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Reduced spontaneous perspective taking in schizophrenia

Lisa Kronbichler[a,b,*], Renate Stelzig-Schöler[c], Brandy-Gale Pearce[c], Melanie Tschernegg[b], Sarah Said-Yürekli[a,b], Julia Sophia Crone[d], Lavinia-Carmen Uscatescu[a,b], Luise Antonia Reich[e], Stefanie Weber[c], Wolfgang Aichhorn[c], Josef Perner[b], Martin Kronbichler[a,b]

[a] Neuroscience Institute, Christian Doppler Medical Centre, Paracelsus Medical University, Ignaz-Harrer Straße 79, 5020 Salzburg, Austria
[b] Centre for Cognitive Neuroscience, University of Salzburg, Hellbrunnerstrasse 34, 5020 Salzburg, Austria
[c] Department of Psychiatry, Psychotherapy & Psychosomatics, Christian-Doppler Medical Centre, Paracelsus Medical University, Ignaz-Harrer Straße 79, 5020 Salzburg, Austria
[d] Department of Psychology, University of California Los Angeles, 502 Portola Plaza, Los Angeles, CA 90095, USA
[e] Department of Child and Adolescent Psychiatry, Psychotherapy, and Psychosomatics, University Medical Center Hamburg-Eppendorf, Martinistraße 52, 20251 Hamburg, Germany

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ABSTRACT

Judgments about another person's visual perspective are impaired when the self-perspective is inconsistent with the other-perspective. This is a robust finding in healthy samples as well as in schizophrenia (SZ). Studies show evidence for the existence of a reverse effect, where an inconsistent other-perspective impairs the self-perspective. Such spontaneous perspective taking processes are not yet explored in SZ. In the current fMRI experiment, 24 healthy and 24 schizophrenic participants performed a visual perspective taking task in the scanner. Either a social or a non-social stimulus was presented and their visual perspectives were consistent or inconsistent with the self-perspective of the participant. We replicated previous findings showing that healthy participants show increased reaction times when the human avatar's perspective is inconsistent to the self-perspective. Patients with SZ, however, did not show this effect, neither in the social nor in the non-social condition. BOLD responses revealed similar patterns in occipital areas and group differences were identified in the middle occipital gyrus. These findings suggest that patients with SZ are less likely to spontaneously compute the visual perspectives of others.

1. Introduction

Schizophrenia (SZ) is characterized by positive symptoms like distorted perception and delusional beliefs, negative symptoms like flattened affect and withdrawal and overall cognitive impairments (Green, 2006; WHO, 1993). Such impairments include deficits in (working) memory, attention, problem solving, processing speed, and social cognition (Green, 2006). Socio-cognitive abilities are especially impaired and reliably predict real-world functioning in patients (Mehl et al., 2010; Roncone et al., 2002). One socio-cognitive function often examined in SZ research is the ability to think about the mental states of other people. Such Theory of Mind (TOM) processes enable us to make sense of the intentions and feelings of others and allow us to respond in an adequate manner (Frith and Frith, 2005). This function seems to be impaired in patients with SZ, since they often fail to correctly attribute mental states to others (Brüne, 2005; Bora et al., 2009). Although numerous behavioral as well as neuroimaging studies examined TOM in SZ, the underlying neural mechanisms remain largely unexplained. Several fMRI examinations reveal increased neural response of patients in TOM-related cortical regions like medial prefrontal cortex, left superior temporal sulcus, left temporo-parietal junction, and precuneus cortex (Brüne et al., 2008; Andreasen et al., 2008; Pedersen et al., 2012), whereas others show the reverse pattern, namely a decreased BOLD response in these areas (Brunet et al., 2003; Das et al., 2012; Walter et al., 2009; Lee et al., 2011). Furthermore, there is an ongoing discussion regarding the extent to which over- and under activation can be equated to over- and under-mentalizing processes as proposed by common theories (Frith and Corcoran, 1996; Abu-Akel, 1999).

One commonly provided explanation is that the tasks used to examine TOM in SZ are highly heterogeneous. However, one thing that most of these studies have in common is that they rely on explicit mentalizing abilities. Participants are explicitly asked to take another person's (visual) perspective in order to select the correct response option (Brüne et al., 2008; Lee et al., 2011; Harvey et al., 2013).

* Corresponding author at: Neuroscience Institute, Christian Doppler Medical Centre, Paracelsus Medical University, Ignaz-Harrer Straße 79, 5020 Salzburg, Austria.
E-mail address: lisa.kronbichler@sbg.ac.at (L. Kronbichler).

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Critically, there is evidence that dysfunctional executive abilities (as evident in SZ) limit TOM performance (Carlson et al., 2002) and that indirect instructions better reveal TOM impairments (Langdon et al., 2017). It is therefore questionable to what extent explicit mentalizing demands can reveal any more 'minimal' TOM abilities in this patient group. Some studies refrain from using explicit mentalizing instructions (Walter et al., 2009; Brunet et al., 2003) and rather ask the participant to select the best fitting response (Das et al., 2012) without any instruction on how this should be achieved.

Whether a task is implicit or explicit is not only defined by means of task instruction but also depends on whether an overt or covert measurement is used. Although many previously published studies use implicit instructions, understanding the other person's belief/perspective is mostly necessary to successfully pass the task (Rapp et al., 2013; Lee et al., 2010). This challenges their true implicit nature, since, given that the participant is aware that mentalizing helps to succeed on the task, he might purposely try to take the other person's perspective. Therefore, the participants' assumptions about the task requirements might be critical for their behavior during the task (for a detailed discussion see O'Grady et al., 2019).

To date, there is an ongoing discussion whether implicit and explicit perspective taking processes are subserved by the same or different mechanisms (Apperly and Butterfill, 2009; Butterfill and Apperly, 2013; Phillips et al., 2015). Implicit mentalizing mechanisms are assumed to be fast, automatic processes which may occur without awareness. By contrast, explicit mentalizing processes are more flexible but slow and require mental effort (Frith and Frith, 2008; Van Overwalle and Vandekerckhove, 2013).

Little is known about implicit mentalizing processes in SZ and the assumption that explicit and implicit mentalizing are subserved by different cortical mechanisms stresses the importance of neuroimaging assessments of implicit TOM processes in this patient group. Furthermore, tasks that tackle rather spontaneous mentalizing seem to more reliably predict TOM dysfunctions in SZ as compared to conventional explicit tasks (Langdon et al., 2017).

Samson et al. (2010) recently proposed a straightforward variant of the dot-perspective task to examine implicit perspective-taking without relying on overt performance measures. Participants saw a human avatar in a room and several discs on a wall. Participants were asked to count the number of discs as fast as possible and respond via button press. In half of the pictures, the human avatar saw the same amount of discs as the participant (consistent perspectives), whereas in the other half, the avatar saw fewer discs (inconsistent perspectives). Participants were neither told to take the other person's perspective nor was perspective-taking helpful in order to succeed in the task. The idea was that if participants spontaneously compute the perspective of the human avatar, their responses should be slowed down when the other-perspective is inconsistent to the self-perspective, compared to when both perspectives are consistent. On the other hand, if participants do not compute the perspective of the avatar (since it is not required and does not happen spontaneously), there should be no differences in response times (RTs) between inconsistent and consistent trials.

Participants revealed slower RTs on inconsistent trials, suggesting that the other-perspective disturbed the processing of the own. The authors argue that participants therefore spontaneously computed the other person's visual perspective, seemingly irrespective of whether it was useful for task performance. Although there is some counter-evidence for this interpretation (Santiesteban et al., 2014), some support for spontaneous perspective-taking is provided by a recent fMRI study (Schurz et al., 2015).

Drayton et al. (2018) were the first to examine Samson's et al. (2010) task in a psychiatric patient sample and showed that psychopaths (as compared to healthy controls) do not spontaneously compute the perspective of others. Furthermore, they argue that impairments in spontaneous perspective-taking might relate to poor social functioning in their daily life since levels of altercentric interference were predictive of real-world criminal behavior.

In order to examine implicit perspective-taking processes in SZ, we adapted the original task by Samson et al. (2010) and examined behavioral and neuroimaging data in a sample of 24 patients with SZ and 24 age- and sex-matched healthy controls (HC). Participants were instructed to count the number of boxes and that they could ignore the human avatar and the triangle of the control condition. Perspective-taking is never required throughout the whole experiment, is not helpful for task completion and is not mentioned in the task instruction. In contrast to previous studies, there was no "YOU" cue presented on the screen and no attention was drawn to the avatar (therefore, our task fulfilled the criteria of "uncued task" as recently described by O'Grady et al., 2019).

To explore whether perspective effects are specific to social cues, we added a control condition where the human avatar was replaced by a spatially directive triangle. If the differences between inconsistent and consistent perspectives in RT and BOLD response are due to spontaneous perspective-taking effects rather than more domain-general effects, inconsistent triangle trials should not lead to decreased RTs or altered BOLD response.

Given that perspective-taking in SZ is not impaired, one would expect slower RTs when the avatars' perspective does not match the self-perspective since computing the other-perspective would impair task performance. Accordingly, there should be no observable differences in response pattern (at the behavioral and neural level) between HC and SZ.

Alternatively, if patients suffer from impaired perspective-taking abilities, this could become evident in two ways: On the one hand, patients with SZ might not (or to a lesser extent) calculate the other person's perspective. This would be reflected in a decreased difference between inconsistent and consistent human avatar trials, since their task performance would not (or to a lesser extent) be disturbed by an inconsistent other-perspective. In this case, their response pattern would resemble that of the previously mentioned psychopaths (Drayton et al., 2018). On the other hand, patients might be more impaired by an inconsistent other-perspective, which would be reflected in even increased RTs (and increased BOLD response) on inconsistent trials.

2. Methods

2.1. Participants

Participants in the patient group were 24 right-handed male adults, who had received a formal ICD-10 diagnosis (which was checked before study participation by certified psychiatrists) in the SZ spectrum group (F20) or the schizoaffective disorders spectrum group (F25). All patients were recruited from the outpatient and inpatient units of the Department of Psychiatry, Psychotherapy and Psychosomatics at the Christian Doppler Medical Centre (Salzburg, Austria). All patients received antipsychotic medication (mean chlorpromazine equivalent = 279.38). Patients were clinically stable with relatively mild symptoms at the time of fMRI assessment (PANSS; Kay et al., 1987). Healthy control participants were 24 right-handed male adults. Exclusion criteria for both, patients and healthy controls, were psychiatric disorders other than SZ or schizoaffective disorders, fMRI incompatibility, current or past neurological insults like head trauma and current substance abuse. Further details are provided in Table 1 and the Supplementary Material. Since the experiment was conducted in the frame of a wider evaluation, there are questionnaires and measures which are not relevant for the current experiment but are listed for the sake of completeness.

2.2. Stimuli and design

Stimuli were pictures of a gray-scaled, three-dimensional room (open to the front) including a protagonist and a varying amount of colored boxes (one, two or three) on the ground (see Supplementary Figure 1). Stimulus material was created with Google Sketchup v3.1 (www.sketchup.com) and presented with Presentation® software

Table 1
Comparison of SZ patients and controls on demographics, psychopathology and social cognition.

	Schizophrenia patients (n = 24)	Healthy controls (n = 24)	p value
Age (y)	26.04 (5.1)	25.73 (4.5)	.623
Years of education	10.1 (1.8)	11.60 (1.1)	.001
EQ[a]	37.21 (12.0)	44.05 (6.4)	.019
SCIP[b]	69.09 (12.6)	84.95 (6.1)	< .001
Eyes minds task[c]	23.96 (4.5)	24.86 (3.6)	.493
CPZ (mg)	279.38 (176.98)	–	–
Duration of illness (y)	4.35 (4.8)	–	–
PANSS + [d]	14.68 (5.9)	–	–
PANSS − [d]	16.00 (7.0)	–	–
VPT task (RT)			
HC (ms)	1238.38 (238.6)	931.32 (159.9)	< .001
HIC (ms)	1250.53 (234.7)	991.70 (153.9)	< .001
TC (ms)	1249.45 (195.2)	977.42 (145.4)	< .001
TIC (ms)	1252.24 (236.9)	957.37 (145.9)	< .001
VPT task (hits)			
HC (% corr)	89.60 (17.8)	85.83 (18.8)	.482
HIC (% corr)	89.89 (13.2)	89.89 (10.5)	1.00
TC (% corr)	89.38 (20.1)	87.71 (18.9)	.769
TIC (% corr)	91.46 (12.6)	91.25 (10.6)	.951

Years of Education, EQ, SCIP and Eyes Minds task were examined by Wilcoxon rank-sum test (Mann–Whitney). All other variables were examined by independent sample t-tests. Standard deviation of each variable is reported in brackets. Abbreviations: VPT = Visual Perspective Taking; HC = Human Consistent; HIC = Human Inconsistent; TC = Triangle Consistent; TIC = Triangle Inconsistent; RT = reaction time.

[1] Baron-Cohen and Wheelwright (2004).
[2] Purdon (2005).
[3] Baron-Cohen et al. (2001).
[4] Kay et al. (1987).

(Version 14.6, www.neurobs.com). Pictures were shown centrally on a white background by means of a MRT-compatible monitor (at a distance of approximately 80 cm) and reflected to the participant by a mirror.

In the experimental condition, the protagonist was a human avatar, facing either one of the three walls or the open front, whereas in the control condition, the human avatar was replaced by a three-dimensional triangle. The perspective of the protagonist was either consistent with the participant's perspective (i.e. the same amount of boxes was visible to both) or inconsistent (more boxes were visible from the participant's perspective than from the protagonist's perspective). Accordingly, stimuli were presented in a 2 × 2 (protagonist, consistency) conditional design resulting in the following four conditions: *human consistent (HC), human inconsistent (HIC), triangle consistent (TC)* and *triangle inconsistent (TIC)*. Each condition consisted of 40 pictures which were divided in two consecutive scan sessions. In addition, each session contained 10 pictures depicting an empty room. Presentation order was pseudo-randomized within sessions. Each trial started with a black fixation cross centered in the middle of the white screen. Subsequently, the stimulus appeared on screen and each stimulus lasted for 3000 ms. Between stimuli, an interstimulus interval (depicting a black fixation cross on a white screen) that lasted for 2000 ms, was presented. Participants reported the amount of boxes via button press and were instructed as follows: "In the current experiment, you will see a room with one, two or three square boxes on the floor. Additionally, there will be either a person or an upright triangle in the room. Your task is to simply count the number of boxes in the room. The person and the triangle are not relevant."

2.3. Image acquisition and data analysis

Functional imaging data were acquired with a Siemens Magnetom Trio 3 Tesla scanner (Siemens AG, Erlangen, Germany) using a 32-channel head-coil. Functional images sensitive to blood oxygen level dependent (BOLD) contrast were acquired with a T2* weighted gradient echo EPI sequence (TR 2250 ms, TE 30 ms, matrix 64 × 64 mm, FOV 192 mm, flip angle 70°). Thirty-six slices with a slice thickness of 3 mm and a slice gap of 0.3 mm were acquired within the TR. Scanning proceeded in two sessions with 206 scans per session. Six dummy scans were acquired at the beginning of each functional run before stimulus presentation started. Additionally, a gradient echo field map (TR 488 ms, TE 1 = 4.49 ms, TE 2 = 6.95 ms) and a high resolution (1 × 1 × 1 mm) structural scan with a T1 weighted MPRAGE sequence were acquired from each participant.

For preprocessing and statistical analysis, SPM12 software (http://www.fil.ion.ucl.ac.uk/spm/), running in a MATLAB R2013a environment (Mathworks Inc., Natick MA, USA), and additional functions from AFNI (https://afni.nimh.nih.gov/) were used. Further details are provided in the Supplementary Material.

For voxel-based group analyses, contrast images for effects of interest were calculated at the first level and rescaled to increase statistical sensitivity and decrease inter-individual variability by the Vascular auto-rescaling of fMRI (VasA fMRI) technique (Kazan et al., 2016) which estimates oscillations in arterial blood CO_2 levels without needing additional reference scans. The rescaled contrast images were used in second level one-way ANOVAs including the patient- and control group for each effect of interest separately. All results from whole brain analyses are reported at a voxel-level threshold of $p < .001$ (uncorrected) with a FDR cluster-level correction of $p < .05$.

3. Results

3.1. Behavioral results

3.1.1. Demographics, psychopathology and social cognition

Information about demographics, psychopathology and social cognition is summarized in Table 1. Patients and controls did not differ significantly in age. Although efforts were made to match the groups for education levels, our healthy controls received significantly longer education compared to patients with SZ (however, the mean difference in education duration was merely 1.5 years). Participants showed significantly lower scores on measures of cognitive (SCIP) and socio-cognitive abilities (EQ). Their performance on the 'Reading the Mind in the Eyes Test was not significantly different from the healthy control sample. Duration of illness (as defined by the time point of first professional help-seeking and diagnosis) was 4.35 years. Patients showed mild symptoms at the time of fMRI assessment (PANSS[36]) and all patients received medication (mean CPZ = 279.38 mg). Behavioral data were analyzed with IBM SPSS 20.0 (NY: IBM Corp.).

3.1.2. Visual perspective-taking task

RTs were analyzed by means of a 2 × 2 × 2 ANOVA with the factors *group* (Patients with SZ vs. controls), *agent* (human vs. triangle) and *consistency* (inconsistent vs. consistent perspective). Mean RTs and Standard Deviations are provided in Table 1.

As evident from Fig. 1, Patients with SZ showed slower overall RTs compared to HC ($F(1,46) = 27.37$, $p < .001$). *Agent* was modulated by consistency as evident from a significant *agent-by-consistency* interaction ($F(1,46) = 12.64$, $p = .001$). This interaction was qualified by the factor *group*, with a significant three-way interaction ($F(1,46) = 7.92$, $p = .007$). HC responded markedly slower when the human avatar's perspective was inconsistent to the self-perspective compared to when perspectives were consistent ($t(23) = 5.05$, $p < .001$). Unexpectedly, they also showed differences in RT between consistent and inconsistent triangle trials. Here, HC were slower when perspectives were consistent ($t(23) = 2.29$, $p = .031$).

In contrast to this marked consistency effect for human agents in healthy participants (a signature of implicit perspective-taking), patients with SZ did not show any signs of such implicit perspective-taking, as post-hoc t-tests showed no significant differences ($ts(23) < 0.79$, $ps > .43$). This group difference was confirmed by a

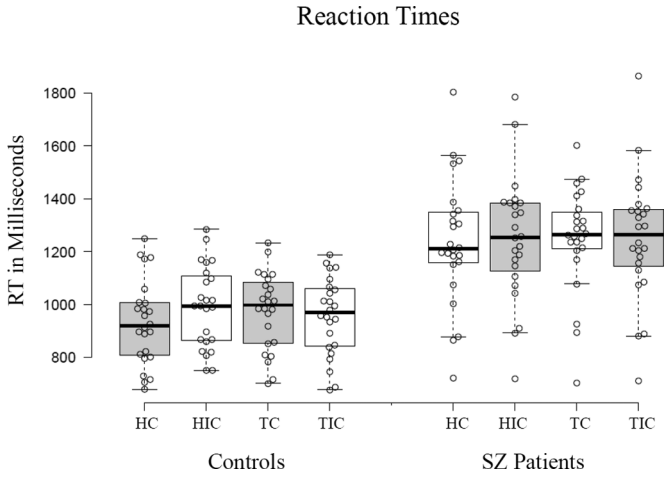

Fig. 1. Tukey Box-plots depict RTs (in ms) of control (left) and schizophrenic (right) participants. Bold horizontal lines indicate the group median, bold crosses show the group mean. End of whiskers indicate the first and third quartile. Abbreviations: SZ = Schizophrenia; *H* = Human; *T* = Triangle; *C* = Consistent; IC = Inconsistent.

significantly larger consistency effect for controls when a human agent was visible ($t(46) = 2.52$, $p = .015$), but not when the triangle agent was presented ($t(46) = 1.05$, $p = .298$). No main effects of agent or consistency (or other interactions) could be observed ($Fs(1,46) < 3.2$, $ps > .08$). All participants achieved adequate hit rates (Table 1) and they did not differ significantly between groups in neither condition ($ts(46) < 0.71$, $ps > .48$).

To rule out possible confounding effects of different education levels (see section above), the ANOVA was repeated including education as a covariate factor. The findings remained the same and no significant interactions with education could be observed ($Fs(1,46) < .69$, $ps > .79$). The analysis is described in detail in the supplementary data.

3.2. Imaging results

The exact coordinates and volumes of regions exhibiting main effects or interactions are listed in Table 2 and the interaction is illustrated in Fig. 2. Main effects are illustrated in Supplementary Figure 2.

3.2.1. Overall effects (both groups)

Increased neural response for trials depicting a human avatar than for trials depicting a triangle was found in a widespread occipital cluster reaching from inferior occipital gyrus to the middle occipital gyrus and right superior parietal lobe in the right hemisphere and from inferior occipital to middle occipital and fusiform regions in the left hemisphere. Further activation was found in right thalamus, left middle frontal gyrus, left precuneus and left orbital gyrus. Increased activation for the reverse effect (*triangle* > *human*) was evident in the right occipital pole. Inconsistent trials showed increased neural response (compared to consistent trials) in the right occipital pole. More activation for consistent compared to inconsistent trials was evident in bilateral fusiform gyri, left occipital pole and in the right inferior occipital gyrus.

A significant agent-by-consistency interaction was identified in occipital areas including bilateral lingual gyrus, left precuneus, right inferior occipital gyrus and right cuneus. Further significant cluster could be observed in right cerebellum, right precentral gyrus and left anterior insula. This interaction was driven by increased differences in neural response between consistent and inconsistent human trials (whereas differences between inconsistent and consistent triangle trials were minimal) in bilateral lingual gyrus and right cuneus. This pattern was reversed in the remaining regions.

Table 2
Significant clusters of the whole brain analysis.

Region	MNI coordinates *x*	*y*	*z*	Volume (voxels)	*F*
HUM vs. TRI overall					
Human > Triangle					
left Middle Occipital Gyrus	−30	−85	10	235	115.35
	−48	−70	13	469	110.07
right Inferior Occipital Gyrus	48	−70	7	508	115.17
left Inferior Occipital Gyrus	−24	−94	−8	33	68.96
left Fusiform Gyrus	−27	−52	−11	156	68.76
right Fusiform Gyrus	39	−52	−20	142	65.72
right Occipital Pole	30	−88	22	152	63.46
	15	−82	−8	55	33.84
right Superior Parietal Lobe	27	−70	40	84	36.70
right Thalamus	3	−16	−5	36	30.91
left Middle Frontal Gyrus	−36	5	49	30	30.59
left Precuneus	−6	−49	49	90	27.78
left orbital gyrus	−30	20	−14	24	21.65
HUM vs. TRI group diff					
n.s.	–	–	–	–	–
IC vs. C overall					
IC > C					
right Occipital Fusiform Gyrus	24	−91	−8	72	102.94
left Occipital Pole	−9	−97	1	406	80.33
right Occipital Pole	12	−97	13	236	61.60
left Fusiform Gyrus	−39	−61	−17	31	32.37
right Inferior Occipital Gyrus	42	−76	−5	65	26.58
IC vs. C group diff					
n.s.	–	–	–	–	–
Agent*Consistency overall					
left Precuneus	−21	−67	28	533	56.48
right Lingual Gyrus	12	−85	−8	100	49.48
left Lingual Gyrus	−6	−85	−8	35	27.05
right Inferior Occipital Gyrus	33	−88	−8	367	42.14
right Precentral Gyrus	39	8	28	77	36.66
right Cerebellum	30	−55	−26	130	30.91
left Anterior Insula	−33	20	−5	34	29.32
right Cuneus	3	−85	19	76	25.74
Agent*Consistency group diff					
right Middle Occipital Gyrus	36	−67	31	35	27.12
left Middle Occipital Gyrus	−36	−82	25	25	26.36

Data were extracted at a voxel-level threshold of $p < .001$ (uncorrected) and a cluster level threshold (FDR) of $p < .05$. Abbreviations: *C* = Consistent; IC = Inconsistent; HUM = Human; TRI = Triangle.

3.2.2. Group differences

Group differences between HC and patients with SZ for the *agent-by-consistency* interaction contrast (technically, this corresponds to an agent-by-consistency-by-group interaction) were identified in the right middle occipital gyrus and were marginally significant in the left middle occipital gyrus (FDR cluster-level corrected $p = .054$). As illustrated in Fig. 3, healthy controls showed increased BOLD response when the human avatar held an inconsistent perspective compared to when perspectives were consistent ($t(23) = 3.86$, $p < .001$). Furthermore, they showed increased response for consistent triangle trials compared to inconsistent triangles ($t(23) = 5.69$, $p < .001$). By contrast, patients with SZ showed relatively indifferent BOLD responses across experimental conditions ($ts(23) < 0.5$, $ps > .58$). Upon visual inspection, the left middle occipital gyrus revealed a similar response pattern. Since the interaction was only marginally significant, we refrained from further analyses.

Similar to the behavioural analysis, we re-examined the three-way-interaction in the right middle occipital gyrus considering effects of education level (for details see supplementary material). Again, using education as a covariate did not change the findings and the three-way interaction remained highly significant ($t(23) = 5.66$, $p < .001$).

No group differences between healthy controls and Patients with SZ could be identified for the *Human* vs. *Triangle* and the *Inconsistent* vs. *Consistent* contrast.

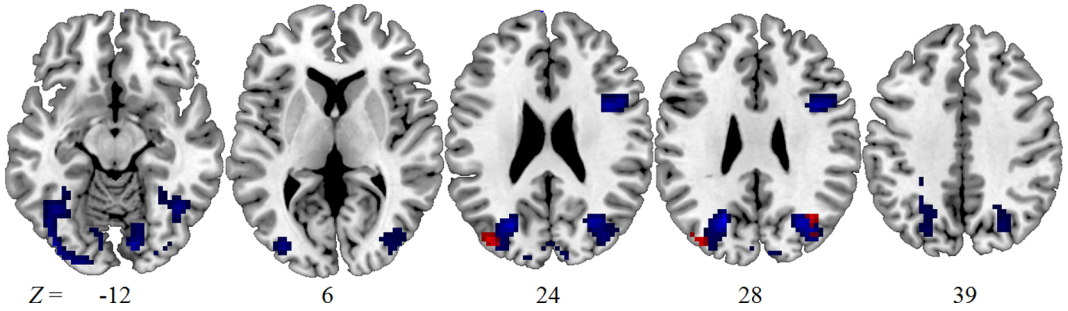

Fig. 2. Activation clusters revealed by the whole brain analyses. Regions that elicited an agent*consistency interaction (irrespective of group) are illustrated in blue. Red spots mark clusters where the agent*consistency interaction differed between groups. All clusters (except for the left MOG; red) were extracted at a threshold of $p < 0.001$ (uncorrected, with a FDR cluster level correction of $p < .05$). For illustration purposes, left MOG was extracted at a more liberal threshold (FDR cluster-level corrected $p = .054$). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

4. Discussion

Impaired mentalizing processes in schizophrenia (SZ) are found in behavioral and several neuroimaging studies (Kronbichler et al., 2017). The current study examined the neural response of patients and healthy controls (HC) during an uncued visual perspective-taking task. We were specifically interested in whether patients show alterations in RTs and neural response when the perspective of a virtual human avatar is inconsistent with the self-perspective (Samson et al., 2010; Schurz et al., 2015; Drayton et al., 2018).

HC revealed a pronounced advantage in RT (60 ms) when the other-perspective equalled the self-perspective, that is, when the avatar saw the same number of boxes on the floor as the participant. Conversely, they were slower when the self- and other-perspective were inconsistent. This was the case even though participants were never required to take the avatar's perspective. In recent studies, this finding was taken as evidence for the existence of spontaneous perspective-taking processes, where participants involuntarily compute the perspective of others even when this is disadvantageous for their task performance (Samson et al., 2010; Schurz et al., 2015). Our control condition, where a directive triangle was presented instead of the avatar, did not evoke this response pattern.

Patients showed overall slower RTs but reached similar accuracy levels compared to healthy controls (>89% for patients and > 85% for healthy controls). With respect to the experimental conditions, RT of patients did not vary with any task manipulation: Their responses were equally slow irrespective of whether a human avatar or a triangle was presented and whether those perspectives were consistent or inconsistent with their own. Accordingly, there was no observable interference effect when the perspective of the human avatar was inconsistent with the self-perspective, that is, responses were equally slow irrespective of whether perspectives were consistent or inconsistent.

Similarly, neural response in patients' bilateral middle occipital gyrus (MOG; marginal group difference in left MOG) was indifferent across task conditions. By comparison, the same cortical region revealed distinct neural response patterns in HC: BOLD response was increased when the avatar's perspective did not match the self-perspective and consistent triangles showed increased BOLD response compared to inconsistent triangles. Taken together, patients with SZ do not show neural evidence for spontaneous perspective-taking. However, several cortical regions (see Fig. 2) did not reveal significant differences between groups, which might be indicative of at least some spared spontaneous perspective computation processes in SZ.

Although prior higher-order perspective-taking studies suggest abnormal neural response in SZ in more anterior regions such as medial prefrontal networks like the ventromedial prefrontal, anterior cingulate, and orbitofrontal cortices (Andreasen et al., 2008; Benedetti et al., 2009; Brüne et al., 2008; Brunet et al., 2003), the finding of abnormal BOLD response in more occipital areas is not surprising. First, there is evidence that perspective-taking involves not only the prefrontal cortex but also tempo-parietal areas and the precuneus (Schurz et al., 2015). Second, differences in neural response during higher-order perspective taking between HC and SZ are also evident in occipito-parietal and occipito-temporal areas and vary depending on the task (Kronbichler et al., 2017). Third, most previous studies used explicit instructions to ensure that participants deliberately take the other-perspective, whereas the current

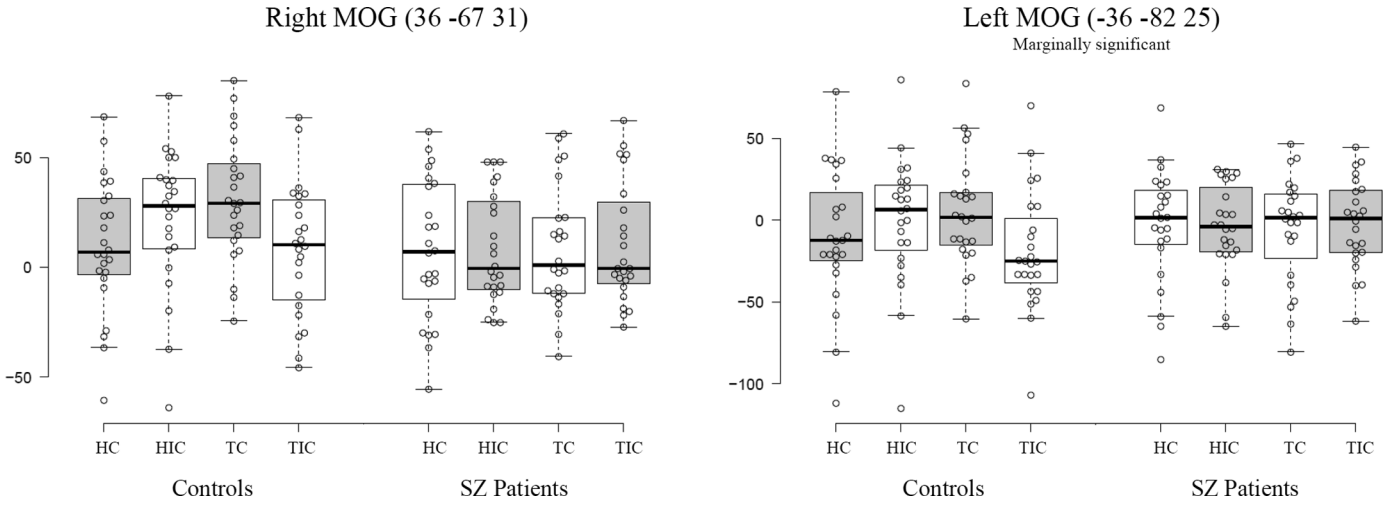

Fig. 3. Tukey Box-plots depict beta estimates extracted from left and right MOG as revealed by the whole brain analysis (sign. group difference in agent*consistency interaction). Bold horizontal lines indicate the group median, bold crosses show the group mean. End of whiskers indicate the first and third quartile. Abbreviations: SZ = Schizophrenia; *H* = Human; *T* = Triangle; *C* = Consistent; IC = Inconsistent.

task aimed at implicit perspective-taking processes which might encompass different neural processes. The number of neuroimaging studies that examined visual perspective-taking in a comparable manner as in the current study is extremely low (Eack et al., 2013; 2017) and they are restricted to predefined regions-of-interest analyses where occipital areas were not examined. Fourth, alterations in occipital areas in SZ are also robustly identified in basic visual tasks like face processing (Spilka et al., 2015; Belge et al., 2017) and during non-social stimulus processing (Kronbichler et al., 2018).

To date, there is some dispute about how a dot-perspective task must be composed to measure directional, spontaneous or automatic effects (and whether these effects can be examined at all with this task). In an elaborate discussion on that topic, O'Grady et al., 2019 argue that a participant's understanding of the task requirements is crucial for whether perspective effects become evident or not: the more salient the perspective of the avatar is to the participant, the more likely it is to find perspective-taking effects (and the less automaticity or spontaneity can be claimed). In fact, experiments that identify such perspective-taking effects either explicitly require perspective-taking (Baker et al., 2016; Furlanetto et al., 2016) or artificially emphasise the importance of the avatar ((Bukowski et al., 2015; Gardner et al., 2018) or the existence of two different perspectives (e.g. Cole et al., 2016; Santiestesban et al., 2014). In the current study, mentalizing is not mentioned in the task instruction (and neither is the word 'perspective') and the avatar is not visually highlighted, therefore minimizing the probability of design-induced perspective-taking effects. Nonetheless, healthy participants responded slower when the perspective of the avatar was inconsistent, which suggests the existence of spontaneous perspective-taking effects. Note that, since we did not address factors like attention, intention, consciousness and controllability, we do not claim that the findings obtained in our study are due to automatic effects (Schurz et al., 2018; Frith and Frith, 2008; O'Grady et al., 2019).

Regarding the absence of significant perspective taking effects in SZ in our study, one could argue that this may not seem surprising, given that perspective taking effects are hardly found in *explicit* mentalizing tasks and that an uninstructed task would necessarily lead to even weaker effects in SZ. However, according to the two-path TOM system approach, (Apperly and Butterfill, 2009; Butterfill and Apperly, 2013) impaired explicit mentalizing does not automatically entail altered implicit mentalizing. For example, Roux et al. (2016) examined eye-movements during a Frith-Happé triangle task. SZ patients showed a similar increase in fixation duration and triangle time (how long triangles were looked at) in TOM conditions. Critically, patients were less accurate in explicitly describing intentional actions of the exact same animations. The authors therefore suggested that early processing of mental states is spared in SZ whereas more complex processing is impaired. Similar evidence comes from Autism Spectrum Disorder (ASD) patients who performed the dot perspective task: Patients, like healthy controls, showed evidence for spontaneous perspective taking, but only patients revealed difficulties when explicitly asked to take the other person's perspective (Schwarzkopf et al., 2014). Again, the authors suggest a dissociation between implicit and explicit visuo-spatial perspective taking. Critically, an examination of cortical areas typically found in explicit mentalizing tasks revealed similar activation pattern in an implicit version of the Sally-Anne task, thus suggesting that both processes are subserved by common brain regions, at least in the healthy population (Naughtin et al., 2017). A direct comparison of implicit and explicit mentalizing in ASD patients furthermore revealed that activation in the right temporo-parietal junction is similarly altered in both processes (Nijhof et al., 2018). It is up to future research to examine the extent to which these processes rely on the same cortical areas and whether these findings also apply to psychiatric samples.

Previous studies on spontaneous perspective-taking also stress the importance of an adequate non-social control condition to show whether interference effects are restricted to the social condition or whether they also occur in the control condition (Santiesteban et al., 2014; Catmur et al., 2016; Heyes, 2014). Although we used control stimuli that were matched in size and orientation to our human avatars, the current study is not able to draw a distinct conclusion about this topic: Even though we do not find evidence for altercentric interference effects in the control condition, one could argue that our control stimuli are not matched in all aspects (e.g. color) to the avatar stimuli. The main focus of the current study was to examine whether patients with SZ show comparable consistency effects in the avatar condition, which they did not. Future studies are needed to examine under which circumstances non-social stimuli elicit consistency effects comparable to those of social stimuli.

The finding of altercentric errors was recently taken as evidence for spontaneous perspective-taking processes (Samson et al., 2010; McCleery et al., 2011; Surtees et al., 2013). Conversely, the absence of altercentric interference would speak against a spontaneous computation of the other person's perspective. In our patient sample, behavioral as well as neuroimaging data show decreased differences between inconsistent and consistent visual perspectives. Accordingly, patients with SZ seem to not (or to a lesser extent) consider the other person's perspective spontaneously. Therefore, the inconsistent condition is equally 'easy' as the consistent condition. This would correspond to the common assumption that patients with SZ tend to under-mentalize about the perspectives and beliefs of others (Frith and Corcoran, 1996) and that they have difficulties in shifting away from their own-perspective (Langdon et al., 2001). In this case, the current study would show that this is not only the case when explicitly told to do so, but also when no direct mentalizing instruction is given and when a covert performance measure is used. Impaired spontaneous mentalizing would also explain poor socializing and unconfident behavior observed in patients with SZ (Ghoreishi et al., 2015) since daily interactions heavily rely on the understanding of other's intentions and beliefs.

Some limitations of the current study should be noted. First, the present sample is limited to male controls and patients with SZ, thus it is unclear how gender may influence the current finding. Second, all our patients were on medication so that we do not know to what extent the abnormal behavioral and neural response patterns are related to medication. Notably, post-hoc correlations between consistency effects (behavioral and neural) and chlorpromazine equivalent values did not show a reliable relation. Third, as shortly mentioned above, we identify several cortical areas that show an agent-by-consistency interaction which is not modulated by participant group. Therefore, either our study is underpowered to examine significant group differences in these regions or, alternatively, patients with SZ do show (at least minimal) spontaneous perspective-taking processes in a subset of those regions commonly engaged in healthy controls.

In sum, the present study provides the first evidence that patients with a psychotic disorder are less likely to spontaneously compute the visual perspective of others and that this might be related to abnormal occipital brain response.

CRediT authorship contribution statement

Lisa Kronbichler: Formal analysis, Visualization, Writing - original draft. **Renate Stelzig-Schöler:** Supervision. **Brandy-Gale Pearce:** Validation. **Melanie Tschernegg:** Data curation. **Sarah Said-Yürekli:** Software. **Julia Sophia Crone:** Methodology. **Lavinia-Carmen Uscatescu:** Validation. **Luise Antonia Reich:** Validation. **Stefanie Weber:** Validation. **Wolfgang Aichhorn:** Supervision. **Josef Perner:** Supervision. **Martin Kronbichler:** Conceptualization, Project administration, Supervision.

Declaration of Competing Interest

All authors declare no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.pscychresns.2019.08.007.

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