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Augmented brain responses to multisensory stimulation in affective/regulation circuits is associated with worse quality of life in adolescents with chronic musculoskeletal pain



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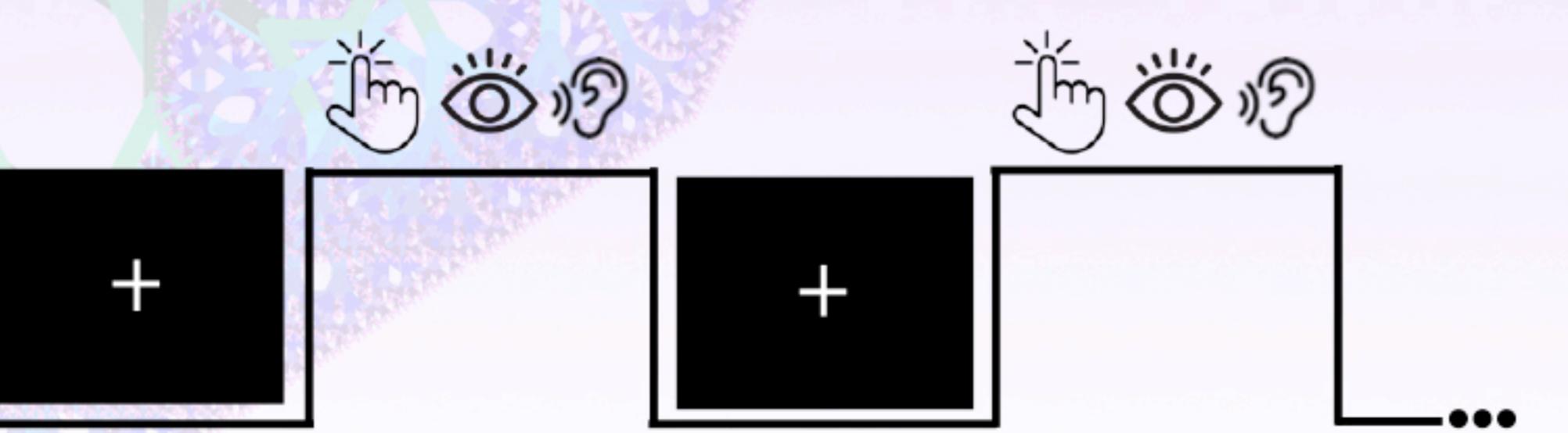
Background & Aims:

- **Chronic musculoskeletal pain (CMP)** affects 30-50% of adolescents, with females experiencing more pain than males¹.
- **CMP negatively impacts** school attendance, physical activity, social relations, and overall **quality of life (QoL)**.
 - Adolescents with CMP often exhibit sensory hypersensitivities, which will undeniably compromise their well-being.²
 - This study aims to investigate the **relationship between brain responses** to non-painful **multisensory stimulation** and self-reported QoL in adolescents with CMP, with a focus on potential sex differences.
 - This study was conducted as an ancillary study as part of the **SPRINT project**³.

Methods:

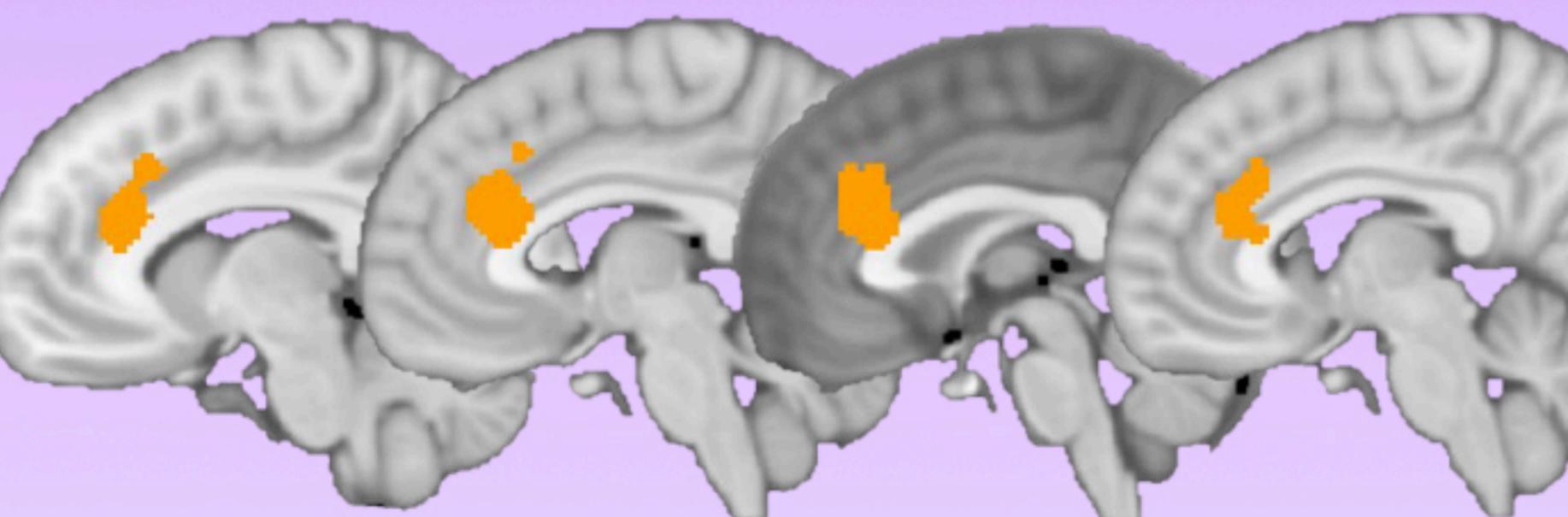
- This study included **129 adolescents** (110 females, 19 males) aged 12 to 18 with CMP from three different sites (Stanford, Cincinnati and Toronto).
- An **fMRI multisensory task** was used to assess brain responses to non-painful multisensory stimulation.
- Self-reported **QoL was measured using the Pediatric Quality of Life Inventory (PedsQL)**, assessing physical and psychosocial dimensions.
- The multisensory task involved concurrent **visual, auditory, and tactile-motor stimulation**, with alternating rest periods⁴.

Multisensory Task:

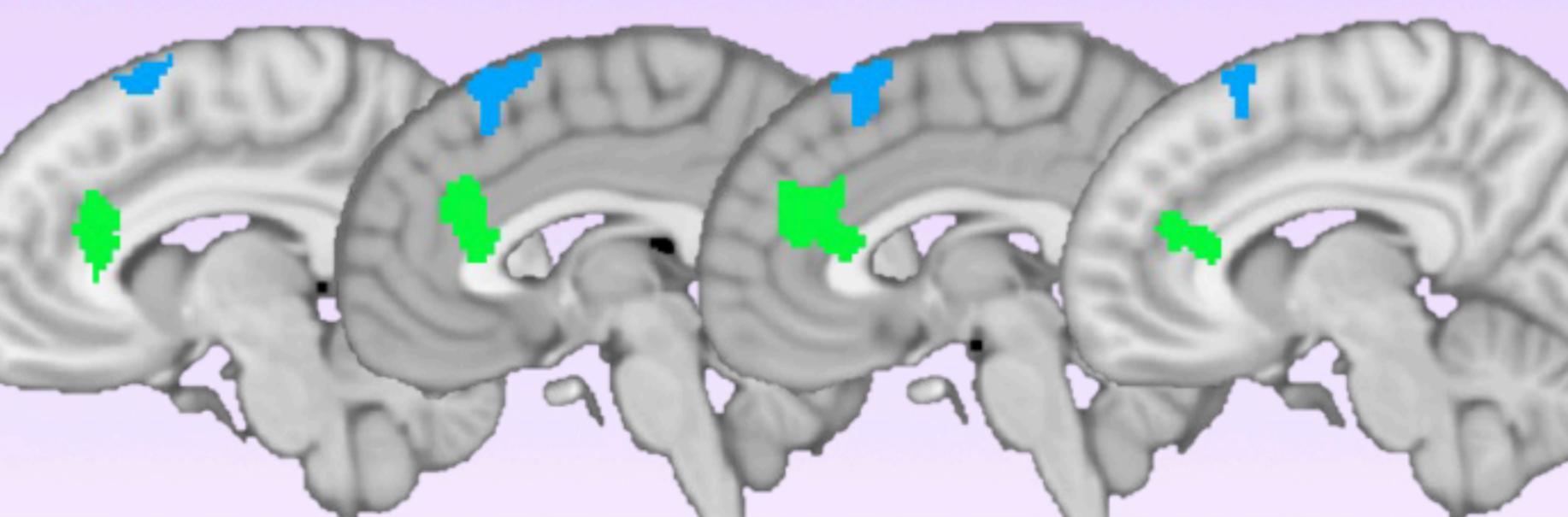


Results

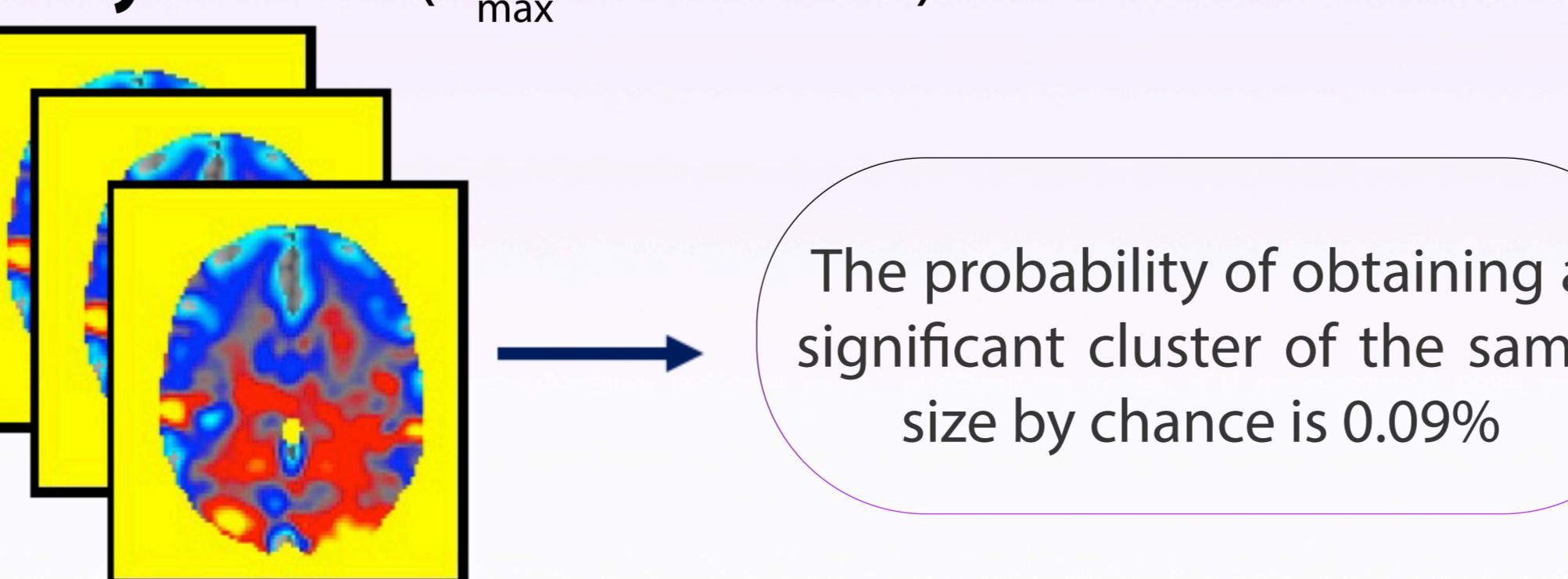
- A significant correlation between the **psychosocial QoL and self-reported multisensory unpleasantness** was found ($r = -0.26, p = 0.002$).
- A **trend towards a negative correlation** was found between **physical QoL** and self-reported multisensory **unpleasantness** ($r = -0.17, p = 0.056$).
 - There were **no significant** associations between **task-evoked brain activation and psychosocial QoL**.
 - **Augmented brain responses to non-painful multisensory stimulation** in the rostral anterior cingulate cortex (ACC) were associated with lower **physical QoL** in the entire sample ($q_{FWE} = 0.001$).



- This correlation was replicated in females, with an additional **significant cluster found in the dorsomedial prefrontal cortex (dmPFC)** ($q_{FWE} = 0.029$).

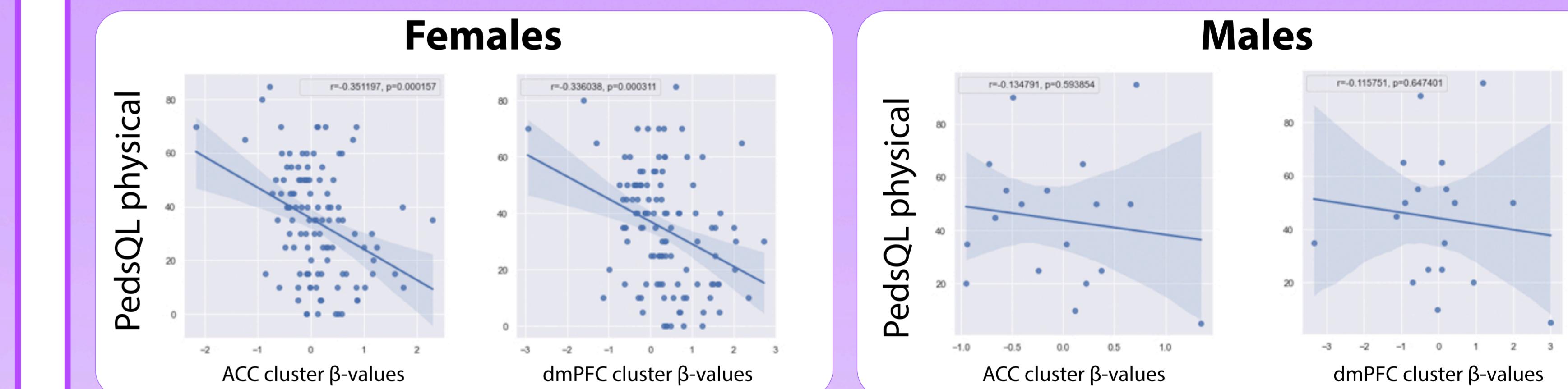


- 10k bootstrap analyses confirmed that the **observed clusters were highly unlikely to occur by chance** ($P_{max} = 0.000909$).

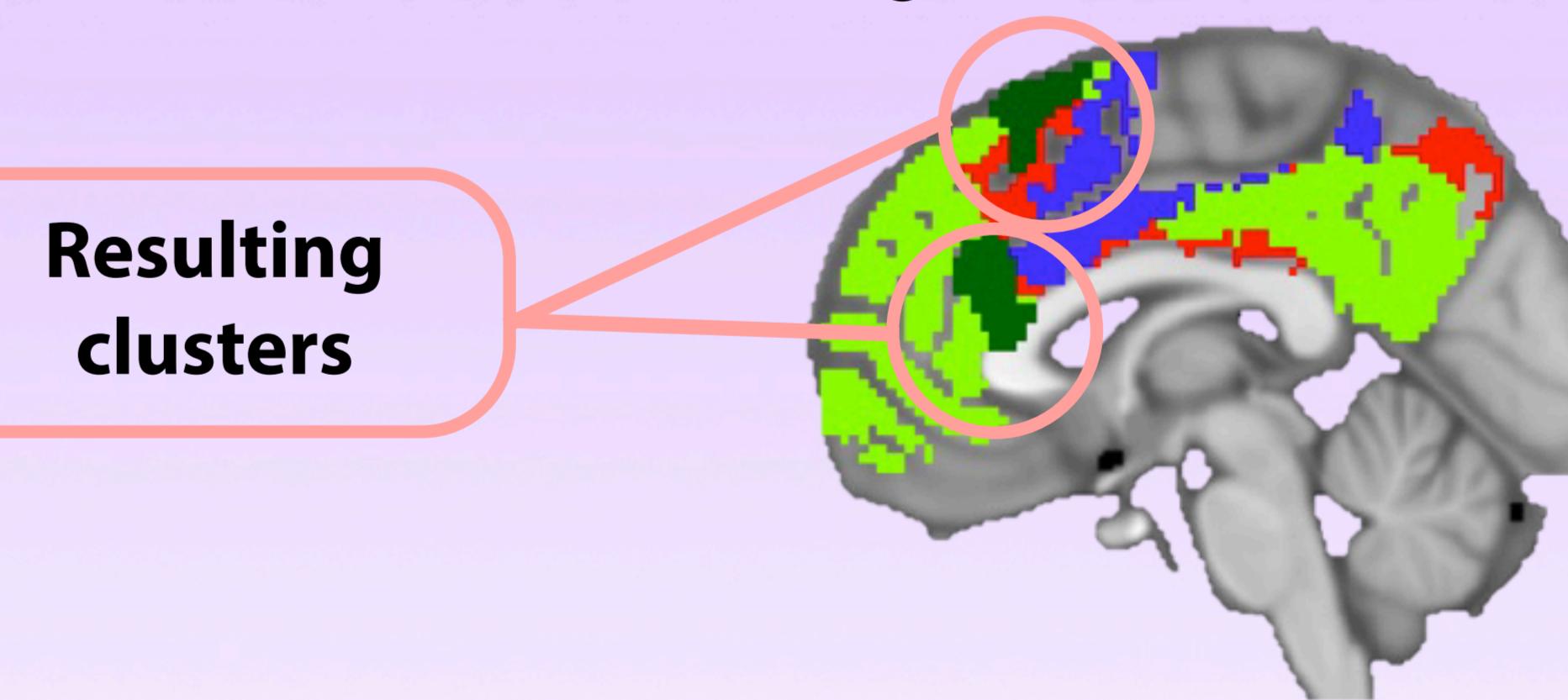


Results

- Significant correlations between the **β -values of the cluster peaks in ACC and dmPFC**, and PedsQL scores were **found in females, but not in males**.



- **Heightened activation in affective/regulation circuits** (intermodal regions at the interface of the Default mode, Salience, and Somatomotor networks) during sensory tasks can contribute to **lower QoL**, particularly in the physical QoL dimension, among adolescents with CMP.



- **Default Mode Network**
- **Salience Network**
- **Somatomotor Network**

Conclusions

Augmented brain responses in the **dmPFC** and **rostral ACC** during **non-painful multisensory tasks** corresponds to **lower physical QoL** in adolescent females with CMP, involving affective/regulation circuits in intermodal regions. Furthermore, Higher self-reported **multisensory unpleasantness** during the task is associated with **lower psychosocial QoL**. However, it's important to note that these results could **not be replicated in the male patients**.