



# Performance in multiple domains of social cognition in parents of patients with schizophrenia



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## ABSTRACT

Social cognition refers to a set of cognitive abilities that allow us to perceive and interpret social stimuli. Social cognition is affected in schizophrenia and impairments have also been documented in unaffected relatives, suggesting that social cognition may be related to a genetic vulnerability to the disease. This study aims to investigate potential impairments in four domains of social cognition (mentalizing, emotion recognition, social knowledge and empathy) in the same group of relatives in order to gather a more complete picture of social cognition difficulties in this population. The *Batterie Intégrée de Cognition Sociale* (BICS) (mentalizing, emotion recognition, and social knowledge) and the *Interpersonal Reactivity Index* (IRI) (empathy) were administered to 31 parents of patients with a psychotic disorder and 38 healthy controls. Parents of patients performed significantly worse than controls on the mentalizing test but significantly better on the social knowledge test. No significant between-group differences were observed for emotion recognition and empathy. This study is the first to evaluate four social cognition domains in this population. The results precise which social cognition processes may be impaired or preserved in unaffected relatives of patients and lead us to propose an hypothesis about a mechanism that could underlie the mentalizing difficulties observed in this population.

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## 1. Introduction

Schizophrenia is a multi-determined psychotic illness characterized by symptoms that can fluctuate widely over time (e.g., hallucinations, delusions, disorganization; APA, 2013), as well as more stable characteristics including cognitive deficits and alterations in brain structure (Nopoulos et al., 1994; Shenton et al., 2001). These more stable features have been the focus of many recent studies about psychosis as they may be trait-related and thus linked to a genetic vulnerability to develop schizophrenia (Braff et al., 2007). Gottesman and Gould (2003) described these trait-related characteristics, or endophenotypes, as measurable intermediate characteristics between the full phenotype and the genotype. These characteristics (e.g., cognitive, neuroanatomical, neurophysiological, or biochemical abnormalities) are thought to be more directly related to the specific genes implicated in schizophrenia than the syndrome itself (Gottesman and Gould,

2003) and represent major targets for prevention and the early treatment of the illness.

Among these stable schizophrenia-related deficits, social cognition difficulties could be an important characteristic to examine. Social cognition refers to a large range of skills that allow people to perceive and interpret social stimuli and that guide daily social interactions (Frith and Frith, 2007; Green et al., 2008; Achim et al., 2012b). Many constructs have been associated with social cognition, though certain inter-related domains have emerged as more central in schizophrenia such as mentalizing, social perception/knowledge, emotion recognition, attributional bias and likely higher order aspects of emotion processing such as empathy (Green et al., 2008; Lee et al., 2011; Savla et al., 2013; Pinkham et al., 2014). *Mentalizing* (also known as Theory of Mind) refers to the capacity to infer the mental states (e.g., beliefs, intentions, desires, and emotions) of others typically based on the integration of complementary information about the person and the context in which the person evolves (Frith and Frith, 2006; Achim et al., 2013). *Social perception/knowledge* can be defined as the body of knowledge one holds in memory about theoretical social situations (e.g., the knowledge of social contexts, social rules, social goals or of what is expected in different social

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situations). *Emotion recognition* refers to the ability to identify affective states from social cues such as facial expressions or prosody. *Empathy* involves the ability to share and respond to others' emotional states (Decety and Jackson, 2004). *Attributional bias* refers to the way in which people explain the cause of social events (Pinkham et al., 2014). The inter-dependent nature of these processes implies that deficits in lower-level aspects of social cognition (emotion recognition and social perception/knowledge) can impact a person's ability to mentalize or to empathize with others (Frith and Frith, 2006; Achim et al., 2012b).

Social cognition impairments have been consistently observed in schizophrenia, both in chronic and recent-onset patients (Edwards et al., 2002; Sprong et al., 2007; Achim et al., 2012b). These impairments are associated with poor social functioning (Fett et al., 2011) and have been shown to mediate the relationship between non-social cognitive deficits and functioning (Brekke et al., 2005). In addition, impairments in social cognition were also observed in remitted patients, suggesting that these impairments are stable during the course of the illness (Bora et al., 2009a; Kohler et al., 2010). The only aspect of social cognition that has not revealed consistent deficits across groups of patients is attributional bias (Savla et al., 2013) and this type of bias seems linked with specific symptoms of the illness rather than the illness itself (Langdon et al., 2013).

Social cognition has also been studied in unaffected first-degree relatives of schizophrenia patients (Irani et al., 2006; Janssen et al., 2003; de Achaval et al., 2010; Montag et al., 2012). In order to correspond to an endophenotype of the illness, deficits observed in patients also have to be observed in relatives, though in a milder form (Gottesman and Gould, 2003), as patients' relatives share part of the genes of the patients even if they are not affected by the illness. Some studies looking for social cognition endophenotypes have observed lower performance in unaffected relatives, compared to control participants, in mentalizing (Mazza et al., 2008; Anselmetti et al., 2009; Riveros et al., 2010; Huepe et al., 2012) and in emotion perception (Bediou et al., 2007; Alfimova et al., 2009; Erol et al., 2010), while others found no significant social cognition impairments in this population (Kelemen et al., 2004; Rasetti et al., 2009; Meijer et al., 2012).

We reviewed and summarized the literature on social cognition abilities of unaffected relatives in a recent meta-analysis. This work revealed mean impairments of moderate effect sizes for both mentalizing ( $d = -0.48$ ) and emotion recognition ( $d = -0.41$ ; Lavoie et al., 2013). Only two studies have targeted social perception/knowledge in relatives of schizophrenia patients. One showed a significant group difference for a task requiring to assess expressions and link them with a social context (Toomey et al., 1999) while the other observed no significant group difference for a task requiring to make trustworthiness judgments (Baas et al., 2007). Only one study has investigated self-reported empathy in this population and no significant difference between unaffected relatives and controls was observed (Montag et al., 2012). In accordance with a previous review (Bora et al., 2009b), the results from our meta-analysis suggested that deficits in at least some domains of social cognition may represent a trait of the illness and may potentially be related to a genetic vulnerability to develop the pathology (Lavoie et al., 2013).

The Consortium on the Genetics of Schizophrenia (COGS), a major initiative addressing neurocognitive endophenotype of schizophrenia, has already considered social cognition among other cognitive measures of interest but have so far focused only on emotion recognition (Gur et al., 2007; Greenwood et al., 2012). Other aspects of social cognition could also represent valuable endophenotypes of schizophrenia, but have received less attention until recently. Studies with healthy relatives of schizophrenia patients have limited their assessments to one or two domains of social cognition (see Lavoie et al. (2013) for a review), often including emotion recognition and more recently mentalizing.

Other aspects of social cognition have received much less attention, making it hard to see a global portrait of social cognitive deficits in this population. Identifying the full range of social cognition processes that are specifically impaired and preserved in healthy relatives of schizophrenia patients represents an important step towards advancing the knowledge of the pathogenesis of schizophrenia.

The aim of this study is thus to investigate the social cognition abilities known to be impaired in schizophrenia in a group of unaffected parents of patients with schizophrenia, including performance on mentalizing, emotion recognition, social perception/knowledge and empathy. In order to enlarge the body of evidence regarding how the different social cognition domains can be related to a genetic vulnerability associated with the illness, this study aimed to specify which of these social cognition processes are impaired or preserved in first-degree relatives of patients with schizophrenia and to establish relations between these aspects within the same population.

## 2. Method

### 2.1. Participants

Thirty-one (31) unaffected parents (mean age of  $56.10 \pm 7.27$  years, nine men) of patients with a non-affective psychotic disorder were recruited through the *Clinique Notre-Dame des Victoires*, a clinic specialized in recent-onset psychosis in Québec City, Canada. Only parents of patients were selected among other first-degree relatives in order to have a more homogeneous group in terms of age. Parents were either related to patients with a diagnosis of schizophrenia ( $n=20$ ), schizoaffective disorder ( $n=4$ ), psychotic disorder not otherwise specified, ( $n=3$ ) or delusional disorder ( $n=4$ ).

Thirty-eight (38) healthy controls (mean age of  $54.55 \pm 6.81$  years, 11 men) were also recruited through advertisements in local media and public places. Healthy controls were excluded if they had 1) a psychiatric illness, 2) a family member with a psychotic disorder (e.g., schizophrenia, schizoaffective disorder or bipolar disorder), or 3) were taking a psychoactive medication. Socio-economic status was assessed using the Hollingshead two-factor index of social position (Miller, 1991).

Participants were excluded if presenting a neurological disorder or an IQ under 70. IQ was estimated from two subscales of the Wechsler Adult Intelligence Scale III (WAIS-III) (Block design and Vocabulary; Ringe et al., 2002). All participants gave informed consent after study procedures were explained.

### 2.2. Tasks

#### 2.2.1. Social cognition assessment

Social cognition was evaluated with the *Batterie Intégrée de Cognition Sociale* (BICS) (Achim et al., 2012b) and with a French version of the self-reported empathy questionnaire, the Interpersonal Reactivity Index (IRI; Davis, 1983). The BICS is composed of three main measures of social cognition evaluating respectively mentalizing (the *Combined Stories test*), social perception/knowledge (the *Social Knowledge test*) and emotion recognition (the *Emotion Recognition test*).

- 1) The *Combined Stories test*. This task is a verbal mentalizing task in which the participants had to read aloud short stories and then answer one or two questions about the mental states of the story characters (e.g., emotions, beliefs, and intentions). Twenty mentalizing stories were presented and each subsequent question was scored 0, 1, or 2 points using a correction grid that takes into account the accuracy and complexity of the answer (e.g., 1 point is given for an answer that is too concrete; 0 point for an incorrect answer). Six of the stories were followed by two questions, for a total of 52 points for the mentalizing stories. The *Combined Stories test* also includes six non-social reasoning stories, constructed similarly to the mentalizing stories but that require non-social reasoning rather than mental states attributions. Questions were also scored 0, 1 or 2 points for a total of 12 points. Each story (mentalizing and non-social reasoning) had a reading control question, scored 0 or 1, in order to confirm that the participant understood the story.
- 2) The *Social Knowledge test*. This task, developed by Achim et al. (2012b), involves presenting a series of situations in which people can find themselves (e.g., "Someone who is chased by a huge dog"). For each of these contexts, the participants were instructed to state the feeling or reaction that would be most common in such situations. No specific character is presented and no action or verbalization is being produced, unlike mentalizing tasks in which mental states are inferred based on what a character is expressing or doing in

an explicit context (Achim et al., 2013). In this task, participants were instructed not to refer to specific people or to themselves, but to focus on how people most typically feel in such situations. Fourteen (14) situations were presented and each answer was scored 0 or 1 point for a total of 14 points.

- 3) The *Emotion Recognition test*. Fourteen (14) printed pictures showing facial affect stimuli from Ekman and Friesen (1976) were presented sequentially. The participants had to name aloud among seven labels (happiness, anger, fear, surprise, sadness, disgust, and neutral), which label describes the emotional state expressed in the picture. The answer to each stimulus was scored 0 or 1 point for a total of 14 points.
- 4) The *Interpersonal Reactivity Index (IRI)*. Empathy was assessed with the *Interpersonal Reactivity Index (IRI)*, a self-report questionnaire developed by Davis (1983). The IRI is composed of four scales that can be organized into two components of empathy: a cognitive component (*Perspective Taking* scale and *Fantasy* scale) and an affective component (*Empathic Concern* scale and *Personal Distress* scale; Shamay-Tsoory et al., 2004). Each IRI scale includes seven items and participants had to indicate on a 5-point scale to what extent each statement describes them.

### 2.3. Analysis

Demographic data were first compared between groups, using *t*-tests for age and IQ, Chi-squared test for gender and Mann–Whitney test for socio-economic categories. The normality of the distributions was assessed in each group and for each of our social cognition measures. Group differences on the social cognition measures were assessed by means of bilateral *t*-tests that were performed separately for each measure from the BICS and for each scale of the empathy questionnaire. Effect sizes *d* were also computed to highlight the magnitude of group differences. For measures in which significant group differences were found, ANCOVAs were repeated using IQ as a covariable. In addition, within each group, Pearson correlations (*r*) were performed between each of the social cognition measures and the two cognitive measures (IQ and non-social reasoning).

### 3. Results

The groups were well matched with respect to age ( $t=0.901$ ,  $d.f.=67$ ,  $P=0.367$ ), socio-economic status ( $P=0.664$ ) and gender ( $P=0.601$ ) (see Table 1 for demographic data). Unaffected relatives, however, had a significantly lower estimated IQ than healthy controls ( $t=-2.231$ ,  $d.f.=66$ ,  $P=0.029$ ).

As shown in Table 1, significant between-group differences were observed on the social cognition measures such that relatives had a lower performance than the healthy controls on the mentalizing items of the Combined Stories Test ( $t=-2.476$ ,  $d.f.=67$ ,  $P=0.016$ ,  $d=-0.64$ ) but a higher performance on the Social Knowledge test ( $t=2.455$ ,  $d.f.=67$ ,  $P=0.017$ ,  $d=0.60$ ). In contrast, no significant between groups differences were observed on the Emotion Recognition test ( $t=-1.223$ ,  $d.f.=67$ ,  $P=0.225$ ,  $d=-0.30$ ) or on any of the four scales of the IRI (all  $P=0.274$ , see Table 1 for all statistics and effect sizes). A lower performance in relatives compared to controls was also observed for the

non-social reasoning items of the Combined Stories Test ( $t=-4.786$ ,  $d.f.=67$ ,  $P<0.001$ ,  $d=-1.17$ ). The group difference observed on the mentalizing items of the Combined Stories Test, on the Social Knowledge test and on the non-social reasoning items of the Combined Stories Test all remained significant after controlling for the effect of IQ (mentalizing items,  $F=74.923$ ,  $d.f.=2$ ,  $65$ ,  $P=0.025$ ; Social Knowledge test,  $F=23.579$ ,  $d.f.=2$ ,  $65$ ,  $P=0.006$ ; non-social reasoning items,  $F=18.934$ ,  $d.f.=2$ ,  $65$ ,  $P<0.001$ ).

Correlations performed between each measures of social cognitive and non-social cognitive performance are reported in Table 2. Notably, a significant correlation was observed between mentalizing and social knowledge in the relatives group ( $r=0.463$ ,  $P=0.009$ ) while the same correlation was less pronounced and did not reach significance in the healthy controls group ( $r=0.250$ ,  $P=0.130$ ). In contrast, a significant correlation was observed between mentalizing and non-social reasoning in the healthy controls group ( $r=0.354$ ,  $P=0.029$ ) while no evidence of such relationship could be observed in the relatives group ( $r=0.035$ ,  $P=0.852$ ). No significant correlation was observed between IQ and any of the social cognition measures in either the relatives or the controls group.

### 4. Discussion

This study investigated four important aspects of social cognition in parents of patients with schizophrenia. Our aim was to identify which domains of social cognition are affected or preserved in this population within the same participants in order to highlight potential endophenotypes of schizophrenia. We observed mentalizing impairments in the parents of patients compared to controls but no significant group differences in emotion recognition or in cognitive or affective self-reported empathy. Surprisingly, we also found that parents of patients performed better than control participants on the social knowledge test, which challenges the idea that relatives of schizophrenia patients present deficits across all aspects of social cognition.

#### 4.1. Current results versus previous meta-analysis/literature

This study allowed us to identify a larger effect size for the mentalizing impairments in parents of patients ( $d=-0.64$ ) than the mean effect size observed in our recent meta-analysis ( $d=-0.48$ ; Lavoie et al., 2013). However, our meta-analysis had demonstrated more important impairments for first-degree

**Table 1**  
Demographic information and descriptive data of the BICS and the self-reported empathy questionnaire.

	N (relatives/controls)	Relatives mean (S.D.)	Controls mean (S.D.)	<i>t</i>	<i>P</i>	<i>d</i>
Demographic information						
Age	31/38	56.10 (7.27)	54.55 (6.81)	0.90	0.367	–
% Male	31/38	29%	29%	–	–	–
SES	31/38	3.39 (1.09)	3.50 (1.00)	–	–	–
IQ	31/38	96.71 (10.10)	102.59 (11.41)	–2.23	0.029	–
BICS						
Mentalizing	31/38	42.68 (3.64)	45.03 (4.05)	–2.48	0.016	–0.64
Social knowledge	31/38	10.68 (1.49)	9.66 (1.88)	2.46	0.017	0.60
Emotion recognition	31/38	11.42 (1.43)	11.84 (1.42)	–1.22	0.225	–0.30
Non-social reasoning	31/38	9.32 (1.33)	10.76 (1.17)	–4.79	<0.001	–1.17
Self-Reported empathy						
IRI-Perspective taking	31/33	25.77 (3.52)	26.09 (4.22)	–0.33	0.746	–0.08
IRI-Fantasy	31/33	20.52 (5.21)	20.67 (4.56)	–0.12	0.902	–0.03
IRI-Empathic concern	31/33	26.55 (4.22)	27.58 (3.19)	–1.10	0.274	–0.28
IRI-Personal distress	31/33	18.45 (5.25)	17.21 (4.10)	1.06	0.295	0.27

**Table 2**  
Correlations between each measure of social cognition and with non-social cognitive measures in healthy relatives and controls group.

	MZ <i>r</i> ( <i>P</i> )	SK <i>r</i> ( <i>P</i> )	ER <i>r</i> ( <i>P</i> )	IRI-PT <i>r</i> ( <i>P</i> )	IRI-F <i>r</i> ( <i>P</i> )	IRI-EC <i>r</i> ( <i>P</i> )	IRI-PD <i>r</i> ( <i>P</i> )	NSR <i>r</i> ( <i>P</i> )
Mentalizing (MZ)	–							
Social knowledge (SK)	<b>0.463** (0.009)</b>	–	–	–	–	–	–	–
Emotion recognition (ER)	0.250 (0.130)	–	–	–	–	–	–	–
IRI-Perspective taking (IRI-PT)	0.100 (0.591)	0.237 (0.199)	–	–	–	–	–	–
IRI-Fantasy (IRI-F)	0.188 (0.258)	0.202 (0.225)	0.277 (0.131)	–	–	–	–	–
IRI-Empathic concern (IRI-EC)	0.345 (0.057)	–0.021 (0.912)	–0.167 (0.352)	–	–	–	–	–
IRI-Personal distress (IRI-PD)	0.218 (0.238)	0.168 (0.367)	0.354 (0.051)	0.019 (0.918)	–	–	–	–
Non-social reasoning (NSR)	–0.153 (0.396)	–0.199 (0.267)	–0.101 (0.576)	<b>0.480** (0.005)</b>	–0.177 (0.341)	–	–	–
Estimated IQ (IQ)	0.085 (0.638)	–0.226 (0.206)	0.065 (0.726)	<b>0.545** (0.002)</b>	<b>0.415** (0.016)</b>	–	–	–
	0.264 (0.151)	0.262 (0.154)	0.078 (0.668)	<b>0.642** (&lt; 0.001)</b>	<b>0.242 (0.190)</b>	–	–	–
	–0.248 (0.165)	–0.114 (0.529)	0.058 (0.756)	–0.184 (0.323)	<b>0.415** (0.016)</b>	–	–	–
	–0.084 (0.655)	0.130 (0.486)	0.018 (0.919)	0.324 (0.065)	<b>0.454** (0.008)</b>	–	–	–
	–0.337 (0.055)	–0.020 (0.911)	0.137 (0.462)	0.223 (0.227)	<b>0.399* (0.026)</b>	–0.001 (0.996)	–0.170 (0.361)	–
	0.035 (0.852)	0.139 (0.457)	0.090 (0.590)	0.004 (0.980)	0.019 (0.916)	0.128 (0.494)	–0.161 (0.371)	–
	<b>0.354* (0.029)</b>	0.232 (0.161)	0.055 (0.770)	–0.001 (0.996)	0.100 (0.591)	–0.183 (0.309)	–0.253 (0.170)	0.119 (0.523)
	0.121 (0.515)	0.060 (0.749)	0.024 (0.887)	–0.052 (0.776)	<b>–0.550** (0.001)</b>	–0.163 (0.382)	–0.158 (0.387)	0.146 (0.389)
	0.228 (0.175)	0.298 (0.074)				–0.182 (0.317)		

relatives in mentalizing tasks that required taking the context into account ( $d = -0.62$ , as in Anselmetti et al., 2009; de Achával et al., 2010; Huepe et al., 2012) than in decontextualized mentalizing tasks ( $d = -0.32$ , as in Kelemen et al., 2004). Thus, the effect size of the present study ( $d = -0.64$ ) is very similar to the effect size established in our meta-analysis for the studies using similar type of mentalizing tasks, which require contextual processing for mental state attributions ( $d = -0.62$ ). Mentalizing difficulties observed in first-degree relatives of patients in this study support the idea that mentalizing impairments could be a valuable endophenotype of schizophrenia (Martin et al., 2013).

In this study, group differences for the emotion recognition test failed to reach significance. Low to moderate impairments in emotion recognition impairments were expected in unaffected first-degree relatives based on our meta-analysis ( $d = -0.41$ ; Lavoie et al., 2013) and we here observed an effect size in the low to moderate range ( $d = -0.30$ ). As emotion recognition deficits in unaffected relatives were expected to be subtle, the size of our groups was probably not sufficient to detect these impairments, thus reflecting a limit of the present study. In addition, the same task had also failed to find a significant impairment in a group of patients with first episode psychosis in a previous study (Achim et al., 2012b), which suggests that the task might also lack sensitivity to detect subtle deficits. Given these limitations, and given that several studies using more sensitive tasks and greater group sizes have demonstrated emotion recognition deficits, the lack of a significant group difference in the current study should be interpreted with care.

We also observed higher performances in unaffected relatives on the social knowledge test. This result was unexpected, as deficits in social knowledge in recent-onset schizophrenia patients have recently been observed in a study using the same task (Achim et al., 2012b). Healthy relatives thus seem to show a different pattern of social knowledge performance than what is observed in affected patients. In addition, a strong association between mentalizing and social knowledge abilities was observed in relatives of patients whereas this relationship was only small and non significant in the control group. It should be noted that the magnitude of the group difference could in part be accountable to the relatively low social knowledge performance of the control group of this study, which performed significantly worse than younger adults (Achim et al., unpublished results). Regardless of whether relatives indeed perform better than expected, we observed that they did not show any impairments on our Social Knowledge task. These results suggest that unaffected relatives could rely more largely on social knowledge when attributing mental states to others, which could compensate for a difficulty to adequately perceive social cues or to recruit general (non-social) cognitive abilities such as general reasoning processes.

Our study also evaluated self-reported empathy, which, to our knowledge, had only been investigated in one previous study in relatives of patients with schizophrenia (Montag et al., 2012). Interestingly, our results are consistent with those reported in that study: there was no significant difference between relatives and controls on either cognitive or affective self-reported empathy. A similar pattern was also observed in a study with recent-onset psychosis patients using the same questionnaire (Achim et al., 2012a). The IRI scale (Davis, 1983) provides an empathy measure relying on self-report of empathic dispositions. It is thus possible that although parents of patients present certain difficulties in attributing mental states to others, as measured by our mentalizing task, they still perceive themselves as being able to share and respond to others' emotional states. Furthermore, several of the IRI's questions are formulated in a way that makes respondents evaluate how much they try to empathize with others, not how much they succeed, leaving open the possibility that they indeed try



but perhaps not with the same success. Given that we used a self-report measure, further studies with tests assessing performance on higher-level aspects of emotional processing are required before drawing conclusions about these abilities in relatives of people with schizophrenia.

#### 4.2. Processes leading to affected mentalizing performance

This study identified mentalizing impairments in healthy relatives of patients with schizophrenia. The results also demonstrate that unaffected relatives of patients present impairments in general cognitive reasoning and a significantly inferior IQ compared to healthy controls. These results raise the important debate regarding the distinct versus non-distinct nature of social cognition and the specificity of social cognition impairments in schizophrenia. Even though there seems to be some processes that are specific to social stimuli (Sergi et al., 2007; Hoe et al., 2012), several cognitive processes are also common to both social and general (non-social) cognition (Kerr and Neale, 1993; Mitchell, 2008; Callejas et al., 2011). In the present study, we observed that group differences on the mentalizing task remain significant after controlling for the effect of IQ, in accordance with previous studies of unaffected relatives of patients (Mazza et al., 2008; Montag et al., 2012; Anselmetti et al., 2009). We also identified a strong association between mentalizing abilities and general reasoning in the controls group but not in the unaffected relatives group. Since the relatives with the greater difficulties in our non-social reasoning measure did not necessarily show greater mentalizing impairments, general cognitive impairments do not seem to be the main factor implicated in mentalizing difficulties.

Still, mentalizing is a complex cognitive ability, and several cognitive processes are at play in the observed deficit. Identifying which specific processes of social cognition are impaired in unaffected relatives of patients will facilitate the identification of endophenotypes closer to the genetic abnormalities of schizophrenia. Our results, combined with previous work in social cognition and unaffected relatives of patients, lead us to propose a hypothesis about a mechanism that could underlie the mentalizing difficulties observed in this population.

Mentalizing relies on a complex combination of information about what is being expressed by a person in a given situation (e.g., facial expression or verbal message) and of information retrieved from memory such as social knowledge (Achim et al., 2013). In real life, there are many reasons why a person may not react in the expected way (i.e., expectations based on social knowledge) and in such cases, what that person expresses or what we know about the context in which that person evolves should influence our judgments about that person's mental state. A participant with difficulties updating mental states attributions in response to unexpected contextual information may fail to make an accurate assessment of mental states (as required in mentalizing task). We hypothesized that this could be the case in unaffected relatives of patients with schizophrenia.

In the present study, unaffected relatives of patients only demonstrated impairments in the mentalizing task, which is the domain of social cognition that requires one to adapt mental state attributions as a function of different contextual information. Our previous meta-analysis (Lavoie et al., 2013) demonstrated more important impairments in contextualized vs. decontextualized mentalizing, and Riveros et al. (2010) proposed that mentalizing impairments in unaffected relatives are present only in context-sensitive social cognition task. Champagne-Lavau et al. (2012) previously demonstrated that contextual processing difficulties in patients with schizophrenia significantly affect their mentalizing abilities. No study directly investigated the impact of context processing on mentalizing performance in unaffected relatives but

MacDonald and Carter (2003) showed contextual processing impairments in unaffected first-degree relatives using a non-social cognitive task. By targeting precise social cognition difficulties in unaffected relatives of patients such as context-sensitive mental state attribution, we may facilitate the identification of neuroanatomic and neurofunctional markers of a genetic liability to schizophrenia, which are likely more proximal to genetic abnormalities than global social cognition abilities per se.

Recent neuroimaging research suggests that the ability to adapt mental state attributions as a function of contextual information may involve a specific brain region, namely the temporo-parietal junction (TPJ). The TPJ is part of the set of brain regions (including also the medial prefrontal cortex, precuneus, temporal poles, anterior cingulate cortex and insula) associated with social cognition and commonly known as the “social brain” (Frith and Frith, 2007). There has been some debate regarding the specific role of the TPJ during mentalizing (Saxe and Kanwisher, 2003; Liepelt et al., 2008; Mitchell, 2008; Aichhorn et al., 2009), but a recent review by Geng and Vossel (2013) highlights substantial evidence supporting the implication of the TPJ in the process of “contextual updating and adjustments of top-down expectations”. The TPJ thus seems to sustain the ability to integrate different pieces of information available in a given situation to adapt an initial mental state attribution. We can hypothesize that unaffected relatives of patients would present a distinct pattern of cerebral activation compared to healthy controls in this brain region during mentalizing tasks. Such pattern, if present, could be a neurofunctional marker of a genetic vulnerability associated with the illness. To date, however, no study has investigated the neural correlates of mentalizing processes in unaffected relatives of patients.

However, the ability to update an attribution based on contextual processing is closely related to executive processes such as cognitive flexibility (i.e., ability to shift between different perspectives). In unaffected relatives of patients, impairments in executive functions such as cognitive flexibility have been observed (Snitz et al., 2006; Lin et al., 2013). Riveros et al. (2010) proposed that executive function may partially influence the performance on social cognitive task, even if social cognition seems distinct from general cognitive functioning. Additional studies are needed to characterize how cognitive flexibility may influence context-sensitive mental state attributions in order to determine the degree to which mentalizing impairments are distinct for executive functioning difficulties.

The results of this study nonetheless suggest that mentalizing difficulties in unaffected relatives of patients are particularly important for context-sensitive mental state attributions. Such refined understanding of the neurocognitive processes that are affected in this population may guide the identification of new targets for research relying on endophenotypes of schizophrenia. Importantly, the identification of the social cognition processes that are linked to a genetic vulnerability for the illness may also contribute to our understanding of schizophrenia and the related social functioning deficits that characterize this psychopathology. Even if such difficulties seem linked to a genetic vulnerability to the illness, they may still be treatable, but may require specific treatments to either improve these functions or help patients manage these difficulties that hinder everyday functioning.

## 5. Conclusion

Assessing several domains of social cognition provided a more comprehensive description of the social cognition processes that are either affected or preserved in parents of patients with schizophrenia. Our study is, to our knowledge, the first to evaluate four main aspects of social cognition within the same group of

first-degree relatives of patients with schizophrenia, and the first to examine social knowledge abilities in this population. Our results revealed impairments in mentalizing, an enhanced performance for social knowledge relative to control participants, but no significant group differences on emotion processing and empathy measures. We suggest that unaffected relatives of patients may present deficits in the ability to flexibly use different sets of contextual information when making mental state attributions, an ability that is specifically involved during mentalizing. Further studies using different techniques such as neuroimaging are needed to investigate this hypothesis directly in this population to determine whether this process is impaired and can stand out as a potential endophenotype of schizophrenia. Overall, this study represents a key step towards identifying specific cognitive characteristics that may be associated with a genetic risk to develop schizophrenia.

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