Distinguishing Oneself from Others: Spontaneous Perspective-Taking in First Episode Schizophrenia and its relation to Mentalizing and Psychotic Symptoms

Arndis Simonsen PhD[1,2,3], Mia Ilsø Mahnkeke MSc[1], Riccardo Fusaroli PhD[2,4], Thomas Wolf PhD[5], Andreas Roepstorff PhD[2], John Michael PhD[5], Chris D. Frith PhD[6], Vibeke Bliksted PhD[1,2,3]

[1]The Psychosis Research Unit, Aarhus University Hospital, Aarhus, Denmark.

[2]The Interacting Minds Centre, Aarhus University, Aarhus, Denmark.

[3]Department of Clinical Medicine, Aarhus University, Aarhus, Denmark.

[4]Cognitive Science, School of Communication and Culture, Aarhus University, Aarhus, Denmark.

[5]Department of Cognitive Science, Central European University, Budapest, Hungary.

[6]The Wellcome Centre for Human Neuroimaging, London, United Kingdom.

Corresponding author

Vibeke Bliksted

Aarhus University Hospital - Psychiatry

Palle Juul-Jensens Boulevard 175, Entrance K, K510-565

DK-8200 Aarhus N, Denmark

vibeke.bliksted@ps.rm.dk

+45 2055 8317

Abstract

Characteristic symptoms of schizophrenia such as thought broadcasting, verbal hallucinations and delusions of being controlled suggest a failure in distinguishing between oneself and others. In addition, patients frequently experience mentalizing deficits, which could be related to such a failure. Here we investigated the tendency to distinguish self and other with a visual perspective-taking task that measures to what extent individuals spontaneously take another's perspective when having to process their own (altercentric intrusion) or vice versa (egocentric intrusion). This was done in 22 patients with first episode schizophrenia and 23 matched healthy controls. We assessed whether patients displayed altered altercentric or egocentric intrusion and whether such alterations are related to mentalizing deficits – as measured with the Animated Triangles Task (ATT) and The Awareness of Social Inference Task (TASIT) – and/or specific psychotic symptoms, suggestive of problems with self-other distinction. The results showed that patients display similar egocentric intrusion and increased altercentric intrusion compared to controls. Degree of altercentric intrusion was associated with severity of delusions and hallucinations that have been tied to problems with self-other distinction but not with unrelated delusions and hallucinations or negative symptom severity. Higher altercentric intrusion was also associated with better TASIT performance in both patients and controls; suggesting that it may also be beneficial. In conclusion, patients display difficulties inhibiting representations of the other when having to process self-relevant information. A failure to control or distinguish the two representations could give rise to the experience that others have access to and control of your thoughts and actions.

2

Introduction

Social interactions require one to inhibit or enhance the representation of oneself and others to varying degrees. For instance, when taking another's perspective, during mentalizing or when empathizing with others, one needs to inhibit one's own perspective, mental or affective state and enhance the representation of the other's, while when performing an action or in order to avoid imitating others, one needs to inhibit the representation of others[1, 2]. This ability to control, distinguish or switch between the representations of self and other is referred to as self-other control or distinction[1-3]. When this mechanism fails, characteristic symptoms of schizophrenia might arise. For instance, echolalia, thought broadcasting, thought insertion or delusions of being controlled all seem suggestive of such a failure. At the same time, patients display large mentalizing impairments[4, 5]. A critical aspect of mentalizing is the ability to keep track of one's own and others' perspectives and to be able to put aside one's own potentially conflicting perspective when taking others'[6-8], i.e. self-other distinction. Previous research on visual perspective-taking in schizophrenia suggests that they also have difficulties with this specific aspect (e.g., see: [7, 9, 10]). However, most of the tasks used to investigate visual perspective taking – and mentalizing in general – assess explicit processes and therefore draw on general cognitive functions (e.g. executive functions, working memory and language)[11, 12]. Since patients are known to have severe cognitive deficits across several domains[13], it is difficult to say whether or to what extent the mentalizing deficits are secondary to these. In addition, mentalizing tasks typically draw on multiple social-cognitive functions. To avoid these issues, and more directly assess core problems with controlling self-other representations, in this study we investigate implicit processes. Specifically, we assessed whether patients with schizophrenia display altered spontaneous perspective-taking compared to healthy individuals and whether such potential alterations are related to higher-order mentalizing deficits or specific psychotic symptoms, suggestive of difficulties with self-other distinction. We used a modified version of the visual perspective-taking task developed by Samson et al. (2010)[6]. The task measures to what extent people spontaneously compute their own perspective when making explicit

3

judgments about the other's perspective (egocentric intrusion) and vice versa (altercentric intrusion).

Both abnormal egocentric and altercentric intrusion could potentially affect higher-order mentalizing ability. As already mentioned, a failure to inhibit one's own perspective could interfere with one's ability to take the other's perspective (increased egocentric intrusion). Interestingly, the opposite could also be the case. Specifically, failing to inhibit the other, when taking one's own perspective (increased altercentric intrusion) has been associated with impaired mentalizing. This has been shown in the motor domain where an individual's ability to control imitation – i.e. the ability to distinguish between self-generated and other generated movements – is associated with better mentalizing performance[3, 14-16]. Finally, reduced altercentric intrusion could suggest strong self-other control processes but it could also reflect a failure to process social information to a sufficient degree. Healthy individuals are known to spontaneously take others into account even in situations where it is not relevant[6, 17] and there is some evidence that patients with schizophrenia fail to do so[18, 19]. Thus, such a failure could impair higher-order mentalizing or at least successful social interactions. Of these alterations in egocentric and altercentric intrusion, increased altercentric intrusion is perhaps the most likely to cause the aforementioned psychotic symptoms that are characteristic of schizophrenia. In particular, the experience that others have access to and control of your thoughts and actions could arise when self-other distinction is impaired in situations where self-relevant information needs to be processed, e.g. during action preparation. A schematic depiction of these relations is presented in Figure 1. Attaining a better understanding of the potential role of self-other control processes in higher-order mentalizing deficits in schizophrenia and in the clinical manifestation of the disorder could provide valuable information concerning the underlying mechanism and help to identify targets for intervention.

4

Methods

Participants

This study was part of a larger project and results from other paradigms are reported in Bliksted et al. (2017, 2019)[20, 21]. Twenty-three patients with first-episode schizophrenia (FES) and 23 healthy controls were included in the study. All patients were recruited from the OPUS Clinic for people with schizophrenia at Aarhus University Hospital. The ICD-10 diagnosis of schizophrenia was confirmed by experienced psychiatrists using Present State Examination (PSE, ICD-10). Patients between the age of 18 and 35 years were included in the study if they had received antipsychotic medication for a period no longer than 3 months prior to the diagnostic interview (life-time exposure).

Controls underwent the entire PSE interview with VB. To be included in the study, controls could not have a history of mental illness, either themselves or among first-degree relatives. Furthermore, both patients and controls were excluded based on the following criteria: a history of neurological illness, severe head trauma or current substance- or alcohol abuse/dependency according to ICD-10 or had an estimated IQ below 70 (based on prior educational achievements). Participants were screened for recent drug use using a urine sample (testing for amphetamine, benzodiazepines, cannabis, codeine, morphine, cocaine).

Patients and healthy controls were matched one to one (when possible) based on age, gender, educational level (based on the last commenced education), community of residence and parental social economic status. One patient was not able to complete the visual perspective-taking task and was excluded from all analyses. Analysis was performed on 22 patients and 23 controls. Of these, two patients and three controls were not matched one to one. Nine patients did not receive antipsychotic medication at the time of testing while 13 had started treatment within the last four weeks. Of these, many received a low dose. Eighteen patients had received their diagnosis within

the last four weeks prior to testing, three patients within the last three months and one patient

approximately a year earlier. See Table 1 for further details on the participants.

General Procedure

In addition to the visual perspective-taking task and mentalizing tasks described below, symptom

severity was assessed with the Scale for the Assessment of Negative/Positive Symptoms

(SANS/SAPS)[22, 23] by VB on the day of testing. We also estimated intelligence based on four subtests

from Weschler Adult Intelligence Scale, Third edition (WAIS-III)[24]: Block design, Vocabulary, Matrix

Reasoning and Similarities. The study was approved by The Central Denmark Region Committees on

Biomedical Research Ethics (Ref: M-2009-0035) and reported to the Danish Data Protection Agency.

The study complied with the Helsinki-II Declaration. Written informed consent was obtained from all

participants after the procedure had been explained.

SAPS sub-scores

To get an indication of the severity of psychotic symptoms related to problems with self-other

distinction as opposed to severity of psychotic symptoms in general, we created two sub-scores

based on SAPS, including severity of specific hallucinations and delusions. The first sub-score

included symptoms that have typically been tied to problems with self-other distinction both

conceptually and in experimental work. These include verbal or auditory hallucinations in general as

well as symptoms referred to as self-disturbances that constitute a large part of the first-rank

symptoms (e.g. delusions of thought interference and being controlled) [25-30]. Here, auditory verbal

hallucinations are assumed to arise from a failure to recognize inner speech as such[31, 32]. Previous

factor analytic work on SANS/SAPS item level suggests that the above mentioned delusions load on

the same factor, while the different types of auditory hallucinations load together on another

6

factor[33, 34]. In addition, delusions of reference or persecution[35-38] have been suggested to be related to problems with self-other distinction on conceptual grounds. Specifically, it has been proposed that such delusions may be a consequence of misattributing one's own (negative) thoughts and emotions about oneself onto others[35, 37]. Aforementioned factor analyses also find that delusions of reference and persecution load on the same factor[33, 34] (although see:[39] for a contradicting finding in a much smaller sample). Thus, the following symptoms were included in the first sub-score: auditory hallucinations, voices commenting, voices conversing, persecutory delusions, ideas and delusions of reference, delusions of being controlled, delusions of mind reading, thought broadcasting, thought insertion and thought withdrawal.

The other sub-score included all other hallucinations and delusions assessed in SAPS: somatic or tactile hallucinations, olfactory hallucinations, visual hallucinations, delusions of jealousy, delusions of sin or guilt, grandiose delusions, religious delusions and somatic delusions. These have, to our knowledge, not been associated with self-other distinction in experimental work. Thus, for instance a grandiose delusion may or may not be related to problems with self-other distinction, depending on the content of the delusion, e.g., believing oneself to be another famous person. This sub-score serves as a general indication of the severity of hallucinations and delusions and at the same time is less likely linked to difficulties with self-other distinction.

Visual Perspective-Taking Task

We used a modified version of the visual perspective-taking task developed by Samson et al. (2010)[6]. Briefly, a human-like avatar was presented on a computer screen (matching the participant's gender), see example in Figure 2. It was facing a left or right wall and 0 to 3 red discs would appear on either or both walls. The task had a 2 x 2 factorial design with the factors Perspective (one's own or the avatar's) and Consistency between the number of discs seen from the two perspectives (consistent, inconsistent).

In the beginning of each trial, participants were presented with a fixation cross for 750ms. 500ms later, the word "DIG" (Eng.: YOU) or "HAM/HENDE" (Eng.: HE/SHE) appeared for 750ms, indicating which perspective had to be judged. 500ms later, the number 0, 1, 2 or 3 appeared for 750ms, specifying how many red discs the participant had to verify were visible from the relevant perspective. Then the room with the avatar appeared until the participant pressed one of two keys (J for "ja" (Eng.: yes) and N for "nej" (Eng.: no)), indicating whether the number matched the relevant perspective. The next trial began automatically after 2000 ms if no response was given.

The task was programmed in E-prime (2.0 Professional). It consisted of 61 trials in total, including nine practice trials. Trials were presented in a pseudo-randomized order that was fixed across participants so that there were no more than three consecutive trials of the same type. There were two versions of this randomization: half of the participants received one version and the other half received the other. On 26 of the 52 test trials, participants were asked to verify their own perspective and on 26 the avatar's. On 18 of the 26 trials, the correct answer was "yes" and on 8 it was "no" (as in previous work[6], the "no" trials were excluded). This resulted in 36 trials, 18 for each perspective. On eight of these, the perspectives were consistent and on 10, they were inconsistent. It took a maximum of 6 minutes to complete the task.

The Awareness of Social Inference Test

We used the Danish version[40] of the Awareness of Social Inference Test (TASIT, Part 2 Social Inference (minimal))[41] to measure explicit higher-order mentalizing ability. The task consists of sincere and sarcastic video clips of everyday-like situations (ten of each). Participants are asked questions about the communicative intentions of the people in the clips. We used the total accuracy score, with higher scores indicating better performance. For further details on the task, see Supplementary Material.

8

The Animated Triangles Task

The Animated Triangles Task[42] (ATT) assesses people's tendencies to spontaneously attribute mental states to shapes that are animate[12]. The video clips are divided into a theory of mind condition and a random condition (four in each). After each clip, participants are asked to describe what happened in the video. We used the total accuracy, with higher scores indicating better performance. For further details, see Supplementary Material.

Data Analysis

We wanted to assess whether patients display 1) increased egocentric intrusion, 2) reduced altercentric intrusion, or 3) increased altercentric intrusion compared to healthy individuals and if so whether it is related to task performance on the two mentalizing tasks and specific psychotic symptoms.

Trials with reaction times (RTs) shorter than 200 ms (0.06 %) and response omissions (patients: 4 %; controls: 0.3 %) due to timeout (no response within 2000 ms) were excluded from all analyses. This resulted in an average of 35.9 trials for controls and 34.5 trials for patients. In addition, errors (patients: 10.1 %; controls: 3.4 %) were excluded from the RT analyses. In order to assess whether patients with schizophrenia display altered spontaneous perspective-taking compared to healthy controls, we built two Bayesian multilevel regression models. The first modeled Accuracy relying on a Bernoulli likelihood function with a logit link. The second modeled RTs of accurate answers relying on a shifted lognormal likelihood function. Both models used the full 2 x 2 x 2 experimental design as predictors (Perspective, Consistency and Group). We modeled two clusters of additional variation in the data (random effects): effects of Perspective and Consistency could vary by participant; and effects of Group could vary by stimulus. Finally, we modeled participant matching between patients

9

and controls (when possible), by relying on the matched participant id and allowing the effect of group to vary by matched id. This corresponds to a maximally conservative random effects structure[43]. Note that the statistical inferences only modeled matches between actually matched participants (shared varying intercept with varying effect of group), while unmatched participants were modeled with an individual varying intercept and no varying effect of group. We defined weakly conservative priors for the models: discounting extreme effects and regularizing individual variability (see Supplementary Material).

From the full models, we then estimated the specific effects to be tested according to our questions. For those, we report 95% credible intervals (CIs), evidence ratios and credibility scores. The evidence ratio provides the ratio of evidence (that is, posterior samples) in favor of the hypothesized effect (e.g., patients display increased egocentric intrusion compared to controls) against the alternative (patients display equal or reduced egocentric intrusion). A common interpretation of evidence ratios is as follows: 1–3 = anecdotal; 3–10 = substantial; 10–30 = strong[44-46]. A credibility score indicates the percentage of posterior estimates compatible with the hypothesis.

When the above analyses yielded group differences, they were followed up by analyses in patients only, testing whether the degree of e.g. altercentric intrusion was associated with performance on the mentalizing tasks and relevant psychotic symptoms. This was done by implementing the modeling procedures detailed above on the patient data only, but replacing "Group" variable with the relevant predictor variable or variables. Mentalizing abilities were operationalized in terms of overall accuracy in the ATT and in TASIT. In the model containing relevant psychotic symptoms, we included both the total SANS score, and the sum of scores of unrelated delusions/hallucinations in order to control for collider bias[47]. For complete details on the model implementations and priors, see Supplementary Material; for the analyses code, see:

https://osf.io/t5qpd/?view_only=9b431f44367249b99dd70d794c1b979e.

10

Results

Task Performance

Patients made more errors and had slower RTs on average compared to controls. Patients were correct 89% of the trials with an RT of 846 ms, while for controls this was 96% and 789 ms, respectively (Accuracy difference on a log-odds scale: β = 1.06, SE = 0.25, 95% CI = 0.65 1.46, ER > 1000, credibility = 1; RT difference on a log-scale: β = -0.09, SE = 0.06, 95% CI = -0.2 0.01, ER = 14.3, credibility = 0.93).

Consistent trials were answered more correctly and faster (95% correct, mean RT = 776 ms) than inconsistent trials (90% correct, mean RT = 848 ms; accuracy difference on a log-odds scale: β = 0.95, SE = 0.25, 95% CI = 0.54 1.36, ER > 1000, credibility = 1; RT difference on a log-scale: β = -0.1, SE = 0.04, 95% CI = -0.17 -0.03, ER = 70.4, credibility = 0.99).

When participants had to take the other's perspective, they responded faster and more correctly (mean RT = 803 ms, 94% correct) than when taking their own perspective (mean = 827 ms, 91% correct; accuracy difference on a log-odds scale: β = 0.37, SE = 0.22, 95% CI = 0.01 0.73, ER = 19.8, credibility = 0.95; RT difference on a log-scale: β = -0.03, SE = 0.03, 95% CI = -0.08 0.01, ER = 9.2, credibility = 0.9).

Perspective-Taking and Schizophrenia

As expected, when healthy controls had to take the avatar's perspective, their own perspective interfered, i.e. they were slower and made more errors on inconsistent trials (egocentric intrusion - Accuracy: β = -0.89, SE = 0.54, 95% CI = -1.81 -0.03, ER = 22.1, credibility = 0.96; RT: β = 0.13, SE = 0.06, 95% CI = 0.05 0.23, ER = 136.9, credibility = 0.99). However, this was also the case for patients and the two groups were not credibly different (difference in egocentric intrusion - Accuracy: β = -0.16, SE = 0.66, 95% CI = -1.25 0.9, ER = 1.4, credibility = 0.59; RT: β = -0.04, SE = 0.08, 95% CI = -0.17 0.09, ER = 2.2, credibility = 0.69), see also Figure 3.

11

When the controls had to take their own perspective, the avatar's perspective also interfered with task performance (altercentric intrusion). Specifically, controls made more errors when the avatar's perspective was inconsistent with their own (β = -0.35, SE = 0.44, 95% CI = -1.08 0.34, ER = 3.7, credibility = 0.79), going from an accuracy of 96% to 94%. However, the RTs were not different in the two conditions (β = 0, SE = 0.06, 95% CI = -0.09 0.09, ER = 1.0, credibility = 0.51). Patients on the other hand, displayed more altercentric intrusion compared to controls, as reflected in the higher number of errors and slower RTs when the two perspectives differed (difference in altercentric intrusion - Accuracy: β = 0.79, SE = 0.57, 95% CI = -0.15 1.7, ER = 10.9, credibility = 0.92; RT: β = -0.12, SE = 0.08, 95% CI = -0.25 0.01, ER = 14.1, credibility = 0.93), see also Figure 3. In particular, accuracy fell from 94% to 82% and RT grew from 814 ms to 901ms. We therefore further tested whether altercentric intrusion in patients was related to mentalizing abilities and relevant psychotic symptoms.

Perspective-Taking, Mentalizing and Psychotic Symptoms

TASIT total score was credibly related to the altercentric intrusion effect for accuracy (β = 4.77, SE = 2.36, 95% CI = 1.05 8.77, ER = 61.5, credibility = 0.98), but not RT (β = -0.12, SE = 0.34, 95% CI = -0.7 0.43, ER = 1.8, credibility = 0.64). In particular, altercentric intrusion increased with better TASIT performance (Figure 4). This is due to the fact that while the higher the TASIT score, the better the performance on both consistent and inconsistent trials, performance on consistent trials increased more. Specifically, performance on consistent trials increased from 83% with a TASIT score at chance level to 98% with a full score, while performance on inconsistent trials only increased from 80% to 84%. TASIT is known to be associated with IQ, also in healthy individuals[48, 49]. We therefore assessed whether the general increase in performance in the perspective-taking task and TASIT was best explained by domain general processes by adjusting for IQ. We found that the association between TASIT and altercentric intrusion remained when adjusting for IQ (β = 3.6, SE = 4.35, 95% CI -3.92 10.27, ER = 3.9, credibility 0.8). More specifically, performance on consistent trials decreased from

12

76% to 61% accuracy as TASIT scores went from chance level to highest score; while performance on inconsistent trials decreased much more: from 75% to 25% accuracy. Thus, while the direction of the effects changed, altercentric intrusion still increased with increasing TASIT score. Interestingly, we saw exactly the same pattern in controls (TASIT alone: β = 5.93, SE = 9.21, 95% CI -9.26 20.89, ER = 3.0, credibility 0.75; TASIT adjusting for IQ: β = 13.11, SE = 12.09, 95% CI -6.3 33.26, ER = 6.3, credibility 0.86).

Performance on the Animated Triangles Task (ATT) was not credibly related to the altercentric intrusion effect for accuracy (β = 0.46, SE = 1.96, 95% CI = -3.7 2.74, ER = 1.4, credibility = 0.59) nor for RT (β = -0.09, SE = 0.24, 95% CI = -0.5 0.31, ER = 0.6, credibility = 0.39). For Accuracy, performance on consistent trials increased from 77% with the lowest ATT score to 99% with the highest score, while performance on inconsistent trials increased from 60% to 95% (Figure 4).

Relevant psychotic symptoms were credibly related to the altercentric intrusion effect for accuracy (β = -3.23, SE = 1.47, 95% CI = -5.66 -0.84, ER = 71.7, credibility = 0.99), but not for RT (β = 0.05, SE = 0.26, 95% CI = -0.36 0.48, ER = 0.8, credibility = 0.43). Altercentric intrusion grew with increased psychotic symptoms (from a difference in accuracy of 1% with 0 score, to a difference of 39% with full score). Interestingly, performance on consistent trials increased from 89% with 0 score to 94% with full score, while performance on inconsistent trials decreased from 88% with 0 score to 33% with full score. Control predictors, i.e. severity of unrelated psychotic symptoms or negative symptoms were not credibly related to altercentric intrusion for accuracy (unrelated psychotic symptoms: β = 0.87, SE = 3.76, 95% CI = -5.63 6.36, ER = 0.6, credibility = 0.37; SANS: β = -0.28, SE = 1.12, 95% CI = -2.1 1.57, ER = 1.5, credibility = 0.6) nor for RT (Unrelated psychotic symptoms: β = -0.03, SE = 0.24, 95% CI = -0.43 0.36, ER = 0.9, credibility = 0.46; SANS: β = -0.08, SE = 0.2, 95% CI = -0.42 0.23, ER = 0.5, credibility = 0.34).

Since both higher TASIT score and higher levels of relevant psychotic symptoms were related to increased altercentric intrusion, we assessed whether TASIT and symptoms were uniquely related to

13

altercentric intrusion. Indeed, there was still an association between altercentric intrusion and both TASIT performance (β = 5.80, SE = 2.90, 95% CI = 1.14 10.60, ER = 49.0, credibility = 0.98) and relevant psychotic symptoms (β = -4.50, SE = 2.78, 95% CI = -9.09 -0.13, ER = 17.1, credibility = 0.94). In particular, adjusting for symptoms, an increase in TASIT score from chance level to highest score brings accuracy on consistent trials from 77% to 96%, and on inconsistent trials from 89% to 77%. Adjusting for TASIT, and irrelevant symptoms, an increase in relevant psychotic symptoms from lowest to highest score brings accuracy in consistent trials from 77% to 80%, and in inconsistent trials from 90% to 42%.

Discussion

The present study sought to investigate whether spontaneous visual perspective-taking is altered in schizophrenia and whether such potential alterations might underlie higher-order mentalizing deficits or specific psychotic symptoms that have been related to problems with self-other distinction. We found increased altercentric intrusion in patients compared to controls, while egocentric intrusion was not credibly different in the two groups. Contrary to this, one previous study[18] found reduced altercentric intrusion in patients. They did not investigate egocentric intrusion. The discrepancy is likely due to the fact that in our study participants were cued to the two perspectives during the task, while in the study by Kronbichler et al. (2019)[18] participants only had to count the number of boxes in the room and were told that the avatar was not relevant. Such cueing may draw attention to both perspectives throughout the task even on trials where it is not relevant[50]. The fact that we did not find a credible difference between patients and controls on egocentric intrusion is interesting given the large literature on mentalizing deficits in schizophrenia. This suggests that a failure to inhibit one's own perspective when trying to take another's might not be at the root of these deficits.

We found that increased altercentric intrusion was associated with better higher-order mentalizing (TASIT performance) in both patients and controls, suggesting that people that tend to process the

14

other's perspective even when this is not relevant actually are more able to infer other's mental states. Previous studies have shown that healthy individuals process other's perspective even when it is not relevant[6, 17] and this automatic tendency to take others into account is arguably beneficial for joint action[17, 51] and possibly fundamental for higher-order mentalizing. Thus, although patients as a whole display increased altercentric intrusion and impaired higher-order mentalizing, increased altercentric intrusion does not seem to impair higher-order mentalizing, rather the opposite seems to be the case.

We did not find a similar association between altercentric intrusion and ATT performance. One reason for this may be that TASIT and ATT tap into different processes related to mentalizing, with the former being more closely related to perspective-taking. Specifically, ATT does not require an understanding of differing perspectives, while this is very much in focus in TASIT. In fact, the two protagonists clearly differ in their perspectives during 9 out of 10 sarcastic videos (e.g. one person thinks he has worked hard, while the other disagrees), but they agree on 9 out of 10 of the sincere videos. Participants are likely using such cues to solve the task. Imaging studies also suggest that visual perspective-taking and ATT to a lesser degree recruit overlapping areas compared to tasks which focus on differing perspectives, i.e. false belief tasks[52].

We found that increased altercentric intrusion was also associated with higher severity of psychotic symptoms related to problems with self-distinction but not with severity of unrelated hallucinations and delusions or severity of negative symptoms. Notably, this association seemed to be largely independent from the association with TASIT. Interestingly, patients with higher symptom severity performed better on consistent trials but worse on inconsistent trials than patients with lower symptom severity. A possible explanation for this is that these patients to a larger degree process both perspectives concurrently, which will result in better performance on consistent trials – where the other's perspective facilitates performance – while it has detrimental effects on inconsistent trials where it interferes more. The findings suggest that these psychotic symptoms may in fact be a

15

consequence of too much weight on or a failure to disengage in processing of other-representations

when having to process self-relevant information. This could naturally lead to misattribution of one's

own thoughts and actions to others and generally blur the distinction between self and other.

Several lines of experimental work suggest that patients with schizophrenia have difficulties

distinguishing themselves from others (e.g. when assessing self or other-produced actions, tactile

sensations, voice recordings)[26, 36, 53-55]. Typically, these impairments are more severe in patients that

are experiencing auditory hallucinations[53, 54, 56] and/or first-rank symptoms[26, 55, 57] compared to

patients that are not. Different theories have been put forward as to why this might be and how it

could result in specific psychotic symptoms. For instance, the comparator model[58] proposes that the

ability to attribute events to oneself (or to others) relies on the correct prediction of the kinematic

and sensory consequences of motor commands. If there is a match, the movement is recognized as

self-generated, while a failure to predict movement will result in an experience of external cause, i.e.

of being moved (delusions of control). Relatedly, others have focused on external cues or the

weighted integration of external and internal cues including prior expectations[38].

Yet, others have focused more on cognitive processes rather than motor processes. For instance,

Bentall and colleagues[37] have, in their attribution-self-representation cycle model, proposed that

persecutory delusions arise because patients try to avoid activating latent negative beliefs about

themselves by attributing negative events to others, such external attributions reduce discrepancies

between actual self-representation and ideals; however, they contribute to building a paranoid

world view. Impaired mentalizing ability may aggravate this problem by increasing the probability of

an external personal attribution rather than a situational attribution[37].

Our current results offer a complementary interpretation, where the continuous processing of

others' perspective even when it is not relevant may lead to such psychotic symptoms. Whether this

abnormality arises as a consequence of noisy and therefore unpredictable internal motor signals

that fundamentally changes how one processes information about the self and others, or whether it

16

is particularly severe in patients that have negative self-representation, or whether these are independent abnormalities should be further explored in future studies. Future studies with larger sample sizes could also assess whether specific psychotic symptoms (e.g. persecutory delusions, delusions of being controlled) are differentially related to the continuous processing of others' perspective.

Another line of research, consistent with our finding, suggests that patients may be overly influenced by others. This is reflected in self-reports of heightened personal distress when observing others in distress[59], but it is also seen on more implicit measures where patients display enhanced automatic imitation of another's actions[60] and increased attitude change based on feedback about others' opinion[61]. Our findings extend these findings by showing that patients have difficulties inhibiting other-representations and this is particularly the case for patients that are experiencing a higher degree of the aforementioned psychotic symptoms. Importantly, we show this in newly diagnosed patients who were either unmedicated or had received antipsychotic medication for less than a month prior to testing, thus reducing such potential confounding factors.

Finally, there is an ongoing debate as to whether this visual-perspective taking task actually measures perspective taking or domain general processes such as attentional orienting[50, 62-64]. So far the literature suggests that participants do compute the perspective of others but only when cued to do so[50]. As participants were cued to the two perspectives in our study, it likely measures some form of perspective-taking. However, future studies could include a non-social control task to disentangle domain specific from domain general processes. Future studies could also extend the investigation of such processes to more ecologically valid social situations[65] to see whether the current findings that are based on highly artificial stimuli in a constrained experimental context, do indeed hold during real social interaction, and thus tap into a meaningful construct. Further, since the current study only included a small sample of newly diagnosed patients, the results should be replicated in a

larger sample and it should be investigated whether the findings generalize to more chronic stages of the disorder.

If patients' difficulties with self-other distinction are indeed a consequence of altered low-level self-other control processes, then it might be possible to improve self-other distinction by providing training for these specific patients. This has been tried in healthy individuals, where short imitation-inhibition training (compared to imitation training) has been found to improve perspective-taking ability[66] and to enhance empathic corticospinal responses and self-reported empathy[2]. The results of these studies suggest that it is possible to modulate self-other control processes through imitation-inhibition training and it would be interesting to see whether this type of training could in fact impact the relevant psychotic symptoms.

In conclusion, we found that patients with schizophrenia, rather than failing to inhibit their own perspective, when taking other's, exhibit difficulties inhibiting the other's perspective when having to take their own (increased altercentric intrusion). Interestingly, the spontaneous readiness to process other's perspective seems to be advantageous in general and is possibly a prerequisite for higher-order mentalizing, in particular when it comes to processing whether perspectives differ or not. However, the degree of altercentric intrusion was also associated with severity of psychotic symptoms that have been tied to problems with self-other distinction. Taken together, the results suggest that it is likely a matter of striking the right balance, since a failure to disengage in representing others when having to represent self-relevant information could contribute to blurring the border between self and others and lead to the experience that others have access to and control of your thoughts and actions or that these are indeed the thoughts or actions of another.

18

Acknowledgements

Financial Disclosures

None of the authors have a conflict of interest.

References

1. Sowden S, Shah P. Self-other control: a candidate mechanism for social cognitive function. *Front Hum Neurosci* 2014;8:789.

2. de Guzman M, Bird G, Banissy MJ, Catmur C. Self–other control processes in social cognition: from imitation to empathy. *Phil Trans R Soc B* 2016;371(1686):20150079.

3. Quesque F, Brass M. The Role of the Temporoparietal Junction in Self-Other Distinction. *Brain Topogr* Nov 2019;32(6):943-955.

4. Chung YS, Barch D, Strube M. A meta-analysis of mentalizing impairments in adults with schizophrenia and autism spectrum disorder. *Schizophr Bull* May 2014;40(3):602-616.

5. Savla GN, Vella L, Armstrong CC, Penn DL, Twamley EW. Deficits in Domains of Social Cognition in Schizophrenia: A Meta-Analysis of the Empirical Evidence. *Schizophr Bull* Sep 4 2012.

6. Samson D, Apperly IA, Braithwaite JJ, Andrews BJ, Bodley Scott SE. Seeing it their way: Evidence for rapid and involuntary computation of what other people see. *J Exp Psychol Hum Percept Perform* 2010;36(5):1255.

7. Langdon R, Coltheart M, Ward PB, Catts SV. Visual and cognitive perspective-taking impairments in schizophrenia: A failure of allocentric simulation? *Cogn Neuropsychiatry* 2001;6(4):241-269.

8. Villatte M, Monestès J-L, McHugh L, i Baqué EF, Loas G. Assessing perspective taking in schizophrenia using relational frame theory. *The Psychological Record* 2010;60(3):413-436.

9. Eack SM, Wojtalik JA, Keshavan MS, Minshew NJ. Social-cognitive brain function and connectivity during visual perspective-taking in autism and schizophrenia. *Schizophr Res* May 2017;183:102-109.

10. Eack SM, Wojtalik JA, Newhill CE, Keshavan MS, Phillips ML. Prefrontal cortical dysfunction during visual perspective-taking in schizophrenia. *Schizophr Res* Nov 2013;150(2-3):491-497.

11. Apperly IA, Butterfill SA. Do humans have two systems to track beliefs and belief-like states? *Psychol Rev* Oct 2009;116(4):953-970.

12. Schneider D, Slaughter VP, Dux PE. What do we know about implicit false-belief tracking? *Psychonomic bulletin & review* Feb 2015;22(1):1-12.

13. Bora E, Binnur Akdede B, Alptekin K. Neurocognitive impairment in deficit and non-deficit schizophrenia: a meta-analysis. *Psychol Med* Oct 2017;47(14):2401-2413.

14. Spengler S, von Cramon DY, Brass M. Resisting motor mimicry: control of imitation involves processes central to social cognition in patients with frontal and temporo-parietal lesions. *Soc Neurosci* 2010;5(4):401-416.

15. Spengler S, Bird G, Brass M. Hyperimitation of actions is related to reduced understanding of others' minds in autism spectrum conditions. *Biol Psychiatry* 2010;68(12):1148-1155.

16. Spengler S, von Cramon DY, Brass M. Control of shared representations relies on key processes involved in mental state attribution. *Hum Brain Mapp* Nov 2009;30(11):3704-3718.

17. Frith CD. The role of metacognition in human social interactions. *Philos Trans R Soc Lond B Biol Sci* Aug 5 2012;367(1599):2213-2223.

18. Kronbichler L, Stelzig-Scholer R, Pearce BG, et al. Reduced spontaneous perspective taking in schizophrenia. *Psychiatry research Neuroimaging* Oct 30 2019;292:5-12.

19. Liepelt R, Schneider JC, Aichert DS, et al. Action blind: disturbed self-other integration in schizophrenia. *Neuropsychologia* Dec 2012;50(14):3775-3780.

20. Bliksted V, Frith C, Videbech P, Fagerlund B, Emborg C, Simonsen A, Roepstorff A, Campbell-Meiklejohn D. Hyper- and Hypomentalizing in Patients with First-Episode Schizophrenia: fMRI and Behavioral Studies. *Schizophr Bull* Mar 7 2019;45(2):377-385.

20

21. Bliksted V, Videbech P, Fagerlund B, Frith C. The effect of positive symptoms on social cognition in first-episode schizophrenia is modified by the presence of negative symptoms. *Neuropsychology* Feb 2017;31(2):209-219.

22. Andreasen NC. *Scale for the assessment of negative symptoms*. Iowa City: University of Iowa; 1983.

23. Andreasen NC. *Scale for the assessment of positive symptoms*. Iowa City: University of Iowa; 1984.

24. Wechsler D. Wechsler Adult Intelligence Scale–Third Edition and Wechsler Memory Scale–Third Edition technical manual. *San Antonio, TX, The Psychological Corporation* 1997.

25. Jeannerod M. The sense of agency and its disturbances in schizophrenia: a reappraisal. *Exp Brain Res* Jan 2009;192(3):527-532.

26. Blakemore SJ, Smith J, Steel R, Johnstone CE, Frith CD. The perception of self-produced sensory stimuli in patients with auditory hallucinations and passivity experiences: evidence for a breakdown in self-monitoring. *Psychol Med* Sep 2000;30(5):1131-1139.

27. Hauser M, Knoblich G, Repp BH, Lautenschlager M, Gallinat J, Heinz A, Voss M. Altered sense of agency in schizophrenia and the putative psychotic prodrome. *Psychiatry Res* Apr 30 2011;186(2-3):170-176.

28. Stephane M, Kuskowski M, McClannahan K, Surerus C, Nelson K. Evaluation of speech misattribution bias in schizophrenia. *Psychol Med* May 2010;40(5):741-748.

29. Jeannerod M. The sense of agency and its disturbances in schizophrenia: a reappraisal. *Exp Brain Res* 2008/08/16 2008;192(3):527.

30. Kendler KS, Mishara A. The Prehistory of Schneider's First-Rank Symptoms: Texts From 1810 to 1932. *Schizophr Bull* Sep 11 2019;45(5):971-990.

31. Jones SR, Fernyhough C. Thought as action: inner speech, self-monitoring, and auditory verbal hallucinations. *Conscious Cogn* Jun 2007;16(2):391-399.

32. Bentall RP, Fernyhough C. Social predictors of psychotic experiences: specificity and psychological mechanisms. *Schizophr Bull* Nov 2008;34(6):1012-1020.

33. Toomey R, Kremen WS, Simpson JC, Samson JA, Seidman LJ, Lyons MJ, Faraone SV, Tsuang MT. Revisiting the factor structure for positive and negative symptoms: evidence from a large heterogeneous group of psychiatric patients. *Am J Psychiatry* Mar 1997;154(3):371-377.

34. Peralta V, Cuesta MJ. Dimensional structure of psychotic symptoms: an item-level analysis of SAPS and SANS symptoms in psychotic disorders. *Schizophr Res* Jul 27 1999;38(1):13-26.

35. Eddy CM. Social cognition and self-other distinctions in neuropsychiatry: Insights from schizophrenia and Tourette syndrome. *Prog Neuropsychopharmacol Biol Psychiatry* Mar 2 2018;82:69-85.

36. van der Weiden A, Prikken M, van Haren NE. Self-other integration and distinction in schizophrenia: A theoretical analysis and a review of the evidence. *Neurosci Biobehav Rev* Oct 2015;57:220-237.

37. Bentall RP, Corcoran R, Howard R, Blackwood N, Kinderman P. Persecutory delusions: a review and theoretical integration. *Clin Psychol Rev* Nov 2001;21(8):1143-1192.

38. Moore JW, Fletcher PC. Sense of agency in health and disease: a review of cue integration approaches. *Conscious Cogn* Mar 2012;21(1):59-68.

39. Kimhy D, Goetz R, Yale S, Corcoran C, Malaspina D. Delusions in individuals with schizophrenia: factor structure, clinical correlates, and putative neurobiology. *Psychopathology* Nov-Dec 2005;38(6):338-344.

40. Bliksted V, Fagerlund B, Weed E, Frith C, Videbech P. Social cognition and neurocognitive deficits in first-episode schizophrenia. *Schizophrenia research* 2014;153(1):9-17.

41. McDonald S, Flanagan S, Rollins J, Kinch J. TASIT: A new clinical tool for assessing social perception after traumatic brain injury. *The Journal of head trauma rehabilitation* 2003;18(3):219-238.

21

42. Abell F, Happe F, Frith U. Do triangles play tricks? Attribution of mental states to animated shapes in normal and abnormal development. *Cognitive Development* 2000;15(1):1-16.

43. Barr DJ, Levy R, Scheepers C, Tily HJ. Random effects structure for confirmatory hypothesis testing: Keep it maximal. *J Mem Lang* 2013;68(3):255-278.

44. Wetzels R, Wagenmakers E-J. A default Bayesian hypothesis test for correlations and partial correlations. *Psychonomic bulletin & review* 2012;19(6):1057-1064.

45. Jeffreys H. *The theory of probability*: OUP Oxford; 1998.

46. Kass RE, Raftery AE. Bayes factors. *Journal of the american statistical association* 1995;90(430):773-795.

47. Pearl J, Glymour M, Jewell NP. *Causal inference in statistics: A primer*: John Wiley & Sons; 2016.

48. McDonald S, Bornhofen C, Shum D, Long E, Saunders C, Neulinger K. Reliability and validity of The Awareness of Social Inference Test (TASIT): a clinical test of social perception. *Disabil Rehabil* Dec 30 2006;28(24):1529-1542.

49. McDonald S, Flanagan S, Rollins J, Kinch J. TASIT: A new clinical tool for assessing social perception after traumatic brain injury. *J Head Trauma Rehabil* May-Jun 2003;18(3):219-238.

50. O'Grady C, Scott-Phillips T, Lavelle S, Smith K. Perspective-taking is spontaneous but not automatic. 2019.

51. Gallotti M, Frith CD. Social cognition in the we-mode. *Trends Cogn Sci* Apr 2013;17(4):160-165.

52. Arora A, Schurz M, Perner J. Systematic Comparison of Brain Imaging Meta-Analyses of ToM with vPT. *BioMed research international* 2017;2017:6875850.

53. Waters F, Woodward T, Allen P, Aleman A, Sommer I. Self-recognition deficits in schizophrenia patients with auditory hallucinations: a meta-analysis of the literature. *Schizophr Bull* Jun 2012;38(4):741-750.

54. Pinheiro AP, Rezaii N, Rauber A, Niznikiewicz M. Is this my voice or yours? The role of emotion and acoustic quality in self-other voice discrimination in schizophrenia. *Cogn Neuropsychiatry* Jul 2016;21(4):335-353.

55. Franck N, Farrer C, Georgieff N, Marie-Cardine M, Dalery J, d'Amato T, Jeannerod M. Defective recognition of one's own actions in patients with schizophrenia. *Am J Psychiatry* Mar 2001;158(3):454-459.

56. Moseley P, Fernyhough C, Ellison A. Auditory verbal hallucinations as atypical inner speech monitoring, and the potential of neurostimulation as a treatment option. *Neurosci Biobehav Rev* Dec 2013;37(10 Pt 2):2794-2805.

57. Daprati E, Franck N, Georgieff N, Proust J, Pacherie E, Dalery J, Jeannerod M. Looking for the agent: an investigation into consciousness of action and self-consciousness in schizophrenic patients. *Cognition* Dec 1997;65(1):71-86.

58. Frith C. Explaining delusions of control: the comparator model 20 years on. *Conscious Cogn* Mar 2012;21(1):52-54.

59. Bonfils KA, Lysaker PH, Minor KS, Salyers MP. Empathy in schizophrenia: A meta-analysis of the Interpersonal Reactivity Index. *Psychiatry Res* Mar 2017;249:293-303.

60. Simonsen A, Fusaroli R, Skewes JC, Roepstorff A, Campbell-Meiklejohn D, Mors O, Bliksted V. Enhanced Automatic Action Imitation and Intact Imitation-Inhibition in Schizophrenia. *Schizophr Bull* Jan 1 2019;45(1):87-95.

61. Simonsen A, Fusaroli R, Skewes JC, Roepstorff A, Mors O, Bliksted V, Campbell-Meiklejohn D. Socially Learned Attitude Change is not reduced in Medicated Patients with Schizophrenia. *Sci Rep* Jan 30 2019;9(1):992.

62. Santiesteban I, Kaur S, Bird G, Catmur C. Attentional processes, not implicit mentalizing, mediate performance in a perspective-taking task: Evidence from stimulation of the temporoparietal junction. *Neuroimage* Jul 15 2017;155:305-311.

22

63. Santiesteban I, Catmur C, Hopkins SC, Bird G, Heyes C. Avatars and arrows: implicit mentalizing or domain-general processing? *J Exp Psychol Hum Percept Perform* Jun 2014;40(3):929-937.

64. Schurz M, Kronbichler M, Weissengruber S, Surtees A, Samson D, Perner J. Clarifying the role of theory of mind areas during visual perspective taking: Issues of spontaneity and domain-specificity. *Neuroimage* Aug 15 2015;117:386-396.

65. Schilbach L. Towards a second-person neuropsychiatry. *Philos Trans R Soc Lond B Biol Sci* Jan 19 2016;371(1686):20150081.

66. Santiesteban I, White S, Cook J, Gilbert SJ, Heyes C, Bird G. Training social cognition: from imitation to Theory of Mind. *Cognition* Feb 2012;122(2):228-235.

23

Figure Legends

Figure 1. The hypothesized relationship between self-other control processes, higher order mentalizing and psychotic symptoms investigated in this study. Here, self-other control processes are probed using the Visual Perspective-Taking Task and measured as altercentric and egocentric intrusion. Both altered egocentric and altercentric intrusion could lead to altered higher order mentalizing, while increased altercentric intrusion could lead to characteristic psychotic symptoms, suggestive of problems with self-other distinction.

Figure 2. The Visual Perspective-Taking Task. The female version of the avatar is presented here facing the left wall. An example of a consistent trial to the left, where both the participant and the avatar see two discs. An example of an inconsistent trial to the right, where the participant sees two discs, while the avatar only sees one. On each trial, prior to the presentation of the room, the participants were presented with information on which perspective they had to take (e.g. "she") as well as the number (e.g. "2"), specifying how many red discs they had to verify were visible from the relevant perspective.

Figure 3. Egocentric (left) and altercentric (right) intrusion in patients and controls. The top panels (A-D) present point range visualizations of the models' estimates in each condition (mean and 95% CIs) for both accuracy and RTs. The bottom panels (E-H) present the posterior estimate distributions of the egocentric and altercentric effects in patients and controls. Note that for RTs, non-decision time, which is equal for the two groups and is estimated as 121.59 ms (95 CIs: 61.90 ms 167.56 ms), is not included in the estimates.
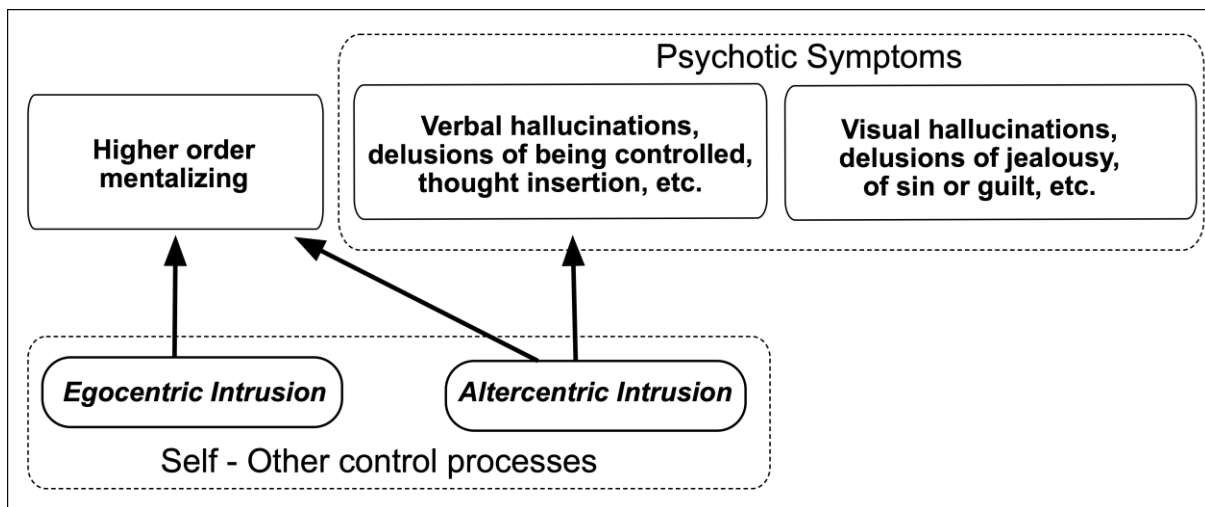
Figure 4. Relations between performance in the perspective taking task (altercentric intrusion) and i) TASIT score (left panel); ii) ATT score (middle panel); and iii) relevant psychotic symptoms score (right panel). The plots represent model estimates.

24

Table 1. Demographics, psychopathology, IQ and mentalizing in FES patients and healthy controls

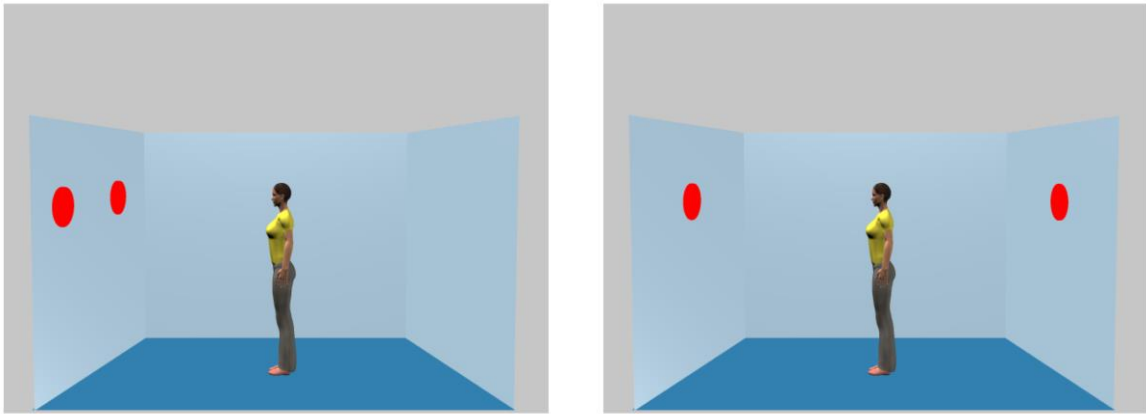|	Schizophrenia (N=22)	Healthy controls (N=23)	Group differences evidence ratio, credibility
Age, mean (95%CI)	23.05 (21.46 ; 24.63)	23.65 (22.10 ; 25.20)	
Females, N (%)	6 (27.3)	7 (30.4)	
Handedness (right : left)	19 : 3	22 : 1	
Current occupation, N (%)			
Unemployed	13 (59.1)	0 (0)	
Work	0 (0)	8 (34.8)	
Student	6 (27.3)	15 (65.2)	
Sick leave	3 (13.6)	0 (0)	
Pension	0 (0)	0 (0)	
SANS[a], mean(95%CI)	9.77 (8.19 ; 11.36)	0 (0)	
SAPS[b], mean(95%CI)	14.45 (13.11 ; 15.80)	0 (0)	
Related hallucinations and delusions[c]	23.4 (6.1 ; 45.9)	0 (0)	
Unrelated hallucinations and delusions[c]	13 (2.1 ; 29)	0 (0)	
TASIT accuracy[d]	64.5 (40.2 ; 77.5)	76.2 (70.1 ; 80)	>1000, 1
ATT accuracy[e]	19.8 (12.6 ; 24)	22.3 (18 ; 24)	399, 1
WAIS-III[f]	91.77 (83.96 ; 99.59)	111.70 (104.05 ; 119.34)	>1000, 1
Years of education, mean (95%CI)	12.14 (11.02 ; 13.25)	15.22 (14.13 ; 16.31)	499, 1

[a]SANS, Scale for Assessment of Negative Symptoms. The score is based on the sum of four global scores (excluding Attention); [b]SAPS, Scale for Assessment of Positive Symptoms. The score is based on the sum of four global scores; [c]The score is based on the sum of individual items. See text for further details; [d]The Awareness of Social Inference Test, the maximum score possible is 80 (0-40 for each of the two conditions: sincere or simple sarcastic); The Animated Triangles Task, the maximum score possible is 24 (0-12 for each of the two conditions: random or theory of mind); [f]Wechsler Adult Intelligence Scale-III (Subtests: Block Design, Vocabulary, Matrix Reasoning and Similarities)
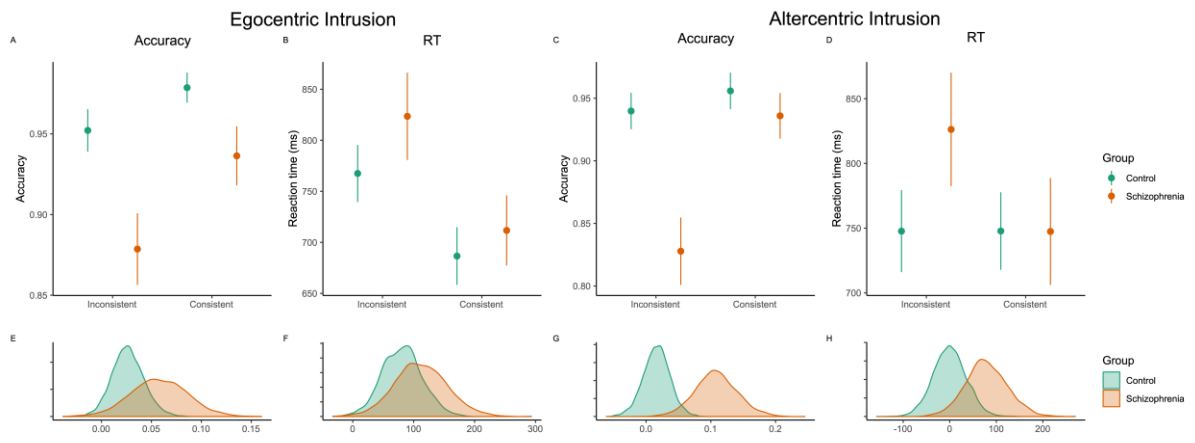
Figure 1

Figure 2

Figure 3

Figure -4