Theory of mind in individuals with paranoid schizophrenia

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CHAPTER 1

Systematic Review

A systematic review of the evidence for Metacognitive Training for individuals with schizophrenia

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Abstract

The evidence for Metacognitive Training (MCT) for individuals with schizophrenia on positive symptoms and the jumping to conclusions reasoning error was systematically evaluated. Nine studies met the inclusion and exclusion criteria. Overall methodological quality was poor and the majority of studies lacked power to detect differences. The ability to compare studies was negatively impacted by variations in how MCT was delivered, assessed and reported. There is emerging evidence that MCT can reduce positive symptoms. However, the evidence from three studies that fully evaluated this was conflicting, and a meta-analysis indicated a small overall effect size (*d* = 0.29; 95% CI -0.18 – 0.77) and did not provide clear support for the efficacy of MCT. Similarly, there is emerging evidence for the effectiveness of MCT in reducing the jumping to conclusions reasoning error. The evidence from one study for MCT augmented with individual metacognitive therapy was the most promising. The limitations of this review and recommendations for future research are discussed.

Keywords: metacognitive training, schizophrenia, positive symptoms, jumping to conclusions bias.

1. Introduction

1.1 Schizophrenia and social cognition

Schizophrenia is a severe and disabling disorder that disturbs perception, is frequently associated with impaired cognition and emotion, and has pervasive effects on an individual's well-being, psychosocial functioning and life opportunities (NICE, 2010; Tarrier and Wykes, 2004). Social cognition, which refers to the cognitive processes that are involved in perceiving and understanding social situations, particularly the behaviours and intentions of others, is also consistently impaired in individuals with serious mental illness (Fizdon and Reddy, 2012; Penn et al., 2008).

There is as yet no consensus on the number of domains in social cognition, however, in a recent review, Fizdon and Reddy (2012), described five domains consisting of emotion processing, social perception, social knowledge, theory of mind (ToM) and attributional bias. Emotion processing involves the identification of emotions, and also refers to the ability to understand and manage emotions (Fizdon and Reddy, 2012). Social perception refers to the ability to make inferences about social situations, and the ability to discern relevant person-related features related to status, mood state, relationship or veracity (Fizdon and Reddy, 2012). ToM refers to the cognitive capacity to represent one's own and other's mental states, for instance, the ability to infer the intentions, beliefs and opinions of self and others (Brüne, 2005). Attributional bias refers to the negative explanations that individuals generate regarding other people's behaviours and their interactions (Fizdon and Reddy, 2012).

1.2 Interventions

The primary treatment for schizophrenia is antipsychotic medication, however there are a number of limitations associated with their use. These include poor response to first-generation or typical antipsychotic drugs; a high incidence and broad range of side effects to typical and second-generation or atypical antipsychotic drugs; patient resistance; and, problems with medication compliance (NICE 2010). In response to these limitations, and in growing recognition of the importance of psychological processes in psychosis, psychological therapies, psychosocial and social cognitive interventions have been the subject of increased research activity.

The use of Cognitive Behaviour Therapy for psychosis (CBTp) in the treatment of schizophrenia is now well-established (Tarrier and Wykes, 2004). Tarrier and Wykes (2004) reviewed 20 randomised controlled trials (RCTs), and concluded that CBTp was associated with modest effect sizes. In addition to established approaches like CBTp, there is currently a focus on the development of social cognitive treatments for schizophrenia. This reflects the significant social cognitive deficits that have been evidenced in schizophrenia (Penn et al., 2008), but also the fact that they are amenable to intervention (Fizdon and Reddy, 2012). Social cognitive interventions for schizophrenia can be classified according to whether they are targeted (focused on a single social cognitive domain), comprehensive (focused solely on social cognition in the absence of any other psychosocial treatments, and addressing a range of social cognitive impairments within a single treatment modality) or broad-based (addressing multiple social

cognitive domains within the context of other psychosocial treatment) (Fizdon and Reddy, 2012).

Metacognitive Training (MCT), a comprehensive social cognitive intervention, is a group, manualised approach that is delivered across eight sessions. It targets the social cognitive biases that are thought to underpin the formation and maintenance of psychotic symptoms, especially delusions (Moritz et al., 2005; Moritz et al., 2011b). MCT focuses upon general types of reasoning errors including attributional bias, jumping to conclusions (JTC) bias, bias against disconfirmatory evidence, ToM impairments, overconfidence in memory errors, and depressive cognitive patterns (Moritz et al., 2005). It aims to raise awareness in participants of cognitive biases, and how these might relate to psychotic symptoms and negative consequences (Moritz et al., 2011a; Moritz et al., 2011b).

Fizdon and Reddy (2012) recently conducted a review of social cognitive treatments for psychosis. Whilst MCT was amongst the approaches that were reviewed, Fizdon and Reddy (2012) did not conduct a systematic review of the literature and did not consider the methodological quality of included studies. To the best knowledge of the author, there has been no systematic review of the evidence for MCT. The current review seeks to address this gap, and in doing so will evaluate the evidence for MCT for individuals with schizophrenia. Specifically, the review will focus on evaluating the effect of MCT on the positive symptoms of schizophrenia and the jumping to conclusions bias.

2. Methods

2.1 Search Strategy

Mental health related bibliographic databases including Excerpta Medica Database (EMBASE) (via OVID), Medical Literature Analysis and Retrieval System Online (MEDLINE) (via OVID), Cumulative Index to Nursing and Allied Health Literature (CINAHL) (via EBSCO), PsychINFO (via EBSCO), Psychology and Behavioural Sciences Collection (via EBSCO), Web of Science, SCOPUS and the Cochrane Library were searched electronically. The search was restricted to 2005 onwards, which reflected the availability of MCT. The electronic database search employed the following search criteria (please note that search terms are separated by Boolean search operators OR and AND):

(metacog* near/2 train*) OR metacog* OR “cognitive bias” OR “cognitive trap$” OR “social cognition” OR “jumping to conclusions bias”

AND

Schizo* OR psychosis OR “positive symptom$” OR delusion$ OR hallucination$ OR (chronic* near/2 ill*) OR (chronic* near/2 disorder*) OR (sever* near/2 ill*) OR (sever* near/2 disorder*).

Search criteria symbols for truncation symbols, wildcards and adjacent searches were modified according to the database employed. The following journals were hand-searched: Behavioural Cognitive Psychotherapy, Behaviour Research and Therapy, BMC Research Notes (from 2008 only), European Psychiatry, European Journal of Psychotherapy and Counselling, Current Opinion in Psychiatry, Journal of Advanced Nursing, Journal of

Behaviour Therapy and Experimental Psychiatry, Psychological Medicine, Schizophrenia Bulletin and Schizophrenia Research. The electronic database search and hand-search of journals was conducted in May 2013. Search results were initially screened for potential relevance using the title, abstract and keywords of articles. Those articles initially selected were subsequently reviewed in greater detail to determine whether they referred to MCT by accessing the full text of the article where possible. Inclusion and exclusion criteria were subsequently applied.

2.2 Inclusion and Exclusion Criteria

The following inclusion criteria were applied:

- Employs MCT modules
- Intervention targets individuals with a schizophrenia spectrum disorder
- Examines outcome on general psychopathology and/or social cognitive biases
- Any age group
- Published in English

The following exclusion criteria were applied:

- Case studies
- Unpublished studies or books
- Other psychiatric diagnoses

2.3 Methodological Quality

The Clinical Trials Assessment Measure (CTAM) (Tarrier and Wykes, 2004) was employed to assess methodological quality. It is designed to assess methodological quality in psychological trials, and is composed of 15 items grouped into six areas of trial design including sample size and recruitment method, allocation to treatment, assessment of outcome, control groups, description of treatments and analysis. The CTAM shows good blind inter-rater agreement, concurrent validity, and adequate internal consistency (Tarrier and Wykes, 2004). Two reviewers independently assessed the articles, and any disagreement in scoring was resolved by discussion.

2.4 Data extraction

A data form was developed to extract study information including study design, intervention, sample size, outcome measures employed and main results. Effect sizes were reported or calculated using an online effect size calculator (Becker, 2000). Effect sizes are reported as Cohen's *d*, with *d* = 0.2 a small effect, *d* = 0.5 a medium effect and *d* = 0.8 a large effect (Cohen, 1988).

2.5 Method of data synthesis

A qualitative synthesis of the included studies was conducted. There was heterogeneity across studies in the measurement of general psychopathology, however the Positive and Negative Syndrome Scale

(PANSS) (Kay et al., 1987) was the most frequently reported measure. Results on the PANSS positive subscale or on individual items from this subscale were considered. This aspect was selected as MCT targets the social cognitive biases that contribute to the formation and/ or maintenance of schizophrenia, in particular delusions (Moritz et al., 2011b). A meta-analysis of three studies that employed full MCT and provided sufficient data on outcome on the positive PANSS subscale was conducted using software provided by Cumming (2012). The meta-analysis examined the effect size for the difference between intervention and control group on the change in positive PANSS score. MCT focuses upon general types of reasoning errors, however JTC was most frequently assessed and was therefore selected to compare studies. Most studies employed the 'Beads Task' (Garety et al., 1991) or variations of this task to assess JTC. The key variables were the number of beads drawn and whether or not a JTC bias was shown.

3. Results

3.1 Study selection

The search strategy returned 4217 results. An initial screen yielded 494 items, which when de-duplicated, resulted in 451 articles requiring further scrutiny. Articles were further screened by accessing the full text where possible, which led to 22 items being identified. In a parallel process, a hand search of journals returned one new result. Following the application of the inclusion and exclusion criteria, nine studies were considered appropriate for

inclusion. Figure 1 illustrates the article selection process and is based on Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) (Moher et al., 2009).

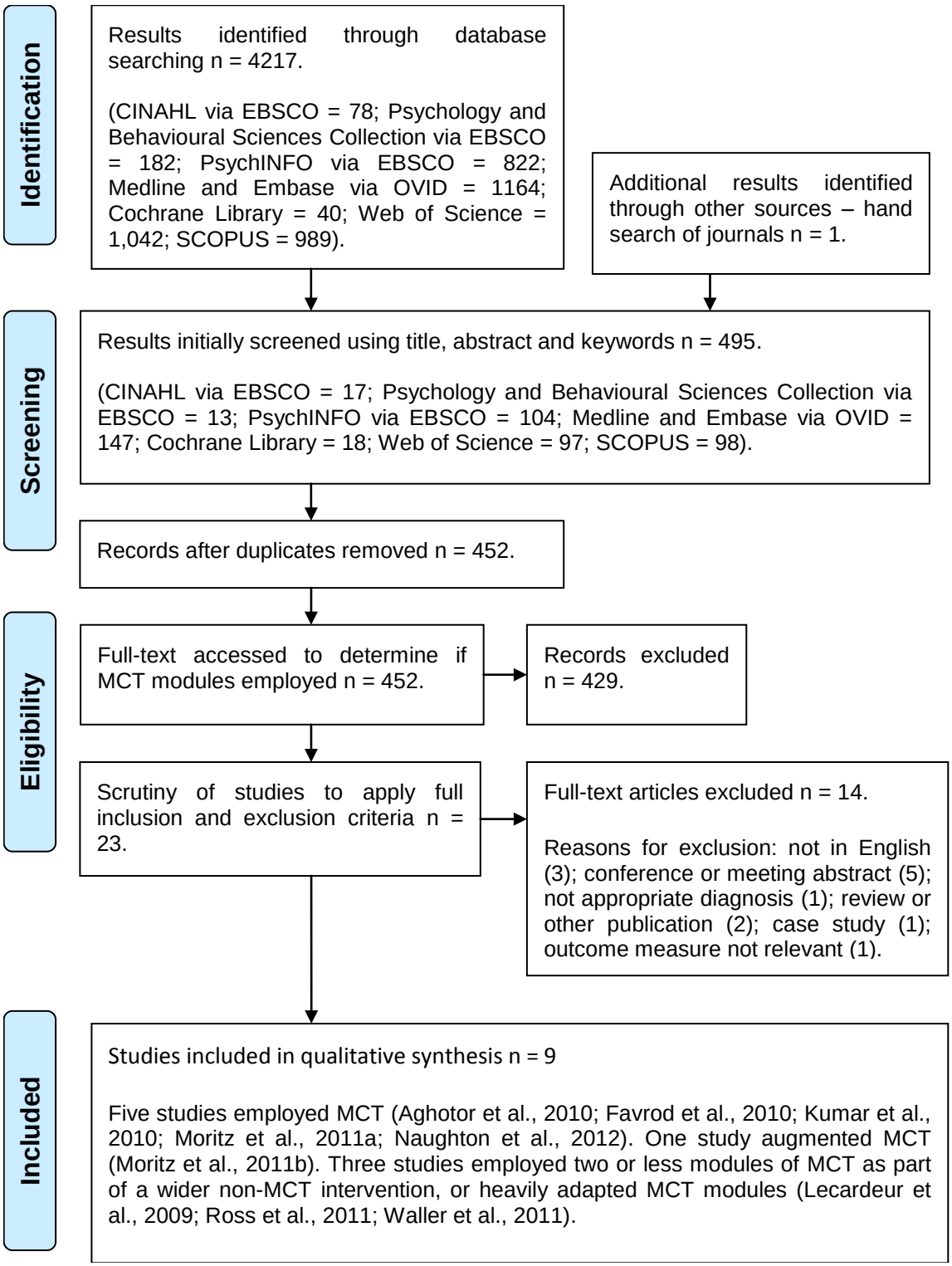

Figure 1: Article selection process.

3.2 Study characteristics

Table 1 provides details of the nine reviewed studies. Seven studies included participants with a schizophrenia spectrum disorder diagnosis. Kumar et al. (2010) specified a diagnosis of paranoid schizophrenia, whilst Naughton et al. (2012) specified a psychotic disorder (including a diagnosis of schizophrenia). Study participants were adults, aged 16 – 65 years. Five studies were RCTs. Five studies employed MCT as described in Section 1.2 (full MCT) (Aghotor et al., 2010; Favrod et al., 2010; Kumar et al., 2010; Moritz et al., 2011a; Naughton et al., 2012). Moritz et al. (2011b) provided MCT and additional individual metacognitive therapy (augmented MCT), whilst three studies incorporated modules of MCT in a wider program or adapted modules of MCT in a wider intervention (modules of MCT) (Lecardeur et al., 2009; Ross et al., 2011; Waller et al., 2011). Across studies, 140 participants received an intervention employing MCT, and data were analysed for 129 of these participants.

3.3 Methodological quality

The CTAM (Tarrier and Wykes, 2004) was employed to evaluate the methodological quality of the studies identified (Appendix 1.1). There was 86.89% agreement across items between two independent raters of the papers, and following discussion to resolve any differences in scoring, 100% agreement was reached. The main areas for discussion were whether the process of randomisation and the methods of rater blinding were adequately described. The median score for the nine studies was 44 (Range 17 – 68).

There was variation in the quality of studies, predominantly in the areas of allocation of participants and use of control groups. CTAM score was used to categorise the methodological quality of studies as ‘very poor’ (0-20), ‘poor’ (21- 40), ‘moderate’ (41 – 60), ‘good’ (61 – 80) and ‘very good’ (81 – 100).

3.4 Synthesis of studies

Studies are considered according to how MCT was employed (Section 3.2) and in order of methodological quality. Table 1 summarises the studies’ methodological quality and key findings.

Table 1: Summary of studies in relation to methodological quality and key findings.

Study	Methodological quality	Design, intervention and sample size	Main results
Full Metacognitive Training Programme			
Moritz et al., 2011a	CTAM: 64/100 Strengths: blinded randomisation; blinded assessments; use of TAU control group. Weaknesses: no active control group; no correction for multiple t – tests.	RCT MCT n = 18 v wait-list group receiving treatment as usual n = 18.	PANSS No significant difference between groups on the change in PANSS positive subscale scores, although a small to medium between group effect was reported (d < 0.38). JTC JTC assessed with computerised variant of the 'Beads Task' (Moritz et al., 2011a). No significant difference between groups in draws to decision score, although a medium effect in favour of the MCT group was reported (*d* = 0.52). No significant difference between groups in the rate of JTC bias between groups, although a small to medium effect in favour of MCT was reported (*d* = 0.45).
Aghotor et al., 2010	CTAM: 52/100 Strengths: active control group. Weaknesses: underpowered; MCT and control group conditions not matched.	RCT MCT n = 16 v active control group n = 14.	PANSS No significant difference between groups on the change in positive PANSS, however an effect in favour of the MCT group was reported (*d* = 0.43, small to medium effect). JTC JTC assessed with BADE procedure (Moritz and Woodward, 2006). No significant difference between groups in pre-post scores of the JTC bias, although a small to medium effect favouring MCT was reported (*d* = 0.31).

Kumar et al., 2010	CTAM: 44/100 Strengths: TAU control. Weaknesses: small sample; no active control.	RCT MCT n = 8 v TAU (pharmacological treatment and ward activities) n = 8.	PANSS No significant difference between groups on the change in PANSS positive subscale score, although a medium to large effect in favour of the MCT group was reported (*d* = 0.68).
Naughton et al., 2012	CTAM: 29/100 Strengths: waiting list control group. Weaknesses: chronological allocation.	Naturalistic cohort study. MCT n = 11 (5 attended all sessions) v waiting list control group n = 8.	PANSS No significant difference in the change scores between groups.
Favrod et al., 2010	CTAM: 21/100 Strengths: used standardised measures. Weaknesses: no control; no blind assessment; no ITT analysis; no reporting of PANSS subscales.	Uncontrolled pilot study MCT n = 24 (18 analysed).	PANSS Uncontrolled within group changes were reported. MCT within group scores decreased significantly on the delusion item (*d* = 1.04, large effect). No significant difference on the hallucinations item (*d* = 0.25).

Augmented Metacognitive Training			
Moritz et al., 2011b	CTAM: 68/100 Strengths: blinded randomisation; blinded assessment; ITT analysis. Weaknesses: idiosyncratic PANSS score.	RCT MCT/MCT+ n = 24 v cognitive remediation program n = 24.	PANSS Authors created a delusional subscale. Significant difference between groups on the PANSS delusion scores in favour of MCT/MCT+ (*d* = 0.66, medium to large effect). JTC JTC assessed with computerised variant of the 'Beads Task' (Moritz et al., 2011a). Significant difference between groups in change scores of the percentage of participants showing the JTC bias in the MCT/MCT+ group relative to control group. A medium effect favouring MCT/MCT+ was reported (*d* = 0.58).
Modules of Metacognitive Training			
Ross et al., 2011	CTAM: 51/100 Strengths: active control group. Weaknesses: general psychopathology outcome not assessed; underpowered.	RCT Reasoning Training Intervention (adapted from MCT) n = 17 v attention control condition n = 17.	JTC JTC assessed with the 'Beads Task'. Intervention effect was examined by estimating the proportional increase in beads drawn. Intervention significantly (p = 0.012) increased the number of beads drawn by 50% compared with the controls.

Lecardeur et al., 2009	CTAM: 22/100 Strengths: TAU control group. Weaknesses: small sample; no random allocation.	Pseudo-randomised controlled trial. Mental State Attribution Therapy (MSAT) (included 2 sessions of MCT) n = 8 v Mental Flexibility Therapy (MFT) n = 8 v TAU n = 8.	PANSS Significant difference between groups on the positive subscale. MFT obtained significantly lower scores than MSAT and TAU.
Waller et al., 2011	CTAM: 17/100 Strengths: limitations acknowledged. Weaknesses: same individual conducted assessment and intervention; no control group; no blinded assessment; underpowered.	A – B design Maudsley Review Training Program (includes one adapted MCT module) n = 14 (13 completed).	JTC JTC assessed with 'Beads Task'. Uncontrolled within group changes were reported. No significant difference in number of beads requested following training within this uncontrolled group, although a small to medium effect was found (*d* = 0.30).

CTAM: Clinical Trials Assessment Measure (Tarrier and Wykes, 2004). BADE: Bias Against Disconfirmatory Evidence procedure (Moritz and Woodward, 2006). ITT: Intention to treat analysis. JTC: Jumping to Conclusions. M = mean. MCT: Metacognitive Training. MCT/MCT+: Metacognitive Training and Individualised Metacognitive Therapy. PANSS: Positive and Negative Syndrome Scale (Kay et al., 1987). RCT: Randomised Controlled Trial. TAU: Treatment as Usual. SD: Standard deviation.

3.4.1 Effect on positive symptoms

Five studies assessed the effect of full MCT on the PANSS. Of these, three studies reported results on the positive subscale (Aghotor et al., 2010; Kumar et al., 2010; Naughton et al., 2012), one study did not differentiate results according to individual PANSS subscales (Moritz et al., 2011a), and Favrod et al. (2010) reported results on individual PANSS items. Moritz et al. (2011b) delivered augmented MCT, and reported an idiosyncratic 'delusion' score. Of the studies employing MCT modules, Lecardeur et al. (2009) used the PANSS to evaluate change, however, Ross et al. (2011) and Waller et al. (2011) employed it as a baseline measure only.

On an individual level most studies did not find significant between group differences when MCT was compared to a control condition. Preliminary evidence suggests that full MCT exerted a small effect on positive symptoms, as assessed by the positive subscale of the PANSS, but that drawing on modules of MCT did not provide any additional benefit over and above treatment as usual. The additional provision of individual MCT was associated with the largest between group effect, which was in the medium to large range (Moritz et al., 2011b).

3.4.1.1 Full MCT

Moritz et al. (2011a) compared MCT to a treatment as usual (TAU) wait-list group in a study that obtained a ‘good’ CTAM score. Insufficient descriptive statistics were provided to report results specifically for the positive subscale.

The authors reported that there were no significant differences between groups on any of the PANSS subscales in terms of change scores, although small to medium between group effect sizes were reported (d < 0.38). It was not clear whether this effect favoured MCT or not, although favourable results for MCT were found on certain items of the Psychotic Symptom Rating Scales (PSYRATS) (Haddock et al., 1999). The study was methodologically robust in terms of employing a control group, blinded randomisation, and assessments being made blind to group allocation. The use of an active control group to control for non-MCT specific effects such as therapeutic contact would have improved this study further.

Aghotor et al. (2010) conducted a pilot RCT, which obtained a 'moderate' score on the CTAM, and was designed to assess the efficacy of MCT versus an active control group. There was no significant difference between groups on the PANSS positive subscale change scores, although a greater attenuation of positive symptoms was noted in the MCT group (d = 0.43, small to medium effect). This pilot RCT was underpowered to detect significant change, and it is possible that the effect described could be due to the non-matched conditions of MCT versus active control group, the former being delivered with increased intensity on a twice-weekly basis compared to the once weekly active control group.

Kumar et al. (2010) conducted a study of 'moderate' methodological quality in which patients were randomly allocated to MCT+TAU or TAU. There was a significant decrease in PANSS positive scores over time, however the group

x time interaction effect was not significant. Despite this, the effect size difference between the two groups was medium to large and favoured MCT (*d* = 0.68). One limitation to this study was the small sample. Additionally, although participants were randomised to group, there was no active control group to control for the non-specific effects arising from an increase in therapeutic contact.

Naughton et al. (2012) explored the effects of MCT for patients with psychosis in a secure forensic psychiatric hospital. This study obtained a 'poor' CTAM score. Participants were allocated to either MCT or a wait-list control group, although this was on a chronological rather than randomised basis. No significant difference was found between groups in the change scores of the PANSS positive subscale, although a small between group effect was found in favour of the control group (*d* = -0.20). The PANSS scores for both groups showed no significant change over time (MCT change score: M = 2.2, SD = 4.9; control group change score: M = 1.3, SD = 3.9). The MCT group had a baseline mean score of 11.4 (SD = 3.7) compared to the controls' baseline mean score of 14.0 (SD = 6.3). One of the limitations to this study was the small sample size, which may lead to missing beneficial or adverse effects.

Favrod et al. (2010) conducted an uncontrolled pilot study, which scored poorly on the CTAM. Twenty-four participants were allocated to MCT, however six were excluded from analysis. The authors only reported scores on individual items of the PANSS. For PANSS positive subscale items there

was significant change on the ‘delusion’ item (*d* = 1.04, large effect), although no significant difference was found on the ‘hallucinations’ item (*d* = 0.25, small effect). No explanation was given for particular items being reported instead of subscale scores. Results must be interpreted cautiously due to the absence of a control group, lack of intention to treat (ITT) analysis and non-blinded assessment.

A preliminary meta-analysis was completed in order to systematically combine the results of studies. Studies that delivered full MCT and reported change on the PANSS positive subscale were included in the meta-analysis. These criteria were applied in an attempt to overcome some of the heterogeneity of studies included in the review. Three studies were included in the meta-analysis (Aghotor et al., 2010; Kumar et al., 2010; Naughton et al., 2012), which delivered full MCT to 35 participants. The meta-analysis was conducted using software provided by Cumming (2012). The combined effect size for these three studies was small (*d* = 0.29; 95% CI -0.18 – 0.77). However, there was no significant effect for MCT versus control as the 95% CI crossed zero. Figure 2 shows the forest plot for these studies. It is of interest that the study with the lowest CTAM rating (Naughton et al., 2012) found negative results pulling the overall effect size down.

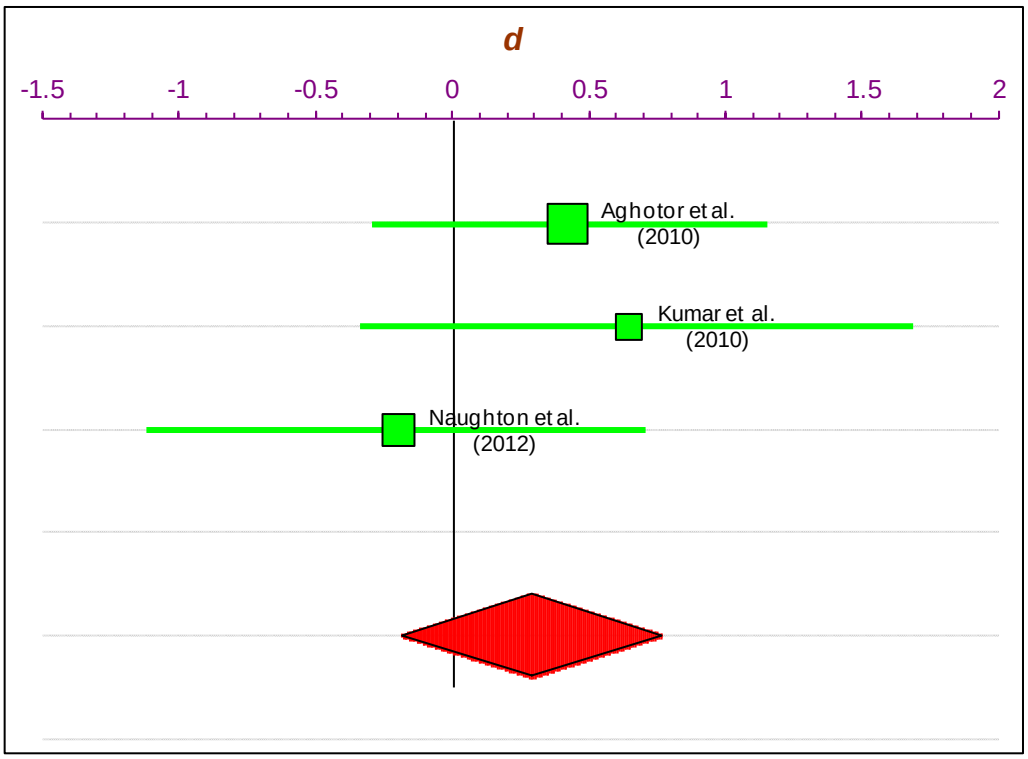

Figure 2: Forest plot of studies using full MCT included in the meta-analysis.

3.4.1.2 Augmented MCT

Moritz et al. (2011b) examined whether a combination of MCT and individual Metacognitive Therapy (MCT/MCT+) exerted an additional effect over an active control group (cognitive remediation training). This study was rated 'good' methodologically, as it employed random allocation of participants, blinded assessment and ITT analysis. However, the main outcome measure for psychopathology was a 'delusional score', composed of the sum of PANSS delusion items from the positive and general psychopathology subscales. Results on this idiosyncratic composite score must be interpreted cautiously as, although it could be argued that targeting change in delusional items is appropriate given the focus of MCT on delusions, there is no data on

the validity or reliability of this particular use of the measure. There was a significant difference between groups on the PANSS delusion scores, with a medium to large effect favouring MCT/MCT+ (*d* = 0.66). The authors also employed three algorithms to calculate positive syndrome scores, although it is difficult to compare results on these algorithms with other studies that reported the positive subscale of the PANSS. All three algorithms indicated medium to large effects in favour of MCT/MCT+ (*d* = 0.59; *d* = 0.66; *d* = 0.77).

3.4.1.3 Modules of MCT

Lecardeur et al. (2009) investigated the impact of two cognitive remediation therapy (CRT) approaches on psychotic symptoms and cognitive complaints versus a TAU control group. This study scored poorly on the CTAM. The first CRT approach targeted mental state attribution (MSAT), with two of eight sessions taken from MCT, whilst the second targeted mental flexibility (MFT). The authors hypothesised that the effect of MSAT on psychotic symptoms would exceed that of MFT, however the contrary was found. A significant difference in PANSS positive subscale scores was reported between the three groups when baseline scores were entered as a covariate, with the MFT group (Estimated Mean EM = 11.62) obtaining significantly lower scores than the MSAT group (EM = 15.57) and the control group (EM = 15.32). There was no significant difference between MSAT and TAU. These results must be interpreted with caution because of the small sample sizes employed and pseudo-randomisation on the basis of availability.

3.4.2 Effect on JTC

Five studies examined the effect of MCT on JTC (full MCT: Aghotor et al., 2010; Moritz et al., 2011a; modules of MCT Ross et al., 2011; Waller et al., 2011). Studies providing full MCT did not find any significant between group differences on the JTC bias or number of draws to decision, although small to medium effects were reported. Ross et al. (2011), using modules of MCT, specifically targeted JTC. Following training, although participants requested more information before making a decision (more draws), the numbers of participants with the JTC bias did not change. Augmented MCT delivered the most promising results (Moritz et al., 2011b).

3.4.2.1 Full MCT

Moritz et al. (2011a) assessed the effect of MCT on JTC using the 'fish task', a computerised and modified variation of the 'Beads Task'. There was no significant difference between groups in the number of draws to decision, however, the results indicated an effect in favour of the MCT group (d = 0.52, medium effect). In terms of the within group change, the MCT group were reported to become more cautious in their decision making behaviour across time (change M = 1.11), whereas the control group showed nearly no change (change M = 0.33). Similarly, there was no significant difference between groups when the JTC bias (defined as a decision after one fish) was examined, although a small to medium effect favouring MCT was reported (d = 0.45). Within group change showed that the rate of the JTC bias was halved in the MCT group (56% to 28%), whereas the decline in the control

group was smaller (50% to 40%).

Aghotor et al. (2010) assessed the JTC bias with the BADE procedure (Moritz and Woodward, 2006). This computerised procedure presents participants with three consecutive and ambiguous pieces of information about a situation. After each presentation of information, participants rate the plausibility of different interpretations on a ten-point scale, and are asked whether they would decide upon one interpretation. A decision after one sentence is judged as JTC bias. No significant difference was found between groups in terms of pre-post scores of the JTC bias, although a small to medium effect favouring MCT was reported (*d* = 0.31).

3.4.2.2 Augmented MCT

Moritz et al. (2011b) examined the effect of augmented MCT on JTC. This was assessed using the same task as Moritz et al. (2011a), although the JTC bias was defined as a decision after one or two fish. There was a significant difference between groups in change scores of the percentage of participants showing the JTC bias in the MCT/MCT+ group relative to controls, and a medium effect favouring MCT/MCT+ was reported (*d* = 0.58). However, the difference between groups may be due to this addition of individual metacognitive therapy to MCT as normal.

3.4.2.3 Modules of MCT

Ross et al. (2011) conducted a RCT that obtained a 'moderate' rating on the CTAM. Participants were allocated to a 45 minute Reasoning Training Intervention (involved three tasks, two adapted from MCT) or an attention control condition (completion of neuropsychological tests). The tasks targeted data gathering, generation and consideration of alternative ideas, and the use of confirmatory and disconfirmatory evidence. JTC was assessed on the 'Beads Task'. The key variable was the number of beads drawn, with the JTC bias defined as requesting two or fewer beads. The effect of the intervention was evaluated by estimating the proportional increase in beads drawn (ratio of beads drawn in the intervention group over the number of beads drawn by controls). The intervention significantly increased the number of beads drawn by 50% compared to the control (point estimate of the ratio = 1.49, p = .012, 95% CI 1.09 – 2.03). However, the numbers of participants with the JTC bias remained consistent, revealing that the amount of improvement was dependent on the baseline measurement. The methodology of this study was strengthened by the use of an a-priori power calculation, the random allocation of participants and adequate description of interventions. However, it would have benefited from a more robust assessment process, for example, employing a rater blind to condition to evaluate outcome.

Waller et al. (2011) examined the effect of the Maudsley Review Training Program (MRTP), which included an adapted MCT module. This study scored very poorly on the CTAM, with a significant weakness being the lack

of a control group. JTC was assessed with the 'Beads Task'. The number of beads drawn before a decision was recorded, and the JTC bias was considered to be a decision after seeing two or fewer beads. There was no significant difference in the number of beads requested following training within the uncontrolled group, although a small to medium effect was found (*d* = 0.30). Participants classified as showing the JTC bias at baseline requested an additional mean of 1.17 (SD = 1.91) beads, whereas those without the bias requested an additional mean of 0.57 (SD = 1.21) beads. The results from this study must be cautiously interpreted as it lacked a control group, employed a small sample and was underpowered to detect change in key outcomes.

4. Discussion

The purpose of this systematic review was to examine the evidence for the effectiveness of MCT for individuals with schizophrenia. The review highlighted sizeable variations in methodological quality across studies and substantial differences in how MCT was provided (e.g. full MCT, augmented MCT, or modules of MCT). These issues are considered in greater detail below in relation to the evidence for MCT.

The methodological quality of studies varied significantly. The overall highest rated study provided augmented MCT (Moritz et al., 2011b), whilst only one of the studies providing full MCT achieved a 'good' CTAM score (Moritz et

al., 2011a). Of the studies using MCT modules, Ross et al. (2011) achieved the highest CTAM score, which was in the 'moderate' category. The areas of strength, for these studies and those achieving a 'moderate' score (full MCT: Aghotor et al., 2010; Kumar et al., 2010), lay in the random allocation of participants, the use of a control group (either TAU or an active control), and a more robust assessment process of the main outcome (e.g. independent assessors, assessment masked to treatment group allocation and/or the use of standardised assessments).

The ratings of all studies, except Ross et al. (2011), were negatively impacted by the use of small samples or the lack of a-priori sample size calculations. For example, sample sizes ranged between 8 - 24 participants per group (Table 1). Moritz et al. (2011b) employed the largest sample, although this still fell short of that required to attract positive ratings on the CTAM. Ross et al. (2011) was the only study to report an a-priori sample size calculation, however the majority of studies were underpowered to detect change.

'Poor' or 'very poor' ratings on the CTAM were received by the remaining studies (full MCT: Naughton et al., 2012; Favrod et al., 2010; modules of MCT: Lecardeur et al., 2009; Waller et al., 2011). In addition to inadequate sample sizes, these studies were weakened by the absence of an independent active control group, lack of randomisation, and weaknesses in

the assessment of the main outcome (e.g. lack of independent assessors, absence of blinded assessment).

In relation to positive symptoms of schizophrenia as assessed by the positive subscale of the PANSS, studies that provided full MCT did not find significant differences between groups when MCT was compared to a control condition. This was the case across studies rated as 'moderate' or 'good', although there was evidence of small to medium (Aghotor et al., 2010; Moritz et al., 2011a), and medium to large (Kumar et al., 2010) effect sizes in favour of MCT. In a preliminary meta-analysis of the most homogeneous studies, only a small effect was found, which did not reach significance. It was possible to include just three studies in the meta-analysis, which is a small number of studies, and the overall effect size reported in the meta-analysis was reduced by the inclusion of the Naughton et al. (2012) study. The Naughton et al. (2012) study was the least methodologically robust study included in the meta-analysis and the only one in this review to be conducted in a forensic setting. It was also the only study delivering full MCT to report negative results, and it may be that the aforementioned factors contributed to this. It attracted lower scores in the allocation and assessment areas of the CTAM. In order to obtain greater clarity regarding the effectiveness of full MCT, further methodologically robust studies are required.

The additional provision of individual metacognitive therapy was associated with the largest between group effect, which fell in the medium to large range (Moritz et al., 2011b). In contrast, Lecardeur et al. (2009) found that MSAT

(which employed modules of MCT) was less effective than MFT (an intervention targeting mental flexibility), which was contrary to the hypothesised direction. This may illustrate the importance of providing full MCT, rather than drawing upon modules of MCT, although this would require further replication.

The effect of MCT on the JTC reasoning error was explored by five studies. Full MCT studies, rated 'moderate' or 'good' methodologically, did not find any significant differences between MCT and control groups in the number of draws to decision or the JTC bias, although small to medium effects were reported (Aghotor et al., 2010; Moritz et al., 2011a). Of the studies that provided modules of MCT, Ross et al. (2011) reported a significant increase in the amount of information that participants requested before making a decision. However, despite specifically targeting JTC, there was no change in the number of participants with the JTC bias after intervention. The Ross et al. (2011) study did not explore outcome on the PANSS, therefore, it is unknown whether this intervention would have led to a general improvement in positive symptoms. When augmented MCT was provided, a significant difference between groups was found in the percentage of participants showing a JTC bias (Moritz et al., 2011b). These results indicate that an individually tailored and intensive intervention, such as augmented MCT, may be required for those individuals who show the severest form of the JTC reasoning error (i.e. meet the criteria for JTC bias). Pre-screening JTC reasoning error severity, for example using the Beads Task (Garety et al.,

1991) to determine whether a JTC bias (decision after a draw of two or fewer beads) is evident, may be helpful in assessing suitability for augmented MCT rather than full MCT.

There was significant variation in the use of outcome measures across studies. Despite the PANSS being the most frequently reported measure of psychopathology, the manner in which it was reported varied significantly. For example, results on individual PANSS items (Favrod et al., 2010), subscales (Aghotor et al., 2011; Lecardeur et al., 2009; Kumar et al., 2010; Moritz et al., 2011b; Naughton et al., 2012) and idiosyncratic composite scores (Moritz et al., 2011b) were reported. This restricted the number of studies that could be directly compared with one another. It may also introduce bias into the literature if items are selectively reported without a justification being provided (Favrod et al., 2010) or if a subscore is developed that has the potential to preferentially assess one intervention over another (Moritz et al., 2011b). As a minimum, results should be reported on the positive subscale to allow comparison between studies.

MCT aims to target a range of social cognitive biases, however, only five studies considered biases, with outcome only assessed in relation to JTC (Aghotor et al., 2010; Moritz et al., 2011a; Moritz et al., 2011b; Ross et al., 2011; Waller et al., 2011). The JTC bias is well studied in psychosis, however, none of the studies justified why this bias was preferentially assessed against others for which standardised measures are also available.

This limits the ability to compare the efficacy of MCT to other social cognitive interventions (Fizdon and Reddy, 2012). Across studies there was variation in how JTC was assessed and the JTC bias determined. Ross et al. (2011) and Waller et al. (2011) employed the 'Beads Task' (Garety et al., 1991). The remaining studies employed different measures, although each argued for similarity to the 'Beads Task'. Aghotor et al. (2010) used the BADE procedure, and reported it as a valid measure of JTC because it maps on to the same JTC parameter as that of the 'Beads Task'. Moritz et al. (2011a) and Moritz et al. (2011b) employed a computerised variant of the 'Beads Task'. They argued that the measure provided similar results to the original task, however they each employed different cut-offs to determine the JTC bias. The ability to compare between studies would have been improved by the use of the same measure.

4.1 Limitations

There was significant heterogeneity across studies in how MCT was delivered, assessed and reported, which restricted the ability to compare studies and limited the studies that could be included in the meta-analysis. It is possible that this heterogeneity reflects the early stage of research within the area. The meta-analysis was conducted in order to try to overcome some of the heterogeneity of studies included in the review by combining evidence across the most similar studies. However, the results should be considered as preliminary and cautiously interpreted as a small number of studies were

included. The meta-analysis could be usefully revisited following the publication of additional studies examining MCT.

Mortimer et al. (2007) proposed that treatment studies should consider outcome as multi-faceted, and that assessment of outcome should focus not only on symptom rating scales, but also encompass meaningful appraisal of cognition, personal, and social functioning. A limitation of this review is therefore the focus on one measure of psychopathology, the PANSS, although this reflects the reviewed studies reliance upon symptom rating scales to assess outcome. Future studies may wish to address this limitation by employing a broader range of measures to assess treatment outcome. The PSYRATS (Haddock et al., 1999) was employed in some studies, and more detailed comparison of the effect of MCT on the PSYRATS may be usefully included in any future reviews. The focus of this review was on examining the evidence for MCT, and as part of this, it would have been of interest to explore the subjective appraisal of MCT. This may be an area for consideration in subsequent reviews.

4.2 Recommendations

Studies could be improved by the use of larger sample sizes. Assuming a medium effect size (*d* = 0.5), an alpha level of .05 and power of 0.80, an a-priori sample size estimation conducted in G*Power3 reveals that 64 participants per group would be required for a two-tailed t-test between two independent groups (Faul et al., 2007). Such sample sizes could be targeted

in future by the development of multi-centre trials. Methodological quality could be improved by the use of active control groups and the random allocation of participants to groups. The addition of individual metacognitive therapy warrants further exploration as results published by Moritz et al. (2011b) appear promising. An interesting avenue for research may lie in examining the effectiveness of augmented MCT versus full MCT or other social cognitive interventions, and in exploring whether any improvement is maintained at follow-up.

4.3 Conclusion

In response to limitations associated with the use of antipsychotic medication in the treatment of schizophrenia, and in growing recognition of the importance of psychological processes in psychosis, psychological therapies, psychosocial and social cognitive interventions have been the subject of increased research activity. MCT is one such intervention, however, further methodologically robust studies are required before it can be firmly established whether or not MCT effectively reduces positive symptoms or improves reasoning in individuals with schizophrenia. As the literature stands at present, there is emerging evidence that MCT can reduce positive symptoms, however, a preliminary meta-analysis was not able to provide clear support for this. A similar picture is also emerging in terms of the effect MCT has on JTC, although this appears to be in the order of a small to medium effect. The additional provision of individual metacognitive therapy

appears promising in terms of its ability to improve positive symptoms and the JTC bias (Moritz et al., 2011b).

If additional methodologically robust studies provide further evidence in support of MCT, then MCT has the potential to inform clinical practice in several ways. MCT could be implemented within in-patient settings in a complementary role to standard treatment programs for individuals with schizophrenia. MCT, delivered as a group intervention, may be more feasibly implemented within such settings as it is less clinician intensive than individualised approaches. As such, it may provide a first step in raising awareness of the social cognitive biases that are thought to underpin the formation and maintenance of psychotic symptoms (Moritz et al., 2005; Moritz et al., 2011b). The additional provision of individualised metacognitive therapy may be more suitable for individuals not wishing to engage in a group intervention, or for individuals who do not benefit from such an intervention. However, as described above, further research is required before MCT can be confidently incorporated into standard treatment programs for individuals with schizophrenia.

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CHAPTER 2

Major Research Project

Theory of mind in individuals with paranoid schizophrenia

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Plain English Summary

Theory of Mind in individuals with paranoid schizophrenia.

Background

Theory of mind (ToM) refers to the ability to represent one's own and other person's thoughts and beliefs. It is impaired in individuals with schizophrenia in comparison to healthy participants. However, the nature of this impairment in individuals with paranoid symptoms is unclear, as some studies have found evidence of impairment and others have not (Brüne, 2005).

Individuals with schizophrenia tend to misperceive emotions, make inflated estimates of the likelihood of future threatening events and pay more attention to threatening stimuli (Kohler et al., 2010; Phillips et al., 2000). ToM can be assessed using tasks that require mental state (i.e. what someone might be thinking or believing) to be deduced from cues (such as eye expressions) or from scenarios (illustrate characters cooperating or deceiving others). These tasks include different emotional content, and it is possible that this might also affect performance given the above tendency to misperceive emotions and attend to threat.

Aim and questions

The aim was to examine whether ToM ability in individuals with paranoid schizophrenia varied according to the emotional content of items within ToM tasks. It addressed three questions:

1. Is there a difference in ToM ability between individuals with paranoid schizophrenia and healthy participants?

2. Is any difference between groups affected by the emotional content of items within the ToM tasks?

3. Are individuals with paranoid schizophrenia more accurate on threat items within ToM tasks?

Methods

All participants were given written information about the study, and informed consent was obtained. The patient group (n = 8) was recruited from in-patient rehabilitation wards and community outreach teams. The inclusion criteria were:

- Diagnosis of paranoid schizophrenia
- Able to provide informed consent
- 16 – 65 years old
- English as first language

- No changes in medication

The group of healthy participants (n = 8) was recruited from a single GP practice. They met the above inclusion criteria, except that they were required to have *no* diagnosed mental health problems. The exclusion criteria applied to both groups included:

- History of traumatic brain injury
- Learning disability
- Active substance dependence

Participants completed two ToM tasks and a measure to estimate pre-morbid intellectual functioning.

Main findings and conclusions

The group of healthy participants performed more accurately than the patient group on ToM tasks, providing further evidence for ToM impairment in individuals with paranoid schizophrenia. On one task, there was a trend towards ToM ability in individuals with paranoid schizophrenia being affected by the emotional content of items. However, this was not in the anticipated direction of those with paranoid schizophrenia more accurately recognising threat emotions. No evidence was found on the second ToM task for the emotional content of the task affecting accuracy. Limitations to the study included small samples that were unmatched for pre-morbid intellectual functioning.

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Abstract

Individuals with schizophrenia show deficits in theory of mind (ToM), however the nature of these deficits in individuals with paranoid symptoms is unclear. This study examined whether ToM ability in individuals with paranoid schizophrenia varied according to the emotional valence of items within ToM tasks. Eight participants with a diagnosis of paranoid schizophrenia (patient group) and eight healthy controls completed two ToM tasks, the revised Eyes Test and a newly developed mental state reasoning task (New ToM Measure). Controls were significantly more accurate than the patient group on both tasks (revised Eyes Test: t (14) = 4.48, p = .001, *d* = 2.24, New ToM Measure: t (14) = 3.63, p = .003, *d* = 1.82). There was evidence of a trend for a mediating role of emotional valence in the patient group on the revised Eyes Test, although contrary to the study's hypothesis, patients were more accurate on positive items than threat items (t (7) = 2.19, p = .07, *d* = 1.01). There was no evidence of a mediating role of emotional valence on the New ToM Measure. This study provides further evidence of ToM deficits in individuals with schizophrenia. The mixed evidence for the mediating role of emotional valence is discussed in relation to existing literature and the study's limitations.

Keywords: theory of mind, paranoid schizophrenia, revised Eyes Test

1. Introduction

1.1 Theory of mind and schizophrenia

Theory of mind (ToM) refers to the cognitive capacity to represent one's own and other person's mental states, and allows an individual to attribute thoughts, beliefs, intentions or feelings to others (Brüne, 2005, Scherzer et al., 2012). A substantial body of evidence demonstrates that this ability is impaired in individuals with schizophrenia versus healthy controls, even when the heterogeneity of tasks employed to assess ToM is accounted for (Bora et al., 2009). Whilst ToM deficits in schizophrenia are well established, contradictory results have been reported regarding ToM impairment in patients in the acute phase of schizophrenia and after remission, in relation to IQ, executive function and memory abilities (Bora et al., 2009). The nature of ToM deficits specifically in patients with paranoid symptoms is also unclear, as some studies have reported impaired ToM capacity, whilst others have failed to confirm this link (Brüne, 2005).

Several different paradigms have been used to assess ToM in schizophrenia. These can be usefully grouped according to mental state reasoning tasks (e.g. assessing false belief, deception and intention understanding, and pragmatic speech comprehension), mental state decoding tasks (e.g. inferring mental states from cues, such as eye expressions), and real-world tasks (e.g. assessing structured interviews) (Bell et al., 2010). It is possible that the inconsistent results in individuals with paranoid symptoms could be related to the nature of these tasks. Support for this was reported by Bora et al. (2009) in a meta-analysis where tasks were

grouped according to whether false belief was assessed using story comprehension or sequencing. The authors found that the distributions of effect sizes were much less heterogeneous for individual tasks compared to combined tasks and total ToM score.

1.2 ToM and paranoid symptoms

A number of cognitive processes are implicated in paranoid symptoms, including disruptions at the neurocognitive and social-cognitive levels, arising from deficits (e.g. poor attention) and/or biases (e.g. a self-serving and personalising bias, and information-processing biases) (Peer et al., 2004). Bentall et al. (2009) conducted an analysis of a range of psychological mechanisms to determine the cognitive and affective processes associated with paranoia, and reported paranoid delusions to be associated with a combination of pessimistic thinking style (low self-esteem, pessimistic explanatory style, and negative emotion) and impaired cognitive performance (executive functioning, tendency to jump to conclusions), and ability to reason about the mental states of others.

Individuals with schizophrenia are less accurate, relative to healthy controls, in recognising facial emotions (Kohler et al., 2010). Interestingly, individuals with schizophrenia have been reported as over-attributing disgusted expressions and under-attributing happy expressions to neutral cues (Kohler et al., 2003), whilst a tendency to misperceive emotions (including happy, sad, fear and surprise emotions) as disgust rather than anger has been

reported in individuals with paranoid symptoms (Peer et al., 2004). This has been assessed using stimuli that consist of facial expressions that represent a range of emotions including happy, sad, angry, disgust or neutral (Kohler et al., 2003; Peer et al., 2004).

The 'Reading the Mind in the Eyes' task (Baron-Cohen et al., 2001), which is similar to the paradigm described above, is contended to be an advanced ToM test because the stimuli consist of only pictures of the eyes (Bell et al., 2010). It measures the ability to identify cognitive emotions that require inferences about others' beliefs or intentions (e.g. being embarrassed or pensive). Cognitive emotions can be distinguished from 'basic emotions', which do not require this kind of inference (e.g. happy or disgusted) (Craig et al., 2004). Craig et al. (2004) reported a poor performance on the Eyes Test by individuals with a diagnosis of paranoid schizophrenia. However, no information was provided regarding whether performance varied according to the direction of emotion (e.g. positive, negative, and neutral) included in the Eyes task.

In addition to a tendency to misperceive emotions, paranoid patients appear to make inflated estimates of the likelihood of future threatening events (Bentall et al., 2009), and demonstrate heightened attention to threatening stimuli (Bentall and Kaney, 1989; cited in Phillips et al., 2000). For example, in an emotional Stroop test, a significantly greater amount of time was required for paranoid individuals to name the print colours of threatening versus depressive and neutral words (Bentall and Kaney, 1989; cited in

Phillips et al., 2000). Many of the mental state reasoning ToM tasks involve the deception of characters. For example, Frith and Corcoran's (1996) False Belief and Deception Story (FBDS) task, commonly employed in schizophrenia research, involves six ToM stories (first-order and second-order) being read to subjects, of which four involve a character being deceived and centre around a theme of stealing. Performance on ToM tasks are not generally considered in relation to the specific emotional content of the task, and it is unclear whether this could be a factor affecting an individual's performance.

Abdel-Hamid et al. (2009) used a five-factor model of the Positive and Negative Syndrome Scale to explore the association of symptom clusters and individual symptoms with ToM ability in schizophrenia. Contrary to their expectations, the authors reported that there was no significant association of positive symptoms and impaired ToM. Unexpectedly, there was a significant interaction of impaired ToM with items included in the 'emotional distress factor'. For example there were significant inverse interactions, all largely independent of IQ or executive functioning, between ToM deficit and the items ‘tension’ and ‘depression’, with decreasing symptom severity on these items associated with better ToM performance. A strong positive interaction between ToM and ‘guilt’ was also found, with participants exhibiting increasing symptom severity achieving greater accuracy on the ToM task. It is possible that several methodological factors could have contributed to these results, including that there was a relatively heterogeneous clinical sample that included a range of both positive and

negative symptoms. In addition, a single measure of ToM was employed.

The ToM task employed by Abdel-Hamid et al. (2009) was Brüne's (2003) Picture Sequencing Task, which comprises picture stories with questions to assess a range of false beliefs, reciprocity, deception and cheating detection (Bell et al., 2010). It is possible that the differing emotional content (e.g. neutral stories and stories involving deception) within this ToM task might have affected performance given the evidence regarding the tendency of individuals with paranoid schizophrenia to attend to threatening stimuli and misperceive emotions (Bentall et al., 2009; Peer et al., 2004).

1.3 Theoretical frameworks

A number of different theoretical frameworks have been proposed in order to account for ToM deficits in schizophrenia. For example, Frith (1992) proposed that positive and negative symptoms in schizophrenia can be accounted for by abnormalities in brain function and circuitry that give rise to the individual's failure to monitor their own and other persons' mental states and behaviour (Brüne, 2005). In contrast, Hardy-Baylé et al. (2003), has proposed that ToM impairments in schizophrenia are primarily related to an executive or planning deficit. Evidence in support of Frith's (1992) and Hardy-Baylé et al.'s (2003) conceptualisations has been mixed (Brüne, 2005; Abdel-Hamid et al., 2009), for example, contrary to Frith's prediction, individuals in remission have also shown ToM impairments relative to non-clinical controls (Bora et al., 2009). This suggests that ToM deficits may be 'trait' rather than

'state' impairments that is, enduring characteristics of the disorder versus being linked to the presence of symptoms (Bora et al., 2009).

An alternative approach to that of Frith (1992) and Hardy-Baylé has been outlined by Gumley (2010). Gumley (2010) has proposed that ToM impairments are rooted in compromised normative developmental pathways, characterised by negative interpersonal experiences (e.g. lack of secure base and/or the presence of relational trauma and loss during childhood and adolescence), which reduce an individual's ability to develop skill in representing one's own and other persons' mental states. Gumley (2010) observes that in schizophrenia, affect regulation strategies tend towards minimising affect and affect laden memories, and that this in combination with ToM deficits may contribute to understanding the development and maintenance of negative symptoms, disorganisation and vulnerability to relapse.

The theoretical frameworks proposed by Frith (1992) and Hardy-Baylé et al. (2003) are limited in their ability to account for the direction of the above findings, for example the tendency to misperceive a range of emotions as disgust. Clarifying whether ToM ability varies according to the emotional content of the specific items of a ToM task could contribute to explaining the inconsistencies that have been reported in the literature, and also contribute to a greater understanding of the theoretical frameworks that attempt to account for ToM impairments in individuals with schizophrenia.

1.4 Aim

To examine whether ToM ability in individuals with paranoid schizophrenia varies according to the emotional valence of items within ToM tasks.

1.4.1 Hypotheses

The research will address several hypotheses including:

- There will be a significant difference in ToM ability in individuals with paranoid schizophrenia compared to controls.
- There will be a significant difference in ToM ability in individuals with paranoid schizophrenia compared to controls, but this will be mediated by the emotional valence of items within the ToM tasks.
- Individuals with paranoid schizophrenia will show greater accuracy on items within ToM tasks that include an element of threat versus items that have no threat.

Additionally, the research will explore the types of errors made by participants.

2. Methods

2.1 Participants

2.1.1 Inclusion and exclusion criteria

The patient group was recruited from NHS Greater Glasgow and Clyde psychiatric rehabilitation wards and rehabilitation outreach teams. The

inclusion criteria for the patient group were: a diagnosis of paranoid schizophrenia; ability to provide informed consent; between 16 and 65 years of age; English as a first language; and, no changes in medication during the study period. The exclusion criteria were a history of traumatic brain injury, learning disability or active substance dependence. The control group was recruited from patients attending appointments at a single GP practice in Glasgow. The inclusion criteria for the control group were similar, except that they were required to have *no* diagnosed mental health problems. The same exclusion criteria were applied to the control group.

2.2 Measures

The Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962) was employed to assess general psychopathology in the patient group. The psychometric properties of the BPRS have been reported as adequate (Kopelowicz et al., 2008). All participants completed the Wechsler Test of Adult Reading (Wechsler, 2001), which provided an estimate of pre-morbid intellectual functioning.

Two tasks were employed to assess ToM. The first was the revised Eyes Test (referred to as the Eyes Test) (Baron-Cohen et al., 2001) available online from the Autism Research Centre (http://www.autismresearchcentre.com/arc_tests). The task involves the attribution of the relevant mental state from photographs of the eye region of faces by making a forced choice between four words (the target word and three distracters) for a total

of 36 items. It has good discriminant validity, and has consistently shown that participants with schizophrenia perform worse than controls (Bell et al., 2010). Outcome on the full Eyes Test was total score calculated as a percentage. A pilot was conducted to identify items for the positive condition and threat condition using a similar procedure to Harkness et al. (2005) (Appendix 2.0). Twelve threat items and eight positive items were identified. The maximum achievable score was twelve for threat items and eight for positive items. Percentage accuracy scores were used to assess performance and to allow comparison between valence conditions.

The second ToM task was developed as part of this study and was based on the Picture Sequencing Task (PST) (Brüne, 2003), which was kindly made available for use by its author. An initial measure was piloted on a small convenience sample (Appendix 2.1). The New ToM Measure consists of a neutral practice item, three scenarios employing a threatening theme, and three scenarios employing a positive theme, each represented by four photographs. The task involves a sequencing component and questions to assess understanding of first-order and second-order belief and false belief; third-order false belief, reciprocity, deception and cheating detection (i.e. one character's detection of another character's intention to deceive them). The total score that can be achieved on the test is 60 and overall scores on the measure were calculated as a percentage. Percentage accuracy scores were used to assess performance according to valence conditions. An example item is provided in Appendix 2.2, and the manual in Appendix 2.3.

2.2.1 Recruitment Procedure

Participants in the patient group were referred to the study by members of their healthcare team. A psychiatrist applied inclusion and exclusion criteria and determined capacity to consent. Participants in the control group opted-in to the study after reading the participant information sheet at their GP Practice. Written informed consent was obtained from each participant.

2.2.2 Research Procedure

Study tasks were administered in a single interview of approximately 30 minutes duration. The Eyes Test was administered in paper format, and in accordance with the procedures outlined in the manual (Baron-Cohen et al., 2001). For each set of eyes, participants were asked to select which word best described what the person in the picture was thinking or feeling.

The New ToM Measure was administered in a similar manner to the PST (Brüne, 2003). The administration process is described in the manual (Appendix 2.3). Briefly, participants were requested to place four photographs in a logical sequence, and then asked a series of questions in the form “what does X believe Y intended to do?”. The RAND function in EXCEL Microsoft Office 2007 was used to randomise the order of photograph presentation within each item and to counterbalance the order with which the three threat items or the three positive items were presented.

The WTAR (Wechsler, 2001) was administered to all participants in accordance with manual instructions. It is composed of 50 words with irregular pronunciations that participants are requested to read aloud. The BPRS was completed in consultation with each patient's named nurse in a separate meeting.

2.3 Design and sample size calculation

A mixed design was employed with Group as between-subjects (patient and control) and emotional valence as within-subjects (positive and threat). Accuracy, defined as the percentage of items where the participant provides a correct response, was the dependent variable. A sample size calculation was conducted for the main comparison of interest, whether there is a significant difference between accuracy on positive items and accuracy on threat items in individuals with a diagnosis of paranoid schizophrenia. Harkness et al. (2005), in a study of dysphoric college students, reported descriptive statistics for positive and negative items in the Eyes Test. These statistics were used to calculate the effect size for the difference in scores between positive and negative items (Cohen's d = 0.74). A sample size calculation for an ANOVA (repeated measures, within-between interaction) with an effect of d = 0.70, α of .05 and power of 0.80, revealed that a total sample of 24 was required (Faul et al., 2007).

2.4 Ethics

NHS Greater Glasgow and Clyde West of Scotland Research Ethics Service (WoSRES) confirmed favourable ethical opinion on 17th April 2012 (Appendix 2.4), and NHS Greater Glasgow and Clyde Research and Development (NHS R&D) approved the project on 18th January 2013 (Appendix 2.5). A major amendment to facilitate recruitment to the control group was approved by WoSRES on 3rd June 2013 (Appendix 2.6) and by NHS R&D on 7th June 2013 (Appendix 2.7).

3. Results

3.1 Analyses

Assumptions of normality and homogeneity of variance were met, therefore parametric tests were employed. Analyses included all participants unless otherwise specified. Effect sizes were calculated using an online effect size calculator (Becker, 2000) or formula 4 provided by Thalheimer and Cook (2002). They are reported as Cohen's *d*, and have been interpreted as small if $d = 0.2$, medium if $d = 0.5$ and large if $d = 0.8$ (Cohen, 1988).

3.2 Participants

3.2.1 Sample

Seventeen participants were referred to the patient group, and of these nine declined to participate. The eight participants in the control group opted-in to

the study, and it was not possible to monitor the number that declined to participate. Participant demographics are reported in Table 1. The mean age of participants was 40.13 years (SD = 11.15). There was no significant difference between groups in age (t (14) = -1.39, p = .19) or gender (Fisher's Exact Test, p = .72). However, controls scored significantly higher on the WTAR than patients (t (13) = 2.78, p = .021). In the patient group, the mean BPRS score was 46.38 (SD = 16.90).

Table 1: Participant Demographics.

	Control (n = 8)	**Patient** (n = 8)
Gender	6 Female, 2 Male	2 Female, 6 Male
Age	M = 36.38 (SD = 13.63)	M = 43.88 (SD = 6.98)
WTAR*	M = 104.86 (SD = 12.19)	M = 87.25 (SD = 12.33)
BPRS	**	M = 46.38 (SD = 16.90)

*p < .05, n = 15, M = mean; SD = standard deviation; WTAR = Wechsler Test of Adult Reading (Wechsler, 2001); BPRS = Brief Psychiatric Rating Scale (Overall and Gorham 1962); **patient group only.

3.3 Theory of Mind tasks

3.3.1 Overall accuracy

Overall accuracy on the two ToM tasks was examined separately for each task (Table 2). The dependent variable was the total expressed as a percentage of the maximum achievable score on each task. There was a significant difference between groups in overall accuracy on the Eyes Test (t (14) = 4.48, p = .001), with the control group (M = 76.39, SD = 10.50) more accurately attributing the mental state of a person than the patient group (M

= 49.65, SD = 13.23) (*d* = 2.24, large effect). A similar result was found for the New ToM Measure, with the control group (M = 76.67, SD = 21.44) achieving greater accuracy on the task than the patient group (M = 44.79, SD = 12.55) (t (14) = 3.63, p = .003, *d* =1.82, large effect). Table 2 provides mean accuracy scores.

Table 2: Means, standard errors and 95% Confidence Intervals for overall accuracy on the Eyes Test and New ToM Measure.

				95 % Confidence Interval	
Task	**Group**	**Mean**	**Standard Error**	**Lower Bound**	**Upper Bound**
Eyes Test	Control	76.39	3.71	67.61	85.17
	Patient	49.65	4.68	38.59	60.72
New ToM Measure	Control	76.67	7.58	58.75	94.59
	Patient	44.79	4.44	34.30	55.28

3.3.2 Performance according to emotional valence

3.3.2.1 Eyes Test

An ANOVA with Group (Control or Patient) as a between-factor and Valence (Threat or Positive) as a within-factor was conducted. The dependent variable was accuracy, defined as the percentage of items for which a correct response was given. Table 3 shows the mean accuracy scores for controls and patients according to the valence of items on the Eyes Test.

Table 3: Means, standard errors and 95% Confidence Intervals for accuracy on the Eyes Test according to valence.

				95 % Confidence Interval	
Group	**Valence**	**Mean**	**Standard Error**	**Lower Bound**	**Upper Bound**
Control	Positive	75.00	3.34	67.84	82.17
	Threat	74.99	7.26	59.44	90.56
Patient	Positive	62.50	3.34	55.34	69.67
	Threat	42.70	7.26	27.14	58.27

There was a significant main effect of group (F (1, 14) = 12.46, p = .003), with participants in the control group (M = 74.99, SE = 4.49, 95% CI 65.38 – 84.62) performing with greater accuracy than participants in the patient group (M = 52.60, SE = 4.49, 95% CI 42.98 – 62.23) (*d* = 1.89, large effect). A marginally non-significant difference was found for the main effect of Valence (F (1, 14) = 4.16, p = .06), although a medium sized effect was calculated (*d* = 0.55). The mean accuracy for positive items was 68.75 (SE = 2.36, 95% CI 63.68 – 73.82) compared with a mean accuracy for threat items of 58.85 (SE = 5.13, 95% CI 47.85 – 69.86). The interaction effect for Group x Valence was similarly marginally non-significant (F (1, 14) = 4.16, p = .06). Figure 1 illustrates that accuracy on positive items and accuracy on threat items was essentially unchanged in the control group (M difference = .00, SD = 9.96), whilst in comparison the mean difference for the patient group was 19.80 (SD = 25.57). The difference in patients' accuracy comparing positive to threat items indicated a trend that did not quite meet significance (t (7) = 2.19, p = .07), although a large effect was found (*d* = 1.01).

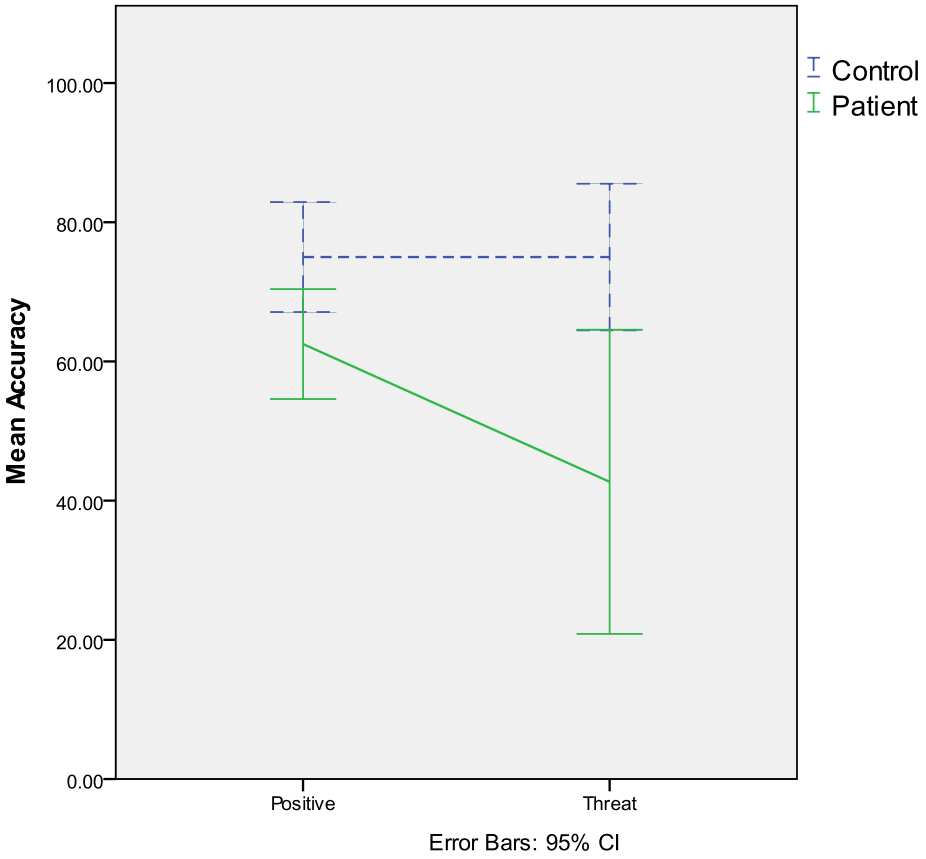

Figure 1: Mean accuracy on the Eyes Test of controls and patients according to valence. The control group is illustrated with a dashed line. Error bars represent 95% confidence intervals.

3.3.2.2 New ToM Measure

An ANOVA with Group (Control or Patient) as a between-factor and Valence (Threat or Positive) as a within-factor was conducted. The dependent variable was accuracy, defined as the percentage of items for which a correct response was given. Table 4 provides mean accuracy scores on the New ToM Measure for controls and patients according to valence.

Table 4: Means, standard errors and 95% Confidence Intervals for the New ToM Measure.

				95 % Confidence Interval	
Group	**Valence**	**Mean**	**Standard Error**	**Lower Bound**	**Upper Bound**
Control	Positive	79.17	6.89	64.40	93.94
	Threat	76.04	7.23	60.53	91.56
Patient	Positive	45.83	6.89	31.06	60.60
	Threat	47.92	7.23	32.40	63.43

There was a significant main effect of Group ($F (1, 14) = 12.14$, $p = .004$), with participants in the control group (M = 77.61, SE = 6.24, 95% CI 64.23 – 90.98) performing with greater accuracy than the patient group (M = 46.87, SE = 6.24, 95% CI 33.50 – 60.25). A large effect was calculated that favoured the control group ($d = 1.32$). However, no significant difference was found for the main effect of Valence ($F (1, 14) = .01$, $p = .91$) (Positive M = 62.50, SE = 4.87, 95% CI 52.06 – 72.94; Threat M = 61.98, SE = 5.11, 95% CI = 51.01 – 72.95) ($d = 0.03$) or the Group x Valence interaction ($F (1, 14) = .31$, $p = .59$). Figure 2 illustrates the mean accuracy of control and patient groups on positive and threat items.

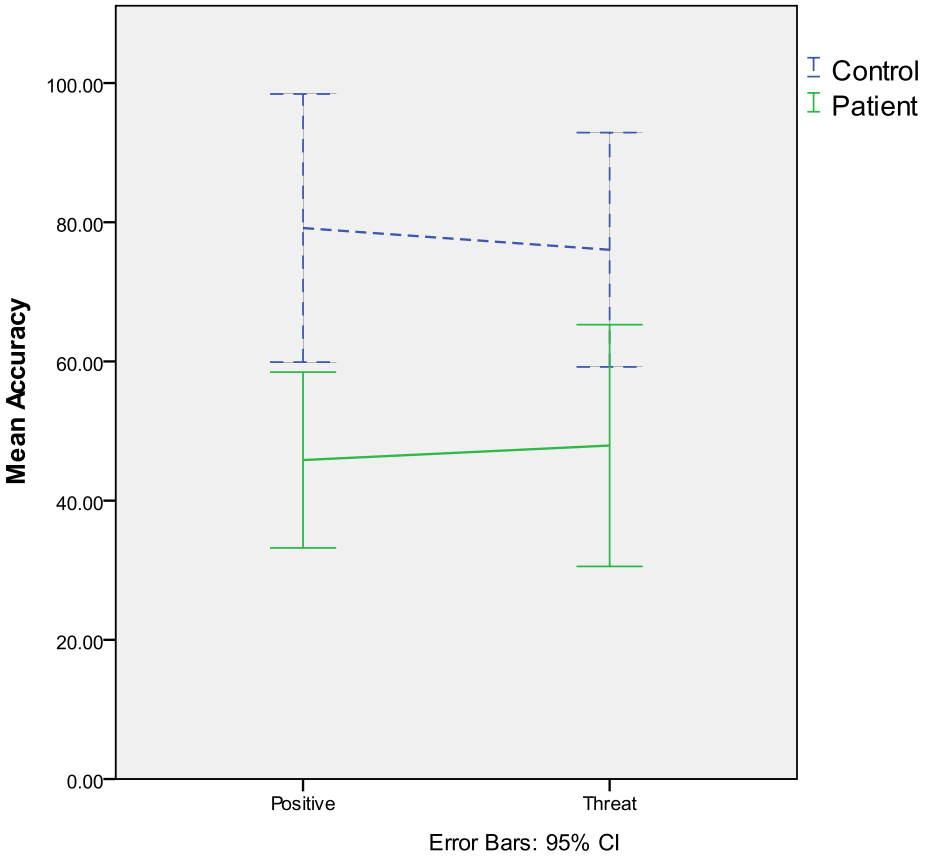

Figure 2: Mean accuracy on the New ToM Measure of controls and patients according to valence. The control group is illustrated with a dashed line. Error bars represent 95% confidence intervals.

3.3.3 Errors

3.3.3.1 Errors on Eyes Test

Differences between groups in the pattern of errors made were examined. The ability to do this was somewhat confounded in that the valence of distracter choices varied. Sometimes, the distracter choices for an item included one that was in the same valence as the target (e.g. the threat item 'distrustful' had two distracters that matched the target valence, 'aghast' and

‘terrified’, and a neutral distracter ‘impatient’), whilst for other items none of the distracters matched the target valence (e.g. the positive item ‘reflective’ had one neutral distracter, ‘impatient’, and two threat distracters, ‘aghast’ and ‘irritated’). Given this confound, a statistical examination of differences between groups in the pattern of errors was not conducted, and the results below are descriptive only.

Distracter items were classified according to whether they were of ‘threat’, ‘neutral’ or ‘positive’ valence (Appendix 2.8). Participants’ errors were categorised according to the valence of the target item, and whether the distracter item was a ‘threat’, ‘neutral’ or ‘positive’ valence. The contingency table of participants’ errors is contained in Table 5. Similar errors were made in both groups overall: when errors were made on positive items, neutral valence distracters were most frequently selected, whereas when errors were made on threat target items, threat valence distracters were most frequently selected. However, when participants made an error on a positive item, patients made more threat attributions compared to controls.

Table 5: Contingency table of participants' errors according to target item and distracter item valence.

		Controls	Patients
Errors on Positive Target Items	**Total Errors**	18	25
	Threat	2 (11.11 %)	7 (28.00 %)
	Neutral	10 (55.56 %)	10 (40.00 %)
	Positive	6 (33.33 %)	8 (32 %)
Errors on Threat Target Items	**Total Errors**	23	57
	Threat	11 (47.83%)	24 (42.11 %)
	Neutral	6 (26.09 %)	21 (36.84 %)
	Positive	6 (26.09 %)	12 (21.05%)

3.3.3.2 Errors on New ToM Measure

The ability to capture information on whether patients scored poorly because of an overall threat interpretation of an item on the New ToM measure is limited in its current format. However, observations by the author noted during the tasks illustrate that three patients and one control misinterpreted an overall positive valence ToM story in a threatening way (Item 3), whilst four participants (two patients and two controls) elaborated on threat valence items (items 4 and 5) in a similar vein. Table 6 describes participants' comments. No observations were noted of any misinterpretations of stimuli in a neutral or positive valence direction.

Table 6: Misinterpretations of items on the New ToM Measure.

Item	Scenario	Observation
3	Two characters work together to give a third character a nice surprise	• Patient B: Described the two characters' intention was to hit the third character with a stick. • Patient C: Reported "he's attacked him", referring to one of characters attacking another. • Patient D: Stated "he's going to kick him" based on interpretation that one of the characters had stolen another's juice. • Control A: Described the two characters' intention was to "mug him" (third character).
4	One character, holding a box, requests assistance to move boxes from two others.	• Patient B: Stated the character holding the box intended to "steal something". • Control A: Stated that the character holding the box intended to "steal that box". • Control B: Stated "he's expecting hostility" in reference to the character holding a box.
5	One character is given a nasty surprise by two others, who offer the first a box of chocolates with a spider in it.	• Patient A: Stated "maybe they've got her [the character who was deceived by the other two characters] as a hostage".

3.3.3.3 New ToM Measure

The New ToM Measure was developed as part of this study, and as such it was of interest to note how participants approached this task. All participants completed the measure, and none became distressed during the completion of any of the study tasks. It would therefore seem reasonable to infer from this that the measure was acceptable to participants. It was observed that several participants (both controls and patients) requested third-order false belief questions to be repeated. These take the form “what does person X assume person Y believes regarding his/her (person X) intentions”. These questions are of increased complexity, however, they minimise the likelihood of ceiling effects and are therefore usefully included in the measure (Bell et al., 2010). The New ToM Measure allows accuracy on the different components (questions or sequencing) to be scored separately and a detailed analysis of this is provided in Appendix 2.9.

3.3.3.4 Post hoc analyses

3.3.3.4.1 New ToM Measure Response Speed

The amount of time taken to sequence items (response speed, seconds) on the New ToM Measure was recorded. Participants were instructed that although the amount of time taken to respond would be measured, the accuracy of sequencing should be prioritised over speed. The assumptions of normality and homogeneity of variance were not met, therefore differences within and between groups were explored using non-parametric tests (Mann-

Whitney Test and Wilcoxon signed-rank test). Data was missing for one control participant.

Average response speed across all items in the New ToM Measure was examined for both groups. There was no significant difference between the control group (Median, Mdn = 21.33) and patient group (Mdn = 26.17) in average response speed (p = .27). Average response speed was examined for both groups according to valence. A non-parametric alternative to a Mixed ANOVA was not available, therefore data were explored using multiple Wilcoxon signed rank tests. In the patient group, average response speed across threat items compared with positive items was examined. There was a significant difference in average response speed, with patients taking longer to respond on threat items (Mdn = 29.00) than positive items (Mdn = 21.67) (p = .04). In the control group, average response speed was not significantly different on threat (Mdn = 23.67) and positive items (Mdn = 17.00).

3.3.3.4.2 Preliminary investigation of construct validity

A preliminary investigation of the construct validity of the New ToM Measure was conducted. The New ToM Measure was based on the Picture Sequencing Task (PST) (Brüne, 2003), however, the PST was not employed in this study. Therefore, this preliminary analysis explores the correlation between the New ToM Measure and the Eyes Test. Overall accuracy data were pooled across groups for the purpose of this analysis, and a bivariate

correlation was conducted. Data met the assumption of normality. There was a significant correlation between the New ToM task and the Eyes Test (r = .59, p = .016). An exploratory analysis of the correlation between the two measures was conducted for controls and patients separately, however, these were not significant (Control group: r = .05, p = .90; Patient group r = .24, p = .57).

4. Discussion

A considerable body of evidence demonstrates that ToM ability is significantly impaired in individuals with schizophrenia versus healthy controls, although the nature of ToM deficits in patients with paranoid symptoms is unclear (Brüne, 2005). The purpose of this study was to examine ToM ability in individuals with paranoid schizophrenia compared to controls, and to explore whether this varied according to the emotional valence of items within ToM tasks.

4.1 Hypothesis 1:

The first hypothesis was that significant differences would be found in ToM ability in individuals with paranoid schizophrenia compared to controls. This study found evidence that controls are significantly more accurate than patients when overall accuracy is considered (Eyes Test: p = .001, *d* = 2.24, large effect; New ToM Measure: p = .003, *d* = 1.82, large effect). This pattern

was maintained when accuracy was explored according to emotional valence, with large between group effects in evidence again on the Eyes Test ($p = .003$, $d = 1.89$) and New ToM Measure ($p = .004$, $d = 1.32$). This study therefore lends further support to the existing body of evidence that has found individuals with schizophrenia to have impaired ToM ability (Bora et al., 2009), and strengthens the evidence that this is similarly the case in individuals with a diagnosis of paranoid schizophrenia.

4.2 Hypothesis 2 and 3

The second hypothesis of the study was that there would be a significant difference in ToM abilities in individuals with paranoid schizophrenia compared to controls, but that this would be mediated by the emotional valence of items within ToM tasks. The third hypothesis concerned the nature of this mediation, and proposed that individuals with paranoid schizophrenia would show greater accuracy on threat items compared to positive items.

In the Eyes Test, an established measure of ToM, controls and patients differed significantly in accuracy, and a trend was found for the interaction between group and valence ($p = .06$). On closer examination, accuracy within the control group was similar for threat and positive items. However, the group with paranoid schizophrenia was more accurate on positive items compared to threat items. This difference was not statistically significant ($p = .07$), however a large effect was found ($d = 1.01$). Therefore, on the Eyes

Test, there would appear to be a trend towards ToM abilities being mediated by the emotional valence of items, although this was in the opposite direction to that hypothesised. There was no evidence from results on the New ToM Measure of a mediating role of emotional valence on ToM ability in terms of accuracy. For both controls and patients there were no significant differences within groups on their performance on positive versus threat items.

4.3 Further considerations

Control and patient groups were unmatched in terms of the WTAR (Wechsler, 2001), with the control group scoring significantly higher than the patient group ($p = .02$). It is possible therefore that the above differences between groups on ToM tasks were due to differences in pre-morbid levels of intellectual functioning. However, there is evidence from other studies to indicate that even when the confounding effects of executive functioning and intelligence are successfully controlled for, patients with schizophrenia still perform more poorly than healthy controls on ToM tasks (Brüne, 2005). The above interpretation of a difference between groups in ToM ability would therefore appear justified.

When accuracy on ToM tasks was examined according to valence, there was a trend towards a mediating role of valence on ToM abilities in terms of accuracy on the Eyes Test. This suggests that there is a degree of variability in performance according to valence in the patient group, and provides some tentative support for the second hypothesis of the study. A large within group

effect (*d* = 1.01) was found in the patient group, and although this difference also showed a trend it too did not quite reach significance. There was no evidence of a mediating role of valence on ToM abilities in terms of accuracy on the New ToM measure.

The nature of the trend in the patient group on the Eyes Test was contrary to hypothesised, with participants with a diagnosis of paranoid schizophrenia performing with greater accuracy on positive valence items than threat valence items. The nature of the trend in these results is consistent with existing literature that suggests that people with schizophrenia recognise facial emotions less accurately than healthy controls (Kohler et al., 2010). For example, Premkumar et al. (2008) found that outpatients with a diagnosis of schizophrenia or schizoaffective disorder performed less accurately than healthy controls on a Facial Emotion Attribution task. Specifically, they noted that patients were significantly less accurate than controls at recognising fear and anger, but did not differ for happy and neutral facial expressions. It may be that the results on the Eyes Test found in this study evidence that the effect of facial emotion recognition deficits exceeds any bias to attend to threatening stimuli (Bentall et al., 2009; Bentall and Kaney, 1989, cited in Phillips et al., 2000).

Alternatively, it may be that the patient group's lower pre-morbid intellectual functioning contributed to the group's larger variation in accuracy scores on threat items. This larger amount of variation, perhaps amplified by the small sample size, may have contributed to a trend being detected. Any

interpretation of this result must be cautiously made given the small sample size, which could increase the chance of a Type 1 error. Response speed was not recorded for the Eyes Test, however, on the New ToM Measure, no between group difference was found for average response speed across all items. This suggests that any difference is not due to impulsive responding. Furthermore, patients spent longer considering the sequencing of threat items compared with positive items. This may indicate that they experienced these items as more difficult, although patients' accuracy on threat and positive items on the New ToM Measure was similar.

The absence of a similar trend towards a mediating role of valence in the patient group on the New ToM measure may be due to the fact that the two tasks employed in this study are based on two different paradigms: the New ToM Measure was primarily a social cognitive ToM task, whilst the Eyes Test was primarily a social-perceptual ToM task (Bell et al., 2010). Social cognitive tasks require the participants to assimilate contextual aspects about characters in a task (e.g. what a character knows or has done) in order to infer mental states (Bell et al., 2010), whilst social-perceptual ToM tasks involve inferring mental states from cues, such as photographs of eyes.

4.4 New ToM measure

When overall accuracy on the New ToM Measure and the Eyes Test was examined, a similar pattern of controls demonstrating greater accuracy than patients was evident. These results indicate that when the New ToM

Measure is scored in full, it is able to distinguish between control and patient groups. In addition, the inclusion of third-order false belief questions appears to have minimised ceiling effects. However, the New ToM Measure could be improved by capturing more information on the errors that participants make. For example, although the original sequence that photographs are placed in by participants is scored, the 'story' that the participant saw when they placed the photographs in a particular order is lost. A simple adjustment, of asking the participant to recount their interpretation of the story in the photographs, and recording this qualitative information would allow future users of the measure to determine whether an overall threatening or positive story was developed by a participant. The measure was acceptable to participants, and all appeared to engage well in trying to sequence the stories and answer the associated questions.

4.5 Limitations

There were several limitations to this study. Firstly, the patient and control groups were not matched in terms of intellectual functioning as determined by WTAR scores (Wechsler, 2001). The patient group were predominantly in-patients on rehabilitation wards, and as reported by Kalidindi et al. (2012), the majority of individuals receiving in-patient mental health rehabilitation services will have a history of psychotic symptoms which are not controlled, and will present with severe psychotic symptoms, which will have a major impact on role functioning. It is possible that recruiting a less severely ill patient group, such as a community patient sample may have overcome the

limitation of groups being unmatched (Kalidindi et al., 2012). The WTAR (Wechsler, 2001) assumes normal pre-morbid development of reading skills, however patients recruited to this study are likely to have experienced disrupted education. It may be that using an alternative estimate of pre-morbid ability would have facilitated the process of matching control and patient groups.

A second limitation to this study was that the recruitment target was not met in the study period. The decision to stop recruitment was based on several considerations. Firstly, a preliminary analysis of the above data revealed that whilst patients performed poorly on the threat items, there was a large amount of variation in the data. In comparison, consistent levels of accuracy were achieved by patients and controls across positive and threat items on the New ToM Measure, again with large variation in accuracy data. This suggested that any mediating role of valence was likely to be small, and that a significantly larger sample would be needed to detect such an effect. In parallel, it was noted that recruitment of participants who met the study's inclusion and exclusion criteria had been exhausted at study sites. Further recruitment would therefore have necessitated the involvement of additional sites, which would not have been possible in a study of this scope. The decision was therefore taken to stop recruitment to the study.

A significant proportion of participants declined to participate in the study, with several citing concerns regarding confidentiality and lack of familiarity with the researcher. This is a recognised barrier in studies relating to

schizophrenia (Woodall et al., 2010). Several steps were taken to overcome these barriers, such as known healthcare team members initially introducing the project and researcher, and the researcher meeting with participants to discuss the project and address any questions or concerns, but despite this the number declining remained high. Alternative adjustments, such as providing general guidance regarding research participation may help to improve participation.

An investigation of the construct validity of the New ToM Measure was conducted by examining the correlation between the New ToM Measure and the Eyes Test. The New ToM Measure was based on the Picture Sequencing Task (PST) (Brüne, 2003), however the PST was not employed in this study. The analysis of construct validity between the New ToM Measure and the Eyes Test can therefore be considered as preliminary only, and is acknowledged as another limitation to the study. Goodwin and Leech (2006) outline that values of r will be greater if there is more variability among the observations than if there is less variability. The amount of variability in the pooled analysis was greater than for the individual analyses of the control and patient group, which may have contributed to a greater value of r being found for the correlation between the New ToM Measure and Eyes Test across groups ($r = .59$, $p = .016$) than for controls ($r = .05$, $p = .90$) and patients ($r = .24$, $p = .57$) separately. Furthermore, correlation estimates are often inaccurate in small sample sizes (Schönbrodt and Perugini, 2013) and so the results obtained, especially for the separate analyses of control group and patient group, should be considered as exploratory only. Future research

could potentially explore the relationship between the New ToM Measure and other tasks, such as the PST.

4.6 Conclusion

The study provides evidence of theory of mind impairments in individuals with paranoid schizophrenia on an established ToM task, the Eyes Test, and a New ToM Measure, with large between group effects found. There was a trend in the patient group towards a mediating role of emotional valence on accuracy on the Eyes Test, however this was not in the hypothesised direction. There were several limitations to this study including the small sample size and samples being unmatched for pre-morbid intellectual functioning, which must be considered when interpreting these results.

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CHAPTER 3

Advanced Clinical Practice: Reflective Account 1

The role of communication in increasing the availability and provision of evidence based psychological therapies

(Abstract only. Full account bound separately in Volume 2)

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Abstract

In Scotland, healthcare policy and Government commitments reflect the current drive to increase the availability and provision of evidence based psychological therapies (Scottish Government, 2011). In order to make a meaningful contribution to this agenda, Wells (2010) argues that clinical psychologists' roles must be extended by concentrating direct clinical work on those with the most complex presentations, and by supporting the wider workforce to deliver psychological care via the provision of training, supervision, consultancy and clinical leadership. I believe that the clinical psychologists' core competence of 'communication' underpins the individuals' ability to engage with this role expansion (British Psychological Society, 2008). In this reflective account, the development of this core competence will be explored via reflections on communication with clients, within supervision and the multi-disciplinary team.

CHAPTER 4

Advanced Clinical Practice: Reflective Account 2

Training formulation skills in clients, other professionals and the multidisciplinary team – the idea of 'chipping in'

(Abstract only. Full account bound separately in Volume 2)

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Abstract

There is an expectation that Clinical Psychologists will contribute to the current Scottish healthcare policy and Government commitments to increase the availability and provision of evidence based psychological therapies by supporting the wider workforce to deliver psychological care by providing training, supervision, consultancy and clinical leadership (Wells, 2010). Formulation is one of the key competence domains for applied psychologists (BPS, 2008), and promoting formulation skills and a psychological based understanding in clients, other professionals and teams is central to achieving good psychological care in Scotland. In this reflective account, I will consider how I have contributed to training formulation skills in others over the course of my first year and third year placements in adult mental health. Informal opportunities for 'chipping in' formulations will be considered in this account (Christofides et al. 2012).

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	Sample	*Available Score*	*Moritz et al. (2011a)*	*Aghotor et al. (2010)*	*Kumar et al. (2010)*	*Naughton et al. (2012)*	*Favrod et al. (2010)*	*Moritz et al. (2011b)*	*Ross et al. (2011)*	*Lecardeur et al. (2009)*	*Waller et al. (2011)*
1	Type of sample: • Geographic cohort (all patients in a particular area) OR • Convenience Sample (e.g. clinic attenders or referred patients) OR • Highly selective (e.g. volunteers)	5 OR 2 OR 0	2	2	2	2	0	2	0	2	0
2	Sample size: Sample size is greater than 27 participants in each treatment group or based on described and adequate power calculations	5	0	0	0	0	0	0	5	0	0
Allocation											
1	There is true randomisation or minimisation allocation to treatment group.	10	10	10	10	0	0	10	10	0	0
2	The process of randomisation is described	3	0	0	3	0	0	0	3	0	0
3	The process of randomisation is carried out independently from the trial research team	3	3	0	0	0	0	3	3	0	0
Assessment (for the main outcome)											
1	The assessments are carried out by independent assessors and not therapists	10	*10*	*0*	*0*	*0*	*0*	*10*	*0*	*0*	*0*
2	Standardised assessments are used to measure symptoms in a standard way OR Idiosyncratic assessments of symptoms	6 OR 3	*6*	*6*	*6*	*6*	*6*	*6*	*6*	*6*	*6*
3	Assessments are carried out blind (masked) to treatment group allocation	10	*10*	*10*	*0*	*0*	*0*	*10*	*0*	*0*	*0*
4	The methods of rater blinding are adequately described	3	*0*	*3*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
5	Rater blinding is verified	3	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*

			Moritz et al. (2011a)	*Aghotor et al. (2010)*	*Kumar et al. (2010)*	*Naughton et al. (2012)*	*Favrod et al. (2010)*	*Moritz et al. (2011b)*	*Ross et al. (2011)*	*Lecardeur et al. (2009)*	*Waller et al. (2011)*
Control Groups		*Available Score*									
1	'Treatment as usual' is a control group AND / OR A control group that controls for non-specific effects or other established or credible treatment	6 AND /OR 10	*6*	*10*	*6*	*10*	*0*	*10*	*10*	*6*	*0*
Analysis											
1	The analysis is appropriate to the design and the type of outcome measure	5	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*
2	The analysis includes all those participants as randomised (i.e. Intention to treat analysis) AND An adequate investigation and handling of drop outs from assessment if the attrition rate exceeds 15%	6 AND 4	*6*	*0*	*6*	*0*	*0*	*6*	*6*	*0*	*0*
Active Treatment											
1	The treatment was adequately described	3	*3*	*3*	*3*	*3*	*3*	*3*	*3*	*3*	*3*
2	A treatment protocol or manual was used	3	*3*	*3*	*3*	*3*	*3*	*3*	*0*	*0*	*3*
3	Adherence to the treatment protocol or treatment quality was assessed	5	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Total			64	52	44	29	21	68	51	22	17

Appendix 2.0: Eyes Test pilot

A pilot was conducted to classify items from the Eyes Test (Baron-Cohen et al., 2001) into three emotional valence categories: positive, neutral and threat. A convenience sample of 10 individuals rated each item according to the procedure employed by Harkness et al. (2005), although a 7-point scale from 'very threatening' to 'very positive' was employed. Stimuli that had mean ratings significantly below neutral were categorised as threatening, those significantly above neutral were categorised as positive, and those that did not differ significantly from neutral were classified as neutral items. If data met assumptions for parametric tests then one sample t-tests were employed, alternatively the Wilcoxon Signed Rank Test was employed. Table 1 provides details the classification of each item. Twelve items were classified as threat valence and eight items as positive valence.

Table 1: Classification of Eyes Test items according to emotional valence.

Valence	Adjective (item number)		
Threat*	Upset (2) Insisting (4) Worried (5) Uneasy (7)	Sceptical (12) Accusing (14) Doubtful (17) Tentative (19)	Hostile (26) Distrustful (34) Nervous (35) Suspicious (36)
Positive *	Playful (1) Desire (3) Anticipating (13)	Contemplative (15) Friendly (20) Interested (28)	Reflective (29) Flirtatious (30)
Neutral	Fantasizing (6) Despondent (8) Preoccupied (9) Cautious (10) Regretful (11) Thoughtful (16)	Decisive (18) Fantasizing (21) Preoccupied (22) Defiant (23) Pensive (24)	Interested (25) Cautious (27) Confident (31) Serious (32) Concerned (33)

* all items $p < .05$.

Appendix 2.1: New Theory of Mind Measure pilot.

The New ToM Measure was based on the Picture Sequencing Task (PST) (Brüne, 2003). The scenarios in the New ToM Measure mirrored those of the PST in incorporating scenarios of mutual cooperation, deception and cooperation of two characters while cheating a third. The key differences were that the New ToM Measure was balanced in having three threat and three positive scenarios, and employed photographs instead of cartoons. Provisional storyboards of the scenarios were developed and photographed. Each scenario was depicted across four photographs.

Individuals in the pilot were requested to place the four photographs for each item in a logical sequence. Following the results of the pilot, three items were amended in order to enhancing cues to the correct sequence order. The changes included having subjects in the photos move from the background to the foreground, and by minimising background information. The manual was taken from Brüne (2003) and questions were modified to reflect the new scenarios.

Appendix 2.2: New Theory of Mind Measure example item

Figure 1. Item 2 from New ToM Measure – a nice surprise

Appendix 2.3: New Theory of Mind Measure manual

Theory of Mind in individuals with paranoid schizophrenia

Theory of Mind Measure – Manual and Scoring Form

Primary Researcher – Ms Liesbeth Scott

Chief Investigator - Dr Sue Turnbull

Co-Investigator – Professor Andrew Gumley

Field Supervisor – Dr Allison Blackett

Please note that this manual is taken from the manual for the Picture Sequencing Task that was kindly provided by Professor Martin Brüne for use in this study (Brüne, 2003). The manual has been adapted slightly to reflect the stimuli employed in this study.

Administration Notes:

Instructions to be read to the client are italicised.

Administer pilot item and then six items.

Pilot item: see corresponding score sheet

To be read to the participant:

> *I have four cards. I am going to put the four cards in front of you.*

Place the cards in order using the numbers 1, 2, 3, and 4. Cards should be placed face up and in a line in front of the participant.

> *When I say 'begin', please arrange the cards in the correct order so that they show a logical sequence of events". Put them in the order that you think is most sensible.*
>
> *When you think you are done, please say 'finished'. I'll be using a clock to measure the time you take, but it's more important to get the cards in the correct order than it is to be fast.*
>
> *Do you understand the instructions?*

If yes, proceed as below. If no, repeat instructions as above, then proceed as below.

Here are the cards for the first story.

Place cards on table in front of the participant. Remember to start timing when you say 'Begin'.

Begin

When the participant has completed the task, by saying 'finished', confirm that the cards are in the correct order. There are letters on the reverse of the cards. Check the sequence in order to confirm whether the cards are in the correct order. For the pilot item the correct order is POUR.

If correct order, then proceed to first test item after saying:

That's right

If incorrect, then put the cards in the right sequence in front of the client and say

This is the right order. They go this way to tell a story.

Use the pilot item to illustrate to the client that each photo adds some additional information, but that you need to look across all four to work out what happens in the story. Say:

You need to look at all four of the cards in order to see what is happening across them, it's like putting together a comic-strip. You need to think about what might possibly be happening, and choose what makes most sense.

Advise client that you are moving to the first test item.

Let's try the next one. With the next ones, I will also ask you some questions about the story you see.

Administration of Test Items:

To be read to the participant:

Let's move on to the next story. There are six stories in total. You may find some easier and some more difficult. Each time, arrange them in an order that makes the most sense. Work through each story in your own time. Do you have any questions?

Let's start.

Place the cards on the table in front of the participant in order using the numbers 1, 2, 3, 4 on the back of the cards.

Say the following to the client, and be ready to start timing.

Are you ready? Begin.

Start timing.

When the client has finished the task, i.e. when they say 'finished', check the sequence of the cards.

Item Number	**Correct Sequence**	**Item Content**
Item 1:	HELP	Biscuit
Item 2:	CAKE	Cake in box
Item 3:	NICE	Present on bench

Item 4:	TRIP	Trip with broom
Item 5:	YUCK	Bug in bag
Item 6:	TAKE	Bike accident

Record sequencing order, time to completion, and circle the scores for each item.

For ease of scoring, correct scores are circled and incorrect ones are crossed out.

Example-

correct sequence	**H**	**E**	**L**	**P**
patient's sequence	H	L	E	P
points (max. 6)	2	1	1	2
Sequencing Time (Sec)	45	Notes:		

If the picture story is sequenced incorrectly, move the pictures into the right order before starting with the questions. Point to the respective picture when asking the theory of mind questions, as indicated on the scoring sheet.

Correct responses are provided on the scoring sheet as a guide.

Once item complete, move to the next item.

<u>Pilot item</u>

Administer pilot item as described above.

Item 1

Correct Sequence	**H**	**E**	**L**	**P**
Participant's Sequence				
Score	2	1	1	2
Sequencing Time (Sec)			Notes:	

Questions:

	Score (0 or 1)
1. What does the person with the black shirt believe the one in the grey shirt intends to do? (2nd order belief) (**Pointing to second picture**). Correct answer – Get biscuits from high shelf.	
2. What does the person with the black shirt expect from the person in the grey shirt (reciprocity) (**pointing to the fourth picture**). Correct answer – Give him a biscuit, share with him.	

Sequencing Score	
Questions Score:	
Time:	
Total Score Item 1:	

Other observations:

Item 2

Correct Sequence	**C**	**A**	**K**	**E**
Participant's Sequence				
Score	2	1	1	2
Sequencing Time (Sec)			Notes:	

Questions:

	Score (0 or 1)
a) What does the person in white believe is in the box? (false belief) (**pointing to photograph 3**). Correct Answer: Work paper/ files.	
b) What's in the box? (reality) **(pointing to the third photograph)**. Correct Answer: Cake	
c) What does the person in white believe the person in red intends to do? (2nd order false belief) **(pointing to third photograph)**. Correct Answer: Give him papers/work files.	
d) What does the person in red assume the person in white believes, regarding her (person in red) intentions? (3rd order false belief) **(pointing to the second photograph)**. e) Correct Answer: Give him work paper/files	
f) What do you think the person in red intended to do? (deception) (whole story). Correct Answer: Do something nice for him, give him a nice surprise.	

Sequencing Score	
Questions Score:	
Time:	
Total Score Item 2:	

Other observations:

Item 3

Correct Sequence	**N**	**I**	**C**	**E**
Participant's Sequence				
Score	2	1	1	2
Sequencing Time (Sec)			Notes:	

Questions

	Score (0 or 1)
a) What does the person in the blue coat intend to do? (intention) **(pointing to 1st picture)**. Correct Answer: Give a present.	
b) What does person in green believe has happened? (false belief) **(pointing to 3rd picture)**. Correct Answer: tripped over branch, injury, fell over	

c) What do the person in the blue and the person in black intend to do? (distraction) **(pointing to 2nd picture)**. Correct Answer: Distract the person in the green shirt and give him a present.	
d) What does the person in blue expect from the person in black? (Reciprocity) **(pointing to 4th photograph)**. Correct Answer: To help him give the surprise present.	
e) What does the Person in green now think that the Person in blue and the person in black intended to do? (intention detection) **(pointing to 4th picture).** Correct Answer: To give him a present.	

Sequencing Score	
Questions Score:	
Time:	
Total Score Item 3:	

Other observations:

Item 4

Correct Sequence	**T**	**R**	**I**	**P**
Participant's Sequence				
Score	2	1	1	2
Sequencing Time (Sec)			Notes:	

Questions

	Score (0 or 1)
a) What does the person in red believe the person in white intends to do? (2nd order belief) **(pointing to picture 2)**. Correct answer – Move boxes.	
b) What does the person with the white shirt expect from the person in the red shirt? **(pointing to picture 2)** (Assistance). Correct Answer – Help, to carry boxes.	

Sequencing Score	
Questions Score:	
Time:	
Total Score Item 4:	

Other observations:

Item 5

Correct Sequence	**Y**	**U**	**C**	**K**
Participant's Sequence				
Score	2	1	1	2
Sequencing Time (Sec)			Notes:	

Questions

	Score (0 or 1)
a) What does the person in blue believe is in the box? (false belief) **(pointing to 2nd photograph).** Correct Answer: A sweet, chocolate (bug is incorrect).	
b) What is in the box (reality**) (pointing to the second photograph)**. Correct Answer: Bug, insect, spider	
c) What does the person in blue believe the person in green intends to do? (second order false belief) **(pointing to the 2nd photograph)**. Correct Answer: Offer a sweet/chocolates	
d) What does the person in green assume the person in blue believes regarding his (the one in green) intentions? (3rd order false belief) **(pointing to the 2nd photograph)**. Correct Answer: Give her sweet/chocolates.	
e) What do you think the person in green intended to do? (deception) (whole story). Correct Answer: scare her, frighten her, shock her.	

Sequencing Score	
Questions Score:	
Time:	
Total Score Item 5:	

Other observations:

Item 6

Correct Sequence	**T**	**A**	**K**	**E**
Participant's Sequence				
Score	2	1	1	2
Sequencing Time (Sec)			Notes:	

Questions

	Score (0 or 1)
a) What does the person with the bike intend to do? **(Pointing to first picture)**. Correct answer – Take laptop bag.	
b) What does the person with the red scarf believe has happened? **(Pointing to the third picture)** (false belief). Correct answer – An accident, an injury.	

a) What do the persons with the bike and grey coat intend to do? **(Pointing to the second photograph)** (cheating). Correct answer – Distract the person in blue and steal the laptop.	
b) What does the person in grey expect from the person with the bike? **(Pointing to the fourth photograph)**. Correct answer – Help to steal the laptop, share the laptop.	
c) What does the person with the red scarf now think that the person with the bike and the person in the grey coat intended to do? **(Pointing to the fourth photograph)**. Correct answer – Steal the laptop.	

Sequencing Score	
Questions Score:	
Time:	
Total Score Item 6:	

Other observations:

Overall Scoring:

	Sequencing	Questions	Time
Item 1			
Item 2			
Item 3			
Item 4			
Item 5			
Item 6			

Overall score

Accuracy on Positive Items (Items 1, 2 and 3) - defined as the percentage of items where the participant identifies a correct response:

Accuracy on Threat Items (Items 4, 5, and 6) – defined as the percentage of items where the participant identifies a correct response:

Appendix 2.4: Ethics approval

WoSRES
West of Scotland Research Ethics Service

NHS
Greater Glasgow and Clyde

West of Scotland REC 2
Ground Floor – The Tennent Institute
Western Infirmary
38 Church Street
Glasgow G11 6NT
www.nhsggc.org.uk

Dr Sue Turnbull
University Teacher, Research Tutor,
Chartered Clinical Psychologist
University of Glasgow, Mental Health and Wellbeing
Gartnavel Royal Hospital,
Administration Building, 1st Floor
1055 Great Western Road
Glasgow G12 0XH

Date 17th April 2012
Your Ref
Our Ref
Direct line 0141 211 2123
Fax 0141 211 1847
E-mail Liz.Jamieson@ggc.scot.nhs.uk

Dear Dr Turnbull

Study title: **Theory of Mind in individuals with paranoid schizophrenia**
REC reference: **11/WS/0115**

Thank you for your letter of 11 March 2012 received on 13th April 2012, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information was considered in correspondence by a sub-committee of the REC. A list of the sub-committee members is attached.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

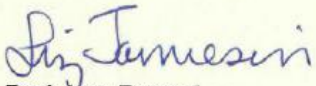
You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

11/WS/0115	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project

Yours sincerely



Dr Adam Burnel
Chair

Email: Liz.Jamieson@ggc.scot.nhs.uk

Enclosures: List of names and professions of members who were present at the meeting and those who submitted written comments

"After ethical review – guidance for researchers"

Copy to: Dr Erica Packard, NHS Greater Glasgow and Clyde - Research and Development

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering Letter		17 November 2011
Investigator CV	1	15 November 2011
Other: Identification of Participants	2	15 November 2011
Other: Poster - Controls	1	15 November 2011
Other: Poster - Patients	1	15 November 2011
Other: Demographic Information - Patient	2	15 November 2011
Other: Demographic Information - Control	2	15 November 2011
Other: Inclusion/Exclusion Criteria - Patient	1	15 November 2011
Other: Inclusion/Exclusion Criteria - Control	1	15 November 2011
Other: CV Student - Suzanne Lake	1	15 November 2011
Other: CV - Key Investigator - Professor Andrew Gumley	1	15 November 2011
Participant Consent Form: Patient	2	11 March 2012
Participant Consent Form: Control	2	11 March 2012
Participant Information Sheet: Patient	2	11 March 2012
Participant Information Sheet: Control	2	11 March 2012
Protocol	1	15 November 2011
Questionnaire: Theory of Mind Picture Stories Task - Administration and Scoring Manual		
Questionnaire: Adult Reading the Mind in the Eyes Test		
Questionnaire: Brief Psychiatric Rating Scale (BPRS)		
Questionnaire: Wechsler Test of Adult Reading		
REC application		17 November 2011
Response to Request for Further Information		11 March 2012

Appendix 2.5: NHS Research and Development approval

NHS
Greater Glasgow and Clyde

Coordinator/Administrator: Dr Erica Packard/Mrs Elaine O'Neill
Telephone Number: 0141 211 6208
E-Mail: erica.packard@ggc.scot.nhs.uk
Website: www.nhsggc.org.uk/r&d

R&D Management Office
Western Infirmary
Tennent Institute
1st Floor 38 Church Street
Glasgow, G11 6NT,

18 January 2013

Ms Suzanne Scott
Trainee Clinical Psychologist
Mental Health and Wellbeing
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow G12 0XH

NHS GG&C Board Approval

Dear Ms Scott,

Study Title:	**Theory of Mind in individuals with paranoid Schizophrenia**
Principal Investigator:	**Ms Suzanne Scott**
GG&C HB site	**Leverndale, Parkhead, Dykebar & Gartnavel Royal Hospitals.**
Sponsor	**NHS Greater Glasgow and Clyde**
R&D reference:	**GN11CP446**
REC reference:	**11/WS/0115**
Protocol no. (including version and date)	**V1; 15/11/11**

I am pleased to confirm that Greater Glasgow & Clyde Health Board is now able to grant **Approval** for the above study.

Conditions of Approval

1. **For Clinical Trials** as defined by the Medicines for Human Use Clinical Trial Regulations, 2004
   a. During the life span of the study GGHB requires the following information relating to this site
      i. Notification of any potential serious breaches.
      ii. Notification of any regulatory inspections.

It is your responsibility to ensure that all staff involved in the study at this site have the appropriate GCP training according to the GGHB GCP policy (www.nhsggc.org.uk/content/default.asp?page=s1411), evidence of such training to be filed in the site file.

NHS
Greater Glasgow and Clyde

2. **For all studies** the following information is required during their lifespan.
   a. Recruitment Numbers on a monthly basis
   b. Any change of staff named on the original SSI form
   c. Any amendments – Substantial or Non Substantial
   d. Notification of Trial/study end including final recruitment figures
   e. Final Report & Copies of Publications/Abstracts

Please add this approval to your study file as this letter may be subject to audit and monitoring.

Your personal information will be held on a secure national web-based NHS database.

I wish you every success with this research study

Yours sincerely,

EPackard

Dr Erica Packard
Research Co-ordinator

Appendix 2.6: Ethics approval of major amendment

WoSRES
West of Scotland Research Ethics Service

NHS
Greater Glasgow and Clyde

West of Scotland REC 3
Ground Floor – The Tennent Institute
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38 Church Street
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www.nhsggc.org.uk

Dr Sue Turnbull
University Teacher, Research Tutor, Chartered Clinical Psychologist
University of Glasgow
Mental Health and Wellbeing
Gartnavel Royal Hospital
Administration Building, Trust HQ, 1st Floor
1055 Great Western Road
Glasgow
G12 0XH

Date 3rd June 2013
Your Ref
Our Ref
Direct line 0141 211 2123
Fax 0141 211 1847
E-mail Liz.Jamieson@ggc.scot.nhs.uk

Dear Dr Turnbull

Study title:	**Theory of Mind in individuals with paranoid schizophrenia**
REC reference:	**11/WS/0115**
Amendment number:	**AM03**
Amendment date:	**20 May 2013**
IRAS project ID:	**87432**

The above amendment was reviewed by the Sub-Committee in correspondence. This amendment covers the recruitment of controls from GP Practices.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Advertisement	1	19 May 2013
Letter of invitation to participant	1	19 May 2013
Participant Information Sheet: GP - Control Group	1	19 May 2013
Protocol	4	19 May 2013
Notice of Substantial Amendment (non-CTIMPs)	AM03	20 May 2013
Participant Consent Form: Control	2	11 March 2012

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

11/WS/0115:	**Please quote this number on all correspondence**

Yours sincerely

Liz Jamieson
Committee Co-ordinator
On behalf of Dr Adam Burnel, Chair

Enclosures:	List of names and professions of members who took part in the review
Copy to:	Dr Erica Packard, R&D - NHS Greater Glasgow and Clyde

Appendix 2.7: NHS Research and Development approval of major amendment

From: O'Neill, Elaine [Elaine.O'Neill2@ggc.scot.nhs.uk]
Sent: 07 June 2013 13:51
To: Suzanne Scott
Subject: Substantial Amendment - R&D Ref GN11CP446 Protocol V4; 19 May 13 Substantial Amendment AM03 (20/05/13)

Dear Ms Scott,

R&D Ref: GN11CP446 **Ethics Ref**: 11/WS/0115
Investigator: Ms Suzanne Scott
Project Title: Theory of Mind in individuals with paranoid Schizophrenia
Protocol Number: V4; 19 May 13
Amendment: Substantial Amendment AM03 (20/05/13)
Sponsor: NHS Greater Glasgow and Clyde

I am pleased to inform you that R&D have reviewed the above study's Amendment AM03 (20/05/13) and can confirm that Management Approval is still valid for this study.

Reviewed Documents:	Version	Dated
Ethics Favourable Opinion Letter		03 Jun 13
Ethics Validation letter		29 May 13
Notice of Substantial Amendment Form	AM03	20 May 13
Advertisement	1	19 May 13
Letter of invitation to participant	1	19 May 13
Participant Information Sheet: GP – Control Group	1	19 May 13
Protocol	4	19 May 13
SSI Form – GP Amendment		

I wish you every success with this research project.

Yours sincerely,

Research and Development
NHS Greater Glasgow & Clyde
Research & Development
Western Infirmary
1st Floor, Tennent Building
38 Church Street
Glasgow
G11 6NT

tel: 0141 211 6208
Web: www.nhsggc.org.uk/r&d

Please note that from the 27th May 2013, R&D will be operating an electronic record system. Please submit your R&D submission via e-mail from this date

Appendix 2.8: Eyes Test distracter items

A list was developed of all distracter items selected by participants when the target item was either a threat valence or positive valence item. Items already categorised in the first pilot as threat or positive were automatically coded as such. The remaining list of distracter items was classified by two independent raters into valence categories. Two items were disputed, and following discussion, full agreement was reached.

Table 4: Classification according to emotional valence of Eyes Test distracter items.

Valence	Adjective	
Threat	Aghast Alarmed Anxious Arrogant Depressed Dispirited Disappointed	Embarrassed Guilty Hostile* Insisting* Irritated Nervous* Terrified
Neutral	Annoyed Apologetic Baffled Bored Convinced Decisive* Dominant Grateful	Indecisive Indifferent Impatient Joking Puzzled Sarcastic Shy
Positive	Amused Affectionate Comforting Contented Contemplative*	Encouraging Friendly* Playful* Relaxed

*****Classified in initial pilot to determine target item valence

Appendix 2.9: New Theory of Mind Measure analysis according to components

An ANOVA with Group (Control or Patient) as a between-factor and component (sequencing or questions) as a within-factor was conducted. The dependent variable was accuracy, defined as the percentage of items for which a correct response was given. There was a significant main effect of group ($F (1, 14) = 11.35$, $p = .005$), with controls ($M = 77.60$, $SE = 6.34$, 95% CI 64.01 – 91.20) performing more accurately than patients ($M = 47.40$, $SE = 6.34$, 95% CI 33.80 – 60.93) ($d = 1.55$, large effect). There was also a significant main effect of component, whereby overall scores were greater on questions ($M = 67.19$, $SE = 4.62$, 95% CI 57.28 – 77.10) than sequencing ($M = 57.81$, $SE = 5.08$, 95% CI 46.91 – 68.72) ($d = 0.67$, medium to large effect). However, there was no significant interaction between component and group ($F (1, 14) = 1.24$, $p = .29$). Paired sample t tests revealed that controls were significantly less accurate on sequencing than questions ($t (7) = -2.63$, $p = .03$), whereas there was no significant difference in patients accuracy according to component ($t (7) = -.96$, $p = .37$) (Figure 1).

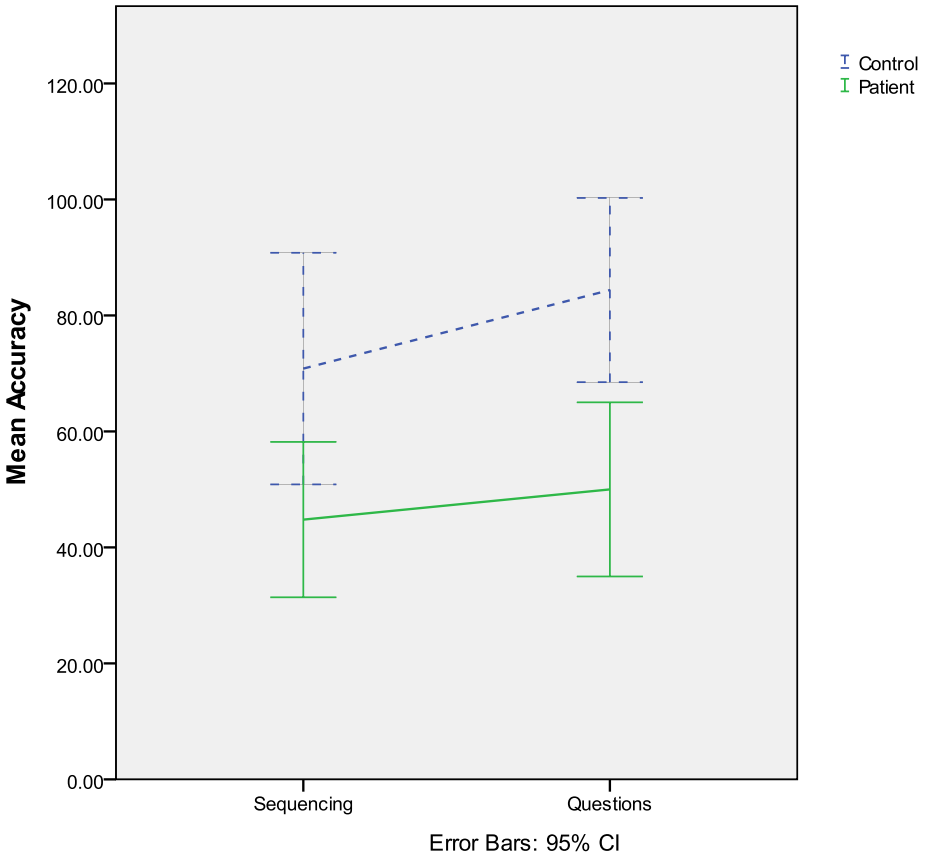

Figure 1: Mean accuracy of control and patients according to sequencing and question components on the New ToM Measure (95% CI are displayed). The control group is illustrated with a dashed line.

Appendix 2.10: Major Research Project proposal

Theory of Mind in individuals with paranoid schizophrenia

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Theory of mind and schizophrenia

'Theory of mind' (ToM) refers to the "cognitive capacity to represent one's own and other persons' mental states, for instance, in terms of thinking, believing, or pretending" (Brüne, 2005, p. 21). A substantial body of evidence demonstrates that this ability is significantly impaired in individuals with schizophrenia versus healthy controls (Brüne, 2005; Sprong et al., 2007), even when the heterogeneity of tasks employed to assess ToM is accounted for (Bora et al., 2009). Whilst ToM deficits in schizophrenia are well established, contradictory results have been reported regarding ToM impairment in patients in the acute phase of schizophrenia and after remission, in relation to IQ, executive function and memory abilities (Bora et al., 2009). The nature of ToM deficits in patients with paranoid symptoms is also unclear, as some studies have reported impaired ToM capacity, whilst others have failed to confirm this link (Brüne, 2005).

Several different paradigms have been used to assess ToM in schizophrenia, and these can be usefully grouped according to social cognitive or mental state reasoning tasks (e.g. assessing false belief, deception and intention understanding, and pragmatic speech comprehension), social perceptual or mental state decoding tasks (e.g. inferring mental states from cues, such as eye expressions), and real-world tasks (e.g. assessing structured interviews) (Bell et al., 2010). It is possible that the inconsistent results in individuals with paranoid symptoms could be related to the nature and content of these tasks, in addition to other

methodological limitations including insufficient power, incomplete reporting of clinical variables (e.g. cognitive data), differences in the battery of ToM tasks employed, and a lack of research regarding the psychometric properties of ToM tasks (Sprong et al., 2007; Bora et al., 2009).

ToM and paranoid symptoms

A number of cognitive processes are implicated in paranoid symptoms, including disruptions at the neurocognitive and social-cognitive levels, arising from deficits (e.g. poor attention) and/ or biases (e.g. a self-serving and personalising bias, and information-processing biases) (Peer et al., 2004). Bentall et al. (2009) conducted an analysis of a range of psychological mechanisms to determine the cognitive and affective processes associated with paranoia, and reported paranoid delusions to be associated with a combination of pessimistic thinking style (low self-esteem, pessimistic explanatory style, and negative emotion) and impaired cognitive performance (executive functioning, tendency to jump to conclusions, and ability to reason about the mental states of others).

Individuals with schizophrenia are less accurate, relative to healthy controls, in recognising facial emotions (Mandal et al., 1998; Kohler et al., 2003). Interestingly, individuals with schizophrenia have been reported as over-attributing disgusted expressions and under-attributing happy expressions to neutral cues (Kohler et al., 2003); whilst a tendency to misperceive emotions

(including happy, sad, fear and surprise emotions) as disgust rather than anger has been reported in individuals with paranoid symptoms (Peer et al., 2004). This has been assessed using stimuli that consist of facial expressions that represent a range of emotions including happy, sad, angry, disgust or neutral (Kohler et al., 2003; Peer et al., 2004).

The 'Reading the Mind in the Eyes' task (Baron-Cohen et al., 2001), which is similar to the paradigm described above, is contended to be an advanced ToM test because the stimuli consist of only pictures of the eyes (Bell et al., 2010). It measures the ability to identify cognitive emotions that require inferences about others' beliefs or intentions (e.g. being embarrassed or pensive). Cognitive emotions can be distinguished from 'basic emotions', which do not require this kind of inference (e.g. happy or disgusted) (Craig et al., 2004). Craig et al. (2004) reported a poor performance on the Eyes tasks by individuals with a diagnosis of paranoid schizophrenia. However, no information was provided regarding whether performance varied according to the direction of emotion (e.g. positive, negative, and neutral) included in the Eyes task.

In addition to a tendency to misperceive emotions, paranoid patients appear to make inflated estimates of the likelihood of future threatening events (Bentall et al., 2009), and demonstrate heightened attention to threatening stimuli (Bentall and Kaney, 1989; cited in Phillips et al., 2000). For example, in an emotional Stroop test, a significantly greater amount of time was

required for paranoid individuals to name the print colours of threatening versus depressive and neutral words (Bentall and Kaney, 1989; cited in Phillips et al., 2000). Many of the mental state reasoning ToM tasks involve the deception of characters. For example, Frith and Corcoran's (1996) False Belief and Deception Story (FBDS) task, commonly employed in schizophrenia research, involves six ToM stories (first-order and second-order) being read to subjects, of which four involve a character being deceived and centre around a theme of stealing. First-order false belief tasks involve identifying the mistaken beliefs held by a character in a story, whilst second-order false belief tasks involve identifying the false belief of one character about the beliefs of another (Sprong et al., 2007; Bell et al., 2010). Performance on ToM tasks are not generally considered in relation to the specific emotional content of the task, and it is unclear whether this could be a factor affecting an individual's performance.

Abdel-Hamid et al. (2009) used a five-factor model of the Positive and Negative Syndrome Scale to explore the association of symptom clusters and individual symptoms with ToM ability in schizophrenia. Contrary to their expectations, the authors reported that there was no significant association of positive symptoms and impaired ToM. Unexpectedly, there was a significant interaction of impaired ToM with items included in the 'emotional distress factor'. For example, there were significant inverse interactions between ToM deficit and the items 'tension' and 'depression', and a strong positive interaction between ToM and 'guilt', all of which were largely

independent of IQ or executive functioning (Abdel-Hamid et al., 2009). It is possible that several methodological factors could have contributed to these results, including that there was a relatively heterogeneous clinical sample that included a range of both positive and negative symptoms. In addition, a single measure of ToM was employed.

The ToM task employed by Abdel-Hamid et al. (2009) was Brüne's (2003) Picture Sequencing Task, which comprises picture stories with questions to assess a range of false beliefs, reciprocity, deception and cheating detection (Bell et al., 2010). It is possible that the differing emotional content (e.g. neutral stories and stories involving deception) within this ToM task might have affected performance given the above evidence regarding an individual's tendency to attend to threatening stimuli and misperceive emotions.

Theoretical frameworks

A number of different theoretical frameworks have been proposed in order to account for ToM deficits in schizophrenia. For example, Frith (1992) proposed that positive and negative symptoms in schizophrenia can be accounted for by abnormalities in brain function and circuitry that give rise to the individual's failure to monitor their own and other persons' mental states and behaviour (Brüne, 2005). In contrast, Hardy-Baylé et al. (2003), has proposed that ToM impairments in schizophrenia are primarily related to an

executive or planning deficit. Evidence in support of Frith's (1992) and Hardy-Baylé et al.'s (2003) conceptualisations has been mixed (Brüne, 2005; Abdel-Hamid et al., 2009), for example, contrary to Frith's prediction, individuals in remission have also shown ToM impairments relative to non-clinical controls (Sprong et al., 2007; Bora et al., 2009). This suggests that ToM deficits may be 'trait' rather than 'state' impairments, that is, enduring characteristics of the disorder versus being linked to the presence of symptoms (Bora et al., 2009).

An alternative approach to that of Frith (1992) and Hardy-Baylé has been outlined by Gumley (2010). Gumley (2010) has proposed that ToM impairments are rooted in compromised normative developmental pathways, characterised by negative interpersonal experiences (e.g. lack of secure base and/or the presence of relational trauma and loss during childhood and adolescence), which reduce an individual's ability to develop skill in representing one's own and other persons' mental states. Reflective functioning (RF) refers to the "psychological processes underlying the capacity to mentalize" (Gumley, 2010, p 51). RF has been found to be impoverished in several studies of individuals with borderline personality disorder, where the Adult Attachment Interview (AAI) has tended to classify individuals as preoccupied with attachment and the transcripts have been unresolved for loss and trauma (Fonagy et al., 1996; Dozier et al., 1999; cited in Gumley, 2010).

The theoretical frameworks proposed by Frith (1992) and Hardy-Baylé et al. (2003) are limited in their ability to account for the direction of the above findings, for example the tendency to misperceive a range of emotions as disgust. Clarifying whether ToM ability varies according to the emotional content of the specific items of a ToM task could contribute to explaining the inconsistencies that have been reported in the literature, and also contribute to a greater understanding of the theoretical frameworks that attempt to account for ToM impairments in individuals with schizophrenia.

Aim

To examine whether ToM ability in individuals with paranoid schizophrenia varies according to the emotional valence of items within ToM tasks.

Hypotheses

The research will address several hypotheses including:

- There will be a significant difference in ToM abilities in individuals with paranoid schizophrenia compared to controls, but this will be mediated by the emotional valence of items within the ToM tasks.
- There will be a significant difference in ToM ability in individuals with paranoid schizophrenia compared to controls.

- Individuals with paranoid schizophrenia will show greater accuracy on items within ToM tasks that include an element of threat versus items that have no threat.

Additionally, the research will explore the types of errors made by participants.

Plan of Investigation

Participants and inclusion/ exclusion criteria

Two groups of participants will be recruited, a clinical group and a control group. The clinical group will consist of participants with a diagnosis of paranoid schizophrenia. Participants will be recruited from Psychiatric Rehabilitation Wards, Rehabilitation Outreach Teams and from Inpatient Wards across NHS Greater Glasgow and Clyde sites (e.g. Gartnavel Hospital, Dykebar Hospital, Leverndale Hospital and Parkhead Hospital). Potential participants from Inpatient Wards will only be recruited if they are no longer in the acute phase of their illness and awaiting move to a Rehabilitation Ward as decided by a member of their healthcare team. The following inclusion criteria will apply to the clinical group:

- Between 16 and 65 years of age
- English as a first language
- Able to provide informed consent

- A diagnosis of paranoid schizophrenia
- No changes in medication during the study period

The following exclusion criteria will be applied to the clinical group:

- A history of traumatic brain injury
- A learning disability
- Active substance dependence

A control group will be recruited from amongst NHS Greater Glasgow and Clyde staff and University of Glasgow staff and students, and from the friends and relatives (excluding first degree relatives) of participating patients. In addition, the control group will also be recruited from patients attending GP practices participating in the study. Similar inclusion and exclusion criteria will apply to the control group, except that they will be excluded if they have received a diagnosis of a mental health problem. The control group will be matched to the clinical group in terms of age and intellectual functioning as determined by scores on the Wechsler Test of Adult Reading (WTAR; Wechsler, 2001).

Recruitment Procedures

Approval of project

Following approval of the Major Research Project Proposal from the Research Director and the West of Scotland Research Ethics Service,

Hospital Management approval will be sought by attending Senior Management Team Meetings across each site. Following approval, the Consultant Psychiatrist Meeting will be attended in order to provide relevant information relating to the project and promote recruitment.

Participant recruitment

The clinical group participants will be recruited via a number of methods. Firstly, the researcher will attend Community Meetings (attended by staff and service users) at the different sites, in order to provide a brief summary outlining the study and allow service users to opt-in to the study. At these meetings, service users will be asked to complete a form where they can a) elect to participate; b) request further information; or c) decline to participate. Secondly, a poster will be used to advertise the study. Thirdly, members of an individual's healthcare team will be able to refer potential participants directly to the researcher. Members of an individual's healthcare team will seek verbal consent from the potential participant for their details to be passed to the researcher prior to referring them to the researcher. Once a participant has indicated that they are interested in participating in the study, the relevant Psychiatrist will then be consulted to apply inclusion and exclusion criteria, and to assess capacity to consent to the study.

The control group will be recruited from amongst NHS Greater Glasgow and Clyde staff and University of Glasgow staff and students, and from the

friends and relatives (excluding first degree relatives) of participating patients. In addition, the control group will also be recruited from patients attending GP practices participating in the study. Participants will be recruited via posters located within appropriate and approved NHS Greater Glasgow and Clyde and University of Glasgow settings and by asking participants if they can suggest friends or relatives (excluding first degree relatives) who can be directly contacted with information about the study. Friends and relatives of patients (excluding first degree relatives) will be informed that their decision not to participate in the study will not affect the care of their friend or relative who is a patient and is taking part in the study. In order to recruit participants from GP Practice settings, all patients attending a GP practice on a particular day will be handed a letter outlining the project and an information sheet regarding the study by GP Practice Reception Staff. GP practice patients will be able to opt-in to the study by completing an opt-in slip or identifying themselves to GP Practice Reception Staff, who will then inform the Primary Researcher. The Researcher will meet with participants on the same day, immediately after their GP appointment. The participant information sheet will be reviewed with each potential participant before consent to participate in the study is sought.

Measures

The following measures will be employed:

The revised Eyes task (Baron-Cohen et al., 2001), which has enhanced psychometric properties, will be employed to assess ToM (Bell et al., 2010). A pilot study using a convenience sample of 10 individuals will be employed to classify the items within the task into emotional valence categories: threatening (e.g. hostile, suspicious), positive (e.g. friendly, interested) and neutral (e.g. pensive, reflective). The classification of items will be guided by adapting the procedure described by Harkness et al. (2005). Each stimuli will be ranked on a 7-point scale from 'very threatening' to 'very positive', and those that have mean ratings significantly below neutral will be classified as threatening, and those rated significantly above will be rated as positive. The piloted task is anticipated to take participants 15 minutes to complete.

Brüne's (2003) Picture Sequencing Task will be employed as the basis for constructing a new ToM task that includes three positive ToM stories, and three threatening ToM stories. Each ToM story will be represented in a series of four photographs. Following the methodology employed in Brüne's (2003) Picture Sequencing Tasks, participants will be asked to place the cards in the correct order so that they show a logical sequence of events. Participants will then be asked a series of questions regarding each story in order to assess ToM ability (e.g. false beliefs, reality). It is anticipated that this task will take 15 minutes to complete. This measure will be piloted using a convenience sample of 10 individuals prior to use.

The Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962) will be employed in order to assess psychopathology. The psychometric properties of the BPRS have been reported as adequate, and four factors are uniformly reported as positive symptoms, negative symptoms, depression-anxiety and agitation (Kopelowicz et al., 2008). Each participant's named nurse or other appropriate member of healthcare staff will be contacted in order to complete this rating scale. It is anticipated that this task will take 15 to 30 minutes to complete.

The Wechsler Test of Adult Reading (Wechsler, 2001) will be employed to provide an estimate of pre-morbid level of intellectual functioning for individuals aged 16-89 years. It is a word-reading test that involves pronouncing irregularly spelled words. The task is anticipated to take 5-10 minutes to complete.

Design

A mixed design will be employed with group as a between-factors (control, clinical) and valence as a within-factors (positive, threat). There will be two dependent variables accuracy on positive items, and accuracy on threat items, defined as the percentage of items where the participant identifies a correct response.

Research Procedures

In the clinical group, once an individual has been identified as able to provide informed consent, the researcher will contact the individual to arrange an appointment. Informed consent will be sought at the start of the appointment. Once written informed consent has been provided, appointments will take approximately 30 minutes to minimise demand on the participant. ToM task presentation will be counterbalanced to minimise bias associated with fatigue. The Eyes Task will be administered according to the instructions provided by Baron-Cohen et al. (2001). Instruction to the new ToM task will be similar to those of Brüne's (2003) Picture Sequencing Task. Instructions will be provided verbally and in brief written format for reference. Participants will be debriefed regarding the purpose of the study, and thanked for their participation. A similar approach will be used for the control group, with informed consent being sought at the start of the appointment.

For the clinical group, following receipt of an individual's informed consent, their named nurse or other appropriate member of staff will be contacted to complete the BPRS (Overall and Gorham, 1962), and to arrange access to case notes in order to obtain relevant demographic (e.g. age, highest level of education) and clinical (age of illness onset, duration of illness, medication) information. If an individual provides consent, their friends/relatives (excluding first degree relatives) will be contacted to invite them to participate in the study. For the control group, relevant information will be sought from individuals.

Justification of sample size

The main comparison of interest will be to explore whether there is a significant difference between accuracy on positive items and accuracy on threat items in individuals with a diagnosis of paranoid schizophrenia. Harkness et al. (2005) reported descriptive statistics for positive and negative items in the Eyes Task. Using these data, Cohen's d was calculated for the difference in scores between positive and negative items, and a large effect of 0.74 was detected. In order to conduct a MANOVA with independent variable of Group (Control, Clinical Group) and two dependent variables (accuracy on positive items, accuracy on threat items), and given an effect size of 0.4, α of .05 and power of 0.80 a total sample of 28 is required for the global effects, with 14 participants in each group (Faul et al., 2007). Harkness et al. (2005) also explored the difference in accuracy between dysphoric and non-dysphoric individuals. The authors reported a significant difference of $t(41) = 2.85$, $p < .025$, and using this, a value of 0.41 was calculated for r. This equates to a large effect size of Cohen's $d > 0.8$. Therefore the above sample size calculation would also appear to be valid for exploring the relationship between the control and clinical groups.

Settings and Equipment

The settings for the study will be a number of hospital sites across NHS Greater Glasgow and Clyde. ToM tasks will be administered in a free clinic room, to be arranged with each Hospital site.

Data Analysis

The main analysis will employ a MANOVA in order to test whether there is a significant difference in ToM ability depending on the emotional valence. This test will be employed to accommodate two dependent variables. Non-parametric alternatives will be explored if necessary.

Health and Safety Issues

The proposed study will be undertaken on different hospital sites within NHS Greater Glasgow and Clyde, therefore local Health and Safety policies and procedures will be adhered to.

Researcher Safety Issues

Researcher safety has been considered and a number of steps will be taken to promote it. Participants with a diagnosis of paranoid schizophrenia are to be recruited, however, a psychiatrist will be consulted prior to any contact with a participant in order to determine whether the individual has the capacity to consent to the study. No participants in the acute phase will be recruited. Additionally, the control group will be recruited from NHS Greater Glasgow and Clyde staff and University of Glasgow staff and students, from friends and relatives (excluding first degree relatives) known to participating individuals, and from patients attending their own GP practice. An identified and appropriate member of staff will be informed of all scheduled meetings

with participants. All appointments will be located on NHS Greater Glasgow and Clyde sites. Local health and safety policies will be adhered to by the Primary Researcher. The Primary Researcher will carry a pin-point alarm and will be familiar with appropriate procedures to raise alarm if necessary.

Participant Safety Issues

Participant safety will be promoted by conducting appointments in suitable settings on NHS Greater Glasgow and Clyde Hospital sites. The Primary Researcher will adhere to local health and safety policies. Participant fatigue will be minimised by limiting the duration of each participant in the study to approximately 30 minutes. The Primary Researcher will monitor participants for signs of fatigue or discomfort, and if indicated, the Primary Researcher will check whether the participant wishes to continue or discontinue with testing. Participants will be provided with written information at the point where consent is sought, which will highlight their right to withdraw from the study at any point.

It is possible that a participant could become distressed during testing (for example, thinking that they are making errors). If the participant becomes distressed, the Primary Researcher will check whether the participant wishes to continue or discontinue with testing. Informed consent will be sought from all participants prior to testing and participants will be provided with written information that highlights their right to withdraw from the study at any point.

If the Primary Researcher has any concerns regarding the participant's well-being or presentation (e.g. they pose a risk to themselves or to others) then testing will be discontinued and the Primary Researcher will report their concerns to an identified and appropriate member of staff (e.g. Clinical Psychologist, Psychiatrist, Named Nurse).

Ethical Issues

Following approval of the proposal by the University of Glasgow, Academic Unit of Mental Health and Wellbeing, management approval will be sought from NHS Greater Glasgow and Clyde Research and Development, whilst ethical approval will sought from the West of Scotland Research Ethics Service. Several ethical issues have been considered such as capacity to provide written informed consent to participate in the study, possible fatigue during testing, and risk.

Each individual's psychiatrist will be consulted to check that they have capacity for consent. Prior to testing, each participant's written informed consent to participate will be sought. Testing will be limited to 30 minutes in order to reduce the demand on the participant, and the researcher will also monitor participants for fatigue or discomfort. Any concerns, for example regarding a participant's risk of harm to self or others or their presentation during the study will be reported by the researcher to an identified and appropriate member of staff, with supervision by the NHS Field Supervisor.

Financial Issues

There is no anticipated cost associated with accessing the measures described above. The Eyes task is available free of charge for research purposes from the Autism Research Centre. The main cost of the study will be associated with photocopying measures, developing photographs, printing consent forms and other study paperwork.

Timetable

Recruitment of participants would commence in January 2013. Recruitment is deferred to January 2013 in order to accommodate a period of maternity leave for the Primary Researcher. The anticipated end date of the study is 27th September 2013.

Practical Applications

The proposed study has the potential to make a significant contribution to the current understanding of ToM ability in individuals with paranoid schizophrenia. Additionally, it is possible may help to inform interventions for ToM deficits in clients with Schizophrenia. For example, Metacognitive Training aims to enhance patient's awareness of cognitive biases and explore alternative strategies that enable the client to make more appropriate inferences (Moritz and Woodward, 2007). Evidence regarding the role of

emotion within ToM deficits in Schizophrenia may serve to refine such interventions.

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