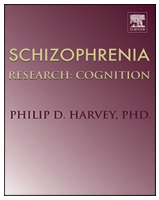
Schizophrenia Research: Cognition 36 (2024) 100306

Contents lists available at ScienceDirect

Schizophrenia Research: Cognition

journal homepage: www.elsevier.com/locate/scog



# Modulation of hemispheric asymmetry in executive control of attention in schizophrenia with atypical antipsychotic treatment: Potential benefits of olanzapine

Yong Zhao [a], Yifan Li [b], Jing Du [c], Chuanlong Fang [a], Wansheng Li [a], Mengyu Lv [h], Yue Wu [c], Kai Wang [b,d,e,f,g], Tingting Wu [h,*], Yanghua Tian [b,c,e,f,**], Juanjuan Zhang [b,e,f,***]

[a] The Sixth People's Hospital of Anqing, Anqing 246000, Anhui, China
[b] Department of Neurology, the First Affiliated Hospital of Anhui Medical University, Hefei 230000, Anhui, China
[c] Department of Neurology, the Second Affiliated Hospital of Anhui Medical University, Hefei 230000, Anhui, China
[d] Institute of Artificial Intelligence, Hefei Comprehensive National Science Center, Hefei 230000, Anhui, China
[e] Anhui Province Key Laboratory of Cognition and Neuropsychiatric Disorders, Hefei 230000, Anhui, China
[f] Collaborative Innovation Center of Neuropsychiatric Disorders and Mental Health, Hefei 230000, Anhui, China
[g] The School of Mental Health and Psychological Sciences, Anhui Medical University, Hefei 230000, Anhui, China
[h] Beijing Key Lab of Learning and Cognition, School of Psychology, Capital Normal University, Beijing 100048, Beijing, China

ARTICLE INFO

*Keywords:*
Attention
Conflict control
Hemispheric asymmetry
Olanzapine
Schizophrenia

ABSTRACT

Deficits in executive control of attention have been reported in schizophrenia patients, but can be ameliorated by treatment of atypical antipsychotics along with the symptoms. However, it remains unclear whether this effect is related to a modulation of hemispheric asymmetry in executive control by the medicine. In this behavioral study, we employed a lateralized version of the attention network test to examine the hemispheric asymmetry of executive control in schizophrenia patients before and after olanzapine treatment, compared to matched healthy controls. Executive control was measured as a conflict effect, indexed as the response time (RT) difference between incongruent versus congruent flanker conditions, and was compared between stimuli presented in the left and the right visual field (i.e., processed by right versus left hemisphere of the brain). Results showed that pre-treatment schizophrenia patients revealed a right hemisphere superiority in conflict effect (i.e., a smaller effect in the right hemisphere than in the left hemisphere), driven by the incongruent condition. Olanzapine treatment reduced this right hemisphere superiority by improving the efficiency of the left hemisphere in the incongruent condition. These results suggested that olanzapine treatment may improve the efficiency of executive control in the left hemisphere in schizophrenia patients.

## 1. Introduction

Schizophrenia is a mental disorder with a lifetime prevalence of about 1 % and is associated with a significant healthcare burden (McCutcheon et al., 2020). It is characterized by symptoms such as hallucinations, delusion, disorganized thinking and speech (McCutcheon et al., 2020). In addition to these symptoms, cognitive deficits are a main category of symptoms in schizophrenia and have a negative impact on the patients' social and occupational abilities (McCutcheon et al., 2020). Among the cognitive deficits, deficits in attention are particularly prominent which plays an important role in supporting other cognitive functions (Spagna et al., 2018a), and have been widely reported in patients with schizophrenia (Backes et al., 2011; Caprile et al., 2015; Carter et al., 1997; Henik and Salo, 2004; Hoonakker et al., 2017; Opgen-Rhein et al., 2008; Orellana et al., 2012; Spagna et al., 2015a; Spagna et al., 2015b; Wang et al., 2005; Westerhausen et al., 2011). Attention can be conceptualized as the three functional networks organized in a hierarchical architectural, with the alerting network (producing and maintaining a state of readiness) and the orienting network (selecting the most relevant information from various inputs) at lower

* Corresponding author.
** Correspondence to: Y. Tian, Department of Neurology, The First Affiliated Hospital of Anhui Medical University, Hefei 230000, Anhui, China.
*** Correspondence to: J. Zhang, Department of Neurology, The First Affiliated Hospital of Anhui Medical University, Hefei 230000, Anhui, China.
*E-mail addresses:* 7003@cnu.edu.cn (T. Wu), ayfytyh@126.com (Y. Tian), zhangjuanjuan0207@126.com (J. Zhang).

https://doi.org/10.1016/j.scog.2024.100306
Received 11 January 2024; Received in revised form 28 February 2024; Accepted 28 February 2024

levels for information selection, and executive control network at a higher level for further reducing uncertainty of information (detecting and resolving conflicting among competing mental processes), which are supported by distinct but interactive brain substrates (Fan et al., 2005; Fan et al., 2002; Fan, 2014; Spagna et al., 2015b; Xuan et al., 2016). Patients with schizophrenia exhibit a particular deficit in the higher-level executive control function (Opgen-Rhein et al., 2008; Orellana et al., 2012; Spagna et al., 2015a; Spagna et al., 2018a; Wang et al., 2005). However, the underlying brain alternations that driver such deficit remains unclear.

The disrupted hemispheric asymmetry observed in schizophrenia patients may contribute to their deficits in executive control of attention. Attention mechanisms typically exhibit hemispheric dominance, with the attention function dominated by the right hemisphere (RH) that is primarily responsible for the processing of information compared to the left hemisphere (LH) (Heilman and Abell, 1980; Mesulam, 1999). This asymmetry in the orienting network attention has been well-documented in neuropsychological studies, where RH lesions often lead to hemisphere neglect (Chambers et al., 2004; Danckert and Ferber, 2006; Nobre et al., 1997). Our recent studies in healthy adults have demonstrated a RH superiority in the executive control network (Spagna et al., 2018b), and this effect has found to be diminished in unilateral stroke patients (Russell-Giller et al., 2021). Compared to health individuals, schizophrenia patients have been observed to reveal disrupted altered hemispheric asymmetry of the brain (see reviews: Ribolsi et al., 2014; Xie et al., 2018), as evidenced by greater complex and cortical folding in the RH, reduced leftward cerebral dominance for language, lower degree of right-sided laterality for the right frontoparietal network, and intricate alternation in asymmetry of functional connectivity (Ke et al., 2010; Leroux et al., 2015; Ribolsi et al., 2014; Rotarska-Jagiela et al., 2010). Despite these observed alterations, the specific role of hemispheric asymmetry changes in executive control deficits in schizophrenia remains largely unexplored.

To gain deeper insights into attention deficits and hemispheric asymmetry in schizophrenia, a promising avenue is through pharmacotherapeutic investigations. Antipsychotic treatments that alleviate clinical symptoms of schizophrenia have been linked to improvements in attention deficits. For instance, our previous study demonstrated enhanced functioning in the orienting network following clozapine treatment (Spagna et al., 2015a). Moreover, a neuroimaging study found diminished impairments in dorsal cortical attention networks in untreated first-episode schizophrenia patients after receiving antipsychotic treatment with risperidone or aripiprazole (Keedy et al., 2015). Olanzapine, an atypical antipsychotic widely used in the treatment of schizophrenia and other psychotic disorders (Bever and Perry, 1998), is recommended as the first-line treatment due to efficacy in managing positive/negative symptoms and its comparatively lower incidence of side effects compared to clozapine. Beyond addressing clinical symptoms, olanzapine has demonstrated efficacy in ameliorating cognitive deficits in schizophrenia patients (Kumar and Chaudhury, 2014; McGurk et al., 2004; Meltzer and McGurk, 1999; Wang et al., 2013), including improvements in the attention domain (Bilder et al., 2002). Exploring the hemispheric asymmetry of executive control before and after an antipsychotic treatment holds promise for shedding light on the role of hemispheric asymmetry in the schizophrenia-related attention deficits.

This study focuses on investigating the impact of olanzapine treatment on deficit of executive control of attention in schizophrenia, with a particular emphasis on alterations in hemispheric asymmetry. Specifically, we employed a lateralized version of the attention network test-revised (LANT-R) to assess the executive control network in each hemisphere by presenting stimuli in the contralateral visual field (Asanowicz et al., 2012; Spagna et al., 2016). This test was administered to a group of schizophrenia patients (SZ group) before and after olanzapine treatment, as well as to matched healthy controls (HC group) before and after a comparable interval. Our hypothesis posited that schizophrenia patients would exhibit a disrupted hemispheric asymmetry in executive control of attention compared to the controls and that this change might be modulated by olanzapine treatment.

## 2. Methods

### 2.1. Participants

A total of 44 participants meeting ICH-10 criteria for schizophrenia were recruited as the SZ group from the in-patient department of No.6 Anqing People's Hospital, an affiliated hospital of Anhui Medical University. Inclusion criteria stipulated the absence of neurological disorder (such as epilepsy, encephalitis, Parkinson's disease, cerebral vascular disease, or traumatic brain injury), no history of mental retardation, and no current substance/alcohol abuse. Seven SZ patients were excluded from the analysis due to high overall error rate (>25 %) and excessively prolonged overall response time (RT, >1200 ms), as outlined in our prior study (Spagna et al., 2014). The final SZ group comprised 37 patients (34 males and 3 females), with 13 diagnosed with paranoia, 2 with disorganized schizophrenia, and 22 undifferentiated schizophrenia. Fourteen of them were the first-time hospitalizations and antipsychotic naive prior to the study. The remaining 23 SZ patients had been hospitalized between 2 and 13 times, averaging 3.6 times ±3.8 times, and drug discontinuance no less than three months. Their average onset age was 23.2 years-old ±6.2 years-old, and the mean course was 6.5 years ±6.3 years. Cognitive ability before treatment was evaluated using the Mini-Mental State Examination (MMSE), and all SZ patients scored >28 (ranging from 28 to 30), indicating a normal cognitive ability. Throughout treatment, the dosage of olanzapine was 13.8 mg/day ±4.6 mg/day. Positive, negative, and general symptoms were assessed using the Chinese version of the Positive and Negative Syndrome Scale for Schizophrenia (PANSS), administered by staff psychiatrists before and after treatment. The interval between the two test sessions were 29.3 days ±17.8 days, ranging from of 7 to 106 days.

The matched HC group comprised thirty-eight healthy individuals (29 males and 9 females) meeting the same inclusion criteria. Demographic information, including gender, age, education, interval of tests, is summarized in Table 1, with no significant between-group differences in gender ratio ($p = .07$), age ($p = .37$), education ($p = .14$), or interval of tests ($p = .88$). All SZ patients and HCs reported right-handedness and had normal or corrected-to-normal vision and hearing. The Clinical Research Ethics Committee of Anhui Medical University approved this study protocol (2019H008), which adhered to the Declaration of Helsinki. Written informed consent was obtained from all participants before participation.

### 2.2. The lateralized attention network test-revised (LANT-R)

The LANT-R is a modified version of the ANT-R introduced by Fan et al. (2009), incorporating a lateralized presentation of stimili achieved by 90° clockwise rotating each stimulus display in the original ANT-R (Russell-Giller et al., 2021; Spagna et al., 2018a, 2018b) (Fig. 1). In essence, participants engaged in a classical Eriksen Flanker task (Eriksen and Eriksen, 1974), where a set of stimuli set—a column of five black arrows pointing either upward or downward—appeared within a box

**Table 1**
Demographic information of participants in schizophrenia and healthy control groups, presented as mean ± standard deviation.

| | Schizophrenia | Healthy control |
|---|---|---|
| N | 37 | 38 |
| Gender (female: male) | 3: 34 | 9: 29 |
| Age (years) | 30.1 ± 8.7 | 32.4 ± 13.6 |
| Education (years) | 11.4 ± 3.1 | 12.6 ± 3.8 |
| Interval of tests (days) | 29.3 ± 17.8 | 29.8 ± 11.7 |

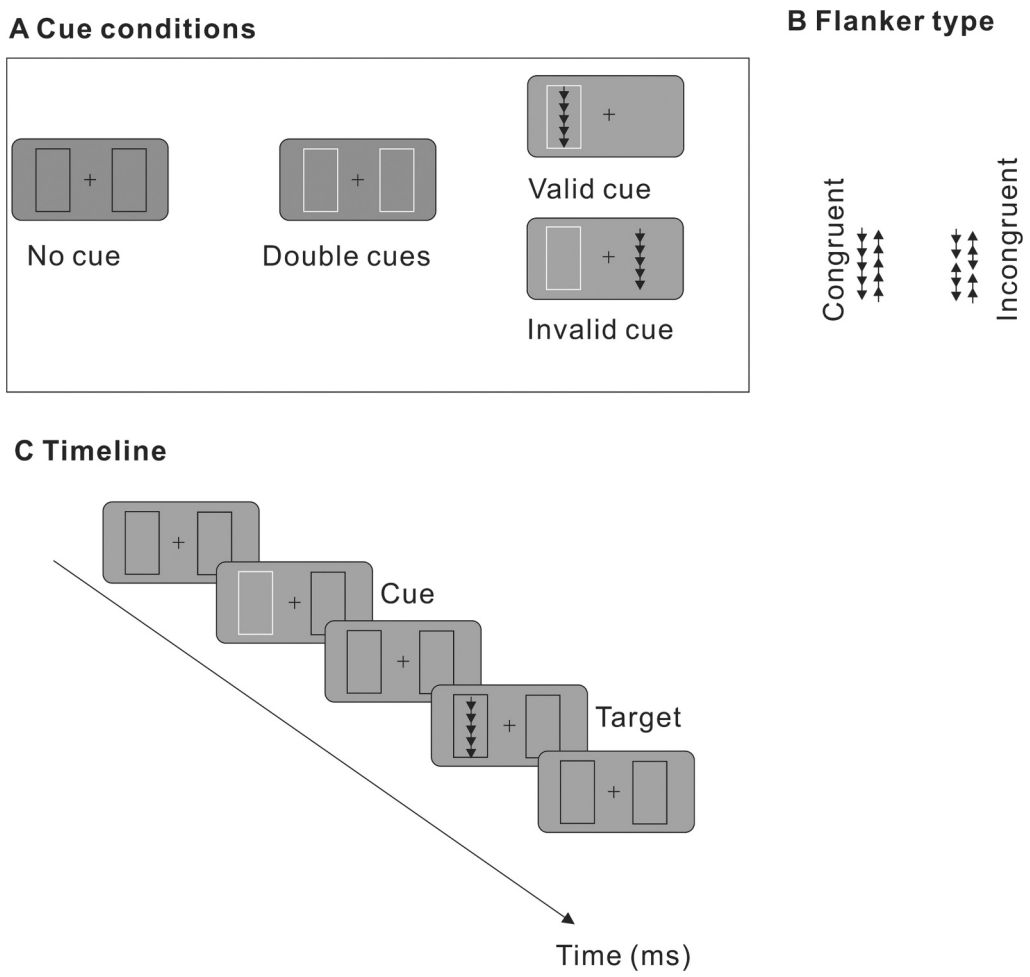



**Fig. 1.** Representation of the Lateralized Attention Network Test-Revised (LANT).
A. Cueing conditions (no cue, double cue, valid cue, and invalid cue). B. Flanker types (congruent and incongruent). C. Timeline of each trail. Each trial began with a fixation period with only the fixation and two boxes displaying for 0 to 2000 ms. Following a cue-to-target interval of 400 ms, an arrows set was presented for 500 ms with a 1700 ms response window starting at arrow set onset, followed by a fixation period of 4000 ms minus the duration of pre-cue fixation period.

situated in the left visual field (LVF, corresponding to the RH) or right visual field (RVF, corresponding to the LH). The target (the central arrow) and its flankers could align in the same direction (congruent condition) or to opposite directions (incongruent condition), each occurring with equal probability. Participants were instructed to disregard the flankers and respond to whether the target arrow pointed up or down by pressing the corresponding buttons. Preceding the arrow set, one or both boxes might flash as a cue, offering temporal and/or spatial information for the arrow set. Details of the task can be found in Supplementary materials. The trials were evenly distributed across congruent-LVF, congruent-RVF, incongruent-LVF, incongruent-RVF conditions. The task implementation was programmed using *E*-Prime (Psychology Software Tools, Pittsburgh, PA, USA; RRID: SCR_009567) on a laptop computer.

### 2.3. Analyzing the behavioral performance in the LANT-R

For each participant, the averaged reaction time (RT) and error rate was computed across trials in each condition (details provided in Supplementary materials). Given the focus on the executive control network of attention in this study, analyses concentrated on the conflict effect, while additional comparative analyses were conducted for the alerting and orienting networks, as well as the overall performance, as detailed in the Supplementary materials.

As an index of executive control of attention, the conflict effect was calculated as the difference between the mean RT/error rate in incongruent and congruent conditions. The conflict effect in RT ($RT_{incongruent} - RT_{congruent}$) signifies the time cost associated with resolving conflict induced by incongruent flankers, with a larger effect denoting less efficient executive control. The conflict effect in error rate was calculated similarly ($Error\ rate_{incongruent} - Error\ rate_{congruent}$). The conflict effect was computed separately for the RH and LH, corresponding to the presentation of arrow sets in the LVF and RVF.

The lateralization index (LI) in RT was determined by $LI = (LH - RH) / [(LH + RH) / 2]$, reflecting the proportion of hemispherical difference relative to the mean RT. Because the error rate of some participants was 0, the LI of error rate was computed as $LI = LH - RH$. A positive LI indicates that greater efficiency in the RH, signifying RH superiority, while a negative LI indicates that greater efficiency in the LH.

### 2.4. Statistical analyses

The primary analyses began with a 2 (Session: pre, post) × 2 (Hemisphere: LH, RH) × 2 (Group: SZ, HC) mixed ANOVA for conflict effect in RT and error rate. "Pre" denotes to the pre-treatment session for SZ patients and the first test for HCs, while "post" refers to the post-treatment session for SZ patients and the second test for HCs. Here conflict effect was used as an executive control index, rather than treating congruency (congruent vs. incongruent) as a main effect,

making the analytic approach more concise. Additionally, a one sample *t*-test was conducted to compare the LI of each measure to zero, examining whether there was a significant RH superiority in each group in each session. Similar analyses were conducted for other measures of the ANT (including altering, orienting, overall performance, each in RT and error rate), which are detailed in Supplementary materials.

Subsequent analyses explore whether the changes in conflict effect by olanzapine treatment in SZ patients was driven by were driven by congruent or incongruent conditions, by conducting 2 (Session: pre, post) × 2 (Hemisphere: LH, RH) × 2 (Congruency: congruent, incongruent) repeated measure. A comparative ANOVA was also conducted for the HCs.

The final analyses explored association between olanzapine treatment effect on the clinical symptoms and behavioral performance. Bootstrap correlation analyses were conducted between conflict effect measures (both RT and error rate, and the corresponding LI) and the PANSS scores (positive, negative, and general symptoms, and total score) before the treatment in SZ patients. Association between the changes (post *minus* pre) in clinical symptoms and the changes in conflict effect and its LIs in SZ patients were also examined. Partial correlation with covariates including age, sex, education, and interval length were also conducted and detailed in Supplementary materials. A significance level of 5 % (two-sided) was maintained for all tests. SPSS 20.0 (RRID: SCR_002865) was used for all statistical analyses.

## 3. Results

Table 2 presented mean and SD of RT and error rate for conflict effect, congruent and incongruent conditions in SZ patients and HCs, separately for each hemisphere, as well as the corresponding LI scores.

### 3.1. Conflict effect and its hemispherical difference

#### 3.1.1. Reaction time

The 2(Session: pre, post) × 2(Hemisphere: LH, RH) × 2(Group: SZ, HC) mixed ANOVA for the conflict effect in RT (Fig. 2A) revealed no significant main effect (Session: $F_{1,73} = 3.106$, $p = .082$, $\eta_p^2 = 0.041$; Hemisphere: $F_{1,73} = 3.286$, $p = .074$, $\eta_p^2 = 0.043$; Group: $F_{1,73} = 1.793$, $p = .185$, $\eta_p^2 = 0.024$). However, the Session by Hemisphere interaction was significant ($F_{1,73} = 7.854$, $p = .006$, $\eta_p^2 = 0.097$). Simple effect analysis for this interaction showed a RH superiority in the first session (RH: 98.0 ms ± 6.1 ms < LH: 112.8 ms ± 5.9 ms, $p = .003$), but not in the second session (RH: 98.0 ms ± 5.4 ms, LH: 96.1 ms ± 5.3 ms, $p = .664$). Other interactions were not significant (Sesson × Group: $F_{1,73} < 1$; Hemisphere × Group: $F_{1,73} < 1$; Session × Hemisphere × Group: $F_{1,73} < 1$).

Similarly, one sample *t*-tests for the LI of conflict effect in RT (Fig. 2B) revealed that a significant RH superiority in the SZ group before treatment (LI = 0.18 ms ± 0.49 ms, $t_{36} = 2.196$, $p = .035$) and in the HC group for the first test (LI = 0.19 ms ± 0.52 ms, $t_{37} = 2.266$, $p = .029$). However, the hemispheric difference was not significant in the SZ group after treatment (LI = −0.11 ms ± 0.66 ms, $t_{36} = -1.038$, $p = .306$) and in the HC group for the second test (LI = 0.005 ms ± 0.41 ms, $t_{37} < 1$).

#### 3.1.2. Error rate

The 2(Session: pre, post) × 2(Hemisphere: LH, RH) × 2(Group: SZ, HC) mixed ANOVA for the conflict effect on error rate (Fig. 2C) revealed that the main effect of Session was significant ($F_{1,73} = 6.614$, $p = .012$, $\eta_p^2 = 0.083$), with a significantly decreased error rates after treatment (post: 3.2 % ± 0.6 % < pre: 4.8 % ± 0.8 %). In contrast, the other two main effects were not significant (Hemisphere: $F_{1,73} < 1$; Group: $F_{1,73} = 2.463$, $p = .121$, $\eta_p^2 = 0.033$). The Session by Group interaction was significant ($F_{1,73} = 4.403$, $p = .039$, $\eta_p^2 = 0.057$). Simple effect analysis for this interaction showed a significantly decreased conflict effect after treatment for the SZ group (post: 3.4 % ± 0.8 % < pre: 6.4 % ± 1.1 %, $p = .002$), while the between-session difference was not significant for the HC group (first test: 3.2 % ± 1.1 %, second test: 2.9 % ± 0.8 %, $p = .737$). Other interactions were not significant (Hemisphere × Group: $F_{1,73} < 1$; Session × Hemisphere: $F_{1,73} = 1.545$, $p = .218$, $\eta_p^2 = 0.021$; Session × Hemisphere × Group: $F_{1,73} < 1$).

Similarly, one sample t-tests for the LI of the conflict effect in error rate (Fig. 2D) showed no significant hemispheric difference for SZ patients (pre: LI = −0.4 % ± 6.7 %, $t_{36} = -0.374$, $p = .710$; post: LI = 1.1 % ± 4.4 %, $t_{36} = 1.542$, $p = .132$) and for HCs (pre: LI = −0.9 % ± 6.5 %, $t_{37} = -0.837$, $p = .408$; post: LI = −0.3 % ± 3.7 %, $t_{37} = -0.456$, $p = .651$).

These findings collectively highlight two key observations: (1) The significant impact of schizophrenia on conflict processing per se was evident primarily in error rate rather than in RT, as a significant decrease in accuracy in conflict processing among SZ patients compared to HCs; (2) Initially, RH superiority in conflict effect was observed in RT during the first session, but this effect diminished in the second session, which was driven by increased efficiency of conflict processing in the LH.

**Table 2**
Behavioral performance of interest (mean ± SD) in the lateralized attention network test-revised.

| | | LH | | RH | | LI | |
|---|---|---|---|---|---|---|---|
| | | Pre | Post | Pre | Post | Pre | Post |
| *Effects in RT (ms)* | | | | | | | |
| SZ | Conflict effect | 121.8 ± 65.6 | 99.9 ± 56.4 | 104.2 ± 61.8 | 103.5 ± 57.2 | 0.18 ± 0.49 | −0.11 ± 0.66 |
| | Congruent | 726.0 ± 163.2 | 701.7 ± 131.4 | 718.6 ± 156.0 | 690.3 ± 134.4 | 0.008 ± 0.04 | 0.02 ± 0.05 |
| | Incongruent | 847.7 ± 172.6 | 801.7 ± 139.4 | 822.8 ± 171.5 | 793.7 ± 147.4 | 0.03 ± 0.04 | 0.01 ± 0.04 |
| HC | Conflict effect | 103.8 ± 32.9 | 92.1 ± 31.3 | 91.8 ± 41.7 | 92.6 ± 32.5 | 0.20 ± 0.52 | 0.005 ± 0.41 |
| | Congruent | 720.2 ± 130.8 | 688.1 ± 115.2 | 711.5 ± 130.4 | 673.4 ± 116.1 | 0.01 ± 0.03 | 0.02 ± 0.04 |
| | Incongruent | 824.0 ± 134.3 | 780.3 ± 126.7 | 803.4 ± 126.7 | 766.0 ± 128.0 | 0.02 ± 0.04 | 0.02 ± 0.04 |
| *Effects in error rate (%)* | | | | | | | |
| SZ | Conflict effect | 6.2 ± 9.0 | 4.0 ± 5.5 | 6.6 ± 7.8 | 2.9 ± 5.5 | −0.41 ± 6.71 | 1.11 ± 4.37 |
| | Congruent | 4.4 ± 4.0 | 2.2 ± 3.8 | 4.4 ± 4.2 | 3.0 ± 4.5 | 0.00 ± 3.75 | −0.86 ± 3.20 |
| | Incongruent | 10.6 ± 10.9 | 6.1 ± 8.1 | 11.0 ± 9.9 | 5.9 ± 7.1 | −0.41 ± 6.25 | 0.24 ± 3.17 |
| HC | Conflict effect | 2.8 ± 5.3 | 2.8 ± 5.3 | 3.7 ± 6.6 | 3.1 ± 4.7 | −0.88 ± 6.46 | −0.27 ± 3.71 |
| | Congruent | 2.3 ± 3.2 | 2.3 ± 3.8 | 2.5 ± 2.4 | 1.5 ± 2.6 | −0.18 ± 2.35 | 0.82 ± 2.84 |
| | Incongruent | 5.1 ± 6.1 | 5.1 ± 7.2 | 6.2 ± 7.8 | 4.6 ± 5.7 | −1.06 ± 5.97 | 0.55 ± 3.52 |

**Note**. SD: standard deviation; SZ: schizophrenia, HC: healthy control, LH: left hemisphere, RH: right hemisphere, RT: response time, LI: lateralized index, Pre: before treatment for schizophrenia patients or the first session for healthy controls; Post: after treatment for schizophrenia patients or the second session for healthy controls.

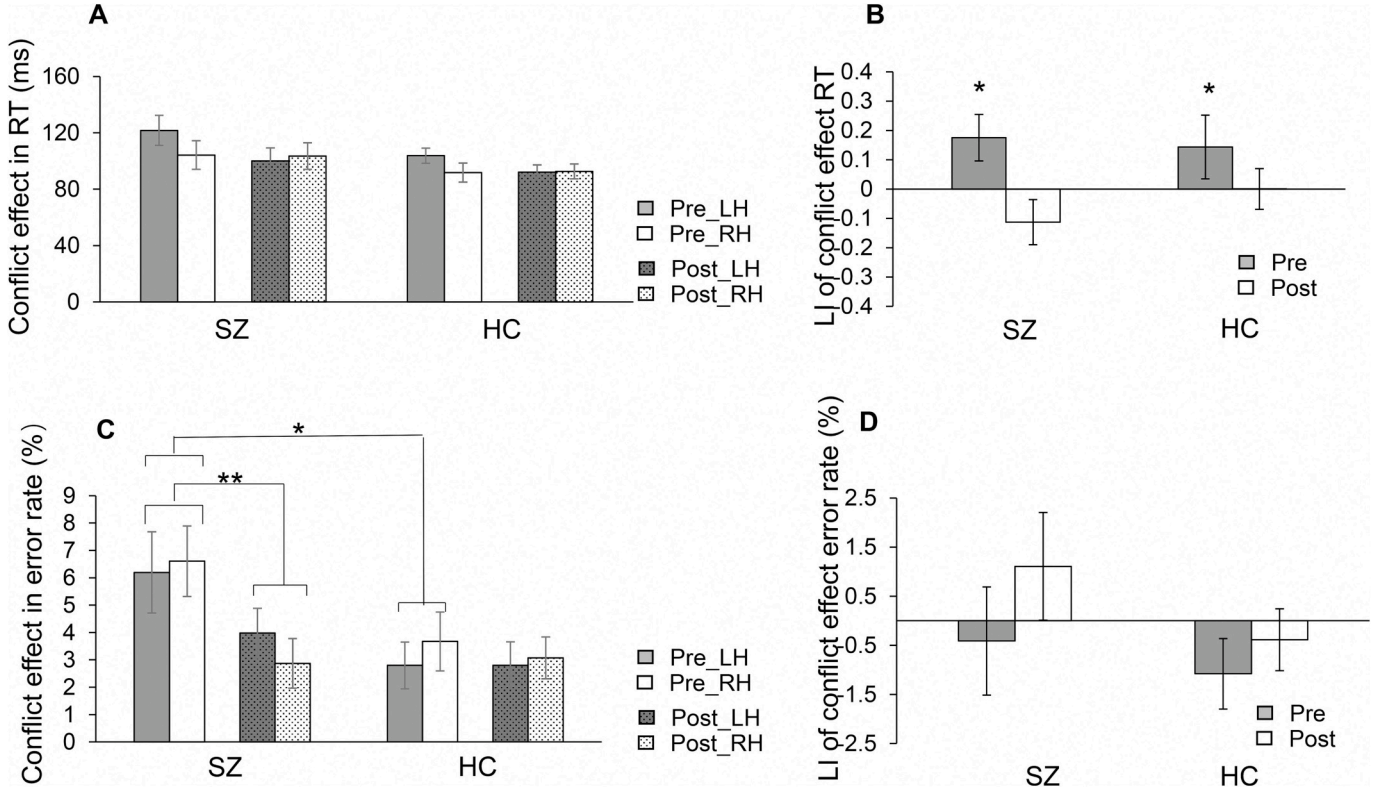



**Fig. 2.** Conflict effect and its lateralized index in response time and error rate in schizophrenia patients and healthy controls. A. Conflict effect in response time (RT). B. Lateralized index (LI) of conflict effect in RT. C. Conflict effect in error rate. D. LI of conflict effect in error rate. Data are represented by mean ± standard error (SEM). SZ: schizophrenia patients, HC: healthy controls, LH: left hemisphere, RH: right hemisphere, Pre: before treatment in schizophrenia patients or the first session in healthy controls, Post: after treatment in schizophrenia patients or the second session in healthy controls., *: $p < .05$, **: $p < .01$.

### *3.2. Hemispherical difference in congruent/incongruent conditions for each group*

#### *3.2.1. Reaction time*

Group mean RT separated in congruent and incongruent conditions were provided in Fig. 3. For schizophrenia patients, the 2(Session: pre, post) × 2(Hemisphere: LH, RH) × 2(Congruency: congruent, incongruent) repeated measures ANOVA revealed that the main effect of Session was not significant ($F_{1,36} = 3.764$, $p = .060$, $\eta_p^2 = 0.095$). In contrast, the main effect of Hemisphere was significant ($F_{1,36} = 11.760$, $p = .002$, $\eta_p^2 = 0.246$), indicating a RH superiority (RH: 756.4 ms ± 23.3 ms < LH: 769.3 ms ± 23.0 ms). The main effect of Congruency was also significant ($F_{1,36} = 165.965$, $p < .001$, $\eta_p^2 = 0.822$), indicating a significant conflict effect (incongruent: 816.5 ms ± 24.3 ms > congruent: 709.1 ms ± 22.6 ms). None of the two-way interactions were significant (Session × Hemisphere: $F_{1,36} = 1.933$, $p = .173$, $\eta_p^2 = 0.051$; Session × Congruency: $F_{1,36} = 1.932$, $p = .173$, $\eta_p^2 = 0.051$; Hemisphere × Congruency: $F_{1,36} = 1.996$, $p = .166$, $\eta_p^2 = 0.053$). However, the three-way Session × Hemisphere × Congruency interaction was significant ($F_{1,36} = 4.910$, $p = .033$, $\eta_p^2 = 0.120$). Simple effect analysis of this three-way interaction suggested that the two-way interaction of Hemisphere × Congruency was significant before treatment ($F_{1,36} = 5.993$, $p = .019$, $\eta_p^2 = 0.143$), but not after treatment ($F_{1,36} < 1$). Simple-simple effect analysis for this two-way interaction before treatment showed a significant RH superiority in the incongruent trials (RH: 822.8 ms ± 28.2 ms < LH: 847.7 ms ± 28.4 ms, $p < .001$), but not in the congruent trials (RH: 718.6 ms ± 25.6 ms, LH: 726.0 ms ± 26.8 ms, $p = .118$). In contrast, simple-simple effect analysis for this two-way interaction after treatment showed that a marginally significant RH superiority in the congruent trials (RH: 690.3 ms ± 22.1 ms < LH: 701.7 ms ± 21.6 ms, $p = .050$), but not in the incongruent trials (RH: 793.7 ms ± 24.2 ms, LH: 801.7 ms ± 22.9 ms, $p = .177$).

For the HC group, this 2(Session: pre, post) × 2(Hemisphere: LH, RH) × 2(Congruency: congruent, incongruent) repeated measures ANOVA showed a significant main effect of Session ($F_{1,37} = 7.458$, $p = .010$, $\eta_p^2 = 0.168$), indicating that the RTs in the second session were shorter than those in the first session (post: 727.0 ms ± 19.5 ms < pre: 764.8 ms ± 20.9 ms). The main effect of Hemisphere was significant ($F_{1,37} = 19.834$, $p < .001$, $\eta_p^2 = 0.349$), indicating a RH superiority (RH: 738.6 ms ± 19.0 ms < LH: 753.2 ms ± 19.1 ms). The main effect of Congruency was also significant ($F_{1,36} = 567.761$, $p < .001$, $\eta_p^2 = 0.939$), indicating a conflict effect (incongruent: 793.4 ms ± 19.6 ms > congruent: 698.3 ms ± 18.5 ms). None of the interactions were significant (Session × Hemisphere: $F_{1,37} < 1$; Session × Congruency: $F_{1,37} = 1.170$, $p = .286$, $\eta_p^2 = 0.031$; Hemisphere × Congruency: $F_{1,37} = 1.327$, $p = .257$, $\eta_p^2 = 0.035$; Session × Hemisphere × Congruency: $F_{1,37} = 2.892$, $p = .097$, $\eta_p^2 = 0.073$, Supplementary materials provided details of the simple effect analysis for this three-way interaction).

These results collectively suggest that reduction of the RH superiority of the conflict effect in RT after olanzapine treatment for SZ patients was mainly driven by a reduction of RH superiority in the incongruent condition. In contract, the HCs did not reveal such effect.

#### *3.2.2. Error rate*

Group mean error rate separated in congruent and incongruent conditions were provided in Fig. 4. For schizophrenia patients, the 2 (Session: pre, post) × 2(Hemisphere: LH, RH) × 2(Congruency: congruent, incongruent) repeated measures ANOVA showed that the main effect of Session was significant ($F_{1,36} = 15.564$, $p < .001$, $\eta_p^2 = 0.302$), with a significantly decreased error rates after treatment (post:

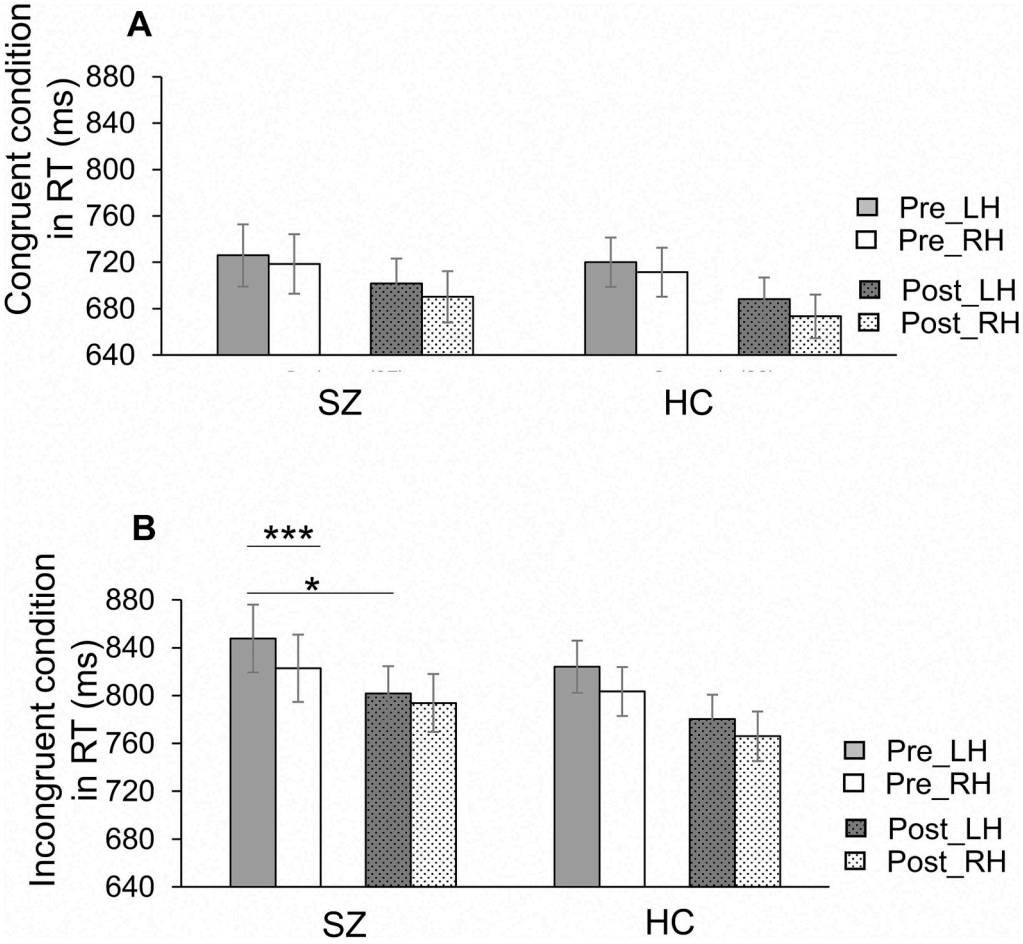



**Fig. 3.** Response time separated in congruent and incongruent conditions. A. Congruent condition. B. Incongruent condition. Data are represented by mean ± SEM. RT: response time, SZ: schizophrenia patients, HC: healthy controls, LH: left hemisphere, RH: right hemisphere, Pre: before treatment in schizophrenia patients or the first session in healthy controls, Post: after treatment in schizophrenia patients or the second session in healthy controls, SEM: standard error of mean. *: $p < .05$, ***: $p < .001$.

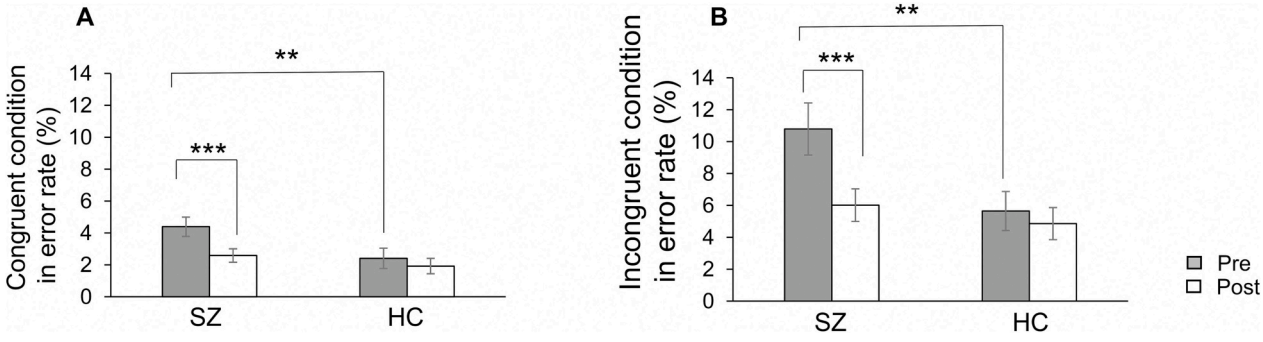



**Fig. 4.** Error rate separated in congruent and incongruent conditions. A. Congruent condition. B. Incongruent condition. Data are represented by mean ± SEM. SZ: schizophrenia patients, HC: healthy controls, Pre: before treatment in schizophrenia patients or the first session in healthy controls, Post: after treatment in schizophrenia patients or the second session in healthy controls, SEM: standard error of mean. **: $p < .01$, ***: $p < .001$.

4.3 % ± 0.9 < pre: 7.6 % ± 1.1 %). The main effect of Congruency was also significant ($F_{1,36} = 26.143$, $p < .001$, $\eta_p^2 = 0.421$), indicating a conflict effect (incongruent: 8.4 % ± 1.3 % > congruent: 3.5 % ± 0.6 %). In contrast, the main effect of Hemisphere was not significant ($F_{1,36} < 1$). The Session × Congruency interaction was significant ($F_{1,36} = 9.422$, $p = .004$, $\eta_p^2 = 0.207$). Simple effect analysis for this interaction showed that the between-session difference was significant in both congruent trials (pre: 4.4 % ± 0.6 % > post: 2.6 % ± 0.6 %, $p = .001$) and incongruent trials (pre: 10.8 % ± 1.6 % > post: 6.0 % ± 1.2 %, $p = .001$), with the amplitude of this effect significantly stronger in incongruent trials. Other interactions were not significant (Session × Hemisphere: $F_{1,36} < 1$; Hemisphere × Congruency: $F_{1,36} < 1$; Session × Hemisphere × Congruency: $F_{1,36} = 1.287$, $p = .264$, $\eta_p^2 = 0.035$).

For the HC group, the 2(Session: pre, post) × 2(Hemisphere: LH, RH) × 2(Congruency: congruent, incongruent) repeated measures ANOVA showed that the main effect of Congruency was significant ($F_{1,37} =$

21.266, $p < .001$, $\eta_p^2 = 0.365$), indicating a conflict effect (incongruent: 5.3 % ± 0.9 % > congruent: 2.2 % ± 0.4 %). In contrast, other effects were not significant (Session: $F_{1,37} < 1$; Hemisphere: $F_{1,37} < 1$; Session × Hemisphere: $F_{1,37} = 3.272$, $p = .079$, $\eta_p^2 = 0.081$; Session × Congruency: $F_{1,37} < 1$; Hemisphere × Congruency: $F_{1,37} < 1$; Session × Hemisphere × Congruency: $F_{1,37} < 1$).

These findings together suggested that decreased conflict effect in the SZ group after treatment was driven by both congruent and incongruent trials.

### 3.3. Correlation analysis

In SZ patients, the scores of positive, negative and general symptoms as well as the total scores assessed by PANSS were all significantly decreased after treatment of olanzapine (all *p*s < 0.001; Table 3). Bootstrap correlation analyses with and without gender, age, education as covariates consistently revealed no significant association between onset age, course of disease, times of hospitalization, and PANSS scores. When controlling for all of these factors, significant or marginally significant negative correlations between the interval of sessions and changes (post *minus* pre) in clinical symptoms were found (positive: $r = -0.334$, $p = .067$; negative: $r = -0.396$, $p = .027$; general: $r = -0.396$, $p = .027$; total: $r = -0.452$, $p = .011$).

Bootstrap correlation analyses revealed no significant correlation between measures of conflict effect (in both RT and ER, and the corresponding LI) and schizophrenia syndromes before treatment in SZ patients (Table 4). Furthermore, no significant correlation was observed between the changes (post *minus* pre) in clinical symptoms and changes in conflict effect either (Table 5). These correlations remained not significant when controlling for gender, age, education, and interval of sessions as covariates (see Supplementary materials).

## 4. Discussion

This study contributes compelling evidence to the modulation of the hemispheric balance of the executive control network in individuals with schizophrenia by olanzapine treatment. Specifically, our findings unveiled a significant RH superiority of the conflict effect in RT among schizophrenia patients before treatment, primarily attributed to the RH superiority in processing time during the incongruent condition. Following olanzapine treatment, this RH superiority was significantly diminished, particularly evident in incongruent condition. These results propose that olanzapine treatment may enhance the efficiency of executive control within the left hemisphere by mitigating reliance on the right hemisphere. Furthermore, our study identified a pronounced conflict effect in error rate among schizophrenia patients compared to the health controls. Remarkably, olanzapine treatment effectively reduced the conflict effect in schizophrenia patients to a level comparable to that observed in health controls. This reduction was marked by diminished error rate in both congruent and incongruent conditions, with a relatively more substantial reduction observed in incongruent trials.

The current study reinforces the evidence supporting the existence of RH superiority of executive control of attention. In alignment with our previous studies involving healthy adults and transient ischemic attack patients (Russell-Giller et al., 2021; Spagna et al., 2018b), our findings revealed a RH superiority of conflict effect in the initial session. Moreover, our observations indicated that this effect was predominantly influenced by an RH superiority of RT during incongruent condition, consistent with earlier research outcomes (Russell-Giller et al., 2021; Spagna et al., 2018b). These results imply a correlation between RH superiority in executive control of attention and the asymmetry of conflict processing in the brain. Additionally, in harmony with our previous studies (Russell-Giller et al., 2021; Spagna et al., 2018b), the RH superiority in the conflict effect manifested exclusively in RT, but not error rate. This underscores the potential importance of interhemispheric communication in the executive control of attention. RH superiority of executive control of attention likely hinges on the processing speed of executive control within and across the two hemispheres, rather than the amount of information that could be accurately processed.

The RH superiority of executive control of attention in SZ patients may be driven by a complex mechanism that differ from that in healthy controls. Schizophrenia is associated with inter-hemispheric hypoconnectivity (Ribolsi et al., 2014), potentially disrupting RH superiority by impeding inter-hemispheric communication. Nonetheless, schizophrenia is also associated with reduced leftward asymmetry in some brain structures (Ribolsi et al., 2014), possibly resulting in compensatory overdevelopment of the right hemisphere, aligning with the observed RH superiority. Thus, these opposing effects may neutralize each other, leading to an apparent RH superiority of conflict effect in SZ patients. In addition, no significant correlation was found between the LI of conflict effect and schizophrenia symptoms, suggesting that the RH superiority of executive control might not significantly contribute to the manifestation of symptoms in schizophrenia. Therefore, caution is warranted when using the LI of conflict effect as a neuropsychological indicator of attention function in individuals with no explicit brain damage, given the potential for complex brain alternations to yield composite effects on this phenomenon.

Examining changes in the LI of conflict effect in the second session offers valuable insights into the plasticity of the executive control

**Table 3**
Comparison of scores of positive, negative, and general symptoms, and total scores assessed by PANSS before and after treatment in SZ patients (mean ± SD).

| PANSS score | Pre | Post |
|---|---|---|
| Positive symptom | 21.9 ± 5.3 | 11.1 ± 2.6 |
| Negative symptom | 17.2 ± 6.3 | 12.4 ± 3.3 |
| General symptom | 34.8 ± 7.6 | 25.2 ± 3.9 |
| Total | 73.9 ± 16.6 | 48.7 ± 7.7 |

**Note**. SD: standard deviation; Pre: before treatment; Post: after treatment.

**Table 4**
Correlation coefficients (*p* values) between measures of conflict effect and the PANSS scores in schizophrenia patients before treatment.

| PANSS score | Conflict effect | | LI of conflict effect | |
|---|---|---|---|---|
| | RT | Error rate | RT | Error rate |
| Total | −0.237 (0.157) | −0.096 (0.574) | −0.078 (0.645) | 0.044 (0.797) |
| Positive | −0.042 (0.084) | −0.219 (0.193) | 0.093 (0.583) | 0.029 (0.865) |
| Negative | −0.167 (0.323) | 0.137 (0.420) | −0.121 (0.474) | 0.007 (0.969) |
| General | −0.164 (0.331) | −0.113 (0.504) | −0.048 (0.777) | 0.100 (0.558) |

**Note**. RT: response time, LI: lateralized index.

**Table 5**
Correlations coefficients (p values) between the changes in clinical symptoms and the changes in conflict effects and their LI in schizophrenia patients.

| PANSS score changes | Change in conflict effect | | Change in LI of conflict effect | |
|---|---|---|---|---|
| | RT | Error rate | RT | Error rate |
| Total | 0.122 (0.474) | 0.002(0.991) | 0.057 (0.739) | −0.038 (0.823) |
| Positive | 0.026 (0.881) | 0.039 (0.821) | 0.019 (0.912) | −0.064 (0.708) |
| Negative | 0.111 (0.511) | −0.017 (0.919) | 0.050 (0.768) | 0.025 (0.884) |
| General | 0.111 (0.515) | 0.085 (0.616) | 0.080 (0.637) | −0.188 (0.319) |

**Note**. RT: response time, LI: lateralized index.

network and the RH superiority. In healthy controls, the RH superiority of executive control diminished in the second session, indicating the plasticity of the executive control network through practice. In the schizophrenia patients, olanzapine treatment significantly reduced the RH superiority, even exhibiting a reversal to LH superiority (although not significant). This change may be resulted from both practice effect observed in healthy controls and an additional impact by olanzapine. Olanzapine may alleviate schizophrenia symptoms by enhancing the activity of the left hemisphere to counteract right hemisphere over-development (Ribolsi et al., 2014), or by facilitating inter-hemisphere communication from LH to RH (Hoptman et al., 2012; Li et al., 2015; Shan et al., 2021). Both mechanisms could enhance information processing efficiency for conflict processing in the left hemisphere. While the study lacks a placebo-treated SZ group for a more nuanced understanding of the practice and treatment effects, ethical considerations limited the inclusion of such a control group.

The current study reveals executive control deficits in schizophrenia, evidenced by a small but significant increase in conflict effect in error rate (approximately 3 % increase) in schizophrenia patients compared to healthy controls, eliminated after olanzapine treatment. This deficit was not observed in RT, excluding a speed-accuracy trade-off in this study. The increased error rate, indicative of information loss tendencies (Fan, 2014; Shannon, 1948; Wu et al., 2016), suggests schizophrenia's impact on cognitive control capacity, potentially mitigated by olanzapine's enhancement of conflict processing. These findings partially align with our previous study using different versions of ANT, which identified a slight yet significant increase in conflict effect in RT among schizophrenia patients before clozapine treatment (Spagna et al., 2015a). The inconsistency observed between the two studies may stem from variations in speed-accuracy trade-off strategies, particularly given the subtle nature of these effects. These insights underscore the complexity of interpreting subtle variations in executive control performance across different antipsychotic treatments and emphasize the need for further investigation into the underlying mechanisms driving these effects.

Olanzapine's modulation of conflict effect and its laterality, coupled with symptoms improvements, suggests potential cognitive enhancement through its influence on prefrontal metabolism or neurotransmission, particularly involving the mesocortical dopamine system (Purdon et al., 2000; Bever and Perry, 1998; Greene et al., 2008). However, changes of clinical symptoms and conflict effect showed no significant correlation, indicating independent pathways. In addition to neurotransmitter effects, olanzapine's modulation of the laterality of conflict effect in schizophrenia patients may involve changes in brain areas associated with executive control. Previous studies have reported increased activation in the frontal cortex during cognitive tasks in schizophrenia patients treated with olanzapine (Del Fabro et al., 2019; Kumari et al., 2015; Schirmbeck et al., 2015), which could explain the observed effect of olanzapine on efficiency of the left hemisphere. However, it remains unclear whether these impacts and the underlying mechanisms are specific to olanzapine. A large-scale unbiased study examining the neurocognitive effects of antipsychotic medications in patients with chronic schizophrenia in the CATIE trial reported that all antipsychotics drugs, including olanzapine, had a small but significant improvement in neurocognition across various of cognitive domains, and they did not find significant difference across antipsychotic medications (Keefe et al., 2007). However, the attention domain was not specifically examined in this study. Since the current study exclusively involved olanzapine but not other antipsychotic medications, further investigation is needed to answer this question and determine whether olanzapine's effects on attentional hemispheric asymmetry are specific to this medication or represent broader trends among antipsychotics in schizophrenia treatment.

Our study presents several notable limitations. Firstly, the small sample size within each schizophrenia subtype hindered differentiation between subtypes. A more extensive study with adequate sample sizes for each subtype is essential for a comprehensive understanding of the association between subtypes and hemisphere asymmetry, offering more robust conclusions on asymmetry and treatment effect. Secondly, our exclusive use of olanzapine treatment limits the ability to compare different antipsychotics' effect on attentional hemispheric asymmetry. Further experiments should incorporate diverse antipsychotics with distinct pharmacological mechanisms to explore their potential differential effects. Additionally, the considerable variation in the interval between test sessions in patients, influenced by clinical factors and patient availability, poses a challenge. Despite our efforts to match intervals in healthy controls, addressing this issue remains complex.

In summary, our study demonstrates that olanzapine treatment significantly enhanced the efficiency of the left hemisphere during the processing the incongruent cue, leading to a reduction in the right hemisphere superiority in the executive control function in individuals with schizophrenia. These findings add valuable insights to the existing literature on hemispheric asymmetries in executive control within the context of schizophrenia. Moreover, our findings underscore the potential positive impact of atypical antipsychotics on the attentional components of cognitive functions in schizophrenia patients. This aspect warrants further attention in the quest for novel pharmacological interventions for schizophrenia treatment.

## Funding

This study was supported by Anqing Science and Technology Program (2019Z1001), Anqing Science and Technology Plan Program of Medical Health (2021Z5001), the National Natural Science Foundation of China (81901135, 32200858) and Construction and Improvement Plan of Scientific Research Platform Base of Anhui Medical University (2020xkjT057).

## CRediT authorship contribution statement

**Yong Zhao:** Writing – original draft, Project administration, Conceptualization. **Yifan Li:** Data curation. **Jing Du:** Data curation. **Chuanlong Fang:** Project administration. **Wansheng Li:** Resources, Conceptualization. **Mengyu Lv:** Data curation. **Yue Wu:** Methodology. **Kai Wang:** Funding acquisition, Conceptualization. **Tingting Wu:** Writing – review & editing. **Yanghua Tian:** Funding acquisition, Conceptualization. **Juanjuan Zhang:** Writing – review & editing, Supervision, Conceptualization.

## Declaration of competing interest

The authors declare having no conflict of interest.

## Data availability

All data generated or used in this study are available upon request from the corresponding authors.

## Acknowledgements

We gratefully acknowledge Prof. Jin Fan from Queens College of the City University of New York for his invaluable assistance in the design of the study and the preparation of the manuscript.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scog.2024.100306.

## References


Asanowicz, D., Marzecová, A., Jaśkowski, P., Wolski, P., 2012. Hemispheric asymmetry in the efficiency of attentional networks. Brain Cogn. 79 (2), 117–128. https://doi.org/10.1016/j.bandc.2012.02.014.

Backes, V., Kellermann, T., Voss, B., et al., 2011. Neural correlates of the attention network test in schizophrenia. Eur. Arch. Psychiatry Clin. Neurosci. 261 (Suppl. 2), S155–S160. https://doi.org/10.1007/s00406-011-0264-9.

Bever, K.A., Perry, P.J., 1998. Olanzapine: a serotonin-dopamine-receptor antagonist for antipsychotic therapy. Am. J. Health-Syst. Pharm. 55 (10), 1003–1016. https://doi.org/10.1093/ajhp/55.10.1003.

Bilder, R.M., Goldman, R.S., Volavka, J., et al., 2002. Neurocognitive effects of clozapine, olanzapine, risperidone, and haloperidol in patients with chronic schizophrenia or schizoaffective disorder. Am. J. Psychiatry 159 (6), 1018–1028. https://doi.org/10.1176/appi.ajp.159.6.1018.

Caprile, C., Cuevas-Esteban, J., Ochoa, S., Usall, J., Navarra, J., 2015. Mixing apples with oranges: visual attention deficits in schizophrenia. J. Behav. Ther. Exp. Psychiatry 48, 27–32. https://doi.org/10.1016/j.jbtep.2015.01.006.

Carter, C.S., Mintun, M., Nichols, T., Cohen, J.D., 1997. Anterior cingulate gyrus dysfunction and selective attention deficits in schizophrenia: [$^{15}$O]H2O PET study during single-trial Stroop task performance. Am. J. Psychiatry 154 (12), 1670–1675. https://doi.org/10.1176/ajp.154.12.1670.

Chambers, C.D., Payne, J.M., Stokes, M.G., Mattingley, J.B., 2004. Fast and slow parietal pathways mediate spatial attention. Nat. Neurosci. 7 (3), 217–218. https://doi.org/10.1038/nn1203.

Danckert, J., Ferber, S., 2006. Revisiting unilateral neglect. Neuropsychologia 44 (6), 987–1006. https://doi.org/10.1016/j.neuropsychologia.2005.09.004.

Del Fabro, L., Delvecchio, G., D'Agostino, A., Brambilla, P., 2019. Effects of olanzapine during cognitive and emotional processing in schizophrenia: a review of functional magnetic resonance imaging findings. Hum. Psychopharmacol. 34 (3), e2693 https://doi.org/10.1002/hup.2693.

Eriksen, B.A., Eriksen, C.W., 1974. Effects of noise letters upon identification of a target letter in a non-search task. Percept. Psychophys. 16, 143–149. https://doi.org/10.3758/BF03203267.

Fan, J., 2014. An information theory account of cognitive control. Front. Hum. Neurosci. 8, 680. https://doi.org/10.3389/fnhum.2014.00680.

Fan, J., McCandliss, B.D., Sommer, T., Raz, A., Posner, M.I., 2002. Testing the efficiency and independence of attentional network. J. Cogn. Neurosci. 14 (3), 340–347.

Fan, J., McCandliss, B.D., Fossella, J., Flombaum, J.I., Posner, M.I., 2005. The activation of attentional networks. Neuroimage 26 (2), 471–479. https://doi.org/10.1016/j.neuroimage.2005.02.004.

Fan, J., Gu, X., Guise, K.G., et al., 2009. Testing the behavioral interaction and integration of attentional networks. Brain Cogn. 70 (2), 209–220. https://doi.org/10.1016/j.bandc.2009.02.002.

Greene, D.J., Barnea, A., Herzberg, K., et al., 2008. Measuring attention in the hemispheres: the lateralized attention network test (LANT). Brain Cogn. 66 (1), 21–31. https://doi.org/10.1016/j.bandc.2007.05.003.

Heilman, K.M., Abell, T.V.D., 1980. Right hemisphere dominance for attention: the mechanism underlying hemispheric asymmetries of inattention (neglect). Neurology 30 (3), 327–330. https://doi.org/10.1212/wnl.30.3.327.

Henik, A., Salo, R., 2004. Schizophrenia and the Stroop effect. Behav. Cogn. Neurosci. Rev. 3 (1), 42–59. https://doi.org/10.1177/1534582304263252.

Hoonakker, M., Doignon-Camus, N., Marques-Carneiro, J.E., Bonnefond, A., 2017. Sustained attention ability in schizophrenia: investigation of conflict monitoring mechanisms. Clin. Neurophysiol. 128 (9), 1599–1607. https://doi.org/10.1016/j.clinph.2017.06.036.

Hoptman, M.J., Zuo, X.N., D'Angelo, D., et al., 2012. Decreased interhemispheric coordination in schizophrenia: a resting state fMRI study. Schizophr. Res. 141 (1), 1–7. https://doi.org/10.1016/j.schres.2012.07.027.

Ke, M., Zou, R., Shen, H., et al., 2010. Bilateral functional asymmetry disparity in positive and negative schizophrenia revealed by resting-state fMRI. Psychiatry Res. 182 (1), 30–39. https://doi.org/10.1016/j.pscychresns.2009.11.004.

Keedy, S.K., Reilly, J.L., Bishop, J.R., Weiden, P.J., Sweeney, J.A., 2015. Impact of antipsychotic treatment on attention and motor learning systems in first-episode schizophrenia. Schizophr. Bull. 41 (2), 355–365. https://doi.org/10.1093/schbul/sbu071.

Keefe, R.S., Bilder, R.M., Davis, S.M., et al., 2007. Neurocognitive effects of antipsychotic medications in patients with chronic schizophrenia in the CATIE Trial. Arch. Gen. Psychiatry 64 (6), 633–647. https://doi.org/10.1001/archpsyc.64.6.633.

Kumar, S., Chaudhury, S., 2014. Efficacy of amisulpride and olanzapine for negative symptoms and cognitive impairments: an open-label clinical study. Ind. Psychiatry J. 23 (1), 27–35. https://doi.org/10.4103/0972-6748.144953.

Kumari, V., Ettinger, U., Lee, S.E., et al., 2015. Common and distinct neural effects of risperidone and olanzapine during procedural learning in schizophrenia: a randomised longitudinal fMRI study. Psychopharmacology 232 (17), 3135–3147. https://doi.org/10.1007/s00213-015-3959-1.

Leroux, E., Delcroix, N., Dollfus, S., 2015. Left-hemisphere lateralization for language and interhemispheric fiber tracking in patients with schizophrenia. Schizophr. Res. 165 (1), 30–37. https://doi.org/10.1016/j.schres.2015.03.028.

Li, H.J., Xu, Y., Zhang, K.R., Hoptman, M.J., Zuo, X.N., 2015. Homotopic connectivity in drug-naïve, first-episode, early-onset schizophrenia. J. Child Psychol. Psychiatry 56 (4), 432–443. https://doi.org/10.1111/jcpp.12307.

McCutcheon, R.A., Marques, T.R., Howes, O.D., et al., 2020. Schizophrenia-an overview. JAMA Psychiatry 77 (2), 201–210. https://doi.org/10.1001/jamapsychiatry.2019.3360.

McGurk, S.R., Lee, M.A., Jayathilake, K., Meltzer, H.Y., 2004. Cognitive effects of olanzapine treatment in schizophrenia. MedGenMed 6 (2), 27 (PMID: 15266253; PMCID: PMC1395781).

Meltzer, H.Y., McGurk, S.R., 1999. The effects of clozapine, risperidone, and olanzapine on cognitive function in schizophrenia. Schizophr. Bull. 25 (2), 233–255. https://doi.org/10.1093/oxfordjournals.schbul.a033376.

Mesulam, M.M., 1999. Spatial attention and neglect: parietal, frontal and cingulate contributions to the mental representation and attentional targeting of salient extrapersonal events. Philos. Trans. R. Soc. Lond. Ser. B Biol. Sci. 354 (1387), 1325–1346. https://doi.org/10.1098/rstb.1999.0482.

Nobre, A.C., Sebestyen, G.N., Gitelman, D.R., Mesulam, M.M., Frackowiak, R.S., Frith, C. D., 1997. Functional localization of the system for visuospatial attention using positron emission tomography. Brain 120 (Pt 3), 515–533. https://doi.org/10.1093/brain/120.3.515.

Opgen-Rhein, C., Neuhaus, A.H., Urbanek, C., Hahn, E., Sander, T., Dettling, M., 2008. Executive attention in schizophrenic males and the impact of COMT Val108/158Met genotype on performance on the attention network test. Schizophr. Bull. 34 (6), 1231–1239. https://doi.org/10.1093/schbul/sbm155.

Orellana, G., Slachevsky, A., Peña, M., 2012. Executive attention impairment in first-episode schizophrenia. BMC Psychiatry 12, 154. https://doi.org/10.1186/1471-244x-12-154.

Purdon, S.E., Jones, B.D., Stip, E., et al., 2000. Neuropsychological change in early phase schizophrenia during 12 months of treatment with olanzapine, risperidone, or haloperidol. The Canadian Collaborative Group for research in schizophrenia. Arch. Gen. Psychiatry 57 (3), 249–258. https://doi.org/10.1001/archpsyc.57.3.249.

Ribolsi, M., Daskalakis, Z.J., Siracusano, A., Koch, G., 2014. Abnormal asymmetry of brain connectivity in schizophrenia. Front. Hum. Neurosci. 8, 1010. https://doi.org/10.3389/fnhum.2014.01010.

Rotarska-Jagiela, A., van de Ven, V., Oertel-Knöchel, V., Uhlhaas, P.J., Vogeley, K., Linden, D.E., 2010. Resting-state functional network correlates of psychotic symptoms in schizophrenia. Schizophr. Res. 117 (1), 21–30. https://doi.org/10.1016/j.schres.2010.01.001.

Russell-Giller, S., Wu, T., Spagna, A., Dhamoon, M., Hao, Q., Fan, J., 2021. Impact of unilateral stroke on right hemisphere superiority in executive control. Neuropsychologia 150, 107693. https://doi.org/10.1016/j.neuropsychologia.2020.107693.

Schirmbeck, F., Mier, D., Esslinger, C., et al., 2015. Increased orbitofrontal cortex activation associated with "pro-obsessive" antipsychotic treatment in patients with schizophrenia. J. Psychiatry Neurosci. 40 (2), 89–99. https://doi.org/10.1503/jpn.140021.

Shan, X., Liao, R., Ou, Y., et al., 2021. Increased homotopic connectivity in the prefrontal cortex modulated by olanzapine predicts therapeutic efficacy in patients with schizophrenia. Neural Plast. 2021, 9954547 https://doi.org/10.1155/2021/9954547.

Shannon, C.E., 1948. A mathematical theory of communication. Bell Syst. Tech. J. 27, 379–423. https://doi.org/10.1002/j.1538-7305.1948.tb01338.x.

Spagna, A., Martella, D., Sebastiani, M., Maccari, L., Marotta, A., Casagrande, M., 2014. Efficiency and interactions of alerting, orienting and executive networks:the impact of imperative stimulus type. Acta Psychol. 148, 209–215. https://doi.org/10.1016/j.actpsy.2014.02.007.

Spagna, A., Dong, Y., Mackie, M.A., et al., 2015a. Clozapine improves the orienting of attention in schizophrenia. Schizophr. Res. 168 (1–2), 285–291. https://doi.org/10.1016/j.schres.2015.08.009.

Spagna, A., Mackie, M.A., Fan, J., 2015b. Supramodal executive control of attention. Front. Psychol. 6, 65. https://doi.org/10.3389/fpsyg.2015.00065.

Spagna, A., Martella, D., Fuentes, L.J., Marotta, A., Casagrande, M., 2016. Hemispheric modulations of the attentional networks. Brain Cogn. 108, 73–80. https://doi.org/10.1016/j.bandc.2016.07.002.

Spagna, A., He, G., Jin, S., et al., 2018a. Deficit of supramodal executive control of attention in schizophrenia. J. Psychiatr. Res. 97, 22–29. https://doi.org/10.1016/j.jpsychires.2017.11.002.

Spagna, A., Kim, T.H., Wu, T., Fan, J., 2018b. Right hemisphere superiority for executive control of attention. Cortex. https://doi.org/10.1016/j.cortex.2018.12.012.

Wang, K., Fan, J., Dong, Y., Wang, C.Q., Lee, T.M., Posner, M.I., 2005. Selective impairment of attentional networks of orienting and executive control in schizophrenia. Schizophr. Res. 78 (2–3), 235–241. https://doi.org/10.1016/j.schres.2005.01.019.

Wang, J., Hu, M., Guo, X., Wu, R., Li, L., Zhao, J., 2013. Cognitive effects of atypical antipsychotic drugs in first-episode drug-naive schizophrenic patients. Neural Regen. Res. 8 (3), 277–286. https://doi.org/10.3969/j.issn.1673-5374.2013.03.011.

Westerhausen, R., Kompus, K., Hugdahl, K., 2011. Impaired cognitive inhibition in schizophrenia: a meta-analysis of the Stroop interference effect. Schizophr. Res. 133 (1–3), 172–181. https://doi.org/10.1016/j.schres.2011.08.025.

Wu, T., Dufford, A.J., Mackie, M.A., Egan, L.J., Fan, J., 2016. The capacity of cognitive control estimated from a perceptual decision making task. Sci. Rep. 6, 34025. https://doi.org/10.1038/srep34025.

Xie, W., Peng, C.K., Huang, C.C., Lin, C.P., Tsai, S.J., Yang, A.C., 2018. Functional brain lateralization in schizophrenia based on the variability of resting-state fMRI signal. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 86, 114–121. https://doi.org/10.1016/j.pnpbp.2018.05.020.

Xuan, B., Mackie, M.A., Spagna, A., et al., 2016. The activation of interactive attentional networks. Neuroimage 129, 308–319. https://doi.org/10.1016/j.neuroimage.2016.01.017.