



Role of hippocampus and orbitofrontal cortex in the association of interdependent self-construal with an acute stress response

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ABSTRACT

Empirical evidence indicates that high interdependent self-construal (InterSC) is correlated with exaggerated acute stress responses; however, the underlying neural correlates remain unclear. Considering the regulatory effect of the prefrontal cortex and limbic system on the acute stress response, the primary aim of this study was to investigate the role of the orbitofrontal cortex (OFC) and hippocampus (HIP) in the relationship between InterSC and acute stress responses. Forty-eight healthy college students underwent a modified version of the Montreal imaging stress task (MIST), while brain activity was recorded using functional magnetic resonance imaging (fMRI). Participants' saliva samples and subjective stress feelings were collected before, during, and after the MIST. Additionally, participants' self-construal was measured using questionnaires. Results revealed that InterSC was positively correlated with the activation of OFC, which, in turn, was associated with higher subjective stress feelings. A higher InterSC was also significantly associated with an enhanced salivary cortisol response in those with lower HIP activity. Furthermore, the HIP moderated the indirect effect of InterSC on subjective stress feelings by moderating the effect of InterSC on neural activity in the OFC. This indicated the mediation of the OFC was stronger in those with higher neural activity in the HIP than in those with lower activity in the HIP. In summary, the current study proposed an important role of the OFC-HIP regions in the relationship between InterSC and acute stress responses, making contribution to broadening the field of personality and stress and deepening our understanding of individual differences in acute stress responses.

1. Introduction

Stress is ubiquitous in our lives and is often accompanied by threats from social evaluation and uncontrollability (Dickerson and Kemeny, 2004; Gunnar and Quevedo, 2007). Any physical or psychological stimulus that exceeds a certain intensity triggers a systemic stress response (Dickerson and Kemeny, 2004). This mainly includes psychological responses such as subjective stress feelings and negative emotions, as well as physiological responses such as increased cortisol concentration, heart rate, and blood pressure (Hellhammer et al., 2009; von Dawans et al., 2021).

Although stress occurs all the time in life, there are significant inter-individual differences in acute stress responses (Kalinichenko et al., 2019; McEwen, 1998). Recent studies suggest that, a personality trait, self-construal, is closely associated with acute stress responses (Cross, 1995; Tsai et al., 2016). Self-construal is jointly shaped by culture and

social environment (Church, 1987; Markus and Kitayama, 1991), and is typically defined as how the individual sees himself in relation to others and how they create meanings for the self (Cousins, 1989; Cross et al., 2011). Specifically, self-construal is divided into interdependent self-construal (InterSC) and independent self-construal (IndeSC). InterSC emphasizes the connection between the individual and others, whereas IndeSC emphasizes individual uniqueness. The main difference between them lies in the relationship between self and others, that is, in the definition of self from the perspective of "I" or "we" (Markus and Kitayama, 1991; Cross et al., 2011).

Previous evidence suggests that InterSC is correlated with exaggerated acute stress responses. For example, studies have revealed that InterSC levels are positively correlated with stress levels among East Asian students (Cross, 1995; Okuno and Kobayashi, 2007). Similarly, some studies found that individuals with higher InterSC levels showed higher subjective stress feelings and greater salivary cortisol responses

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during acute stress than individuals with lower InterSC levels (Hu et al., 2018; Hu et al., 2019). Interestingly, He et al. (2021) suggested that individuals with high InterSC show a more effective stress response pattern than those with low InterSC, manifested by fast stress reactivity and rapid recovery. Additionally, compared with self-support priming, individuals with high InterSC provided with social support present lower cortisol responses (Ren et al., 2019). Furthermore, those with high InterSC levels who solicit a high level of instrumental support are predicted to have slightly greater diastolic blood pressure reactivity and faster recovery in acute stress (Lee et al., 2015). In general, these studies indicate that InterSC is an important personality trait that influences acute stress responses.

The brain is the core organ involved in stress responses (McEwen, 2007; Qiu et al., 2022), especially, the prefrontal lobe and limbic system (Lupien et al., 2009; Ulrich-Lai and Herman, 2009). Although it has been suggested that InterSC is associated with acute stress responses, the underlying neural correlates remain unclear. Therefore, this study aimed to investigate the possible roles of the limbic system and prefrontal cortex in the relationship between InterSC and individual acute stress responses.

Previous studies have revealed that the frontal lobe (e.g., the orbitofrontal cortex [OFC]) plays an important role in regulating emotional processing and cognitive assessment, and also affects acute stress responses (Davidson, 2000; Goldin et al., 2008; Rolls, 2019). For example, Seo et al. (2011) revealed that a higher activation of the OFC predicts stronger subjective stress feelings in acute stress conditions. Another study showed that a smaller volume of the OFC was associated with greater subjective stress feelings (Ansell et al., 2012). These studies suggested an important role of the OFC in experience of subjective stress feelings. Meanwhile, previous studies have shown that individuals with higher InterSC exhibit greater subjective stress feelings (Hu et al., 2018; He et al., 2021). Considering the aforementioned role of the OFC on subjective stress feelings, we speculated that OFC activation during acute stress would regulate the relationship between InterSC and subjective stress feelings. Taken together, we hypothesized that InterSC might be linked to subjective stress feelings through the regulatory effect of the OFC on emotional processing and cognitive assessment.

In addition to the prefrontal cortex, the limbic system, especially the hippocampus (HIP), is an important brain region that regulates stress responses through negative feedback regulation of the hypothalamus-pituitary-adrenal (HPA) axis (Herman et al., 2005; Lupien et al., 2009). Weak activation of the HIP reflects a decreased negative feedback regulation on the HPA axis, which allows quick secretion of cortisol (Lupien et al., 2009; Herman et al., 2016; Seo et al., 2019), and mobilization of physical and mental resources to efficiently cope with acute stress situations (Habib et al., 2001; Kim et al., 2015; Pruessner et al., 2010). In contrast, strong activation of the HIP indicates an increased negative feedback regulation on the HPA axis and further inhibits the secretion of cortisol, which helps prevent cortisol from being kept at a high concentration for a long time and promotes individual physical and mental health (Abercrombie et al., 2006; Dickerson and Kemeny, 2004). Previous studies revealed that higher InterSC was associated with a higher cortisol response (Hu et al., 2018; He et al., 2021). Considering the aforementioned role of the HIP on cortisol response, we cautiously speculated that higher activation of the HIP would inhibit cortisol response through its negative feedback regulation on the HPA axis. Further, we hypothesized that higher InterSC might be associated with stronger cortisol response among those individuals with low activation of the HIP.

Additionally, many researchers have demonstrated that the prefrontal cortex and HIP are interconnected and influence each other via direct and indirect neural activity (McEwen, 2007). For example, both the OFC and HIP work together to mediate the responses to stressful experiences and are associated with impaired cognition and emotion during stress (Feng et al., 2022). In addition, the OFC interacts with the HIP during the storage of long-term memories (Ramus et al., 2007), and

the HIP may participate in regulating the cognition and emotion of acute stressors by supporting memory retrieval (Andrews et al., 2013; Goldfarb et al., 2020). Moreover, previous studies suggested that the HIP could change stress reactions by generalizing from prior stressful contexts and increasing reliance on habitual coping strategies (Goldfarb and Phelps, 2017; McEwen, 1998), which might further affect neural activity in the OFC (Feng et al., 2022; McEwen, 2007). Meanwhile, those with high InterSC levels tends to pay more attention to the surrounding environment and interpersonal relationships with others and is more sensitive to social evaluations and threat information in the environment (Church, 1987; Cross et al., 2011). Considering the role of OFC in emotional processing and cognitive assessment (Rolls, 2019), we speculated that the HIP and InterSC might contribute together to neural activity in the OFC. Taken together, we hypothesized that there would be an interaction effect between InterSC and the HIP on the neural activity in the OFC, and a further link to subjective stress feelings.

In summary, the purpose of this study was to explore the possible role of the OFC and HIP in the relationship between the InterSC and individual acute stress responses. Three neural models were proposed: a) InterSC would be associated with subjective stress feelings through its connection with the OFC (Fig. 1A); b) neural activity in the HIP would moderate the association between InterSC and cortisol response (Fig. 1B); c) neural activity in the HIP would moderate the indirect effect of InterSC on subjective stress feelings through its moderation of the effect of InterSC on the OFC (Fig. 1C).

2. Material and methods

2.1. Participants

To confirm the sample size required for this study, we used G*power and set a medium effect size (0.15) to identify the interaction effect with $\alpha = 0.05$, and power $(1-\beta) = 0.8$ (Faul et al., 2009), and the sample size was determined to be $n = 33$. In this study, 48 healthy Chinese college students were recruited through online advertisements. Four participants were excluded because of excessive head movement during fMRI (mean FD > 2 SD) (Yan et al., 2013) or missing data (lack or insufficient volume of saliva), and the final sample consisted of 44 participants (21 males; mean [SD] age = 19.07 [1.11] years). Based on self-reports, all women were in the luteal phase, and all participants reported no mental health diagnoses or drug and alcohol abuse. Participants were asked not to eat or exercise strenuously for 1 h before the experiment. This study was approved by the Research Ethics Board of Southwest University, China, and all the participants provided written informed consent.

2.2. Outcome measures

2.2.1. Self-construal scale

Self-construal was measured using the self-construal scale (Singelis, 1994), which includes 24 items and employs a 7-point Likert scale ranging from 1 (strongly disagree) to 7 (strongly agree). Half of items were used to measure InterSC, for instance, "My happiness depends on the happiness of those around me". Rest of the items were used to measure IndeSC, for instance, "I do my own thing, regardless of what others think". Li et al. (2006) translated the self-construal scale into Chinese and it has been shown to exhibit acceptable psychometric properties when tested on Chinese populations (Wang and Wang, 2016). In the current study, Cronbach's alpha coefficients were 0.778 for InterSC, 0.628 for IndeSC, and 0.765 for the total scale. These two dimensions were scored separately, and according to the suggested methods (Chiao et al., 2010; Ma et al., 2014), InterSC was defined as the sum score of interdependent items minus the sum score of independent items. Higher score indicates a stronger tendency toward interdependence than independence.

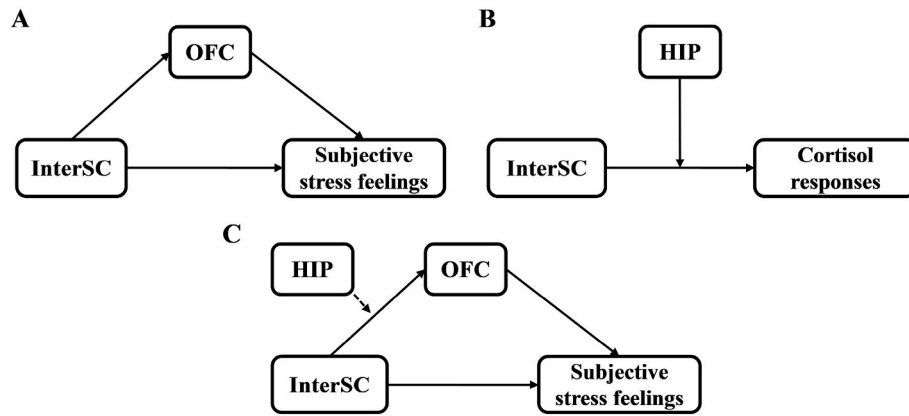


Fig. 1. Visualization of three neural models. Note. InterSC = Interdependent self-construal; OFC = Orbitofrontal cortex; HIP = Hippocampus.

2.2.2. The Montreal Imaging Stress Task

Participants completed a modified version of the Montreal imaging stress task (MIST) (Dedovic et al., 2005). Details of the MIST have been

elaborated in a previous article (Ren et al., 2022). Briefly, a block design consisting of three imaging runs was adopted for the MIST. Each run consisted of two conditions: a stressful experimental condition and a

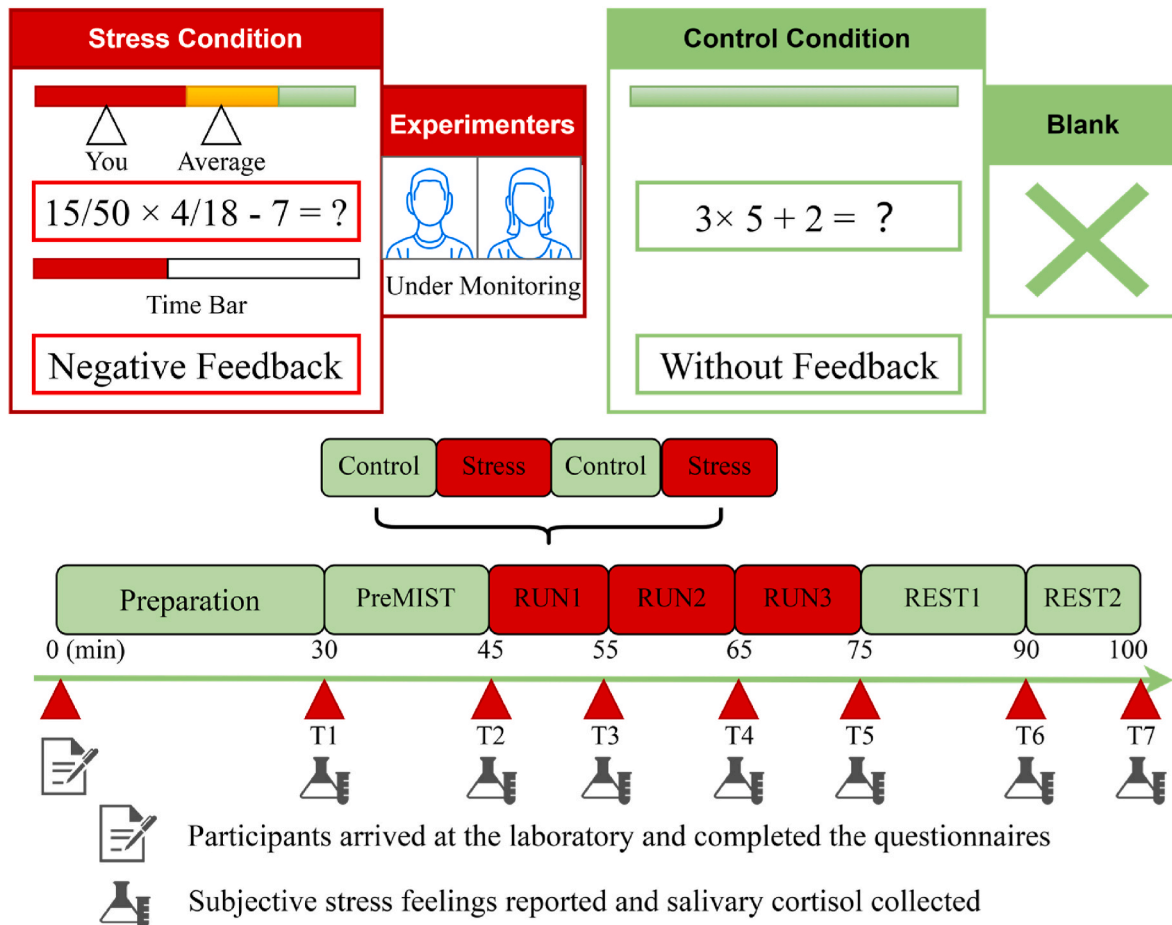


Fig. 2. Visualization of The MIST paradigm and experimental procedure.

(A) In stress condition, participants were asked to complete difficult mathematical operations within the time limit, which was manifested by a visible progress bar (generally, the fastest speed is selected), and this process was monitored and evaluated by the experimenter. The correct answer rate was maintained at around 20 to 45 percent through automated monitoring with MIST, moreover, participants were provided with negative verbal feedback via headphones between each run. To increase participants' feelings of being socially evaluated, the original MIST was modified by creating a monitoring screen with the image of a strict evaluator's face under the stress condition. (B) In control condition, participants needed to answer simple arithmetic questions without a time limit and they would not receive any feedback on their performance, they would not be monitored, too. (C) An overview of experimental procedure, at the end of each run, the experimenter provided a saliva tube to the participant to collect saliva samples, participants put the tube in their mouth and chewed for about 50 s. Subjective stress feelings were assessed by oral reports via the microphone in the scanner, just after the saliva sample collection. MIST = Montreal Imaging Stress Task.

nonstressful control condition. In the stress condition, participants were asked to complete a difficult mathematical task accompanied by a social evaluative threat and uncontrollability (Fig. 2A), whereas in the control condition, participants were required to complete a simple task without any social evaluative threat and uncontrollability (Fig. 2B). The stress and control conditions in each run were repeated once (sequence: control-stress-control-stress, 70 s for the control condition, and 140 s for the stress condition). Notably, the stress task lasted twice as long as the control task, which could have generated a relatively strong stress effect. Because of the experimental program setting, when one condition ended, the experimenter had to click a “continue button” to jump to the next condition. To avoid unnecessary confusion, we set aside time that distinguish the “continue button” click trials with other trials, and name it as the blank condition. Specifically, there were 16 s for the blank condition per run.

2.2.3. Procedure

The experiment lasted for approximately 100 min and was conducted between 1:30 p.m. and 5:00 p.m. to control for the cortisol circadian rhythm (Fig. 2C). After the participants arrived at the laboratory, they were allowed 30 min to rest and complete the questionnaires. Subsequently, the participants entered the scanner and the task was begun. During the entire experiment, salivary cortisol and subjective stress feeling data were collected seven times (T1–T7): T1 called “Preparation” was collected immediately before participants entered the scanner; T2 called “PreMIST” was collected after the resting-state fMRI and T1 image acquisition; T3 called “Run1” was collected after the first run; T4 called “Run2” was collected after the second run; T5 called “Run3” was collected after the third run; T6 called “Rest1” was collected after a 15-min rest in the scanner; and T7 called “Rest2” was collected after another 10 min rest outside the scanner. Data on cortisol and subjective stress feelings were simultaneously collected.

2.3. Data collection and analyses

2.3.1. Subjective stress feelings

Participants’ subjective stress feelings (SS) were used to present the psychological responses, which were evaluated by a one-item question about “Rate your feeling of stress on a 7-point Likert scale ranging from 1 (not stressful) to 7 (terribly stressful) ”.

2.3.2. Salivary cortisol

Salivary cortisol was used to present physiological responses, and saliva samples were collected with a specific sampling device (Salivette; SARSTEDT, Nümbrecht, Germany) to assess cortisol levels during the experiment. Briefly, as soon as the experiment was completed, the saliva samples were stored in a -20°C refrigerator for subsequent analysis and an enzyme-linked immunosorbent assay (ELISA; IBL, Hamburg, Germany) was used to analyze the cortisol concentrations, following the manufacturer’s instructions. The results indicated that the sensitivity of the cortisol assay was $0.005\ \mu\text{g}/\text{dL}$, and the inter-assay and intra-assay coefficients of variation for the cortisol assay were 3.2% and 6.1%, respectively. In particular, the area under the curve with respect to ground (AUC_g) and with respect to increases (AUC_i) in these data (including SS and cortisol response) were calculated to reflect the level of acute stress responses (Pruessner et al., 2003).

2.3.3. fMRI data acquisition and preprocessing

All fMRI data were acquired using a 3 T Siemens Trio MRI scanner. A total of 218 vol of functional images were acquired from each participant using a T2*-weighted gradient-echo-planar imaging sequence. Thirty-two echo-planar images per volume sensitive to blood oxygenation level-dependent contrast were acquired (repetition time [TR] = 2000 ms; echo time [TE] = 30 ms; 64×64 matrix with $3 \times 3 \times 3\ \text{mm}^3$ spatial resolution; field of view [FOV] = $192 \times 192\ \text{mm}^2$). High-resolution T1-weighted three-dimensional fast-field echo sequences

were obtained for anatomical reference (176 slices; TR = 1900 ms; TE = 2.52 ms; slice thickness = 1 mm; FOV = $256\ \text{mm} \times 256\ \text{mm}$; voxel size = $1\ \text{mm} \times 1\ \text{mm} \times 1\ \text{mm}$).

All preprocessing was performed using the Data Processing & Analysis for (Resting-State) Brain Imaging software toolbox (Yan et al., 2016). The preprocessing steps included removing the first five volumes, slice timing, and realigning images to the first image of the task to correct for head motion. Structural images were coregistered to the mean functional image after realignment and subsequently segmented into gray matter, white matter, and cerebral spinal fluid (Ashburner and Friston, 2005). The DARTEL tool (Ashburner, 2007) was used to compute transformations from individual native space to the Montreal Neurological Institute (MNI) space, and normalized to the standard T1 MNI template image with a voxel size of $3 \times 3 \times 3\ \text{mm}^3$ to remove the nuisance signals. The images were subsequently smoothed with a 6 mm full-width-half-maximum Gaussian kernel.

2.3.4. fMRI data analysis

The preprocessed data were analyzed using SPM12 software (Statistical Parametric Mapping Software, SPM; Wellcome Department of Imaging Neuroscience, London, United Kingdom; <http://www.fil.ion.ucl.ac.uk>). A First-level general linear model incorporating the three conditions (a stress, control, and blank) was built and convolved with the canonical hemodynamic response function and six movement parameters as covariates of non-interest. A high-pass temporal filter with a cut-off period of 256 s was applied (Zschucke et al., 2015). Second-level analyses were conducted using random effects models to assess any stress effects (stress versus control). The contrast image of the stress condition versus the control condition was obtained using a one-sample *t*-test. To generate a clear result, a relatively strict correction of 2-tailed voxel-level false discovery rate (FDR) corrected ($p < .05$) was adopted, consistent with previous acute stress-related studies (Dahm et al., 2017; Lederbogen et al., 2011).

Region-of-interest (ROI) analyses were conducted to investigate the role of brain activity in the contrast of stress versus control condition in the effects of InterSC on the acute stress response (including subjective stress and cortisol response). Based on the existing literature on acute stress, ROIs with a radius of 6 mm centered at the OFC (MNI coordinates: 51/28/-11) (Seo et al., 2011) and HIP (MNI coordinates: $-24/-13/-17$) (Corr et al., 2021) were chosen to explore the underlying neural activity on the relationship between InterSC and acute stress response. The level of activation in the two ROIs under the Stress > Control contrast were extracted for subsequent analyses.

2.4. Statistical analysis

To test the validation of the stress induction, repeated analysis of variance with time as a within-subject variable was used to analyze both SS and cortisol responses. To explore the relationship between InterSC and stress response, the Pearson correlation between InterSC and acute stress responses (including SS and cortisol responses, and neural activity) was conducted, besides, data from the peak point of SS and cortisol responses were also include in the correlation analysis. Further, to test our hypothesis, we used a mediation model using InterSC as the independent variable, activation of the OFC as the mediation variable, and SS as the dependent variable. Similarly, a moderation model was developed using InterSC as the independent variable, activation of the HIP as the moderation variable, and cortisol response as the dependent variable. In addition, we built a moderated mediation model to test the last hypothesis, using InterSC as the independent variable, activation of the OFC as the mediation variable, activation of the HIP as the moderation variable between InterSC and activation of the OFC, and SS as the dependent variable. Both in the moderation model and in the moderated mediation model, the low, medium, and high HIP activity indicates 1 Standard deviation (SD) below the mean, the mean, and 1 SD above the mean HIP activity, respectively. Data were analyzed using SPSS Macro-

PROCESS (Bolin, 2014).

3. Results

3.1. Acute stress response

The participants' SS and salivary cortisol responses (COR) during the MIST are shown in Fig. 3A. Repeated analysis of variance with time as a within-subject variable was conducted for SS and COR. The results revealed a significant effect of time on SS ($F(6,258) = 78.12, p < .001, \eta_p^2 = 0.64$) and the post-hoc analysis revealed that participants reported the highest levels of SS at T5 (after Run3, approximately 30 min after the MIST began). Moreover, results also revealed a significant effect of time on COR ($F(6,258) = 2.62, p = .02, \eta_p^2 = 0.057$), showing the cortisol at T5 was significantly higher than that at T4 ($p_{T5-T4} = 0.013$), however, it was neither significantly different from cortisol at T6 ($p_{T5-T6} = 0.34$) nor at T7 ($p_{T5-T7} = 0.28$).

At the neural level, compared with the control condition, whole-brain analysis (2-tailed voxel-level FDR-corrected $p < .05$) revealed stress-induced extensive activation and deactivation (Table 1). This included activation in the OFC, frontal gyrus, cingulate gyrus, thalamus, insula, and parahippocampal gyrus, and deactivation in the hippocampus, temporal and angular gyri (Fig. 3B).

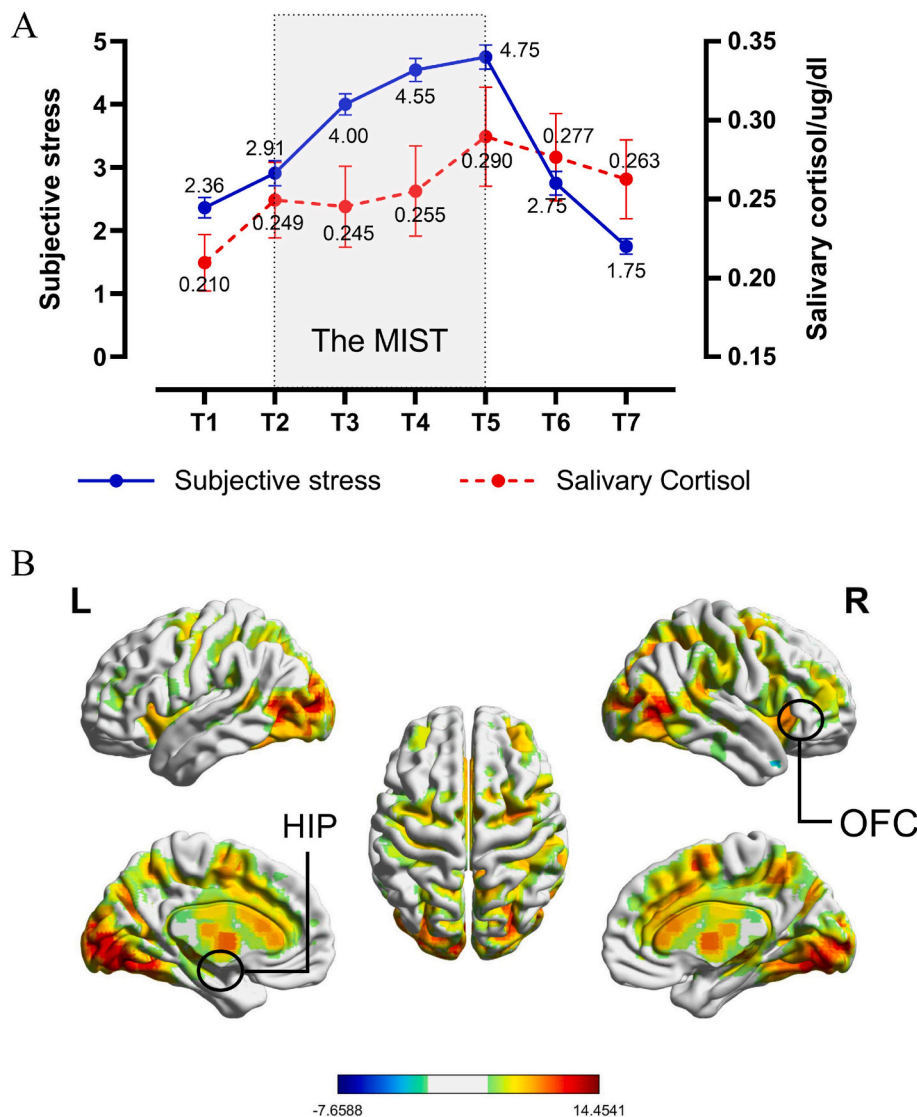


Fig. 3. Acute stress responses induced by the MIST.

(A) Participants' subjective stress feelings and salivary cortisol ($\mu\text{g}/\text{dl}$) responses during the MIST. Both subjective stress feelings and salivary cortisol peaked immediately at T5. (B) Neural activity in the MIST paradigm. 2-Tailed voxel-level FDR-corrected $p < .05$. Values and their error bars represent the mean \pm SEM. MIST = Montreal Imaging Stress Task; OFC = Orbitofrontal cortex; HIP = Hippocampus; SEM = standard error of the mean.

3.2. Statistical analysis

3.2.1. Correlation analysis

The correlation results showed positive correlations were found between participants' InterSC levels with the SS level at T5, which was the peak point of SS ($r = 0.33, p < .05$; Fig. 4A) and with the AUCg of SS ($r = 0.32, p < .05$; Fig. 4B). In addition, InterSC was positively correlated with OFC activity during acute stress ($r = 0.33, p < .05$; Fig. 4C), and the SS level at T5 was positively correlated with OFC activity during acute stress ($r = 0.39, p < .01$; Fig. 4D). Moreover, the AUCg of salivary cortisol was negatively correlated with HIP activity during acute stress ($r = -0.40, p < .01$; Fig. 4E), and the participants' InterSC was not significantly correlated with salivary cortisol. The results of the total correlation analysis are shown in Fig. 4F.

3.2.2. Mediation role of the OFC

The results revealed that OFC activity mediated the relationship between InterSC and SS at T5 (Table 2 and Fig. 5B). Specifically, a higher InterSC was associated with greater OFC activation, and was further linked to the strong SS at the peak point (T5).

3.2.3. Moderation role of the HIP

Neural activity in the HIP moderated the relationship between

Table 1
Activation and Deactivation of Stress VS Control in the MIST paradigm.

Stress vs Control	Region	Peak Coordinate			k	BA	t _{peak}	
		X	Y	Z				
Activation	Frontal_Mid_L	-27	-3	54	448	6	7.75	
	Frontal_Mid_R	27	48	18	627	6	8.42	
	Frontal_Sup_L	-24	-6	57	299	6	7.87	
	Frontal_Sup_R	15	3	57	432	6	11.04	
	Temporal_Sup_L	-45	-42	12	173	21	6.19	
	Temporal_Sup_R	57	-36	18	393	42	9.4	
	Parietal_Sup_L	-18	-60	54	272	7	8.21	
	Parietal_Sup_R	15	-54	54	177	5	8.67	
	Parietal_Inf_L	-24	-66	45	385	7	8.13	
	Parietal_Inf_R	30	-48	48	215	40	9.03	
	Cingulum_Ant_L	0	36	18	338	32	7.82	
	Cingulum_Ant_R	6	33	24	364	32	8.7	
	Cingulum_Post_L	-12	-42	15	41	29	7.26	
	Cingulum_Post_R	6	-39	21	43	26	7.17	
	Hippocampus_L	-24	-30	-3	145	36	9.27	
	Hippocampus_R	33	-30	-6	186	20	9.29	
	ParaHippocampal_L	-33	-39	-3	59	30	5.88	
	ParaHippocampal_R	36	-39	-6	137	37	6.25	
	Amygdala_L	-27	3	-15	13	34	3.13	
	Amygdala_R	39	0	-12	22	34	5.95	
	Insula_L	-36	15	9	472	48	9.77	
	Insula_R	36	21	0	410	47	8.95	
	Thalamus_L	-18	-21	12	299	27	11.21	
	Thalamus_R	9	-21	0	307	27	11.82	
	Precuneus_L	-15	-66	33	571	5	10.3	
	Precuneus_R	18	-63	42	618	7	10.67	
	Angular_L	-30	-51	36	56	40	4.71	
	Angular_R	27	-60	42	161	7	8.94	
	Deactivation	Hippocampus_L	-24	-12	-24	11	36	-4.81
		Hippocampus_R	27	-12	-21	15	20	-4.53
		Angular_L	-42	-72	39	71	19	-7.13
		Temporal_Pole_Mid_L	-33	9	-33	45	20	-6.11
		Temporal_Pole_Sup_L	-42	3	-21	18	21	-4.01
Temporal_Inf_L		-36	6	-36	43	36	-6.83	

Note. All p values are <.05, and 2-tailed voxel-level FDR has been corrected for the whole brain.

InterSC and the AUCi of salivary cortisol during acute stress ($\beta = -0.36$; $p < .05$; Table 3). Specifically, InterSC was positively correlated with the AUCi of COR among participants with a lower HIP (1 SD below the mean) activation during acute stress ($p < .05$; Fig. 5C).

The moderated mediation model revealed that the interaction between InterSC and HIP activation significantly predicted OFC activation in acute stress ($\beta = 0.30$, $p < .05$; Table 4), suggesting that the HIP moderated the relationship between InterSC and the OFC. Especially, InterSC was positively correlated with the level of activation in the OFC among participants with higher HIP (1 SD above the mean) activation in acute stress ($p < .01$; Fig. 5D), and further, a higher InterSC was linked to greater SS at the peak point (T5) through its association with stronger OFC activation.

* indicates $p < .05$. ** indicates $p < .01$.

4. Discussion

In this study, we used the MIST paradigm to investigate the possible role of the OFC and HIP in the relationship between InterSC and acute stress responses. Results revealed that higher InterSC was significantly associated with greater neural activity in the OFC, which, in turn, was associated with higher subjective stress feelings. Additionally, a higher InterSC was significantly associated with an enhanced salivary cortisol response in participants with low HIP activity. Furthermore, neural activity in the HIP moderated the indirect effect of InterSC on subjective stress feelings through its moderation of the effect of InterSC on neural activity in the OFC. This indicated that the mediation of the OFC was stronger in participants with higher neural activity in the HIP than in those with lower activity in the HIP.

Consistent with previous studies (He et al., 2021; Hu et al., 2018),

our research found a positive correlation between InterSC and subjective stress feelings during acute stress, indicating that individuals with higher InterSC experience stronger subjective stress feelings. Importantly, we found that a higher InterSC predicted stronger activation of the OFC during acute stress. Acute stress situations include uncontrollability and negative social evaluation and increase the load of emotion and cognition (Herman et al., 2005; McEwen, 1998), especially for individuals with higher InterSC (Cross et al., 2011; Seo et al., 2011). Our results suggest that individuals with higher InterSC will maintain a higher activation of the OFC in acute stress, which helps them efficiently meet the emotional and cognitive requirements (Davidson, 2000; Rolls, 2019). Further, consistent with our hypothesis, we discovered that OFC activation mediated the relationship between the InterSC and subjective stress feelings in acute stress. As mentioned earlier, the OFC plays an important role in regulating emotional processing and cognitive assessment (Goldin et al., 2008; Rolls, 2019), while subjective stress feelings mainly include the processing of affective arousal, emotion regulation, and cognitive appraisal (Epel et al., 2018; Gross, 2002). In acute stress, an individual's cognition and emotion are highly aroused and produce strong subjective stress feelings (Dickerson and Kemeny, 2004), especially in individuals with higher InterSC (Cross et al., 2011; Seo et al., 2011). Neural activity in the OFC makes a great contribution to regulating an individuals' emotions and cognition (O'Doherty, 2011; Rolls, 2019), and further affects subjective stress feelings. Taken together, our study emphasizes the role of the OFC in subjective stress feelings, and the OFC might be a possible neural pathway mediating the relationship between InterSC and subjective stress feelings.

Additionally, consistent with previous studies (Corr et al., 2021), the current study found that the level of activation in the HIP was negatively correlated with the salivary cortisol response in acute stress, which

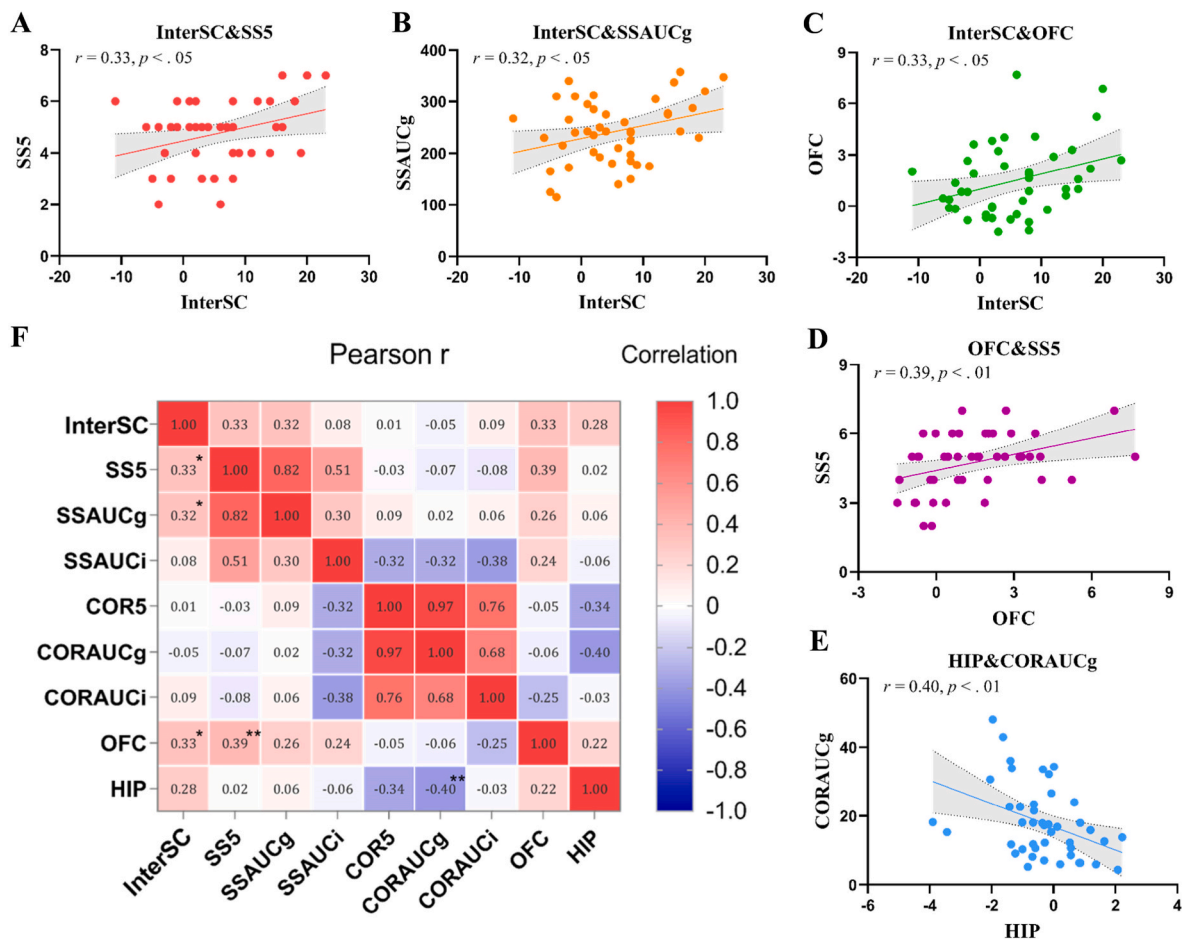


Fig. 4. Correlation analysis results.

(A) Correlation between InterSC and subjective stress feelings on the time point of T5 (SS5). (B) Correlation between InterSC and the AUCg of subjective stress curve (SSAUCg). (C) Correlation between InterSC and OFC activity. (D) Correlation between OFC activity and subjective stress on the time point of T5 (SS5). (E) Correlation between HIP activity and the AUCg of cortisol response curve (CORAUCg). (F) The total correlation analysis results. AUCg = area under the curve with respect to ground. * indicates $p < .05$. ** indicates $p < .01$.

Table 2

Mediation effect of OFC between InterSC and subjective stress feelings.

Mediator	Path	Effect	95%CI	p
OFC	Total (c)	0.0525	[0.0055, 0.0995]	0.0295
	Direct (c')	0.0359	[-0.0121, 0.0839]	0.1384
	Indirect (ab)	0.0166	[0.0009, 0.0399]	0.0428

Note. OFC = Orbitofrontal cortex; CI = Confidence interval.

reflects the negative feedback regulation of the HPA axis by the HIP (Pruessner et al., 2010). In acute stress, the hypothalamus secretes corticotropin-releasing hormone (CRH), and this in turn triggers the pituitary to secrete adrenocorticotropic hormone (ACTH). This eventually leads to the secretion of the glucocorticoid hormone cortisol, which is a vital biomarker of the physiological response to acute stress and is called the “stress hormone” (Hellhammer et al., 2009). This process is regulated by the HIP through its negative feedback effect on the HPA axis (Lupien et al., 2009; Uhart et al., 2006). Consistent with our hypothesis, neural activity in the HIP moderated the relationship between InterSC and cortisol response in acute stress. Specifically, individuals with a higher InterSC with low HIP activation presented an enhanced cortisol stress response. As mentioned earlier, low activation of the HIP reflects a reduced negative feedback regulation of the HIP on the HPA axis, which leads to weak inhibition of the cortisol response in acute stress (Herman et al., 2016; Jacobson and Sapolsky, 1991), and further

causes the cortisol concentration to increase rapidly in a relatively short time. Increased cortisol levels promote energy metabolism by increasing an individual’s blood glucose levels (Habib et al., 2001; Pruessner et al., 2010), helping the individual deal with the acute stress situation more effectively. Although previous studies have shown that InterSC is positively correlated with cortisol response (Hu et al., 2018; Hu et al., 2019), our study emphasizes the role of the HIP in the relationship between InterSC and cortisol response, and demonstrates that the HIP might be a possible neural pathway moderating the association between InterSC and cortisol response.

Interestingly, our results suggest that the HIP and OFC together regulate the relationship between InterSC and subjective stress feelings, aligning with the moderated mediation model. In this model, both the HIP and OFC belong to the prefrontal-limbic cortex, which plays a crucial role in the acute stress response (Hu et al., 2022; Tabibnia, 2020; Ulrich-Lai and Herman, 2009). Previous studies have suggested that neural damage in the HIP and OFC compromises cognitive and affective functions, including emotion regulation, and increases vulnerability to stress-related disorders, including substance abuse, depression, and anxiety (Arnsten, 2009; Russell and Lightman, 2019). In addition, the synergistic and separate regulation of stress response by the HIP and OFC promotes adaptive stress responses (Metz et al., 2019); Ulrich-Lai and Herman (2009). From a positive psychology perspective, this model reflects that activation of the HIP and OFC contributes to efficiently coping with acute stress situations, especially in individuals with higher InterSC.

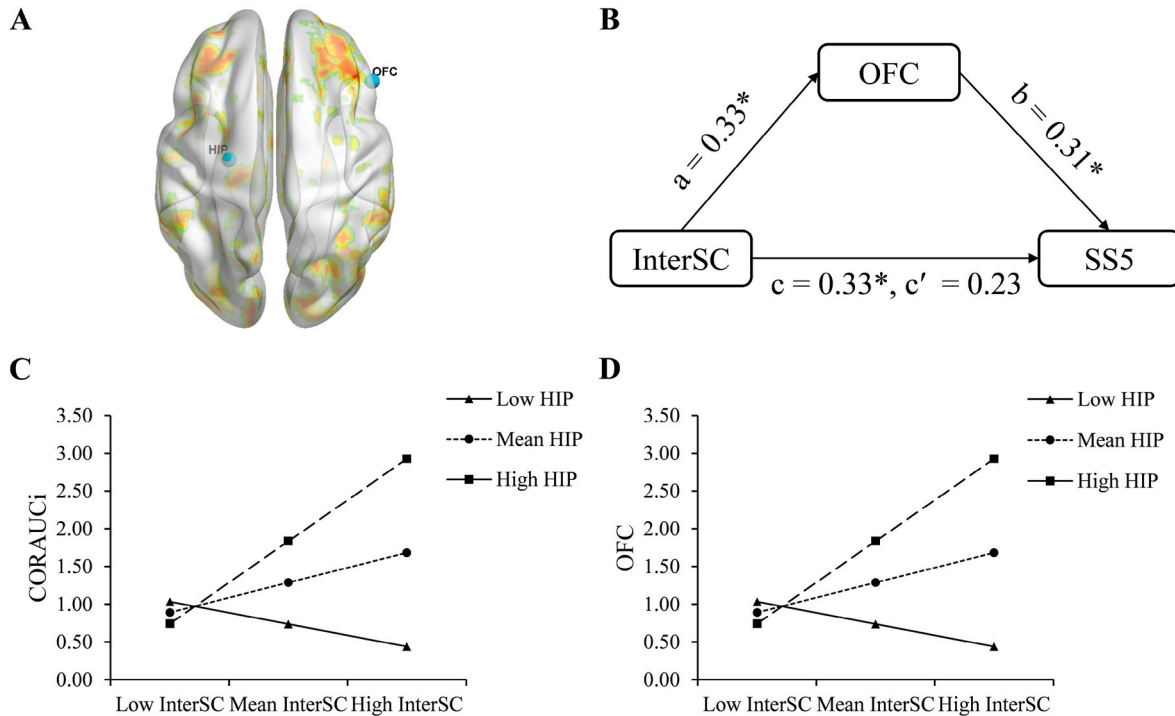


Fig. 5. The mediation effect of OFC and moderation effect of HIP.

(A) Visualization of ROIs, including OFC and HIP. (B) Mediating effect of OFC between InterSC and SS5. Total (path *c*), direct (path *c'*), and indirect (*ab*) with its components (paths *a* and *b*). (C) Moderating effect of HIP between InterSC and salivary cortisol. (D) Moderating effect of HIP between InterSC and the activation of OFC. SS5 = Subjective stress feelings on the time point of T5; CORAUCi = area under the curve with respect to increases in cortisol response; OFC = Orbitofrontal cortex; HIP = Hippocampus; Mean HIP = Mean activation of HIP; Low HIP = - 1 SD + Mean; High HIP = 1SD + Mean 1SD; SD = standard deviation.

Table 3
Moderation effect of HIP between InterSC and salivary cortisol.

Predictor	<i>b</i>	<i>b</i> 95% CI [LL, UL]	<i>beta</i>	<i>beta</i> 95% CI [LL, UL]	<i>sr</i> ²	<i>sr</i> ² 95% CI [LL, UL]	<i>r</i>	Fit
(Intercept)	3.10	[-0.82, 7.03]						
InterSC	0.14	[-0.25, 0.54]	0.11	[-0.20, 0.42]	.01	[-.05, .07]	.09	
HIP	0.48	[-2.15, 3.12]	0.06	[-0.27, 0.39]	.00	[-.03, .03]	-.03	
InterSC * HIP	-0.40*	[-0.75, -0.05]	-0.36	[-0.68, -0.04]	.12	[-.06, .29]		
								<i>R</i> ² = .126 95% CI [.00, .28]

Note. A significant *b*-weight indicates the beta-weight and semi-partial correlation are also significant. *B* represents unstandardized regression weights. *Beta* indicates the standardized regression weights. *Sr*² represents the semi-partial correlation squared. *R* represents the zero-order correlation. *LL* and *UL* indicate the lower and upper limits of a confidence interval, respectively. * indicates *p* < .05. ** indicates *p* < .01.

Table 4
Testing the moderated mediating effect of InterSC on subjective stress.

Predictors	On OFC			On SS5		
	<i>beta</i>	<i>t</i>	95%CI	<i>beta</i>	<i>t</i>	95%CI
InterSC	0.29	1.22	[-0.01, 0.58]	0.22	1.51	[-0.07, 0.53]
HIP	0.04	1.65	[-0.28, 0.35]			
OFC				0.31	2.09*	[0.01, 0.61]
InterSC*HIP	0.30	2.04*	[0.01, 0.61]			
<i>R</i> ²	0.21*			0.19*		
<i>F</i>	3.55*			4.93*		

Note. *Beta* represents standardized regression weights. SS5 = Subjective stress feelings on the time point of T5; OFC = Orbitofrontal cortex; HIP = Hippocampus; CI = Confidence interval. * indicates *p* < .05. ** indicates *p* < .01.

Moreover, there has been growing literature suggesting that anterior and posterior HIP may function differently (Grady, 2020). For example, Poppenk et al. (2013) suggested that the anterior HIP toward pattern integration and the posterior HIP toward pattern separation, and the

anterior HIP is more involved in the social cognitive and emotion processes than the posterior segment (Grady, 2020). In the current study, the ROI of HIP is located in the anterior part, thus, its activity may contribute to the integration of information from the environment and the regulation of individual emotions during acute stress. Meanwhile, this may also make HIP-related results apply only to activity in the anterior HIP where the 6 mm sphere was placed.

There are some limitations to this study, and certain possible future research directions are proposed. First, in the current study, the Cronbach's alpha coefficient for independent self-construal was 0.628, which is lower than that in a previous study (Luo et al., 2015; Ma et al., 2014). We speculated that this could be due to two reasons: a) the sample was from China, which has a collectivist culture, in which most individuals tend to form interdependent self-construal rather than independent self-construal; b) the relatively small sample size might cause our Cronbach's alpha coefficient to be relatively low. Second, the Self-construal scale contain two dimensions: interdependence and independence, some studies used the sum score of interdependent items measured by the Self-construal scale to reflect the tendency toward

interdependence (Wang and Wang, 2016), whereas the present study used the sum score of interdependent items minus the sum score of independent items to represent the InterSC. Although similar methods have been proposed or adopted in previous studies (Li et al., 2018; Ma et al., 2014; Wang et al., 2017), future studies could attempt to specify the exact differences between them. Third, the MIST is a psychosocial task that uses math problems to combine key situational components that trigger stress responses, including the presence of social evaluative threat, a highly challenging atmosphere, and a sense of uncontrollability (Dickerson and Kemeny, 2004). Although the MIST is effective in inducing stress responses, the difficulty of math problems differed between the stress and the control conditions, and this difference may induce some brain activity unrelated to psychological stress. Finally, this study was conducted using a sample from China, which is dominated by interdependent self-construal owing to its collectivist culture (Markus and Kitayama, 1991). In terms of verifying the findings in diverse samples or samples with a range of self-construals, future studies can explore the neural mechanism underlying the relationship between self-construal and acute stress responses in a more culturally diverse sample.

5. Conclusion

From the perspective of association between interdependent self-construal and the acute stress response, this study explored the possible role of the prefrontal cortex and limbic system in this relationship. Based on the results of the current study, we cautiously propose important regulatory roles for the HIP and OFC in the relationship between InterSC and acute stress response, especially the neural moderation effect of the HIP. In general, this study is helpful in further broadening the research scope of personality and stress and deepening our understanding of individual differences in acute stress responses.

Credit author statement

Jiahao Luo: Conceptualization; Data curation; Methodology; Visualization; Software; Validation; Writing – original draft; Writing – review & editing. **Yadong Liu:** Data curation; Visualization; Methodology; Software; Writing – review & editing. **Kaige Guo:** Investigation; Methodology; Software. **Xi Ren:** Data curation; Investigation. **Zheni Wei:** Conceptualization; Data curation. **Yipeng Ren:** Methodology; Software. **Weiyu Hu:** Data curation; Software. **Juan Yang:** Funding acquisition; Conceptualization; Supervision; Project administration; Writing – review & editing.

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Declarations of competing interest

The authors declare no conflict of interest. None.

Data availability

Data will be made available on request.

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