Adolescent Maturation of Stress Regulatory Brain Circuits

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BACKGROUND

- **Adolescence is an important period for the maturation of fronto-limbic circuits, and a time for the onset of many neuropsychiatric disorders**
- **Aberrant stress reactivity and regulation have been linked to clinical neuropsychiatric symptoms (1) and may pose risk for neuropsychiatric disorders**
- **Fronto-limbic brain circuits are critical for regulation of the stress response**

HYPOTHESES

H1: Limbic regions will show decreased activation while executive regions will show increased activation during social evaluative stress.

H2: Aberrant stress reactivity and regulation in the cortico-limbic circuitry will demonstrate significant age-related maturational changes.

H3: Fronto-limbic circuits will be significantly associated with trait anxiety measures

METHODS

Participants:

32 typically developing adolescents aged 9-16 years old.

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)

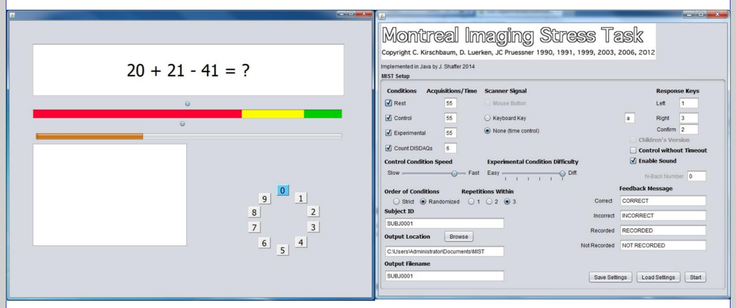
•All covariate analyses were corrected using a FWE at z>2.3 (p<.01 cluster thresholded)

Montreal Imaging Stress Task:

•3 Mental Math runs, 5 min each

•Negative feedback between runs

•Button response to all stimuli

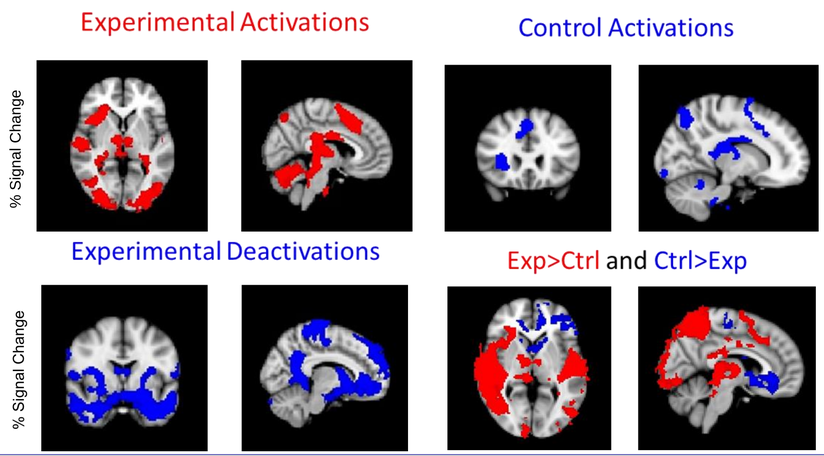


Anxiety Measures:

Trait anxiety was measured pre-scan using the State-Trait Anxiety Inventory for children (STAI-CH).

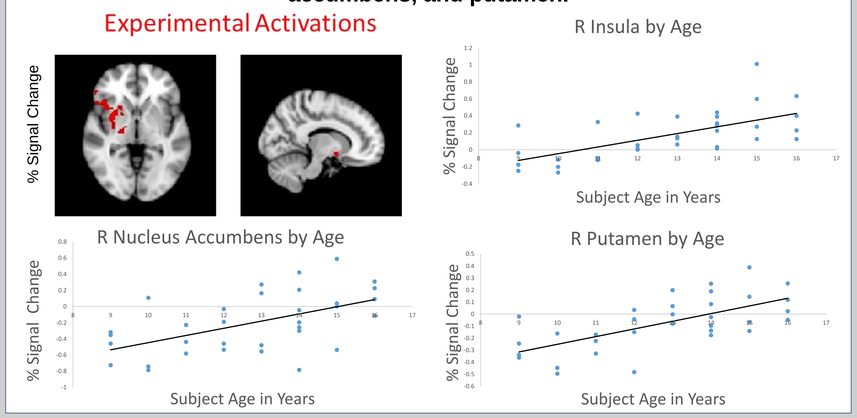
MAIN RESULTS

Stress blocks <u>significantly activated</u> multiple regions including the thalamus, insula, frontal operculum, and paracingulate regions, supporting findings in adults from Dedovic et al. (2009). Other areas were <u>significantly deactivated during stress</u>, including the amygdala and nucleus accumbens.



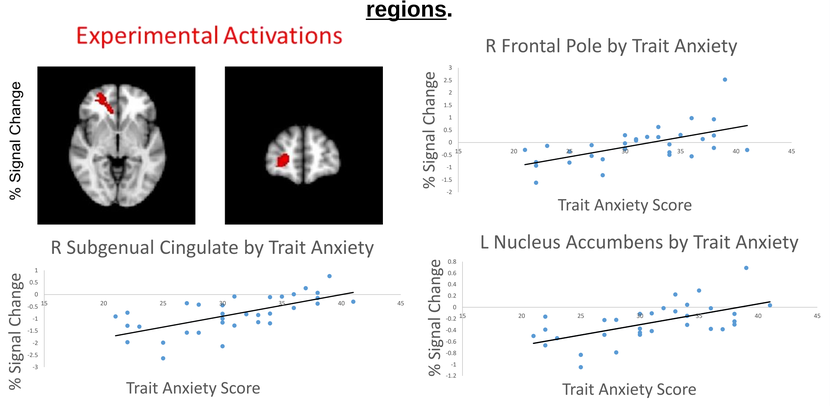
AGE RESULTS

Covariate analyses revealed <u>significant age-dependent maturational changes in stress</u> activation in the anterior insula, frontal operculum, nucleus accumbens, and putamen.



TRAIT ANXIETY RESULTS

Covariate analyses also revealed significant correlations between <u>trait anxiety scores and stress-induced activation in the frontal pole and paracingulate regions</u>.

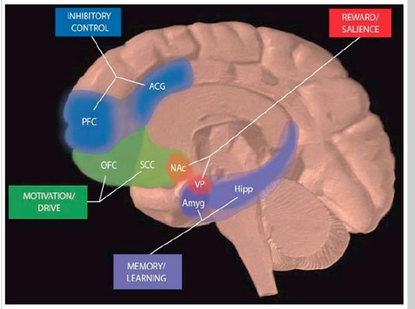


DISCUSSION and CONCLUSION

- **Stress may cause domain effects: increases cognition in some areas but may inhibit it in others**
- **Deactivation of amygdala and NAcc during stress may indicate a temporary blunting of emotional response to reward**
- **Age-dependent maturation during adolescence:**
  - **Significantly increased activation of anterior insula and frontal operculum with age may indicate increased interoception and awareness of emotion and bodily state under stress**
- **Age-dependent neural nodes may play key roles in the emergence of neuropsychiatric disorders during adolescence**
- **Multiple nodes of stress response circuitry covaries significantly with trait anxiety:**
  - **Decreased suppression of frontal pole under stress covaries with trait anxiety and may underscore the decreased sensitivity to emotional reward as a function of baseline anxiety**
  - **Decreased suppression of subgenual cingulate with increased trait anxiety levels may indicate a hyperreactivity or greater intolerance to task uncertainty among individuals with more anxious baselines**

NEXT STEPS

- **Are there significant age x anxiety interactions?**
- **Are there any correlations with gender, RSA, genetics, pubertal stage, and other clinical measures?**
- **How will stress affect memory and reward circuitry?**
- **How will high-risk adolescents diverge from these results?**
- **What are potential neurodevelopmental implications for chronic stress exposure in childhood and adolescence?**



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1. Dedovic, K., Duchesne, A., Engert, V., Lue, S.D., Andrews, J., Efanov, S., Beaudry, T. & Pruessner, J. (2014). Psychological, endocrine and neural responses to social evaluation in subclinical depression, *SCAN, 9,* 1632-1644.
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