



Emotion processing and theory of mind in schizophrenia patients and their unaffected first-degree relatives

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ABSTRACT

Previous studies have suggested that social cognition is affected in individuals with schizophrenia. The purpose of this study was to explore to what extent social cognition deficits are shared by unaffected first-degree relatives, and the nature of the relationship between performance in different paradigms of social cognition. 20 Schizophrenia patients (7 females, 31 ± 10 years), 20 healthy age- and gender-matched individuals, 20 unaffected first-degree relatives of the schizophrenia patients (11 females, 50 ± 20 years), and 20 healthy individuals matched for age and gender were recruited. Patients showed deficits in the detection of social Faux Pas (0.80 ± 0.17 vs. controls: 0.94 ± 0.09 , $p = 0.025$) and the correct identification of Theory of Mind stories (0.71 ± 0.13 vs. controls: 0.82 ± 0.12 , $p = 0.038$). Relatives performed poorly in the Faces Test (0.83 ± 0.14 vs. controls: 0.9 ± 0.08 , $p = 0.048$), the Reading the Mind in the Eyes Test (0.59 ± 0.17 vs. controls: 0.71 ± 0.14 , $p = 0.046$) and the detection of social Faux Pas (0.8 ± 0.2 vs. controls: 0.93 ± 0.09 , $p = 0.024$). Abnormalities were independent of age, years of education, and general cognitive performance in patients and their relatives. Performance in an Emotion Processing task (Faces Test) was correlated with performance in theory of mind tests in healthy individuals and relatives of patients with schizophrenia only. These results suggest that schizophrenia patients and their unaffected first-degree relatives display similar but nonidentical patterns of social cognition processing.

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1. Introduction

Schizophrenia is characterized by psychotic symptoms such as formal thought disorder, hallucinations, and delusions (American Psychiatric Association, 1994). Although the essential feature of schizophrenia is disruption of the interpersonal world, impaired social functioning frequently precedes the onset of overt psychosis resulting in severe functional loss in different social settings (Kee, Horan, Mintz, & Green, 2004; Penn, Corrigan, Bentall, Racenstein, & Newman, 1997). This has been recognized since the inception of the concept of schizophrenia, thus, in Kraepelin's (1919) words:

"Frequently the patients have already shut themselves off from their family and surroundings long before the appearance of the more striking symptoms (. . .), which is connected with a suppression driven to the limit of the possible of all natural emotions."

Over the past decades, most neuropsychiatric studies in schizophrenia have largely focused on disorders of cognitive processes such as executive function, attention, or working memory (Cirillo & Seidman, 2003; Evans, Chua, McKeena, & Wilson, 1997) which may affect patients' psychosocial skills. Only more recently have researchers shifted their attention towards social cognition in schizophrenia (Brüne, 2005; Irani et al., 2006; Penn et al., 1997; Pinkham, Penn, Perkins, & Lieberman, 2003). Social cognition refers to the mental operations underlying social interactions, which include processes involved in perceiving, interpreting, and generating responses to the intentions and emotions of other persons (Adolphs, 2003; Brothers, 1990; Fiske & Taylor, 1991; Kunda, 1999; Ostrom, 1984).

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Two dimensions of social cognition have received particular attention in the literature, namely Emotion Processing (EP) and Theory of Mind (ToM) (Green, Olivier, Crawley, Penn, & Silverstein, 2005; Penn, Addington, & Pinkham, 2006). EP refers to aspects of perceiving and using emotion, and the empirical knowledge of this aspect of social cognition is usually based in studies of affect perception in faces and eyes (Adolphs, Damasio, Tranel, & Damasio, 1996; Green, Olivier, Crawley, Penn, & Silverstein, 2005). Whereas sometimes it has been considered an EP task, akin to traditional facial emotional recognition paradigms (Fertuck et al., 2009), the Reading the Mind in the Eyes is usually considered a ToM test in that it probes the inference of mental states of others. ToM can be defined as the understanding that others also have minds, with different and separate beliefs, desires, mental states, and intentions from our own (Green et al., 2005; Premack & Woodruff, 1978).

The relationship between EP and ToM has recently been put into question, with some data indicating that these are closely interrelated phenomena (Ochner, 2008). Assessing other persons' intentions necessarily involves the appraisal of their emotional status as well as one's own emotional response to them (Ochner, 2008). This is most evident in tests involving recognition of facial expressions, which are often used in the measurement of either variable (Ochner, 2008).

Initially developed for application in the field of autism (Saxe, Carey, & Kanwisher, 2004), measures of ToM and EP have been extended to schizophrenia, in part because of the similarity between aspects of social dysfunction in autism and schizophrenia (Brüne, 2005; Corcoran, 2001; Frith, 1992). In fact, Frith was the first to suggest that many symptoms associated with schizophrenia could be explained in terms of a compromised ToM (Frith, 1992). Preliminary data suggest that EP and ToM deficits are present in unaffected first-degree relatives of patients with schizophrenia (Aleman, Swart & van Rijn, 2008; Irani et al., 2006) and this may indicate that the performance in ToM tasks is genetically influenced, possibly constituting an endophenotype (Corcoran, 2001; Gottesman & Gould, 2003). More recently, Gur and colleagues have estimated the heritability of emotion processing deficits using a simple, short test of this function (Gur et al., 2007), and attempts have been made to map this important dimension of social cognition to specific chromosomal loci (Almasy et al., 2008; Hill et al., 2008). However, there is a paucity of studies on familial aggregation of social cognitive deficits characteristic of schizophrenia. The few studies that investigate Theory of Mind in unaffected first-degree relatives often offer conflicting results (Janssen, Krabbendam, Jolles, & van Os, 2003; Marjoram et al., 2006). Whereas one study found an association between performance in Theory of Mind tests and genetic liability to schizophrenia (Janssen et al., 2003), another study suggested that Theory of Mind abnormalities were psychotic state-dependent, and not due to genetic traits of schizophrenia (Marjoram et al., 2006).

With regard to EP deficits in unaffected relatives of schizophrenic patients, some studies suggest that this population has similar, although less severe abnormalities than those found in patients (Phillips & Seidman, 2008). However, this has not been a consistent finding. Instead EP deficits may be difficult to separate from general cognitive impairments in patients and their unaffected relatives (Pomarol-Clotet et al., 2009).

Regardless of differences between reports studying individuals affected by schizophrenia and those genetically loaded for it, there are indications that ToM involves an amygdala centred processing system while EP involves the medial prefrontal cortex and superior temporal sulcus (Frith & Frith, 1999; Frith & Frith, 2001), but it is not clear if alterations in these social cognitive abilities have a shared pathophysiology or heritability. Preliminary data indicate that patients with schizophrenia display different correlation patterns for ToM and EP from healthy controls (Brüne, 2005), but to

our knowledge this relationship has not been tested in unaffected relatives of schizophrenia patients.

We tested the hypothesis that ToM and EP performance are familial traits; therefore unaffected first-degree relatives of schizophrenia patients might display similar, but less intense abnormalities than patients in ToM and EP performance. Secondly, we sought to determine whether performance in both these dimensions of social cognition showed the same relationship in schizophrenia patients, unaffected first-degree relatives and healthy individuals.

2. Methods

This was a cross-sectional study on the relationship between measures of social cognition in patients with schizophrenia, their unaffected first-degree relatives and healthy control groups.

2.1. Subjects

Two consultant psychiatrists (SMG, EYC) and a psychologist (DDA) assessed all participants, who were seen at the Cognitive Neurology Section and the Psychiatry Department at FLENI Hospital, Buenos Aires, between July 1, 2007 and September 30, 2008. All participants gave written informed consent as approved by the local bioethics committee, and have therefore been performed in accordance with the ethical standards set by the 1964 Declaration of Helsinki.

2.2. Patients (P)

Psychiatry outpatients were invited to participate in the study if they (a) received a DSM-IV-TR diagnosis of schizophrenia (any subtype), confirmed with a Composite International Diagnostic Interview (Robins, Wing, Wittchen, & Helzer, 1988) administered by a consultant psychiatrist (EYC), (b) were aged 18–75 years, and (c) had been on the same medications for at least two weeks. Exclusion criteria were (a) misuse or addiction to illegal substances in the previous 6 months, (b) active symptoms having warranted antipsychotic dose adjustment or admission to the hospital, day hospital, or intensive outpatient treatment, in the preceding 2 weeks or (c) a history of mental retardation. Current symptom severity was assessed with the Positive and Negative Syndrome Scale (PANSS; Kay, Fiszbein, & Opler, 1987). Twenty patients with schizophrenia (7 females, age 30.9 ± 10 years, range 19–55 years) were recruited for this study. Two patients were siblings.

2.3. Relatives (R)

First-degree biological relatives of the recruited patients were included from 16 families and consisted of the parents (six mothers, four fathers) and the siblings (five sisters, five brothers), aged 18–75 years, of schizophrenia patients as defined above (age 50.1 ± 19.6 years, range 19–75 years). Exclusion criteria included (a) the lifetime presence of any DSM-IV-TR Axis I psychotic disorder diagnosis as detected by a psychiatric interview with consultant psychiatrist (EYC) and (b) treatment with antipsychotics, antidepressants, or mood stabilizers.

2.4. Controls

Healthy volunteers were recruited from local community attendees to free lectures related to health promotion as advertised in posters and the media, from staff, and colleagues in other institutions. Exclusion criteria included (a) the lifetime presence of any DSM-IV-TR Axis I anxiety, mood, or psychotic disorder diagnosis as detected by a psychiatric interview with a consultant psychiatrist and (b) a medication history of antidepressants, antipsychotics, or mood stabilizers. A schizophrenia patient control group (PC; $n = 20$, 7 females, age 28.2 ± 5.6 years, range 20–47 years) and a first degree relatives control group (RC; $n = 20$, 11 females, age 44.2 ± 17 years, range 25–69 years) were recruited to the study.

2.5. Procedures

2.5.1. Cognitive Screening Tests

All participants were screened for general cognitive impairments with the Mini Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975), Addenbrooke's Cognitive Examination (ACE; Mathuranath, Nestor, Berrios, Rakowicz, & Hodges, 2000), Frontal Assessment Battery (FAB; Dubois, Slachevsk, Litvan, & Pillon, 2000), and Facial Recognition Test (FRT; Benton & Van Allen, 1968). The latter test was used to control for possible impairments in face perception which could interfere with recognition of facial expressions.

2.5.2. Social Cognition Tests

The Spanish version of the Faces Test, Reading the Mind in the Eyes Test, Faux Pas Test and ToM Stories Test as provided by their authors were used.

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