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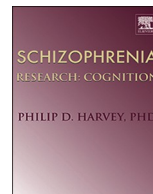
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Research Paper

Atypical meta-memory evaluation strategy in schizophrenia patients

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ABSTRACT

Background: Previous research has reported that patients with schizophrenia would regard false memories with higher confidence, and this meta-memory deficit was suggested as a neurocognitive marker of schizophrenia. However, how schizophrenia patients determine their memory decision confidence has received scant consideration. This study, therefore, aimed to characterize the extent to which meta-memory evaluation strategy differs between schizophrenia patients and healthy individuals, and how such difference contributes to the patients' meta-memory performance.

Methods: 27 schizophrenia patients and 28 matched healthy controls performed a temporal-order judgement (TOJ) task, in which they judged which movie frame occurred earlier in an encoded video, and then made retrospective confidence rating. Mixed effect regression models were performed to assess the between-group metacognitive evaluation strategy difference and its relationship to clinical symptoms.

Results: Compared to the control group, the patients' confidence ratings were correlated more with the recent confidence history and less with the TOJ-related evidence. The degree of dependence on recent history of confidence was negatively correlated with the severity of positive symptoms. Furthermore, by controlling for the first-order TOJ performance, we observed that the patients discriminated correct memory decisions from the incorrect ones as accurately as the controls.

Conclusion: The present investigation revealed that schizophrenia patients tend to use more heuristics in making meta-memory evaluations, and such atypical strategy is related to their clinical symptoms. This study provides new insights into how schizophrenia patients perform meta-memory processes. Future research could consider examining such metacognitive deficits in light of other cognitive domains in psychosis.

1. Introduction

Metacognition refers to the capacity to monitor one's own cognitive

processes, and it plays a crucial role in human adaptation to the environment (Yeung and Summerfield, 2012). However, in both clinical interviews and cognitive experiments, schizophrenia (Scz) patients are

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reported to having a limited metacognitive insight, particularly on the memory domain (Balzan, 2016; Berna et al., 2019; Lysaker et al., 2014; Mayer and Park, 2012; Moritz et al., 2006; Stephan et al., 2009). Recent theories suggest that the psychotic symptoms (i.e. hallucinations and delusions) of Scz result from abnormal Bayesian belief updating, in essence inappropriately evaluating and integrating prior beliefs and incoming sensory evidence (Corlett et al., 2019; Fletcher and Frith, 2009; Sterzer et al., 2018). In this sense, it could be further hypothesized that it is the inaccurate mnemonic metacognition or meta-memory evaluation on previous experiences (e.g., tagging false memories as trustworthy) that leads to the abnormal reliance of sensory inputs in Scz (Eisenacher and Zink, 2017; Moritz and Woodward, 2006).

Notably, one's metacognitive performance is dependent on the primary or first-order cognitive performance (Maniscalco and Lau, 2012; Pouget et al., 2016). If an individual accumulates sufficient amount of evidence for the first-order decision-making, they will also have more knowledge to evaluate whether the decision is correct. Recent investigations found that Scz patients did not exhibit impaired perceptual metacognition after controlling for the first-order decision accuracy (Favre et al., 2021; Koizumi et al., 2020; Powers et al., 2017; Rouy et al., 2021). Given the well-reported Scz-associated primary memory deficit (Brébion et al., 2012; Danion et al., 1999; Kwok et al., 2020) and the functional correlation between perceptual and mnemonic metacognition (McCurdy et al., 2013; Morales et al., 2018; Zheng et al., 2021), it is likely that Scz patients' meta-memory deficit in fact results from their primary memory deficit.

Even though the meta-memory ability is preserved in the Scz patients, it would be possible that the underlying evaluation strategy differs in the Scz and healthy populations. Existing literature has indicated that metacognitive evaluation is informed by multiple cues in addition to the first-order decision evidence (Shekhar and Rahnev, 2021). For instance, the response time (RT) for the first-order decision could influence metacognitive judgements independent of the first-order decision accuracy (Kiani et al., 2014; Palser et al., 2018). In addition, trial-by-trial metacognitive judgements can be influenced by preceding metacognitive judgements (Rahnev et al., 2015), presumably through forming a confidence prediction or a global self-belief (Boldt et al., 2019; Seow et al., 2021). As Scz patients tend to be less willing to exert cognitive effort than healthy counterparts (Gershman and Lai, 2021; Gold et al., 2015), it is likely that they would rely more on the heuristics than the first-order decision related information when making metacognitive evaluations compared to the healthy counterparts.

The current study therefore aimed to address the following issues: i) compared to the healthy individuals, whether Scz patients' meta-memory evaluation strategy would be different; ii) whether Scz patients' meta-memory ability would be impaired.

2. Methods

2.1. Participants

Data from 27 schizophrenia patients and 28 matched healthy controls were analyzed. Scz patients were inpatients at Shanghai Mental Health Center (SMHC) and met ICD-10 diagnostic criteria for schizophrenia. They all had received antipsychotic medications. Controls were recruited by public advertisements. All Scz patients and controls were interviewed by a research psychiatrist to ensure they met the criteria of no history of neurological illness, no severe physical disease, and no substance/alcohol use disorder. The patients were further assessed with the positive and negative syndrome scale (PANSS) for their severity of clinical symptoms (positive: including hallucinations and delusions; negative: including flattening of affect, loss of pleasure and social withdrawal; general: including impairments in attention, impulse control and motor function; Kay et al., 1987).

All participants had normal or corrected-to-normal vision. The study was approved by the Ethics Committee at SMHC. All participants gave

their written informed consent for their participation. Participants' sociodemographic and clinical data were summarized in Table 1. Five additional Scz patients were tested but were not included in the analysis because they selected only one memory task response and/or confidence rating throughout the experiment, rendering their data unusable for analysis. Trials with response times below 100 ms or above three standard deviations from per-subject means were discarded (2.5% of all trials discarded).

2.2. Task procedure

Participants were required to perform the temporal-order judgement (TOJ) task in three sessions on a 14-inch computer monitor with 1920 * 1080 resolution. Session 1 served the purpose of both encoding and testing (see Fig. 1). In this session, participants watched 12 distinct 20-s video clips [six clips were played in forward order (FW), six in reversed order (RV), counterbalanced between participants].

Two seconds after viewing each clip, participants completed three consecutive two-alternative forced choice (2-AFC) TOJ trials, where they judged which one of the two images extracted from the video occurred earlier in the video. Participants then indicated their TOJ decision confidence with a four-point Likert-type scale (1 = very uncertain, 4 = very certain). In each TOJ trial, the two images were centred on the left and right half of the display. The location of the correct response was randomized at the trial level but counterbalanced for each session.

Sessions 2 and 3 were conducted 2-h and 24-h after the first session, respectively. Participants were only required to perform the TOJ trials followed by confidence ratings without video viewing in sessions 2 and 3. In each of these two testing sessions, three new pairs of images extracted from each of the twelve encoded videos were presented as TOJ probes. Probes pretraining to the same video clip were presented sequentially. Thus, there were 36 (3 * 12) TOJ trials in each session, and 108 trials in total for each participant. Video presentation order in session 1, as well as the presentation order of TOJ probe sets in session 2 and 3, was randomized.

Table 1
Sociodemographic data and clinical profile.

	Scz (N = 27)	Control (N = 28)	Group comparison (between-subjects two-sided <i>t</i> -test)
Age (mean ± SD)	37.41 ± 12.10	37.79 ± 15.06	<i>t</i> (51.88) = 0.103, <i>p</i> = .918
Gender			<i>t</i> (52.94) = -0.125, <i>p</i> = .901
Male	48.1%	46.4%	
Female	51.9%	53.6%	
Education level (1-4)			<i>t</i> (49.97) = 2.311, <i>p</i> = .025
1-Primary school	3.7%	–	
2-Junior middle school	14.8%	7.1%	
3-Senior middle school	51.9%	35.7%	
4-University	29.6%	57.2%	
Illness duration (in year; mean ± SD)	13.52 ± 9.72	–	–
Medication (in chlorpromazine equivalents mg/day; mean ± SD)	570.95 ± 784.43	–	–
PANSS scores (mean ± SD)			
Positive symptoms	15.52 ± 4.26	–	–
Negative symptoms	20.63 ± 4.46	–	–
General symptoms	34.41 ± 4.08	–	–
Total	70.56 ± 8.80	–	–

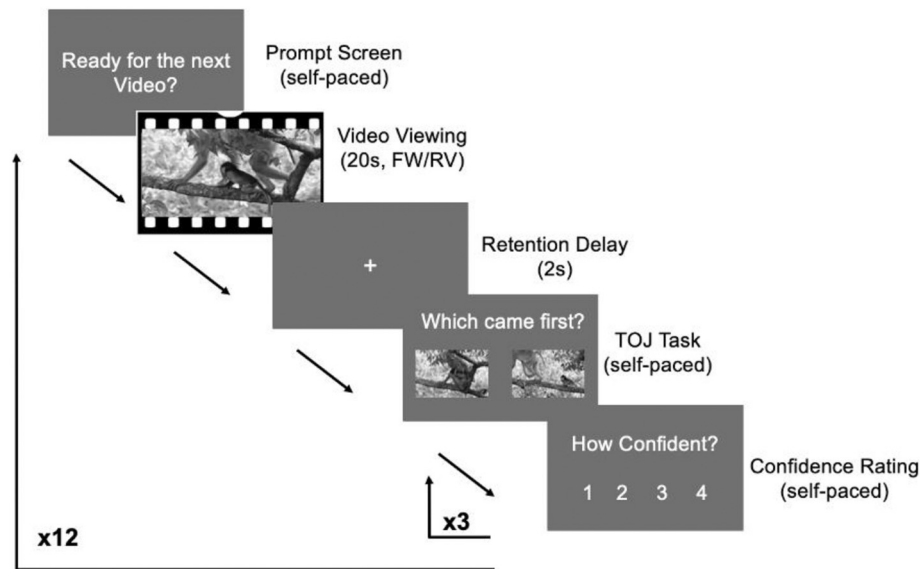


Fig. 1. Procedure of Session 1. The procedure of Session 2 and 3 were identical with Session 1 except that there were no video viewing and retention delay periods.

2.3. Stimuli

2.3.1. Video clips

Video clips were compiled from Youtube. All video content was footage of non-human animals in their natural environment, and pre-screened to be of similar, moderate emotional valence. A pool of 12 video clips was reproduced, each one having a FW and RV version, for a total of 24 videos. For each participant, 6 of 12 original video clips were randomly selected for the FW condition, and the remaining 6 video clips were reserved for the RV condition.

Video content was edited with Corel VideoStudio. All clips were exactly 20-s in length and depicted only one scene. Within each video clip, the footage contained no more than 4 camera cuts (“cuts” are defined as a change in camera perspective) per 10 s of footage. Back-and-forth movement of the camera or subjects, stagnant footage of subjects, tracking shots, or shot-reverse-shots were only tolerated if this shot lasted for less than 2 s. All selected video content was High Definition (HD) quality (720 ppi or higher), had a frame rate of 30 frames per second (fps), and played out in real-time (i.e., not slow-motion or time-lapsed). All clips contained no audio content.

2.3.2. Probe image extraction

Each TOJ probe consisted of a pair of images extracted from a video clip with a temporal distance (TD) of either 2 s, 5 s, or 10 s. Nine TOJ probes that were evenly divided for each TD were generated from each of the 12 original (i.e., FW) videos; the same was done for the RV videos. Image pairs were carefully selected so that no image pairs contained the exact same narrative content as another pair. This minimized the extent to which memory of one's answer on a previous probe can be used to answer a subsequent probe, both within a given session and across sessions.

2.4. Statistical analysis

The pre-processing of behavioral data was implemented in Python 3.7.6. Metacognition modelling and regression model analyses were performed with R 4.0. *t*-Tests and analysis of variance (ANOVAs) were carried out with IBM SPSS 22. Although the interval between memory encoding and retrieval was 2 s in Session 1, given the length of video presentation (20s), we considered it as a long-term memory task. Thus, we combined data from all the three sessions together to examine the difference between controls' and Scz patients' meta-memory

performance. Moreover, we should note that the rationale of introducing RV videos here was merely to induce some systematic memory retrieval errors (Wang et al., 2020) so that we could examine the relationship between confidence and performance in the Scz patients.

2.4.1. Meta-memory evaluation strategy

According to Shekhar and Rahnev (2021), we fit the following linear mixed-effect model (Model 1) with the data to investigate the meta-memory evaluation strategy difference between Scz patients and healthy controls. Here, trial-by-trial confidence rating was the dependent variable, confidence rating cues (i.e., TOJ Correctness and RT, Confidence History) and their interaction with group and video conditions were independent variables, and participant ID was a random effect. Recent confidence history was measured by the average of the five prior confidence ratings. For the comparability of regression coefficients, we computed the z-scores for all the regressors (except for “Video Type”, “Correctness” and “Group” as they were binary).

Model 1. TOJ Confidence \sim Group * Video Type * (TOJ Correctness + TOJ RT + Confidence History) + Age + Gender + Education + (1|Participant).

2.4.2. Meta-memory ability quantification

Participants' meta-memory bias was measured by the average value of their confidence ratings, while meta-memory sensitivity was quantified in a non-hierarchical Bayesian meta- d' model using R packages (<https://github.com/metacoglab/HMeta-d>; Fleming, 2017). We computed an Mdiff score ($meta-d' - d'$) to represent participants' meta-cognitive ability to discriminate correct TOJ from incorrect ones after controlling for first-order TOJ performance influence.

2.4.3. Relationship with clinical symptoms

To examine the relationship between Scz patients' clinical symptom severity (particularly the positive and negative symptoms; McLeod et al., 2014) and meta-memory performance, we fit the data with Models 2-4 respectively. In line with Rouault et al. (2018), we log-transformed each clinical score first before computing its z-score.

Model 2. Meta-memory Bias \sim Positive Symptoms + Negative Symptoms + General Symptoms + Video Type + Age + Gender + Education + Illness duration + Medication.

Model 3. Meta-memory Efficiency \sim Positive Symptoms + Negative Symptoms + General Symptoms + Video Type + Age + Gender +

Education + Illness duration + Medication.

Model 4. TOJ Confidence ~ (TOJ Correctness + TOJ RT + Confidence History) * (Positive Symptoms + Negative Symptoms + General Symptom) + Video Type + Age + Gender + Education + Illness Duration + Medication + (1|Participant).

3. Results

3.1. Memory performance

TOJ accuracy was analyzed as a function of the within-subjects factor video type (FW vs RV) and between-subjects factor group (Scz vs healthy controls) using a one-way, repeated-measures ANOVA. A significant main effect of group ($F(1,53) = 13.132, p = .001, \text{partial } \eta^2 = .199$) and video type ($F(1,53) = 4.771, p = .033, \text{partial } \eta^2 = 0.083$) was returned, with no interaction effect between factors ($F(1,53) = 1.629, p = .207$). Scz patients' performance was worse than the controls in both FW and RV conditions (Fig. 2A).

3.2. Meta-memory bias by condition

A repeated-measures ANOVA was used to assess changes in confidence as a function of video type (FW vs RV), decision correctness (correct vs incorrect), and group (Scz vs controls; between-subjects factor). Across groups, confidence ratings were higher when preceded by a correct decision (Correctness, $F(1,53) = 39.507, p < .001, \text{partial } \eta^2 = 0.427$), although Scz patients reported lower overall confidence than the controls (Group, $F(1,53) = 11.108, p = .002, \text{partial } \eta^2 = 0.173$). The difference in confidence between correct and incorrect responses were larger in the healthy controls than in the Scz patients (Group: Correctness, $F(1,53) = 4.493, p = .039, \text{partial } \eta^2 = 0.078, \text{Fig. 2B}$). Moreover, confidence differences between correct and incorrect trials varied as a function of video type (Video: Correctness, $F(1,53) = 6.339, p = .015, \text{partial } \eta^2 = 0.107$), irrespective of group (Video: Correctness: Group, $F(1,53) = 0.285, p = .596$), indicating participants in both groups

reported higher confidence in correct TOJ response in the FW condition.

3.3. Meta-memory evaluation strategy

Using the mixed-effect linear regression outlined in Section 2.4.1, we found that, across groups, trial-by-trial confidence ratings were positively correlated with the correctness of TOJ response (estimate = 0.078, $p < .001$) and the recent history of confidence ratings (estimate = 0.447, $p < .001$), and negatively correlated with TOJ RT (estimate = -0.175, $p < .001$). Compared to the controls, Scz patients' trial-by-trial confidence was more strongly correlated with the recent history of confidence ratings (Group: Confidence History, estimate = -0.146, $p < .001, \text{Fig. 3C}$), and less strongly correlated with TOJ correctness and RT (Group: Correctness, estimate = -0.040, $p < .001, \text{Fig. 3A}$; Group: RT, estimate = -0.093, $p < .001, \text{Fig. 3B}$). Video types did not influence the interaction effect between group and metacognitive resources (i.e., correctness, RT, confidence history) or confidence ratings (Video: Group: Correctness, estimate = 0.015, $p = .270$; Video: Group: RT, estimate = -0.004, $p = .750$; Video: Group: Confidence History, estimate = 0.017, $p = .157$).

3.4. Relationship between TOJ confidence and clinical factors

We observed that the overall TOJ decision confidence was negatively correlated with the severity of general symptoms (estimate = -0.629, $p < .001$), but not with positive (estimate = -0.092, $p = .489$) nor negative symptoms (estimate = 0.028, $p = .840$).

Regarding confidence rating strategy, a mixed-effect linear regression analysis (Model 4) revealed that the clinical symptoms only modulated the relationship between trial-by-trial confidence ratings and recent history of decision confidence (Confidence History: P scores, estimate = -0.073, $p = .007$; Confidence History: N scores, estimate = -0.120, $p < .001$; Confidence History: G scores, estimate = 0.203, $p < .001$), but not the relationship between confidence and decision correctness (Correctness: P scores, estimate = 0.039, $p = .236$; Correctness: N scores, estimate = -0.019, $p = .486$; Correctness: G scores, estimate =

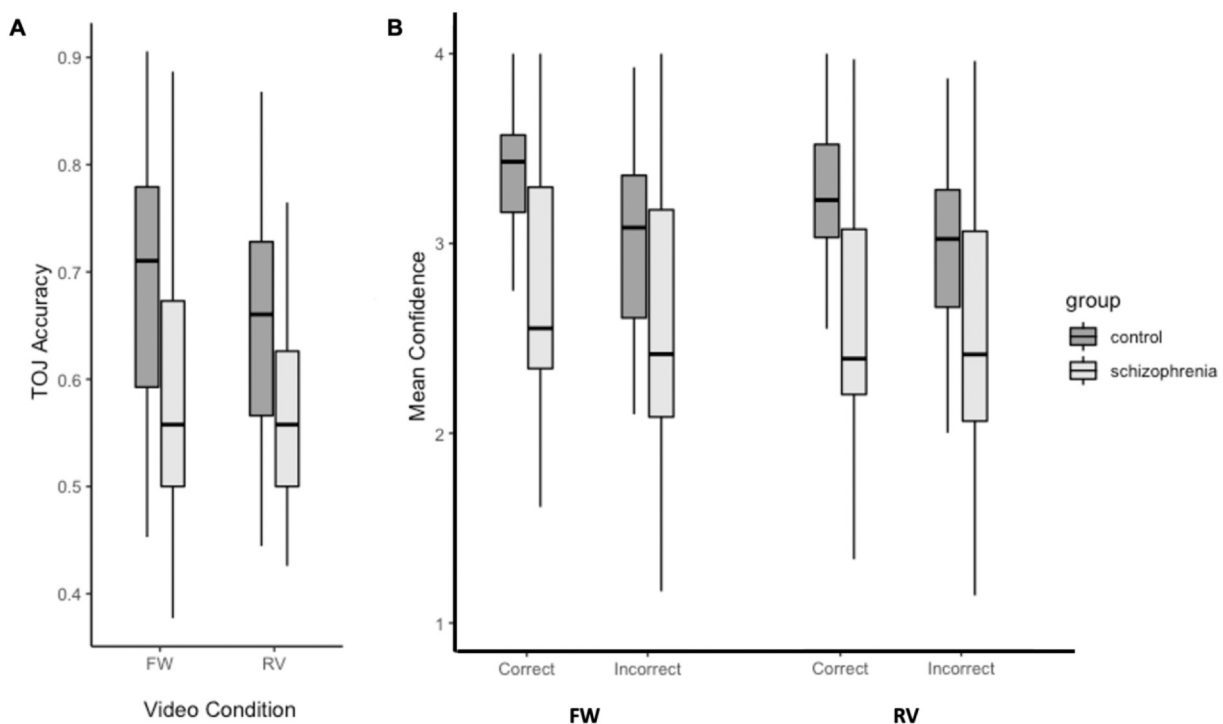


Fig. 2. Scz patients and healthy controls' TOJ accuracy (A); and mean confidence in correct and incorrect TOJ response (B) in both forward-displayed (FW) and reversed-displayed (RV) conditions.

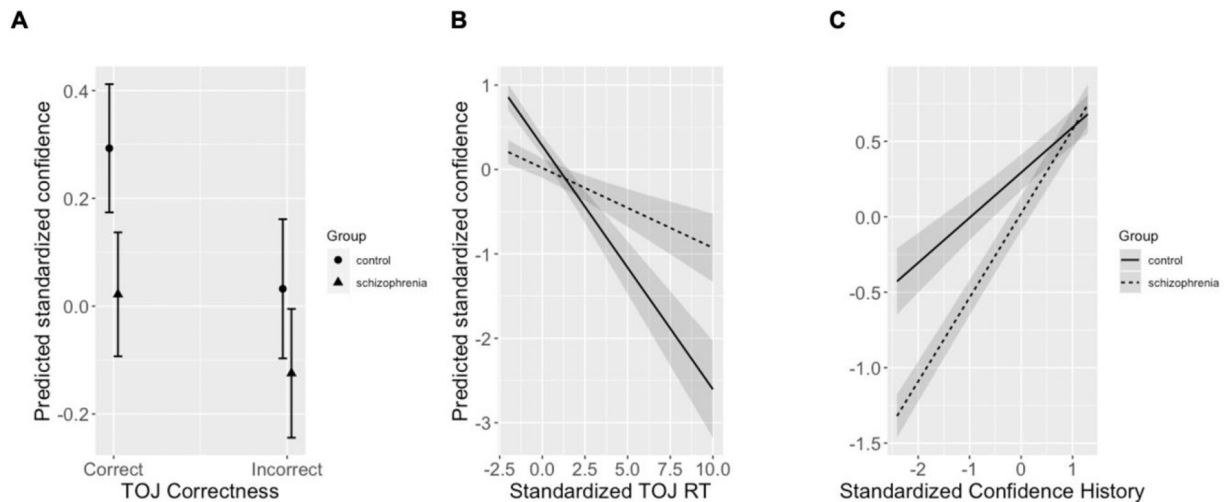


Fig. 3. Regression model predicting TOJ performance confidence within a given trial as a function of decision correctness (A), reaction time (B), and recent history of confidence (i.e., the average of 5-trial-back ratings; C) for both schizophrenia and healthy control groups. Error bars in A, and the light grey areas in B–C, represent the 95% confidence interval of the estimation. The values of all non-binary variables were standardized using z-scores.

0.010, $p = .769$) nor RT (RT: P scores, estimate = -0.025 , $p = .223$; RT: N scores, estimate = 0.030 , $p = .007$; RT: G scores, estimate = 0.017 , $p = .366$). The more severe patients' positive and negative symptoms were, the weaker their dependence on prior confidence (Fig. 4A–B); while the pattern was opposite for general symptoms (Fig. 4C).

3.5. Meta-memory efficiency

To meet the assumption of meta- d' quantification (see Section 2.4.1), we excluded 11 Scz patients and 3 healthy whose TOJ performance was below the chance level (i.e., 50%, Scott et al., 2014) before examining the between-group meta-memory efficiency differences. Patients and controls were demographically matched in this analysis (p -values for between-group differences in age, gender and education level were all larger than 0.23).

Results from a one-way, repeated-measures ANOVA indicated no group differences in meta-memory efficiency in either video conditions (Video, $F(1,38) = 0.313$, $p = .578$; Group, $F(1,38) = 2.947$, $p = .090$; Video: Group, $F(1,39) = 0.403$, $p = .528$). In addition, through a multiple

regression analysis (Model 3), we found that Scz patients' meta-memory efficiency did not correlate with positive, negative, or general symptoms (P scores, estimate = 0.144 , $p = .742$; N scores, estimate = 0.484 , $p = .306$; G scores, estimate = -0.941 , $p = .168$).

Notably, within this subset of participants, we replicated the above-mentioned group differences in the confidence rating strategy (Group: Correctness, estimate = 0.083 , $p = .246$; Group: RT, estimate = -0.205 , $p < .001$; Group: Confidence History, estimate = -0.151 , $p < .001$).

4. Discussion

Memories are closely linked to conscious perceptions and beliefs (LeDoux and Lau, 2020). Previous studies have reported that patients with Scz tend to report false memories with stronger conviction (e.g., Berna et al., 2019), and this memory monitoring (i.e., meta-memory) deficit is speculated as the root of positive symptoms in Scz (Moritz and Woodward, 2006). By using a temporal-order memory task with naturalistic material, here, we replicated that Scz patients had smaller differences in confidence between correct and incorrect memory

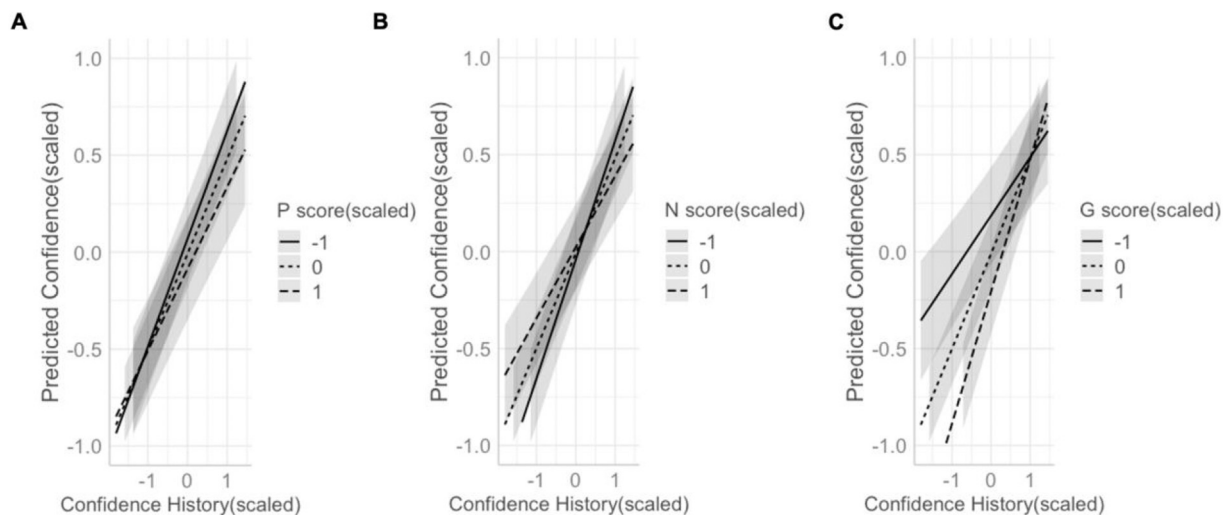


Fig. 4. Modulation effects of positive (P; A), negative (N; B), and general (G; C) symptoms on the relationship between trial-by-trial confidence and recent history of confidence. Values of all the non-binary variables, including the total score of each symptom type measured from the PANSS scale, were standardized by z-scores. Regarding the P/N/G scores, “0” is the mean score, while “1” and “-1” refer to scores that are 1 standard deviation above and below the mean, respectively. The light grey areas represent the 95% confidence interval of the estimation.

decisions. A linear mixed-effect model further revealed that the Scz patients relied less on first-order memory decision information (i.e., TOJ correctness and RT in this case) and more on recent confidence history when selecting trial-by-trial confidence.

As severer negative symptoms were correlated with weaker serial dependence of confidence, it is not likely that Scz patients simply rely on previous confidence ratings due to cognitive effort avoidance. A more plausible explanation might be drawn from the abnormal belief updating perspective. Scz patients are reported to have a stronger reliance on the prior beliefs (Powers et al., 2017; Schmack et al., 2013; Teufel et al., 2015). Through recent confidence ratings, participants might form a prediction or a prior belief in the likelihood of making a correct response in the upcoming task (e.g., Seow et al., 2021). Therefore, it is likely that stronger serial dependence of confidence could reflect Scz patients' atypical use of the prior beliefs. Moreover, previous research has shown the degree of prior belief reliance is negatively correlated with delusion proneness in higher-level cognitive decisions (Stuke et al., 2019). Here we observed that the severity of positive symptoms negatively modulated serial dependence in metamemory judgements.

Recent research has also demonstrated that prior self-belief or confidence prediction was able to modulate upcoming first-order decision processes: a high confidence prediction might lead to not only a high retrospective decision confidence but also a correct first-order decision (Boldt et al., 2019; Rouault et al., 2019). In this study, we found that Scz patients can monitor their memory retrieval as accurately as the healthy participants after having controlled for the first-order performance influence. Therefore, it is likely that a Scz patient's retrospective confidence could track the memory decision accuracy because of the stronger reliance on the confidence prediction. By measuring confidence predictions, future research could test whether this variable would modulate the liberal acceptance of false memories and the overconfidence in memory errors (Hoven et al., 2019), since Scz-associated overconfidence in semantic knowledge errors was moderated by patients' subjective self-competence (Moritz et al., 2015). Future research could also consider measuring confidence predictions, to further examine how Scz patients compute trial-by-trial confidence and whether the patients use an atypical strategy to achieve control-equivalent meta-memory performance.

The patients in this study suffered from chronic Scz and were inpatients receiving medication on a daily basis. A few studies suggested that Scz patients with first-episode psychosis (FEP) and high-risk healthy subjects, who had lower medication treatments, exhibit different perceptual metacognitive performance compared to the chronic patients and healthy controls (Bliksted et al., 2017; Davies et al., 2018). It is important to know whether the observed behavioral pattern would be generalized to other cognitive domains such as perception, psychosocial functions, and semantic knowledge (Hoven et al., 2019). Additionally, in contrast to explicit mnemonic metacognition tested here, it might be possible that the Scz patients suffer from abnormal metacognition at an implicit level, for example, in terms of reality monitoring, giving rise to first-order false memories (Lau, 2019), and thereby giving us a worthwhile hypothesis for future research.

CRediT authorship contribution statement

L.W., D.J.G., J.W., Y.T., and S.C.K. designed the study and wrote the protocol; D.J.G., W.D. and X.W. collected experiment data; Y.Z. conducted data analysis and wrote the first draft of manuscript with the help from J.Y., C.Y., M.A., F.B., Y.T., and S.C.K.; all authors contributed to and approved the final manuscript.

Declaration of competing interest

The authors declare no conflict of interests.

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