Taking others into account: combining directly experienced and indirect information in schizophrenia

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Abstract

An abnormality in inference, resulting in distorted internal models of the world, has been argued to be the common key to heterogeneous psychopathology in schizophrenia. However, findings have been mixed as to wherein the abnormality lies and have typically failed to find convincing relations to symptoms. The limited and inconsistent findings may have been due to methodological limitations of the experimental design, such as conflating other factors (e.g., comprehension) with the inferential process of interest, and a failure to adequately assess and model the key aspects of the inferential process.

Here, we investigated probabilistic inference based on multiple sources of information using a new digital version of the beads task, framed in a social context. Thirty-five patients with schizophrenia or schizo-affective disorder with a wide range of symptoms and 40 matched healthy controls performed the task, where they guessed the color of the next marble drawn from an urn based on a sample from the urn as well the choices and expressed confidence of four people, each with their own independent sample (which was hidden from participant view). We relied on theoretically motivated computational models to assess which model best captured the inferential process and investigated whether it could serve as a mechanistic model for both psychotic and negative symptoms. We found that ‘circular inference’ best described the inference process, where patients over-weighed and over-counted direct experience and under-weighed information from others. Crucially, over-counting of direct experience was uniquely associated with most psychotic and negative symptoms. In addition, patients with worse social cognitive function had more difficulties using others’ confidence to inform their choices. This difficulty was related to worse real-world functioning. The findings could not be ascribed to differences of working memory, executive function, intelligence or antipsychotic medication.

These results suggest hallucinations, delusions and negative symptoms could stem from the a common underlying abnormality in inference, where directly experienced information is assigned an unreasonable weight and taken into account multiple times. By this, even unreliable first hand experiences may gain disproportionate significance. The effect can lead to false perceptions (hallucinations), false beliefs (delusions) and deviant social behavior (e.g. loss of interest in others, bizarre and inappropriate behavior). This may be particularly problematic for patients with social cognitive deficits, as they may fail to make use of corrective information from others, ultimately leading to worse social functioning.
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Introduction

Abnormal inference mechanisms in the nervous system, resulting in distorted internal models of the world, have been argued to be key to schizophrenia (Fletcher and Frith, 2009). Within this hierarchical Bayesian approach to brain function, beliefs and percepts emerge from an optimal integration of prior expectations and new observations (Adams, 2018). However, failures in this process may cause abnormal perceptions (hallucinations), abnormal beliefs (delusions) and possibly even negative symptoms such as asociality (Fletcher and Frith, 2009). Despite the elegance of this theory of one common mechanism giving rise to such diverse symptoms, empirical evidence for this is yet scarce (Jardri et al., 2017). Findings have been mixed as to wherein the abnormality lies (Chambon et al., 2011; Moutoussis et al., 2011; Ross et al., 2015; Jardri et al., 2017; Powers et al., 2017; Baker et al., 2019; Valton et al., 2019). Furthermore, the identified inferential abnormalities are typically only associated with one type of symptom (e.g. delusions), if any at all (Ross et al., 2015; Baker et al., 2019; Valton et al., 2019). However, the limited and inconsistent findings could be due to methodological limitations of the experimental design, where other factors such as task comprehension and working memory abilities are conflated with the inferential process of interest, and a failure to adequately model the inferential process (Dudley et al., 1997; Speechley et al., 2010; Moutoussis et al., 2011; Balzan et al., 2012; Ross et al., 2015; Baker et al., 2019).

Typically, studies have used variations of the classical beads task to investigate explicit probabilistic inference in schizophrenia. This is a data-gathering paradigm, where participants sample beads from a hidden jar until they feel confident enough to guess which of two jars the beads are sampled from (e.g. the jar with most blue beads or most yellow beads) based on the color of the sampled beads. The task was originally adapted to assess the relation between inference and delusions, and although patients are consistently found to gather less information and tend to “jump to conclusions” (i.e., show fewer draws-to-decision (DTD)), the relation between DTD and delusions has been found weak at best (Ross et al., 2015). In fact, recent studies addressing limitations of the original task have found that both delusion-proneness in healthy individuals and delusion severity in patients are associated with increased information seeking behavior (i.e., increased DTD) (Baker et al., 2019; McLean et al., 2020). Further computational analyses showed that delusional patients displayed stronger reliance on beliefs formed early in the inferential process, or in other words, they had “sticky” beliefs that were resistant to new evidence (Baker et al., 2019; Schmack and Sterzer, 2019).
A reliable model of how patients perform sequential integration of one type of information could indeed prove essential in understanding a key abnormality in schizophrenia. However, this research neglects that we usually make inferences based on a multitude of information sources that vary both in type and reliability. This is the case for low-level perception (Deroy et al., 2016), but perhaps even more so for our social lives, where we constantly have to deal with different people that say or do different things with different degrees of certainty. This information has to be combined with our own experiences and beliefs, which may be more or less certain. In short, the classical beads task fails to address how we simultaneously balance and integrate heterogeneous information sources. This is of particular relevance in schizophrenia, where patients typically struggle with such everyday situations. Schizophrenia has even been described as a disorder of self-other processing, displaying problems with self-other integration and distinction that range from self-disturbances (e.g. delusions of being controlled) to altered mimicry (e.g. echolalia) and difficulties inferring others’ mental states and distinguishing them from one’s own (van der Weiden et al., 2015).

Indications of inferential problems were reported in a recent study by Jardri et al. (2017). In this study, participants had to integrate two different sources of information that both varied in degree of certainty to decide which lake a fish (which was red or black) was from: a prior (the basket size associated with each of two lakes reflecting probability of catching a fish in them) and sensory evidence (distribution of red and black fish in each lake). Interestingly, patients relied more on the most recent evidence (contrary to Baker et al.’s (2019)) and this tendency was related to psychotic symptoms. There may be several reasons for this. First, participants could only see the lake fish distributions (sensory evidence) and not the basket sizes (prior information) when making the decision. Patients may have disregarded the prior information due to working memory deficits, which are prevalent in schizophrenia (Schaefer et al., 2013), rather than mis-weighting priors in some integrative process. Indeed, weighing of prior information was associated with working memory performance (Jardri and Deneve, 2013). Second, the task is highly abstract. It may not be clear to patients how they should interpret and use the basket size compared to the number of red fish in the lakes. Such comprehension difficulties may contribute to larger reliance on sensory evidence. Finally, the task design conflates information type (basket or lake) and time (prior or new evidence). Thus, it is possible that if the lakes and baskets were presented in reversed order or simultaneously, we would still see a larger reliance on the lake distributions, i.e. it may be qualities of the information source rather than order that matters.
To address some of these alternative interpretations and directly investigate probabilistic inference based on multiple sources of information, we used a new version of the beads task (Campbell-Meiklejohn et al., 2017). On each trial, participants had to guess the color (red or green) of the next marble drawn from a hidden jar based on a sample from the jar (8 marbles) and the choice and confidence of four other people. Each of the others’ choices were said to be based on their own sample of 8 marbles from the same jar. By systematically varying the evidence for a specific color in the sample and the others’ choices, we could assess how patients integrate different sources of information varying in degree of certainty. Importantly, all information was present when they had to make a choice to avoid confounding inference with working memory abilities. To ease task comprehension and make the task less abstract, we gave careful task instructions (see Materials and Methods) and framed the task in a social context, since reasoning is known to be easier in social contexts (Cosmides, 1989), thus reducing such potential confound of misunderstanding. Altered inference may become particularly evident in social contexts (Lincoln et al., 2011), given the pronounced social cognitive deficits in schizophrenia (Savla et al., 2012) and the very social nature of many symptoms (e.g., hearing voices, mind reading, feeling persecuted, displaying reduced interest in others).

In order to investigate the patients’ information integration processes, we relied on theoretically motivated computational models based on Bayes theorem. A common concern in the study of psychiatric conditions is the lack of adequate modeling of behavioral data, with strong arguments in favor of theoretically motivated computational models replacing more traditional statistical techniques (Adams et al., 2016). In this study, we compared four different Bayesian models as well as two control models: i) simple Bayes, ii) weighted Bayes, iii) circular inference with and iv) without interference, v) a heuristic model and vi) the generalized linear model (for details, see Methods section). The Bayesian framework provides a formal solution to optimal integration of information under uncertainty where each source of information is weighed according to its precision or reliability. While simple and weighted Bayes are established models to integrate information, circular inference is a biologically informed model that is shown to account for psychotic symptoms (Jardri and Deneve, 2013; Jardri et al., 2017). The model builds on the theory that a failure to maintain the balance in excitatory/inhibitory neural processing may cause reverberation of sensory and prior information, so that sensory information is misinterpreted as prior beliefs (or vice versa). The net result is an inflated sense
of confidence in unreliable information, which might lead abnormal perception (hallucinations) and abnormal beliefs (delusions) (Jardri and Deneve, 2013; Jardri et al., 2017).

We compared patients’ performance to a matched healthy control group, and we investigated whether symptoms and social functioning were related to the observed information integration style. In addition, we assessed whether altered inference was related to social cognitive deficits, a relationship that is not yet well understood (Chambon et al., 2011; Takeda et al., 2018). Specifically, we assessed whether there was a relation between inferences made in the two contexts, i.e. inferences based on integration of direct experience and information from others, and mental state inferences based on integration of multiple social cues. Finally, we assessed how potential confounders (working memory, executive function, intelligence, antipsychotic medication) affect the observed information integration style. We hypothesized that patients would discount information from others in favor of directly experienced information (i.e. their own sample) relative to controls, and that this information integration style would be related to more severe psychotic symptoms, more severe negative symptoms, larger social cognitive deficits and lower social functioning.

**Materials and methods**

**Participants**

Forty patients with an ICD-10 DCR diagnosis of schizophrenia or schizoaffective disorder and forty matched healthy controls were included in the study. Diagnosis was confirmed using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) (Wing et al., 1998; Celik, 2005). Controls were pairwise matched to the patients according to age, gender, childhood residence as well as commenced educational level (or parents’ educational attainment if higher than the patient’s) and parental socioeconomic status when possible (see Table 1).

Patients were recruited through the Psychiatric Centre of the National Hospital of the Faroe Islands. Controls were contacted based on age and gender and, if they fulfilled the inclusion criteria and matched a patient, were offered to participate in the study. Participants were between 18 and 55 years old. The inclusion criteria were: no current psychoactive substance use disorders (except nicotine), no head trauma, neurological or medical disorder that could affect brain functioning, and an estimated IQ above 70 based on prior history or testing. In addition, the controls should not be taking psychotropic drugs or have a history of severe
mental disorder either among themselves or a first-degree relative. The participants were screened for recent use of psychoactive substances (THC/cannabis, opiates, amphetamine, MDMA, benzodiazepines, cocaine) using a urine stick (NanoSticka® 200-32). Patients without a prescription who had a positive test were excluded. None of the controls had a positive test. Two patients were excluded after initial inclusion as it became clear that they did not fulfill the inclusion criteria. In addition, two patients did not perform the task because they did not understand the task instructions and one patient opted out due to lack of time. Thus, data from thirty-five patients (four with schizoaffective disorder) and 40 controls was included in the analyses. Thirty-two of these patients were taking antipsychotic medication at the time of testing (see Table 1). Antipsychotic dose was converted to Chlorpromazine equivalents (Gardner et al., 2010; Leucht et al., 2014).

**General procedure**

The task was administered as part of a larger battery of cognitive tests. In addition, symptom severity and level of functioning were assessed with the Scale for the Assessment of Positive/Negative Symptoms (SAPS/SANS) (Andreasen, 1983, 1984) and the Personal and Social Performance Scale (PSP) (Morosini et al., 2000), respectively. We used the Danish version of ‘The Awareness of Social Inference Test’ (TASIT, Part 2: Social Inference–Minimal) (Bliksted et al., 2014) to assess social cognition. This is a criterion referenced test depicting short video vignettes of everyday interactions. The test is designed for clinical assessment of social perception where participants answer yes/no questions about the protagonists’ thoughts, feelings, intentions and meaning (McDonald et al., 2003; McDonald et al., 2006). The test requires social cue integration (e.g. intonation, facial expression, body language, verbal content) in order to infer when the protagonists are being sincere or sarcastic. We used four subtests (Vocabulary, Similarities, Block Design, and Matrix Reasoning) of the Wechsler Adult Intelligence Scale-IV (Wechsler, 2011) to estimate intelligence (IQ). Working memory (WM) and executive function (EF) were assessed with Spatial Working Memory (SWM) and the Intra-Extra Dimensional Set Shift (IED) from the Cambridge Neuropsychological Test Automated Battery (CANTAB) (Cognition, 2012), respectively (see Table 1). The study was performed in accordance with the relevant national guidelines and regulations and with the Helsinki Declaration. Written informed consent was obtained from all participants after the procedure had been explained.
Experimental paradigm

We used a shortened version of the urn task described in Campbell-Meiklejohn et al. (2017). To ensure task comprehension, participants received detailed task instructions, practice trials and debriefing after the task. In addition, they performed an individual pre-task prior to the actual task. It contained 16 trials plus practice trials. They were presented with a random sample of eight marbles (zero to eight red and green marbles) from a series of mixed hidden urns and were instructed to infer the color (red or green) of the next marble drawn from each urn as well as state confidence in that choice (high or low) (see Figure 1, right top corner for the four response options). The marbles were said to be replaced before the decision had to be made. This pre-task was used in order to make sure that the participants understood the responses of the other people (agents) during the following task, including how they might be using confidence.

During the experimental task, participants were again presented with a new hidden jar on every trial and were instructed to infer the color of the next marble drawn from that jar. Before deciding, however, participants were presented with a sample of eight marbles and the decisions of four other people (agents), which each stated their choice as well as the confidence in that choice (see Figure 1). Others’ decisions were said to be based on their own sample of eight marbles randomly drawn from the same jar and all the marbles were said to be replaced before the participant had to make a decision. Due to the specific patient group, we deliberately avoided providing an elaborate cover story about these other people. Agents’ confidence was communicated as an explicit cue (identical to the response options during the pre-task): the smug (confident cue) or perplexed (unconfident) animated smiley that appeared within the indicated choice (red or green marble) (see Figure 1). To avoid that participants made hasty guessing to reduce task duration, all information was available on the screen for 500 ms before a decision could be made. After a choice, confirmation of the choice was displayed. No feedback was provided. The task consisted of 105 trials (plus 10 practice trials) that were generated by creating every possible combination, across trials, of: the number of others choosing red or green, confidence of others choosing red or green, and participants’ samples - all varying independently of one another. For each number of others choosing red (0 – 4), there were 21 trials - three for every possible participant sample (1 – 7 reds). To reduce the number of necessary trials, agents that chose the same color had the same confidence level. The trials were randomized. The task had no extrinsic gain or loss. There was no explicit or implicit cost.
to weighting one’s sample and the information from the agents, other than the intrinsic incentive to provide a correct response.

**Statistical analyses and computational modelling**

In order to assess the dynamics underlying the decisions made by the participants, we implemented four theory-driven models of information integration, simple Bayes, weighted Bayes and circular inference (with and without interference) (Jardri et al., 2017), as well as two control analyses: the traditional generalized linear model (GLM) and a heuristic model. The models are briefly described below and their full implementation (relying on R, Stan and brms (Bürkner, 2017; Carpenter et al., 2017)) is detailed in the Supplementary Material, including additional control analyses and the implementation code. All models were implemented in a Bayesian multilevel fashion: partially pooling information from all participants to improve our inferences and explicitly accounting for the uncertainty in the parameter estimates. For comparison we also report individually fitted models (no pooling of information) in the Supplementary Material. We chose to use regularizing priors, that is, priors weakly skeptical of the effects, to decrease chances of model overfitting (McElreath, 2015). We compared the models using estimated out-of-sample-error (Pareto-smoothed Information Sampling Leave-One-Out Information Criteria, PSIS-LOO) (Vehtari et al., 2015), which estimates the likely generalizability of the model to new data.

**Simple Bayes model.** This model assumes that the directly experienced information (i.e. the participant’s sample) and the information from the agents are fully trusted, thus weighing them equally, i.e. one’s own sample weighs as much as the information provided by the choice of one of the agents. In this situation, the optimal form of inference is to directly combine the sources of information using Bayes’ theorem, expressed by the equation:

\[
red_{ij} \approx bias_j + S_{ij} + \sum_{k=1}^{4} C_{kij} O_{kij}
\]

For computational simplicity, we express the simple Bayes model in terms of log odds. \(\text{Red}_{ij}\) is the log odds of the probability of choosing red for participant \(j\) during trial \(i\). \(S\) (for self) is the log odds of the proportion of red marbles in the participant’s sample. \(O_k\) indicates the
evidence for red provided by the other agents’ choices (log odds of 0.9 for choice of red, log odds of 0.1 for choice of green), and C_k their confidence in the choice (low, coded as 0.5, or high, coded as 1), with k indexing the four agents. The bias term indicates a potential bias towards one of the two colors. Bias is conditioned on group and matched participant pair. The two components of bias are modeled as hierarchical and correlated, that is, as both fixed and random effects. This allows us to account for individual variability, participant matching and variability in participant matching. The estimated outcome choice is calculated according to a Bernoulli distribution. Note that the simple Bayes model – although it is unlikely to capture the actual decision-making process – it is the best model when participants treat the different sources of information equally, and the model acts as a stepping stone to understand and build the more complex models.

**Weighted Bayes model.** This model builds on the previous model, but allows the participant to attribute different degrees of trust to the directly experienced information and the agents’ information and therefore to weigh their impact on the decision differently:

\[
red_{ij} \approx bias_j + F(S_{ij}, w_S) + \sum_{k=1}^{4} F(O_{kij}, w_O + \beta_j C_{kj})
\]

where

\[
F(L, w) = \log \frac{w e^L + 1 + w}{(1 - w) e^L + w}
\]

In other words, the probability of choosing red on a given trial is parametrized by a possible bias, a weight \(w_S\) that indicates the trust placed on the directly experienced information and a weight \(w_O\) that indicates the trust placed on information from the agents. Note that \(w_O\) is the same parameter for all four agents (identified by the index \(k\)) as they are not uniquely identifiable and we assume participants treat them indifferently. The weight for the agents’ information is modified by the confidence expressed by the agents: a low confidence should involve a lower weight, a high confidence a higher one. The parameter \(\beta\) expresses the amount of variation that a high level of confidence has on the weight (compared to a low level), and is the same for all four agents. The function \(F(L,w)\) corresponds to the weighting of the evidence from a given source (L or likelihood) by a weight (w) in a log odds space.
Analogue to bias in the previous model, the estimated bias, weight and $\beta$ parameters are allowed to vary by diagnosis, as well as by participant accounting for the matching between participants. Note that when the two weights are equal and fully trusted ($w_S = w_O = 1$), the weighted Bayes model is equivalent to the simple Bayes model (see Figure S1).

Circular Inference. According to this model, prior beliefs and sensory input reverberate in a non-linear fashion, and can be mixed and accounted for multiple times (Jardri and Deneve, 2013; Jardri et al., 2017). Here we extend the model to directly experienced information and information from others, as well as more than two sources of information. The mathematical formulation of the model builds on the weighted Bayes model by adding two components: i) a free parameter per information source, indicating the strength of the reverberation, and ii) interference between the sources of information. In the weighted Bayes model, directly experienced information and information from the agents are considered only once, while in the circular inference model, the information can be counted multiple times. A high loop value for directly experienced information ($\alpha_S$) indicates over-counting of this information and analogously for the agents’ information ($\alpha_O$). Note that even if a source of information might be considered multiple times, participants do not need to trust it fully, thus maintaining meaningful weight parameters.

$$\text{red}_{ij} \approx \text{bias}_j + F(\alpha_S S_{ij} , w_{Sj}) + \sum_{k=1}^{4} F(\alpha_O O_{kij} , w_{Oj} + \beta_j C_{kij})$$

Further, the circular inference model also involves the corruption of information sources (Jardri et al., 2017). The second circular inference model we implemented includes this in the form of an interference term, combining the different sources of information in non-linear ways, thus rendering them non-separable (Interference or $I$).

$$\text{red}_{ij} \approx \text{bias}_j + F(S_{ij} + I, w_{Sj}) + \sum_{k=1}^{4} F(O_{kij} + I, w_{Oj} + \beta_j C_{kij})$$

Where $I$ is defined as:

$$ I = F(\alpha_S S_{ij} , w_{Sj}) + \sum_{k=1}^{4} F(\alpha_O O_{kij} , w_{Oj} + \beta_j C_{kij})$$
The circular inference model with and without interference has six parameters: bias, $w_s$, $w_0$, $\beta$, $\alpha_s$, and $\alpha_0$, each of them allowed to vary by participant and diagnosis in a hierarchical fashion as in the previous models. Note that as in the weighted Bayes model there is only one weight, one confidence and one loop parameter for the four agents. The circular inference model is equivalent to the weighted Bayes model when both alphas ($\alpha_s$ and $\alpha_0$) are equal to one and no interference is present. If in addition, the weights are both equal to one, the model is equivalent to the simple Bayes model (See Figure S2).

Generalized Logistic Regression. In order to make our findings more easily comparable with traditional statistical approaches (including previous uses of the paradigm (Campbell-Meiklejohn et al., 2017)), we also included a logistic regression model. Choice of color (red vs. green) was modeled as a Bernoulli distribution where the log odds of choosing red were determined by the following function:

\[
\text{red}_{ij} \approx \beta_0 + \beta_1 S_{ij} + \beta_2 \left( \sum_{k=1}^{4} O_{kij} \right) + \beta_3 \left( \sum_{k=1}^{4} C_{kij} O_{kij} \right) + \beta_4 G + \beta_5 G S_{ij} \\
+ \beta_6 G \left( \sum_{k=1}^{4} O_{kij} \right) + \beta_7 G \left( \sum_{k=1}^{4} C_{kij} O_{kij} \right)
\]

As in the previous models, the same beta coefficients apply to all of the other agents (as indicated by the parentheses) and the beta parameters are hierarchically structured to enable them to vary by participant. Note that we only model confidence in interaction with social information: the level of confidence on its own should not affect the participants’ choice, without knowing what others have actually chosen.

Heuristic model. Finally, previous studies suggest that participants may use simpler reasoning strategies (Speechley et al., 2010; Moutoussis et al., 2011; Culbreth et al., 2016), we therefore assessed whether participants were using simple heuristics to solve the task as opposed to the Bayesian models presented above. The heuristic model had the following probabilistic decision rules and always relied on one type of information only (i.e. no information integration): i) choose the color that is most of in the sample, if indecisive then ii) choose the color that most others choose, if indecisive then iii) choose the preferred color (bias). Note that confidence is ignored in this model. This model was implemented by creating two additional variables: HeuristicSelf, which is 1 if the red and green marbles sampled are in equal proportion (4 and
4), 0 otherwise; HeuristicOther, which is 1 if more than 2 others choose red, -1 if less than 2 others choose red and 0 if exactly 2 others choose red. We then built the following model:

\[
red_{ij} = \beta_0 + \beta_1 S_{ij} + \beta_2 (HeuristicSelf_{ij} \times HeuristicOther_{ij}) + \beta_3 G + \beta_4 G S_{ij} + \beta_5 G (HeuristicSelf_{ij} \times HeuristicOther_{ij})
\]

**Cognitive and clinical features in parameter estimation**

After identifying the best fitting model via model comparison, we further assessed in this model whether cognitive and clinical factors were related to the patient’s use of information. In particular, we assessed whether cognitive function (e.g. TASIT, IQ), specific symptom clusters (e.g. hallucinations, delusions), general symptom severity (SANS or SAPS total score), antipsychotic medication dose (CPZ) and level of functioning (PSP) would modulate the integration of the directly experienced and the indirect information, by affecting the model parameters. All of these analyses were conducted on the patients only by conditioning the estimated parameters on each patient and the additional variable of interest (i.e., we expected the parameters to vary by individual – random effect – and by e.g. global rating of hallucinations – fixed effect). For ease of comparison with previous studies not relying on multilevel modeling, and in order to assess the contribution of a symptom cluster when adjusting for the others, we also report the analysis of the relation between symptoms and individually fit model parameters in the Supplementary Material.

**Evidence ratio**

To quantify the support for our hypotheses, we calculated an evidence ratio (ER) in the form of the posterior probability of the directed hypothesis (e.g. parameter > 0) against the posterior probability of the opposite hypothesis (e.g. parameter ≤ 0) (Burnham et al., 2011) with the following interpretation of evidence: 1–3 = anecdotal; 3–10 = moderate; 10–30 = strong (Jeffreys, 1998). Additionally, we report a credibility score for the hypothesis, that is, the percentage of the samples from the posterior conforming to the prediction.

**Data availability**

The dataset analyzed is available from the corresponding author on reasonable request. The implementation code is available at

**Results**
Model comparison

We first compared the six models (simple Bayes, weighted Bayes, circular inference with and without interference, GLM and heuristic). The circular inference model with interference was the most likely given the data, credibly minimizing estimated out-of-sample error. PSIS-LOO indicated credible differences from all other models, with GLM stacking as second (see Table 2). Circular inference with interference was also the most likely model within each group (for patients, circular inference without interference was second, Tables S8-9). Individual-level fitted models confirmed that circular inference (with or without interference) was most likely for 70 out of 75 participants (see Supplementary Material). Given the evidence for participants’ performance being best described by the circular inference model, we focus on this model, but parameter estimates for all models are available in the Supplementary Material (Tables S1-6).

Schizophrenia and circular inference

Participants generally took confidence into account, did not take any source of information at face value (weights below 1, indicating uncertainty in the use of information), and over-counted information (loop parameters above 1, indicating that participants paid more attention to the direction of the evidence than to small differences in it). Participants were also more affected by directly experienced than by information from others (indirect information), but patients more so than controls. Specifically, patients overweighed and over-counted directly experienced information (mean weight: 0.92 in patients vs. 0.89 controls; mean loops of 6.24 in patients vs. 2.66 in controls). In other words, small amounts of evidence in their samples (e.g. 6 red gumballs instead of 5) made a larger difference in the patients’ propensity to guess that the next marble would be red, than it did for controls. Patients also underweighed indirect information (both choice and confidence of others) more than controls (mean weight for others of 0.64 for high confidence and 0.57 for low confidence in patients vs. 0.74 and 0.62 for high and low confidence in controls), but showed similar over-counting (2.05 vs. 2.01). See Table 3 for details and Figure 2.

Cognitive function and circular inference

There was strong evidence for an association between TASIT performance and the use of others’ confidence in informing choice behavior (Table S10, ER >1000, credibility = 1), i.e., the better patients were at inferring others’ mental states, the more they relied on others’ confidence to weight information from them. In particular, patients with the minimum TASIT
score would weight low and high confident others 0.55 and 0.58 respectively; while patients with the maximum TASIT score 0.58 and 0.68.

We assessed whether this could be related to IQ, since IQ is known to be related to TASIT performance (McDonald et al., 2006). Indeed, there was a similar association, i.e., the higher the patients’ IQ, the more they relied on others’ confidence to weight information from them (Table S11, ER >1000, credibility = 1). In particular, patients with the minimum IQ score would weight low and high confident others 0.54 and 0.57 respectively; while participants with the maximum IQ score 0.58 and 0.69. However, when adjusting for IQ, there was still strong evidence for a positive association between TASIT performance and use of others’ confidence (Table S12, \( \beta = 1.02, 95\% \text{ CIs} = 0.52 \text{ } 1.52, \text{ ER > } 1000, \text{ credibility } = 1 \)).

There was no evidence for a negative association between loops for self and IQ (ER = 0.08, credibility = 0.08). In fact, the evidence was in the opposite direction, i.e. the higher the IQ, the higher the loops for self (Table 11, mean loops for Self changing from 3.78 to 5.05 from lowest to highest IQ, ER = 12.3, credibility = 0.92). There was no credible evidence that working memory or executive function were associated with patients’ task performance (Tables S13-14). Model comparison also showed that models including IQ, SWM or IED gained 0 weight, while the model including TASIT was the most likely given the data (Table S15, stacking weight TASIT model: 0.89; baseline model: 0.11).

**Psychopathology and circular inference**

There was strong evidence for a positive association between loops for Self and hallucinations (5.42 with a score of 0, 7.00 with a score of 5, ER = 18.1, credibility = 0.95, Table S16), delusions (5.31 to 6.62, ER = 11.7, credibility = 0.92, Table S17), bizarre behavior (5.36 to 7.02, ER = 20.6, credibility = 0.95 Table S18) and SAPS score (5.21 to 7.1, ER = 29.9, credibility = 0.97, Table S20), while it was moderate for formal thought disorder (5.58 to 6.69, ER = 5.5, credibility = 0.85, Table S19). Similarly, there was strong evidence for a positive association between loops for Self and anhedonia-asociality (5.21 to 7.1, ER = 28.7, credibility = 0.97, Table S24), avolition-apathy (5.31 to 6.89, ER = 12.0, credibility = 0.92, Table S23), attention (5.42 to 6.75, ER = 10.5, credibility = 0.91, Table S25) and SANS score (5.26 to 6.82, ER = 13.7, credibility = 0.93, Table S26), while it was moderate for affective flattening (5.47 to 6.36, ER = 4.2, credibility = 0.81, Table S21) and not credible for alogia (5.37 to 5.70, ER = 1.6, credibility = 0.62, Table S22). For the other model parameters (weight for Self, weight
for high or low confident Others, loops for Others), there was either no or only moderate evidence for associations with different symptoms (see Supplementary Material). We also assessed whether medication could be confounding the results. However, the evidence for a positive association between antipsychotic medication dose and loops for Self was only moderate (ER = 3.1, credibility = 0.75, mean loops changing from 5.5 for no medication to 6.3 for highest medication dose, Table S27). Finally, we also assessed parameters fitted at the individual level (no pooling), as done in previous studies (e.g. Jardri et al., 2017). Here, there was in most cases strong evidence for a positive association between loops or weight for Self and all symptom clusters (except for formal thought disorder). There was a similar picture for loops and weight for Others, where there was moderate to strong evidence for a negative association with all symptoms (except formal thought disorder). On the other hand, there was no credible evidence for an association between confidence and symptoms, expect for bizarre behavior, where the evidence was moderate (see Table S30). Importantly, since some of the symptoms co-varied (see correlation matrix S32 and network structure Figure S5), we also assessed associations between the model parameters and each psychotic or negative symptom cluster while controlling for the other psychotic or negative symptom clusters, respectively. Many of the associations survived this correction. For instance, hallucinations, delusions, bizarre behavior, anhedonia-asociality, alogia and attention were uniquely associated with loops for Self. Similarly, hallucinations, delusions, affective flattening, avolition-apathy and attention were uniquely associated with weight for Others (for full details see Table S31).

**Level of functioning and circular inference**

There was a similar pattern for PSP and IQ. Specifically, there was evidence for a positive association between PSP score and the importance attributed to others’ confidence (ER = 36.6, credibility = 0.97). Participants with minimum PSP score used an average weight of 0.56 for low confident and 0.61 for high confident others; while participants with the highest score 0.57 and 0.64 respectively (Table S28). This was the case even when controlling for IQ (ER = 4.37, credibility = 0.81, Table S29). In addition, there was moderate evidence for a positive association between PSP and loops for Self (ER = 8.7, credibility = 0.90, Table S28), which disappeared when controlling for IQ (ER = 1.15, credibility = 0.54, Table S29).
Note that we also report a control experiment including 66 healthy individuals, where we used a simplified version of the task with only one other source of information (instead of four). Here, we assessed whether framing the indirect source of information in a social (a person) or non-social (a computer) context had any effect on how participants’ treated the information. Results showed that while there was no credible difference in how they used their own sample in the two contexts, there was a difference in how they used the other information source. Specifically, while they equally relied on a low confident algorithms and confident people, they relied more on a confident person than on a confident algorithm (beta = 0.66, 95% CIs 0.07 1.24, ER = 72.4, credibility = 0.99, Table S33). This was despite the fact that the social and non-social trials were randomly interleaved.

**Discussion**

We investigated the hypothesis that the diverse symptoms characteristic of schizophrenia could stem from a common abnormality in inference mechanisms (Fletcher and Frith, 2009). This was done using a new version of the Beads task, designed to investigate inference based on concurrent integration of multiple sources of information. By comparing different computational models of how inference could be altered in schizophrenia, we found that different degrees of circular inference best described choice behavior in both patients and controls.

This is concordant with circular inference being the best model to describe the integration of sensory and prior information in a previous study (Jardri et al., 2017). Patients tend to put more weight on and over-count directly experienced information compared to controls and, conversely, they tended to put less weight on the information from others (indirect information). The findings are in line with the study by Jardri et al. (2017), which found that patients put more weight on and over-counted sensory evidence and less weight on prior information. Importantly, our results suggest that over-counting of direct experience may not only be a key mechanism underlying psychotic symptoms as previously reported (Jardri et al., 2017) but also negative symptoms. The fact that over-counting of direct experience was associated with most symptom clusters cannot be simply ascribed to general disorder severity or high correlations between symptoms. Although some symptoms were correlated, many of the psychotic and negative symptoms were uniquely related to over-counting of direct experience. Over-weighing of direct experience as well as under-weighing and under-counting
of indirect information also likely play a role in the psychopathology, although the evidence for this was not as strong.

We framed the task in a social context to make it less abstract, but also because social cognitive deficits are central in schizophrenia and patients typically display impairments in social functioning (Savla et al., 2012). The social aspect could therefore play a key role. Indeed, we found that the patients’ ability to make inferences about others’ mental states and their level of functioning were both specifically related to how they used information from others. Patients that were better at mentalizing and had a higher level of functioning relied more on cues about others’ confidence to weight information from others in their decisions. This was also the case when controlling for IQ. The results suggest that these patients were more attuned to the cues from others and/or better at making inferences based on them and therefore more able to make use of them, and ultimately to function in the real world. Our results suggest that it is important to keep in mind that social cognitive function presumably interacts with the inference process. In particular, the way information from others is treated may be instrumental in the shaping an maintenance of hallucinations and delusions as well as directly affect behavior in social contexts. This is something that would not be evident from the use of non-social tasks (e.g. the classical Beads task (Takeda et al., 2018). Note, that although the basic inference mechanism may be the same, and our main study does not discriminate between a specific social or more general cognitive domain atypicality, our control experiment shows that placing the task in a social vs. non-social context affects how the information is treated. In particular, we show that directly experienced information is treated similarly in the two contexts. However, and crucially, that is not the case for the indirect information. Confidence expressed is treated differently according to whether it comes from an algorithm (non-social source) or a person (social source) and it is used to inform one’s decisions more in the social context. In addition, the fact that neither context nor social cognitive function was related to over-counting of direct experience suggests that this specific abnormality, which may be key to schizophrenia symptomatology, is unrelated to social impairments.

The fact that patients focused more on directly experienced information as opposed to information from others compared to controls, could not be easily explained by general cognitive deficits. First, both patients and controls differentiated between high and low confident others. This is arguably the most complex part of the task and suggests that they did not have problems with processing the information provided. Second, both patients and
controls often stated during debriefing that they put more trust in their own sample (higher certainty) than the others’ decisions and not that they had problems with considering all the available information. Third, patients’ working memory and executive function were not related to task performance. While, patients’ IQ was related to how they used others’ confidence, over-counting of directly experienced information was not associated with a lower IQ.

Our results provide further evidence of the benefit in using biologically informed computational models to critically investigate the underlying mechanisms of disorders like schizophrenia, beyond the immediate behavioral data. They also point to the limitation of conceptualizing abnormal inference in schizophrenia as solely a problem of sequential belief updating of one type of information. In fact, a key abnormality may lie in how multiple sources of information are integrated simultaneously and in particular how directly experienced information is processed compared to other types of information, e.g. information from others. This only becomes evident when moving beyond one information source. Future studies could further investigate how different sources of information (direct experience vs. indirect information) are treated during sequential belief updating.

Some limitations of this study should be mentioned. We cannot, based on the current data, determine whether circular inference is causally related to the formation of psychotic and negative symptoms. While it seems unlikely that over-counting of direct experience should stem from all types of schizophrenia psychopathology, it is possible that for instance putting less weight on information from others could be a consequence of the distrust experienced by patients with severe delusions. Future studies could assess circular inference in prodromal stages of the disorder or in high-risk groups as well as across diagnoses with or without psychotic symptoms. This could also circumvent the problem with antipsychotic medication being a potential confounder, although the evidence for this was weak. Future studies could also investigate the purported underlying neural mechanisms of the circular inference model to provide further medium for hypothesis testing and establish a better understanding of the link between abnormal inference and the heterogeneous psychopathology of schizophrenia.

In conclusion, our results suggest that hallucinations, delusions and negative symptoms could stem from the same underlying abnormality in inference, where directly experienced information is assigned an unreasonable weight and taken into account multiple times, so that even random and unreliable experiences may gain disproportionate significance. This may
eventually lead to false perceptions (hallucinations), false beliefs (delusions) and deviant social behavior (e.g. loss of interest in others, bizarre and inappropriate behavior). This may be particularly problematic for patients with social cognitive deficits, as they to a larger degree may miss or fail to make use of corrective information from others, ultimately leading to worse social functioning.

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Competing interests
The authors report no competing interests.

Supplementary Material
References


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

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


Table 1. Characteristics of the participants

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Schizophrenia mean (SD)</th>
<th>Controls mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size (n)</td>
<td>35</td>
<td>40</td>
</tr>
<tr>
<td>Age</td>
<td>38.0 (10.7)</td>
<td>39.3 (10.5)</td>
</tr>
<tr>
<td>Sex, males/females (n)</td>
<td>22/13</td>
<td>27/13</td>
</tr>
<tr>
<td>Handedness, right/left (n)</td>
<td>32/3</td>
<td>36/4</td>
</tr>
<tr>
<td>Educational level commenced(^a)</td>
<td>2.1 (0.7)</td>
<td>2.3 (0.7)</td>
</tr>
<tr>
<td>Years of education</td>
<td>12.6 (2.7)</td>
<td>14.3 (3.1)</td>
</tr>
<tr>
<td>Parental socioeconomic status(^b), high/middle (n)</td>
<td>12/23</td>
<td>13/27</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cognitive functions</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated IQ</td>
<td>93.3 (14.4)</td>
<td>(13.8)</td>
</tr>
<tr>
<td>The awareness of social inference test</td>
<td>44.5 (7.3)</td>
<td>49.7 (5.4)</td>
</tr>
<tr>
<td>Spatial Working Memory, total errors</td>
<td>16.1 (10.5)</td>
<td>7.6 (9.0)</td>
</tr>
<tr>
<td>Intra Extra Dimensional Set Shift, total errors adjusted</td>
<td>42.1 (39.3)</td>
<td>18.6 (16.1)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level of functioning</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal and Social Performance Scale</td>
<td>59.8 (13.7)</td>
<td>86.1 (5.1)</td>
</tr>
<tr>
<td>Living independently/with parents/in institution (n)</td>
<td>13/15/7</td>
<td>37/3/0</td>
</tr>
<tr>
<td>Early retirement or other financial support(^c) (n)</td>
<td>30</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Illness duration, psychopathology, medication status</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Illness duration in years</td>
<td>14.7 (9.8)</td>
<td>-</td>
</tr>
<tr>
<td>SAPS(^d) total score [range]</td>
<td>4.20 (4.13) [0-13]</td>
<td>-</td>
</tr>
<tr>
<td>Global rating of severity of hallucinations [range]</td>
<td>1.31 (1.94) [0-5]</td>
<td>-</td>
</tr>
<tr>
<td>Global rating of severity of delusions [range]</td>
<td>1.89 (2.03) [0-5]</td>
<td>-</td>
</tr>
<tr>
<td>Global rating of severity of bizarre behavior [range]</td>
<td>0.49 (0.92) [0-3]</td>
<td>-</td>
</tr>
<tr>
<td>Global rating of positive formal thought disorder [range]</td>
<td>0.51 (0.98) [0-3]</td>
<td>-</td>
</tr>
<tr>
<td>SANS(^f) total score [range]</td>
<td>7.66 (4.63) [0-20]</td>
<td>-</td>
</tr>
<tr>
<td>Global rating of affective flattening [range]</td>
<td>1.34 (1.11) [0-4]</td>
<td>-</td>
</tr>
<tr>
<td>Global rating of alogia [range]</td>
<td>0.86 (1.31) [0-4]</td>
<td>-</td>
</tr>
<tr>
<td>Global rating of avolition – apathy [range]</td>
<td>2.34 (1.21) [0-5]</td>
<td>-</td>
</tr>
<tr>
<td>Global rating of anhedonia – asociality [range]</td>
<td>1.97 (1.48) [0-5]</td>
<td>-</td>
</tr>
<tr>
<td>Global rating of attention [range]</td>
<td>1.14 (1.40) [0-4]</td>
<td>-</td>
</tr>
<tr>
<td>Chlorpromazine equivalent dose</td>
<td>703 (577)</td>
<td>-</td>
</tr>
</tbody>
</table>

\(^a\) Commenced educational level divided into 4 levels: 1: primary school (up to 10 years of education), 2: secondary school/professional training, 3: bachelor program or shorter further education, 4: master program.  
\(^b\) Parental socioeconomic status (SES) was based on the parent with the highest education and an estimated salary according to their employment. It was divided into 3 levels: low, middle, high. None of the parents had a low SES.  
\(^c\) e.g. cash benefits, sickness benefits.  
\(^d\) Scale for the assessment of positive symptoms.  
\(^f\) Scale for the assessment of negative symptoms.
Figure 1. The Urn Task. Modified from Campbell-Meiklejohn et al. (2017). At the beginning of each trial the words "next jar" were displayed for 1000ms. This served as a remainder to the participants that each jar was different. During 'pre-task', the jars were numbered, to make this explicit. When a new jar appeared, contents were hidden. A display of five hands reaching for five different samples from the jar was then animated. Next, the decisions of the four agents were shown with their confidence in those decisions. Agent faces were represented with neutral expression. To avoid association between answers and specific agents, agents were randomly drawn from a set of 30 faces on each trial. Agent answers were expressed by the colour of the circle next to their faces. Confidence was indicated as the expression within the circle as well as the speed at which the answer was shown (rapid + smug = high confidence). Individual agent answers took between 300 and 2800ms to appear. The contents of the participant’s sample then moved up from the bottom (~500ms). All information was displayed for a further 500ms before the participant could make his/her choice (red or green). The chosen colour was highlighted for 1000ms, followed by the next trial.
Table 2. Model comparison

<table>
<thead>
<tr>
<th>Model</th>
<th>Δ ELPD</th>
<th>SE</th>
<th>weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple Bayes</td>
<td>-3581.4</td>
<td>125.9</td>
<td>0</td>
</tr>
<tr>
<td>Heuristic model</td>
<td>-2052.5</td>
<td>46.1</td>
<td>0</td>
</tr>
<tr>
<td>Weighted Bayes</td>
<td>-466.2</td>
<td>23.0</td>
<td>0</td>
</tr>
<tr>
<td>GLM</td>
<td>-56.0</td>
<td>18.6</td>
<td>.33</td>
</tr>
<tr>
<td>Circular Inference (no Interference)</td>
<td>-81.9</td>
<td>13.5</td>
<td>0</td>
</tr>
</tbody>
</table>

| Circular inference        | 0      | NA  | .67    |

ELPD indicates the expected log predictive density of the model, calculated using PSIS-LOO. In other words, it indicates the estimated out-of-sample error of the model: the relative likelihood of the model given the data, adjusting it for potential overfitting and influential data points. Δ ELPD thus indicates the difference in ELPD compared to the best model: the lower the score, the bigger the distance from the best model. SE indicates the standard error in the estimate of the difference. Weight indicates the stacking weights based on PSIS-LOO, that is, how strong the preference for a given model should be. 0 indicates a very unlikely model, 1 the most likely model having no likely competitors amongst the models analyzed, intermediate values indicate relative uncertainty as to which model is best (Yao et al., 2017).

Table 3. Parameter estimates for the circular inference model including group

<table>
<thead>
<tr>
<th>Model</th>
<th>Mean</th>
<th>2.5% CI</th>
<th>97.5% CI</th>
<th>Evidence ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bias for red (controls)</td>
<td>-0.07</td>
<td>-0.16</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Group-level diff in bias for red</td>
<td>0.01</td>
<td>-0.10</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td>Confidence (controls)</td>
<td>2.07</td>
<td>1.85</td>
<td>2.30</td>
<td></td>
</tr>
<tr>
<td>Group level diff in confidence</td>
<td>-0.18</td>
<td>-0.48</td>
<td>0.13</td>
<td>7.1, 88% credibility</td>
</tr>
<tr>
<td>Weight for self (controls)</td>
<td>1.25</td>
<td>1.06</td>
<td>1.44</td>
<td></td>
</tr>
<tr>
<td>Group level diff in weight for self</td>
<td>0.39</td>
<td>0.11</td>
<td>0.67</td>
<td>362.6, 100% credibility</td>
</tr>
<tr>
<td>Weight for others (controls)</td>
<td>-2.19</td>
<td>-2.41</td>
<td>-1.98</td>
<td></td>
</tr>
<tr>
<td>Group level diff in weight for others</td>
<td>-0.61</td>
<td>-0.91</td>
<td>-0.32</td>
<td>&gt;1000, 100% credibility</td>
</tr>
<tr>
<td>Loops for self (controls)</td>
<td>0.98</td>
<td>0.77</td>
<td>1.17</td>
<td></td>
</tr>
<tr>
<td>Group level diff in loops for self</td>
<td>0.88</td>
<td>0.61</td>
<td>1.17</td>
<td>&gt;1000, 100% credibility</td>
</tr>
<tr>
<td>Loops for others (controls)</td>
<td>0.72</td>
<td>0.21</td>
<td>1.16</td>
<td></td>
</tr>
<tr>
<td>Group level diff in loops for others</td>
<td>-0.02</td>
<td>-0.60</td>
<td>0.58</td>
<td>1.1, 53% credibility</td>
</tr>
</tbody>
</table>

Note that the parameters can be on transformed scales, e.g. weights are on a log odds scale, and loops on an exponential scale, see the Materials and methods section and the Supplementary Material for more details.
Figure 2. The upper panels represent the influence of the agents on controls (top left) and patients (top right). The x-axis indicates the amount of combined evidence for red provided by the other agents on a log-odds scale, the y-axis indicates the probability of choosing red. The color indicates the level of evidence for red in the sample. The average patient shows less influence from others (shallower slopes) and more influence from directly experienced information (more spread curves). Note that for simplicity of representation we have collapsed others’ confidence and choices, to construct a continuous one-dimensional scale of indirect evidence for red. The lower panels represent the influence of directly experienced information on controls (top left) and patients (top right). The x-axis indicates the amount of red marbles contained in one’s own sample, the y-axis indicates the probability of choosing red. The color indicates the level of evidence for red provided by the other agents. Note, how the colored lines are steeper and more collected in the average patient compared to the average control; this indicates a more decided role of directly experienced information (steeper slopes) and a lower influence of indirect information (as the lines are more similar to each other, no matter the level of indirect evidence). See Supplementary Figures S3, S4A and S4B for participant-level representations of the model.