Progressively decreased functional coupling within task positive networks during acute stress signals stress resilience: the promotion role of reward system

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January 19, 2023

Abstract

Over the past decade, studies have demonstrated that a shift in attentional patterns from goal-oriented top-down attention to bottom-up attention to external stimuli under acute stress involve reallocating resources between different neurocognitive networks,which is a heterogeneous process. However, it remains unclear that how this neural functional coupling regulates the activation and termination of hypothalamic-pituitary-adrenal (HPA) axis, the major endocrine stress system. To bridge this konwledge gap, seventy-seven participants (age, 17–22 years, 37 women) were recruited for a ScanSTRESS brain imaging study, and their salivary cortisol levels during stress were collected. In addition, we assessed individual differences in the sensitivity of behavioral activation system (BAS) and funtional connectivity of the brain in all participants. We found that functional couplings among the dorsal attention network (DAN), central executive network (CEN) and visual network (VN) decreased significantly during repeated stress induction. The decline of functional connectivity could single a rapid cortisol recovery and the level of BAS could moderate the relationship between neural changes and cortisol reactivity and recovery. In all, this study suggested the important role of functional connectivity between CEN and DAN in the process of stress resilience, and the promotive effects of reward sensitivity measured by behavioral activation system.

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Over the past decade, studies have demonstrated that a shift in attentional patterns from goal-oriented top-down attention to bottom-up attention to external stimuli under acute stress involve reallocating resources between different neurocognitive networks,which is a heterogeneous process. However, it remains unclear that how this neural functional coupling regulates the activation and termination of hypothalamic-pituitary-adrenal (HPA) axis, the major endocrine stress system. To bridge this konwledge gap, seventy-seven participants (age, 17–22 years, 37 women) were recruited for a ScanSTRESS brain imaging study, and their salivary cortisol levels during stress were collected. In addition, we assessed individual differences in the sensitivity of behavioral activation system (BAS) and funtional connectivity of the brain in all participants. We found that functional couplings among the dorsal attention network (DAN), central executive network (CEN) and visual network (VN) decreased significantly during repeated stress induction. The decline of functional connectivity could single a rapid cortisol recovery and the level of BAS could moderate the relationship between neural changes and cortisol reactivity and recovery. In all, this study suggested the important role of functional connectivity between CEN and DAN in the process of stress resilience, and the promotive effects of reward sensitivity measured by behavioral activation system.

Key words:neural functional coupling; stress resilience; behavioral activation system; dorsal attention network (DAN); central executive network (CEN)

1 Introduction

Stress is one of the important potential pathogenic factors in modern society. However, not all individuals experiencing stress events will suffer from stress-related diseases, such as depression, anxiety, PTSD and so on. The principal cause of stress-related disorders is not the stressors *per se* , but rather the physiological and psychological response to the stressors (Franklin, Saab, & Mansuy, 2012; Walker, Pfingst, Carnevali, Sgoifo, & Nalivaiko, 2017). When exposed to stressors, the speed of reactivity and recovery is crucial for dividing stress resilience and stress vulnerability (McEwen & Gianaros, 2011). Rapid response and rapid recovery of multiple stress-related biological systems can facilitate adaptation and resilience (McEwen & Gianaros, 2011). The hypothalamic–pituitary–adrenal (HPA) axis, as the major endocrine stress system, its rapid activation and termination in time contribute to the maintenance of homeostasis during and after acute stress(McEwen, 1998). On the countrary, its inadequate initialization or a delayed termination may undermine mental and physical health (McEwen & Gianaros, 2011).

Brain is the central mediator of stress resiliency and vulnerability processes(McEwen, 2016). It regulates the physiological and psychological response via altering the activation and functional connectivity (FC) within and between different neurocognitive networks(McEwen, 2016). This process involves the strategic reallocation of resources to deal with transition in cognitive demands under acute stress. It is not a homogeneous process that may be manifested as the continuous increase or decrease of neural activity over a period of time, but a heterogeneous process, which reflects the efficiency of reallocation of resources at the neural level (Hermans, Henckens, Joels, & Fernandez, 2014). However, it remains unclear how the heterogeneous changes of neural activity would affect the HPA axis, including reactivity and recovery, which may provide a new perspective for the division of stress vulnerability and stress resilience.

It has been established that stress-induced re-allocation of neural resources involving increases in the salience network (SN) connectivity at the cost of decreases in the central executive network (CEN) connectivity(Hermans, et al., 2011; Qin, Hermans, van Marle, Luo, & Fernandez, 2009; van Marle, Hermans, Qin, & Fernandez, 2010), accompanying upregulation of the default mode network (DMN) (Hermans, Henckens, Joels, & Fernandez, 2014; Vaisvaser, et al., 2013; van Oort, et al., 2017b). The responsiveness and interconnectivity within SN increased as magnitude of the stress response increases(Hermans, et al., 2011). Besides, the ventral media prefrontal cortex (vmPFC), one of the core regions of DMN was also found show sustained increase under stress conditions (Sinha, Lacadie, Constable, & Seo, 2016). In contrast to SN and DMN, there is much less information about constant changes in CEN(Van Oort, et al., 2017a). Given that communication between networks is also crucial for supporting complex brain function, we speculate that there may be other networks that work together with CEN to support advanced cognitive functions and exhibit progressive decoupling during stress, such as the dorsal attention network (DAN) and sensor cortex systems.

DAN along with SN and CEN is known as the task positive network, which shows consistent activations across different tasks(Di & Biswal, 2014). However,given the unpredictable and uncontrollable nature of stressful events, people in acute stress tend to respond quickly rather than accurately when dealing with higher order cognitive tasks(Qin, Hermans, van Marle, Luo, & Fernandez, 2009). This process involves a shift in attention patterns from goal-oriented top-down attention to bottom-up attention to external stimuli(Broeders, et al., 2021), which results in greater activation and increased functional connectivity of the SN for its critical role in focusing on salient information, accompanied by DAN and CEN offline(Gagnon & Wagner, 2016; Sinha, Lacadie, Constable, & Seo, 2016). Early animal studies have shown that stress can lead to reorganization of the prefrontal lobe structure (dorsal frontal regions), which is related to impaired perceptual attention, behavioral flexibility and decision-making ability, involving a wide range of brain regions related to DAN and CEN (Arnsten & Goldman-Rakic, 1998; Soares, et al., 2013b). In some human research, DAN was reported to show a decreased connectivity during chronic stress and increased when recovery from stressors(Soares, et al., 2013b). Besides, during recovery from acute stress, DAN also showed increased functional interconnectivity (Broeders, et al., 2021). Since the two networks both are functionally related to the external attention orientation task(Fox, et al., 2005), we hypothesized that during acute stress, they will coordinate their activities to support the completion of cognitive tasks, but their functional connectivity will show a sustained decrease due to negative feedback and time constraints(McEwen, 1998).

Further, sensor cortex systems also play a vital role in stressful situations. Previous studies have found a greater activation of the visual (VN) and sensorimotor (SMN) networks, which suggest a hyper-sensitized perception-action system to support the fight-or-flight reaction (Soares, et al., 2013a; Zhang, et al., 2020). Recent evidence from our lab also demonstrated that connection between CEN, SMN and VN in the resting state is associated with lower social evaluation threats experienced during stress tasks, which means that the top-down control mechanism is supported by both three networks, and such a mechanism is very essential for reduction of negative emotions during acute stress (Liu, et al., 2022; Yao, et al., 2019). Based on this, we resonably speculate that during acute stress induction, the control mechanism supported by the perceptual cortical system and the task active network (major the DAN and CEN) will be significantly activated by the stress task and gradually decoupled as the task progresses.

In addition to exploring the neural mechanisms of adaptive cortisol response under acute stress, we also focus on the possible individual differences. Over the past decade, studies have demonstrated that the reward system play a critical role in promoting stress resilience(Holz, Tost, & Meyer-Lindenberg, 2020). It refers to the tendency and responsiveness of individuals to approach and respond to reward - related stimuli(Corral-Frias, et al., 2015). People with higher reward sensitivity had lower cortisol levels in acute stress, experienced less subjective stress and were more likely to buffer the negative effects of stress(Corral-Frias, Nadel, Fellous, & Jacobs, 2016; Dutcher & Creswell, 2018). As an important component of motivation system, reward sensitivity can be measured by the the sensitivity of the behavioral activation system (BAS)(Abaied & Emond, 2013; Gray, 1987). On the neural level, the reward circuit involve neural pathways supporting by the ventral tegmental area, limbic system (including amygdala, thalamus and ventral striatum) and

prefrontal cortex(Kalivas & Nakamura, 1999; Tabibnia, 2020). It has been proved that stronger activation of the mesostriatal reward regions during stress is associated with more positive emotional experiences and more rapid cortisol recovery, reflecting an active coping with stress(Hu, et al., 2022; Jiang, Kim, & Bong, 2014). Considering the characteristics of individuals with high reward sensitivity, we speculate that they would exhibit motivational behavior, such as fun-seeking and pursuing intrinsic rewards during acute stress, which would buffer the adverse effects of acute stress and thus enable more effective neurological and endocrine stress response.

In this study, we aimed to better understand how HPA axis can be timely activated and terminated by examining changes in functional connectivity of brain networks induced by a standardized acute stress paradigm (ScanSTRESS paradigm)(Streit, et al., 2014), and investigate whether motivational system sensitivity regulates the relationship between neural and endocrine response. Under acute stress, the re-allocation of neural resources is not a homogeneous process, so there might be individual differences in reallocation efficiency, which will further affect the reactivity and recovery of HPA axis. Therefore, based on comparing stress vs. control, we further compared the changes between different sessions under stress condition, observing the changes of FC between brain networks from a longitudinal perspective.

2 Methods and Materials

2.1 Participants

More information about the participants has been reported in Hu, et al. (2022). Briefly, seventy-seven college students participated in the current study (age: 20.18 $\pm$ 1.97 years (18-26 years); 35 females). None of the participants had reported any history of alcoholism, drug abuse, head injury or any psychological disorders. Participants were instructed not to smoke, drink coffee or wine, or do any heavy exercise on the day of their appointment. The study was approved by the ethics committee of the Southwest University. Written informed consent was attained from all participants.

2.2 ScanSTRESS paradigm and Experiment procedure

Stress response were induced by an adapted version of the ScanSTRESS paradigm, which included a stress condition and a control condition(Streit, et al., 2014). In the stress condition, participants had to perform challenging cognitive tasks (included mental arithmetic task and mental rotation task) under time pressure. Besides, they were monitored by two juries (a man and a woman), which aimed to induce the social evaluative threat. When participants made some incorrect answers or out of the time limit, a negative feedback would be shown on the screen immediately ("Error!", "Work faster!"). In the meanwhile, two injuries would also give disapproving message that they have recorded the bad performance of the participants (Figure 1A). In the control condition, participants do the similar but much easier tasks (found matched figure or number) without time limit and negative feedback, furthermore, the social evaluative threat were also reduced to a great extent as the injuries need to look away during the control condition (Figure 1B). There are two imaging runs in the ScanSTRESS paradigm. Each run consist of 8 blocks: half of stress conditions (2 serial subtraction blocks and 2 mental rotation blocks) and half of control conditions (2 figure matching and 2 number matching, Figure1 C).

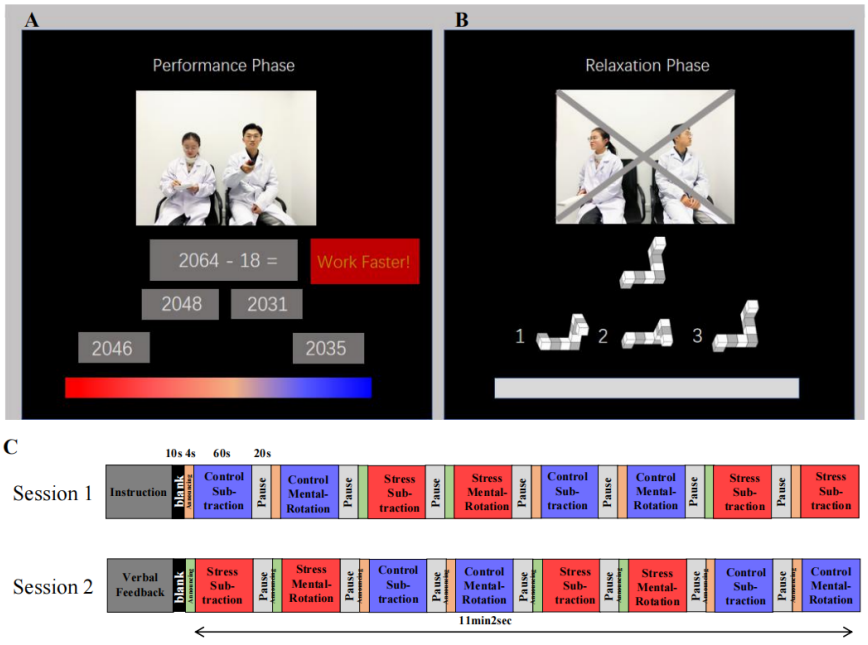

Figure 1. Stress condition and control condition in the ScanSTRESS paradigm

All experiments were conducted in the mid-afternoon, between 12:00 and 3:00pm, to control the effect of cortisol rhythm on the experimental results. After arriving at the laboratory, participants were asked to rest for 30 min and fill out the questionnaires. Following the training session of the ScanSTRESS task, participants entered the MRI scanner. A T1 image was acquired first, followed by a resting-state image. Therafter, 2 sessions of ScanSTRESS task were performed for 22 min. The second resting-state image and a DTI image were then collected. Before participants left the laboratory, they were debriefed in detail. During the experiment, five saliva samples were collected in total. Participants' subjective stress reports were assessed by oral reports just after the saliva sample collection (Figure 2).

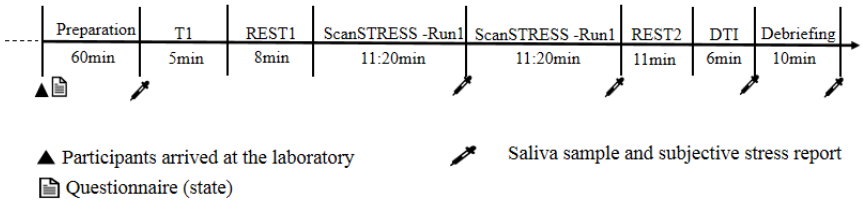

Figure 2. An overview of the experimental procedure

2.3 Data acquisition

2.3.1 Psychological and Physiological Measures

Self-reported subjective stress (SS) was evaluated by a 7-point Likert scale ranging from 1, corresponding to 'Not stressful', to 7, corresponding to 'Terribly stressful'. Saliva samples were collected with a sampling device (Salivette, SARSTEDT, Germany) to assess cortisol levels (CORT) throughout the experiment. All saliva samples were stored at room temperature until the completion of the experiment, after which they were stored at -20°C until analysis. Cortisol concentrations were analyzed using an ELISA kit (IBL-Hamburg,

Germany) following the manufacturer's instructions. The sensitivity of the cortisol assay was 0.005 μg/dl, and the inter-and intra-assay coefficients of variation for the cortisol assay were 3.2% and 6.1%, respectively.

2.3.2 Behavioral Activation Scale (BAS)

BAS was used to measure the individual difference in the sensitivity of behavioral activation systems. BAS contains 13 items with a 4-point Likert scale ranging from 1, corresponding to 'very true for me', to 4, corresponding to 'very false to me'. There are 3 subscales in BAS: BAS Drive (BASD), BAS Fun-Seeking (BASF) and BAS Reward Responsiveness (BASR). BASD reflects behavioral maintenance and sustained effort (4 items; e.g. "I go out of my way to get things I want."); BASF represents the willness to seek potentially rewarding event and the tendency to pursuit novel rewards (4 items; e.g. "I will often do things for no other reason than that they might be fun."); BASR denotes that people make positive response to the reward-attainment (5 items; e.g. "When I'm doing well at something, I love to keep at it"). The Cronbachα for the BAS is .842 (Carver & White, 1994).

2.3.3 fMRI data acquisition

Functional and anatomical whole-brain images were acquired using a 3T Siemens Trio MRI scanner. 242 volume-functional images were acquired from each subject with a T2*-weighted gradient echo-planar imaging sequence during resting-state. We obtained 32 echo-planar images per volume sensitive to blood oxygenation level-dependent contrast (repetition time: TR = 2000 msec, echo time: TE = 30 msec, 64 × 64 matrix with 3 × 3 × 3 mm3 spatial resolution, FOV = 192 × 192mm2). Slices were acquired in an interleaved order and oriented parallel to the AC-PC plane with a 0.99 mm gap. High-resolution T1-weighted 3D fast-field echo sequences were obtained for anatomical reference (176 slices, repetition time: TR = 1900 msec; echo time: TE TE = 2.52 msec; slice thickness = 1 mm; FOV = 256 mm × 256 mm; voxel size = 1 mm × 1mm × 1 mm).

2.4 fMRI data analysis

2.4.1 preprocessing

fMRI data were processed with MATLAB software using the DPABI toolbox (Yan et al., 2016). Firstly, 3-dimensional images were transformed into 4-dimensional images, which were then sliced time-corrected in ms for each slice individually. After that, all images were realigned to correct for the head motion for acquisition, co-registered with individual participants' T1-weighted images, spatially normalized to the Montreal Neurological Institute template using the Dartel segments, and smoothed using a 4 mm full-width at half-maximum Gaussian kernel.

2.4.2 Task fMRI analysis

The generalized Psychophysiological Interaction (gPPI, McLaren et al., 2012) was carried out using CONN version 19c software (https://www.nitrc.org/projects/conn/) to examine the task-dependent changes in ROI-to-ROI connectivity. Predefined regions-of-interest were chosen based on templates developed by Yeo et al. as seeds to create connectivity maps of the ventral attention (SN), default mode (DMN), dorsal attention (DAN), central executive (CEN), visual, limbic and somatomotor networks. First, we extracted an averaged BOLD time-course across selected voxels for each ROI/network and used it as a physiological regressor. For a subject-level analysis, we generated a PPI regressor for each condition by calculating the element-by-element product between psychological and physiological regressors. Second, we computed how strongly the time-course of one ROI/network is correlated with the PPI regressor of another. Unlike correlational analysis, gPPI is based on multiple regression, thereby generating different beta values when the seed and target regions are reversed. This pair-wise computation was made for every possible pair-wise combination of selected ROIs/networks to measure task-dependent changes in FC for each participant. We conducted one sample T test to obtain the contranst images of stress versus control on the group level, therefore the general effects of stress induction can be estimated.

To further calculate the level of neural change between different sessions, statistical inferences were made

using a one-sample paired t-test comparing ROI/network connectivity for the run1 vs. run2. We corrected for the rate of type1 errors with the FDR at the analysis-level (the number of tests performed; that is, each possible pair combination of ROIs/network) instead of the ROI/network-level (the number of ROIs/networks selected). In particular, the interested networks were extracted using the template developed by Yeo, et al. (2011).

2.5 Correlational and moderation analysis

To estimate the relationship between neural changes and acute stress response, Pearson's bivariate correlation analyses between the level of neural changes and stress response (endocrine and subjective) were performed. For this purpose, we firstly calculated the change rate of stress response, including stress reactivety and stress recovery. To more specific, we took time interval between before and after stress induction as the change amount of reactivity (denoted as ΔX_{up}, ΔX_{up} = 35.5 min) and time interval after stress induction and before leaving the laboratory as the change amount of recovery (denoted as ΔX_{rec}, ΔX_{rec} = 27 min). Based on this, reactivity slope was magnituded as ($Peak_{CORT/SS}$ – $Baseline_{CORT/SS}$) / ΔX_{up}; recovery slope as ($Peak_{CORT/SS}$ – $Post_{CORT/SS}$) / ΔX_{rec}.

To further estimate the effect of BAS on the relationship between neural changes and stress response, we defined moderate models with the level of neural change as the independent variable, the slope of stress reactivity and recovery as independent variables, and BAS as the moderate variable. All statistical analyses were performed using SPSS (version 22) and all p-value in statistical analysis were corrected using the false discovery rate (FDR) approach.

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`image3.emf` available at https://authorea.com/users/577551/articles/619899-progressively-decreased-functional-coupling-within-task-positive-networks-during-acute-stress-signals-stress-resilience-the-promotion-role-of-reward-system

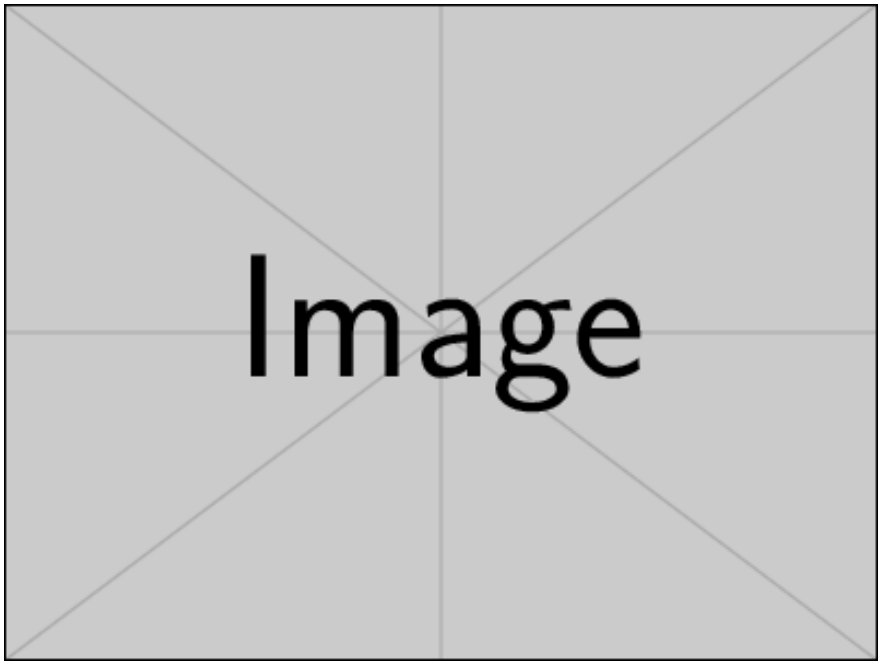
3 Results

3.1 Stress-induced changes in neuroendocrine and functional connectivity between brain networks

The overall changes in stress response are illustrated in Figure 3A. A repeated analysis of variance revealed that time period was determined to be a signigicant within-subject variable both in subjective stress self-reports (F (4,73) = 47.821, p <0.001,η_π^2 = 0.724) and salivary cortisol levels (F (4,73) = 4.162, p =0.004,η_π^2 = 0.186).

On the neural levels, the gPPI results revealed enhanced functional coupling in 11 pairs of networks and decreased functional coupling in only 1 pair of networks during the stress condition as compared to control condition. Specifically, except DMN and Limbic network showed a decreased connectivity during stress condition, SN, DAN and CEN all displayed an increased connectivity with other networks, which revealed a main condition effect (Figure 3B).

A



B

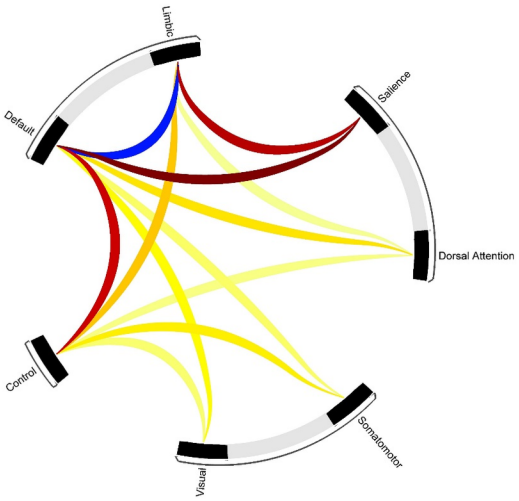


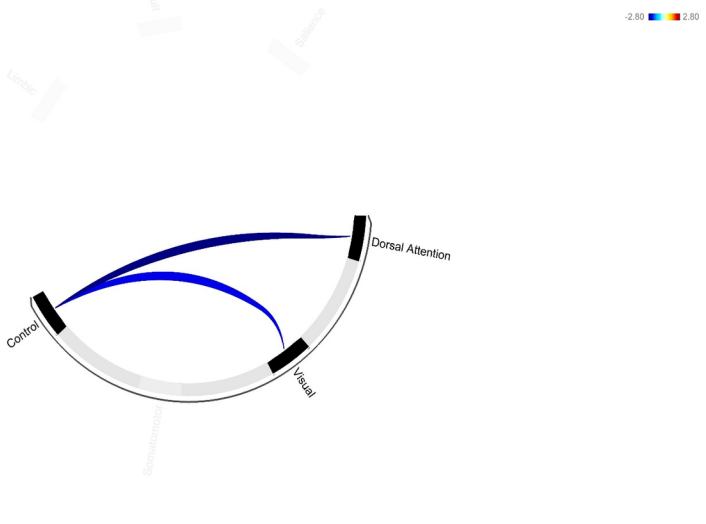
Figure3. Multiple changes induced by stress (A) Subjective stress and salivary cortisol at five-time points. **(B)**Differences in ROI-to-ROI functional connectivity for stress vs. control. Depicted lines indicate pairs of ROIs that demonstrate increased functional connectivity for stress relative to control (red lines) and increased functional connectivity for control relative to stress (the blue line).

3.2 Neural changes during repeated stress induction

For the contrast between different session (stress condition only), only 2 pairs of networks (Figure 4A) showed decreased connectivity. More specifically, as hypothesized, with repeated stress induction, decreased

functional coupling among CEN, DAN and VN was observed. Brain changes were quantified by the amplitude difference between 2 sessions for further analysis. Correlation results showed that decreased connectivity between CEN and DAN was accompanied by an efficient cortisol recovery (r = 0.3014, p $_{\text{-FDR}}$ = 0.017, p $_{\text{-uncorrected}}$ = 0.003, Figure 4B).

A



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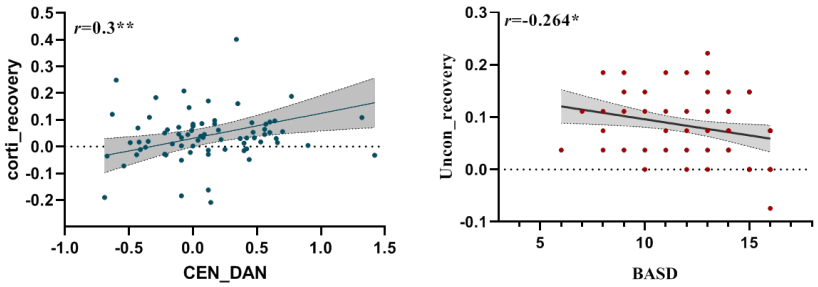

Figure4. Neural changes between different sessions and correlation analyses (A) Differences in ROI-to-ROI functional connectivity for run1 vs. run2. (B) Correlation between neural changes (run1 – run2) and stress recovery slope.

3.3 Motivation moderated the association between the decreased functional coupling of task positive networks and efficient cortisol responses

Moderate analysis with brain changes as the independent variable, cortisol response slope (reactivity and recovery) as the dependent variable, and individual difference in BAS as the moderate variable found that the BASF could moderate the decreased functional coupling between DAN and CEN and efficient cortisol reactivity, and BASR could moderate the decreased functional coupling between DAN and CEN and efficient

cortisol recovery. More specifically, the relationship between great functional connectivity between DAN and CEN decline and efficient stress response only exist in participants with a high level of BASF and BASR (Figure 5, Table 1).

Table 1. moderating effect of BAS between neural changes (run1 – run2) and cortisol response Predictor	Table 1. moderating effect of BAS between neural changes (run1 – run2) and cortisol response *b*	Table 1. moderating effect of BAS between neural changes (run1 – run2) and cortisol response *b* 95%CI [LL, UL]	Table 1. moderating effect of BAS between neural changes (run1 – run2) and cortisol response *t*	Table 1. moderating effect of BAS between neural changes (run1 – run2) and cortisol response *p*	Table 1. moderating effect of BAS between neural changes (run1 – run2) and cortisol response Fit
Model 1					
constant	0.153*	[0.022, 0.284]	2.320	0.023	
DAN-CEN	-0.000067	[-0.037, 0.037]	-0.004	0.997	
BASF	-0.008	[-0.017, 0.001]	-1.703	0.093	
BASF*(DAN-CEN)	0.016*	[0.002, 0.029]	2.360	0.021	
					$R^2 = 0.103^*$
Model 2					
constant	-0.086	[-0.308, 0.136]	-0.770	0.444	
CEN-DAN	0.055	[-0.007, 0.166]	1.769	0.081	
BASR	0.009	[-0.007, 0.024]	1.078	0.285	
BASR*(CEN-DAN)	0.044**	[0.011,0.078]	2.671	0.009	
					$R^2 = 0.144^*$

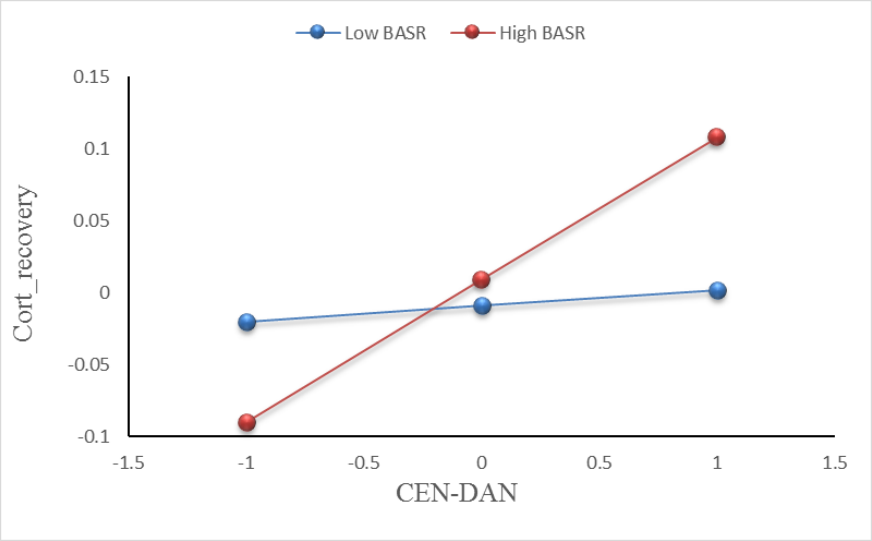

Figure5. Moderating effect of resilience between neural changes (run1 – run2) and cortisol response

4. Discussion

This study investigated stress-induced changes in functional connectivity between different brain networks. We found that functional couplings among the DAN, CEN and VN decreased significantly during repeated stress induction. The decline of functional connectivity could single an adaptive cortisol recovery. Moreover, the level of BAS could moderate the relationship between neural changes and adaptive cortisol reactivity and recovery, which underlies the mechanism by which motivation system can generate promotive effects on stressful situations.

Consistent with our hypotheses, we found that the decreased functional connectivity between DAN and CEN was positive correlated with the slope of cortisol recovery. Rapid stress recovery is considered as the maker of effective coping under stressful situations. Delayed arrest of the stress response means that the body is difficult to maintain physiological and behavioral stability during stress, leading to physical and mental overload (Franklin, Saab, & Mansuy, 2012; McEwen & Gianaros, 2011). Previous studies have demonstrated the close relationship between CEN and DAN in supporting advanced cognitive tasks(Liu, et al., 2022). To more specific, CEN represents information about task context in working memory and that the DAN translates this information into commands to guide the deployment of spatial attention to specific objects and locations (Dixon, et al., 2018). In this study, the reduced functional connectivity between the two networks indicated that the ability to complete higher-order cognitive tasks in stressful situations was inhibited and implied a subsequent faster recovery from stress. This finding further proves that in the process of stress response, it is an adaptive stress response pattern for individuals to exchange the speed of response for the accuracy of response (Qin, Hermans, van Marle, Luo, & Fernandez, 2009).

Besides, we also found an enhanced functional coupling of VN and CEN increased significantly during the stress condition as compared to control condition. But with the repeated application of stressors, the connection between them decreased significantly. The CEN can flexibly and quickly respond to current tasks by adjusting interaction modes with other networks (Cole, et al., 2013). This result explains the significant increase in CEN and VN functional connectivity at the beginning of the stress task, which suggests an effort to try to complete the task. Due to the negative effects of stress induction on executive functions such as cognitive flexibility and working memory (Plessow, Kiesel, & Kirschbaum, 2012), the functional connectivity of CEN-VN showed a downward trend during repeated stress. It further proves that the re-allocation of neural resources by stress needs a process (Zhang, et al., 2020).

Results also showed that individual difference in motivation system could moderate the relationship between neural decline and blunted stress response. To be specific, the score of fun seeking (BASF) could moderate the neural decline in DAN-CEN connectivity and cortisol reactivity slope, people with higher BASF will have greater neural decline in DAN-CEN connectivity and faster cortisol reactivity. The decreased functional connectivity between DAN and CEN, as mentioned above, could reflect the inhibition of higher-order congnition (Hermans, Henckens, Joels, & Fernandez, 2014) and make adaptive preparations for rapid response to potential threats. During stress induction, the feeling of uncontrollability is induced repeatedly, those who are better at taking on new challenges in daily life can quickly adjust their mindset and maintain a higher level of motivation during unpleasant circumstances (Fresco, Mennin, Heimberg, & Ritter, 2013), allowing them to make sufficient endocrine stress response. Similarly, people with higher BASR will have greater neural decline in DAN-CEN connectivity and faster cortisol recovery. Reward Responsiveness can be defined as one's ability to experience pleasure in the anticipation and presence of reward-related stimuli(Carver & White, 1994). Individuals with higher reward responsiveness were more likely to focus on pleasurable stimuli and expected rewards(Taubitz, Pedersen, & Larson, 2015), which allows them to disengage from repeated failures more quickly after the end of the task and focus on the rewards they might receive in the future, a mechanism that gives them the possibility of a quick recovery from acute stress.

In general, based on the perspective of functional coupling between different large-scale brain networks, this study explores the neural changes during stress situations and its impact on cortisol reactivity and recovery. Compared with previous theoretical studies on motivational dysregluations caused by acute stress induction(Carroll, Lovallo, & Phillips, 2009), we proved from another aspect that the motivation system,

as an important personality trait, plays a promotion role stress responses. This provides a new perspective and possibility for the treatment of adverse stress response. In addition, this study further supports the important role of the central executive network and the dorsal attention network in the process of stress, and explains the less consistent findings of previous human studies on these two networks from the perspective of functional connectivity(Van Oort, et al., 2017a). Finally, this study took both reactivity and recovery of the HPA axis into consideration and explored the underlying neural mechanisms, which may provide a basis for the prevention and treatment of stress-related adverse diseases in the future.

This study has some limitations. First, in this study, changes in DAN-CEN functional connectivity during the task did not establish a direct correlation with the slope of the cortisol reactivity phase. We speculate that this could be due to the HPA axis as a slow response system, cortisol reactivity takes a period of time (Gunnar & Quevedo, 2007), and the brain regulation of the HPA axis may begin before the start of the task. Therefore, future research should take into account the brain activity of the pre-task preparation state and explore how it affects the HPA axis response in subsequent tasks. Secondly, the ScanSTRESS paradigm contains two different conditions (stress and control) in which participants need to shift their states repeatedly. But this study only considered neural changes under stress conditions, future studies should further explore the neural changes under control conditions in different sessions. Thirdly, the experiment consisted of two cognitive tasks (computation and graph rotation), so differences in cognitive patterns may affect the results. Finally, our study was conducted on healthy college students, so whether it can be extended to other groups remains to be further verified.

5 Conclusions

We found that the functional connectivity within and between the active networks changed significantly during the experiment, and this decline could signal an adaptive endocrine stress recovery. Besides, the level of BAS could moderate the relationship between neural changes and endocrine response. This study provides a possible neural mechanism for the rapid recovery of the HPA axis and demonstrates the promotion role of the motivation system, also how personality factors such as motivational system respond to threats to promote survival.

Acknowledgments

This work was supported by the National Natural Science Foundation of China [31971019; 32271133], the National Key Research and Development Program of China [2022ZD0211000], Chongqing Research Program of Basic Research, Frontier Technology [cstc2019jcyj-msxmX0016], and the Social Science Foundation of Chongqing [2021YC029], China.

Disclosures

The authors report no biomedical financial interests or potential conflicts of interest.

References

Abaied, J.L., & Emond, C. (2013). Parent psychological control and responses to interpersonal stress in emerging adulthood: Moderating effects of behavioral inhibition and behavioral activation.*Emerging Adulthood* , **1** , 258-270.

Arnsten, A.F., & Goldman-Rakic, P.S. (1998). Noise stress impairs prefrontal cortical cognitive function in monkeys: evidence for a hyperdopaminergic mechanism. *Arch Gen Psychiatry* , **55** , 362-368.

Broeders, T., Schoonheim, M., Vink, M., Douw, L., Geurts, J., van Leeuwen, J., & Vinkers, C. (2021). Dorsal attention network centrality increases during recovery from acute stress exposure. *NeuroImage: Clinical* , **31** , 102721.

Carroll, D., Lovallo, W.R., & Phillips, A.C. (2009). Are large physiological reactions to acute psychological stress always bad for health? *Social and Personality Psychology Compass* , **3** , 725-743.

Carver, C.S., & White, T.L. (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: the BIS/BAS scales. *Journal of Personality and Social Psychology* ,**67** , 319.

Cole, M.W., Reynolds, J.R., Power, J.D., Repovs, G., Anticevic, A., & Braver, T.S. (2013). Multi-task connectivity reveals flexible hubs for adaptive task control. *Nat Neurosci* , **16** , 1348-1355.

Corral-Frias, N.S., Nadel, L., Fellous, J.M., & Jacobs, W.J. (2016). Behavioral and self-reported sensitivity to reward are linked to stress-related differences in positive affect.*Psychoneuroendocrinology* , **66** , 205-213.

Corral-Frias, N.S., Nikolova, Y.S., Michalski, L.J., Baranger, D.A.A., Hariri, A.R., & Bogdan, R. (2015). Stress-related anhedonia is associated with ventral striatum reactivity to reward and transdiagnostic psychiatric symptomatology. *Psychological Medicine* , **45** , 2605-2617.

Di, X., & Biswal, B.B. (2014). Modulatory interactions between the default mode network and task positive networks in resting-state.*PeerJ* , **2** , e367.

Dixon, M.L., De La Vega, A., Mills, C., Andrews-Hanna, J., Spreng, R.N., Cole, M.W., & Christoff, K. (2018). Heterogeneity within the frontoparietal control network and its relationship to the default and dorsal attention networks. *Proc Natl Acad Sci U S A* ,**115** , E1598-E1607.

Dutcher, J.M., & Creswell, J.D. (2018). The role of brain reward pathways in stress resilience and health. *Neuroscience and Biobehavioral Reviews* , **95** , 559-567.

Fox, M.D., Snyder, A.Z., Vincent, J.L., Corbetta, M., Van Essen, D.C., & Raichle, M.E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proc Natl Acad Sci U S A* , **102** , 9673-9678.

Franklin, T.B., Saab, B.J., & Mansuy, I.M. (2012). Neural mechanisms of stress resilience and vulnerability. *Neuron* , **75** , 747-761.

Fresco, D.M., Mennin, D.S., Heimberg, R.G., & Ritter, M. (2013). Emotion Regulation Therapy for Generalized Anxiety Disorder. *Cogn Behav Pract* , **20** , 282-300.

Gagnon, S.A., & Wagner, A.D. (2016). Acute stress and episodic memory retrieval: neurobiological mechanisms and behavioral consequences.*Annals of the New York Academy of Sciences* , **1369** , 55-75.

Gray, J.A. (1987). The neuropsychology of emotion and personality.

Gunnar, M., & Quevedo, K. (2007). The neurobiology of stress and development. *Annu Rev Psychol* , **58** , 145-173.

Hermans, E.J., Henckens, M., Joels, M., & Fernandez, G. (2014). Dynamic adaptation of large-scale brain networks in response to acute stressors.*Trends in Neurosciences* , **37** , 304-314.

Hermans, E.J., van Marle, H.J.F., Ossewaarde, L., Henckens, M., Qin, S.Z., van Kesteren, M.T.R., Schoots, V.C., Cousijn, H., Rijpkema, M., Oostenveld, R., & Fernandez, G. (2011). Stress-Related Noradrenergic Activity Prompts Large-Scale Neural Network Reconfiguration.*Science* , **334** , 1151-1153.

Holz, N.E., Tost, H., & Meyer-Lindenberg, A. (2020). Resilience and the brain: a key role for regulatory circuits linked to social stress and support. *Molecular Psychiatry* , **25** , 379-396.

Hu, W., Zhao, X., Liu, Y., Ren, Y., Wei, Z., Tang, Z., Tian, Y., Sun, Y., & Yang, J. (2022). Reward sensitivity modulates the brain reward pathway in stress resilience via the inherent neuroendocrine system.*Neurobiol Stress* , **20** , 100485.

Jiang, Y., Kim, S.I., & Bong, M. (2014). Effects of reward contingencies on brain activation during feedback processing.*Front Hum Neurosci* , **8** , 656.

Kalivas, P.W., & Nakamura, M. (1999). Neural systems for behavioral activation and reward. *Current opinion in neurobiology* ,**9** , 223-227.

Liu, Y., Ren, X., Zeng, M., Li, J., Zhao, X., Zhang, X., & Yang, J. (2022). Resting-state dynamic functional connectivity predicts the psychosocial stress response. *Behav Brain Res* , **417** , 113618.

McEwen, B.S. (1998). Stress, adaptation, and disease: Allostasis and allostatic load. *Annals of the New York Academy of Sciences* ,**840** , 33-44.

McEwen, B.S. (2016). Central Role of the Brain in Stress and Adaptation.*Stress: Concepts, Cognition, Emotion, and Behavior* (pp. 39-55).

McEwen, B.S., & Gianaros, P.J. (2011). Stress- and allostasis-induced brain plasticity. *Annu Rev Med* , **62** , 431-445.

Plessow, F., Kiesel, A., & Kirschbaum, C. (2012). The stressed prefrontal cortex and goal-directed behaviour: acute psychosocial stress impairs the flexible implementation of task goals. *Exp Brain Res* ,**216** , 397-408.

Qin, S.Z., Hermans, E.J., van Marle, H.J.F., Luo, J., & Fernandez, G. (2009). Acute Psychological Stress Reduces Working Memory-Related Activity in the Dorsolateral Prefrontal Cortex. *Biological Psychiatry* , **66** , 25-32.

Sinha, R., Lacadie, C.M., Constable, R.T., & Seo, D. (2016). Dynamic neural activity during stress signals resilient coping. *Proc Natl Acad Sci U S A* , **113** , 8837-8842.

Soares, J.M., Sampaio, A., Ferreira, L.M., Santos, N.C., Marques, P., Marques, F., Palha, J.A., Cerqueira, J.J., & Sousa, N. (2013a). Stress Impact on Resting State Brain Networks. *Plos One* , **8** , e66500.

Soares, J.M., Sampaio, A., Marques, P., Ferreira, L.M., Santos, N.C., Marques, F., Palha, J.A., Cerqueira, J.J., & Sousa, N. (2013b). Plasticity of resting state brain networks in recovery from stress.*Front Hum Neurosci* , **7** , 919.

Streit, F., Haddad, L., Paul, T., Frank, J., Schafer, A., Nikitopoulos, J., Akdeniz, C., Lederbogen, F., Treutlein, J., Witt, S., Meyer-Lindenberg, A., Rietschel, M., Kirsch, P., & Wust, S. (2014). A functional variant in the neuropeptide S receptor 1 gene moderates the influence of urban upbringing on stress processing in the amygdala.*Stress* , **17** , 352-361.

Tabibnia, G. (2020). An affective neuroscience model of boosting resilience in adults. *Neurosci Biobehav Rev* , **115** , 321-350.

Taubitz, L.E., Pedersen, W.S., & Larson, C.L. (2015). BAS Reward Responsiveness: A unique predictor of positive psychological functioning. *Pers Individ Dif* , **80** , 107-112.

Vaisvaser, S., Lin, T., Admon, R., Podlipsky, I., Greenman, Y., Stern, N., Fruchter, E., Wald, I., Pine, D.S., Tarrasch, R., Bar-Haim, Y., & Hendler, T. (2013). Neural traces of stress: cortisol related sustained enhancement of amygdala-hippocampal functional connectivity.*Frontiers in Human Neuroscience* , **7** .

van Marle, H.J.F., Hermans, E.J., Qin, S.Z., & Fernandez, G. (2010). Enhanced resting-state connectivity of amygdala in the immediate aftermath of acute psychological stress. *NeuroImage* , **53** , 348-354.

Van Oort, J., Tendolkar, I., Hermans, E., Mulders, P., Beckmann, C., Schene, A., Fernández, G., & van Eijndhoven, P. (2017a). How the brain connects in response to acute stress: A review at the human brain systems level. *Neuroscience & Biobehavioral Reviews* ,**83** , 281-297.

van Oort, J., Tendolkar, I., Hermans, E.J., Mulders, P.C., Beckmann, C.F., Schene, A.H., Fernandez, G., & van Eijndhoven, P.F. (2017b). How the brain connects in response to acute stress: A review at the human brain systems level. *Neuroscience and Biobehavioral Reviews* ,**83** , 281-297.

Walker, F.R., Pfingst, K., Carnevali, L., Sgoifo, A., & Nalivaiko, E. (2017). In the search for integrative biomarker of resilience to psychological stress. *Neurosci Biobehav Rev* , **74** , 310-320.

Yao, Z., Shi, J., Zhang, Z., Zheng, W., Hu, T., Li, Y., Yu, Y., Zhang, Z., Fu, Y., Zou, Y., Zhang, W., Wu, X., & Hu, B. (2019). Altered dynamic functional connectivity in weakly-connected state in major depressive disorder. *Clin Neurophysiol* , **130** , 2096-2104.

Yeo, B.T., Krienen, F.M., Sepulcre, J., Sabuncu, M.R., Lashkari, D., Hollinshead, M., Roffman, J.L., Smoller, J.W., Zollei, L., Polimeni, J.R., Fischl, B., Liu, H., & Buckner, R.L. (2011). The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *J Neurophysiol* , **106** , 1125-1165.

Zhang, Y., Dai, Z., Hu, J., Qin, S., Yu, R., & Sun, Y. (2020). Stress-induced changes in modular organizations of human brain functional networks. *Neurobiol Stress* , **13** , 100231.