Theory of mind reasoning in schizophrenia patients and non-psychotic relatives

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Abstract

Research consistently demonstrates that schizophrenia patients have theory of mind (ToM) impairments. Additionally, there is some evidence that family members of schizophrenia patients also demonstrate impairments in ToM, suggesting a genetic vulnerability for the disorder. This study assessed ToM abilities (i.e., sarcasm comprehension) in schizophrenia patients and their first-degree biological relatives during video-taped social interactions, to be representative of real-world interactions and to assess for disease-specific and/or genetic liability effects. Additionally, we assessed whether ToM abilities predicted social and global functioning in schizophrenia patients, and whether symptoms were associated with ToM deficits. Schizophrenia patients demonstrated impairments in sarcasm comprehension compared to controls and relatives, whereas relatives showed intact comprehension. Symptoms of schizophrenia significantly predicted worse ToM abilities. Furthermore, in schizophrenia patients, impaired ToM reasoning predicted worse social and global functioning. Given schizophrenia patients demonstrated impairments in ToM reasoning in a task that resembles real-life interactions, this might be a key area for remediation.

Keywords:
Theory of mind
Schizophrenia
First-degree relatives
Family study
Social functioning
Social cognition

1. Introduction

Theory of mind (ToM) refers to the ability of an individual to attribute mental states, such as beliefs and intentions, to another individual. ToM abilities are consistently found to be impaired in schizophrenia patients (reviewed in Bora et al., 2009a). Moreover, recent research suggests that ToM abilities are more strongly associated with social functioning than any other aspect of social cognition or neurocognition (Fett et al., 2011). Research is also beginning to assess whether ToM impairments are related to the genetic vulnerability for the disorder (e.g., Irani et al., 2006). Additionally, recent research has moved towards using more ecologically valid measures of ToM; however, these tools have been under-utilized to study schizophrenia, and have not frequently been used in genetic liability studies. The goal of the present study was to investigate ToM deficits using a more ecologically valid task in schizophrenia patients and non-psychotic first-degree biological relatives. Investigating both patients and family members allowed for a better examination of genetic (familial) liability, as well as disease-related processes.

Current research undoubtedly indicates the presence of ToM deficits in schizophrenia with large effect sizes of $d=1.21–1.26$ (Sprong et al., 2007; Bora et al., 2009a). Furthermore, ToM abilities have been associated with several aspects of social functioning in schizophrenia patients, namely better interpersonal communication skills and participation in more social activities (Bora et al., 2006). In fact, research shows that mental state attribution abilities in schizophrenia patients are one of the best predictors of difficulties with social interactions and behaviors (e.g., Bora et al., 2006; Brüne et al., 2007). One hypothesis is that a lack of integrity in fronto-limbic networks of the brain are related to both social cognitive (e.g., ToM) impairments, as well as deficits in emotion regulation abilities in schizophrenia patients (Rowland et al., 2012).

A more recent debate has focused on whether these symptoms are more state- or trait-related. To date there have been conflicting findings. Evidence for the state argument has come from findings that impairments in ToM abilities are strictly present during the acute stages of the illness (Drury et al., 1998), as well as findings that suggest state-dependent ToM deficits associated with specific behavioral symptoms of schizophrenia (e.g., Frith and Corcoran, 1996; Pickup and Frith, 2001). There is some evidence that suggests ToM deficits are present early in the course of the illness, and may be maintained throughout the course of the illness (e.g., Green et al., 2012); however, it has been postulated that these...
prolonged deficits may also be related to a more general neurocognitive impairment also present in schizophrenia (Green et al., 2012). ToM deficits have been found to be related to both positive and negative symptoms of schizophrenia (Brüne, 2005). For example, “over-attributing” the intentions of others may lead to the development of delusions, and individuals with paranoid symptoms may be unable to use contextual information to accurately understand others’ intentions (Brüne, 2005). In contrast, negative symptoms are hypothesized to be related to “under-attributing” or failing to utilize available information to interpret the intentions of others (Fridh and Corcoran, 1996). Taken together, current research suggests that ToM deficits are likely present throughout the course of schizophrenia, are significantly related to both positive and negative symptomatology, and predict impairments in social situations.

In contrast, evidence for the trait-dependent view has identified similar ToM deficits in individuals with high levels of schizotypal traits as in those with schizophrenia (Langdon and Coltheart, 2004), while other studies have found impairments in schizophrenia patients with remitted symptoms compared to both healthy controls (Janssen et al., 2003) and psychiatric controls (Mitchley et al., 1998). In a recent meta-analysis, ToM impairments were described as being more pronounced in non-remitted patients, though remitted patients still performed significantly worse than healthy controls (Bora et al., 2009a).

One particularly useful method for resolving the state vs. trait debate is to assess whether ToM deficits are associated with the genetic liability for the disorder by studying the first-degree biological relatives of schizophrenia patients. Family studies are a particularly useful method for investigating genetic liability for the disorder, as non-psychotic relatives of patients share genes for the disorder, but not the illness process. Previous studies of family members of schizophrenia patients have demonstrated discrepant results. In some studies, first-degree relatives performed significantly worse than healthy controls at correctly interpreting hints in a series of vignettes (the Hinting Task; Janssen et al., 2003; Versmissen et al., 2008), and on a written second-order false belief task (Mazza et al., 2008), though it has been suggested that some of the relative samples used in this literature were experiencing sub-clinical psychotic symptoms themselves (Martin et al., 2014). Other studies have found no difference in ToM between relatives of schizophrenia patients and healthy controls on the Revised Mind in the Eyes Test (Kelemen et al., 2004), a cartoon picture task (Marjoram et al., 2006b), or on a written second-order false belief task, after controlling for the effects of IQ (Pentaraki et al., 2008).

A recent review has suggested the need for the literature to further expand upon the possibility of ToM deficits being an endophenotype (i.e., vulnerability marker) for schizophrenia (for review, see Martin et al., 2014). A possible explanation for the inconsistent findings in schizophrenia family studies is the widely differing tasks used to measure ToM. In fact, an issue in the ToM literature is the heterogeneity amongst the tasks used (e.g., Bora et al., 2009a). Psychometric properties (i.e., reliability and validity) of ToM measures are widely under-studied, and there is a lack of task standardization across this literature. For example, though false-belief tasks are one of the most widely used tasks to tap into ToM abilities, there is a great deal of variability relating to the number of stories that are presented, how comprehension questions are phrased, and the method of story presentation (e.g., cartoon vs. written). In general, the majority of studies have used either written short stories or cartoon vignette tasks to assess ToM, which may not be representative of real-world encounters where tone and intonation cues, as well as facial expressions, give valuable information. The correct interpretation of the intentions of others goes beyond the simple understanding of language and requires the ability to use contextual information in order to recognize non-literal or sarcastic utterances of speech (Langdon et al., 2002). Previous research has shown that the processes and strategies associated with detecting non-literal statements — including irony, sarcasm, and metaphor — differ depending on whether the statements are received in video/conversational form versus written form (Carvalho et al., 2009). As a result, ToM tasks utilizing written short stories and cartoons may not be adequately assessing the same abilities that are required in real-world social contexts. Taken together, this suggests further research is needed to determine whether ToM deficits are associated with schizophrenia using more ecologically valid tasks. Moreover, it can be argued that, in taking steps towards developing a standardized ToM assessment battery, video-taped stories should be included to improve ecological validity.

This study uses The Awareness of Social Inference Test (TASIT; McDonald et al., 2003), which consists of a series of videotaped vignettes that are designed to assess the detection of sarcasm, an important component of ToM (Kern et al., 2009). The TASIT has been used successfully to measure social perception abilities, and has the added benefit of being more representative of daily life encounters due to its video format (McDonald et al., 2003). Relatively few studies have utilized this task in schizophrenia research (e.g., Mancuso et al., 2011; Horan et al., 2012), with, to the best of our knowledge, no study utilizing the TASIT in a family study.

Given that ToM has been associated with critical aspects of social functioning (e.g., Roncone et al., 2002; Fett et al., 2011), it is important to understand the underpinnings of ToM deficits in schizophrenia and identify associated vulnerabilities in non-psychotic relatives. The present study investigated more ecologically valid ToM abilities in schizophrenia patients, first-degree biological adult relatives, and healthy controls in an effort to clarify whether ToM deficits are a state or trait marker for the disorder and whether the deficits are associated with the genetic liability for the disorder. Second, we investigated whether these more ecologically valid ToM impairments are associated with real-world social and global functioning in schizophrenia, as well as symptomatology. We hypothesized that schizophrenia patients would demonstrate ToM impairments compared to controls, and relatives would demonstrate an intermediate level of performance between schizophrenia patients and controls. Furthermore, we hypothesized that greater ToM impairment would predict worse social and global functioning and greater symptomatology in schizophrenia patients.

2. Methods

2.1. Participants

A total of 85 individuals participated: 30 schizophrenia or schizoaffective patients (hereafter referred to as schizophrenia patients), 28 adult non-psychotic first-degree biological relatives, and 27 healthy controls. Demographic characteristics are shown in Table 1. Schizophrenia patients were recruited through outpatient clinics at Foothills Hospital, and through community support programs in Calgary, Canada. Research staff identified first-degree biological relatives by completing a pedigree with the proband. Not all probands met recruitment criteria for the study; however, to enhance the sample, all first-degree biological relatives of schizophrenia or schizoaffective patients that met recruitment criteria were included. Thus, 22 of the 28 relatives were not related to the patients who participated in the study. A total of four relative-patient pairings were living together (1 patient-sibling pairing, and 3 patient-parent pairings). On average, the relative-patient pairings have lived together for 27 years (S.D. = 4.9 years). Healthy controls were recruited through flyers and advertisements around the community of Calgary. The University of Calgary ethics board approved the protocol and all participants provided informed written consent.

Inclusion criteria for all participants included: (1) age 18–65, (2) minimum IQ of 70, (3) no current diagnosis of drug or alcohol dependence or abuse, (4) no history of head injury or being unconscious for more than 20 min, (5) no history of electroconvulsive therapy, and (6) no history of stroke or other neurological
condition. Further criteria for inclusion of first-degree relatives were no lifetime
diagnosis of a psychotic disorder or bipolar disorder, or history of anti-psychotic
medication use. Further criteria for inclusion of healthy controls were no personal
or family history of a psychotic disorder or bipolar disorder, or personal use of an
anti-psychotic medication.

2.2. Diagnosis and assessment

All participants were interviewed using the Structured Clinical Interview for
DSM-IV Axis I Disorders (SCID-I; Spitzer et al., 1992). The Structured Interview for
Schizophrenia, with supplemental questions, was used to measure Axis II Cluster A
disorders in relatives and controls (Kendler et al., 1989). Diagnoses were assigned
according to DSM-IV-TR criteria via case conferences. No relatives or controls met
diagnosis of a psychotic disorder or bipolar disorder, or history of anti-psychotic
medication use. Evidence for the

2.3. Theory of Mind Tasks

Parts 2 and 3 of the TASIT were used to measure ToM abilities. Evidence for the
ecological validity of the TASIT has been shown, as TASIT scores were found to
 correlate significantly with spontaneous social behavior in impaired adults
(McDonald et al., 2004). The TASIT consists of a series of videotaped interactions
with two or three professional actors in each scene. Part 2 (Social Inference – Minimal)
is made up of 15 vignettes (20–60 s each), with five sincere and 10
sarcastic exchanges and associated comprehension questions. In the sarcastic
examples, the viewer must correctly interpret contextual cues, such as facial
expressions and tone of voice, in order to differentiate them from sincere remarks.

Table 1
Participant Characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Schizophrenia</th>
<th>Relative</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>30</td>
<td>28</td>
<td>27</td>
</tr>
<tr>
<td>Age (years)</td>
<td>39.0 (11.5)</td>
<td>41.9 (15.6)</td>
<td>40.7 (11.1)</td>
</tr>
<tr>
<td>Gender ( % female)</td>
<td>50</td>
<td>60.7</td>
<td>51.9</td>
</tr>
<tr>
<td>Country born</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canada (%)</td>
<td>88.2</td>
<td>89.3</td>
<td>81.5</td>
</tr>
<tr>
<td>Outside of Canada (%)</td>
<td>11.8</td>
<td>10.7</td>
<td>18.5</td>
</tr>
<tr>
<td>Education (years completed)</td>
<td>13.9 (3.0)</td>
<td>16.2 (2.5)</td>
<td>15.3 (2.4)</td>
</tr>
<tr>
<td>Annual income $0–30,000 (%)</td>
<td>55.9 ab</td>
<td>71</td>
<td>7.4</td>
</tr>
<tr>
<td>$30,000–50,000 (%)</td>
<td>14.7</td>
<td>17.9</td>
<td>32.2</td>
</tr>
<tr>
<td>$50,000–95,000 (%)</td>
<td>20.6</td>
<td>50.0</td>
<td>37.0</td>
</tr>
<tr>
<td>$95,000 + (%)</td>
<td>8.8</td>
<td>25.0</td>
<td>33.3</td>
</tr>
<tr>
<td>Maternal education (%)</td>
<td>13.9 (3.2)</td>
<td>13.0 (3.6)</td>
<td>13.5 (3.4)</td>
</tr>
<tr>
<td>Matrix Reasoning Raw Score</td>
<td>26.4 (2.9)</td>
<td>27.4 (3.1)</td>
<td>27.0 (5.6)</td>
</tr>
<tr>
<td>Vocabulary Raw Score</td>
<td>56.9 (5.9)d</td>
<td>62.1 (5.8)</td>
<td>59.1 (7.9)</td>
</tr>
<tr>
<td>Handedness (% right handed)</td>
<td>89.3</td>
<td>85.3</td>
<td>96.3</td>
</tr>
<tr>
<td>Duration of illness (%)</td>
<td>16.8 (11.4)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>PANSS: General Range</td>
<td>55.6 (12.6): 30–79</td>
<td>36.4 (5.5): 31–53c</td>
<td>33.2 (5.1): 30–54c</td>
</tr>
<tr>
<td>PANSS Negative Range</td>
<td>12.9 (4.1): 7–22</td>
<td>7.7 (1.1): 7–1</td>
<td>7.2 (0.6): 7–10c</td>
</tr>
<tr>
<td>PANSS Positive Range</td>
<td>15.4 (5.4): 7–25</td>
<td>8.7 (1.7): 7–14</td>
<td>7.9 (1.3): 7–10c</td>
</tr>
<tr>
<td>Axis I (% with any lifetime non-psychosis diagnosis)</td>
<td>–</td>
<td>35.7</td>
<td>25.9</td>
</tr>
<tr>
<td>Anti-psychotic (Atypical, Typical; % on)</td>
<td>94.1, 14.7</td>
<td>0, 0</td>
<td>0, 0</td>
</tr>
<tr>
<td>Anti-depressants (% on)</td>
<td>38.2</td>
<td>7.1</td>
<td>3.7</td>
</tr>
<tr>
<td>Mood Stabilizer (% on)</td>
<td>11.8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anti-anxiety (% on)</td>
<td>8.8</td>
<td>3.6</td>
<td>0</td>
</tr>
<tr>
<td>Anti-parkinson (% on)</td>
<td>8.8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other Psychiatric (% on)</td>
<td>5.9</td>
<td>3.6</td>
<td>0</td>
</tr>
</tbody>
</table>

Note: Mean and standard deviation presented where appropriate. The following annotations were used to denote group differences other than for medication information.

* Less than relatives.

b Less than controls.

c Less than patients.

by interpreting the voice tone of the speaker. The other five sarcastic exchanges
involve paradoxical sarcasm, where the verbal interaction does not make sense
unless it is correctly interpreted that one of the speakers has made a sarcastic
remark.

Part 3 (Social Inference –Enriched) consists of 16 vignettes (15–60 s each), with
eight lies and eight sarcastic exchanges and accompanying comprehension questions.
In this section of the TASIT, the viewer must correctly identify statements
that are contrary to what the actor believes (lies) and statements that are contrary
to what the actor is trying to convey (sarcasm). Again, information regarding the
actor’s intentions must be interpreted through various contextual cues.

Following each scene, a series of four forced choice (yes/no) comprehension
questions are posed to the viewer. Each set of questions assesses comprehension of
(1) what the actor is trying to communicate to other actors in the scene; (2)
whether the actor is trying to communicate a literal or non-literal message;
(3) the actors’ beliefs and knowledge in the situation; and (4) the emotional state of
the actor.

2.4. Statistical analysis

Analyses were conducted using SPSS version 19.0. First, the normality of the data
was tested using the one-sample Kolmogorov–Smirnov analysis. The distribution
of scores was not normal for all three conditions (sincere, simple sarcasm, and
paradoxical sarcasm) of Part 2 (Social Inference – Minimal) of the TASIT
(p < 0.001), or for lie comprehension on Part 3 (p < 0.01). Specifically, significantly
skewed scores were noted for the sincere (skewness = –1.12), simple sarcasm
(skewness = –2.01), and paradoxical sarcasm (skewness = –2.23) conditions of
Part 2 of the TASIT. Significantly skewed scores were noted for the lie condition
(skewness = –1.44) of Part 3 of the TASIT. Due to the significant deviation from
normality for many of the conditions, all data analyses were conducted with both
the raw and Blom’s transformed data. As both analyses revealed similar results, the
raw data are presented in the manuscript.

Repeated measures analyses of variance (ANOVA)s were used to analyze the
effect of condition and group on task performance. For Part 2 of the TASIT, a
3 condition (sincere, simple sarcasm, paradoxical sarcasm) by three group
(schizophrenia, relatives, controls) repeated measures ANOVA was conducted. For Part 3 of
the TASIT, a two condition (sarcasm, lies) by three group (schizophrenia, relatives,
controls) repeated measures ANOVA was conducted. Greenwood–Geisser
corrections are reported for repeated measures ANOVA analyses. Follow-up ANOVAs and LSD post-hocs were conducted as necessary. The same analyses were also conducted using gender and education as covariates, and the results were similar when these covariates were included. Verbal IQ was not included as a covariate, given the literature suggesting that ToM abilities and verbal IQ scores are highly related constructs (e.g., Milligan et al., 2007). Thus, removal of verbal abilities would likely also remove a large proportion of the variance attributed to ToM abilities. Moreover, the use of covariates is not recommended for groups that have pre-existing differences on the variable that is to be covaried (Miller and Chapman, 2001). Given the pre-existing differences between schizophrenia patients, relatives, and healthy controls on verbal IQ, it is not advised to use verbal IQ as a covariate (Miller and Chapman, 2001).

To assess the relationship between total sarcasm comprehension (simple sarcasm plus paradoxical sarcasm) and verbal IQ, Pearson’s two-tailed correlations were conducted to test the model that symptom severity (i.e., total PANSS scores), duration of illness, years of education, and total sarcasm comprehension predicted both SFS and GAF scores. Next, two hierarchical multiple regression analyses were conducted to identify whether total sarcasm comprehension incrementally predicted SFS and/or GAF scores above and beyond verbal IQ. Finally, linear regression was used to assess the relationship between symptom severity and ToM abilities separately in all three groups.

3. Results

3.1. Participants

Participant characteristics are presented in Table 1. The three groups did not differ for age (F(1, 88) = 0.39, p = 0.68), for gender distribution (χ²(2) = 0.78, p = 0.68), or for country of origin (χ²(18) = 18.75, p = 0.41). There was a significant difference between groups on number of years of education (F(2, 88) = 5.72, p = 0.005), with schizophrenia patients having fewer years of education than relatives (p = 0.001) and controls (p = 0.05). There was also a significant difference between groups on average annual income (χ²(10) = 31.78, p < 0.001), with schizophrenia patients earning significantly less than both controls (p = 0.003) and relatives (p = 0.002). Maternal level of education did not differ between groups (F(2, 85) = 0.56, p = 0.59). While groups did not differ on matrix reasoning scores of the WASI (F(2, 83) = 0.40, p = 0.67), there was a significant difference between groups on vocabulary scores (F(2, 83) = 4.40, p = 0.02), with schizophrenia patients scoring significantly lower than relatives (p = 0.004). Groups did not differ on handedness (χ²(2) = 1.94, p = 0.38). Relatives and controls were comparable for lifetime history of any Axis I disorder (χ²(1) = 1.54, p = 0.46). All 30 schizophrenia patients were on anti-psychotic medication, with two patients being solely on atypical medication, 25 patients being solely on atypical medication, and three patients being on both types of medication.

### Table 2

Means, standard deviations, and effect sizes for group differences on the TASIT.

<table>
<thead>
<tr>
<th></th>
<th>Schizophrenia Mean</th>
<th>S.D.</th>
<th>Relative Mean</th>
<th>S.D.</th>
<th>Control Mean</th>
<th>S.D.</th>
<th>Schizophrenia vs. Control Cohen’s d</th>
<th>Schizophrenia vs. Relative Cohen’s d</th>
<th>Relative vs. Control Cohen’s d</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Part 2: Social Inference</strong>&lt;br&gt;Minimal</td>
<td>Sincere (max = 20)</td>
<td>17.67</td>
<td>2.56</td>
<td>17.43</td>
<td>2.94</td>
<td>17.63</td>
<td>2.60</td>
<td>0.02</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>Simple sarcasm (max = 20)</td>
<td>16.10</td>
<td>4.02</td>
<td>18.54</td>
<td>1.82</td>
<td>18.63</td>
<td>2.13</td>
<td>0.79</td>
<td>0.78</td>
</tr>
<tr>
<td></td>
<td>Paradoxical sarcasm (max = 20)</td>
<td>17.57</td>
<td>2.88</td>
<td>19.29</td>
<td>0.76</td>
<td>18.82</td>
<td>1.49</td>
<td>0.55</td>
<td>0.82</td>
</tr>
<tr>
<td></td>
<td>Total (max = 60)</td>
<td>51.34</td>
<td>3.15</td>
<td>55.26</td>
<td>1.84</td>
<td>55.08</td>
<td>2.07</td>
<td>1.40</td>
<td>1.52</td>
</tr>
<tr>
<td><strong>Part 3: Social Inference</strong>&lt;br&gt;Enriched</td>
<td>Sarcasm (max = 32)</td>
<td>24.33</td>
<td>3.23</td>
<td>27.46</td>
<td>3.45</td>
<td>27.56</td>
<td>3.15</td>
<td>1.01</td>
<td>0.94</td>
</tr>
<tr>
<td></td>
<td>Lies (max = 32)</td>
<td>25.07</td>
<td>4.65</td>
<td>28.89</td>
<td>2.39</td>
<td>28.11</td>
<td>2.61</td>
<td>0.81</td>
<td>1.04</td>
</tr>
<tr>
<td></td>
<td>Total (max = 64)</td>
<td>49.40</td>
<td>3.94</td>
<td>56.35</td>
<td>2.92</td>
<td>55.67</td>
<td>2.88</td>
<td>1.82</td>
<td>2.00</td>
</tr>
</tbody>
</table>

3.2. TASIT Part 2: Social Inference — Minimal

Means, standard deviations, and effect sizes for group comparisons are presented in Table 2. A three condition (sincere, simple sarcasm, paradoxical sarcasm) by three group (schizophrenia, relatives, controls) repeated measures ANOVA demonstrated a main effect of condition (F(1,61.131,57) = 3.87, p = 0.03), with paradoxical sarcasm being less difficult than both the simple sarcasm (p = 0.007) and sincere (p = 0.01) conditions. Additionally, a significant main effect of group was found (F(2,82) = 6.38, p = 0.003), with schizophrenia patients performing generally worse than controls (p = 0.004) and relatives (p = 0.002), but no difference between controls and relatives (p = 0.89). Furthermore, there was an interaction between condition and group (F(3,21.131,57) = 3.00, p = 0.03). To follow up on this significant interaction, three condition × two group repeated measures ANOVAs were conducted to specifically compare performance amongst the groups on the sincere, simple sarcasm, and paradoxical sarcasm conditions (see Fig. 1).

A three condition (sincere, simple sarcasm, paradoxical sarcasm) by two group (schizophrenia, controls) repeated measures ANOVAs and LSD post-hocs were conducted necessary. The same analyses were conducted separately in all three groups. To assess the relationship between symptom severity and ToM abilities separately in all three groups.
ANOVA demonstrated no main effect of condition ($F(1,70,93.29) = 1.50, p = 0.23$). However, a significant main effect of group was found ($F(1,55) = 7.01, p = 0.01$), with schizophrenia patients scoring lower overall than controls. Moreover, there was a significant condition by group interaction ($F(1,70,93.29) = 3.51, p = 0.04$). One-way ANOVA follow-up tests demonstrated that schizophrenia patients scored significantly lower on simple sarcasm comprehension ($F(1,56) = 8.52, p = 0.005$) and paradoxical sarcasm comprehension ($F(1,56) = 4.07, p = 0.05$), but not comprehension of sincere exchanges ($F(1,56) < 0.001, p = 0.96$) compared to controls.

A 3 condition (sincere, simple sarcasm, paradoxical sarcasm) by two group (schizophrenia, relatives) repeated measures ANOVA demonstrated no main effect of condition ($F(1,53,85.68) = 3.04, p = 0.07$). However, a significant main effect of group was found ($F(1,56) = 8.18, p = 0.006$), with schizophrenia patients scoring significantly lower overall than relatives. Importantly, there was a significant condition by group interaction ($F(1,53,85.68) = 4.25, p = 0.03$). One-way ANOVA follow-up tests demonstrated that schizophrenia patients scored significantly lower than relatives on comprehension of simple sarcasm ($F(1,57) = 8.63, p = 0.005$) and paradoxical sarcasm ($F(1,57) = 9.32, p = 0.003$), but not sincere exchanges ($F(1,57) = 0.11, p = 0.74$) compared to relatives.

A three condition (sincere, simple sarcasm, paradoxical sarcasm) by two group (relatives, controls) repeated measures ANOVA found a significant main effect of condition ($F(1,57,83.12) = 7.15, p = 0.003$), with sincere questions being more difficult than both simple sarcasm ($p = 0.04$) and paradoxical sarcasm ($p < 0.001$). No main effect of group was found ($F(1,53) = 0.04, p = 0.85$). Similarly, there was no significant condition by group interaction ($F(1,57,83.12) = 0.38, p = 0.63$).

3.3. TASIT Part 3: Social Inference – Enriched

Means, standard deviations, and effect sizes for group comparisons are presented in Table 2. A two condition (lies, sarcasm) by three group (schizophrenia, relatives, controls) repeated measures ANOVA demonstrated no main effect of condition ($F(1,82) = 3.08, p = 0.08$). However, a main effect of group was found ($F(2,82) = 19.35, p < 0.001$), with schizophrenia patients scoring significantly lower overall than both controls ($p < 0.001$) and relatives ($p < 0.001$), but no difference between controls and relatives ($p = 0.80$). There was no significant condition by group interaction ($F(2,82) = 0.26, p = 0.77$). Given the main effect of group, follow-up testing was conducted to evaluate which groups differed for which conditions (see Fig. 2).

Looking more specifically at the group differences, follow-up one-way ANOVAs demonstrated that schizophrenia patients scored significantly lower on lie comprehension than both controls ($F(1,56) = 9.07, p = 0.004$) and relatives ($F(1,57) = 15.29, p = 0.001$). In addition, schizophrenia patients scored significantly lower than both controls ($F(1,56) = 14.46, p < 0.001$) and relatives ($F(1,57) = 10.59, p = 0.002$) on enriched sarcasm comprehension. No significant differences were observed between controls and relatives on either lie detection ($F(1,54) = 1.34, p = 0.25$) or enriched sarcasm detection ($F(1,54) = 0.27, p = 0.61$).

3.4. Relationship between ToM abilities and verbal IQ

Verbal IQ was significantly correlated with total sarcasm comprehension (simple sarcasm plus paradoxical sarcasm) on the TASIT across all participants ($r = 0.33, p = 0.002$). More specifically, verbal IQ was significantly correlated with sarcasm comprehension for schizophrenia patients ($r = 0.39, p = 0.04$), but not relatives ($r = 0.19, p = 0.32$) or controls ($r = 0.15, p = 0.46$). However, the difference between these correlations was not statistically significant between schizophrenia patients and relatives ($Z = 0.72, p > 0.05$) or schizophrenia patients and controls ($Z = 0.84, p < 0.05$).

3.5. Relationship between ToM abilities with daily functioning and symptoms in schizophrenia patients

A total of seven regression analyses were conducted. In the first model, SFS scores were the dependent variable, and total PANSS scores, duration of illness, number of years of education, and TASIT scores (i.e., total sarcasm comprehension) were entered as independent variables. Together, the predictors accounted for approximately 32% of the variance in SFS scores ($R^2 = 0.32$), with total PANSS scores ($β = 0.49$) being the only significant predictor in the model ($t(18) = -2.29, p = 0.03$). In the second model, GAF scores were the dependent variable, and total PANSS scores, duration of illness, number of years of education, and TASIT scores were entered as independent variables. Together, the predictors accounted for approximately 51% of the variance in GAF scores ($R^2 = 0.51$), with total PANSS scores ($β = -0.66$) being the only significant predictor in the model ($t(20) = -3.67, p = 0.002$).

Third, to examine the incremental contribution of total sarcasm comprehension above and beyond verbal intelligence in predicting daily functioning, a hierarchical regression analysis was conducted with SFS scores as the dependent variable, and verbal IQ, and total sarcasm comprehension on the TASIT entered as independent variables (in steps 1 and 2, respectively). Results demonstrated that total sarcasm comprehension on the TASIT was significantly incrementally predictive of SFS scores over and above verbal IQ ($R^2 = 0.19$, $F$ Change$(1,20) = 5.06, p = 0.04$). Moreover, TASIT scores ($β = 0.48$) were a significant predictor in this model ($t(20) = 2.25, p = 0.04$). Fourth, a hierarchical regression analysis was conducted with GAF scores as the dependent variable, and verbal IQ and total sarcasm comprehension on the TASIT entered as independent variables (in steps 1 and 2, respectively). Results suggested that total sarcasm comprehension on the TASIT was significantly incrementally predictive of GAF scores over and above verbal IQ ($R^2 = 0.16$, $F$ Change$(1,22) = 4.29, p = 0.05$). Moreover, TASIT scores ($β = 0.41$) were a significant predictor in this model ($t(22) = 2.07, p = 0.05$).
The last three models examined the relationship between symptoms and ToM abilities in each of the three groups separately (i.e., schizophrenia patients, relatives, and controls), with total sarcasm comprehension on the TASIT entered as the dependent variable, and total PANSS scores (i.e., positive and negative symptoms) as the independent variable in each model. Linear regression analysis suggested that total PANSS scores significantly predicted ToM abilities in schizophrenia patients, as measured by total sarcasm comprehension on the TASIT ($F(1,24)=4.50$, $p=0.04$). PANSS scores ($\beta=-0.40$) accounted for approximately 16% of the variance in sarcasm comprehension on the TASIT in patients. In contrast, total PANSS scores did not significantly predict ToM abilities in first-degree relatives ($\beta=-0.14$, $F(1,21)=0.45$, $p=0.52$) or controls ($\beta=-0.13$, $F(1,25)=0.41$, $p=0.53$).

4. Discussion

This study investigated ToM abilities using a more ecologically valid task in schizophrenia patients, adult non-psychotic first-degree biological relatives, and healthy controls to identify whether ToM impairments represent a state or trait marker and are associated with the genetic liability for the disorder, as well as whether these impairments are related to daily functioning in patients. Overall, schizophrenia patients demonstrated an intact ability to understand sincere exchanges, but demonstrated an impaired ability to detect and comprehend simple and paradoxical sarcasm compared to both controls and relatives. In contrast, relatives demonstrated intact performance.

Consistent with our hypotheses, schizophrenia patients demonstrated impairments in interpreting intentionality. Taken together, these results support the previous literature suggesting that schizophrenia patients have impairments in ToM reasoning compared to controls (reviewed in Brune, 2005; Sprong et al., 2007; Bora et al., 2009a). More specifically, deficits in understanding the pragmatics of language, including sarcasm comprehension, have been reported in schizophrenia patients in the past (e.g., Langdon et al., 2002; Covington et al., 2005; Leitman et al., 2006). It has been postulated that impairments in sarcasm detection may be due to right prefrontal cortex damage or deficits in basic auditory and visual processing that are commonly reported in schizophrenia (Rabinowicz et al., 2000; Shamy-Tsory et al., 2005; Leitman et al., 2006). Specifically, some research has also utilized the TASIT to assess sarcasm comprehension abilities in schizophrenia. The current study supports previous findings, which have consistently reported impairments in schizophrenia patients compared to controls on simple and paradoxical sarcasm detection measures of the TASIT (e.g., Sparks et al., 2010; Wynn et al., 2010; Green et al., 2012). Furthermore, this study demonstrates that these impairments also exist in comparison to non-psychotic adult relatives, providing further support for disease-specific effects.

Contrary to our hypotheses, the current study found no impairments in ToM reasoning in non-psychotic relatives compared to controls. Similar to our findings, studies assessing the ability to identify mental states through the images of eyes (Kelemen et al., 2004), second-order false belief reasoning (Pentaraki et al., 2008, 2012), and comprehension of hinting statements (Marjoram et al., 2006b) have found no differences in relatives compared to controls. In contrast, other studies have found genetic liability effects, with relatives demonstrating impairments in false belief reasoning (Janssen et al., 2003) and difficulty interpreting cartoon jokes that tap into mentalizing abilities (Marjoram et al., 2006a). Overall, differences in findings between our study and previous results that have found ToM impairments in relatives may be due to differences in task choices, as the majority of previous research in this area has utilized paper-and-pencil or image-based tasks that are not generally representative of real-world social encounters (e.g., Corcoran et al., 1995; Anselmetti et al., 2009). In contrast to these traditional measures, the TASIT provides viewers with important social cues that are available in live social encounters, including voice intonation, pitch, and facial expression cues. It is possible that these cues are providing family members with the additional information that they require to correctly interpret sarcastic remarks. Moreover, these ToM findings based on a task using video-taped social interactions support findings that healthy relatives do not show the same degree of impairments in real-life social interactions as schizophrenia patients, and their daily social behavior is similar to healthy controls (e.g., Dodell-Feder et al., 2014). Taken together, these results suggest that traditional ToM tasks may not be measuring the same abilities that are required in daily social interactions. However, further replication of these findings using the TASIT, as well as other dynamic ToM measures, is needed to provide further support for this theory. In addition, future research on ToM impairments in schizophrenia should work towards developing a standardized assessment battery for measuring social cognitive functioning. In doing so, the importance of ecological validity when assessing abilities that are highly dependent on specific cues that are available in real-life social interactions, is necessary.

Alternatively, it is possible that the null findings between relatives and controls were due to the study being underpowered (i.e., a small sample size for these groups). However, the effect sizes for relatives vs. controls on all measures of sarcasm comprehension were negligible to small. This provides further support for the conclusion that relatives do not differ from controls in their understanding of sarcasm through video-taped interactions. Moreover, the sample size recruited for this study was similar to most studies investigating ToM impairments in first-degree biological relatives (Lavioie et al., 2013). Finally, it is possible that the null findings between relatives and controls were due to ceiling effects with the ToM task. Thus, future research would benefit from the development of more challenging ecologically-valid ToM assessment tools.

The current finding of ToM impairments in schizophrenia patients compared to both controls and relatives, coupled with the lack of impairment in relatives, suggests that more real-world ToM reasoning could be a transient marker of the disorder that is associated with the clinical status of schizophrenia patients. Further support for the state hypothesis comes from our finding that positive and negative schizophrenia symptoms significantly predicted ToM abilities in patients. These results are similar to previous studies that have found greater schizophrenia symptomatology in patients with greater ToM impairments (e.g., Abdel-Hamid et al., 2009; Kern et al., 2009). Importantly, schizophrenia symptoms did not significantly predict ToM abilities in first-degree relatives or controls, likely due in part to the comparative lack of symptoms (and/or lack of variability in symptoms) in these two groups.

The current results differ from a recent meta-analysis of schizophrenia patients in remission, first-episode patients, persons at high risk for psychosis, and relatives, which concluded that the literature provides support for ToM deficits also being a trait characteristic of schizophrenia rather than just a state characteristic (Bora et al., 2009b). However, almost all of the studies included in this analysis utilized paper-and-pencil, cartoon, or static image tasks. Notably, the single study included in the analysis that utilized a dynamic ToM task (the TASIT) found no differences between individuals with high schizotypy scores and those with low schizotypy scores (Jahshan and Sergi, 2007), providing evidence that on more real-life interactions, the level of impairment in other groups demonstrating a genetic liability for schizophrenia is reduced. In a more recent meta-analysis, first-degree relatives were again shown to
have deficits in ToM reasoning (Lavoie et al., 2013); however, similar to the aforementioned analysis, almost all of the tasks used to assess ToM were static images or stories. The one study that utilized a dynamic task, the Movie for the Assessment of Social Cognition (MASC), only found subtle deficits in relatives of schizophrenia patients on only cognitive ToM reasoning, with no impairments in affective (i.e., emotional) ToM reasoning (Montag et al., 2012).

Limitations of this study include that only one measure of ToM reasoning was used and, thus, we are unable to make direct statements about how measuring sarcasm comprehension through the TASIT is related to other measures of ToM, such as irony comprehension, metaphor comprehension, or false belief reasoning. Additionally, it would have been useful to evaluate the relationship between ToM reasoning and other forms of social cognition and neurocognition. Finally, given the difficulties associated with collecting reliable information from schizophrenia patients regarding the number of years they had been taking different classes of medication and dosages, we were unable to assess the relationship between medication use and theory of mind abilities.

Despite the limitations, this study has a number of strengths, including use of a more ecologically valid task to assess ToM reasoning in an attempt to mimic day-to-day social interactions. This study also used age- and sex-matched comparison groups in order to more accurately assess for ToM impairments in both schizophrenia patients and relatives. Finally, this study was able to recruit a sample size that is on par with or exceeds most family studies (Lavoie et al., 2013).

In sum, while schizophrenia patients appear to show impairments with sarcasm comprehension, non-psychoptic first-degree relatives seem to benefit from the dynamic cues associated with video-taped social interactions, including voice intonation and facial cues. These results may help explain in part why first-degree relatives do not show similar impairments in daily functioning that are generally seen in persons with a diagnosis of schizophrenia. In addition, ToM deficits in patients appear to be related to daily functioning. In general, the current findings suggest that future ToM research may benefit from utilizing tasks that incorporate dynamic social cues that are available in everyday social communication in order to obtain a more accurate assessment of ToM abilities. Furthermore, in the future, investigating healthy relatives, who share a genetic liability for the disorder, but do not demonstrate behavioral impairments, may allow for an analysis of compensatory mechanisms that could be useful for remediating deficits in their affected relatives.

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