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Associations between acceptance of the implausible bias, theory of mind and delusions in first-episode psychosis patients; A longitudinal study

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ABSTRACT

Multiple different cognitive biases, among them the liberal acceptance (LA) bias, have been suggested to contribute to reality distortion in psychotic disorders. Earlier studies have been cross-sectional and considered a limited set of cognitive correlates of psychosis, thus the relationship between LA bias and psychosis remains poorly known. We studied a similar bias (acceptance of the implausible (AOI)) in 62 first-episode psychosis (FEP) patients and 62 control subjects, who watched movie scenes with varying degrees of realism and were asked to evaluate the probability of these events occurring in real life. We assessed theory of mind (ToM) performance using the Hinting task and delusion severity using Brief Psychiatric Rating Scale item 11. We correlated the magnitude of AOI with the severity of delusions and performance in the ToM task. Furthermore, we used 1-year follow-up data from 40 FEP patients and 40 control subjects to disentangle state vs trait-like characteristics of AOI. At baseline FEP patients expressed more AOI than control subjects, and the magnitude of AOI correlated positively with the severity of delusions and negatively with ToM performance. At the one-year follow-up, when most patients were in remission, patients still displayed increased AOI, which no longer correlated with delusions. These findings support the notion that the AOI bias could represent a trait rather than a state feature and support further studies to test the hypothesis that it could be one of the causal factors of psychotic disorders, possibly associated with ToM.

1. Introduction

Schizophrenia and other psychotic disorders are characterized by a disrupted sense of reality, manifesting as delusions and hallucinations. Such reality distortion symptoms have been suggested to be explained by multiple factors, including abnormal processing of salience, distortions in predictive coding, and cognitive biases related to probabilistic reasoning (Broyd et al., 2017; Howes and Murray, 2014). Patients with psychotic disorders tend to display a more liberal acceptance (LA) towards implausible outcomes than healthy control subjects when evaluating multiple options with low probability (Moritz et al., 2009; Moritz et al., 2004; Reininghaus et al., 2019). In addition, a recent study has linked LA to anomalistic beliefs, possibly leading to increased delusion proneness (Prike et al., 2018).

Most of the studies on cognitive biases focus on either first-episode psychosis (FEP) patients or patients diagnosed with chronic schizophrenia, and very little is known about the stability of cognitive biases throughout the progression of psychotic disorders. Prospective studies on at-risk patients are sparse due to the potentially massive cohorts required. In absence of such studies, longitudinal studies on FEP patients may provide valuable information when deciphering whether cognitive biases are a cause of the psychotic disorder or a risk factor predisposing for these disorders (e.g., state vs trait). Although theorized to represent a trait-like bias (Moritz and Woodward, 2004), it is still unclear whether the LA bias manifests as a result or a correlate of the psychosis itself or represents a trait-like bias predisposing for psychotic symptoms. Cross-sectional studies evaluating LA in patients in an at-risk mental state for psychosis provide conflicting evidence, with results suggesting this bias could be present (Eisenacher et al., 2015) or absent (Eisenacher et al., 2016) before psychosis develops.

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Relatively few studies on LA have been conducted, and they are substantially outnumbered by studies on other cognitive biases, such as the jumping to conclusions (JTC) bias (Huq et al., 1988). While LA and JTC have often been studied separately, LA has been suggested to account for the JTC tendency (Moritz and Woodward, 2004). JTC manifests as a tendency to require less evidence when making decisions, and it has been demonstrated in delusional patients (Dudley et al., 2016; McLean et al., 2017) and delusion-prone individuals (Colbert and Peters, 2002; van der Leer et al., 2015). In addition, persistence of said bias is correlated with persistence of delusions in FEP patients (Falcone et al., 2015). In the general population JTC is associated with perceptual aberrations and paranoid thoughts (Moritz and Woodward, 2004), also suggesting this bias is a trait more than a state (Garety and Freeman, 2013).

A recent meta-analysis concluded that LA and JTC were more prevalent in psychiatric illnesses when delusional symptoms were present, supporting a causal relationship between cognitive biases and delusions (McLean et al., 2017). Support for the suggestion was, however, limited by the lack of longitudinal studies.

In addition to longitudinal course, it remains poorly known how LA relates to social cognitive alterations that have also been associated with delusions. Theory of mind (ToM) refers to the ability to understand the mental states of others (Premack and Woodruff, 1978). Deficits in ToM are well documented in both patients with schizophrenia and FEP patients (Bertrand et al., 2008; Corcoran et al., 1995; Green et al., 2015; Healey et al., 2016; Lindgren et al., 2018). Connections between impaired ToM and JTC have been observed in patients with schizophrenia (Langdon et al., 2010), suggesting a possible common mechanism, although conflicting results have also been presented (Woodward et al., 2009). ToM deficits have previously been associated with delusions and theorized to contribute to the formation of reality distortions (Garety and Freeman, 1999). A more recent review, however, suggested that while the connection between JTC and delusions seems robust, ToM deficits correlate more significantly with negative symptoms in psychotic individuals (Garety and Freeman, 2013). To our knowledge, no studies have assessed relationships of LA, ToM and delusions in the same sample.

In the original LA task (Moritz and Woodward, 2004) participants are instructed to view different paintings and assign probability to four title alternatives for each painting, and patients with psychotic disorders generally assign higher probabilities to implausible or absurd answers than the control subjects. To study a similar reasoning bias, we used fantasy scenes from Tim Burton's movie Alice in Wonderland that are generally considered implausible in the real world. We then asked FEP patients and control subjects to evaluate how probable the movie events they had just viewed are to occur in real life.

We measured this bias, referred to as acceptance of the implausible (AOI), ToM and delusions in FEP patients and control subjects. Furthermore, we assessed AOI and delusions at follow-up 12–15 months later to study the stability of this bias in FEP patients.

2. Methods

2.1. Participants

97 FEP patients were selected from psychiatric wards and outpatient clinics within the Hospital District of Helsinki and Uusimaa and City of Helsinki as a part of the Helsinki Early Psychosis Study (HEPS) (Mäntylä et al., 2015; Mäntylä et al., 2018; Rikandi et al., 2017). Exclusion criteria for patients were psychotic symptoms caused by substance abuse or organic causes. 62 FEP patients originally enrolled participated in all tests included in this study. Symptoms were evaluated using the Brief Psychiatric Rating Scale Extended (BPRS-E)(Ventura et al., 1993), and psychosis was defined as a score of four or higher for either hallucinations (BPRS-10) or unusual thought content (BPRS-11, a general measure of delusion severity). 62 age- and sex-matched control subjects living in the Helsinki region were invited from the civil registry, excluding individuals with history of psychotic episodes (Table 1). 40 patients and 40 control subjects participated in a follow-up study 12–15 months after the baseline study. See Fig. 1 for visualization of subject inclusion.

All participants gave written consent before participating in the study. This study was approved by the Ethics Committee of the University Hospital District of Helsinki and Uusimaa.

2.2. Clinical measures

Delusions and hallucinations were scored by using the BPRS-11 and BPRS-10 items. Level of functioning was assessed using the Social and Occupational Functioning Assessment Scale (SOFAS) (*Diagnostic and statistical manual of mental disorders: DSM-IV,* 1994), and negative symptoms using the combined scores of BPRS-16 (blunted affect) and the SANS (Andreasen, 1989) scores for apathy, anhedonia and alogia. All measures were acquired at baseline and at the one-year follow-up. Dosages of antipsychotic medication were verified from patient records. Chlorpromazine equivalent doses were calculated using the Defined Daily Doses (DDD) method (Leucht et al., 2016).

For control subjects, cognitive testing was evaluated at baseline, where ToM performance was assessed using the Finnish version of the Hinting task (Corcoran et al., 1995). For patients, cognitive testing was done at a 2-month follow-up to avoid confounding by the most severe psychotic symptoms. General neurocognitive performance (g-score) was estimated using a factorial model of 20 common cognitive variables (Lindgren et al., 2018).

Diagnoses were based on the Research Version of the Structured Clinical Interview for DSM-IV Disorders – Axis I (SCID-I) (First et al., 2002) and a review of medical records from all lifetime mental health care records. Written permission to access the medical records was obtained from the participants. Diagnoses reported here are based on all information available, and evaluation was done by a senior psychiatrist (JS). In an earlier publication of an overlapping material from the HEPS-study the difference in performance in ToM was mainly driven by lower performance in those patients who would receive a diagnosis of schizophrenia within one year (Lindgren et al., 2018). To assess whether this was true regarding the variables studied, the FEP group was split into two subgroups based on the DSM-IV diagnosis codes at follow-up (Table 1). Schizoaffective disorder (DSM-IV 295,7) and schizophreniform disorder (DSM-IV 295,4) were included in the "other psychosis" group.

2.3. Experiment

FEP patients and control subjects were presented audio-visual scenes from the movie "Alice in Wonderland" (Tim Burton, Walt Disney Pictures, 2010, Finnish soundtrack. License to present the movie was purchased from the local right holder M&M Viihdepalvelut Inc.) for a duration of 7 min and 21 s while undergoing fMRI scanning (Rikandi et al., 2017). The scenes, which have been described in detail in the Supplementary material of (Rikandi et al., 2017), were selected to contain both realistic and unrealistic content.

In short, the first 80 s take place at a garden party, with content consisting of realistic, non-animated live-action scenes. Alice then sees an animated rabbit dressed in a blue jacket and holding a pocket watch, whom she follows to a rabbit hole. She leans over the edge, slips, and falls into the rabbit hole. During the fall, which takes almost 30 s, she sees multiple flying pieces of furniture and decorative objects before bouncing of a flying bed. She ends up in a room where she eats a piece of cake and grows tremendously, and then drinks a potion causing her to shrink in size. She then enters Wonderland, where most content is to some degree unrealistic, with content such as giant flying insects, a flying rocking horse and plants with faces. She meets multiple animated, unrealistic characters such as the twins Tweedledee and Tweedledum,

Table 1
Demographic, clinical, and behavioral information of FEP group subjects, diagnostic subgroups, and control subjects at baseline.

	Control[a] N = 62	FEP[a] N = 62	SCZ[a] *N* = 24	OP[a] *N* = 38	Group difference Control - FEP[b]	Group difference Control - SCZ[b]	Group difference Control - OP[b]	Group difference SCZ - OP[b]
Male	40 (64.5)	37 (59.7)	13 (54.2)	24 (63.2)	$p = 0.579$	$p = 0.460$	$p = 1.000$	$p = 0.711$
Age	24.0 (7.0)	25.4 (7.1)	24.5 (6.7)	25.7 (7.6)	$p = 0.776$	$p = 0.610$	$p = 0.435$	$p = 0.378$
Years of education	14.8 (3.6)	13.0 (5.0)	12.3 (3.9)	13.5 (5.0)	$p = 0.064$	**p = 0.006**	$p = 0.537$	$p = 0.054$
BPRS-10 hallucination score	1.0 (0.0)	2.0 (4.0)	2.0 (4.0)	1.0 (4.0)	**p < 0.001**	**p < 0.001**	**p < 0.001**	$p = 0.939$
					d = 0.994	d = 0.921	d = 0.921	d = 0.018
					pw = 100	pw = 95.6	pw = 99.1	pw = 5.1
BPRS-11 delusion score	1.0 (0.0)	5.0 (2.3)	5.0 (2.0)	4.0 (5.0)	***p* < 0.001**	**p < 0.001**	***p* < 0.001**	**p = 0.050**
					d = 1.830	d = 1.988	d = 1.449	d = 0.503
					pw = 100	pw = 100	pw = 100	pw = 45.8
Negative symptoms	1.0 (0.0)	6.0 (5.3)	9.0 (6.0)	4.5 (4.0)	**p < 0.001**	***p* < 0.001**	**p < 0.001**	***p* < 0.001**
					d = 2.302	d = 2.392	d = 1.805	d = 1.511
					pw = 100	pw = 100	pw = 100	pw = 100
AOI score	2.0 (4.0)	5.0 (16.3)	12.5 (41.0)	3.5 (14.0)	**p = 0.003**	**p < 0.001**	$p = 0.102$	p = 0.053
					d = 0.554	d = 0.831	d = 0.324	d = 0.501
					pw = 84.8	pw = 91.6	pw = 33.1	pw = 45.5
Identification with movie protagonist	11.0 (32.3)	42.5 (55.3)	49.5 (53.0)	39.5 (53.50)	**p < 0.001**	**p < 0.001**	**p = 0.001**	p = 0.285
					d = 0.793	d = 0.814	d = 0.688	d = 0.274
					pw = 99.0	pw = 90.1	pw = 89.8	pw = 17.2
Hinting task score	18.0 (3.0)	16.5 (3.0)	15.0 (4.0)	17.0 (2.5)	***p* = 0.005**	**p < 0.001**	$p = 0.300$	**p = 0.006**
					d = 0.513	d = 0.942	d = 0.206	d = 0.740
					pw = 79.0	pw = 96.6	pw = 16.2	pw = 77.8
G-score	0.5 (1.1)	−0.6 (1.0)	−0.9 (1.1)	−0.3 (1.0)	***p* < 0.001**	**p < 0.001**	**p < 0.001**	$p = 0.056$
CPE	0.0 (0.0)	249.4 (328.1)	300.0 (337.5)	240.0 (328.2)				$p = 0.290$
SOFAS	90.0 (5.0)	40.0 (8.5)	40.0 (9.8)	40.0 (10.5)	**p < 0.001**	**p < 0.001**	**p < 0.001**	***p* = 0.001**

AOI = Acceptance of the implausible, CPE = chlorpromazine equivalent doses, FEP = first-episode psychosis patient, SCZ = patients diagnosed with schizophrenia during follow-up (paranoid schizophrenia ($n = 10$), schizophrenia undefined ($n = 14$)), OP = other psychosis (patients not diagnosed with schizophrenia during follow-up; schizophreniform disorder ($n = 14$), schizoaffective disorder ($n = 2$), bipolar type 1 disorder ($n = 6$), major depressive affective disorder with psychotic features ($n = 3$), brief psychotic disorder with psychotic features ($n = 3$), unspecified psychosis ($n = 10$)).

[a] Frequency (%) or median (IQR).

[b] Mann-Whitney *U* test or Fishers exact test. *P*-value or *p*-value, Cohen d effect size and post-hoc power. Significant results shown in bold.

who engage in a discussion whether or not she is the "real Alice". In the final scenes she walks through a dark forest, where she meets the talking Cheshire Cat, who occasionally appears as only a flying head.

After seeing all the scenes, participants were asked to evaluate realism of the movie, i.e., how probable they thought it would be for the movie events to occur in real life. AOI was assessed on a visual analogue scale of 0 to 100 with 0 labelled as "very unlikely" and 100 labelled as "entirely possible". A similar scale was used to ask how much the participants identified with the main character Alice with endpoints "not at all" and "very much". The same stimulus was shown to patients and control subjects during the baseline and follow-up studies.

2.4. Analyses

All statistical analyses were performed using the SPSS software (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp) at $p < 0.05$. As a significant majority of the parameters did not follow normal distribution when controlled using the Shapiro-Wilk test, we used non-parametric tests for all statistical analyses. We used a nonparametric Mann-Whitney *U* test to compare FEP patients, control subjects and diagnostic subgroups. We calculated effect sizes based on the Mann-Whitney U value (Fritz et al., 2012; Lenhard and Lenhard, 2017), and calculated post-hoc power for group analyses based on the calculated effect sizes using the G*power software (Faul et al., 2007). We performed a Wilcoxon signed-rank test to control for longitudinal within-subject effects between baseline and follow-up. We used a Spearman's correlation test to analyze behavioral correlates within the FEP group. When analyzing which baseline variable displayed the strongest correlation with AOI at follow-up, i.e., which of the variables better explains the common third variable, we used a Williams T2 test (Dunn and Clark, 1969; Williams, 1959).

We observed a significant correlation between the AOI score and age in the FEP group, thus we repeated our correlation analyses within this group using an age adjusted AOI. Additionally, as general neurocognition and antipsychotic medication could affect cognitive bias, we adjusted the AOI score using the g-factor and chlorpromazine equivalent doses. We adjusted for these variables by calculating the unstandardized residuals using linear regression in SPSS.

3. Results

3.1. Baseline

Table 1 presents demographic, clinical, and behavioral characteristics of the FEP patients and control subjects, as well as of the two diagnostic subgroups of the FEP sample based on DSM-IV diagnoses obtained at the one-year follow-up. The groups did not differ regarding age and sex at baseline, and only the schizophrenia subgroup differed significantly from control subjects for years of education. Patients with a future diagnosis of schizophrenia presented with significantly more severe delusions and negative symptoms at baseline but we did not observe large differences in antipsychotic medication doses.

FEP patients rated the fantasy movie to be more realistic than control subjects. We observed a similar result when comparing the schizophrenia subgroup to the control subjects, while the effect was less clear between the "other psychosis" group and control subjects. While not statistically significant, AOI of the schizophrenia group tended to be higher than that of "other psychosis" group. ToM performance was significantly lower in the FEP group when compared to control subjects. The subjects who would receive a diagnosis of schizophrenia during the one-year follow-up performed worse than the control subjects and those patients who had not been diagnosed with schizophrenia during the first year of clinical follow-up. The schizophrenia subgroup displayed significantly higher scores in the BPRS-11 item and significantly more negative symptoms than the "other psychosis" group. (Table 1).

Table 2 presents the associations between AOI and other behavioral

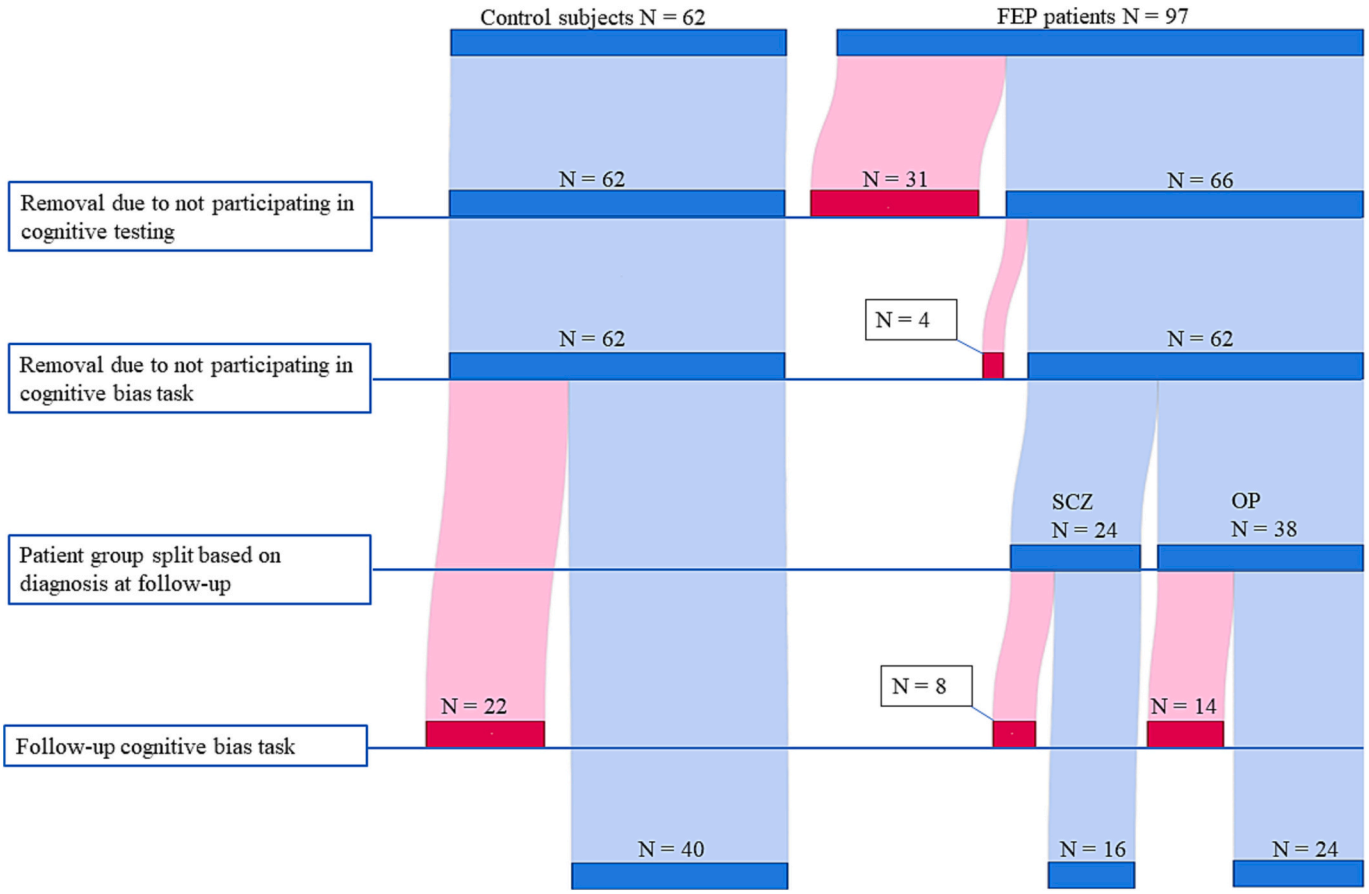

Fig. 1. Inclusion of FEP patients and control subjects in this study. Only control subjects who participated in cognitive testing and fMRI scanning (during which the AOI task was performed) are included from the parent study (HEPS). Already during the baseline study, the patient group was split based on which patients would receive a diagnosis of schizophrenia during the follow up period of one year. FEP = first-episode psychosis, SCZ = patients diagnosed with schizophrenia during follow-up, OP = other psychosis (patients not diagnosed with schizophrenia during follow-up)

variables of interest at baseline. Among the FEP patients AOI correlated positively with identification with the protagonist and delusion severity, and negatively with the Hinting task score and age. The correlations between AOI and the Hinting task score and AOI and delusion severity remained significant after adjustment for g-score, chlorpromazine equivalent doses and age. The Hinting task score correlated negatively with negative symptoms and neurocognitive performance (g-score).

3.2. Follow-up

Table 3 presents behavioral results at the one-year follow-up. As in the baseline phase, the FEP group displayed significantly higher AOI scores than the control group as did the schizophrenia subgroup when compared to control subjects. Patients who had been diagnosed with schizophrenia during follow-up used higher doses of antipsychotic medications when compared to other FEP patients. Patients in the schizophrenia group had lower SOFAS scores when compared to control subjects and the "other psychosis" group as did the FEP group when compared to control subjects. Fig. 2 presents the associations of baseline AOI score at baseline with BPRS-11 delusions score at baseline, Hinting task score at baseline and AOI score at follow-up.

Table 4 displays the associations of AOI score at one-year follow-up. The AOI score displayed a strong intercorrelation between baseline and follow-up, which remained significant after adjusting for g-score, chlorpromazine equivalent doses and age. The negative correlation with the 2 months Hinting task was still observable for the follow-up AOI score, even when adjusting for g-score, chlorpromazine equivalent doses and age. AOI did not change from baseline to follow-up (Wilcoxon signed-rank test, $Z = -0.467$, $p = 0.640$) in the FEP group, while the BPRS-11 score ($Z = -4.413$, $p < 0.001$) and the level of identification with the main protagonist ($Z = -3.529$, $p < 0.001$) significantly decreased. In direct comparison, AOI score at follow-up was better explained by AOI score at baseline than by the BPRS-11 score at baseline (Williams formula, $T2 = 3.667$, $p = 0.001$) or the BPRS-11 score at follow-up (Williams formula, $T2 = 2.790$, $p = 0.006$), suggesting AOI to be rather an independent trait than a consequence of reality distortion.

4. Discussion

To our knowledge this is the first study to differentiate state and trait characteristics of a cognitive bias and its relation to both delusion severity and ToM performance in individuals with recent onset of FEP. Our findings suggest that FEP patients differ significantly from control subjects in their estimations whether events of a fantasy movie can happen in real life. This AOI bias remained stable even when the psychotic symptoms alleviated at the one-year follow-up, suggesting a trait-like feature. Magnitude of the bias correlated positively with the severity of delusions at baseline and negatively with ToM performance.

There is robust evidence for developmental changes partaking in the formation of psychotic illness through dysfunctional dopaminergic signaling (Howes and Kapur, 2009). While it is possible that such a common factor could give rise to the illness in question and the associated abnormal probabilistic reasoning as parallel entities, LA has been theorized to provide a causal explanation for delusions (Moritz et al., 2017). Biases similar to LA have previously been shown to correlate with delusion severity. In a metamemory task, employing the

Table 2
Associations of AOI score, adjusted AOI score (adjusted for g-score, CPE and age), BPRS-11 delusion score, and Hinting task score in the FEP group at baseline.

	AOI score[a] *N* = 62	G-score, CPE and age adjusted AOI score[a] *N* = 62	BPRS-11 delusion score[a] N = 62	Hinting task score[a] N = 62
Sex	*p* = 0.365	*p* = 0.704	*p* = 0.400	*p* = 0.065
Age	**−0.321** ***p* = 0.011**	–	0.099 *p* = 0.443	0.103 *p* = 0.427
BPRS-10 hallucination score	0.187 *p* = 0.145	**0.250** ***p* = 0.050**	**0.336** ***p* = 0.008**	0.109 *p* = 0.398
BPRS-11 delusion score	**0.441** ***p* < 0.001**	**0.523** ***p* < 0.001**	–	−0.179 *p* = 0.165
Negative symptoms	0.169 *p* = 0.188	0.148 *p* = 0.250	**0.278** ***p* = 0.029**	**−0.308** ***p* = 0.015**
Hinting task score	**−0.380** ***p* = 0.002**	**−0.370** ***p* = 0.003**	−0.179 p = 0.165	–
G-score	0.081 *p* = 0.531	–	−0.076 *p* = 0.556	**0.466** **p < 0.001**
Identification with movie protagonist	**0.302** ***p* = 0.017**	0.125 *p* = 0.333	0.241 *p* = 0.059	−0.013 *p* = 0.920
CPE	0.080 *p* = 0.538	–	0.039 *p* = 0.763	−0.220 *p* = 0.086
SOFAS	−0.212 *p* = 0.098	−0.231 *p* = 0.071	**−0.441** ***p* < 0.001**	0.242 *p* = 0.058

AOI = Acceptance of the implausible, CPE = chlorpromazine equivalent doses.
[a] Spearman's rho and p-value or Mann-Whitney *U* test *p*-value. Significant results shown in bold.

Deese–Roediger–McDermott paradigm studying confidence in false memories, Eisenacher et al. observed correlations between smaller confidence gap and delusion severity in FEP patients (Eisenacher et al., 2015). In a study investigating bias against disconformity evidence, Riccaboni et al. observed a relationship between LA of implausible outcomes and delusion severity (Riccaboni et al., 2012). Mirroring these results, our study shows a correlation between the severity of delusions and AOI in agreement with the idea that a lower threshold for accepting implausible or absurd outcomes is associated with a higher confidence in beliefs that are objectively classified as implausible (delusions). AOI did not correlate with general neurocognition and correcting for neurocognitive measures did not have significant effects on our results. During follow-up, measured magnitude of AOI did decrease but was still significantly higher than that of the control subjects. At the same time, delusions markedly decreased, and no longer correlated with AOI. We observed a strong correlation between the baseline and follow-up AOI, and baseline AOI predicted follow-up AOI better than baseline or follow-up delusion severity. These findings support the trait-like quality and suggest this bias to remain relatively stable through changes in positive symptoms. Due to the lack of prospective data and the relatively short follow-up time, these results cannot be interpreted as direct evidence that cognitive biases represent a trait like risk factor for the development of psychotic disorders. They are, however, in line with this hypothesis, and if AOI develops in tandem with reality distortion, AOI resolves slower than delusions alleviate. Prospective studies and longer follow-up times could provide further insight into how this (and other) cognitive biases behave in relation to the development of reality distortion symptoms.

Considering both ToM deficits and cognitive biases have been theorized to lead to delusion formation, surprisingly few studies have analyzed these cognitive variables in the same sample (Corcoran et al., 2008; Langdon et al., 2010). Corcoran et al. observed increased tendency to JTC and lower ToM performance in both patients with depression and schizophrenia when delusions were present, while Langdon et al. observed a tendency to JTC and lower ToM performance in patients with schizophrenia in subsamples with and without delusions, and both measures correlated with delusional ideation. In addition, they observed a correlation between ToM anomalies and JTC.

Table 3
Demographic information and behavioral variables of FEP group subjects, diagnostic subgroups, and control subjects at the one-year follow-up.

	Control[a] N = 40	FEP[a] N = 40	SCZ[a] *N* = 16	OP[a] *N* = 24	Group difference Control - FEP[b]	Group difference Control - SCZ[b]	Group difference Control - OP[b]	Group difference SCZ - OP[b]
Male	29 (72.5)	20 (50.0)	6 (37.5)	14 (58.3)	*p* = 0.066	***p* = 0.030**	*p* = 0.280	p = 0.333
Age	25.5 (8.1)	27.2 (7.0)	27.2 (9.0)	26.5 (7.7)	*p* = 0.969	*p* = 0.549	*p* = 0.608	*p* = 0.576
BPRS-10 hallucination score	1.0 (0.0)	1.0 (0.0)	1.0 (0.0)	1.0 (0.0)	*p* = 0.162 d = 0.132 pw = 8.8	*p* = 0.481 d = 0.058 pw = 5.4	*p* = 0.109 d = 0.169 pw = 9.6	*p* = 0.774 d = 0.092 pw = 5.9
BPRS-11 delusion score	1.0 (0.0)	1.0 (1.0)	1.0 (1.0)	1.0 (1.0)	**p < 0.001** d = 0.501 pw = 60.0	***p* = 0.001** d = 0.537 pw = 41.3	**p = 0.006** d = 0.422 pw = 34.9	*p* = 0.633 d = 0.158 pw = 7.5
Negative symptoms	1.0 (0.0)	4.0 (5.8)	6.5 (8.0)	3.0 (3.8)	**p < 0.001** d = 1.326 pw = 100	***p* < 0.001** d = 1.824 pw = 100	**p < 0.001** d = 0.892 pw = 91.3	***p* = 0.007** d = 0.923 pw = 77.6
AOI score	2.0 (3.8)	4.0 (11.8)	6.0 (23.5)	3.5 (9.0)	***p* = 0.038** d = 0.472 pw = 45.3	***p* = 0.033** d = 0.589 pw = 48.0	*p* = 0.174 d = 0.341 pw = 24.6	*p* = 0.292 d = 0.341 pw = 17.1
Identification with movie protagonist	6.5 (44.5)	15.0 (38.3)	19.5 (47.0)	14.0 (26.8)	*p* = 0.557 d = 0.132 pw = 8.8	*p* = 0.340 d = 0.257 pw = 0.132	*p* = 0.906 d = 0.029 pw = 5.1	*p* = 0.486 d = 0.224 pw = 10.1
CPE	0.0 (0.0)	167.5 (295.3)	212.5 (264.4)	120.0 (300.0)				**p = 0.012**
SOFAS	87.5 (10.0)	55.0 (32.3)	45.0 (17.5)	70.0 (27.3)	**p < 0.001**	**p < 0.001**	**p < 0.001**	***p* = 0.002**

AOI = Acceptance of the implausible, CPE = chlorpromazine equivalent doses. FEP = first-episode psychosis patient, SCZ = patients diagnosed with schizophrenia during follow-up, OP = other psychosis (patients not diagnosed with schizophrenia during follow-up).
[a] Frequency (%) or median (IQR).
[b] Mann-Whitney *U* test or Fishers exact test. *P*-value or *p*-value, Cohen d effect size and post-hoc power. Significant results shown in bold.

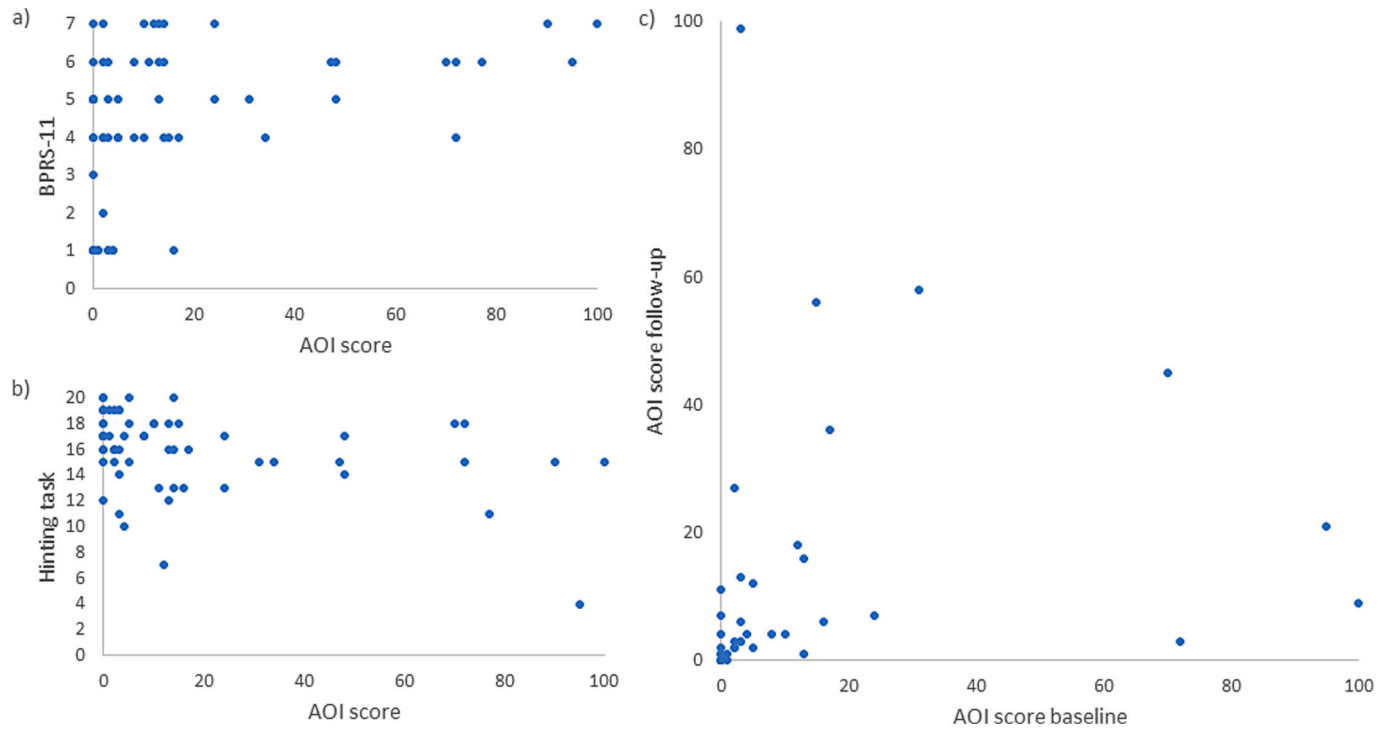

Fig. 2. Distribution of AOI score, BPRS-11 delusion score and Hinting task score at baseline and AOI score at follow-up in FEP patients.
FEP = first-episode psychosis, AOI = acceptance of the implausible.
a) FEP patient AOI score and BPRS-11 at baseline.
b) FEP patient AOI score at baseline and Hinting task score at 2 months.
c) FEP patient AOI score at baseline and follow-up.

We observed similar, but not identical results when comparing AOI, ToM and delusion severity. In our study, ToM performance correlated with AOI at both baseline and follow-up, but we did not observe significant correlations between ToM and delusions severity at either baseline or follow-up. The settings in the studies differ, as does the studied bias and the grouping of subjects. ToM impairment has been theorized to be associated with the formation of paranoid delusions, as both are related to inferring mental states or intentions to others (Harrington et al., 2005). Our results are in line with the more recent review on the subject (Garety and Freeman, 2013), where ToM was considered a correlate of negative symptoms in lieu of delusions. Of secondary interest to the correlations between ToM, AOI and delusion severity, we considered that individuals with lower ToM performance could be less likely to identify with fictional characters. The validity of this question is somewhat more difficult to interpret, as the movie includes realistic content that could be relatable to a varying degree based on personal experiences. We did not, however, observe correlations supporting this hypothesis.

AOI was more prevalent among FEP patients than control subjects at baseline and follow-up. This difference seemed to be driven mainly by the subgroup of patients diagnosed with schizophrenia during the first year of follow-up. The difference in AOI between the schizophrenia group and other psychosis group was non-significant ($p = 0.053$), but due to the small sample size the study was most likely underpowered, Further studies should examine whether the severity of cognitive bias carries predictive value in disease severity and other clinical outcomes.

5. Limitations of this study

Due to time limitations, we only showed one set of movie scenes and assessed AOI only once for baseline and follow-up. Thus, we do not know if and how much the groups differ when evaluating objectively realistic scenes. It is possible that some participants misunderstood the question, as three control subjects thought that it would be very likely for the events in the movie to occur in real life (AOI > 90/100). In two of the three subjects, AOI score was, however, above average during both baseline and follow-up, decreasing likelihood of misunderstanding. In addition, one patient answered the baseline question as very unlikely (3/100) and the follow-up question as very likely (99/100). There was no major change in the severity of delusions that could have explained this, and most likely this subject's answer is incorrect during the follow-up study. However, we did not interview the subjects afterwards, and could not verify this. Thus, we elected not to exclude outliers, and all results presented include these values. The rating of identification did not affect the results in a significant way, and only correlated with the AOI score at baseline. We elected to retain this variable, as the results suggest that even severely delusional patients responded to the questions presented. While there was an observable correlation between identification score and AOI score, the difference in mean and median values was lowest for control subjects, and highest for patients with a future diagnosis of schizophrenia. In addition, BPRS 11 did not correlate with the identification score (while it did correlate with AOI-score). In case patients with severe symptoms had answered the questions randomly, we would have expected the mean and median values to be closer for these groups. While this is not a certified sanity check, it still suggests that even patients with severe symptoms did answer the questions instead of randomly assigning an answer.

As this study is a part of a larger parent study (HEPS), no a priori power calculations were conducted for the variables and cohort sizes analyzed here. While post hoc power analyses remain a controversial topic (Hoenig and Heisey, 2001; Zhang et al., 2019), we elected to include these calculations due to the small sample sizes, especially when comparing diagnostic subgroups. This study is most likely underpowered regarding these analyses.

ToM performance was only measured at two-months after baseline, and thus we were unable to assess the possible temporal changes of this

Table 4
Associations of AOI score, adjusted AOI score (adjusted for g-score, CPE and age), BPRS-11 delusion score, and Hinting task score in the FEP group at follow-up.

	AOI score follow-up[a] $N = 40$	G-score, CPE and age adjusted AOI score follow-up[a] $N = 40$	BPRS-11 delusion score follow-up[a] N = 40	Hinting task score 2 months[a] N = 40
Sex	$p = 0.149$	$p = 0.461$	$p = 0.127$	$p = 0.512$
Age follow-up	−0.221 $p = 0.171$	–	−0.119 $p = 0.464$	−0.037 $p = 0.821$
BPRS-10 hallucination score baseline	−0.211 $p = 0.191$	−0.275 $p = 0.086$	0.034 $p = 0.837$	0.111 $p = 0.496$
BPRS-10 hallucination score follow-up	−0.132 $p = 0.416$	−0.173 $p = 0.285$	0.189 $p = 0.242$	0.063 $p = 0.701$
BPRS-11 delusion score baseline	0.109 $p = 0.505$	0.092 $p = 0.573$	0.218 $p = 0.178$	−0.297 $p = 0.062$
BPRS-11 delusions score follow-up	0.190 $p = 0.239$	0.147 $p = 0.366$	–	0.040 $p = 0.806$
Negative symptoms baseline	0.065 $p = 0.692$	0.086 $p = 0.600$	0.103 $p = 0.527$	**−0.394** $\mathbf{p = 0.012}$
Negative symptoms follow-up	0.274 $p = 0.088$	**0.341** $\mathbf{p = 0.031}$	0.311 $p = 0.051$	**−0.484** $\mathbf{p = 0.002}$
Hinting task score 2 months	**−0.352** $\mathbf{p = 0.026}$	**−0.510** $\mathbf{p < 0.001}$	0.040 p = 0.806	–
G-score 2 months	0.038 $p = 0.817$	–	0.036 $p = 0.826$	**0.647** $\mathbf{p < 0.001}$
AOI score baseline	**0.647** $\mathbf{p < 0.001}$	**0.490** $\mathbf{p = 0.001}$	0.284 $p = 0.076$	**−0.316** $\mathbf{p = 0.047}$
Identification with movie protagonist baseline	**0.392** $\mathbf{p = 0.012}$	0.289 $p = 0.070$	0.159 $p = 0.327$	−0.026 $p = 0.872$
Identification with movie protagonist follow-up	0.233 $p = 0.148$	0.180 $p = 0.267$	−0.096 $p = 0.556$	−0.123 $p = 0.449$
SOFAS follow-up	−0.236 $p = 0.143$	**−0.356** $\mathbf{p = 0.024}$	**0.583** $\mathbf{p < 0.001}$	−0.274 $p = 0.087$
CPE follow-up	0.142 $p = 0.382$	–	−0.288 $p = 0.072$	0.121 $p = 0.459$

AOI = Acceptance of the implausible, CPE = chlorpromazine equivalent doses.
[a] Spearman's rho and *p*-value or Mann-Whitney *U* test *p*-value. Significant results shown in bold.

variable. The G-score was assessed during the one-year follow-up but was not available for all subjects, and thus we omitted the second evaluation of neurocognition and controlled AOI at follow-up using the initial g-score obtained at 2 months after admission, however the g-score was rather stable on average.

All but four of the FEP patients were already using antipsychotic medication before admission to the study. Multiple patients were using mood-altering medications and some had medications for somatic disease, which were not considered in the analysis.

Patients and control subjects underwent fMRI scanning while watching the movie at both the baseline and follow-up studies. Due to a change of the MRI-scanner during the baseline study and omission of subjects due to excessive head movement, the sample size for imaging studies is smaller for both the baseline and follow-up studies. For clarity and to maintain maximal statistical power (Hoenig and Heisey, 2001) for the behavioral variable analyses we omitted imaging data from this paper.

6. Conclusion

Our study suggests that AOI is a trait-like feature rather than a correlate or a short-term consequence of delusion. While a causal relationship cannot be established based on these results, they support the hypothesis that this bias, possibly related to LA, could represent a trait-like risk factor for psychotic illness.

The AOI bias was not explained by lower general neurocognition, while the severity of this bias correlated with deficits in ToM performance. Deficits in these functions seem to be more common in psychotic patients, and our results agree with the view that cognitive bias could be predictive of the severity of delusions during psychotic episodes.

Finally, our results were mostly driven by those patients diagnosed with schizophrenia during the one-year follow-up time. ToM and negative symptoms are known to carry predictive value for functional outcomes (Fett et al., 2011; Lindgren et al., 2020), but to our knowledge no previous study has examined possible similar effects of LA. These findings support further studies to assess whether AOI measures can predict future schizophrenia in risk groups.

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Conflict of interest

The authors have declared that there are no conflicts of interest in relation to the subject of this study.

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