two-tailed; ** $p < 0.01$, two-tailed

All psychosis-proneness measures were significantly correlated with Eyes Test performance, with the exception of scores on the Magical Ideation Scale. Controlling for either verbal or performance IQ reduced correlations between psychosis-proneness and Eyes Test performance, but correlations between negative psychosis-proneness measures and Eyes Test scores remained significant.

Discussion. The current findings suggest that the relationship between FER and psychosis-proneness generalizes to measures of complex emotion perception, but is more robust for negative than positive psychosis-like characteristics. In an analysis using multiple self-report scales and controlling for IQ differences, FER was robustly related to measures of negative psychosis-proneness. FER was also related to measures of positive psychosis-proneness, but this relationship was not significant after controlling for differences in IQ.

This finding agrees with previous literature indicating that FER deficits are more closely related to the presence of negative than positive symptoms (Sergi et al., 2007).

Experiment #4: Psychosis-proneness and self-referential processing

Introduction. Previous evidence has indicated that individuals with schizophrenia have trouble judging the origin of information, or source monitoring (Vinogradov et al., 1997). In particular, they have difficulties with remember the source of self-generated information (Vinogradov et al., 1997; Fisher et al., 2008), showing a greater tendency to identify self-generated information as arising from external sources. Harvey et al. (2011) similarly found that schizophrenia patients had a smaller recognition memory advantage for self-referential information than healthy control participants.

In a study of self-referential source memory and social perception, Fisher et al. (2008) further found that source memory for self-generated information predicted face emotion perception and identity recognition in healthy control and schizophrenia participants – but that once the influence of other neurocognitive variables was removed, this relationship was only significant in healthy control participants. In other words, self-referential source memory specifically contributed to social perception ability in healthy control participants, but not in

patients with schizophrenia. This suggests that self-referential processing deficits contribute to deficits in social cognition in schizophrenia.

Two paradigms were taken from the schizophrenia literature for measuring self-referential source memory (Fisher et al., 2008; Vinogradov et al., 1997) and self-referential recognition memory (Harvey et al., 2011) to see whether self-referential processing (1) is related to positive and/or negative psychosis-proneness, (2) whether self-referential processing ability is related to FER ability, and (3) whether the relationship between psychosis-proneness and FER ability could be explained by differences in self-referential processing, as suggested by Fisher et al. (2008).

Experiment 4a - Self-referential source memory.

Method. This study was conducted in the lab, using the same sample of 55 participants that completed Experiment #3. The paradigm and stimuli were taken from Vinogradov et al. (1997) and Fisher et al. (2008) to assess source memory for self-generated, experimenter-generated, and new words. During the study phase, the participant was given a list of 20 short sentences, where ten of the sentences had words already filled in and underlined and ten had blank lines (e.g. “The boy threw the ball”, “The cat chased the ___”). The participant read each sentence out loud, filling in the blank with a word where no word was given. The experimenter recorded all words generated by the participant. Approximately two hours later, participants were presented with a list of 30 word pairs (e.g. boy-ball, cat-mouse), with 10 word pairs from sentences that the participant had previously read aloud (experimenter-generated), 10 word pairs from sentences where the participant had filled in the blank with a word (self-generated), and 10 new word pairs. Participants were asked to identify whether the second word in the pair was experimenter-generated, self-generated, or new.

Patterns of errors were calculated as dependent measures using the same procedure as Vinogradov et al. (1997). For each category of word pair (self-generated, experimenter-generated, and new) errors could be classified as misattribution errors or source discrimination errors. For self-generated word pairs, for example, a judgment of “experimenter-generated” or “new” would be a source discrimination error – a failure to remember the source of the word pair. Where experimenter-generated or new word pairs were judged as self-generated, this was classed as a self-generated misattribution error, or the incorrect judgment that oneself was the source of a word pair. Thus, there were six classes of errors: self-generated source discrimination errors, self-generated misattribution errors, experimenter-generated source discrimination errors, experimenter-generated misattribution errors, new source discrimination errors, and new misattribution errors.

People tend to be better at remembering the source of self-generated information than experimenter-generated information (Vinogradov et al., 1997). Also, when new information is falsely recognized, the source of that information is more likely to be attributed to the experimenter than to oneself. The goal was to replicate these previous findings in this sample. The main hypothesis with respect to psychosis-proneness was that higher psychosis-proneness would be associated with a greater tendency to make self-generated source discrimination errors (failure to remember that a self-generated word was self-generated), but that this could not be explained by a greater tendency to make source discrimination errors overall. Finally, the role of IQ in any observed relationships was examined.

Results. Due to significant positive skew in all variables, nonparametric tests were used. Across all participants, significantly fewer self-generated source discrimination errors (9% error) were made than experimenter-generated source discrimination errors (46%) (Wilcoxon signed

rank test: $z = -5.9$, $p < 0.001$). Similarly, participants made fewer self-generated misattribution errors (mistakenly judging a word-pair as self-generated: 4%) than experimenter-generated misattribution errors (14%) ($p < 0.001$). The most common errors were new misattribution errors (49%), which correspond to a failure to recognize a word pair. For new word pairs that were falsely recognized (new source discrimination errors), participants were much more likely to judge the word pair as experimenter-generated (13%) than self-generated (0.2%) ($z = -4.6$, $p < 0.001$). Thus, these findings agree with previous literature on biases in source memory.

Greater positive psychosis-proneness was related to a significantly higher number of self-generated source discrimination errors (Spearman rank correlation; $\rho = 0.31$, $p < 0.05$), but not other types of source discrimination errors ($\rho = 0.09$, $p = 0.5$). Post hoc comparisons revealed no other error types that were significantly related (even at trend level) to positive psychosis-proneness. When controlling for other type of errors (total errors – self-generated source discrimination errors), the correlation between positive psychosis-proneness and self-generated source discrimination errors remained significant ($\rho = 0.29$, $p < 0.05$). Controlling for IQ did not significantly impact this relationship either (performance IQ: $\rho = 0.31$, $p < 0.05$; verbal IQ: $\rho = 0.29$, $p < 0.05$). Negative psychosis-proneness was not related to any of the error types, at significant or trend levels.

Finally, variations in self-generated source discrimination errors were looked at in relation to FER performance based on the Eyes Test. There was no significant relationship ($\rho = -0.08$, $p = 0.5$) indicating that differences in self-referential source memory do not explain FER ability based on the current measures.

Experiment 4b - Self-referential recognition memory.

Method. This experiment was conducted on TestMyBrain.org, in two separate web-based samples. In the first sample (n = 2006), the brief version of the Schizotypal Personality Questionnaire was used as a measure of psychosis-proneness (Raine & Benishay, 1995). In the second sample (n = 5071), the Revised Social Social Anhedonia Scale was used (Eckblad et al., 1982). A new FER task was also included. In this task, participants were shown three faces expressing either happiness, sadness, anger, fear, surprise, or disgust. Two of the faces expressed the same emotion, and the third face expressed a different emotion. Participants were asked to choose which of the three faces was the “odd one out”, that is the face that expressed a different emotion from the other two (three alternative forced choice: 3AFC). Faces were shown on screen all at once, for 4500ms. There were 50 trials in total.

As a measure of self-referential recognition memory, the paradigm and stimuli from Harvey et al. (2011) were adapted for web-based administration. There were four conditions in the encoding phase, each with 12 trials. Participants were presented with a prompt for 2000ms, followed by a target adjective for another 2000ms. The prompt was one of four questions. (1) Is this word uppercase? (structural condition), (2) Does this word describe you? (self condition), (3) Is this word socially desirable? (social desirability condition), and a final question that was created for this version of the task: (4) Does this word describe your computer? (object condition). For each question the participant was to press 1 for yes, and 0 for no (response options always on screen). The object condition was added to be certain that any memory biases found were not due to deeper encoding arising from processing an adjective with reference to some person/thing that is present in the local environment and could be used as a memory cue

(oneself or one's computer). Within each condition, half the words were presented in uppercase and half in lowercase. Half were positively valenced and half were negatively valenced.

After judging all 48 words, participants were taken to another test that lasted 10 minutes. After this delay participants were tested in an unexpected recognition memory task. Participants were asked to judge whether each of 96 adjectives were old or new. Half of the adjectives were new, and these were matched to the other half in terms of number of letters and syllables. Both lists were also matched in terms of how appropriate each adjective was for describing a computer, using ratings from an in lab sample.

Harvey et al. (2011) used d' prime as an index of sensitivity for recognition memory in each condition. Harvey et al. (2011) used the difference between d' for self vs. social desirability conditions as their index of self-referential memory biases. The d' difference between self and object conditions was also calculated as an additional index of self-referential memory biases. As subtracting a control measure from a measure of interest can introduce confounds owing to variations in the baseline (Wilmer, Garrido, & Herzmann, *in prep*), self-referential memory bias was also computed by regressing d' social or d' object scores out of d' self scores and using the residuals as the dependent measure.

Unfortunately, due to an error in transitioning tests to a new web server, demographic information was lost for these participants. Thus, it is unknown whether any findings or lack of findings might be explained by differences in participant age, sex, or education that would have otherwise been collected.

Results. *Revised Social Anhedonia Scale.* Average d' scores were 1.35 (SD = 0.88) for the self condition, 1.04 (SD = 0.79) for the social desirability condition, 1.91 (SD = 1.43) for the object condition, and 1.4 (SD = 1.1) for the structural condition. The magnitude of the self-

referential memory bias in the sample (self-social desirability) was 0.3 (SD = 0.73). This bias was similar in magnitude to the bias found by Harvey et al. (2011) when comparing these two (self and social desirability) conditions (M = 0.32, SD = 0.47 in Harvey et al., 2011). When using the object condition as a comparison, however, there was no longer a self-referential memory bias (M = -0.57, SD = 1.2).

Social anhedonia scores were related to d' recognition sensitivity measures in the self ($r = -0.042$, $p < 0.01$), social desirability ($r = -0.038$, $p < 0.01$), object ($r = -0.055$, $p < 0.001$), and structural conditions ($r = -0.04$, $p < 0.01$). Based on the measure used by Harvey et al. (2011) (d' self minus d' social desirability for each participant), there was no relationship between social anhedonia scores and self-referential memory biases ($r = -0.009$, $p = 0.66$). When self-referential memory biases were calculated with reference to the object condition (d' self minus d' object), there was a small, but significant association in the opposite direction as predicted ($r = 0.035$, $p < 0.01$). When regression based dependent measures were used, neither relationship was significant (d' self regressing out d' social desirability: $r = -0.006$, $p = 0.66$; d' self regressing out d' object: $r = 0.01$, $p = 0.46$).

In this sample, participants had an average 70% correct (SD = 11%) on the 3AFC FER task. Social anhedonia scores were significantly related to FER scores ($r = -0.15$, $p < 0.0001$). Since no robust relationship was found between measures of self-referential processing and social anhedonia, however, no additional analyses were performed.

Schizotypal personality questionnaire (brief:SPQ-B). Averages across this sample in each condition were very similar to the independent sample that completed the Revised Social Anhedonia Scale. Average d' scores were 1.33 (SD = 0.93) for the self condition, 1.02 (SD = 0.76) for the social desirability condition, 1.9 (SD = 1.46) for the object condition, and 1.36 (SD

= 1.0) for the structural condition. The magnitude of the self-referential memory bias was 0.31 (SD = 0.76) in this sample when comparing self and social desirability conditions, and -0.57 (SD = 1.3) when comparing self and object conditions, similar to the social anhedonia sample.

The SPQ-B includes subscales for positive (cognitive-perceptual distortions), negative (interpersonal difficulties), and disorganized symptoms. There was a slight relationship between SPQ-B total scores and d' self – d' social ($r = -0.047$, $p < 0.05$), in the predicted direction. This relationship was driven by a small but significant relationship between cognitive-perceptual/positive psychosis-proneness characteristics and reduced self-referential memory biases ($r = -0.055$, $p < 0.01$). These correlations were the same when using regression-based measures. No significant relationships were found between the interpersonal or disorganized subscales and self-referential memory biases with either subtraction or regression measures. No significant relationships were found between self-referential memory biases and psychosis-proneness when d' object was used as the comparison measure.

In this sample, participants again had an average 69% correct (SD = 10%) on the 3AFC FER task. FER scores were related to SPQ-B total scores ($r = -0.13$, $p < 0.0001$), as well as scores on each subscale (cognitive-perceptual distortions: $r = -0.12$; interpersonal difficulties: $r = -0.09$; disorganization: $r = -0.10$). FER scores were not related to self-referential memory biases when either the social desirability ($r = 0.03$, $p = 0.16$) condition or the object condition ($r = 0.01$, $p = 0.54$) were used as comparison measures, so no further analyses were conducted.

Discussion. The findings of Harvey et al. (2011) were replicated in terms of the direction and magnitude of a self-referential memory bias (when comparing self judgments with social desirability judgments) across participants. The overall findings of this experiment are difficult to interpret, however, as there was no self-referential memory bias when comparing self

judgments with the other two conditions. In fact, accuracy was highest for adjectives where participants judged whether or not the adjective described their computer.

Relationships with psychosis-proneness were weak and/or inconsistent. A weak relationship was found between a measure of positive psychosis-proneness (SPQ-B cognitive-perceptual subscale) and self-referential memory biases, but this relationship was only found when comparing memory for words judged with respect to oneself with words judged for social desirability. No relationship was found when self-referential memory biases were computed with respect to memory for words judged for how well they described a computer. It is possible that this was due to some problem or confound in this new condition (object) that has not been identified, but these results do not support a relationship between self-referential memory biases and psychosis-proneness.

Experiment #5: Psychosis-proneness and Voice Emotion Recognition

In Experiment #1, a relationship was observed between psychosis-proneness and FER, but it is unclear whether this relationship extends to emotion recognition in other modalities. A similar relationship between psychosis-proneness and voice emotion recognition would imply that this relationship generalizes beyond visual perception of emotion.

Method. To answer this question, a voice emotion recognition task developed by Sauter et al. (2010) was adapted for web-based administration on TestMyBrain.org. In this paradigm, two male and two female British English speakers produced emotionally-inflected neutral content speech (three-digit words) expressing one of ten positive or negative emotions: amusement, anger, contentment, disgust, fear, relief, sadness, sensual pleasure, surprise, and triumph. After hearing a brief audio clip, participants were asked to choose which of the ten

emotion words (all displayed on screen) best described the emotion being expressed. The original experiment included 100 trials, with 10 trials of each emotion type, with an average score of 72% (SD = 8%) based on 23 control participants. 5/10 trials of each emotion were chosen to create a shorter version of this test more suitable for web administration.

As measures of psychosis-proneness, the Revised Social Anhedonia Scale (Eckblad et al., 1982; Mishlove and Chapman, 1985; See Study #2 and #3) and the brief version of the Schizotypal Personality Questionnaire (SPQ-B; Raine, 1991; Raine & Benishay, 1995; See Study #1) were used. Due to technical difficulties, however, this experiment was only conducted using the SPQ-B.

At the beginning of the experiment, an audio clip of a beeping sound was played continuously in order to adjust volume for each participant. Participants were asked to adjust the volume on their computers until the beeping sound was only just audible. This was followed by three practice stimuli, with feedback, and 50 trials of the actual test. All measures were administered over the web on TestMyBrain.org.

Results. Audio presentation over the web presented a wide range of problems evident by very high attrition rates and numerous reports of technical issues. Also, cross browser compatibility was an issue and no clear solution was found that allowed the test to be run in all popular web browsers. When a major update of Firefox's popular web browser created compatibility problems for a significant proportion of users, the experiment was terminated early and without administering the social anhedonia measure in a second sample. Thus, final sample sizes were smaller than expected for this study and the voice emotion recognition task was only administered in conjunction with one measures of psychosis-proneness, the brief version of the Schizotypal Personality Questionnaire.

Based on a sample of 451 participants, mean performance was 63% (SD = 14) suggesting this version was significantly more difficult than the original version --- although this performance mean may have been reduced by technical problems with the test. Preliminary data suggest a small but nonsignificant relationship between voice emotion recognition performance and the SPQ-B interpersonal subscale (negative psychosis-proneness; $r = -0.07$, $p = 0.14$, two-tailed) and the cognitive-perceptual subscale (positive psychosis-proneness; $r = -0.07$, $p = 0.16$), but no relationship with the disorganized symptom subscale ($r = 0.04$, $p = 0.35$) or total SPQ-B scores ($r = -0.04$, $p = 0.34$). Given the reduced mean and higher standard deviation of this sample relative to the original control sample collected by Sauter et al. (2010), technical difficulties likely interfered with the ability to accurately measure voice emotion recognition ability in this experiment.

Discussion. No significant relationship was found between psychosis-proneness and voice emotion recognition, but technical difficulties likely interacted with the results as suggested by the relatively low performance means on this test. Previous comparisons between web and lab using TestMyBrain.org for tests of social perception, including emotion recognition, have revealed comparable means and standard deviations between web and lab samples (Germine et al., *submitted*). Although this difference may arise from a difference in forms, it also suggests problems for these web-based data that make results difficult to interpret.

Discussion and Conclusion

Summary of Findings

In this dissertation, it has been shown that both positive and negative psychosis-like characteristics predict face emotion recognition (FER) abilities, even in otherwise healthy individuals. This relationship was not explained by variations in IQ, visual perception, face processing, body representation, or self-referential processing. Greater psychosis-proneness was also related to reduced neural activity in brain regions thought to underlie normal FER. Altogether, the current evidence indicates that behavioral and neural abnormalities in FER are related to the expression of psychosis-like characteristics in otherwise healthy individuals. This suggests that FER deficits are related to psychosis vulnerability, rather than secondary characteristics of schizophrenia and other psychotic disorders.

Psychosis-proneness and FER: Interpretation of Behavioral Findings

Previous research has produced mixed findings regarding the relationship between FER and psychosis-proneness (Brown & Cohen, 2010). This was addressed in the current set of studies by using very large samples (Experiment #1, #4b, #5) and a range of psychosis-proneness measures (Experiment #1, #3c, #4). A relationship between FER and psychosis-proneness was identified and replicated using four different FER paradigms, five measures of psychometric psychosis-proneness, and multiple control or comparison conditions. These findings indicate that the relationship between FER and psychosis-proneness is highly replicable and generalizes to different measures of FER when sample sizes are adequate and sensitive tests are used.

Another contribution of the current research is addressing whether the relationship between FER and psychosis-proneness can be explained by differences in more general cognitive factors that also vary with psychosis-proneness (Siever et al., 2002). It was found that psychosis-proneness related variations in FER could not be explained by differences in face processing (Experiment #1), IQ (Experiment #3c), flexibility of body representations (Experiment #3b), or differences in self-referential processing (Experiment #4). Across experiments, no single factor was identified that could explain the relationship between FER and psychosis-proneness. Although there are many other possible neurocognitive factors that may underlie FER deficits in psychosis-prone individuals, these findings indicate relative specificity in psychosis-proneness related FER variations. This is in contrast with studies of schizophrenia patients where specific deficits are difficult to isolate against a background of generalized cognitive impairment (Kerr & Neale, 1993).

In the schizophrenia and psychosis-proneness literature, emotion recognition deficits are typically linked with negative symptoms or characteristics (Lincoln et al., 2011). In the studies reported here, both positive and negative psychosis-like characteristics were associated with FER. There was some support, however, for a more robust link between negative psychosis-proneness and FER. Although in experiments #1 and #4 the relationship between positive and negative psychosis-like characteristics and FER was comparable, experiment #3c revealed a stronger relationship between FER and negative psychosis-proneness measures. When controlling for IQ in a smaller sample ($n = 55$), only negative psychosis-proneness still significantly predicted FER ability. It should be noted though that in Experiment #3c, composite measures of psychosis-proneness were used that may have masked symptom heterogeneity. That is, some aspects or dimensions of positive psychosis-proneness (e.g.

perceptual distortions) may be better predictors of FER than others. Nevertheless, these data suggest that FER may be broadly related to a range of psychosis-proneness characteristics and not any single dimension, with the most consistent relationships between FER and negative psychosis-like characteristics.

Psychosis-proneness and FER: Interpretation of Neural Findings

In Experiment #2, neural measures of FER were obtained using functional magnetic resonance imaging (fMRI) in participants that differed in their expression of negative psychosis-proneness, as indexed by social anhedonia. Social anhedonia is a lack of pleasure from social interactions, and is one of the strongest predictors of psychosis development (Kwapil, 1998). In participants with higher levels of social anhedonia / negative psychosis-proneness, reduced responses were observed in *a priori* defined emotion perception brain regions including the anterior medial frontal cortex, right superior temporal gyrus, and somatosensory cortices. These regions have been implicated in previous studies of FER in healthy participants (Adolphs et al., 2000; Adolphs, 2002; Haxby et al., 2000).

The right superior temporal sulcus (and neighboring regions of the right superior temporal gyrus) is thought to be involved in integration of information across modalities, contributing to social perception and processing dynamic social cues including eye gaze (Allison et al., 2000), face emotion (Haxby et al., 2000), and voice emotion (Phillips et al., 1998). Single cell recordings in monkeys have indicated that individual cells in superior temporal regions code particular directions of head orientation and gaze (Allison et al., 2000). Thus, superior temporal cortex seems to contain high-level representations of social stimuli and integrates semantic, spatial, verbal, and perceptual information (Haxby et al., 2000). Psychosis-proneness related

differences in this region may reflect reduced recruitment of these computational processes for FER, and may contribute to reduced FER ability among psychosis-prone individuals.

In Experiment #2, variations in neural activity in the anterior rostral subdivision of the medial frontal cortex (arMFC; Amodio & Frith, 2006) were also observed. Numerous studies have found activity in this region when judging emotional faces as compared to non-emotional faces (Dolan et al., 1996; Kestler-West et al., 1991; Phillips et al., 1998; Wright et al., 2002) and deficits in this region during emotion processing in schizophrenia (Hempel et al., 2003). Social understanding, person perception, and mentalizing also engage arMFC across a range of tasks (Frith & Frith, 2003; Gobbini et al., 2004; Iacoboni et al., 2004; Mitchell, Banaji, & Macrae, 2005; Saxe, Carey, & Kanwisher, 2004).

There is consistent evidence that arMFC is also involved in self-referential processing. For example, Johnson et al. (2002) found that this region was more active when participants were asked to reflect on their own personal characteristics than on information-based statements (e.g. 'I have a quick temper' as opposed to 'You need water to live'). Another study by Macrae et al. (2004) found that not only was arMFC more active when judging self-related words, but activity in arMFC also predicted subsequent memory for those words. Altogether, evidence suggests that the arMFC is involved in processing self-related information, information about other individuals, and information about the relationship between oneself and others.

In Experiment #2, regions of somatosensory and somatosensory-related cortex were also found to be less active during emotion discrimination in psychosis-prone participants. Somatosensory regions have been implicated in aspects of both self processing and social-emotional processing (Adolphs, 2002). Somatosensory cortex is thought to contribute to

representation of the bodily self through touch and contributions to proprioception, as well as to FER (Adolphs et al., 2000).

Neural findings reported in Paper #2 suggest that psychosis-proneness is related to reduced neural activity in emotion processing regions, including regions that have been implicated in processing self-related and social information. In addition to specifying potential neural mechanisms that underlie psychosis-proneness related differences in FER, these findings also suggest other areas of inquiry that may contribute to our understanding of the underlying causes of FER deficits in psychosis-prone individuals.

Psychosis-proneness, Self-representation, and FER

Although differences in neural activity do not demonstrate differences in any particular cognitive process or behavior, they do suggest further areas of investigation. Experiment #2 revealed that psychosis-proneness is related to variations in regions that putatively contain neural substrates for representing self and others, suggesting that differences in self-representation may contribute to differences in FER based on simulation or action-perception theories of social cognition (Brunet-Gouet & Decety, 2006). Previous research supports this possibility, as schizophrenia is associated with deficits in somatosensory processing (Arnfred & Chen, 2004) and self-referential processing (Vinogradov et al., 1997). Moreover, Fisher et al. (2008) found that differences in self-referential processing might contribute to differences in social cognition among schizophrenia patients. Experiments #3 and #4 were designed to investigate the relationship between self-representation and psychosis-proneness, and whether any observed relationship contributes to psychosis-proneness related differences in FER. Experiment #3a-b investigated the relationship between psychosis-proneness, FER, and flexibility of the body

representation. Experiment #4 investigated the relationship between psychosis-proneness, FER, and self-referential processing.

Based on indications of somatosensory and body representation abnormalities in schizophrenia and psychosis-prone individuals (Lenzenweger, Nakayama, Chang, & Hooley, 2003), the rubber hand illusion was used as a way of gaining traction on disturbances of the bodily self that are related to psychosis-proneness (Experiment #3a-b). The rubber hand illusion is an illusion of body ownership where stroking the participant's hand with a paintbrush at the same time as stroking a rubber hand induces the subjective experience of body ownership over the rubber hand in approximately 40% of healthy participants (Botvinick & Cohen, 1998). In this experiment, it was observed that greater psychosis-proneness was related to greater susceptibility to the rubber hand illusion. The relationship was found only for positive psychosis-proneness though, with no relationship between rubber hand illusion susceptibility and negative psychosis-proneness. Contrary to hypothesis, rubber hand illusion susceptibility was related to better FER, not poorer FER as predicted. Thus, although these findings suggest that positive psychosis-like characteristics are linked with susceptibility of body representations to distortion, this susceptibility does not appear to contribute to psychosis-proneness related differences in FER ability.

The relationship between this finding and the finding of differences in somatosensory regions in Experiment #2 cannot be interpreted based on the current data. Experiment #2 used a measure of negative psychosis-proneness and Experiment #3a-b only identified a relationship between bodily self-representation and positive psychosis-proneness. The lack of relationship between negative psychosis-proneness (including social anhedonia) and the rubber hand illusion

suggests that the somatosensory differences observed in Experiment #2 are probably not related to the differences in body representations observed in Experiment #3.

In Experiment #4, the relationship between psychosis-proneness and self-referential processing was investigated. One previous study has reported that self-referential source memory deficits may contribute to social cognition deficits (including FER) in schizophrenia (Fisher et al., 2008). Experiment #4 focused on the relationship between self-referential processing and FER in psychosis-proneness. Two forms of self-referential processing were tested: (1) self-referential source memory, or memory for the source of a word pair as generated by oneself, the experimenter, or a new word pair (Vinogradov et al., 1997; Fisher et al., 2008); and (2) self-referential recognition memory, or memory for information that has been processed with reference to oneself (Harvey et al., 2011). There was no consistent relationship between self-referential recognition memory and psychosis-proneness. There was, however, a significant relationship between self-referential source memory biases and positive psychosis-proneness. Greater positive psychosis-proneness was associated with a greater tendency to judge a self-generated word pair as being experimenter-generated or new. This replicates previous findings in the literature with schizophrenia patient samples (Vinogradov et al., 1997). These findings did not, however, replicate the finding of Fisher et al. (2008) showing a relationship between self-referential source memory and FER, as FER was unrelated to self-referential source memory in the current sample.

As before, the relationship between positive psychosis-proneness, self-referential processing, and neural findings in Experiment #2 are difficult to interpret. Although neural responses in medial prefrontal cortex are consistently linked with self-referential processing (Amodio & Frith, 2006), no relationship was found between negative psychosis-proneness and

biases in self-referential source memory. Neural findings in Experiment #2 were based on negative psychosis-proneness measures only.

Experiments #3 and #4 indicate that aspects of self-representation do vary with psychosis-proneness, but are more closely linked with positive psychosis-like characteristics and may not contribute to differences in FER.

Psychosis-proneness and Voice Emotion Recognition

Based on the finding that psychosis-proneness is related to differences in multimodal cortical regions (arMFC and right superior temporal gyrus), the next question was whether psychosis-proneness might be related to differences in emotion recognition in other modalities. Deficits in voice emotion recognition have been observed in schizophrenia patients (Edwards, Jackson, & Pattison, 2002). Thus, Experiment #5 looked at the relationship between voice emotion recognition and psychosis-proneness.

Technical difficulties made results from Experiment 5 difficult to interpret. A weak, nonsignificant relationship was observed between psychosis-proneness and voice emotion recognition. Further experiments would be needed to clarify whether there is a relationship between psychosis-proneness and voice emotion recognition, or whether psychosis-proneness related deficits in emotion recognition are limited to FER.

The Relationship between Self-representation and Positive Symptoms

The current findings are consistent with a relationship between abnormalities in self-representation and psychosis vulnerability, but only based on positive psychosis-like characteristics.

Positive symptoms include distortions of self, such as attributing one's own actions or thoughts to an external agent (Frith, 1992) and the sense of not fully inhabiting one's body, experiences, thoughts, and actions (Sass & Parnas, 2003). Evidence from schizophrenia research indicates that source monitoring deficits (e.g. self-referential source monitoring) are more closely linked with positive symptoms (Sterling, Helliwell, Ndlovu, 2001) and perhaps even inversely related with negative symptoms (Brebion et al., 2002). Positive symptoms have been specifically linked with a failure to recognize one's own actions as one's own (Franck et al., 2001) and discriminating self touch from other touch (Blakemore, Smith, Steel, Johnstone, & Frith, 2000).

The specificity of the relationship between self-representation and positive symptoms and/or positive psychosis-proneness calls into question the theoretical model that psychosis-related deficits in self processing contribute to FER. Prominent theories of schizophrenia development posit that self-representation and theory of mind (other representation) arise from the same basic abnormality. For example, Frith (1992) suggested that both impairments arise from failure of metarepresentation. If both theory of mind deficits and deficits in self-representation are related to the same underlying abnormalities, they should show a similar pattern of association with psychosis symptoms or dimensions of psychosis-proneness. As noted above and suggested by the findings of Experiments #3 and #4, source monitoring and self-representation deficits are more closely linked with positive symptoms whereas theory of mind deficits (Pickup & Frith, 2001; Langdon et al., 2001; Garety & Freeman, 1999) and FER deficits (Mandal, Jain, Haque-Nizamie, Weiss, & Schneider, 1999; Sergi et al., 2007) are more closely linked with negative symptoms. Although self and other representations are thought to arise from shared mechanisms in healthy individuals (Carruthers, 1996; Frith, 1994; Gopnik,

1993) deficits in representing one's own mind and representing other minds may arise from dissociable mechanisms in psychosis (Lysaker et al., 2005; Nichols & Stich, 2002). The current findings support a relationship between FER and both positive and negative symptom dimensions. However, the current findings also are consistent with dissociable mechanisms underlying differences in self-representation and FER in psychosis-proneness. Further research would be needed to resolve these discrepancies and advance our understanding of how different dimensions of self-representation are related to one another and to social-emotional processing in schizophrenia and in psychosis-prone individuals.

Limitations

The studies included in the current dissertation examined variations in psychosis-proneness and attempted to link these variations with differences in social-emotional processing. This approach was necessarily correlational, and relied on cross-sectional samples. Based on this approach, it is not possible to ascertain whether these relationships are causal or the direction of causality. That is, it is not clear whether FER deficits contribute to psychosis-like characteristics, whether psychosis-like characteristics impact FER, or whether some third variable influences FER and the expression of psychosis-like characteristics with no causal relationship between the two. Studies that could begin to address questions of causality include longitudinal studies examining the relationship between FER ability and the emergence of psychosis-like characteristics over time and intervention studies targeting FER ability to see if improvements in FER lead to improvements in symptoms or reduced psychometric psychosis-proneness.

Another question is how specific FER deficits are to psychosis and psychosis-proneness, or whether they represent a general neurocognitive impairment that is found in any disorder that impacts social functioning. Some evidence suggests that social anhedonia, which has been treated here as a psychosis vulnerability marker, also occurs in disorders such as major depressive disorder (Blanchard, Horan, & Brown, 2001). One critical difference is that social anhedonia in major depressive disorder is episodic as opposed to trait-like, whereas in schizophrenia, anhedonia is thought to be a stable characteristic (Blanchard et al., 2001). Still, investigations of social anhedonia tend to focus on psychotic disorders and psychosis vulnerability so evidence about the relationship between social anhedonia and other disorders is limited.

Even if we assume social anhedonia is a similar feature and risk factor for psychotic disorders and mood disorders, this does not necessarily present a challenge to the importance of social-emotional deficits (including social anhedonia) in psychosis development. There is an increasing appreciation that many disorders are not as etiologically distinct as would be suggested based on symptom-based classification. Evidence for boundaries between diagnostic categories and boundaries with normality may be artifacts of a diagnostic system that emphasizes reliability over validity, as well as research and funding practices that tend to reify these original diagnoses (Hyman, 2010). Thus, differences between disorders may be more apparent than real, and symptoms dimensions that cut across diverse categories may contain meaningful information about underlying causes of mental disorders (Insel et al., 2010). Indeed, severe depression can be accompanied by psychotic symptoms and schizophrenia spectrum disorders often include significant mood symptoms (APA, 2000). The fact that these two phenomena are given different classifications does not mean that they do not arise from many common environmental,

genetic, neural, or psychological risk factors (Bora, Yucel, & Pantelis, 2009) including a tendency towards social-emotional withdrawal. In fact, there is significant inconsistency in these diagnoses over time (Ruggero et al., 2011) with high rates of conversion from primary mood disorders to primary psychotic disorders.

Concluding Thoughts

One can view the development of psychosis as a “perfect storm” where cognitive-perceptual abnormalities, poor social-emotional functioning, and deficits in neurocognition contribute to the break from reality that marks the transition to psychotic illness (Sergi et al., 2007). In this view, social-emotional and cognitive/perceptual abnormalities (e.g. deficits in source monitoring) can contribute to psychosis development in different ways. The primary deficit that differentiates psychosis from other disorders is a fundamental disconnect between beliefs and reality, but this is accompanied by an equally profound and important disconnect between oneself and the social world. FER provides a crucial feedback mechanism for developing social affiliations and correctly interpreting social signals and it may be for this reason that FER significantly predicts social functioning in schizophrenia (Hooker & Park, 2002). Deficits in FER and other social-emotional processes may lead to impoverished social feedback, allowing odd beliefs to develop and proliferate unchallenged in individuals with a predisposition to abnormal associations (Meehl, 1962/1990), aberrant salience attributions (Kapur, 2003), or source monitoring deficits (Frith, 1992). Over time, social-emotional processing deficits may contribute to social-emotion withdrawal, social anhedonia, and affective flattening as well as reducing stress resilience.

Given the complexity and diversity of plausible models linking emotion recognition to the development of psychosis, it is difficult to say based on current evidence how FER is linked with psychotic disorders. In this dissertation, I have reported a consistent relationship between FER and psychosis-proneness as well as results from experiments linking positive psychosis-proneness and aspects of self-representation. Unfortunately, self-representation is a broad concept in the psychology literature that is often inconsistently operationalized. It may be that certain dimensions of self-representation are related to negative psychosis-proneness and to FER ability in psychosis-proneness, but simply not the dimensions studied here. Nevertheless, the consistent link between FER and psychosis-proneness provides a challenge to theories of schizophrenia and psychosis development that only account for positive symptom characteristics at the exclusion of perhaps equally important social-emotional impairments.

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