IMAGING STRESS EFFECTS ON WORKING MEMORY CAPACITY IN ADOLESCENTS AT-RISK

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BACKGROUND

Psychosocial stress has been identified as a key trigger for numerous neuropsychiatric disorders, many of which emerge in adolescence. The late maturation of prefrontal neural networks that regulate the stress response creates a unique target for stress-induced modulation of adolescent brain and cognition[1]. In addition, animal models demonstrate this stress response may be different in males and females[2]. The present study examined the impact of acute stress on neural networks responsible for working memory (WM) in adolescents at risk for complex neuropsychiatric disorders.

HYPOTHESES

H1: As working memory load increases, there will be a change in pattern in prefrontal activation.
H2: Similarly, prefrontal activation will be interrupted after a psychosocial stressor.
H3: Adolescents at a higher-risk for neuropsychiatric disorders will be particularly sensitive to this stress affect.
H4: Females will perform worse than males and thus, show a greater prefrontal disruption.

METHODS

Participants:

60 adolescents, aged 9-16 years old, 34 males
- 33 typically developing
- 27 diagnosed ADHD/Anxiety and/or at a familial high-risk for psychosis

Study:

1 clinical assessment, 1 EEG session, 1 fMRI session

Functional Imaging Parameters:

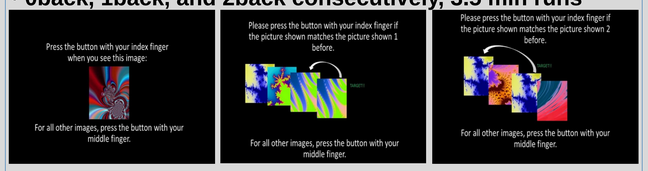
Scanner: GE MR750 3T
Spiral acquisition sequence: TR=2000ms; TE=30ms; Flip angle=60˚
Voxel size: 3.75 * 3.75 * 4 mm; 34 oblique-axial slices (FOV=24 cm)

Image Analysis:

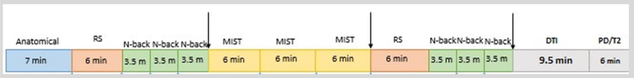
- Voxel-based analyses of activation using FSL (1)
- All covariate analyses were corrected using a FWE at z>2.3 (p<.01 cluster thresholded)

Working Memory Task (nBack):

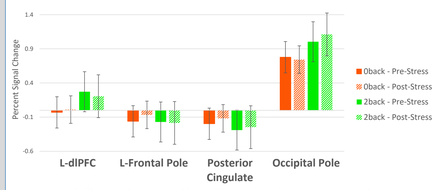
- 0back, 1back, and 2back consecutively, 3.5 min runs



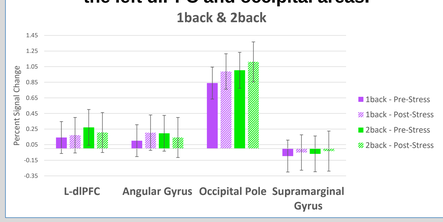
- One set before a stressor (Montreal Imaging Stress Task[3]) and one set afterwards

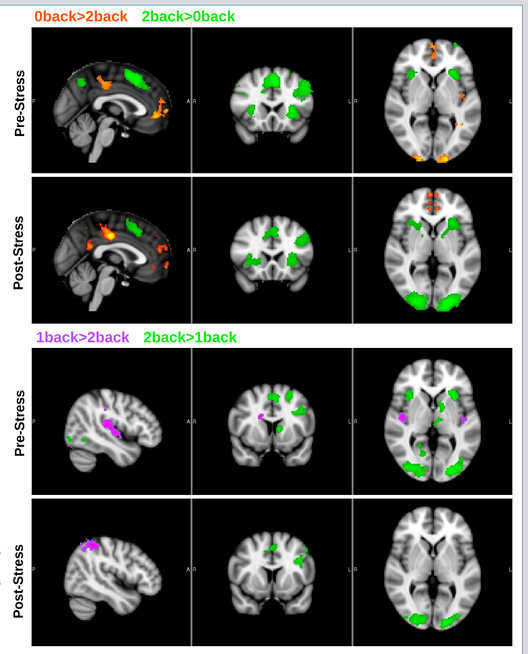


1. LOAD EFFECTS

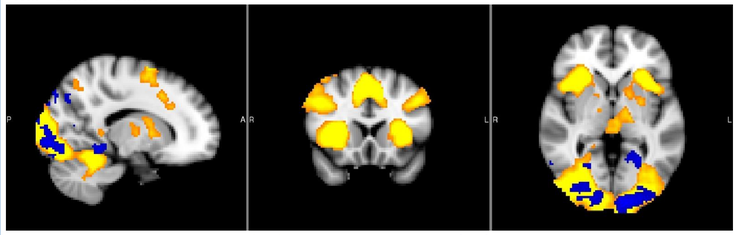


After stress, the 2back shows greater suppression of part of the DMN (posterior cingulate) and increased activation in the left dlPFC and occipital pole compared to the 0back. Compared to the 1back, the 2back activation shows less suppression of the supramarginal gyrus, decreased activation in the angular gyrus, and increased activation in the left dlPFC and occipital areas.

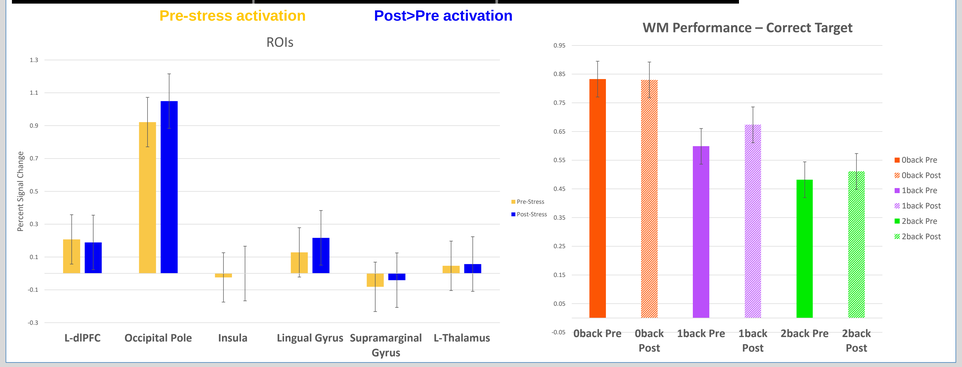




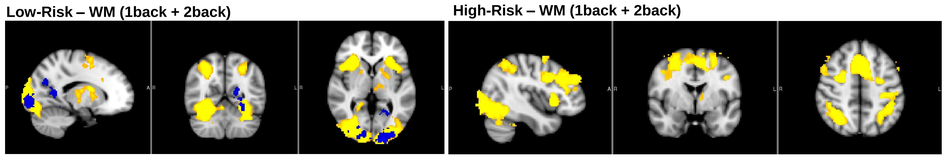
2. STRESS EFFECTS



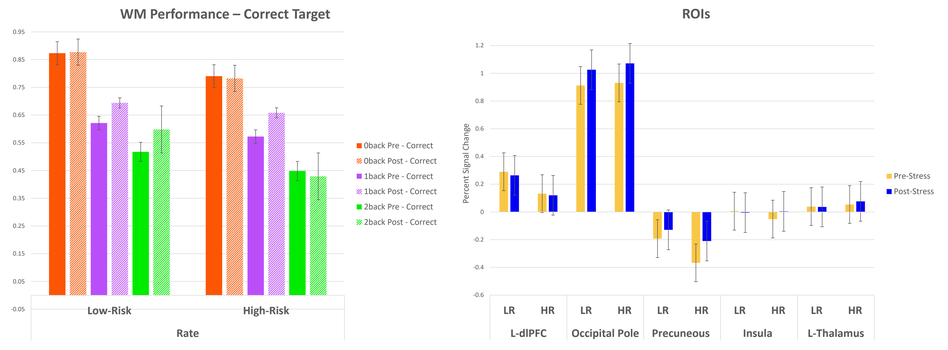
After an acute, psychosocial stressor, adolescents show less suppression of the insula and supramarginal gyrus and an increase in activation in the thalamus, lingual gyrus, and occipital areas dealing with vision.



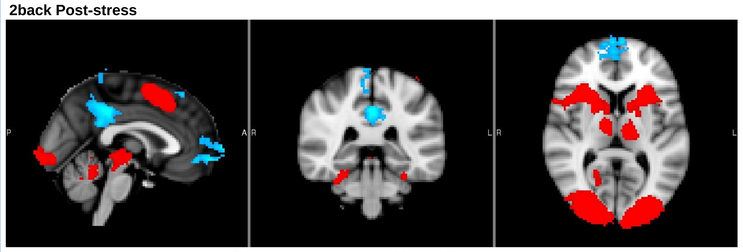
3. HIGH-RISK VS LOW-RISK



Those at a lower risk for neuropsychiatric disorders show increased occipital pole activation, suppression of the insula, and decreased thalamus post-stress compared to pre-stress while those at a higher-risk show increased insula and increased thalamus. Both groups show decreased dlPFC activation, increased occipital pole activation, and less suppression of the precuneous.



4. MALES VS FEMALES



Post-stress, males show less suppression of the frontal pole and posterior cingulate during a high working memory load (2back). However, females show more occipital activation and, on average, perform better than males at that high working memory load both before and after stress.

DISCUSSION and CONCLUSION

- Adolescent brain activation at high load WM suggests two things: 1) adolescents work harder on completing a 2back than a 0back, and 2) due to the left lateralization of the dlPFC, adolescents are utilizing covert retrieval to complete a harder WM task.
- After an acute stressor, adolescents employ a visual strategies to complete WM tasks.
- Both groups of adolescents, regardless of risk for neuropsychiatric disorders, contribute to the overall stress effect in different ways. The thalamic and insular activation of high-risk adolescents mirror the main stress effect as well as the statistically significant increase in occipital pole activation post-stress of the lower-risk group.
- Females employing a visual strategy may be advantageous for performance on a spatial WM task.

SEE ALSO

C36. Electrophysiological Markers of Stress on Working Memory Networks in Adolescents – Campbell, Alana
C41. Anxiety Modulates Autonomic Regulation and Neural Activation During High-Load Working Memory Following Acute Stress in Adolescence – Graham, Jessica

NEXT STEPS

- Look at the difference between ADHD/Anxiety and familial high-risk
- Analyses with clinical and neurocognitive assessments
- Integrate information about cortisol and heart rate as a stress reactivity measurement
- Analyze the functional connectivity between active regions

REFERENCES

[1]Holtzman, C. W., Shapiro, D. I., Trotman, H. D. & Walker, E. F. (2012). Stress and the prodromal phase of psychosis. *Curr Pharm Des* 18, 527-533.
[2]Holmes, A. (2017). Sex and Orexins: Uncovering a Mechanism Underlying Sex Differences in Stress Susceptibility. *Biological Psychiatry, 81*(8), 642-644.
[3]Dedovic, K., Renwick, R., Mahani, N. K., Engert, V., Lupien, S. J., & Pruessner, J. C. (2005). The Montreal Imaging Stress Task: using functional imaging to investigate the effects of perceiving and processing psychosocial stress in the human brain. *Journal of Psychiatry and Neuroscience*, *30*(5), 319–325.

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