Supplemental Data

Stress task and procedure

The Montreal Imaging Stress Task (MIST), a widely used stress paradigm and adapted for functional magnetic resonance imaging (fMRI), was induced the psychosocial stress by using elements of the uncontrollability and social evaluative threat. The MIST paradigm used a block design consisting of 3 different conditions (rest, control and experimental). The rest condition recorded a baseline state in 30 seconds and the interface of the computer program remained on the screen without tasks. Subjects were asked to keep their eyes open and not to press buttons until the next mental arithmetic task appeared. The control condition (90 seconds) aimed at recording brain activation related to mental arithmetic aspects of the task specifically that without stress components. The arithmetic tasks were presented as in the experimental condition, but without time pressure. Subjects were told to try to perform the task as quickly and accurately as possible. Average performance could reach to about 90% under the control condition. Finally, during the experimental condition (90 seconds), time pressure was induced by a time bar adapting to each subject's performance in order to enforce about 50% correct rate. Subjects received "correct" or "incorrect" feedback after each math question, and a simulative performance bar at the top of the screen showed that their performances were below the correct rate of the 'average subject', which was artificially set to 80% . The order of conditions was repeated once within a measurement sequence, resulting in a total duration of seven minutes. After each scanning run, the investigator criticized the subjects' insufficient performance via headphone (about 30 seconds), emphasizing the need for better performance to enhance subjects' perceived stress. We investigated the contrasts experimental minus control to assess the effects of stress.

Four from eight saliva samples were collected in the scanner during the intervals of scanning sequences. Because of the constraints of the neuroimaging environment, the subjects were still in the scanner without movement when saliva collecting. The investigator placed the sterile salivette into the subject's mouth with sterile gloves. The subject was instructed to refrain from chewing on the salivette to minimize the head movement. After about 2 minutes (usually sufficient to saturate the salivette with saliva), the subject was asked to expel the salivette using the tip of the tongue so that the investigator can get it from his/her mouth. This procedure was repeated for each saliva sample obtained during scanning, and it was conducted after a negative verbal feedback between MIST runs.

Comparison of findings

Several prior fMRI studies have used the MIST to investigate specific neural stress responses of some disorders, or to explore potential associations between cortisol responses and brain regional activation. Our results were not fully consistent with the findings of these studies, with some studies highlighting other brain regions. To make a clear presentation, we summarized the comparisons of previous and our findings in those brain regions highlighted by prior studies in STable 4.

Supplementary references

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STable 1 Stress-induced Activation and Deactivation (experimental minus control condition).

	Region	Hemi-sphere	MNI coordinate			*t*
			x	y	z	
Activation	Middle temporal gyrus	R	48	-66	0	17.20
	Middle occipital gyrus	R	18	-93	9	15.85
	Declive	R	24	-72	-18	14.70
	Lingual gyrus	R	21	-75	-15	14.33
	Middle occipital gyrus	L	-18	-93	12	14.27
	Supplementary motor area	R	3	0	51	14.24
	Fusiform gyrus	R	27	-57	-12	14.05
	Declive	L	-30	-63	-18	13.99
	Cingulate gyrus	R	3	12	42	13.90
	Lingual gyrus	L	-21	-72	-9	13.87
	Middle frontal gyrus	R	27	3	57	13.86
	Insula	L	-33	15	3	12.19
	Superior frontal gyrus	R	30	42	30	12.12
	Thalamus	R	3	-18	6	11.84
	Insula	R	33	18	3	11.29
	Thalamus	L	-18	-24	9	10.93
Deactivation	Superior temporal gyrus	R	39	12	-39	-11.48
	Middle temporal gyrus	L	-39	9	-36	-10.11
	Anterior cingulate cortex	L	-6	30	-6	-10.03
	Angular gyrus	R	51	-69	42	-8.62
	Medial prefrontal cortex	L	-3	36	-9	-7.80
	Parahippocampal gyrus	R	24	-6	-27	-7.66
	Angular gyrus	L	-39	-78	45	-7.16

All $p<.001$, family-wise error rate corrected.

STable 2 Regions of a Main Effect of Group by ANOVA among Three Groups.

Region	**Hemi-sphere**	**MNI coordinate**			***F***	η^2
		x	**y**	**z**		
Precuneus	R	9	-48	48	17.50	.26
Paracentral lobule	L	-12	-33	54	15.12	.23
Ventromedial prefrontal cortex	L	-6	42	-9	14.55	.22
Middle cingulate cortex	L	-6	-12	45	13.66	.21
Dorsolateral prefrontal cortex	L	-24	42	21	12.11	.19
Caudate	R	18	18	6	10.50	.17
Putamen	L	-21	9	6	9.83	.16
Putamen	R	24	15	-3	9.07	.15

All p<.001, uncorrected.

STable 3 Comparison of Stress-related Activation among Three Groups with Controlling for Childhood Traumas.

Contrast	Region	Hemi-sphere	MNI coordinate[a]			*t*	*p* uncorrected	*P* corrected[b]	Cohen's *d*
			x	y	z				
Current depression > Healthy Control	Precuneus	Right	9	-48	48	4.99	<.001	<.001	1.19
	Paracentral lobule	Left	-9	-33	48	4.71	<.001	.001	1.13
	Middle cingulate cortex	Left	-3	-12	42	4.03	<.001	.012	.96
Current depression < Healthy Control	Ventromedial prefrontal cortex	Left	-3	39	-9	3.99	<.001	.014	.95
Remitted depression > Healthy Control[c]	Precuneus	Right	9	-48	48	4.85	<.001	.001	1.19
	Putamen	Left	-21	6	6	4.78	<.001	.001	1.17
	Caudate	Right	18	18	6	4.67	<.001	.001	1.14
	Middle cingulate cortex	Left	-6	-9	48	4.43	<.001	.003	1.08
	Paracentral lobule	Left	-15	-33	57	4.28	<.001	.005	1.05
	Dorsolateral prefrontal cortex	Left	-24	42	21	4.24	<.001	.006	1.04
	Putamen	Right	27	12	-3	3.87	<.001	.02	.95
Remitted depression < Healthy Control[c]	Ventromedial prefrontal cortex	Left	-6	36	-9	5.34	<.001	<.001	1.30
Remitted depression > Current depression	Putamen	Right	27	18	6	2.98	.002	.24	.73
	Caudate	Right	21	21	6	2.85	.003	.31	.70
	Putamen	Left	-21	9	6	2.79	.003	.35	.69
	Dorsolateral prefrontal cortex	Left	-24	42	18	2.19	.015	.80	.54

[a] Montreal Neurological Institute coordinate;

[b] Family-wise error rate correction;

[c] Beck Depression Inventory scores were controlling for as well when comparing remitted depression with healthy control group.

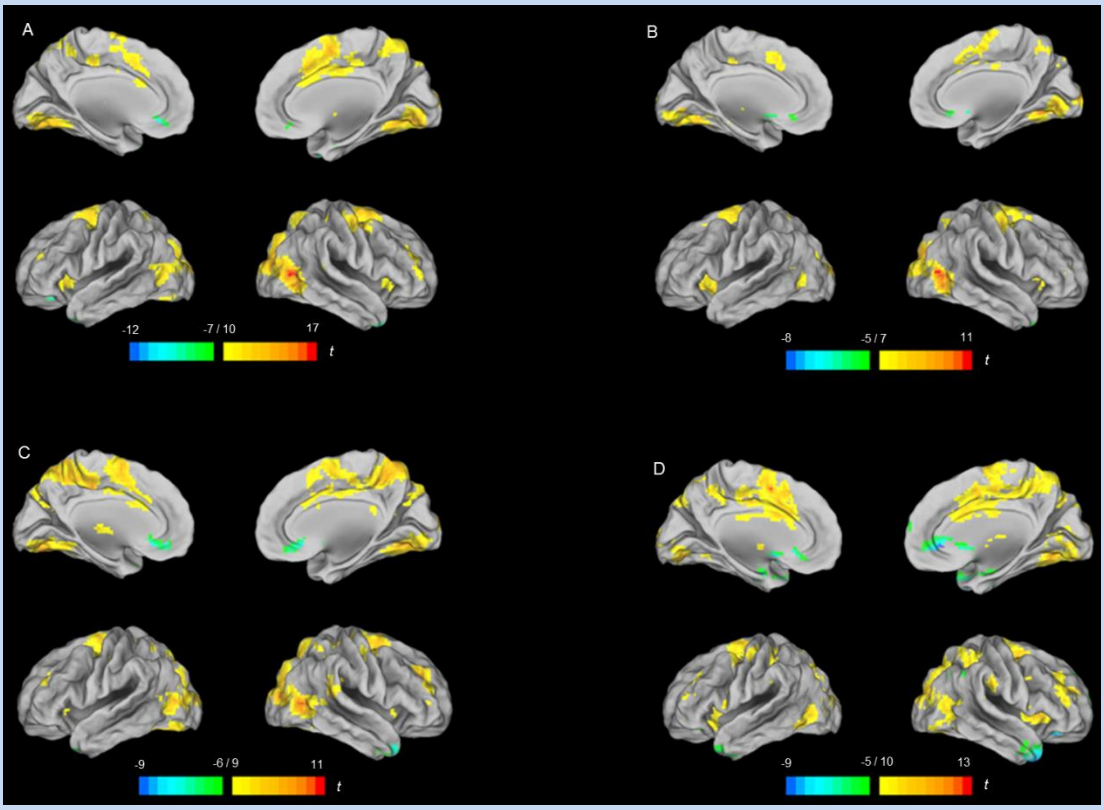
STable 4 Findings in Brain Regions Highlighted by Previous Studies Using Montreal Imaging Stress Task.

Study	Participants	Brain region	MNI coordinate[a]			Stress-induced activity	Stress-induced activity in our study	Group difference/ Association with cortisol	Related findings in our study
			x	y	z				
Ashare et al. 2016 (1)	Nicotine withdrawal	Inferior frontal gyrus	38	30	16	Activation	Activation	Increased activity in nicotine withdrawal	None
	Nicotine non-withdrawal	Anterior/para cingulate cortex	-2	38	28	Activation	Activation	Increased activity in nicotine withdrawal	None
		Precuneus	2	-64	20	Activation	Activation	Increased activity in nicotine withdrawal	None
		Supramarginal gyrus	52	-26	30	Activation	Activation	Increased activity in nicotine withdrawal	None
Castro et al. 2015 (2)	Schizophrenia	Subgenual anterior cingulate cortex	2	44	0	Activation in controls	Deactivation	Decreased activity in schizophrenia	Decreased activity in depression groups
Dedovic et al. 2014 (3)	Subclinical depression	Precuneus	—	—	—	Activation	Activation	Decreased activity in subclinical depression	Increased activity in depression groups
		Temporoparietal junction	-46	-52	24	Activation in controls	Activation	Decreased activity in subclinical depression	None
		Insula	40	-6	10	Activation in controls	Activation	Decreased activity in subclinical depression	None
		Hippocampus	—	—	—	Activation	Activation/ Deactivation	None	None
		Subgenual anterior cingulate cortex	8	22	-4	Deactivation	Deactivation	None	Decreased activity in depression groups
		Medial orbitofrontal cortex	-.3	43	-20	Deactivation in subclinical depression	Deactivation	None	Decreased activity in depression groups
Lord et al. 2012 (4)	Postpartum obsessive-compulsive disorder	Orbitofrontal cortex	6	36	-17	Activation in patients, deactivation in controls	Deactivation	Increased activity in postpartum obsessive-compulsive disorder	Decreased activity in depression groups
		Superior temporal gyrus	48	12	-32	Activation in patients, deactivation in controls	Deactivation	Increased activity in postpartum obsessive-compulsive disorder	None
		Insula	-45	-4	-2	Activation in patients, deactivation in controls	Activation	Increased activity in postpartum obsessive-compulsive disorder	None
		Medial prefrontal cortex	6	36	-17	Activation in patients, deactivation in controls	Deactivation	Increased activity in postpartum obsessive-compulsive disorder	Decreased activity in depression groups

Pruessner et al. 2008 (5)	Healthy subjects	Hippocampus	—	—	—	Deactivation	Activation/ Deactivation	Deactivation positively correlated with cortisol responses	None
		Medial orbitofrontal cortex	17	44	-16	Deactivation	Deactivation	Decreased activity in cortisol responders	Decreased activity in depression groups, deactivation correlated with cortisol increases
		Anterior cingulate cortex	-12	47	-3	Deactivation in cortisol responders, activation in nonresponders	Activation	Decreased activity in cortisol responders relative to nonresponders	None
		Dorsolateral prefrontal cortex	-29	44	20	Deactivation in cortisol responders, activation in nonresponders	Activation	Decreased activity in cortisol responders relative to nonresponders	Increased activity in remitted depression
Soliman et al. 2011 (6)	Negative symptom schizotypy	Putamen	-26	-16	10	Deactivation	Activation	Decreased activity in Negative symptom schizotypy	Increased activity in remitted depression
	Positive symptom schizotypy	Caudate body	-10	8	10	Deactivation	Activation	Decreased activity in Negative symptom schizotypy	None
		Amygdala-parahippocampal gyrus	-22	0	-18	Deactivation	Deactivation	Decreased activity in Negative symptom schizotypy	None
		Anterior cingualte	-4	42	-2	Deactivation	Deactivation	Decreased activity in Negative symptom schizotypy	Decreased activity in depression groups
		Cingulate white matter	18	-4	26	Activation	Activation	Decreased activity in Negative symptom schizotypy	None
		Superior frontal white matter	26	-26	28	Activation	Activation	Decreased activity in Negative symptom schizotypy	None
Wheelock et al. 2016 (7)	Healthy subjects	Ventromedial prefrontal cortex	6	62	-10	Activation in nonresponders	Deactivation	Decreased activity in cortisol responders	Decreased activity in depression groups, deactivation correlated with cortisol increases
		Posterior cingulated cortex	-10	48	30	Activation in nonresponders	Activation	Decreased activity in cortisol responders	None

[a]Montreal Neurological Institute coordinate.

SFigure 1 Brain Activation during Stress Processing.



Significantly activated regions (*p*<.05, family-wise error rate corrected) of the experimental > control contrast in A: all subjects as a whole; B: healthy control group; C: current depression group; D: remitted depression group.