

# Associations between Perceived Stress, Stress-related Negative Affect, and Anxious/Depressive Symptoms with Representational Similarity in the Amygdala's Reactivity to Negative vs. Neutral Stimuli

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**Research Question:** How does the amygdala's response to emotional stimuli relate to levels of perceived stress, anxiety, depressive symptoms, and negative affect in daily life?

## Background

- Anxiety and depression commonly observed in patients with Alzheimer's Disease may promote neurobiological changes that accelerate cognitive decline.<sup>1, 2</sup>
- 20% of US adults report anxiety and depressive symptoms.<sup>3</sup>
- Higher perceived stress (people's subjective perception of their recent experienced events and their capacity to cope) is associated with more anxiety and depressive symptoms.<sup>4, 5</sup>
- The amygdala plays a crucial role in emotional processing,<sup>6</sup> integral in studies linking amygdalar responses to emotional stimuli with experiences and responses to stress.<sup>7, 8, 9</sup>
- Understanding how emotional processes in the brain contribute to stress, stress-related negative affect, anxiety, and depressive symptoms is important for providing insights into the neural basis of mental health and emotional wellbeing, which may have implications for mitigating the impacts of stress, depression, and anxiety on AD risk.

## Methods

Participants from the Midlife in the U.S. (MIDUS) study 3<sup>rd</sup> follow-up of the Core and 1<sup>st</sup> Refresher waves.

- N = 259 (fMRI task).
- mean age = 57.57 ± 13.47 (SD) years, age range = 26-95.
- 57% female, 30% Black, Indigenous, and/or People of Color.
- Education: 25% high school or less, 31% some college or technical training, and 44% bachelor or higher.
- "Daily Diary" subset N = 137, providing stressor reactivity.

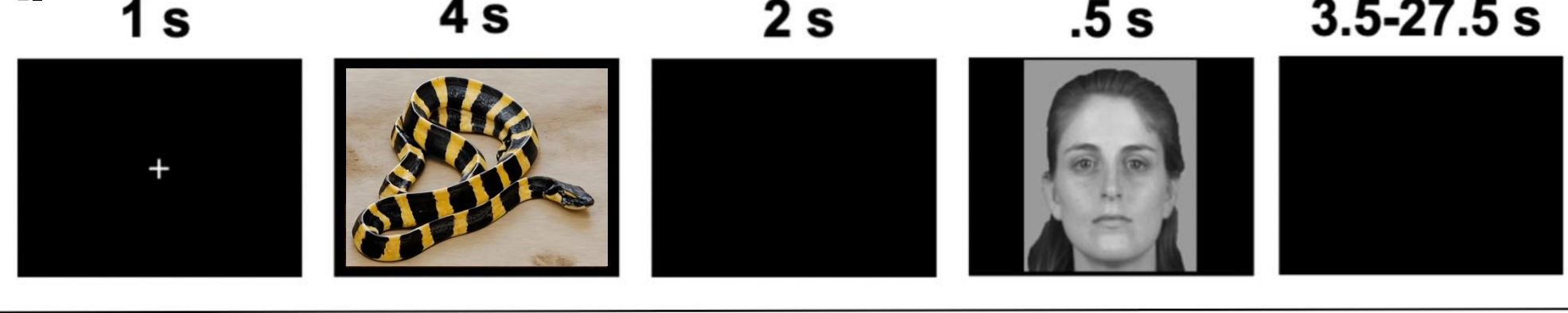
**Perceived stress:** the degree to which situations in life are perceived as stressful, measured by the Perceived Stress Scale.<sup>10</sup>

**Daily Diary:** participants reported whether they experienced stressors and the frequency of negative emotions over the past 24 hours in 8 daily phone interviews.

**Stressor reactivity:** reflects increase in negative affect on Daily Diary stress days compared to non-stress days.<sup>11, 12</sup>

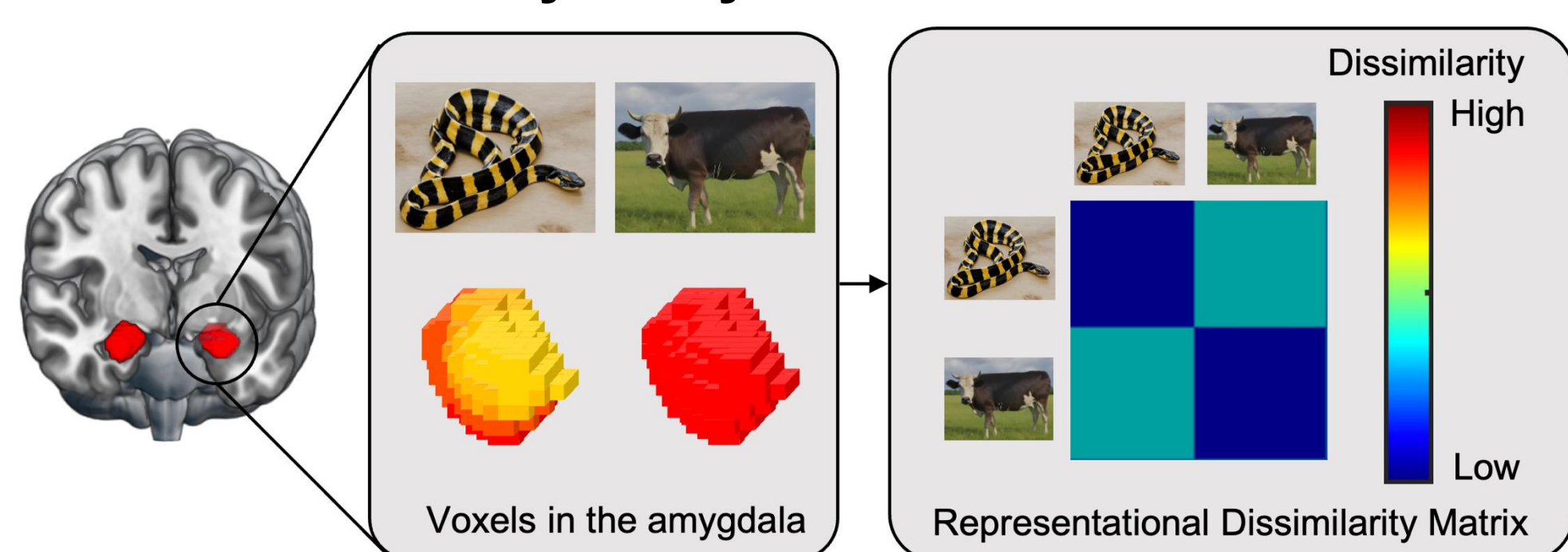
**Anxiety Symptoms and Depressive Symptoms:** measured by Mood and Anxiety Symptoms Questionnaire (MASQ)<sup>13, 14, 15</sup> General Distress-Anxious Symptoms and General Distress-Depressive Symptoms subscales.

## Task fMRI



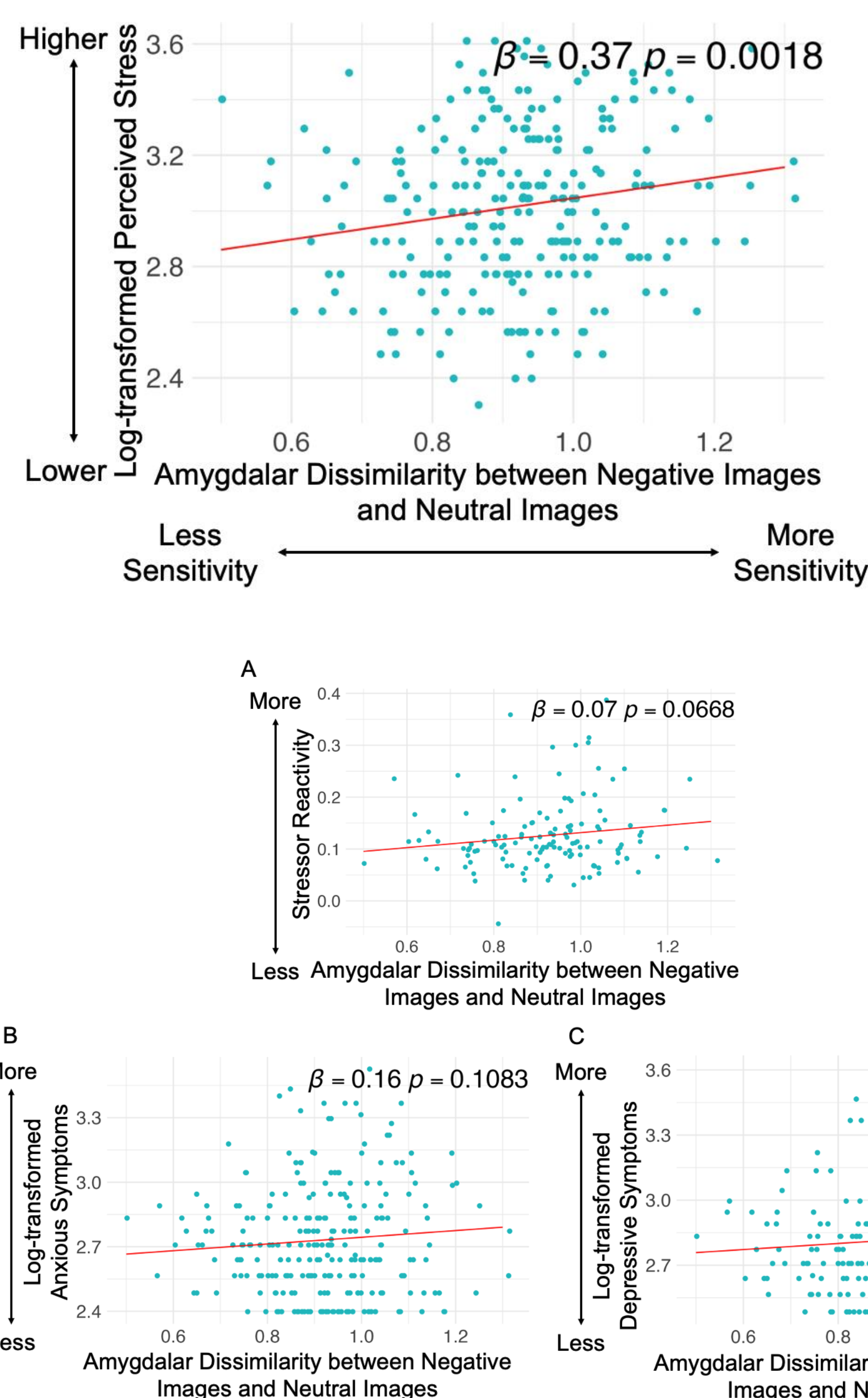
90 trials: 30 negative, 30 neutral, 30 positive emotional images (IAPS)<sup>16</sup> paired with a neutral face that followed 2 s after the image.

## Representational Similarity Analysis



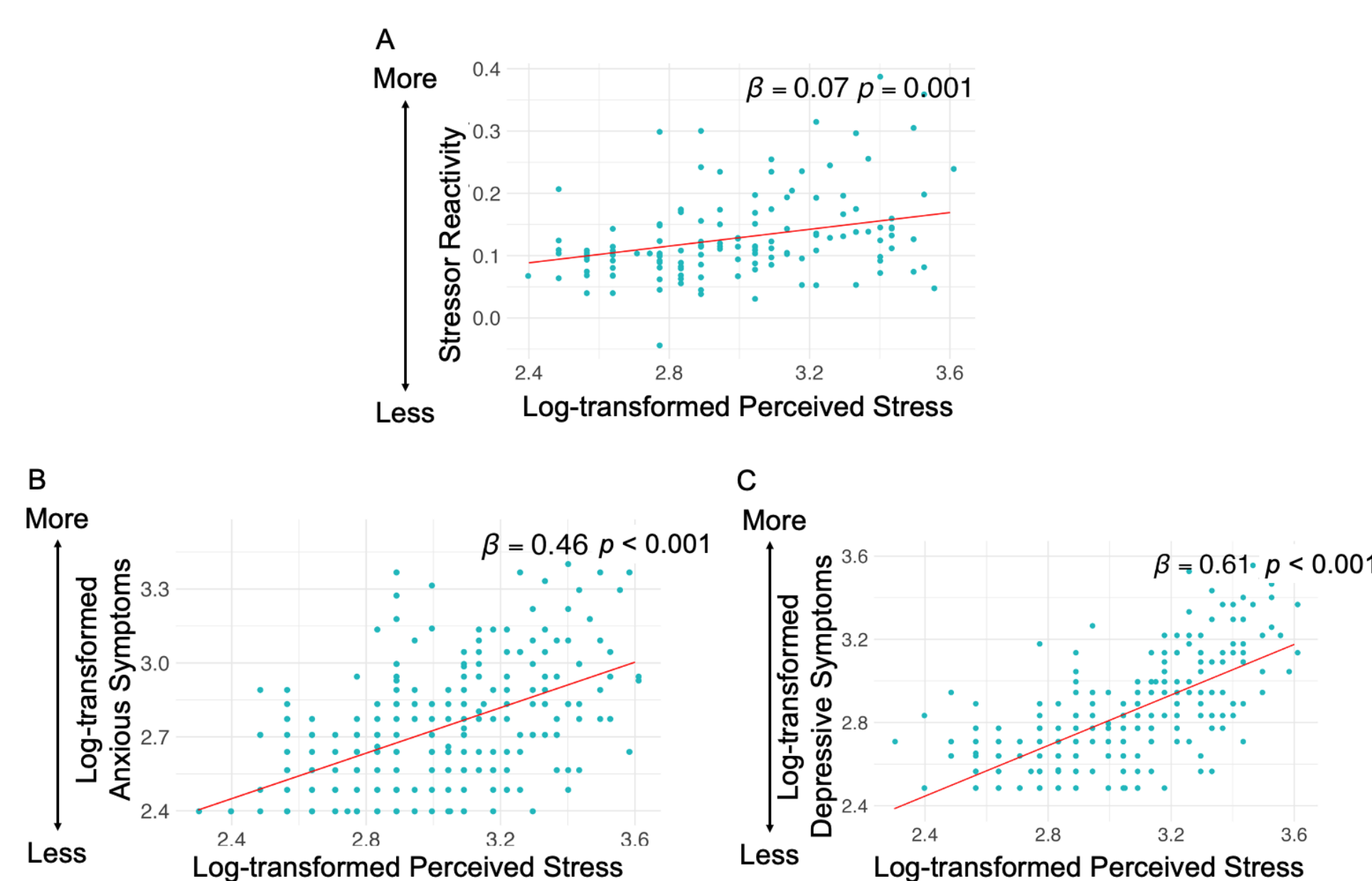
**Emotional reactivity:** pattern dissimilarity in amygdalar responses to negative versus neutral images.

## Results

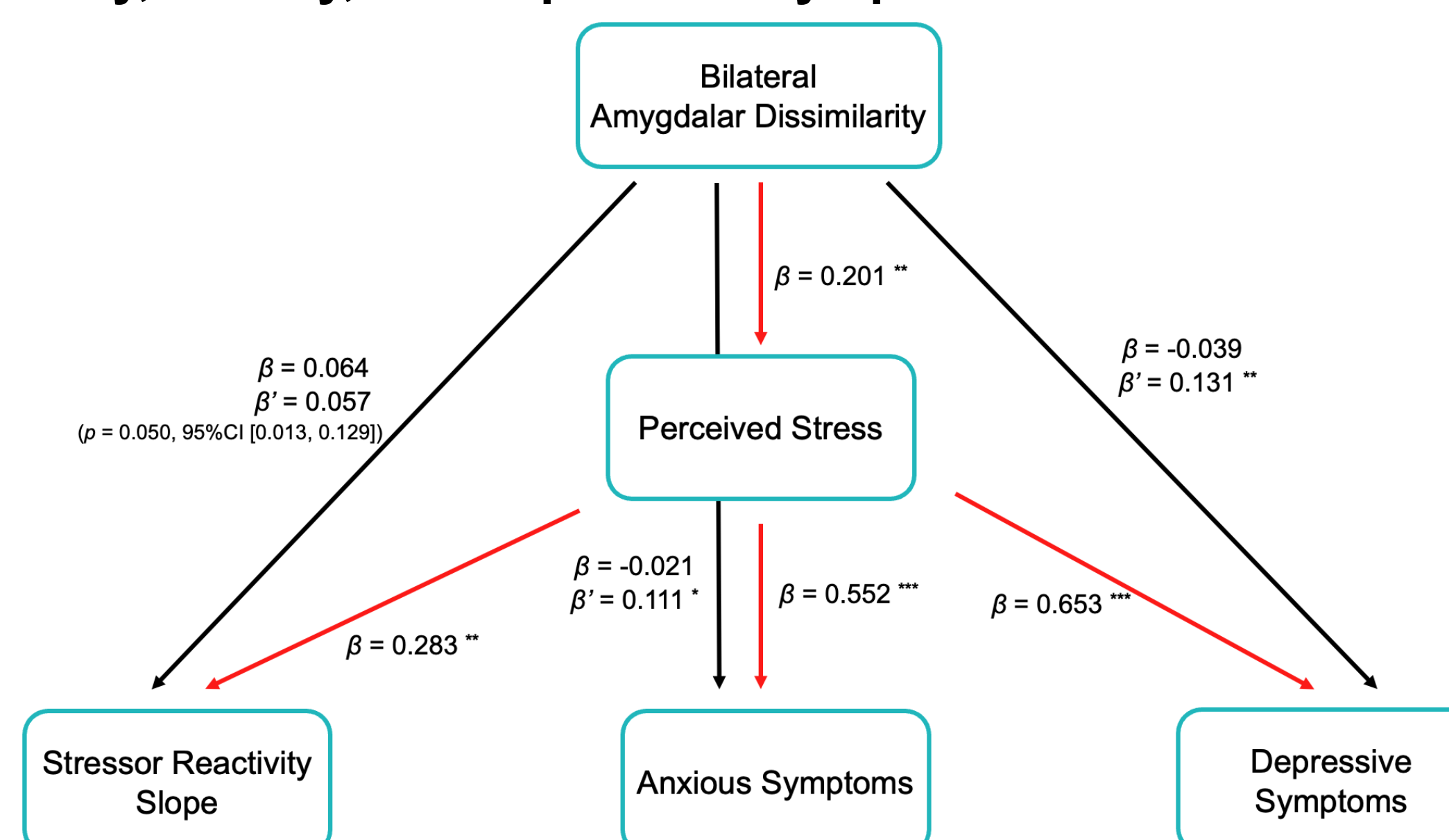


**Greater perceived stress was significantly associated with greater bilateral amygdala dissimilarity (reflecting greater pattern differentiation between negative and neutral stimuli).**

Bilateral amygdala dissimilarity was not significantly associated with stressor reactivity, anxiety, or depressive symptoms, but note the similar trending relations.



**Perceived stress was significantly associated with more stressor reactivity, anxiety, and depressive symptoms.**



**Significant indirect effects of bilateral amygdalar pattern dissimilarity on stressor reactivity, anxious symptoms, and depressive symptoms through levels of perceived stress.**

## Conclusions

Higher levels of perceived stress were associated with more bilateral amygdala dissimilarity between negative and neutral stimuli (suggesting greater amygdalar sensitivity to negative emotional stimuli).

Perceived stress indirectly linked amygdalar pattern dissimilarity with greater stressor reactivity (negative affect due to stress), anxiety, and depressive symptoms.

Our findings suggest that greater amygdalar sensitivity to negative emotional content might contribute vulnerability to greater negative affect, anxiety, or depression symptoms based on people's subjective perception of recent stressful events and their capacity to handle them.

## Future directions:

- Examine functional connectivity in emotional regulatory circuitry (e.g. prefrontal cortex and amygdala) and how it explains these relationships.
- Perceived stress is significantly associated with cognitive decline in these samples, so we will examine how amygdala responses and perceived stress levels are associated with cognitive function and biomarkers of ADRD in MIDUS.

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