

# LEARNING-RELATED CEREBELLAR CONNECTIVITY IN ADOLESCENT CHRONIC PAIN

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## BACKGROUND

- Chronic pain is common in young people and can have a major impact across life domains.
- Mechanisms underlying the development of chronic pain and its persistence are still poorly understood.
- Alterations in learning processes are a strong predictor of pain-related disability.
- It is important to understand the neural mechanisms underlying these learning processes.
- The focus within this field of research has primarily been on the cerebrum, excluding potential cerebellar contributions.
- Research in pain-free adults suggests that differential responses to threat and safety cues may be apparent in the cerebellum.

**Do adolescents with chronic pain differ in cerebellar activation in threat learning compared to pain free peers?**

## METHODS

### Participants

- Adolescents (age M = 15.7y, SD = 2.91y), with chronic pain (n=44) compared with pain-free peers (n=32)

### Data Acquisition

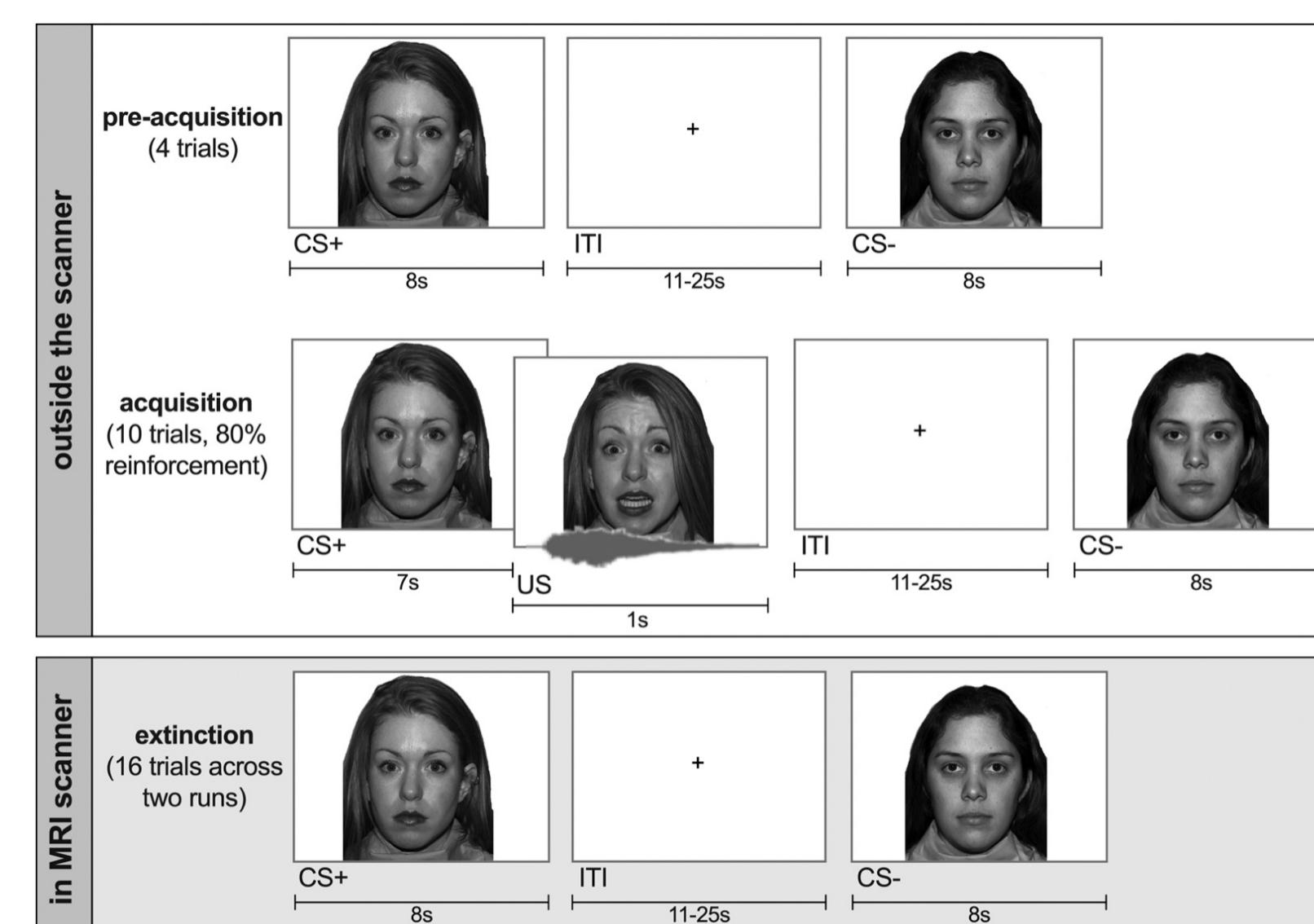
- For the functional images, a T2\*-weighted standard echo-planar imaging (EPI) sequence was used to acquire 51 axial slices (3 mm isotropic) covering the entire cortical volume, using the following parameters: repetition time (TR) = 1110 ms, echo time (TE) = 30 ms, flip angle = 70°, field of view (FOV) = 228 × 228 mm, matrix size = 76 × 90, slice acceleration factor = 3.

### Data Processing

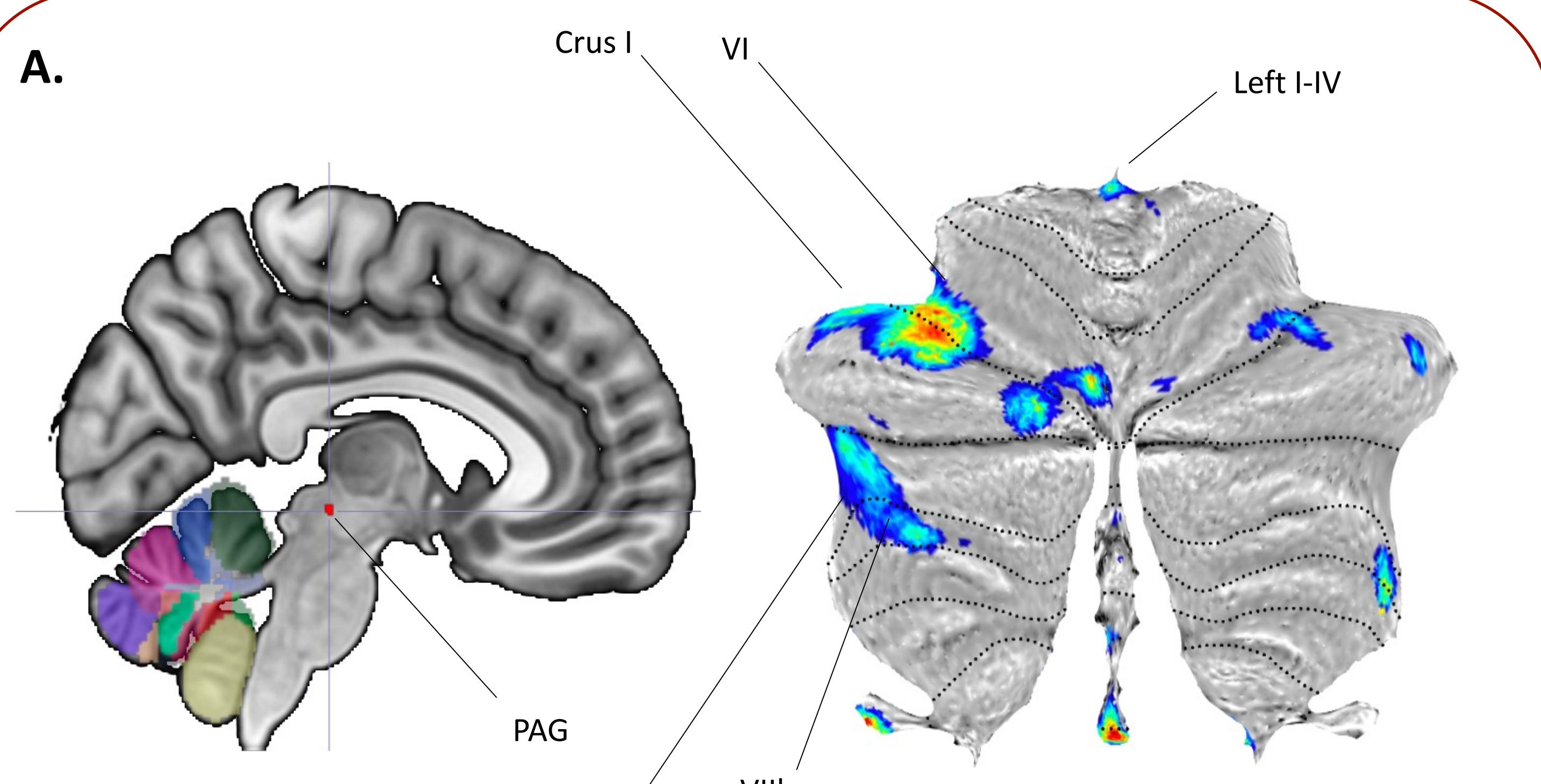
- fMRIprep was used for preprocessing of the functional task-evoked MRI data. Analysis of cerebellar task-evoked responses used the SUIT toolbox, including isolation of cerebellum from cerebral cortex and spatial normalization into atlas space. CONN was used for connectivity analyses.

### Functional seed selection

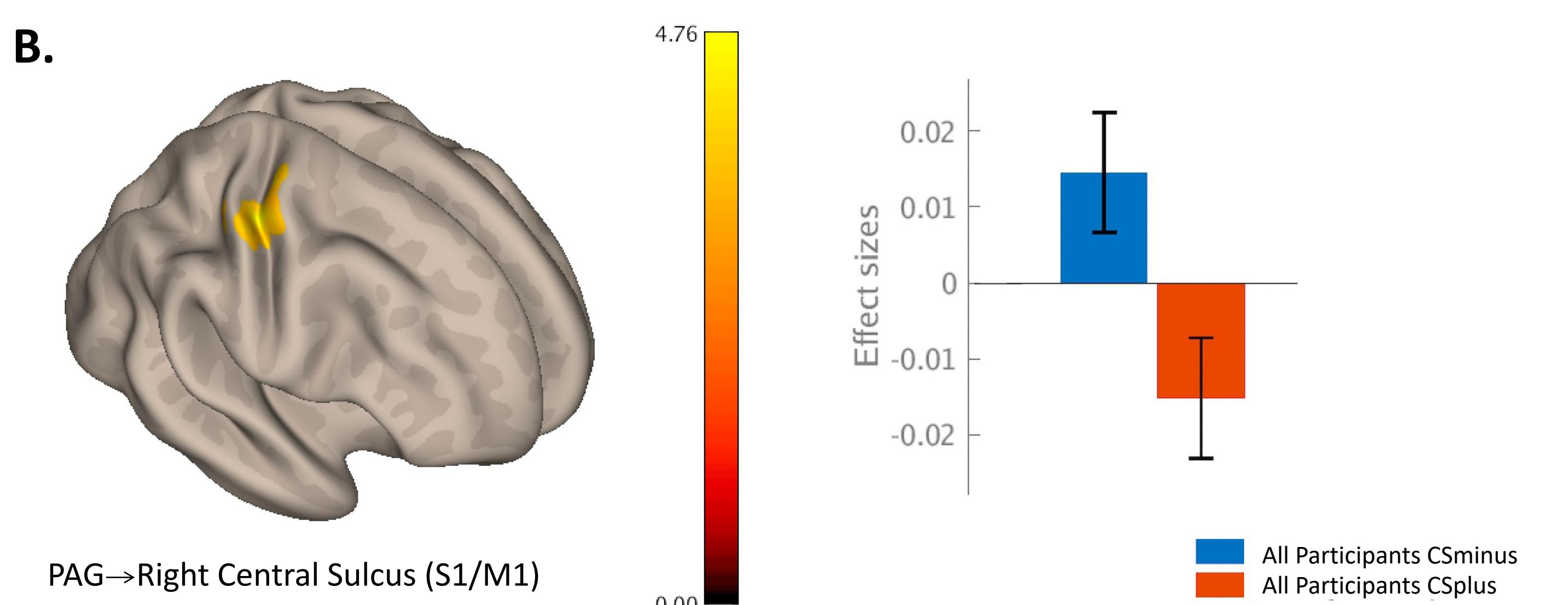
- In the first level analyses, a general linear model was used to examine responses to the CS+ and CS-. The comparisons between CS+ >/< CS- were calculated and used for a second level analysis, including age and sex as covariates.



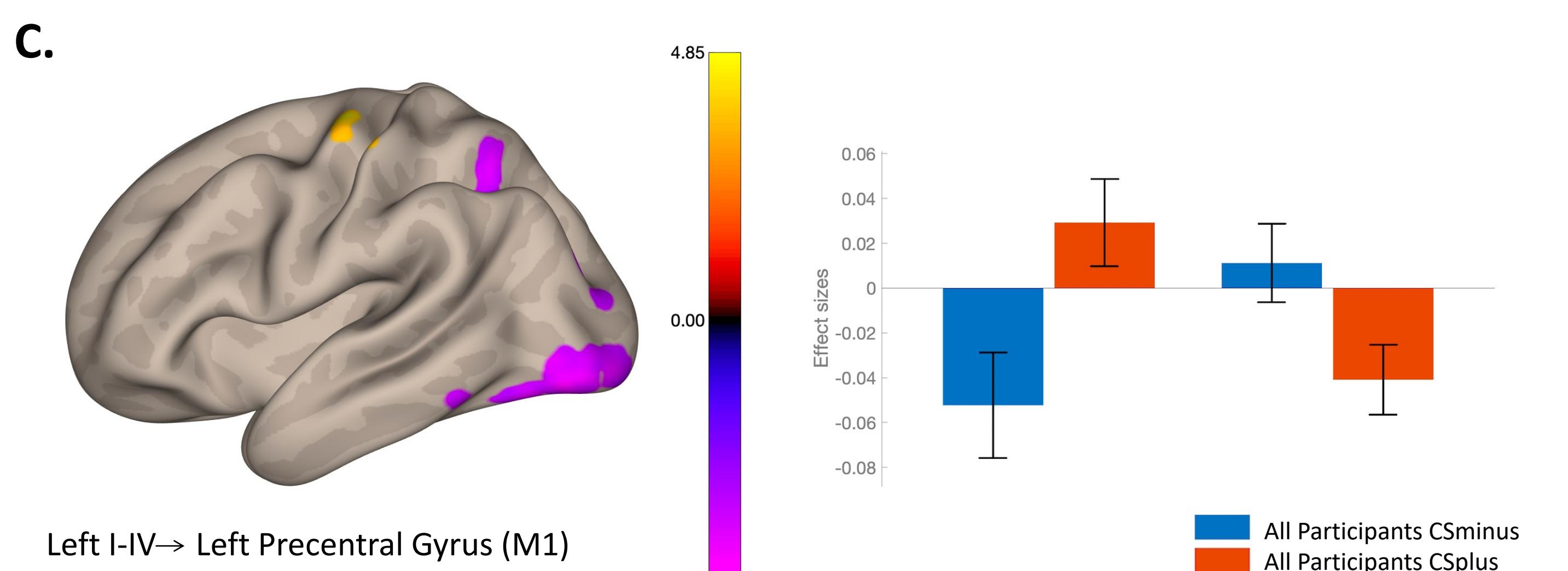
## RESULTS



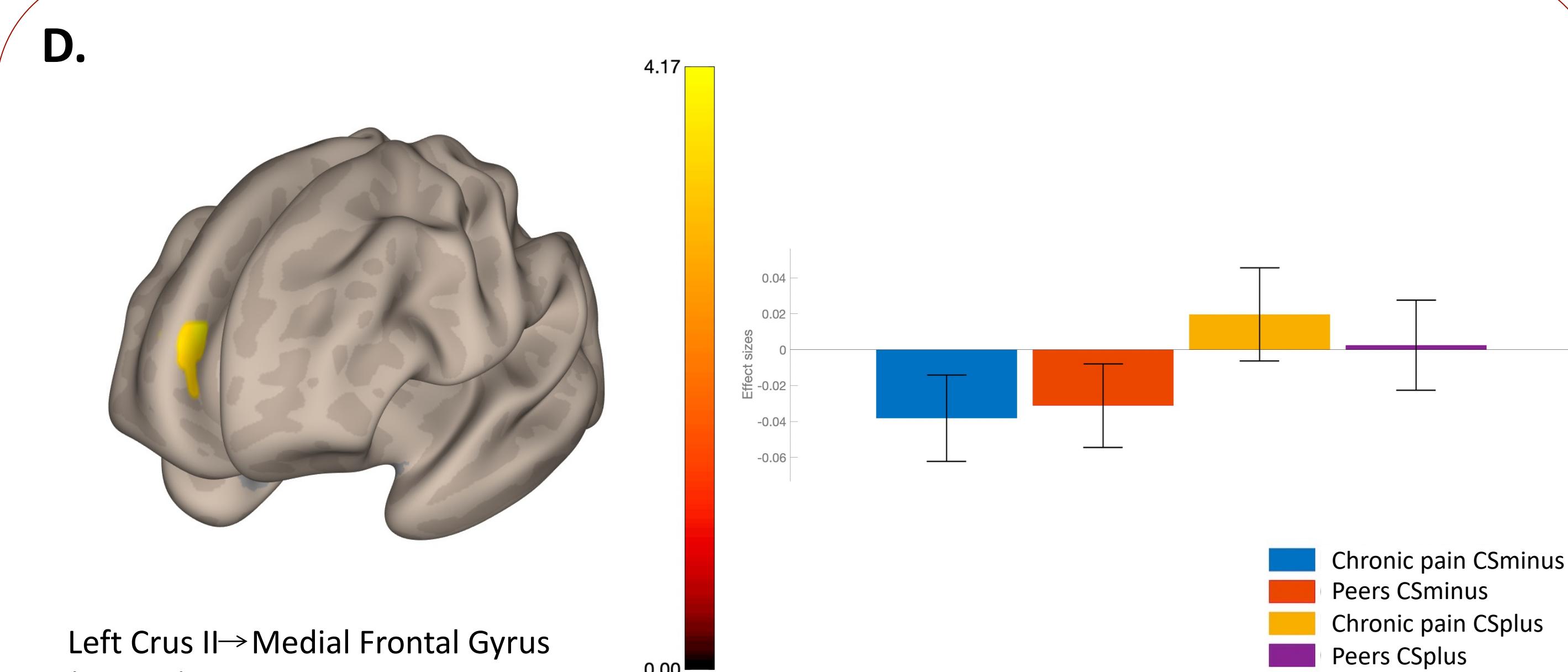
There were ten significant clusters (uncorrected threshold  $p<.001$ , cluster size threshold = 10 voxels) in the cerebellum that showed greater responses for CS+ over CS- (see above), with one cluster in PAG surviving FWE-correction (see A).



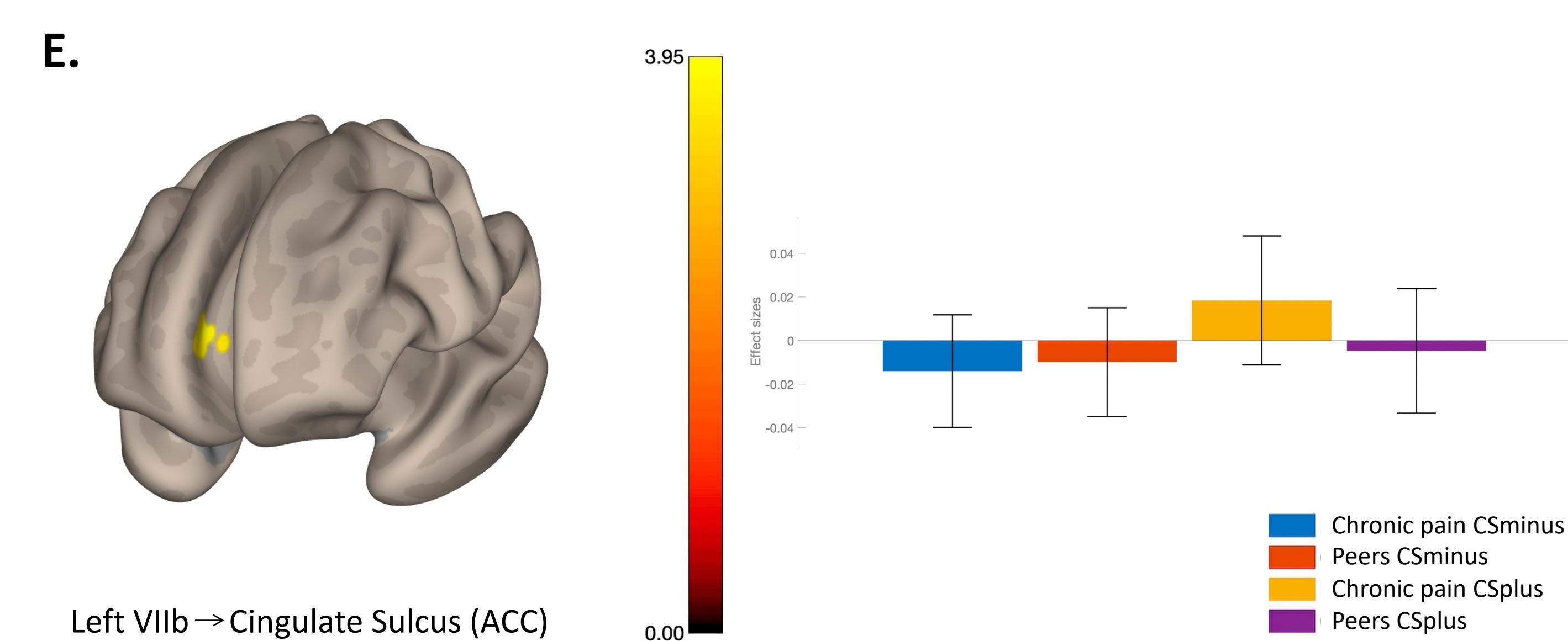
The clusters in Figure A. were used as seeds in a gPPI analysis. Figures B and C are from the second level analysis for all participants for the contrast CS+>CS-. Whole brain analysis, FDR corrected at  $p<.05$ .



## RESULTS



Figures D and E are from the second level analysis comparing the chronic pain group to pain free controls for the contrast CS+>CS-. Whole brain analysis, FDR corrected at  $p<.05$ .



We observed modulated functional connectivity between cerebellum and primary sensory areas when comparing CS+ to CS- during extinction. In addition, we observed differential connectivity between cerebellum and prefrontal regions dependent on pain status for the same contrast.

## CONCLUSIONS

Understanding mechanistically how fear and emotional processing are influenced in a developmentally critical time point in youth with chronic pain could help providers better treat and care for both adults and children suffering from chronic pain and other disorders and diseases where learned fear can influence many factors such as function, disability, mental and physical health, and pain.

### Contact Information

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### Funding

Supported by The National Institutes of Health (No. R01HD083270 to LES)

### Scan me!

