Empathy and theory of mind in schizophrenia and anxiety disorders

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Abstract

This study examined the factors that lead people with schizophrenia to perform poorly on experimental theory of mind (ToM) paradigms. A group with psychosis (n=26) was compared to a group with anxiety disorders (n=27) and a healthy control group (n=25) on two tests of ToM (the Eyes and Hinting tests) and a measure of global empathy (the Empathy Quotient). The psychosis group performed worse than controls on all measures, with negative symptoms as the key negative predictive factor. When divided by remission status, only the non-remitted psychotic group differed from the other two groups on ToM measures. The anxiety group performed worse than controls on the measure of global empathy, and social anxiety was associated with poor performance on ToM and global empathy paradigms. Further research into the role of anxiety in ToM performance is warranted. The role of paradigm and specific psychotic symptoms in ToM performance is discussed.

Résumé

Cette étude a examiné les facteurs qui contribuent au mauvais rendement des individus atteints de schizophrénie dans les paradigmes expérimentaux de la théorie de l'esprit (TdE). Un groupe avec psychose (n = 26) a été comparé à un groupe avec des troubles anxieux (n = 27) et un groupe contrôle en bonne santé (n = 25) avec deux échelles sur la TdE (soit le test des yeux et la tâche d'inférence) ainsi qu'une échelle d'empathie globale (le quotient d'empathie). Le rendement du groupe de psychose a été moindre que le rendement du groupe contrôle sur toutes les échelles, les symptômes négatifs étant déterminants dans ces résultats. Lorsque séparées par statut de rémission, seules les personnes avec symptoms actifs de psychose différaient de deux autres groupes sur les échelles de TdE. Le rendement du groupe des troubles anxieux a été moindre que le rendement du groupe contrôle sur l'échelle de l'empathie globale; l'anxiété sociale étant associée à une mauvaise performance au TdE et aux paradigmes de l'empathie globale. Plus d'études sur le rôle de l'anxiété sur la performance au TdE est nécessaire. Le rôle des paradigmes et des symptômes psychotiques spécifiques sur la performance au TdE est discuté.

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1. Introduction

Empathy is a complex psychological phenomenon that defies easy definition. In general it refers to the process by which people identify another person's emotional and mental state. This ability allows us to sense another's silent distress, share in the euphoria of an athlete's gold medal performance on television, and make sense of why someone has behaved in a certain way. The instantaneous information received is used to facilitate social interactions, and is fundamental to how we come to know other people. For this reason it is often equated with "mind-reading"[1]. Though seemingly an innate and unconscious process, the ability to empathize varies between individuals and is affected by particular emotional states and in certain psychiatric and neurological conditions.

Psychosis is one of the clinical conditions in which pronounced empathy deficits are often evident. This observation is supported by a large body of research that demonstrates that in general, psychotic individuals perform poorly on a variety of paradigms assessing empathy[2]. However, it is not yet clear what specific factors influence this poor performance. This thesis explores the relationship between a number of clinical factors and performance on paradigms assessing different components of empathy. The link between anxiety symptoms and empathy performance will be a particular focus. Although anxiety symptoms are prominent in psychotic disorders, the association between anxiety and empathy has yet to be studied.

The next section will give a brief historical account of the concept of empathy, and then the many factors that have been associated with poor empathy performance in psychosis will be reviewed.

2. Empathy and Theory of Mind

2.1 Definitions of empathy

Nineteenth century German aesthetics used the word *Einfuhlüng* (meaning "feeling into") to describe the sensation one feels when viewing an inspiring piece of art. For example a particularly stunning portrait of a tree standing firm in howling wind might induce a feeling of solidity or strength in the observer. In the early 20th century Lipps proposed that this same process may be involved in coming to understand the minds of others. Titchener translated Lipp's conception of *Einfuhlüng* to "empathy" in 1909 [3].

Contemporary authors have offered a variety of definitions to the term "empathy". Feshbach[4] felt the process of empathy involved three components:

1) the ability to discriminate and identify the emotional state of another
2) the capacity to take the perspective of the other
3) the evocation of a shared affective response

These components factor into most authors' use of the word although some also emphasize other points. For example, some point out the importance of a sustained self-other distinction during the shared affective response (e.g. the person realizes it is "as if" he had won the gold medal using the above example)[5, 6]. Others broaden the concept to include mimicked motor movements that result from observing another move as a type of "motor empathy"[7].

In the cognitive neuroscience literature, authors tend to divide these factors into two groups: cognitive empathy and affective empathy [8, 9]. Cognitive empathy involves the ability to apprehend the mental state of someone else (1 and 2 from Feshbach's model), while affective empathy involves feeling something emotionally as a result of witnessing emotion occurring in someone else (3 from Feshbach's model). Although related, these are two different processes.

For example, imagine attending a funeral reception and seeing a grieving family member sitting alone, not speaking to anyone. Through the process of cognitive empathy you might deduce they are not simply antisocial and rude, but instead are feeling sad and not able to speak to others. Due to the affective empathy component, you might begin to feel sad yourself just from observing their sadness, even if you did not know the deceased person.

Feshbach believed that the affective empathy experience required the cognitive empathy piece. The independence of each module is still debated, although preliminary evidence suggests that these are dissociable components[10].

2.2"Theory of mind" and its relationship to empathy

Twenty-five years ago Simon Baron-Cohen proposed that children with autism had a core deficit in "theory of mind" or the ability to accurately assess the thoughts and feelings of another person[11]. This initiated an enormous body of research focused on assessing theory of mind in autism spectrum disorders as well as in a variety of other psychiatric and neurological conditions such as schizophrenia [2, 12], bipolar disorder [13-15], amygdala lesions [16], frontotemporal dementia [17, 18], and traumatic brain injury [19], among others. When used as a verb, theory of mind is also referred to as "mentalizing" or "mindreading".

Theory of mind maps very well onto the concept of cognitive empathy and most authors use the terms interchangeably. Indeed, some subdivide the components of theory of mind into (1) mental state decoding (i.e. correctly identifying emotion), and (2) mental state reasoning (i.e. understanding why they feel that way)[20]. These two components correspond very well to the first two factors of Feshbach's model of empathy.

Although research into the broader concept of empathy has recently begun to build, due to large body of theory of mind literature, there is far more research concerning the cognitive dimension of empathy than on the affective dimension.

3. Theory of Mind Deficits in Psychosis

After the autism spectrum disorders, psychosis is the clinical condition that has received the most attention from theory of mind researchers. Two recent meta-analyses both found clear theory of mind deficits in schizophrenia with an effect size of approximately -1 relative to healthy controls [2, 12]. While it is clear that deficits exist, moving beyond this general finding has been problematic. Several questions remain unanswered: what specific factors are associated with theory of mind deficits in schizophrenia? Are the deficits state-dependant (i.e. related to symptoms) or an enduring trait? If mentalizing deficits are related to specific symptoms, which ones? To what extent are these deficits dissociable from other general and specific cognitive deficits? Are they related to problems with real-world functioning?

The studies examining these more specific questions have thus far found inconsistent and often contradictory findings. Research in this area is hampered by small samples sizes, no standardized theory of mind measures, and often incomplete reporting of relevant clinical variables[12, 21, 22]. The next sections will review the studies addressing these questions and other factors that may moderate theory of mind performance in psychosis.

3.1 Factors known to moderate theory of mind performance

3.1.1 Trying to measure mentalizing: the variety of theory of mind paradigms

Perhaps the most basic challenge to identifying theory of mind deficits is to figure out how to measure it. A variety of ingenious paradigms have been developed measuring different skills thought to require a functioning theory of mind, yet it is unclear whether they are all measuring the same thing.

Most of the theory of mind paradigms used early on in psychosis research tested false beliefs. These tasks typically involve participants listening to a story or brief vignette involving a social interaction, followed by questions about the mental state of the

characters. For example, one of the classic theory of mind paradigms is the Sally and Ann test, a task developed for research with children [23]. In this test, participants are told a story in which a girl Sally puts her doll in a box and leaves the room. While she is away her friend Ann enters and hides the doll under the bed. The participant is then asked where Sally will look for her doll. Answering correctly requires an understanding that other people can hold beliefs different than one's self. Even though the participant knows the doll is now under the bed, they understand that Sally would falsely believe the doll was in the box. When these tests are adapted for adults, the details are changed to an adult situation (i.e. cigarettes are hidden rather than dolls).

The Sally and Ann test is an example of a "first-order" false belief test because it tests the simple ability to recognize another person's false belief. Paradigms using first-order false beliefs are the simplest, and children over four usually answer them correctly [24]. More difficult "second-order" tests require participants to understand characters in the stories can have false beliefs about *another* character's mental state. Other paradigms have used social vignettes involving indirect language that require social inferences such as understanding *faux pas* [19], metaphor and irony [25, 26], humour [27], and hinting[28].

One criticism of these paradigms is that psychotic participants may score poorly on the tasks due to problems with low general IQ or specific neuropsychological deficits in working memory and executive functioning. For example, listening to vignettes (especially the more elaborate ones in second-order tests) may place too great a load on working memory and lead to incorrect answers. Some of the more carefully controlled studies added control questions to assess memory for story details, or "non-mental" reasoning such as changes in an object, and found the deficits were not accounted for by memory deficits (for example see Pickup[29]). Nevertheless, even with these controls, there is evidence that small details like how the vignettes are presented can alter the results.

For example, despite using the same theory of mind vignettes, Frith and Corcoran [30] found schizophrenic patients had difficulty with both first-order and second order false-beliefs, while Doody et al. [31]found only problems with second-order false beliefs. While

the vignettes were the same, in the Doody et al. study, the stories were acted out with props in addition to being read aloud. When Pickup and Frith [29] repeated the paradigm using props, they replicated the finding of Doody et al. and found only problems with second order false beliefs.

To mitigate the issue of low verbal IQ in schizophrenia, a handful of studies have used non-verbal paradigms such as interpreting cartoons or picture sequencing [32]. These methods have demonstrated deficits in psychosis [33, 34], and in a non-clinical population that scored high on schizotypy[32]. Although an interesting format, it is unclear whether they measure the same underlying skill as the verbal tests. For example, Harrington et al. used both verbal and non-verbal tasks and found a schizophrenia population only impaired on the verbal tasks, with no correlation between verbal and non-verbal performance[21]. By contrast, Sarfati et al found that deficits on the non-verbal task improved in a subgroup with disorganized symptoms when written sentences replaced images on the answer cards[34]. Similarly, Corcoran et al found that schizophrenia spectrum patients did worse on a strictly non-verbal picture sequencing task than on a verbal false belief test administered with illustrations to support the narrative[35].

It is difficult to interpret these conflicting results. It may be that the more sensory modalities the paradigm engages, the better the performance of the psychotic participants. For example, paradigms that use strictly auditory information seem to yield more severe deficits than those that supplement the vignettes with written or acted-out information. Similarly, performance improves on non-verbal tasks when written or verbal information is added. Thus, it may not be the verbal/non-verbal distinction that is important, but rather that presenting the vignettes in multiple formats increases the chances of understanding the vignette and making the correct choice. If the deficits truly relate to faulty mentalizing, then providing as much information as possible should not change the performance.

Unfortunately there is no standardized protocol for any of the tasks and each study administers false belief and social inference tests slightly differently. In some studies the

vignettes are read aloud and supplemented with pictures describing the vignettes[30], in others participants are also given the script[21], and in others they are acted out with dolls[31, 36]. Obviously this makes generalizing difficult, even from meta-analytic data. It is likely that the lack of standardized measures is an important factor in the inconsistent results.

Furthermore, it suggests the deficits may be due (at least in part) to the cognitive demands of these non-naturalistic paradigms rather than mentalizing per se. In fact, in one study that analyzed real-life interactions by studying actual interviews, no mentalizing deficits were found, even in those with large symptom burdens[37].

Baron-Cohen and colleagues developed the "In the Eyes Test" as a difficult theory of mind task for adults with autism-spectrum disorders [38]. In the task, subjects are presented with photographs of actors showing only their eyes, and they must infer what emotion they are portraying from a list of four options. The emotions displayed are complex (e.g. flirtatious, excited, despondent) to avoid performance ceiling effects. Both adults with autism-spectrum disorders[38] and patients with amygdala lesions[39] show deficits relative to normal controls. It is an appealing measure to use with a psychosis population as it uses a naturalistic everyday task (identifying emotion) that correlates well with standard theory of mind tasks in those with autism spectrum disorders. It has both verbal and non-verbal components, and emotions are presented in written format to minimize memory demands. These features may make it less demanding on working memory and general cognition as compared to the standard read-aloud tasks. A handful of studies have used it in psychosis with an effect size similar to false belief and other standard measures[12], and it has been shown to correlate better with real-world social functioning than standard false belief or language inference tests[40].

3.1.2 The role of general and specific cognitive function in theory of mind performance

As discussed in the previous section, an obvious confounder in trying to assess potential theory of mind deficits in psychotic individuals is the general and specific cognitive

deficits that are at the heart of the illness[41]. Many studies have added both general (e.g. IQ) and domain-specific cognitive assessments in the theory of mind studies. In individual studies, the role of general IQ has frequently been shown to moderate theory of mind performance, while specific domains such as executive functioning have not (for recent review see Pickup[42]).

For the purposes of meta-analysis, there is only sufficient data to consider the effect of general IQ. Sprong et al[2] reported that general IQ did not affect overall effect sizes. Bora et al.[12] found a trend for the IQ deficit to negatively affect performance overall, and this was more pronounced and statistically significant for remitted patients.

Research from the autism spectrum literature supports the moderating role of general IQ in theory of mind performance. Studies comparing autism spectrum, mental retardation and control populations generally show deficits in both clinical groups[43, 44]. Only one study has added an intellectually impaired control group in the schizophrenia literature. Doody et al[31] compared those with schizophrenia, those with a learning disability and those with both schizophrenia and a learning disability to a depressed clinical control group and a healthy control group. They found the comorbid group had the largest deficits, with the non-psychotic learning disability group also worse than controls.

Thus while specific cognitive deficits have yet to be consistently associated with theory of mind deficits, general intellectual deficits influence performance and are an important moderating variable.

3.1.3 The role of specific symptoms in theory of mind deficits

Research on theory of mind in schizophrenia began after Frith published an influential neuropsychological model of schizophrenia [45]. He proposed that three core neuropsychological deficits could account for many of the symptoms seen in schizophrenia. Deficits in self-monitoring (the ability to distinguish between internally and externally generated events) lead to passivity experiences and hallucinations,

difficulties with initiating willed actions lead to negative and disorganized symptoms, and deficits in theory of mind lead to paranoid ideas and delusions. He called this a "meta-representational" model of schizophrenia because all three deficits involve the difficulty to reflect upon the conscious processes of self or others.

The idea that problems with theory of mind underlie paranoid thinking has intuitive appeal. Paranoid individuals show explicitly poor mentalizing when they mislabel the intentions of others as malevolent or suspicious. Frith points out that this subgroup shows not an *absence* of theory of mind (as in autism), but rather a *dysfunction* of the theory of mind domain[46]. By contrast, he felt those with many "behavioural signs" (i.e. observable signs such negative symptoms or disorganized behaviour and speech), like those with autism, would show no capacity for mentalizing. He felt this was attributable to generalized cognitive deficits rather than theory of mind deficits *per se*. Lastly, he predicted that those with only passivity symptoms or those in remission would be no different from controls.

Subsequent research has neither clearly supported nor disproved his theory. Many symptom clusters have been associated with theory of mind deficits, with no particular symptom showing specificity. According to Frith's model, one would expect that theory of mind deficits would be primarily found in patients with paranoid delusions. While a number of studies found this association[21, 28, 47], many did not [25, 27, 31, 48-50], and some only with the more difficult second order tasks[30].

There have been a handful of studies looking at disorganized symptoms. Safarti completed a number of studies demonstrating deficits in patients with disorganized symptoms[33, 34, 51]. Other investigators have found deficits only in second order tests[52], or that poor theory of mind performance in those with disorganized schizophrenia did not differ from controls after controlling for IQ[53]. While the meta-analysis of Sprong et al found more pronounced deficits in those with disorganized symptoms, they noted this is possibly explained by higher overall rates of symptoms in this group[2, 21]. In general,

interpreting the findings in disorganized patients is complicated by the fact that there are few studies and almost all of them are by the same researcher.

Theory of mind deficits are perhaps seen most consistently in those with negative symptoms[31, 49, 52, 54, 55]. Despite this, negative symptoms are rarely the focus in any of the studies, and are often lumped in a category of "behavioural symptoms" along with disorganized symptoms. It is curious this symptom cluster has not been considered in more detail given Frith's prediction that these symptoms would be associated with greater cognitive deficits and thus secondarily more theory of mind deficits. While Frith found this in an early study[30], many studies found an association between negative symptoms and theory of mind deficits over and above any cognitive deficits. No study has yet addressed this hypothesis directly, and there is insufficient data for a meta-analytic study of the question.

Thus, it is not yet clear whether specific symptoms or overall symptom number influence theory of mind performance. This ambiguity is due in part to a lack of specific clinical measures in many studies. Often groups were organized around a score on a particular symptom dimension (i.e. disorganization or paranoia), and global assessments using a standardized measure such as the PANSS[56] or SAPS/SANS[57, 58] are often absent. Some have advocated that trying to link performance with specific symptoms may bear more fruit than with a particular diagnosis or symptom cluster [21].

3.1.4 Are theory of mind deficits in schizophrenia a state or trait characteristic?

A related question is whether the observed theory of mind deficit constitutes a state or trait marker in schizophrenia. Frith's theory predicted that mentalizing deficits would be a state phenomenon related to the presence of paranoid symptoms. This argument has been supported by the finding in some studies that remitted patients did not differ from controls[25, 28-30, 47, 59]. Additionally, a medication treatment study demonstrated that over the course of inpatient treatment for acute psychosis, patients' performance on a theory of

mind task improved to normal levels (although the improvement was not statistically related to symptom improvement)[49].

The trait argument is supported by studies demonstrating deficits during remission[60], in children that would go on to develop schizophrenia[61], in unaffected relatives[62, 63], and in those with high schizotypy scores[32].

Meta-analytic data makes a strong case for the trait argument. Both meta-analyses[2, 12] found remitted patients showed a moderate to large effect size of about -0.7 relative to normal controls, meaning they scored 70% worse than the control group on theory of mind measures. Pousa et al. argued that this conclusion ought to be tentative given the relative paucity of studies that have used clear remission criteria[22]. This is certainly true, and many of the data points grouped under "remission" in both papers used very loose criteria for remission. For example, Bora considered inpatients nearing discharge and all outpatients as "remitted". It is clear that further study of stable outpatients using consensus criteria for remission is required to better address this controversy.

3.2 Questions not yet explored in the theory of mind and psychosis literature

3.2.1 Are there deficits in affective or global empathy?

Although there is a wealth of studies assessing theory of mind or cognitive empathy in schizophrenia, relatively few have addressed potential deficits in affective empathy or considered the relationship of the two. People with schizophrenia show consistent deficits in identifying emotions[64], and they persist after symptom stabilization [65]. Given this fact and the deficits seen in cognitive empathy, one would expect deficits in affective empathy as well.

Montag et al[66] compared schizophrenic participants with healthy controls on the Interpersonal Reactivity Index (IRI)[67]. The IRI is a self-report measure of empathy that provides scores in four different domains: perspective taking, empathic concern, personal distress and fantasy. The perspective taking score maps onto the concept of cognitive

empathy, while empathic concern roughly maps onto that of affective empathy. The schizophrenia group scored lower than controls on cognitive empathy, but not on affective empathy. Neither score was influenced by PANSS rated positive or negative symptoms in a regression model.

Bora et al[68] used a more recently developed measure, the Empathy Quotient[9] (EQ) to assess potential deficits in global empathy in schizophrenia. Like the Eyes test, the EQ was developed for use in autism-spectrum disorder research. It is a self-report measure that asks participants to rate their skills on a number of areas related to both cognitive and affective empathy (e.g."I am good at predicting how someone will feel"; "I can't always see why someone should have felt offended by a remark"). To control for under-reporting, Bora et al. not only had the psychotic participant complete the questionnaire, but also had a family member complete it separately giving their rating of the participant's ability for each question. The family-rated EQ score showed significant deficits relative to healthy controls while the self-report was milder and did not reach statistical significance. This study highlights the potential limitations of self-report measures in this population.

Despite this potential limitation, there are virtually no studies investigating potential deficits in affective or global empathy using something other than a self-report measure. Very recently Derntl et al.[69] reported deficits in emotion recognition, emotional perspective taking and affective responsiveness in paradigms that required participants to put themselves in the place of actors in a photograph. They showed poor performance relative to controls in all three tasks. Similar to Bora et al., this study also found that their empathy self-report measure underestimated the deficits seen in the computer based tasks.

Thus although deficits in the affective components of empathy are suspected, there has been little research on this question so far, perhaps owing to a lack of paradigms to measure affective and global empathy.

3.2.2 The role of co-morbid psychiatric symptoms in theory of mind impairment in schizophrenia

One area that has received little attention is the role that mood states and comorbid symptoms may play in theory of mind deficits in schizophrenia. This is an important lacune given that non-psychotic symptoms can influence theory of mind performance, and rates of co-morbid symptoms are very high in psychosis.

For example, poor performance on theory of mind measures have been reported in Major Depression[13, 70], Borderline Personality Disorder[71], and some studies of psychopathy[72], but not others[7, 73]. There is also evidence in the theory of mind literature that mood states such as depression can impact theory of mind performance in a non-clinical population[74]. Two recent reports using self-report measures of general empathy found that compared to non-clinical controls, those with alcohol dependence had lower empathy scores [75], and those with the hoarding subtype of OCD showed higher scores [76]. No published work has yet looked at possible theory of mind deficits in anxiety disorders or focused on the effect anxiety may have on theory of mind performance in any population.

Anxiety symptoms are very common in psychotic disorders. Among those with schizophrenia, recent estimates suggest a 30% prevalence for specific anxiety disorders[77]. The rates for sub-syndromal anxiety symptoms are even higher. For example, data from the Epidemiological Catchment Area study found a 45% lifetime rate of panic attacks in those with schizophrenia[78]. Rates of social anxiety co-morbidity have been reported as high as 36%[79].

Symptoms of social anxiety may be particularly germane to theory of mind performance. To begin with, social anxiety is considered a core feature of the broader schizophrenia spectrum known as schizotypy[80]. This notion is reflected clinically in the DSM-IV, which lists social anxiety as a symptom in the DSM-IV diagnostic criteria for schizotypal personality disorder[81]. Secondly, socially anxious people have a cognitive bias towards perceiving others as mocking, critical and judgmental. This expectation of ridicule and

contempt is part of what fuels anxiety and subsequent avoidance of social interactions. Therefore, just as Frith theorized about paranoia, it is possible that the mislabelling of other's mental states found in social anxiety results from problems with theory of mind. Lastly, people suffering from social anxiety tend to have behavioural patterns such as avoiding social situations, making poor eye contact and excessive self-focused attention that interfere with processing social cues[82].

There is currently no published literature examining social anxiety and theory of mind, but there is some preliminary evidence suggesting difficulties with identifying emotions. For example, children with social anxiety disorder are poorer than controls at correctly labelling emotions[83], and studies in adults have shown a greater likelihood of labelling neutral emotions as negative[84].

There is also virtually no indirect information concerning this question in the existing psychosis and theory of mind literature. Some studies have compared the psychosis group to a clinical control group, usually a group of non-psychotically depressed patients [25, 27-31, 33]. However, it is rare that any clinical information regarding depressive or anxiety symptoms are collected or reported. One study using a non-clinical population found that anxiety and depression symptoms were stronger predictors than schizotypal traits of low scores on an empathy self-report[85].

Therefore, despite theoretical reasons to expect anxiety may be a moderating factor in theory of mind performance, no work has yet to investigate this possibility. In particular, social anxiety may be particularly relevant in psychosis.

4.0 Present study – Design and Rationale

This study had two purposes. Firstly, it was a pilot study investigating the potential role of anxiety in theory of mind performance among those with psychosis. It compared a group with psychosis to a group with anxiety disorders and healthy controls on two theory of mind tests and a measure of global empathy. By collecting a range of clinical measures of anxiety and other psychiatric symptoms, it investigated the association of specific symptoms to theory of mind and general empathy deficits.

A second aim of the investigation was to further explore unresolved questions in the theory of mind and psychosis literature. The psychosis group had a full clinical assessment and had remission status assessed based on consensus criteria. This allowed assessment of the role that remission status and residual symptoms play in theory of mind performance. Comparing two theory of mind tasks, one traditional narrative based (Hinting task) and one more naturalistic (the Eyes test), allowed comparison of whether the effect of general cognitive deficits differentially affects performance on each type of measure. Participants also completed the EQ to investigate potential deficits in general empathy and to assess the extent to which performance on it correlates with theory of mind performance.

There were a number of hypotheses:

1. Those with anxiety disorders would perform in an intermediate range to those with psychosis and healthy controls on all measures.
2. Both non-remitted and remitted psychotic participants would show deficits on all measures, however, that the participants with more symptoms would perform worse.
3. In the psychosis group, it was predicted that social anxiety scores would correlate negatively with performance on theory of mind and empathy tasks.

5. Methods

5.1 Participants:

The study sample consisted of 26 participants with psychosis, 27 with an anxiety disorder, and 25 community volunteers. All participants provided written informed consent as approved by the research ethics board of the McGill University Health Centre (MUHC). Clinical participants were drawn from the outpatient department of the MUHC department of Psychiatry and the McGill Student Mental Health clinic. The MUHC provides secondary and tertiary psychiatric care to the urban population of Montreal, Canada. All clinical participants were being actively followed by a psychiatrist.

Participants were recruited through the use of posters announcing the project in the hospital and by invitation from their mental health care provider. Inclusion criteria included age 18-65, ability to read and speak either French or English, and the ability to give consent to participate in the study. Exclusion criteria included current or past diagnosis of a pervasive developmental disorder, history of neurological illness or injury such as traumatic brain injury or stroke, and active heavy substance use. No compensation was provided for participating in the study. Diagnoses were established by consulting with the participant's treating psychiatrist, review of their chart, and by clinical interview by one of the study's psychiatrists (JM). The majority of participants were English speaking; 5 in the psychosis group and 4 in the anxiety group completed the study using materials in French.

Participants in the psychosis group were all recruited from the MUHC Schizophrenia Tertiary Services outpatient program. This included 18 with paranoid schizophrenia, 5 with schizoaffective disorder, bipolar type; 2 with residual schizophrenia, and 1 with undifferentiated schizophrenia. They had varying levels of symptom severity, chronicity, medication doses, and demographic background. All were assessed by the same psychiatrist to determine symptomatic 6-month remission status using recently published criteria [86], and to assess symptom severity using the Positive and Negative Syndrome

Scale (PANSS)[56]. All but one participant took medication, primarily antipsychotic medication. Nine took olanzapine (mean dose 19.44 mg, range 7.5-40 mg), seven patients took risperidone (mean dose 3.2 mg, range 1.5-6 mg), three took clozapine (mean dose 408.33 mg, range 400-425 mg)), one took quetiapine (600 mg), one took zuclopenthixol 40 mg, one took a combination of perphenazine 20 mg and quetiapine 300 mg, one took trifluoperazine 9 mg and risperidone 3 mg, and one took risperidone 1.5 mg and quetiapine 500 mg. Medication data is missing for one subject. Medication dosages were converted to Chlorpromazine units using published criteria [87, 88] for the purposes of the analysis. Additional medications included small doses of anticholinergics (n=3, max dose 5mg/d procyclidine), benzodiazepines (n=3, max dose 2 mg/d lorazepam), anticonvulsants (n=6), antidepressants (n=4), and gabapentin (n=1). Although duration of illness information was not available for all participants, the majority had been ill for more than 10 years, and the shortest duration of illness was 1 year.

Those in the anxiety disorders group were recruited from the tertiary care Anxiety disorders program (n= 9), the MUHC Cognitive-Behavioural Therapy Unit (n=11), and the McGill Student Mental Health clinic (n= 7). Diagnoses were established in the same manner as for the psychosis group. This consisted of 8 with social anxiety disorder, 7 with obsessive compulsive disorder, 6 with generalized anxiety disorder, 3 with panic disorder, and 3 with anxiety disorder not otherwise specified. None had a history of psychosis. Twenty took medications, seven did not. For the most part this consisted of antidepressant medications, although three took low dose antipsychotics (quetiapine 100 mg, olanzapine 2.5mg, risperidone 0.5 mg).

Community volunteers were recruited by posters in the hospital and consisted largely of students and staff from the McGill University Health Centre.

5.2 Procedure:

The testing for each participant was completed in a single session at a dedicated office at the McGill University Health Centre. Each participant completed a series of empathy

measures, the two subtests format of the Wechsler Abbreviated Scale of Intelligence (WASI)[89] as a global measure of IQ and cognitive function, the Beck Depression Inventory II (BDI-II)[90] to assess for depressive symptoms, the Symptom Checklist-90 R (SCL-90)[91] to assess general level of psychopathology, and the Social Phobia Inventory (SPIN)[92] for symptoms of social anxiety.

5.2.1 Empathy measures:

Three different measures were used: the Empathy Quotient (EQ)[9], the Adult "Reading the Mind in the Eyes" test[38], and the Hinting task[28]. All three measures were translated into Quebecois French by a professional translator and then verified by two bilingual native French speakers to ensure coherence and fidelity. The order of presentation for the three tasks was counterbalanced to avoid order effects.

The *EQ* is a 60 item self-report questionnaire that provides a measure of global empathy. It asks participants to respond to questions related to how they feel or perform in various social situations (e.g. "I often find it difficult to judge if something is rude or polite"). 40 items relate to dimensions of cognitive and affective empathy and 20 are control questions which are not scored. It uses a four point Likert scale (strongly agree, slightly agree, slightly disagree, strongly disagree), and participants can score 0, 1, or 2 for each item with a maximum score of 80, and a minimum score of 0. For example, on the example question above, "strongly disagree" would score 2 points, "slightly disagree" would score 1 point, and any other answer would score 0. This measure has been validated in autism spectrum and general populations, and in several languages (including French[93]).

During the *"Eyes" test*, participants view a series of 36 pictures presented on a computer screen. Each picture shows a horizontal rectangle showing only the eyes from photographs of men and women of different ages. Participants are then asked to identify the emotion portrayed in the photo from a list of four options. They are also asked to guess the sex of the subject as a control measure. One point is scored for a correct answer

and zero for an incorrect answer leading to a maximum score of 36, and a minimum score of 0.

In the *Hinting task*, participants listen to a series of 10 social vignettes involving dialogue between two people. At the end of each vignette, they are asked to identify the hidden meaning in remarks made by one of characters. Minor modifications were made to the original Hinting task to adapt it to North American English (e.g. "Cor! Those treacle toffees look delicious." was changed to "Wow! Those Oreo cookies look delicious."). A correct answer scores 2 points. If answered incorrectly, participants are given a more obvious clue and asked again. A correct answer scores 1 point, while an incorrect answer scores 0. There is a maximum of 20 points and a minimum of 0.

5.2.2 Additional Measures and Demographic Information

The two subtest WASI involves two tasks (defining words, and matrix reasoning) that give an estimate of general intellectual ability. This IQ measure was used to control for the potential confounding effects of IQ in performance on the outcome measures.

Demographic information was collected from all participants. Parental social-economic status was assessed using the Hollingshead Two-Factor Index of Social Position[94]. This is a validated measure that uses parental employment and education to estimate socio-economic rank. No attempt was made to match subjects between groups along demographic parameters.

5.3 Statistical Analysis:

Statistical analysis was performed using SPSS 13.0[95]. A power analysis showed that having 25 participants per group, based on standard deviations from previous work (generally 4-5), would be sufficiently powered to detect differences of 4 on the Eyes test at β=0.8. This was also sufficient to detect a clinically meaningful difference of 1.5 on

the Hinting task. It was difficult to calculate for the EQ as the measure had never been used in schizophrenia.

Demographic information across the three groups was compared using a one-way ANOVA for continuous variables and a Chi-square test for categorical data (see table 1). Variables that demonstrated a statistically significant difference were used as covariates in an ANCOVA and regression model for comparisons of the main outcome measures.

A Pearson correlation compared the three theory of mind measures, both collapsed across groups and within each group. An ANCOVA was performed to test for group differences in the three outcome measures controlling for the relevant continuous variables (IQ, age and SES measure). A linear regression model was also constructed for each measure comparing across the three groups. In constructing the models, factors that have been established in previous research as clear factors in influencing theory of mind scores (e.g. gender, presence of psychosis) were entered as the first steps with other candidate factors taken from between group differences in demographic parameters and those factors that showed a moderate or better correlation with the outcome measures. Similarly a regression model was built for each of the clinical groups to look at group specific factors that may explain their performance (e.g. such as PANSS scores in the psychosis group). An ANOVA was used to test the effect of diagnosis within both clinical groups, and remission status in the psychosis group on performance in the outcome measures. An alpha level of 0.05 was used for all statistical tests. Bonferroni comparisons (α=0.05) were used for post-hoc pairwise comparisons. In variables that showed unequal variance between groups, post-hoc pairwise comparisons were done using Tamhane's test (α=0.05) for the continuous variables and Chi Square comparison for the categorical variables.

6. Results

6.1 Demographic and clinical measures

Due to low frequencies of certain groups in the marital and working categories, they were organized into dichotomous groups. The two marital groups were married/common law and single/divorced, and the two work groups were working/student and unemployed/disability. Table 1 presents the demographic variables for the three groups. One way ANOVA and Chi Square analysis showed significant differences between the groups on gender, marital status, education and IQ. Specifically, the psychosis group had more males, was less likely to be married or common law or be working, had fewer years of school and had lower scores on the WASI verbal and spatial subscales. The anxiety and clinical groups did not differ from each other on any demographic measure. One participant in the psychosis group had missing data for the WASI and Social Position Score (SPS).

Table 2 presents means for each group on the general clinical measures. Table 3 presents group means for the clinical measures related to psychosis for those in the psychosis group. An analysis of variance comparing BDI-II, SPIN, and SCL-90 subscale scores by group showed a statistically significant group effect for each measure except the SCL-Hostility subgroup score. As the Levene statistic demonstrated non-homogeneity of variance in some groups, post-hoc tests were run using both Bonferroni and Tamhane test (α=0.05). Both yielded the same result. For all but two SCL-90 subgroups, the anxiety and psychosis groups differed from the control group but not from each other. The anxiety group reported more somatic symptoms than the psychosis or control group, and also reported more obsessive-compulsive symptoms than the psychosis group who in turn reported more than the control group.

There was a number of missing clinical measure data. Due to incomplete responses on the SCL-90, subscale means could not be calculated at all for 1 psychotic participant and only the Somatic, Obsessive-Compulsive, and Interpersonal subscale for another. As the

majority of questions had been answered their total for the positive symptom total was used. There were also 2 from the psychosis group missing BDI data, and missing SPIN data from 4 in the psychosis group, 3 in the anxiety group, and 1 in the control group.

6.2 Performance on theory of mind and empathy tests – between group comparisons

6.2.1 Correlation analysis

Table 4 presents the two tailed Pearson correlations between the three outcome measures. The Eyes test showed a moderate-strong correlation with the Hinting test ($r = .496$, $p<.001$), and a mild-moderate correlation with the EQ ($r =.295$, $p=.004$). The Hinting test and the EQ also showed a mild correlation ($r =.214$, $p=.03$).

Next, two-tailed Pearson correlations analysed the relationship between these three test scores and the continuous demographic and clinical variables. Spearman's rho was used for categorical variables. The Eyes test showed a moderate positive correlation with WASI verbal ($r=.421$, $p<.001$), WASI spatial ($r=0.416$, $p<0.001$), and with years of education ($r=0 .431$, $p<.001$). There was a negative correlation with being single ($\rho=-0.241$, $p=0.033$), male gender ($\rho=-0.364$, $p=0.001$), not working or studying ($\rho=-0.362$, $p=0.001$), SPIN score ($r=-0.316$, $p=0.007$), and the Phobic Anxiety ($r=-0.444$, $p<0.001$), Paranoid Ideation ($r=-0.290$, $p=0.011$), Psychoticism ($r=-0.260$, $p=0.023$), Global Severity Index ($r=-0.234$, $p=0.042$) and Positive Symptom Total ($r=-0.227$, $p=0.045$) scores of the SCL-90.

The Hinting test showed a moderate-strong correlation with the WASI verbal score ($r = .498$, $p=.000$) and years of education ($r=0.477$, $p=0.000$), and a mild correlation with WASI spatial ($r=0.235$, $p=0.04$). There was a negative correlation with being single ($\rho=-0.233$, $p=0.039$).

The EQ showed a positive correlation with years of education (r=.234, p=.039), and a negative correlation with male gender (ρ=-0.362, p=0.001), not working or studying (ρ=-0.224, p=0.049), BDI (r=-0.266, p=0.023) and SPIN score (r=-0.240, p=0.44).

6.2.2 Analysis of variance and covariance

A distribution histogram and Shapiro-Wilk test was used to check for normality of the distribution of each measure. The EQ showed a normal distribution for each group. The Eyes test showed a slight right skew towards higher scores in the anxiety and control group, with the Shapiro-Wilk statistic significant for the control group (0.97, df=25, p=0.045). The psychosis group showed a normal distribution. The Hinting task showed a significant right skew in the anxiety and control groups due to ceiling performance. In the psychosis group there is a bimodal distribution with several participants scoring at ceiling level, and the rest spread in a roughly normal fashion. The Shapiro-Wilk test was significant for all three groups on the Hinting.

As a result, to compare overall group means, a non-parametric test (Kruskal-Wallis) was used for the Hinting test, and parametric tests (ANOVA) for the EQ and Eyes. Parametric tests were run for the Eyes test because the normality violation was slight, Levene's test of homogeneity of variance was not significant, and running the comparison using a non-parametric test yielded the same results. After the initial comparison, an analysis of covariance was used to control for the potential confounding effect of verbal IQ. Verbal IQ was used as the sole covariate due to its importance as a moderating variable in previous research and the strong correlations it showed with the theory of mind measures in the correlation analysis. Also, adding other potential confounders such as age, years of education, or social position score did not change the results.

Table 5 presents the group means on all three outcome measures and the results of the between group comparisons. Figure 1 presents these means in graphic format. The groups differed significantly on the Eyes test, and post-hoc testing showed the psychosis group scored significantly lower than both the anxiety group and the control group. There

was no difference between the control and anxiety groups. In the analysis of covariance, the main effect of group persisted ($F(2, 74)=4.375$, $p=0.016$). However, post-hoc comparisons showed the psychosis group (mean= 24.50, 95% CI: 22.82-26.17) scored lower than the control group (mean=27.95, 95% CI: 26.34-29.57), but was not statistically different from the anxiety group (mean=27.21, 95% CI: 25.69-28.73). There was no difference between the three groups in accuracy of identifying the sex of the person portrayed in the photographs ($F(2,76)= 0.275$, $p=0.794$).

Overall group differences on the Hinting test were not significant (χ^2 $(2,76)=5.5$, $p=0.062$). Paired group comparisons using the Mann-Whitney U test ($\alpha=0.5/3=0.17$) showed a trend ($U=213.5$, $p=0.033$) between the psychosis (mean= 15.92, 95%CI: 14.22-17.63) and both control group (mean=18.36, 95%CI: 17.67-19.05), and ($U=246.5$, $p=0.059$) with the anxiety group (mean=18.22, 95%CI: 17.56-18.88). When the Hinting task was analyzed using parametric tests, it showed a main effect of group that was eliminated when verbal IQ was controlled for.

The groups also differed on the EQ. Post-hoc testing showed both the psychosis group and the anxiety group scored significantly lower than the control group. There was no difference between the psychosis and anxiety groups. These differences persisted following the ANCOVA.

6.2.3 Linear regression models

Linear regression models were constructed for each of the 3 main outcome measures. The enter method was used for each model, with gender, followed by WASI verbal score, and then presence of psychosis entered in successive steps as they had been shown to influence theory of mind performance in previous research. The presence of psychosis variable is a dichotomous variable created to test the effect of having psychosis in the regression model. Any of these factors that did not make a statistically significant contribution to the model were removed. Then, the factors that showed a significant Pearson correlation with the given outcome measure were entered as a block. Any of

these additional factors that were statistically significant were retained to build the final model. For the Eyes test these additional factors included WASI verbal and spatial, being single, male gender, not working, SPIN score, and SCL-90 Phobic Anxiety, Paranoid Ideation, Psychoticism, Global Severity Index and Positive Symptom Total scores. The additional factors for the Hinting test included WASI verbal and spatial, and being single. For the EQ male gender, not working, BDI and SPIN scores were added as potential factors. Table 6 presents the regression models for each of the three outcome measures.

The model for the Eyes test only included the three factors used for each regression: male gender (β_{stand}=-0.236, p=0.03), WASI verbal (β_{stand}=0.347, p=0.001), and presence of psychosis (β_{stand}=-0.253, p=0.027). This accounted for 31.6% of the variance in Eyes test scores (Adjusted R^2 = 0.316). None of the other factors that had a significant correlation made a significant contribution to the model. Tests of collinearity were in the normal range (e.g. lowest tolerance=0.719, highest VIF=1.391, both for the presence of psychosis factor).

Two factors emerged in the Hinting test model: WASI verbal (β_{stand}=0.424, p=0.00), and presence of psychosis (β_{stand}=-0.244, p=0.019). This model accounted for 28.4% of the variance (Adjusted R^2 = 0.284) in Hinting test scores. The effect of gender in the first step was not significant, nor was years of education and being single in the fourth step.

As the anxiety disorder group scored significantly lower on the EQ than the control group, the presence of an anxiety disorder was added in the fourth step in the EQ model. As the effect of WASI verbal in the second step was not significant, it was removed. Three significant factors emerged: male gender (β_{stand}=-0.264, p=0.023), presence of psychosis (β_{stand}=-0.359, p=0.009), and presence of anxiety disorder (β_{stand}=-0.301, p=0.014). This model accounted for19.4% of the variance in EQ scores (Adjusted R^2 = 0.194). Tests of collinearity were in the normal range (e.g. lowest tolerance=0.615, highest VIF=1.626, both for the presence of psychosis factor).

In addition to collinearity testing, one-way ANOVA compared performance on the Eyes and EQ by gender with the psychotic participants removed to further assess whether the effect of gender was overly influenced by the preponderance of men in the psychosis group. Women performed better than men on both the Eyes ($F(1,50)=4.82$, $p=0.033$) and the EQ ($F(1,50)=8.05$, $p=0.007$).

6.3 *Correlates and linear regression models for performance on theory of mind and empathy tests for individual groups*

6.3.1 Psychosis group

The same correlation analysis was repeated for individual clinical groups (see Table 4). Within the psychosis group, the Eyes test showed a moderate correlation with the Hinting task ($r=0.443$, $p=0.012$), while the EQ showed no significant correlation with the other two measures. On the clinical and demographic measures, the Eyes test showed negative correlations with the PANSS negative subscale ($r=-0.474$, $p=0.015$), PANSS Composite score ($r=-0.405$, $p=0.04$), Chlorpromazine equivalents of medication ($r=-0.467$, $p=0.019$), and the Somatic ($r=-0.535$, $p=0.006$) and Phobic Anxiety ($r=-0.496$, $p=0.14$) subscales of the SCL-90. The Hinting task showed a strong positive correlation with WASI verbal ($r=0.500$, $p=0.011$) and years of education ($r=0.478$, $p=0.014$), and negative correlation with the PANSS negative subscale ($r=-0.672$, $p<0.001$), and the PANSS Composite score ($r=-0.526$, $p=0.006$). The EQ showed a negative correlation with the PANSS negative subscale score ($r=-0.457$, $p=0.019$), as well as positive correlations with the Interpersonal ($r=0.442$, $p=0.027$), Hostility ($r=0.441$, $p=0.031$), Anxiety ($r=0.528$, $p=0.008$) and Positive Symptom Distress ($r=0.439$, $p=0.032$) subscales of the SCL-90.

The clinical factors found to correlate with the three outcome measures in each group were added to male gender and WASI verbal to try to develop regression models for each group. The same “Enter” approach was used as for the combined groups wherein gender, then WASI verbal, then the other factors as a block where entered into the model. Due to missing SCL-90 subscale data, the Eyes and Hinting models involved 24 participants

while the EQ model involved 23. Table 7 presents the regression models for the psychosis group.

In the psychosis group the best model for the Eyes test had two factors: SCL-90 Somatic subscale score and PANSS negative subscale score. Although the PANSS negative factor just misses statistical significance, it was included as it improved the model's ability to account for the variance by 9%, to a total of 34.5%. As the Somatic score being significant was a surprising finding, several factors were entered into the model to see if its significance could be explained by collinearity with more theoretically likely variables such as medication dose, PANSS symptom scales, BDI, SPIN or overall SCL-90 symptom burden. None of these factors entered on their own without the Somatic subscale reached significance.

One factor emerged in the model for the Hinting test: the PANSS Negative subscale score, which accounted for 42.9% of the variance in Hinting scores within the psychosis group. The effect of Verbal IQ and years of education were not significant.

The EQ model had two significant factors: SCL-90 Anxiety subscale score, and the PANSS Negative subscale score. These two factors accounted for 57.9% of the variance in EQ scores within the psychosis group (Adjusted $R^2 = 0.579$). The other three SCL-90 subscale scores that had significant correlations (Interpersonal, Hostility and Positive Symptom total) showed moderate collinearity with the Anxiety score, and only Anxiety showed a strong independent contribution to the model.

6.3.2 *Anxiety group*

Within the anxiety group there were no significant correlations between any of the three outcome measures (see Table 3). The EQ showed a moderate negative correlation with age ($r=-0.389$, $p=0.045$), and the Eyes test showed a moderate negative correlation with social position score ($r=-0.395$, $p=0.041$). The Hinting task showed a moderate negative correlation with presence of the diagnosis social anxiety disorder ($\rho= -0.440$, $p=0.017$).

The Eyes model had one factor, Social Position Score (β_{stand}= -0.395, p=0.041), that accounted for 12.2% of the overall variance (R=0.395; R^2=0.122; SE=3.421; df=1,25; F=4.622; p=0.041). For the Hinting task there was no significant factor. There was a trend for the factor of diagnosis of social anxiety disorder (β_{stand}= -0.335, p=0.088) which accounted for 7.7% of the variance (adjusted R^2=0.077). Two significant factors emerged in the EQ model: age (β_{stand}= -0.418, p=0.023) and male gender (β_{stand}= -0.373, p=0.041). These factors accounted for 23.0% of the overall variance (R=0.538; R^2=0.230; SE=11.567; df=2,24; F=4.885; p=0.017). The factor of having a diagnosis of social anxiety disorder had a trend towards significance (β_{stand}= -0.334, p=0.062) and increased the explanatory power of the model by an additional 8%.

6.3.3 Control group

In the control group there was a strong correlation between the Eyes test and the Hinting test (r=0.625, p=0.000), and the EQ showed a moderate negative correlation with male gender (r=-0.443, p=0.026) and BDI score (r=0.433, p=0.031).

For the Eyes test there were no significant factors. For the Hinting task there was a trend for Verbal IQ (β_{stand}=0.393, p=0.052) that accounted for 11.8% of the variance (Adjusted R^2=0.112). A regression model for the EQ was possible(R=0.609; R^2=0.311; SE=8.554; df=2,23; F=6.197; p=0.008). Male gender (β_{stand}=-0.442, p=0.019) and BDI score (β_{stand}=-0.366, p=0.048) predicted 31.1% of the variance (Adjusted R^2 = 0.311). There was a trend for SPIN score (β_{stand}=0.369, p=0.059) which accounted for an additional 8% of the variance.

6.4 Does remission of psychosis influence performance?

To evaluate the effect of remission, the psychosis group was split into a group of remitted (n=10) and non-remitted (n=16) participants. There were no significant differences between the remitted and non-remitted group on any of the demographic variables, nor on

the WASI verbal, BDI-II, SPIN or Anxiety or Somatic subscales of the SCL-90. Table 3 presents group means on the psychosis related clinical measures, and Table 8 presents the group means and group comparisons for the remitted and non-remitted groups as well as the anxiety and control groups on the outcome measures. One-way analysis of variance found a significant effect of group for all three measures. Mean scores for the non-remitted group was lower for every measure. For the Eyes test, post hoc tests showed that the non-remitted group was significantly lower than both the anxiety and control group, while the remitted group did not differ from any group. This pattern was also found for the Hinting test. On the EQ both the remitted and non-remitted groups scored lower than controls but not the anxiety group or each other. Controlling for verbal IQ did not change this finding for the Eyes, however in the EQ the non-remitted group no longer differed from the control group. For the Hinting test, both the overall group effect and group differences disappeared.

6.5 Is there an effect of diagnosis or symptoms in the psychosis group?

Due to low numbers of diagnoses other than paranoid schizophrenia, direct comparisons between different subtypes of psychosis were not possible. An analysis of variance comparing paranoid schizophrenia and non-paranoid schizophrenia revealed no differences in the outcome measures or in any of the other demographic or clinical variables. Similarly, having paranoid schizophrenia showed no significant correlation with any of the outcome measures.

As negative symptoms were such key predictors of performance in all measures, the psychosis group was split into high and low negative symptom groups to see if demographic or clinical differences could account for these strong effects. Participants were placed in the high negative symptom category if their mean PANSS negative symptom subscale score was greater than 2 (i.e. 15 or higher total symptoms). There were significant group differences on the Hinting ($t=2.207$, $df=24$, $p=0.037$) and EQ ($t=2.547$, $df=24$, $p=0.018$), with a trend for the Eyes test ($t=1.847$, $df=24$, $p=0.077$). There were no group differences on any demographic measure, WASI verbal or spatial,

medication dose, BDI, SPIN, Composite PANSS scale, SCL-90 Anxiety or Positive Symptom Total subscales.

As a final way to analyze the relationship between symptoms and theory of mind/empathy, Table 9 shows a matrix of Pearson correlations (two-tailed, $\alpha=0.05$) of the three measures and individual PANSS items in the psychosis group. Only one item, blunted affect, showed a significant correlation for all three measures. Virtually all the items that denote impaired cognition (i.e. disorganization, difficulty in abstract thinking, stereotyped thinking, poor attention, disorientation) showed strong negative correlations with the two theory of mind measures, especially the Hinting test. For the EQ, four items from the negative subscale showed negative correlations (blunted affect, social withdrawal, poor rapport, lack of spontaneity). As an interesting mirror to the regression model, the four General Psychopathology measures related to anxiety (somatic concern, anxiety, guilt feelings, tension) were all significantly positively correlated to EQ score.

7. Discussion

The purpose of this study was to investigate the specific factors that lead people with psychotic disorders to perform poorly on measures of empathy. As expected, the psychosis group showed deficits in measures of theory of mind and global empathy. Those in symptomatic remission exhibited milder deficits, and deficits were most strongly associated with negative symptoms. In addition, the anxiety group showed deficits in global empathy with performance that did not differ significantly from the psychosis group. To my knowledge, this is the first study to find empathy deficits in those with anxiety disorders. Social anxiety was not as strong a predictor variable as hypothesized, however it showed moderate to strong correlations with the Eyes and EQ. These results inform a number of important issues relevant to empathy research in schizophrenia and other psychiatric disorders.

7.1 The impact of paradigm on theory of mind performance

Both measures of theory of mind correlated strongly both overall and in the psychosis and control groups. Although verbal IQ was an important predictor in the regression models for both measures, co-varying out verbal IQ completely eliminated group differences for the Hinting, while with the Eyes test the psychosis and control group remained different. These results partially support the hypothesis that the Eyes test would be less influenced by general IQ deficits than the Hinting. This underlines the importance of developing paradigms to minimize the load on general cognitive functioning, and that this dimension should be taken into consideration when comparing performance between different paradigms.

These measures also differed in that sex was a significant predictor for the Eyes test but not with the Hinting. In the psychosis literature, sex has not typically been found to be a moderating variable in theory of mind performance. However, as it is an emotion identification test, it is likely that performance on the Eyes test in part tests affective empathy skills as well as cognitive. In this way it may be closer to a test of global

empathy than the Hinting task. As they did in this study, women usually score higher on tests of global empathy than men[9], and this may explain why women performed better on the Eyes test. Alternatively, this difference might reflect that there are sex differences in mental state decoding (Eyes) but not in mental state reasoning (Hinting). Two previous studies that compared mental state reasoning vs. decoding in schizophrenia did not comment on sex differences[40, 96]. This is an area worthy of further exploration.

There was no correlation between the Eyes and the Hinting tests in the anxiety group. This may be because the Hinting is too easy a test for this population. In this study, almost all participants in the anxiety and control groups scored at or near the ceiling performance of 20. Even in the psychosis group 14 of 26 participants scored an 18 or better. Ceiling effects not only obscure potential differences in the higher range of performance, but also leads to problems with unequal variances and skewed distributions that make statistical analysis problematic. This skewed data throws into question the validity of several surprising results. For example, because of the skewed distributions and heterogeneity of variance, non-parametric tests had to be used in the between group comparison for the Hinting test. As these tests have less power than parametric ones, it is likely the lack of significant difference between psychosis and the other groups is attributable to using this type of statistic (ANOVA comparison showed psychosis as different from the other groups). This type of distribution does not appear to be a quirk of this study's data as the means and standard deviations are similar to other studies. Other researchers have either not mentioned normality/homogeneity of variance and run parametric tests anyway[14, 59], not reported means or standard deviations at all[96], dichotomized the measure into perfect score/not perfect score and analysed percentages[62], or used it in a longitudinal repeated measures study[49]. This test is probably best suited to compare populations in which pronounced deficits are expected, such as two different groups of psychotic participants or in a longitudinal design. This situation is a good example of the difficulties that arise when using measures with no known psychometric properties or reliability data. Unfortunately this is currently the case with all theory of mind measures.

7.2 The relationship between theory of mind and global empathy

Overall, the EQ showed milder associations with the theory of mind measures than they did with each other. This is not surprising and reflects the fact that this measure captures both cognitive and affective dimensions of empathy. In contrast to earlier studies, evaluating global empathy with a self-report measure did not seem to affect accuracy. Although information from confederates was not collected, the group means for the psychosis group correspond to the means found by the family member report in the Bora et al study[68].

Most interesting were the similarities and differences in the predictors of performance between the theory of mind and empathy measures. Negative symptoms were important negative predictors of performance in all measures. This is consistent with numerous studies in which negative symptoms were linked with theory of mind deficits. However, in contrast to Frith's hypothesis, the connection between negative symptoms and theory of mind was not attributable to general cognitive deficits. Those with high negative symptoms did not have a lower IQ or worse overall severity of psychotic symptoms, yet scored worse on the Hinting and EQ and with a trend to worse on the Eyes.

In the few studies of global or affective empathy, there are conflicting results: one study that also used the EQ found a strong correlation between empathy and negative symptoms[68], while two studies that used different measures did not[66, 69]. In fact, the latter study found those with negative symptoms performed better than those with predominantly positive symptoms in an affective responsiveness task. At this point there are too few studies to say whether negative symptoms are as important for the affective dimension of empathy.

The results from this study form an interesting parallel with studies in the emotion processing literature. Negative symptoms have been consistently linked with emotion processing deficits in schizophrenia[97]. In particular the symptom of flat affect has been linked with emotion recognition dysfunction, wherein psychotic participants with flat

affect do worse on a variety of emotion processing tests, and have poorer social adjustment that those without flat affect[98]. These differences are not accounted for by general cognitive deficits, and the men with flat affect do worse than the women. The present study results mirror these findings. Indeed, the PANSS item "blunted affect" was the only PANSS item that showed a strong correlation with all three measures. In the case of the Eyes test, this overlap could be because it is a sort of hybrid paradigm, considered by some as more of an emotion identification test, despite it being developed as a theory of mind test[99]. However, this does not explain the negative symptom association with a more pure cognitive empathy/mental state reasoning test like the Hinting, or a global empathy measure like the EQ. Perhaps negative symptoms and flat affect in particular, are a phenotypic marker signalling dysfunction in several domains of social cognition.

An interesting difference between the empathy and theory of mind measures was that general cognition had little relation to EQ score. This finding is consistent with the three earlier studies of psychosis and affective or global measures of empathy [66, 68, 69]. It may be that general cognition is less relevant to affective dimensions of empathy. Affective empathy tends to be more automatic requiring less deliberate reasoning and thus perhaps is less dependent on general cognitive functioning. As the EQ evaluates both cognitive and affective dimensions of empathy, the contribution of general cognition may be less pronounced. It is also important to consider that the EQ is a self-report questionnaire, and thus likely less cognitively demanding than the other two performance oriented measures.

7.3 The role of anxiety in empathy performance

Another difference between the theory of mind and global empathy measures is that those with anxiety disorders performed worse than controls only on the measure of empathy. As a group their performance was intermediate between the psychosis group and the control group, and was statistically different from the controls.

A surprising finding was that in the psychosis group, higher anxiety scores were associated with *higher* levels of global empathy. It does not appear this was a chance

finding as this association was noted in both the self-report SCL-90 scores, and clinician-rated PANSS items related to anxiety. It is also not simply a consequence of those with many negative symptoms reporting little anxiety as there was no correlation between negative symptoms and anxiety. This contrasts sharply with both the control and anxiety groups where anxiety symptoms were associated with lower scores. Also, in the theory of mind measures, anxiety symptoms and in particular somatic concerns were associated with poor performance. It is difficult to explain why anxious psychotic patients would express more empathic attitudes. It is possible that anxiety is related to an unmeasured clinical factor such as insight. Replication of this finding with different empathy measures will be important in establishing whether this was a chance or more pervasive finding.

The role of social anxiety in empathy deficits were not as robust as predicted. SPIN scores correlated moderately with the Eyes and EQ, and within the anxiety group, there was a strong negative correlation between Hinting score and the diagnosis of social anxiety disorder (SAD). In regression models, SPIN scores and SAD diagnoses were not statistically significant predictors, however they accounted for 7-8% of the variance in the Hinting and EQ scores within the anxiety group, and for the EQ in the control group. These results are encouraging given that there were only 8 participants with SAD, limiting the power of finding significant effects. Certainly these results are promising enough from this pilot investigation to warrant further investigation into theory of mind deficits and social anxiety.

7.4 The role of remission and specific symptoms in theory of mind performance

As predicted, those with active symptoms performed more poorly than those with remitted symptoms. When the psychosis group was subdivided along this dimension, only the non-remitted group differed significantly from the anxiety and control group on the theory of mind measures. However, the means of the remitted group were much closer to those of the non-remitted psychosis group than they were to the anxiety group or

controls. Dividing the group would dramatically reduce statistical power, and this is likely why the remitted group was not statistically different.

This study did not support Frith's hypothesis that theory of mind deficits would be seen in those with paranoid delusions. Positive symptoms did not correlate strongly with any measure, nor did the specific symptom of delusions from the PANSS. In fact in our sample, those with PANSS item 1 (Delusions) scores >=3, actually had *higher* mean scores than the rest of the group on all measures. Rather, as discussed earlier, negative symptoms were clearly the most important factor in the poor performance on all measures in the psychosis group.

Taken together these findings support the idea that deficits in theory of mind in schizophrenia are both state and trait characteristics[40]. Studies early on in theory of mind and psychosis research tended to study participants in the acute phase of illness and found deficits that disappeared when symptoms remitted. In recent years, studies with stable and remitted outpatients have shown ongoing deficits, particularly in those with residual symptoms. Overall it appears that in the acute phase, deficits are more pronounced and correspond with active positive symptoms, particularly paranoia. In the stable phase, deficits persist in an attenuated form, and are mediated by cognitive and negative symptoms.

Importantly, these ongoing deficits appear to be clinically meaningful. Mental state decoding deficits in particular have been associated with poor social adjustment and functioning. An important question is whether the empathy deficits themselves lead to poorer social functioning, or whether they are simply part of a wider negative symptom deficit syndrome involving problems in multiple areas of social and general cognition. There are so far few studies examining the connection between empathy deficits and real world functioning, and further research is required. More data linking these would add impact to recent efforts to include theory of mind skills as part of a cognitive remediation program for those with schizophrenia in the stable phase[100].

7.5 Strengths and Limitations of the Study

This study was unique in that it is the first to investigate potential deficits in cognitive and global measures of empathy in those with anxiety disorders. It is also the first study to explore the role anxiety symptoms play in empathy performance. It used good clinical assessment of specific symptoms of psychosis and defined remission status based on published criteria. Lastly it used multiple measures of empathy in order to compare and contrast the features of different paradigms.

There were also a number of limitations to this study. While the anxiety and control group was well matched on demographic features, the psychosis group differed on most parameters. This was mitigated by the use of ANCOVA and regression analysis to assess the effect of the different variables. Similarly, the control group was a convenience sample rather than a true community sample. Nonetheless, the mean for the Hinting and Eyes is not substantially different from community norms (28 vs. 26-28 on the Eyes[38], 18 vs. 16.7-19.9 for the Hinting[28]), while that for the EQ was slightly higher (51.6 vs. 45.2[9]). Missing data from the SCL-90 and SPIN may have affected results, particularly on the regression models as those with missing data were excluded from the analysis. Lastly, information on duration of illness was not systematically collected and thus was not available for analysis. This should not have affected our conclusions as this variable has not been shown systematically to be an important predictor of empathy performance.

7.6 Future Directions

An urgent project for theory of mind researchers is to develop and agree on some standardized paradigms. Movement in this direction has already begun[101]. Certainly this task is a difficult one. The concept of theory of mind and affective empathy are fairly easy to define in global terms, but very difficult to operationalize in a specific task. Each of the many paradigms has intuitive appeal for the way it tries to capture and measure theory of mind; however it is likely each are measuring slightly different things. In many ways this is no different than trying to measure a particular dimension of cognition with a

neuropsychological test. No one paradigm can measure "attention" but several measures pooled together likely gives a reasonable approximation. Theory of mind research would benefit greatly from a consensus battery of tests. One approach would be to develop a composite test that combines the features of many tests in the way that the Montreal Cognitive Assessment (MOCA)[102] used pieces of several different dementia screening tools to develop a more robust overall screening instrument. This could include 1st and 2nd order false beliefs, humour, irony, hinting, emotion identification, and both verbal and non-verbal tests to give a more robust overall measure of theory of mind ability. Once this is established important features like psychometric properties, responsivity to change, etc. can be elucidated.

Work on affective dimensions of empathy and schizophrenia is just beginning. Again, a major limitation to further research in this area is the development of paradigms. It is likely there are large overlaps between affective empathy and emotion identification and processing. Given there is already a large body of research and a few standardized tests for emotion processing, further research comparing performance on these measures to paradigms considered to measure empathy would be valuable. In particular, neuroimaging data that compared the activated neural circuitry for each measure would help to better understand the similarities and differences in these related concepts.

Lastly, this study provided some initial evidence for the role of anxiety in theory of mind and global empathy performance. Further research considering both the role of anxiety in psychotic disorders, and in anxiety disorders such as social anxiety disorder are warranted. A particularly interesting study would see a comparison of psychotic participants with and without SAD and a non-psychotic SAD group to compare the relative effects of psychosis and social anxiety on theory of mind performance. Similarly, a replication study focused on anxiety disorders using multiple measures of empathy would add strength to the findings of this study.

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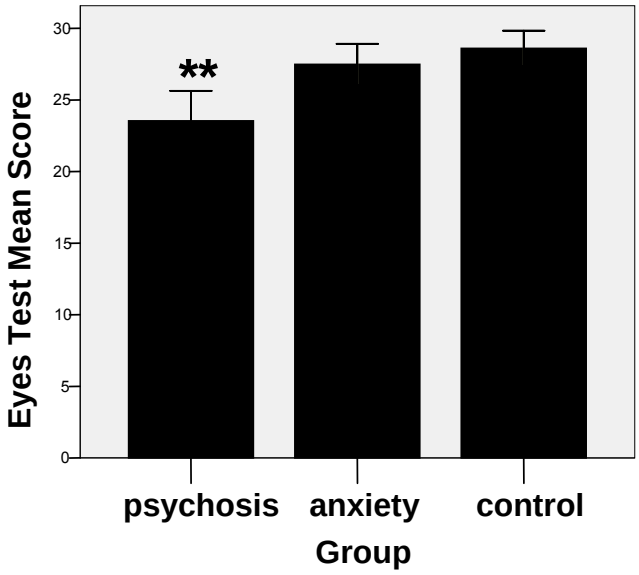
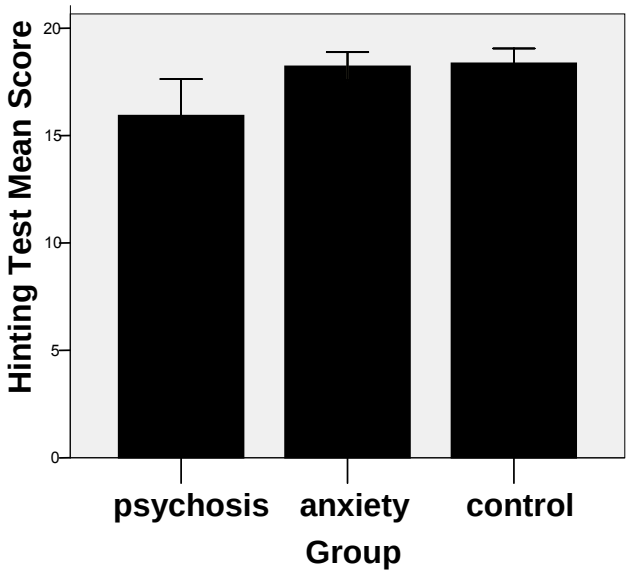
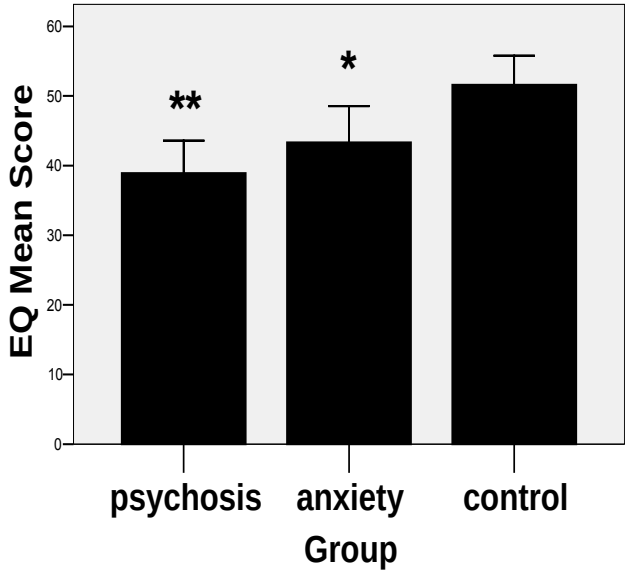
Figure 1 – Theory of mind/empathy scores in the psychosis, anxiety and control groups.





Psychosis group significantly different from the anxiety and control groups (p<.001)



Psychosis and anxiety groups significantly different from controls (p<.001 and .05 respectively)
EQ= Empathy quotient, Error bars show 95% confidence interval
* = post-hoc comparison significant at <0.05, ** = significant at <0.001

Table 1 – Demographic data showing differences between the psychosis group and both the anxiety and healthy control groups

	Psychosis (n=26)	Anxiety (n=27)	Control (n=25)	Test Statistic	p	Post hoc
Mean age (SD)	39.73 (11.76)	32.19 (11.85)	35.20 (11.43)	F(2,75) = 2.79	.068	Non signif
Male sex (%)	23 (88.5)	12 (44.4)	10 (40.0)	χ^2(2,75) = 15.23	<.001	P>A^{++},C^{++}
Martial Status - Married/Common law (%)	1 (3.8)	8 (39.5)	14 (56.0)	χ^2 (2,75) = 16.67	<.001	P<A^{+},C^{++}
Work Status - Working/Student (%)	8 (30.8)	23 (85.2)	22 (88.0)	χ^2(2,75) = 24.80	<.001	P<A^{++},C^{++}
Education Status - Years of school (SD)	13.31 (2.51)	15.44 (1.67)	15.76 (1.56)	F(2, 75) = 11.96	<.001	P<A*,C**
Social Position Score (SD)	27.72 (16.31)	26.0 (13.9)	26.44 (17.19)	F(2, 74) = 0.08	.922	Non signif
- Class I (%)	9 (36.0)	5 (18.5)	10 (40.0)			
- Class II (%)	5 (20.0)	11 (40.7)	6 (24.0)	χ^2(4,72) = 8.39	.399	Non signif
- Class III (%)	4 (16.0)	8 (29.6)	5 (20.0)			
- Class IV (%)	6 (24.0)	3 (11.1)	3 (12.0)			
- Class V (%)	1 (4.0)	0 (0.0)	1 (4.0)			
WASI - verbal raw score (SD)	59.92 (14.78)	66.15 (7.74)	68.28 (8.98)	F(2, 74)= 4.011	.022	Non signif
- spatial raw score (SD)	23.76 (6.48)	27.44 (3.04)	28.84 (4.01)	F(2, 74) = 7.831	.001	P<A*,C*

*Bonferroni test significant<0.05, ** <0.001

$^{+}$ Chi Square test significant <0.05, $^{++}$ <0.001

Table 2 – Means and analysis of variance of the clinical measures by group

	Psychosis [Mean (SD)]	n	Anxiety [Mean (SD)]	n	Control [Mean (SD)]	n	Test Statistic	p value	Post hoc[a]
General Clinical Measures									
- BDI	12.25 (7.60)	24	15.85 (9.06)	27	5.72 (4.78)	25	F(2,73) = 12.35	.000	P*,A**>C
- SPIN	21.18 (14.59)	22	23.16 (15.2)	24	8.54 (7.00)	24	F(2,68) = 9.22	.000	P*,A**>C
SCL-90 Subscales:									
- Anxiety	1.18 (1.00)	24	1.56 (1.04)	27	0.35 (0.48)	25	F(2,73) = 12.56	.000	P*,A**>C
- Phobic Anxiety	0.83 (0.93)	24	0.91 (0.88)	27	0.06 (0.13)	25	F(2,73) = 9.89	.000	P*,A**>C
- Obsessive Compulsive	1.16 (0.71)	25	1.70 (0.74)	27	0.52 (0.56)	25	F(2,74) = 19.41	.000	A*>P*>C
- Dependant	1.00 (0.72)	24	1.54 (0.70)	27	0.47 (0.57)	25	F(2,73) = 16.73	.000	P*,A**>C
- Psychoticism	0.88 (0.77)	24	0.76 (0.52)	27	0.14 (0.30)	25	F(2,73) = 12.50	.000	P**,A**>C
- Paranoid Ideation	0.97 (0.87)	24	0.94 (0.91)	27	0.25 (0.33)	25	F(2,73) = 7.40	.001	P*,A*>C
- Hostility	0.58 (0.64)	24	0.76 (0.75)	27	0.38 (0.48)	25	F(2,73) = 2.31	.106	No diff
- Somatic	0.53 (0.57)	25	1.05 (0.83)	27	0.33 (0.36)	25	F(2,74) = 9.23	.000	A>P*,C**
- Interpersonal	1.16 (0.97)	25	1.33 (0.89)	27	0.44 (0.52)	25	F(2,74)= 8.70	.000	P*,A**>C
- Positive Symptom Distress	1.73 (0.61)	24	1.99 (0.47)	27	1.35 (0.33)	25	F(2,73) = 11.40	.000	P*,A**>C
- Positive Symptom Total	43.69 (21.99)	25	51.70 (19.28)	27	20.84 (16.83)	25	F(2,74) = 17.29	.000	P**,A**>C
- Global Severity Index	0.93 (0.69)	24	1.20 (0.64)	27	0.35 (0.36)	25	F(2,73) = 14.44	.000	P*,A**>C

[a]Post hoc is Bonferroni test (α=0.05), *p<0.05, **p<0.001

Table 3 – Clinical measures specific to psychosis for the remitted, non-remitted and total psychosis group

	Total Psychosis Group (n=26)			Remitted Psychosis (n=10)			Non-remitted psychosis (n=16)		
Schizophrenia Clinical Measures	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range
- PANSS Total Score	50.12	13.90	32-94	39.10	4.46	32-47	57.00	13.36	37-94
- PANSS Positive Subscale Score	11.77	4.74	7-24	8.50	1.84	7-13	13.81	4.88	7-24
- PANSS Negative Subscale Score	14.04	5.55	7-29	10.00	2.87	7-14	16.56	5.37	7-29
- PANSS General Psychopathology	24.31	6.75	16-41	20.60	4.06	16-30	26.63	7.15	16-41
- Medication dose (mg CPZ equivalents*)	355	161.70	0-800	270.00	78.88	150-400	411.67	179.50	0-800
- Anticholinergic medication use	3/26			2/10			1/16		

*Medication doses converted to chloropromazine equivalents as per Woods et al [87]

Table 4 - Pearson correlation matrices showing the relationship between the three outcome measures by group

All Groups Combined

	EQ	Hinting	Eyes
Eyes	0.295*	0.496**	1
Hinting	0.214*	1	
EQ	1		

Psychosis Group

	EQ	Hinting	Eyes
Eyes	0.031	0.443*	1
Hinting	0.297	1	
EQ	1		

Anxiety Group

	EQ	Hinting	Eyes
Eyes	0.312	-0.084	1
Hinting	0.089	1	
EQ	1		

Control Group

	EQ	Hinting	Eyes
Eyes	0.144	0.625**	1
Hinting	-0.118	1	
EQ	1		

* Correlation is significant at 0.05 level (1-tailed)

**Correlation is significant at 0.001 level (1-tailed)

Table 5 – Group means and analysis of variance results on performance on the theory of mind/empathy measures

	Psychosis (n=26)		Anxiety (n=27)		Control (n=25)		Group Comparisons			ANCOVA[b]		
	Mean	SD	Mean	SD	Mean	SD	Test Statistic[a]	P	Post hoc	F	P	Post hoc
Theory of Mind/ Empathy Measure												
- Eyes test	23.54	5.19	27.48	3.65	28.60	3.00	$F(2,75) = 11.04$	<0.001	P<A*,C**	10.66	<0.001	P<C*
- Hinting test	15.92	4.22	18.22	1.67	18.36	1.68	$X^2(2,75) = 5.55$	0.062		10.56	<0.001	Non-signif
- Empathy Quotient	38.92	11.51	43.33	13.18	51.60	10.15	$F(2,75) = 7.67$	0.001	P**,A*<C	4.85	0.004	P*, A*<C

[a] One-way analysis of variance for Eyes and Hinting, Kruskal-Wallis test for Hinting test

[b] Corrected for verbal IQ; n=25 for the psychosis group due to missing WASI data

* Bonferroni test significant at $p < 0.05$, ** <0.001

Table 6 – Linear regression models for performance on theory of mind/empathy measures across psychosis, anxiety and control groups combined

Measure and Predictor	β	t	p	r^2 change	Partial correlation
Eyes Test[a]					
Male Gender	-0.236	-2.209	0.030	0.117	-0.250
Verbal IQ	0.347	3.434	0.001	0.180	0.373
Presence of Psychosis	-0.253	-2.259	0.027	0.046	-0.256
Hinting Test[b]					
Verbal IQ	0.424	4.162	0.000	0.248	0.436
Presence of Psychosis	-0.244	-2.399	0.019	0.054	-0.269
Empathy Quotient[c]					
Male Gender	-0.264	-2.315	0.023	0.130	-0.260
Presence of Psychosis	-0.352	-2.697	0.009	0.030	-0.299
Presence of Anxiety Disorder	-0.301	-2.517	0.014	0.066	-0.281

[a] Model summary: R=0.585; R^2adj=0.316; SE=3.783; F=12.681; df=3,73; p=0.000

[b] Model summary: R=0.550; R^2adj=0.284; SE=2.534; F=16.036; df=2,74; p=0.000

[c] Model summary: R=0.475; R^2adj=0.194; SE=11.394; F=7.193; df=3,74; p=0.000

n=77 for the EQ model, and n=76 for the Eyes and Hinting model due to missing WASI data in one participant

Table 7 – Linear regression models for performance on theory of mind/empathy measures within the psychosis group

Measure and Predictor	β	t	p	r^2 change	Partial correlation
Eyes Test[a]					
SCL-90 Somatic score	-0.438	-2.552	0.018	0.286	-0.478
PANSS Negative Subscale	-0.351	-2.044	0.053	0.114	-0.399
Hinting Test[b]					
PANSS Negative Subscale	-0.672	-4.444	0.000	0.451	-0.672
Empathy Quotient[c]					
SCL-90 Anxiety score	0.854	4.313	0.000	0.279	0.703
PANSS Negative Subscale	-0.525	-4.214	0.000	0.337	-0.695

[a] Model summary: R=0.632; R^2adj=0.345; SE=4.282; F=7.331; df=2,23; p=0.004 (due to missing data n=25)

[b] Model summary: R=0.672; R^2adj=0.429; SE=3.192; F=19.751; df=1,25; p<0.001 (n=27)

[c] Model summary: R=0.785; R^2adj=0.579; SE=7.663; F=16.815; df=2,22; p<0.001 (due to missing data n=24)

Table 8 – Group means, analysis of variance and analysis of covariance of performance on measures of theory of mind and empathy between remitted and non-remitted psychotic participants, anxiety and control groups

	Non-Remitted Psychosis (n=16)		Remitted Psychosis (n=10)		Anxiety (n=27)		Control (n=25)		ANOVA[a]			ANCOVA[b]		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F[+]	P	Post hoc	F	P	Post hoc
ToM/ Empathy Measure														
Eyes test	22.81	5.08	24.70	5.44	27.48	3.65	28.60	3.00	7.84	0.000	NR<A*,C**	4.55	0.006	NR<A*,C**
Hinting test	15.44	5.09	16.70	2.31	18.22	1.67	18.36	1.68	4.58	0.005	NR<A*,C**	1.94	0.131	Non-signif
EQ	38.92	10.47	39.20	13.6	43.33	13.18	51.60	10.15	5.05	0.003	NR*, R*<C	3.77	0.014	R<C*

ToM=Theory of Mind; EQ=Empathy Quotient, R= remitted psychosis group, NR = non-remitted psychosis group, A=anxiety group, C=control group

[a] One-way analysis of variance

[b] Corrected for verbal IQ, F reported as ANOVA from estimated marginal means, n=25 due to missing WASI data

* Bonferroni test significant at $p < 0.05$, ** < 0.01

[+] Degrees of freedom = (3, 74)

Table 9 – Significant correlations between individual PANSS items and performance on theory of mind/empathy tests.

PANSS Item	Eyes	Hinting	EQ
Positive Symptoms			
- Delusions			
- Conceptual Disorganization	-0.532**	-0.429*	
- Hallucinations			
- Excitement		-0.434*	
- Grandiosity			
- Suspiciousness			
- Hostility		-0.431*	
Negative Symptoms			
- Blunted affect	-0.398*	-0.531**	-0.396*
- Emotional withdrawal			
- Poor rapport		-0.526**	-0.489*
- Passive-apathetic social withdrawal			-0.394*
- Difficulty in abstract thinking	-0.444*	-0.529**	
- Lack of spontaneity		-0.510**	-0.428*
- Stereotyped thinking	-0.404*	-0.722**	
General Psychopathology			
- Somatic concern			0.641**
- Anxiety			0.506**
- Guilt feelings			0.630**
- Tension			0.431*
- Mannerisms and posturing			
- Depression			
- Motor retardation			
- Uncooperativeness			
- Unusual thought content			
- Disorientation	-0.475*	-0.478*	
- Poor attention	-0.518**	-0.754**	
- Lack of judgment/insight			
- Disturbance of volition		-0.576**	
- Poor impulse control			
- Preoccupation		-0.603**	
- Active social avoidance			

* Pearson correlation significant at 0.05 (two-tailed)
** Pearson correlation significant at 0.01 (two-tailed)