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Is the Theory of Mind deficit observed in visual paradigms in schizophrenia explained by an impaired attention toward gaze orientation?

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ABSTRACT

Schizophrenia is associated with poor Theory of Mind (ToM), particularly in goal and belief attribution to others. It is also associated with abnormal gaze behaviors toward others: individuals with schizophrenia usually look less to others' face and gaze, which are crucial epistemic cues that contribute to correct mental states inferences. This study tests the hypothesis that impaired ToM in schizophrenia might be related to a deficit in visual attention toward gaze orientation.

We adapted a previous non-verbal ToM paradigm consisting of animated cartoons allowing the assessment of goal and belief attribution. In the true and false belief conditions, an object was displaced while an agent was either looking at it or away, respectively. Eye movements were recorded to quantify visual attention to gaze orientation (proportion of time participants spent looking at the head of the agent while the target object changed locations).

29 patients with schizophrenia and 29 matched controls were tested. Compared to controls, patients looked significantly less at the agent's head and had lower performance in belief and goal attribution. Performance in belief and goal attribution significantly increased with the head looking percentage. When the head looking percentage was entered as a covariate, the group effect on belief and goal attribution performance was not significant anymore.

Patients' deficit on this visual ToM paradigm is thus entirely explained by a decreased visual attention toward gaze.

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1. Introduction

It is now well established that individuals with schizophrenia have impaired performance in Theory of Mind (ToM) tasks (Brune, 2005): they perform usually less well than control participants on tasks requiring the attribution of goals (Zalla et al., 2004; Liepelt et al., 2012), intentions (Brunet et al., 2003; Koelkebeck et al., 2010) and beliefs (Brune, 2005; Bora et al., 2009; Langdon et al., 2010) to others. A better understanding of poor ToM performance in schizophrenia is particularly important as it is one of the strongest predictor of functional outcome among the other social as well as non-social cognitive domains (Fett et al., 2011). ToM also mediates the relationship between neurocognition and social competence (Couture et al., 2011).

However, poor performance in ToM tasks is open to multiple interpretations. Many classical false belief tasks have heavy executive and verbal demands, such that failure in these tasks may reflect impairments in several different cognitive processes other than pure mentalizing. Limitations of classical false belief tasks have been appreciated for a long time (Bloom and German, 2000), and many efforts have been dedicated to designing tasks that tap belief attribution in a purely visual manner, bypassing language and reducing executive demands. In the present study, we investigate the ability of patients with schizophrenia to attribute mental states, using a visual and non-verbal version of the false belief paradigm (Forgeot d'Arc and Ramus, 2011). Yet, poor performance in even purely visual and non-verbal ToM tasks may also be due to deficits at levels other than mental state attribution, e.g., at more perceptual or attentional levels.

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Indeed, another important schizophrenic symptom is the avoidance of eye contact during conversational situations (Davison et al., 1996), particularly for negative situations (Choi et al., 2010). When they are presented with pictures or videos involving human characters, individuals with schizophrenia make fewer fixations and shorter scan paths on faces, particularly on salient facial features like eyes (Loughland et al., 2002; Green et al., 2003; Delerue et al., 2010). Individuals with schizophrenia seem to be particularly impaired in gaze direction discrimination (Hooker and Park, 2005; Tso et al., 2012) which is nevertheless a powerful epistemic cue: it is necessary to focus one's attention toward the gaze of others in order to infer their visual knowledge, i.e. what they have seen or not. This in turn raises the question whether the poor performance of patients with schizophrenia in visual ToM tasks might be due, in whole or in part, to an impaired attention toward gaze orientation. Indeed, ToM abilities are often assessed using scenarios in which the accurate processing of an agent's gaze direction plays a crucial role in task performance.

Recently, eyetracking was used to record looking behavior on a standard Sally-Anne false belief paradigm in which an agent sees a toy being hidden in location A, and the toy is later moved to location B while the agent is looking away. Authors found anticipatory eye movements toward location A (where the agent should search the toy according to his false belief about its location), suggesting an implicit mentalizing ability (Onishi and Baillargeon, 2005; Schneider et al., 2012) that was lacking in autism (Senju et al., 2009). However, these authors have paid little attention to whether participants tracked the agent's gaze when the object location change occurred. Nevertheless, it seems important in any visual false belief paradigm to rigorously control whether patients do acquire the crucial pieces of information about the object's location and the agent's gaze. We believe this exploration is a prerequisite before testing whether individuals with schizophrenia make anticipatory saccades toward the expected location of an object according to belief attribution.

In this study, we presented patients with schizophrenia and a control group with animated cartoons showing true and false belief situations in which an object was displaced while an agent was either looking at it or looking away. The paradigm required participants to predict the behavior of the agent depending on his goal and belief about the object's location. Based on previous research, we predicted that individuals with schizophrenia would make less accurate predictions based on goal and belief attribution than control participants. Furthermore, eye movements were recorded in order to quantify the amount of visual attention devoted to the agent's gaze orientation and to the object translocation. We hypothesized that individuals with schizophrenia would perhaps look less at the agent's gaze than controls. Finally, we tested to what extent the decreased performance in goal and belief attribution found in schizophrenia could be explained by their decreased visual attention toward the agent's gaze orientation.

2. Materials and methods

2.1. Participants

29 patients with schizophrenia and 29 control participants were recruited for this study. All participants had normal or corrected-to-normal vision. Exclusion criteria for both groups comprised substance or alcohol dependence within the past 6 months and current or prior history of untreated significant medical or neurological illness. All diagnoses in the schizophrenia group were confirmed by two licensed psychiatrists according to the DSM-IV-R criteria for schizophrenia. Individual with schizophrenia were recruited from community mental health centers and outpatient clinics in the Versailles area. At the time of testing, all participants with schizophrenia were taking antipsychotics. The control participants were recruited in Ile-de-France area. The control group was screened for current or past psychiatric illness and participants were excluded if they met criteria for any axis I disorder of the DSM-IV-TR. Groups were matched on age, gender and educational level. The experiment was approved by the local medical ethics committee. All participants received a complete description of the study in verbal and written form. Written informed consent was obtained from each participant.

2.2. Cognitive and clinical measures

General intelligence was estimated by means of four WAIS-III subtests: Vocabulary and Similarities for verbal intelligence; Pictures Completion and Matrices for non-verbal intelligence. We rated the severity of schizophrenic symptoms in all patients with the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987).

2.3. Belief and goal attribution paradigm

We adapted a silent animated cartoons paradigm based on non-verbal scenarios split into three minimally differing conditions (Forgeot d'Arc and Ramus, 2011). Each scenario is divided into four successive phases: Beginning, Change, Suspense, and End. The Beginning phase (common to all conditions) sets up the general situation, the main agent and his goal. In the Change phase, the target object is displaced while the main agent is either looking at it (Seen Change condition) or looking away (Unseen Change condition). In the third condition (No Change), the same situation is displayed as in the Unseen Change condition, but the object is not displaced. In the Suspense phase (common to all conditions), the main agent approaches the area where the change took place and is about to perform one of two actions (corresponding to the two possible object locations). In the End phase, the scene freezes and the two possible behavioral outcomes of the corresponding condition are displayed. Subjects were instructed to choose the most plausible end for the story and gave their response on a response box during an 8-second window. A correct mental states attribution (goals and beliefs) leads one to predict the same end for the Unseen Change and No Change conditions, but the opposite end in the Seen Change condition. Examples and detailed descriptions of animations can be seen at http://www.lscp.net/persons/forgeot/stim/. At the beginning of the test session, participants were trained on this forced choice task using 3 different stimuli with the same structure as test stimuli but involving reasoning on physical causation. Twelve different scenarios were used. The 36 trials (12 scenarios in each of the three conditions) were pseudo-randomized such that two successive stimuli never belonged to the same scenario and that there were never more than three consecutive trials in the same condition. The test lasted approximately half an hour.

2.4. Eye movements recording

Stimuli were presented on a 17-inch display with a 60 Hz refresh rate and an 800 × 600 pixels resolution, viewed from 63 cm in a dimly lit room. The experiments were run with Matlab using the Psychophysics and Eyelink Toolboxes (Brainard, 1997; Pelli, 1997). Eye movements were recorded monocularly with a video-based desktop-mounted eyetracker (see Supplement 1 for a description of the eyetracking apparatus).

2.5. Data analysis for the belief and goal attribution paradigm

2.5.1. 2 alternative forced-choice responses

3% of the trials did not yield any response and were discarded from the analysis (see Supplement 2 for an analysis of non-responses). Following Forgeot d'Arc and Ramus (2011), we ran a signal detection analysis (SDT) by computing sensitivity (d') to both beliefs and goals, as well as response bias ($\ln\beta$) (Macmillan and Creelman, 2005). For belief attribution sensitivity, we considered as a hit the choice of the correct end of the story in the Unseen Change condition, and as a false alarm the

(incorrect) choice of the same end in the Seen Change condition. For goal attribution sensitivity, we considered as a hit the choice of the correct end of the story in the Seen Change condition, and as a false alarm the (incorrect) choice of the same end in the No Change condition.

2.5.2. Eye movement measures

First, trials were discarded from the analysis when the percentage of recorded ocular samples during the Change phase was below 70% (due to blink, artifact or other technical reasons). Then we computed two ocular measures: (1) the *object looking percentage* as the ratio between ocular samples that fell into the area where the change occurred and the total number of ocular samples during the Change phase (2) the *head looking percentage* as the ratio between ocular samples that fell into the head of the agent and the total number of ocular samples during the Change phase. Object looking percentage measured the attention allocated to the object translocation whereas head looking percentage measured the attention allocated to gaze orientation.

2.6. Statistical analyses

Groups' demographical and cognitive characteristics were compared with Student's t-test or Chi-squared tests when appropriate. To test whether patients had lower performances than controls in goal and belief attribution, a repeated-measures ANOVA was run on mental state attribution sensitivities and bias with one within-subject factor, Mental state (two modalities: belief or goal) and one between-subject factor, Group (two modalities: schizophrenia or control).

To test whether patients had a different ocular behavior compared to controls, two successive repeated-measures ANOVAs were run: first on object looking percentage and then on head looking percentage, with one within-subject factor, Condition (three modalities: Unseen Change, Seen Change, No Change) and one between-subject factor, Group.

A simultaneous linear regression analysis was run to analyze the relation between ocular behavior and performance in goal and belief attribution. Mental state attribution sensitivity was the repeated, dependent variable, while Mental state (belief, goal), estimated IQ, object looking percentage, head looking percentage, and Group were the independent variables. In the belief condition, head looking percentages were computed on Unseen Change and Seen Change conditions whereas in the goal condition they were computed on Seen Change and No Change conditions.

3. Results

3.1. Participants

Demographic, cognitive and clinical characteristics of the groups are shown in Table 1. Patients had a marginally lower IQ but were matched on age, gender, and educational level.

3.2. Belief and goal attribution sensitivities

Results are presented in Fig. 1. The sensitivity analysis revealed significant effects of Group ($F(1,56) = 6.4$, $p = 0.02$) and Mental state ($F(1,56) = 81.9$, $p < 0.001$). Thus, sensitivity was overall higher in both groups, for goal attribution than for belief attribution. The interaction between Group and Mental state wasn't significant ($F(1,56) = 0.2$, $p = 0.68$). The bias analysis revealed no significant effect of Group ($F(1,56) = 0.1$, $p = 0.76$) but a significant effect of Mental state ($F(1,56) = 69$, $p < 0.001$), reflecting a general bias for "No Change/Unseen change" responses. These results demonstrated that individuals with schizophrenia did not significantly differ from controls in terms of response bias. Thus differences in sensitivity between patients and controls couldn't be explained by differences in response bias. Results of exploratory associations between patients' performances and their clinical characteristics are presented in Supplement 3.

3.3. Ocular measures

16 trials were excluded due to a low quality of the eyetracking recording (13 for patients, 3 for controls). Results are presented in Fig. 2. The repeated-measures ANOVA run on object looking percentage revealed a main effect of Condition ($F(2,112) = 721.8$, $p < 0.001$). Post hoc comparisons showed that the object looking percentage was higher for Seen Change ($F(1,57) = 1103.1$, $p < 0.001$) and Unseen Change ($F(1,57) = 1134.4$, $p < 0.001$) than for No Change conditions. The

Table 1
Characteristics of participants.

Variable	Patients	Controls	Statistics	*p* Value
N	29	29		
Gender ratio (M/W)[a]	21/8	19/10	$X^2 = 0.1$	0.78
Visual correction (Co/Gl)[b]	1/12	3/9	$X^2 = 0$[c]	0.99
	Mean (SD)	Mean (SD)	Statistics	*p* Value
Age (years)	39 (12.5)	40.7 (13.5)	$t(56) = 0.5$	0.63
Educational level (years)	12 (2.3)	12.4 (1.5)	$t(56) = 0.9$	0.39
Estimated general intelligence[d]	8.3 (2.1)	9.3 (2.1)	$t(56) = 1.8$	0.067
Illness duration (years)	18	11.1		
Hospitalizations duration (months)	16.5	19.3		
Haloperidol equivalents (mg/24 h)	11.7	8.6		
PANSS Total	90.6	12		
PANSS Positive scale	21.8	4		
PANSS Negative scale	24.3	4.9		
PANSS General Symptoms scale	44.5	6.8		
PANSS Positive factor	20.7	3.5		
PANSS Negative factor	24.1	4.5		
PANSS Disorganization factor	20.2	3.8		
PANSS Excitement factor	14.6	2.5		
PANSS Anxiety/Depression factor	8.2	2.9		

[a] Men/women.
[b] Contact lenses/glasses.
[c] Contact lenses and glasses categories were collapsed into one category because the size of the contact lenses category was below 5.
[d] Mean scaled scores, from 1 to 19. Wechsler intelligence scaled scores have a mean of 10 and a standard deviation of 3 in the general population.

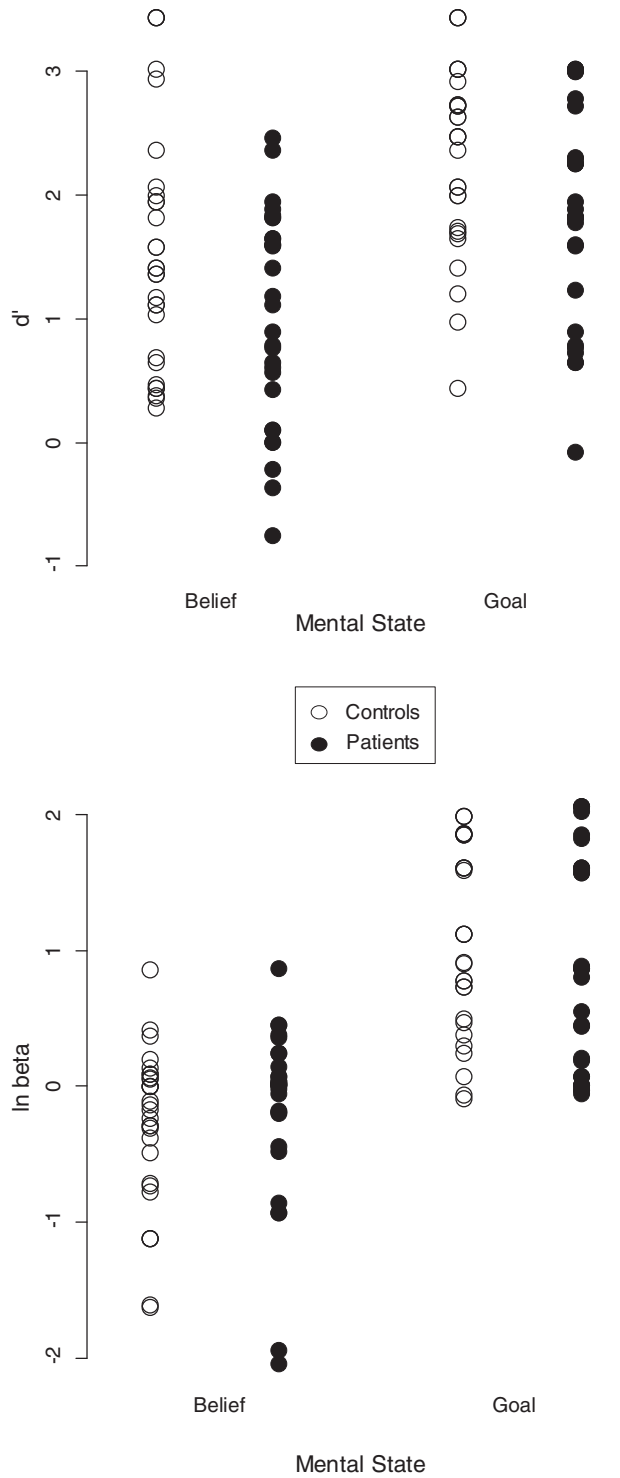

Fig. 1. Scatter plots of individual sensitivity and bias in belief and goal attribution.

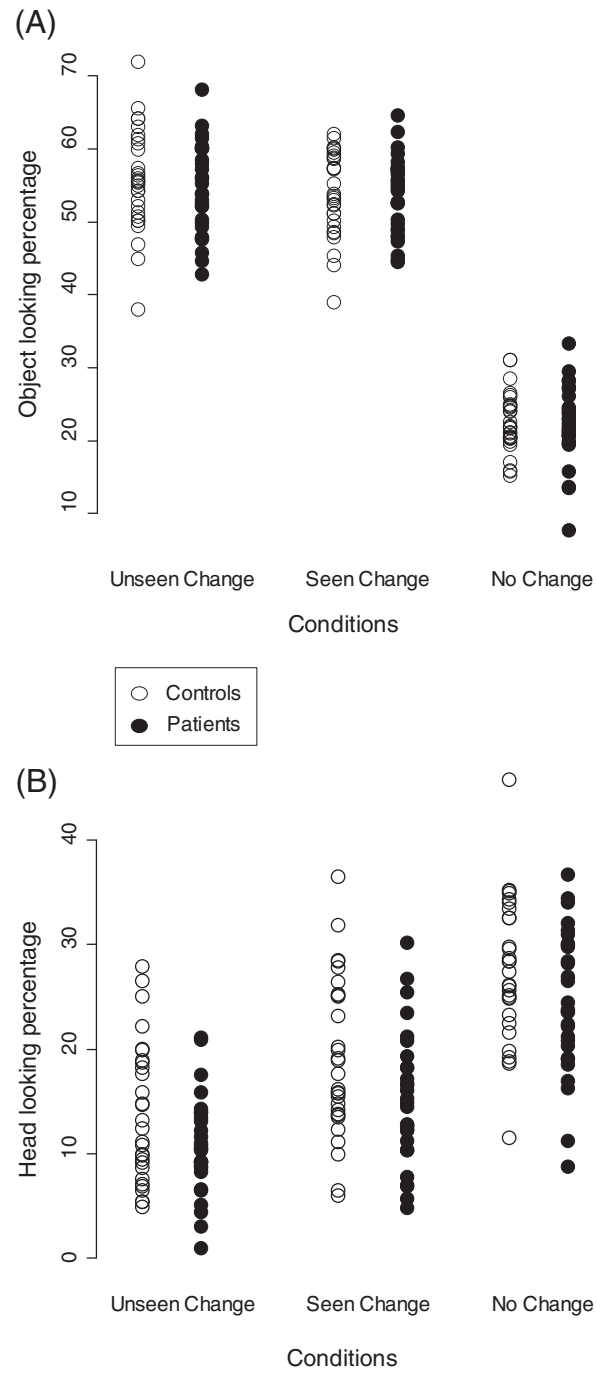

Fig. 2. Scatter plots of individual (A) object and (B) head looking percentages for Unseen Change, Seen Change and No Change conditions.

difference between Seen Change and Unseen Change conditions was not significant ($F(1,57) = 2.5, p = 0.12$). Furthermore, there was a non significant effect of Group effect ($F(1,52) = 0.2, p = 0.64$), and a non significant interaction between Group and Condition ($F(2,112) = 0.2, p = 0.80$).

The repeated measures ANOVA run on head looking percentage revealed significant main effects of Group ($F(1,52) = 5.3, p = 0.03$) and Condition ($F(2,112) = 122.7, p < 0.001$). Thus controls looked overall more at heads than patients did. Post hoc comparisons revealed that the head looking percentage was lower in Unseen Change than in Seen Change condition ($F(1,57) = 29.1, p < 0.001$), and lower in Seen Change than in No Change condition ($F(1,57) = 151.2, p < 0.001$). The interaction between Group and Condition was not significant ($F(2,112) = 0.2, p = 0.84$). Results of exploratory associations between patients' performances and their PANSS subscales scores are presented in Supplement 4.

3.4. Relation between ocular measures and mental state attribution sensitivities

The results of the simultaneous linear regression analysis run on mental state attribution sensitivities are presented in Table 2. On top

Table 2
Simultaneous linear regression analyses ran on mental state attribution sensitivities.

Independent variables	$R^2 = 56.7\%$[a]			
	β[b]	95% CI[c]		*p* Value
General intelligence	0.132	−0.06	0.32	0.16
Head looking percentage	0.574	0.33	0.817	<.001
Object looking percentage	0.211	−0.015	0.437	0.066
Mental state	0.574	0.33	0.817	<.001
Group	−0.04	−0.436	0.357	0.84

[a] R squared coefficient based on likelihood ratio for mixed models.
[b] Standardized fixed effect coefficients.
[c] 95% Confidence intervals.

of the significant effect of Mental state ($t(56) = 9$, $p < 0.001$: participants were more sensitive to goals than to beliefs), the effect of head looking percentage was strongly significant ($t(53) = 4.4$, $p < 0.001$): belief and goal attribution sensitivities increased with the head looking percentage. The effect of Object looking percentage was also significant ($t(53) = 2.1$, $p = 0.04$): belief and goal attribution sensitivities also increased with the object looking percentage. The effect of general intelligence was marginally significant ($t(53) = 1.9$, $p = 0.058$) and the effect of group was not significant anymore ($t(53) = -0.4$, $p = 0.66$). Thus the group difference in mental state attribution sensitivity was explained by the decreased head looking percentage found in patients.

4. Discussion

In this study, we used an animated cartoons paradigm to measure the ability to attribute beliefs and goals in individuals with schizophrenia. Visual attention devoted to the agent's gaze orientation was also measured via the recording of participants' eye movements.

As expected according to the previous literature in the field, individuals with schizophrenia showed a decreased sensitivity to belief and goal attribution compared to controls. This decrease could not be attributed to differences in response bias between patients and controls, nor could it be attributed to differences in language skills, since the task involved no language at all. Individuals with schizophrenia also had a different ocular behavior compared to controls: although they looked as much as controls at the displaced object, they spent less time looking at the head of the agent. We interpret this result as reflecting an impairment in visual attention toward gaze orientation. This deficit is not explained by a generally restricted visual scanning strategy, since patients attended the object translocation as much as controls.[2] It was also not explained by a general impairment in cognitive abilities measured by four subtests of the WAIS, including the Picture Completion subtest which is related to visual attention.

The main result of this study is the demonstration that the lower performance of the patients with schizophrenia in goal and belief attribution was predicted by their decreased attention dedicated to gaze orientation. This result can be interpreted in two different ways: according to a bottom-up interpretation, poor mental state attribution might be the consequence of a lack of attention toward gaze orientation. In contrast, according to a top-down interpretation, a primary deficit in mental state attribution would decrease the tendency to search for relevant epistemic information such as gaze orientation. It is also conceivable that the two levels might be affected independently from each other. Interestingly, the two contrasting interpretations differ in their clinical predictions. Indeed, a remediation program focused on increasing visual attention to gaze might help improve the performance of schizophrenic patients in visual ToM tasks according to the bottom-up hypothesis, but not according to the top-down one.

[2] Supplementary analyses taking into account scanning abilities did not change the present conclusions and are reported in Supplement 5.

Obviously, the conclusions that can be drawn from this study are limited to visual ToM paradigms in which crucial epistemic information is acquired through the perception of cartoon depictions of gaze orientation. It seems unlikely that the attentional deficit toward gaze orientation would explain ToM impairments in schizophrenia when epistemic information is acquired verbally, such as in the classic false belief tasks or in ToM tasks unrelated to belief (ex: hinting task, irony comprehension…). Another potential limitation of the present study is the use of rather sketchy cartoon faces used instead of real human faces. One might argue that schematic faces are less salient for individuals with schizophrenia compared to controls, which may not be necessarily the case for real face. For example, a decreased sensitivity to gaze cues has been reported in schizophrenia when the gaze was schematic (Akiyama et al., 2008) whereas this sensitivity was increased in patients when the stimuli were real gaze pictures (Langdon et al., 2006; Magnée et al., 2011). This clearly affects generalizability and ecological validity of the study and would require a replication using real human faces.

To conclude, this study suggests that earlier studies reporting visual ToM impairments in schizophrenia, insofar as they relied on the processing of cartoon depictions of gaze orientation, should be replicated with a proper measure of looking strategies. Future studies should control the acquisition of visual epistemic information by participants more systematically before drawing conclusions on high-level cognitive impairments. Furthermore, our results suggest that existing programs of ToM remediation in schizophrenia (Kayser et al., 2006; Bechi et al., 2012) should attempt to increase the attentional orientation toward gaze cues. Further research is needed to establish whether improvements in ToM task performance obtained in this manner generalize to real-life situations that are important to the adaptive functioning of individuals with schizophrenia.

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Contributors
The study was designed by PR, BFA and FR. The data was collected by PR, analyzed by PR and FR, and interpreted by all authors. The paper was written by PR and reviewed and approved by all authors.

Conflict of interest
All authors reported no biomedical financial interests or potential conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.schres.2014.04.031.

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