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# The interaction between positive schizotypy and high sensitivity C-reactive protein on response inhibition in female individuals

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ABSTRACT

This study aimed to measure the associations between high sensitivity C-reactive protein (hsCRP), childhood maltreatment (CM), schizotypy and response inhibition, and to explore the interactions between hsCRP, CM and schizotypy on response inhibition. Two hundred and fourteen participants completed the Stop-Signal Task (SST), the Schizotypy Personality Questionnaire (SPQ) and the Childhood Trauma Questionnaire-Short Form (CTQ), which measured response inhibition, schizotypy and history of CM respectively. The level of hsCRP was also measured. The high schizotypy group ($n$ = 114) had higher scores on SPQ and CTQ, higher hsCRP levels and longer SST reaction times (SSRTs) than the low schizotypy group ($n$ = 100). In female participants, SSRT had a positive correlation with the SPQ positive factor and the disorganized SPQ factor and a positive correlation with physical neglect. HsCRP was positively correlated with the SPQ negative factor and positive SPQ factor. In male participants, SSRT was negatively correlated with emotional neglect and physical neglect. The majority of correlations between CTQ and SPQ variables were significant in both female and male participants. In female participants, hsCRP significantly predicted SSRT, and hsCRP significantly interacted with positive schizotypy in predicting SSRT.

## 1. Introduction

The term schizotypy, a multidimensional personality organization, covers a range of personality traits that resemble the symptoms of schizophrenia (Grant et al., 2018; Mason, 2014), including the positive or psychotic-like dimension, the negative or deficit dimension, and the cognitive-behavioural disorganization dimension of schizophrenia. A meta-analysis has examined sex differences in schizotypal traits and found no major sex differences in positive schizotypal traits (Miettunen and Jaaskelainen, 2010), while men tend to score higher than women in negative schizotypal traits. All healthy individuals possess schizotypal traits to some degree, which is normally distributed throughout the general population and is thought to represent a continuum of psychosis risk (Verdoux and van Os, 2002). Schizotypy is a valuable and unifying concept for investigating the causes, development and manifestation of a range of schizophrenia-like pathological traits, called schizophrenia-spectrum disorders. The Schizotypal Personality Questionnaire (SPQ), developed based on the DSM-III-R criteria, serves as a measure to assess schizotypal traits in the general population.

Cognitive impairment, which is a hallmark of schizophrenia, includes deficits in attention, memory and executive functions (Harvey, 2013; Heinrichs and Zakzanis, 1998; Orellana and Slachevsky, 2013; Reichenberg et al., 2009). Cognitive impairment, which is present before the onset of psychosis (Reichenberg et al., 2009), is consistently exhibited by patients with first-episode schizophrenia (Mesholam-Gately et al., 2009), and it is relatively unresponsive to pharmacological treatment (Heinrichs, 2007). People with high levels of schizotypal traits, compared with those with schizophrenia, show attenuated or mild impairments in the same areas of cognitive function (Snitz et al., 2006).

Response inhibition, which is the capacity to inhibit unwanted or inappropriate behaviours, is a core feature of executive function (Barkley, 1997). A number of studies have found that people with schizophrenia-spectrum disorders exhibit poor response inhibition on the stop-signal task (SST) (Bellgrove et al., 2006; Davalos et al., 2004;

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Enticott et al., 2008; Ross et al., 2008; Thakkar et al., 2011). The SST is the main paradigm used to study response inhibition (Logan et al., 1984). The trials in the task start with a "go" stimulus to which the study participant must respond with speed and accuracy (the go task). A second stimulus (the "stop" stimulus) is presented after the "go" stimulus in some trials, signaling that participants have to inhibit the "go" response (the stop-signal task). The amount of time taken to inhibit the "go" response, called the stop signal reaction time (SSRT) (Logan et al., 1984), is the primary dependent variable of the SST. SSRT is longer in patients with schizophrenia than matched healthy controls (Bellgrove et al., 2006; Enticott et al., 2008; Lipszyc and Schachar, 2010). Moreover, longer SSRTs have been found in children who are at-risk of developing schizophrenia (Davalos et al., 2004) and their SSRTs do not improve on subsequent testing (Ross et al., 2008). These findings suggest that poor inhibition on the SST may be an endophenotype for schizophrenia (Gottesman and Gould, 2003). Poor executive function also occurs in high schizotypy individuals (Ettinger et al., 2015; Giakoumaki, 2012), including perseverative errors on the Wisconsin Card Sorting Test (Gooding et al., 1999; Lenzenweger et al., 1991; Suhr, 1997; Tallent and Gooding, 1999). Furthermore, schizotypy, especially its disorganized dimension, has been found to be correlated with poor inhibitory performance across a number of tasks (e.g., the Stroop Task and the Simon Task) (Ettinger et al., 2017), which supports the importance of the disorganized schizotypy dimension in cognitive control (Kerns, 2006). Previous studies examining sex differences in response inhibition have reported that women have stronger inhibition control abilities than men, who may have more frequent engagement in risk-taking and sensation-seeking behaviours (Li et al., 2006; Liu et al., 2013).

There is evidence for an association between childhood maltreatment and schizotypal traits, especially positive schizotypy (Velikonja et al., 2015). Among different types of childhood maltreatment, emotional abuse (Powers et al., 2011) and neglect (Berenbaum et al., 2003) are the strongest risk factors for psychosis. Individuals with schizotypal traits have also been shown to have increased likelihood of experiencing childhood maltreatment than healthy controls (Berenbaum et al., 2003; Campbell and Morrison, 2007; Velikonja et al., 2015). Empirical findings suggest that childhood maltreatment (CM) may lead to altered brain changes, including a reduced volume of the hippocampus and the amygdala, and abnormal fronto-temporal electrical activity (Teicher et al., 2002, 2003). These changes have a significant detrimental effect on cognitive function and may cause poor executive function (e.g., inhibitory control) in children (Koenen et al., 2003), diminished cognitive flexibility in adolescents (Spann et al., 2012), and deficits in intellectual and academic functions and memory in adulthood (Bremner et al., 2004; Navalta et al., 2006). However, one study found no association between executive function and any type of CM (Majer et al., 2010). In addition, two studies of individuals aged over 50 years reported associations between childhood sexual abuse and better executive function, including processing speed (Feeney et al., 2013) and a lower risk of impaired verbal fluency (Ritchie et al., 2011). CM could affect episodic narrative, working memory, cognitive performance, learning and visual-context processing in people with schizophrenia-spectrum disorder (Aas et al., 2011; Aas et al., 2012; Lysaker et al., 2001; Schenkel et al., 2005; Shannon et al., 2011), in people with ultra-high risk for psychosis (Ucok et al., 2015) and in people in the early stages of psychosis (Aas et al., 2011). One study found that maltreated individuals (both patients and healthy subjects) exhibited significantly greater dysfunction in inhibitory control, compared with healthy participants without a history of CM, suggesting that early maltreatment might adversely influence the development of brain circuits that underlie aspects of executive function related to inhibitory control irrespective of psychiatric diagnosis.

High sensitivity C-reactive protein (hsCRP) is an acute-phase protein that is thought to be one of the most reliable indicators of inflammation, which might be involved in both the pathogenesis and symptomology of psychiatric disorders (Haroon et al., 2012). Previous studies have reported high hsCRP levels in individuals with schizophrenia (Dargel et al., 2015; Miller et al., 2014), and it has been found to be associated with more severe psychopathology (Fan et al., 2007), especially negative symptoms (Fawzi et al., 2011; Garcia-Rizo et al., 2012) and poorer cognitive function, such as memory and executive function (Bulzacka et al., 2016; Dickerson et al., 2007; Dickerson et al., 2012; Johnsen et al., 2016; Micoulaud-Franchi et al., 2015). A recent meta-analysis revealed that serum CRP levels were higher in patients with schizophrenia, particularly in patients from African and Asian countries who were less than 30 years-old, irrespective of other variables, such as body mass index, study region, sample size or age of onset of schizophrenia (Wang et al., 2017). Other meta-analyses have suggested that CM may induce a low-grade immune system response, as indicated by increased circulating levels of CRP (Baumeister et al., 2016; Coelho et al., 2014). In addition, a life-course study has shown that CM was linked to higher levels of hsCRP in participants 20 years later, after controlling for the effects of early-life risks, stressors and adult health (Danese et al., 2007). Several studies with small sample sizes ($N < 50$) have found higher levels of CRP in schizophrenia patients with CM (Dennison et al., 2012; Hepgul et al., 2012). A recent cross-sectional study also confirmed that CM severity is linked to elevated hsCRP in schizophrenia patients (Aas et al., 2017), and a recent longitudinal study found that long-term decline in cognitive function was significantly associated with hsCRP levels, suggesting that hsCRP could be used as a biomarker for cognitive deficits (Zheng and Xie, 2017). Furthermore, individuals differ consistently in the magnitude of their inflammatory responses to acute stressors, with females often showing greater responses than males (Marsland et al., 2002; Marsland et al., 1995).

Since CM and hsCRP have been found to influence executive function deficits in individuals with schizophrenia and schizotypy is thought to be a mental state representing "psychosis-proneness", understanding the nature of the association between poor response inhibition and schizotypy may provide a more comprehensive description of inhibition-related performance deficits across the schizophrenia spectrum. Previous studies have also reported sex differences in schizotypal traits, response inhibition and inflammation response. Therefore, we proposed the following hypotheses:

1 Similar to schizophrenia, individuals with high levels of schizotypal traits would show longer SSRTs, more severe CM, and higher levels of hsCRP than individuals with low levels of schizotypal traits, and there would be associations between these variables (i.e., schizotypal traits, CM, SSRT and hsCRP).
2 Cognitive function would be affected by schizotypal traits, CM, and hsCRP, and these variables would predict SSRT. There would be interactions between CM and schizotypal traits, and between hsCRP and schizotypal traits on SSRT, and there would be sex differences in these effects.

## 2. Methods

### 2.1. Participants

A total of 1469 freshmen from two local universities responded to an initial survey questionnaire that included the Schizotypal Personality Questionnaire (SPQ) and the Childhood Trauma Questionnaire (CTQ). To minimize random responding, if three or more items of the questionnaire were unanswered, a participant was excluded from further analysis. A total of 1329 participants satisfied our inclusion requirement. The exclusive criteria were: (1) a history of physical illness; (2) a history of neurological disorders; (3) a history of substance abuse; (4) a history of head injury; and (5) a family history of psychiatric disorders. Participants were also excluded if they had a history of any psychotic disorders according to the Structured Clinical

Interview for DSM-IV Axis I Disorder (non-patient Edition). Participants with infectious diseases and autoimmune diseases were also excluded. According to Raine (1991), people scoring in the top 10% of the Schizotypal Personality Questionnaire (SPQ) can be considered as exhibiting schizotypal traits. Based on this criterion, 130 individuals with a SPQ score over 36 (cut-off for 10%) were classified as exhibiting schizotypal traits and 114 of them were randomly selected to form the high schizotypy group. At the same time, 100 participants who scored in the bottom 10th percentile of the entire sample on the SPQ were classified as the low schizotypy group. Both groups were invited to the laboratory for further testing, which included the SST and serum hsCRP testing. The average age of the participants was 18.86 ± 0.86 years. The average family income per person per month was RMB1,661.52 ± 1492.83. Seventy-one participants (31.0%) reported they were a single-child and 146 (63.76%) reported they were not a single-child, while 12 (5.24%) did not respond to this question. This study used a subsample of the participants from a previous study (Gong et al., 2017). The Ethics Committee of the Hunan University of Chinese Medicine approved the study. Written informed consent was obtained from all participants.

### 2.2. Psychometric measures

#### 2.2.1. Schizotypal traits

The SPQ is a self-report measure of schizotypal traits that consists of 74 items in a yes/no format. The item scores are combined to form a total score and nine subscale scores, which included: Constricted Affect, Excessive Social Anxiety, Ideas of Reference, No Close Friends, Odd Beliefs or Magical Thinking, Odd or Eccentric Behaviour, Odd Speech, Suspiciousness and Unusual Perceptual Experiences. The scale consists of three factors: Interpersonal Schizotypy (negative schizotypy), Cognitive-Perceptual Schizotypy (positive schizotypy), and Disorganized Schizotypy (Raine et al., 1994). A higher score on the SPQ indicates a higher level of schizotypal traits. The SPQ has been shown to have good reliability, validity and internal consistency across all three factors (Chen et al., 1997). In our sample, the Cronbach's alpha was 0.78, and 0.76 to 0.78 for the three factors respectively. Classification method for the high and low schizotypal traits groups have been described earlier.

#### 2.2.2. Childhood maltreatment

Exposure to early maltreatment was rated using the Childhood Trauma Questionnaire-Short Form (CTQ) (Bernstein et al., 2003), which is a 28-item retrospective self-report measure that assesses different forms of maltreatment: physical abuse (PA), physical neglect (PN), sexual abuse (SA), emotional abuse (EA), and emotional neglect (EN). Each subscale is composed of five items measured on a five-point scale (1 = never true; 5 = very often true), with scores ranging from 5 to 25. The total CTQ score is the sum of the scores of the five subscales, with scores ranging between 25 and 75. There are three additional items designed to detect responders' tendency to under-report or deny maltreatment (e.g., I had a perfect childhood). Two items of the PN subscale and five items of the EN subscale are reverse-coded. Previous studies in many countries have demonstrated that the CTQ has good validity and reliability (Bernstein et al., 2003; Gerdner and Allgulander, 2009). In our sample, the Cronbach's alpha for the whole scale was 0.78, and 0.79–0.80 for the five subscales.

#### 2.2.3. Stop signal task (SST)

The SST is a frequently used paradigm to investigate the neural correlates of response-inhibition deficits in healthy individuals and clinical populations (Logan et al., 1984). The participants performed a computerized stop-signal task based on the paradigm used by Tian et al., (2012), which consisted of 64 trials containing 48 "go" trials and 16 "stop" trials. Each trial started with the presentation of a white fixation cross displayed at the centre of a black background for 500 ms, followed by a 1500 ms "go" stimulus. For "go" trials, participants were instructed to press the J or F keys on the computer keyboard as quickly as possible in response to the letters O and X, which were presented with equal probability. For "stop" trials (randomly selected 25% of the trials), a visual "stop" signal (a white frame) appeared shortly after the "go" stimulus, requiring the participants to withhold their "go" response. The time interval between the "go" signal and the "stop" signal (the stop-signal delay; SSD) was determined by the percentage of "go" responses that were successfully inhibited. Reaction time (RT) on the "go" trials, and the time needed to inhibit a "go" response after the "stop" signal was presented (the stop-signal reaction time, SSRT), which was calculated by subtracting the SSD from the mean RT in "go" trials. SSRT, which is the speed of reacting to the "stop" signal, is the most important index of the SST, with longer SSRTs indicating poorer response inhibition (Logan et al., 1984).

#### 2.2.4. Serum level of hsCRP

Five ml of venous blood was drawn into EDTA tubes from all participants in the morning in the fasting state. The blood specimens were centrifuged at 4000 rpm for 10 min and the separated sera were extracted into small tubes and stored at −80 °C. Serum hsCRP levels were measured in all subjects on the same day. A code number was utilized to identify all participants until all biochemical analysiss were completed. Plasma levels of hsCRP were measured by a Cusabio ELISA Kit (Bersinbio, InC., Guangzhou, China).

### 2.3. Statistical analyses

All analyses were performed with SPSS version 22 with the significance level set at $p < 0.05$. Descriptive statistics were used to illustrate the characteristics of the participants, with continuous variables presented as means and standard deviations. In order to examine sex differences in these effects, Pearson correlations were calculated to test the relationships among schizotypal traits, CM, hsCRP and SSRT in male and female participants separately. Hierarchical regression analysis was conducted to examine the predictive strength of hsCRP, schizotypal traits and CM on SSRT in Model 1. We further tested the interactions between schizotypal traits and CM, as well as schizotypal traits and hsCRP on SSRT in Model 2.

## 3. Results

### 3.1. Sample characteristics

Table 1 shows the mean scores and standard deviations of the two groups on the SST, CTQ and SPQ. The high schizotypal traits group had higher total and subscale scores on the SPQ, compared with the low schizotypal traits group. They also reported more emotional abuse and sexual abuse on the CTQ, had higher levels of hsCRP, and longer SSRTs. In the high schizotypal traits group, male participants reported more severe sexual abuse and emotional neglect than female participants, but there was no significant sex difference on the SPQ total and subscale scores, hsCRP level and response inhibition.

### 3.2. Sex differences for the correlations between SSRT, hsCRP, schizotypal traits and CM in the entire sample

Correlation analyses showed that in female participants, SSRT was positively correlated with scores on the positive SPQ factor($P < 0.01$) and the disorganized SPQ factor ($P < 0.05$) and positively correlated with physical neglect ($P < 0.05$). Serum hsCRP level was positively correlated with scores on the positive SPQ factor and negative SPQ factor ($Ps < 0.05$). Emotional abuse was positively correlated with all three SPQ factors (all $p$-values $< 0.01$). The positive SPQ factor was positively correlated with sexual abuse ($P < 0.01$), physical abuse ($P < 0.01$) and physical neglect ($P < 0.05$) (see Table 2). In male

**Table 1**
Mean scores (and standard deviations) of the two groups on the study variables.

| | High schizotypy group Male ($n$ = 38) | Female ($n$ = 76) | $P$ | Low schizotypy group Male ($n$ = 33) | Female ($n$ = 67) | $P$ | $p$ |
|---|---|---|---|---|---|---|---|
| Age | 18.84(0.92) | 18.66(0.74) | *NS* | 18.88(0.99) | 19.10(0.82) | *NS* | 0.008 |
| Family income | 1679.39(1810.12) | 1642.67(1322.52) | *NS* | 1928.33(1331.61) | 1648.25(1665.05) | *NS* | 0.682 |
| SPQ_total | 46.26(6.38) | 45.61(7.92) | *NS* | 20.24(7.90) | 20.07(7.63) | *NS* | < 0.001 |
| SPQ_pos | 20.18(4.88) | 19.67(5.02) | *NS* | 8.42(3.16) | 9.91(4.56) | *NS* | < 0.001 |
| SPQ_neg | 18.95(4.75) | 19.78(5.08) | *NS* | 8.51(5.00) | 7.21(4.21) | *NS* | < 0.001 |
| SPQ_dis | 11.13(2.38) | 10.83(2.70) | *NS* | 4.82(2.52) | 4.31(2.64) | *NS* | < 0.001 |
| CTQ_total | 45.74(12.02) | 40.45(11.12) | 0.022 | 38.24(9.70) | 38.73(11.10) | *NS* | 0.018 |
| EA | 9.29(3.06) | 9.22(3.16) | *NS* | 7.12(2.47) | 7.58(2.70) | *NS* | < 0.001 |
| PA | 7.26(2.63) | 6.49(2.66) | *NS* | 6.97(2.31) | 6.12(2.00) | *NS* | 0.300 |
| SA | 7.16(2.83) | 6.08(1.88) | 0.017 | 5.52(1.09) | 5.87(1.82) | *NS* | 0.013 |
| EN | 12.87(5.36) | 10.30(4.12) | 0.006 | 9.85(4.53) | 10.84(4.71) | *NS* | 0.314 |
| PN | 9.16(3.01) | 8.47(3.49) | *NS* | 8.42(3.19) | 8.33(3.47) | *NS* | 0.458 |
| SSRT_CC | | | | | | | |
| SSRT_RT | 250.34(72.90) | 265.92(58.92) | *NS* | 241.48(53.23) | 242.09(56.21) | *NS* | 0.023 |
| hsCRP | 26.10(26.07) | 36.99(34.81) | *NS* | 27.90(17.13) | 25.00(17.26) | *NS* | 0.042 |

*Note:* SPQ = Schizotypy Personality Questionnaire, SPQ_pos = SPQ_positive factor, SPQ_neg = SPQ_negative factor, SPQ_dis = SPQ_disorganization factor, EA = emotional abuse, PA = physical abuse, SA = sexual abuse, EN = emotional neglect, PN = physical neglect, hsCRP = High sensitivity C-reactive protein, SSRT = stop-signal reaction time.

participants, SSRT was negatively correlated with emotional neglect ($P < 0.01$) and physical neglect ($P < 0.05$). Emotional abuse, emotional neglect and physical neglect were positively correlated with all the three SPQ subscales. Sexual abuse was positively correlated with the positive SPQ factor and the disorganized SPQ factor (see Table 3).

### *3.3. Hierarchical regression model of emotional neglect, positive schizotypy and hsCRP in predicting SSRT in female participants*

According to our correlation analysis, in female participants, the positive SPQ factor, the disorganized SPQ factor and physical neglect were correlated with SSRT. Although hsCRP was not correlated with SSRT, hsCRP is an important research variable for this study. Thus hsCRP was also included. Hierarchical regression analysis was conducted to examine the effects of hsCRP, the positive SPQ factor, the disorganized SPQ factor, and physical neglect on SSRT. The ppositive SPQ factor and the disorganized SPQ factor were the dependent variables, physical neglect and hsCRP were the moderator variables, and SSRT was the independent variable. Model 1 of the regression analysis included physical neglect, the positive SPQ factor, the disorganized SPQ factor and serum hsCRP level. We found that hsCRP negatively predicted SSRT ($\beta = -0.7$, $P = 0.029$). Based on Model 1, Model 2 tested the interactions between the positive SPQ factor and physical neglect, between the positive SPQ factor and hsCRP, the disorganized SPQ factor and physical neglect, and between the disorganized SPQ factor and hsCRP on SSRT. We found that the interaction between the positive SPQ factor and hsCRP on SSRT was significant ($P = 0.046$) (see Table 4).

## 4. Discussion

To the best of our knowledge, this is the first study examining the interactions between hsCRP, childhood maltreatment and schizotypy on response inhibition. There were two main findings in this study. First, consistent with our hypotheses and the findings of Ettinger et al. (2017) that schizotypy is correlated with inhibitory performance across a number of tasks, individuals with high levels of schizotypal traits in the present study showed longer SSRT on the SST, which indicates that executive function is impaired in individuals with high levels of schizotypal traits (Ettinger et al., 2015; Giakoumaki, 2012). Generally, poor inhibitory control, as indicated by a longer SSRT, has been found in patients with schizophrenia (Bellgrove et al., 2006; Enticott et al., 2008; Ettinger et al., 2017; Hughes et al., 2012) and children at-risk of developing schizophrenia (Davalos et al., 2004). Our results provide further evidence for an impairment in response inhibition in individuals with schizotypal traits, which supports the idea that inhibitory dysfunction may be an endophenotype of schizophrenia spectrum disorders (Gottesman and Gould, 2003).

The second main finding is that sex difference was demonstrated in the effect of schizotypy, childhood maltreatment and hsCRP on

**Table 2**
Pearson correlations between the SPQ scores, CTQ scores, SSRT, and hsCRP in female participants ($n$ = 143).

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| 1.SSRT | 1 | | | | | | | | | |
| 2.SPQ_pos | 0.242** | 1 | | | | | | | | |
| 3.SPQ_neg | 0.139 | 0.669** | 1 | | | | | | | |
| 4.SPQ_dis | 0.167* | 0.666** | 0.756** | 1 | | | | | | |
| 5.EA | 0.073 | 0.345** | 0.258** | 0.304** | 1 | | | | | |
| 6.PA | 0.017 | 0.257** | 0.061 | 0.071 | 0.555** | 1 | | | | |
| 7.SA | 0.093 | 0.278** | 0.121 | 0.054 | 0.330** | 0.361** | 1 | | | |
| 8.EN | 0.002 | −0.041 | 0.034 | −0.008 | 0.462** | 0.362** | 0.216** | 1 | | |
| 9.PN | 0.167* | 0.187* | 0.094 | 0.081 | 0.560** | 0.345** | 0.129 | 0.539** | 1 | |
| 10.hsCRP | −0.029 | 0.192* | 0.174* | 0.129 | 0.093 | 0.051 | 0.003 | 0.043 | 0.064 | 1 |

*Note.* SPQ = Schizotypy Personality Questionnaire, SPQ_pos = SPQ_positive factor, SPQ_neg = SPQ_negative factor, SPQ_dis = SPQ_disorganization factor, EA = emotional abuse, PA = physical abuse, SA = sexual abuse, EN = emotional neglect, PN = physical neglect, hsCRP = High sensitivity C-reactive protein, SSRT = stop-signal reaction time.

* $p < 0.05$.

** $p < 0.01$.

**Table 3**
Pearson correlations between the SPQ scores, CTQ scores, SSRT, and hsCRP in male participants ($n$ = 71).

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| 1.SSRT | 1 | | | | | | | | | |
| 2.SPQ_pos | 0.07 | 1 | | | | | | | | |
| 3.SPQ_neg | 0.041 | 0.648** | 1 | | | | | | | |
| 4.SPQ_dis | −0.032 | 0.778** | 0.734** | 1 | | | | | | |
| 5.EA | −0.171 | 0.390** | 0.455** | 0.408** | 1 | | | | | |
| 6.PA | −0.126 | 0.173 | 0.108 | 0.112 | 0.469** | 1 | | | | |
| 7.SA | −0.124 | 0.343** | 0.194 | 0.281* | 0.456** | 0.542** | 1 | | | |
| 8.EN | −0.324** | 0.369** | 0.542** | 0.375** | 0.431** | 0.353** | 0.234* | 1 | | |
| 9.PN | −0.246* | 0.261* | 0.331** | 0.289* | 0.295* | 0.311** | 0.101 | 0.614** | 1 | |
| 10.hsCRP | 0.113 | −0.072 | 0.02 | −0.031 | −0.081 | −0.092 | 0.028 | −0.19 | −0.126 | 1 |

*Note.* SPQ = Schizotypy Personality Questionnaire, SPQ_pos = SPQ_positive factor, SPQ_neg = SPQ_negative factor, SPQ_dis = SPQ_disorganization factor, EA = emotional abuse, PA = physical abuse, SA = sexual abuse, EN = emotional neglect, PN = physical neglect, hsCRP = High sensitivity C-reactive protein, SSRT = stop-signal reaction time.

* $p < 0.05$.

** $p < 0.01$.

**Table 4**
Hierarchical regression model predicting SSRT from physical neglect, positive schizotypy factor, disorganized schizotypy factor and hsCRP in female participants.

| | Unstandardized coefficients | | Standardized coefficients | $t$ | Sig. |
|---|---|---|---|---|---|
| | B | Std. Error | Beta | | |
| (Constant) | 223.637 | 37.447 | | 5.972 | 0.000 |
| SPQ_pos | −1.175 | 2.931 | −0.137 | −0.401 | 0.689 |
| SPQ_dis | 5.067 | 4.537 | 0.364 | 1.117 | 0.266 |
| PN | 5.238 | 4.004 | 0.310 | 1.308 | 0.193 |
| hsCRP | −1.535 | 0.652 | −0.747 | −2.356 | 0.020 |
| SPQ_pos* PN | 0.106 | 0.317 | 0.167 | 0.334 | 0.739 |
| SPQ_pos*hsCRP | 0.073 | 0.035 | 0.763 | 2.084 | 0.039 |
| SPQ_dis*PN | −0.579 | 0.481 | −0.489 | −1.203 | 0.231 |
| SPQ_dis*hsCRP | 0.003 | 0.059 | 0.016 | 0.053 | 0.958 |

*Note:* SPQ = Schizotypy Personality Questionnaire, SPQ_pos = SPQ_positive factor, SPQ_dis = SPQ_disorganization factor, PN = physical neglect, hsCRP = high sensitivity C-reactive.

response inhibition. Our correlation analyses showed that in female participants, SSRT was significantly correlated with positive schizotypal traits and disorganized schizotypal traits, but not with negative schizotypal traits. This is consistent with reduced controlled processes (Neill et al., 2014; Stefaniak et al., 2015) in positive schizotypy and higher level of automatic processes. This result is also supported by studies by Bullen and Hemsley (1987) and Steel et al. (2002), in which inhibition was associated with scores on scales measuring a predisposition for hallucinations, like the Unusual Perceptual Experiences subscale of the SPQ, which measures positive schizotypy. This association of "inhibitory" information processing with positive schizotypy provides support for Hemsley (1994)'s observation that positive schizotypy predicts the inhibitory effects of contextual cues on RTs. Previous studies (Barneveld et al., 2013; Bullen and Hemsley, 1987; Peters et al., 1994; Steel et al., 2002) have reported that performances on cognitive tasks, which appears to be governed by contextually driven inhibitory processing, are commonly associated with measures of positive schizotypy and disorganized schizotypy (Gooding et al., 2001). Disorganized schizotypy may serve as a marker for cognitive control problems in people at genetic risk of developing schizophrenia (MacDonald et al., 2003), and in schizophrenia, disorganization symptoms have been strongly and consistently associated with poor cognitive control (Cohen et al., 1999; Kerns and Berenbaum, 2002, 2003). Although the relationship between negative symptoms and impairment in multiple cognitive domains has been one of the clearest findings in studies of schizophrenia (Li et al., 2018), we did not observe any correlations between SSRT and negative symptoms in both female and male participants. Furthermore, consistent with previous studies showing gender differences in cognitive function associated with schizotypal symptoms in healthy college students (Gruzelier, 1994; Lubow and De la Casa, 2002; Lubow et al., 2001), the present study also found positive symptoms and disorganized symptoms were associated with SSRT in female participants, while no any significant correlations between all SPQ factors and SSRT in male participants.

Contrary to previous studies in which poor cognitive function was found in adults with childhood physical neglect and emotional abuse (Majer et al., 2010) and adolescents with childhood physical abuse/neglect (Spann et al., 2012), we found a significant negative correlation between SSRT and physical neglect in our female participants, and between SSRT and emotional neglect and physical neglect in our male participants. This result suggests that severe emotional and physical neglect may be associated with better response inhibition on the SST, which may be suggestive of a resilience factor. Similarly, several studies have reported that experiencing childhood physical or sexual abuse is associated with better cognitive functioning in some domains (Feeney et al., 2013) or a lower risk of cognitive impairment (Ritchie et al., 2011). In the present study, the majority of associations between CTQ variables and SPQ variables were significant, which is consistent with the results of previous studies (Gong et al., 2017; Sheinbaum et al., 2015; Varese et al., 2012; Velikonja et al., 2015), suggesting that childhood adversity is associated with the development of clinical and subclinical psychotic symptoms.

The serum level of hsCRP in individuals with high level of schizotypy in our study was higher than the hsCRP level in individuals with low level of schizotypy, and correlation analyses showed that hsCRP level was positively correlated with negative and positive schizotypal traits in female participants, but not with SSRT or any type of childhood trauma. This finding is similar to the results of several studies that focused on the positive association between CRP levels and clinical characteristics in schizophrenia. Two studies in particular reported that CRP level is positively correlated with the severity of negative symptoms (Fawzi et al., 2011; Garcia-Rizo et al., 2012). A possible explanation for the lack of association between hsCRP and SSRT is that the biomarker was not measured at the same time as the SST, but six to eight months apart, during which CRP levels might have fluctuated. Contrary to previous studies (Baumeister et al., 2016; Coelho et al., 2014; Danese et al., 2007), we did not find any associations between hsCRP level and various types of childhood trauma, which may be due to the small number of cases with severe childhood maltreatment in our sample.

Previous studies have demonstrated the effects of schizotypy and elevated levels of hsCRP on inhibitory performance. However, no study has explored whether there is an interaction between schizotypy and hsCRP level on response inhibition. We found an interaction between

positive schizotypy and hsCRP level on SSRT in our female participants, suggesting that positive schizotypy in conjunction with an elevated level of hsCRP may produce poorer response inhibition. However, the mechanisms underlying these results need to be explored further. It is possible that schizotypy and hsCRP (a marker of inflammation) are both markers for schizophrenia (Zheng and Xie, 2017) such that individuals with positive schizotypy and higher levels of hsCRP may have a greater risk for schizophrenia, manifesting as more severe inhibition deficits.

In conclusion, this is the first study that demonstrates sex difference in the interaction between positive schizotypy and hsCRP on response inhibition. However, our results should be interpreted in the context of several limitations. First, hsCRP measurement and the stop signal task were not administered at the same time. However, the inclusion of the time of blood sampling into the model did not improve the model or change the findings. Secondly, we relied on the CTQ, which is a retrospective questionnaire, to assess childhood maltreatment. Although retrospective designs have been found to be valid and reliable sources for collecting information about childhood experiences in patients with severe mental disorders, data from retrospective designs are always subject to recall bias. In addition, neuroticism may be linked to this recall bias regarding the retrospective assessment of childhood maltreatment, and neuroticism has been shown to exhibit considerable variance with the SPQ (Gross et al., 2014). Future studies should consider the potential effect of neuroticism. Thirdly, this was a cross-sectional study and as such we were unable to ascertain whether the relationship among the study variables were causal or not. Future longitudinal studies could help to better determine the causal relationship between response inhibition and inflammatory markers and the developmental course of schizotypy.

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2019.02.064.

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