Using a Deep-Phenotyping Approach to Test the Efficacy of an Enhanced Acceptance-based Mindfulness Strategy for Pain Across Multiple Body Sites

Cognitive and Affective Neuroscience Lab

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INTRODUCTION

BACKGROUND

In recent years, empirical research has increasingly validated the benefits of meditation, linking it to improvements in attention, emotional regulation, and overall well-being. Recent imaging research has identified regions of the posterior cingulate cortex (PCC) and medial prefrontal cortex (mPFC) as playing a critical role in emotional and cognitive regulation (Prakash et al., 2013; Brewer et al., 2011; Hölzel et al., 2007). These studies have suggested differing patterns of activation in regards to the effect of mindfulness on neural correlates, but they have not demonstrated a consolidated activation pattern as a result of mindfulness and acceptance in response to pain.

QUESTION

We used a novel enhanced mindfulness strategy that combines pain education, imaginal exposure, mindfulness, reappraisal, and habituation for boosting psychological pain analgesia.

We initially hypothesized that the enhanced-acceptance strategy would show decreased activation in the PCC, and increased activation in the mPFC.

METHODS

PARTICIPANTS

n = 8 participants, mean age = 39 years

SCAN & ANALYSIS PARAMETERS

- EPI BOLD imaging on 3T Siemens Magnetom Prisma (TR = 1000 ms, 2.5 × 2.5 × 2.5 mm isotropic voxels, 240 mm FoV, 96 x 96 matrix, 90° flip angle)
- Pre-processing and 1st level analysis with SPM2
- Second-level analysis was conducted using CANlab's neuroimaging tools from Dartmouth College, implemented in MATLAB (R2019b)

STIMULI

Thermal stimulus with a Peltier thermode at painful heat intensities repetitively for 12-13 seconds for 8 runs over two sessions (days)

TRIAL STRUCTURE

Session #1				Session #2			
Run #1	Run #2	Run #3	Run #4	Run #1	Run #2	Run #3	Run #4
Site A	Site B	Site A	Site B	Site A	Site B	Site A	Site B

Conditions 'Experience' and 'Regulate' are assigned interchangeably to the two sessions, with no fixed order. Site A and Site B are randomly assigned to either the left face or one of the following: Right Face, Right Arm, Left Arm, Chest, Abdomen, or Right Leg.

ANALYSIS PATHWAY

Step 1: Creation of Linear Models to Investigate Pain Intensity Variations
Created linear models to explore individual and interactive effects of experimental conditions on pain intensity, revealing significant variability across subjects and conditions, visualized through detailed heatmaps.

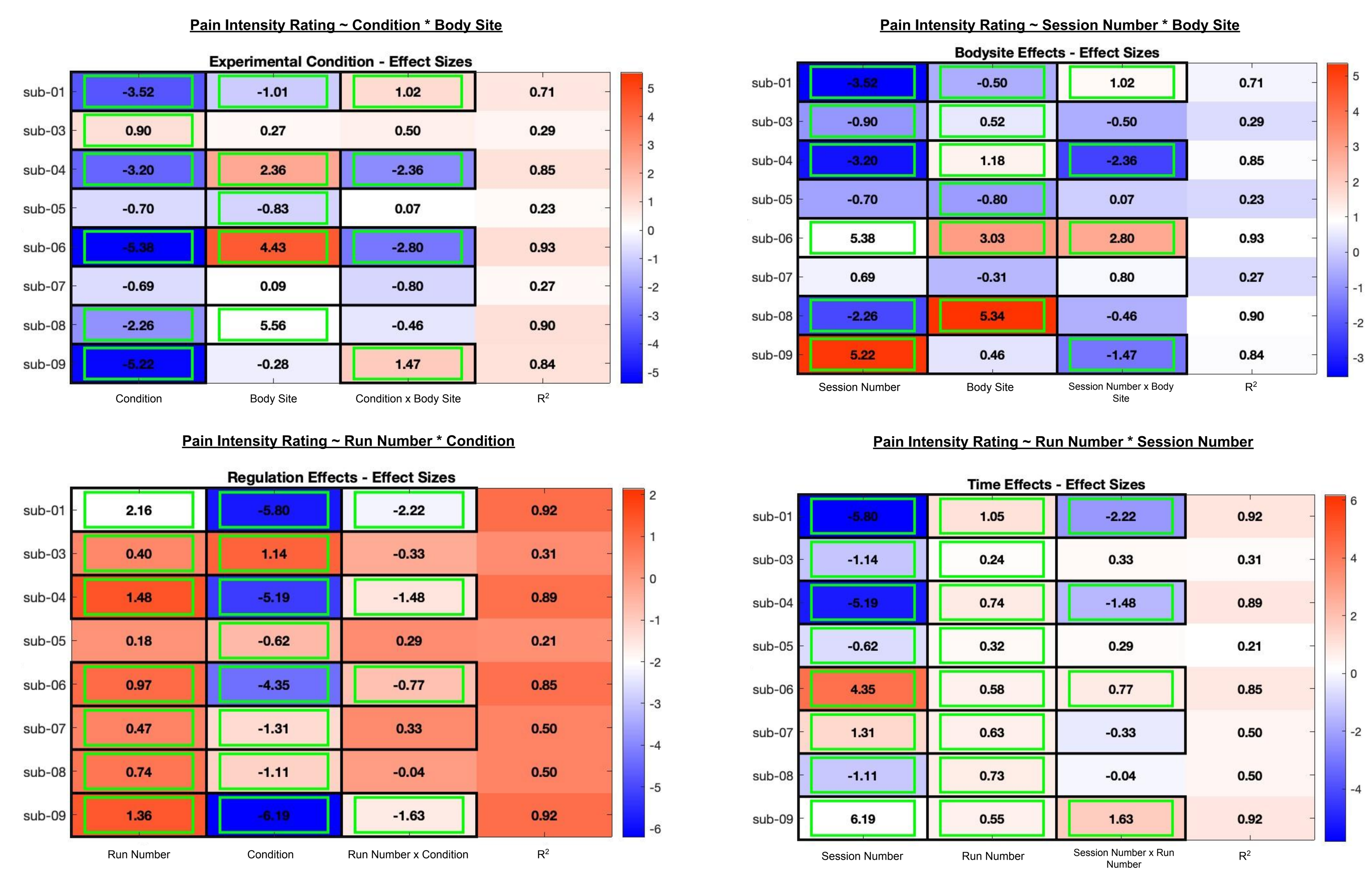
Step 2: Group-Level Analysis of Pain Intensity Ratings
Visualizations demonstrate that pain regulation strategies effectively reduce pain from 'Experience' to 'Regulate' across various body sites.

Step 3: Whole Brain Robust Regression Voxelwise Analysis at the Group Level
Performed a robust voxelwise analysis of whole brain data to identify neural correlates of pain regulation, contrasting 'Regulate' with 'Experience' conditions, excluding Subject 3 due to anomalous data. The analysis was conducted at an uncorrected threshold of $p < 0.05$ and FDR threshold of $q < 0.05$.

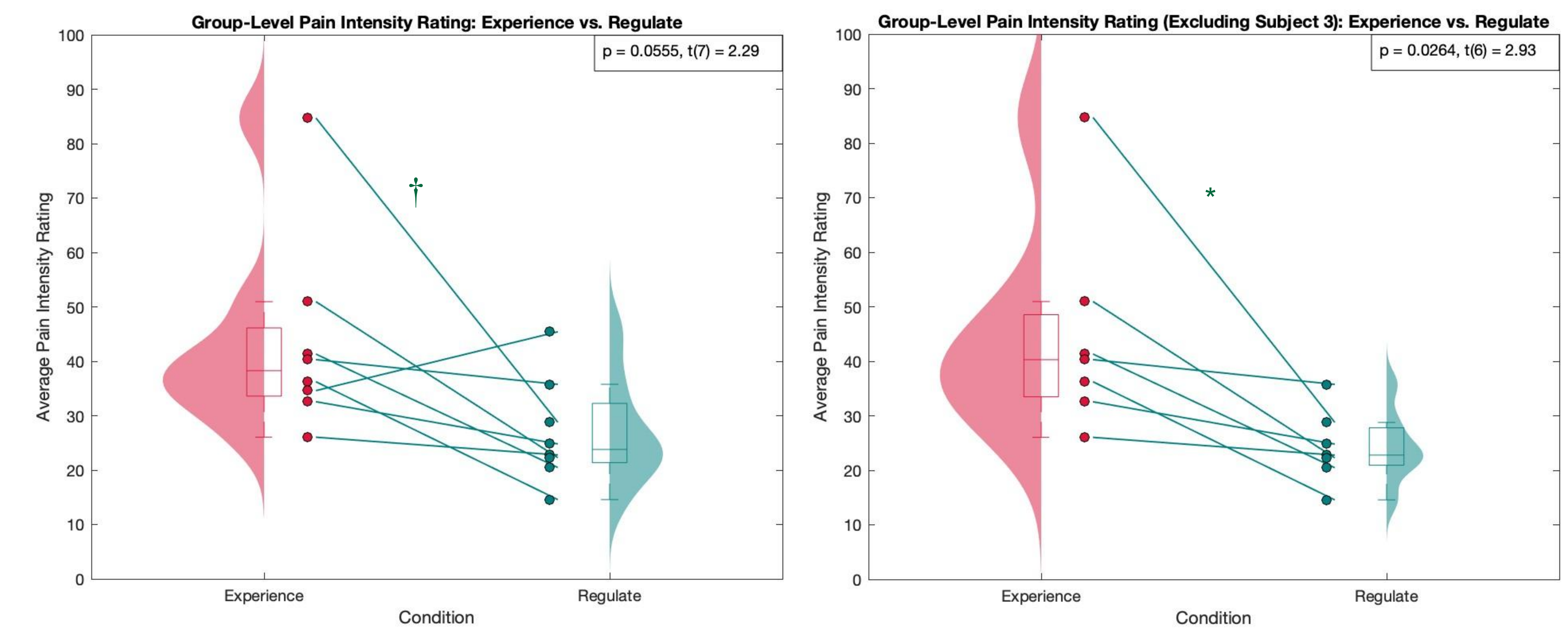
Step 4: Comparative Analysis of NPS and SIIPS1
Conducted a robust brain activity under 'Experience' and 'Regulate' conditions against established pain signatures (NPS and SIIPS1). Utilizing cosine similarity metrics, the study assessed how closely brain responses aligned with the typical pain response pattern

RESULTS

Step 1: Creation of Linear Models to Investigate Pain Intensity Variations



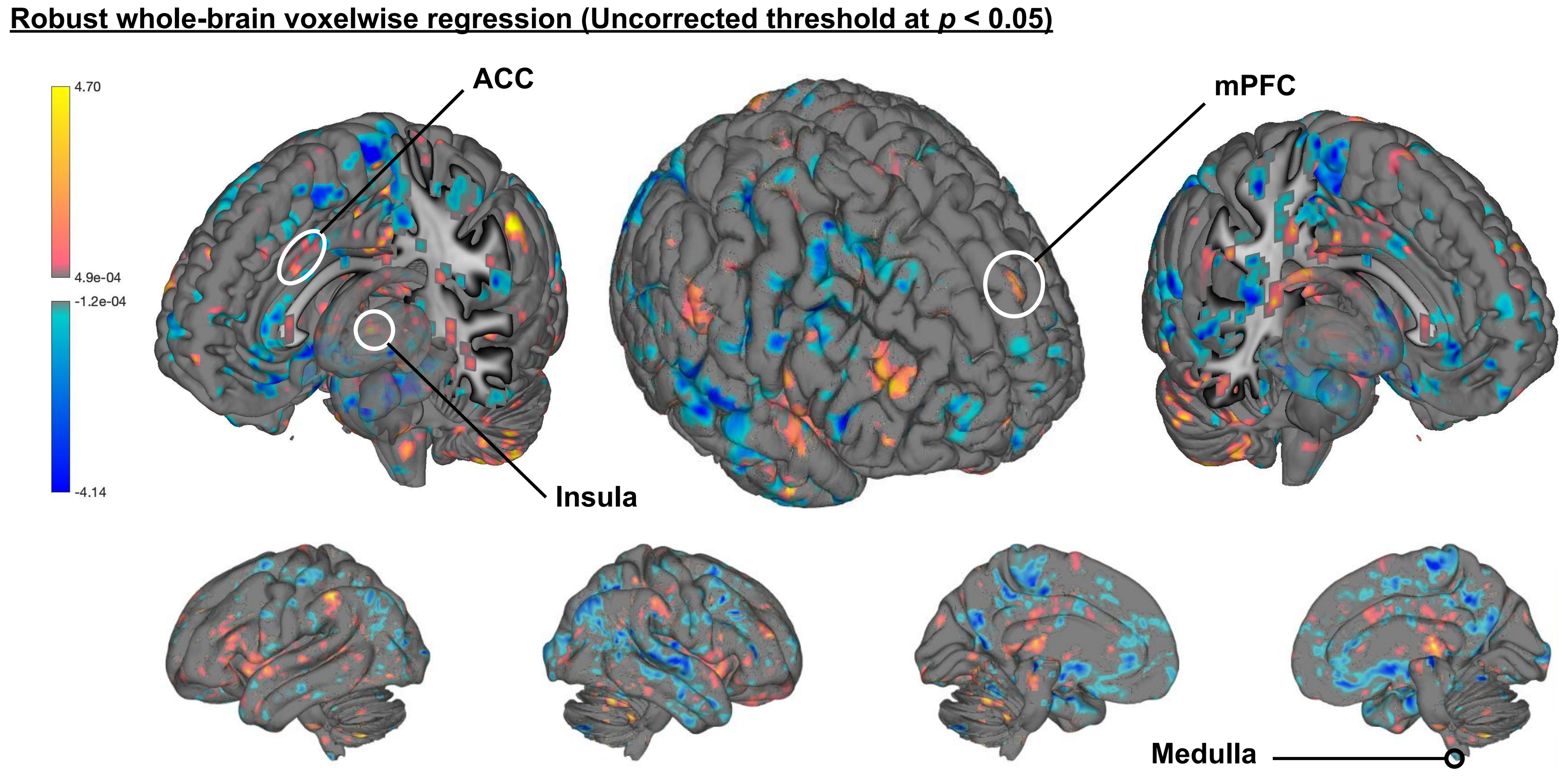
Step 2: Group-Level Analysis of Pain Intensity Ratings



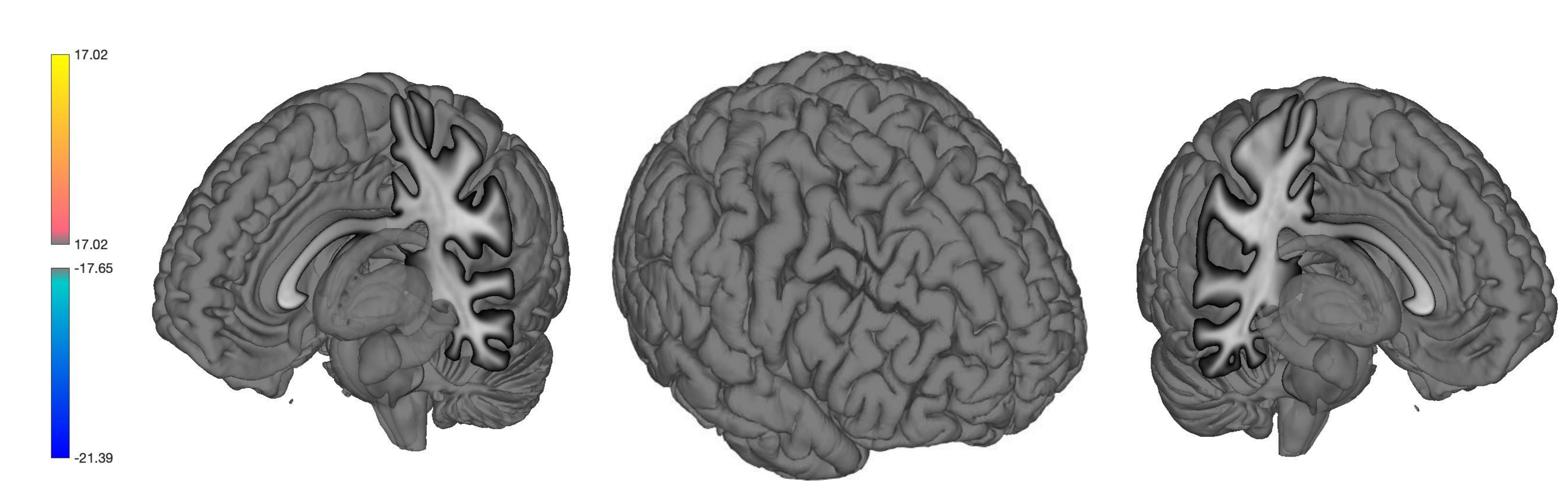
Group-level pain intensity ratings showed that contrasting the 'Experience' and 'Regulate' conditions resulted in overall pain reductions of **40.0152% (p = 0.0264)**, with specific decreases at the left face by **40.4881% (p = 0.0179)**, and at other body sites by **39.2516% (p = 0.0438)**; inclusion of Subject 3 still showed decreases across all conditions, albeit with slightly higher p-values of 0.055 for the overall, 0.0401 for the left face, and 0.0823 for other body sites.

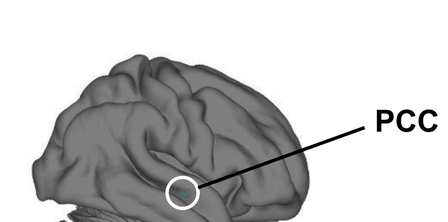
Step 3: Whole Brain Robust Regression Voxelwise Analysis at the Group Level

Robust whole-brain voxelwise regression (Uncorrected threshold at $p < 0.05$)



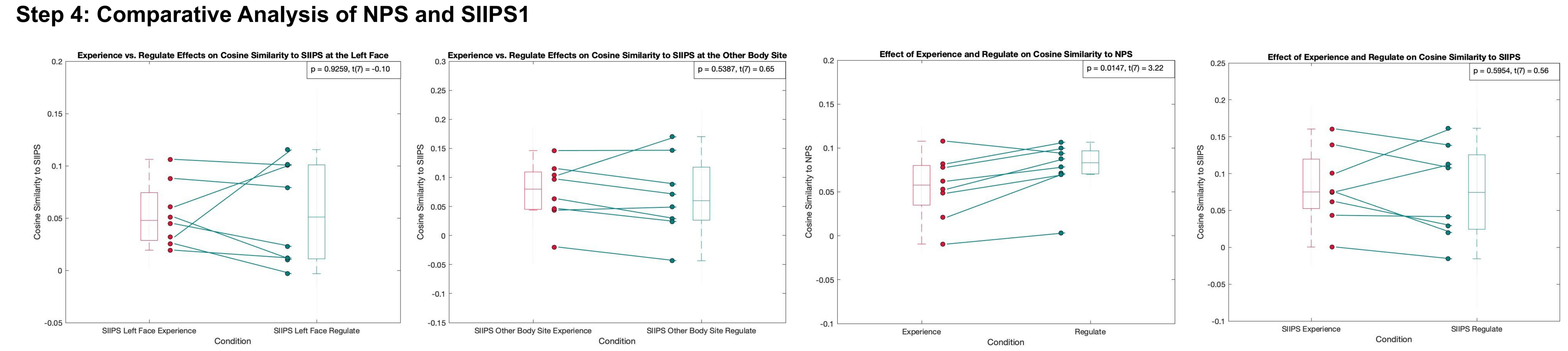
Robust whole-brain voxelwise regression (FDR corrected threshold at $q < 0.05$)





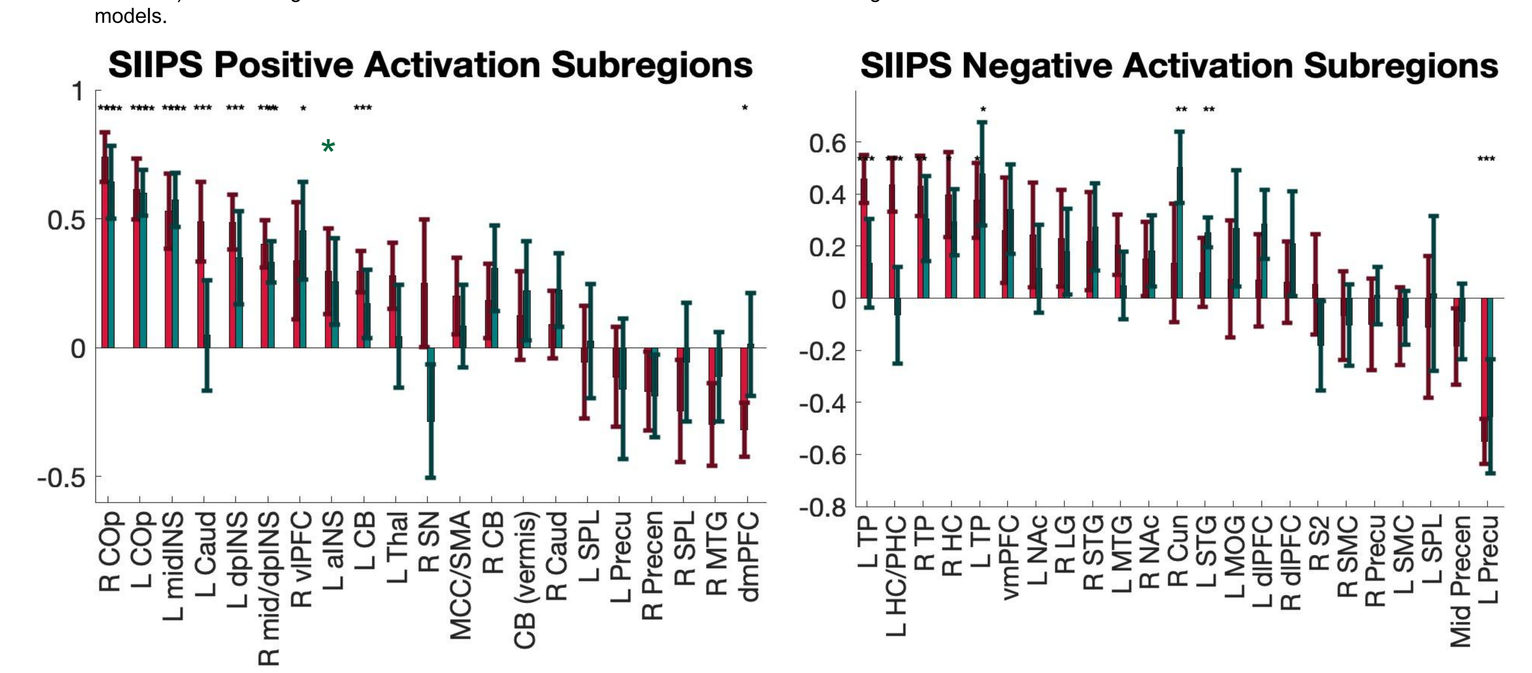
Positive effects were observed in the **left somatomotor operculum**, while negative effects were noted in the **right auditory association cortex** and the **right posterior cingulate cortex**.

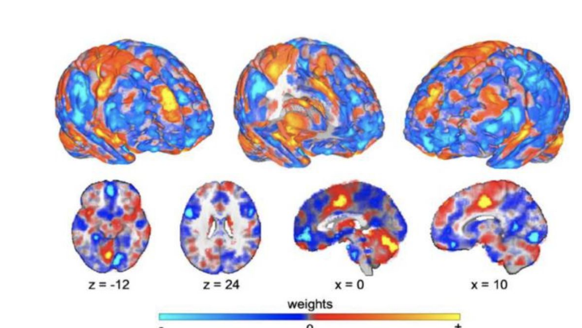
Step 4: Comparative Analysis of NPS and SIIPS1



Satterthwaite-corrected ANOVA revealed a significant two-way interaction for Condition & Body Site with SIIPS1 (**p = 7.8707e-09**); however, individual contrasts at the Left Face (**p = 0.9259**) and other sites (**p = 0.5387**) were not significant. It is the difference between the two conditions that aligns with the linear models.

The 'Regulate' condition significantly increased the cosine similarity to the NPS signature (**p = 0.0147**), but did not significantly affect the cosine similarity to SIIPS1.





Compared to the **SIIPS1 signature**, the 'Regulate' condition demonstrated a decrease in cosine similarity in the **left hippocampal/parahippocampal complex (p = 0.0273)** relative to the 'Experience' condition, although it is uncertain if this p-value will withstand Bonferroni correction.

SUMMARY AND CONCLUSIONS

- The significant reduction in pain intensity under the 'Regulate' condition illustrates the efficacy of cognitive strategies in managing pain, a finding corroborated across various body sites. Different body sites exhibited higher pain intensities, indicating the influence of anatomical sites on pain perception.
- The robust voxelwise analysis affirmed the initial hypothesis that the PCC would show negative effects as a result of the implementation of acceptance and mindfulness based strategies. This suggests that mindfulness and regulatory strategies not only modulate sensory pathways but also engage cognitive and emotional circuits, aiding in pain reduction.
- The somatomotor operculum's proximity to areas involved in emotional processing (like the insula and cingulate cortex) may allow it to contribute to the emotional regulation aspects of mindfulness and acceptance strategies.
- Active regulation can modulate the typical neural coding of pain, reducing the standard pain signature's presence in key pain-processing areas.

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