Ventromedial Prefrontal Cortex and Amygdala Functional Connectivity May Be Associated with Social Anxiety in Autism Spectrum Disorder

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Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by social impairment, among other symptoms. Neuroimaging research on individuals with ASD has primarily focused on social deficits and their relationship with the over-/under-activation of the amygdala—a brain region known to play a role in social anxiety. To expand on previous neuroimaging research exploring the neural faculties responsible for social impairment in ASD, I intend to observe the relationship between social anxiety level and the co-activation (functional connectivity) of the amygdala and the ventromedial prefrontal cortex (vmPFC). Animal studies have demonstrated that the vmPFC and the amygdala are anatomically connected. Further, neuroimaging studies have observed that the vmPFC plays a role in inhibiting the activation of the amygdala in response to emotionally salient stimuli.
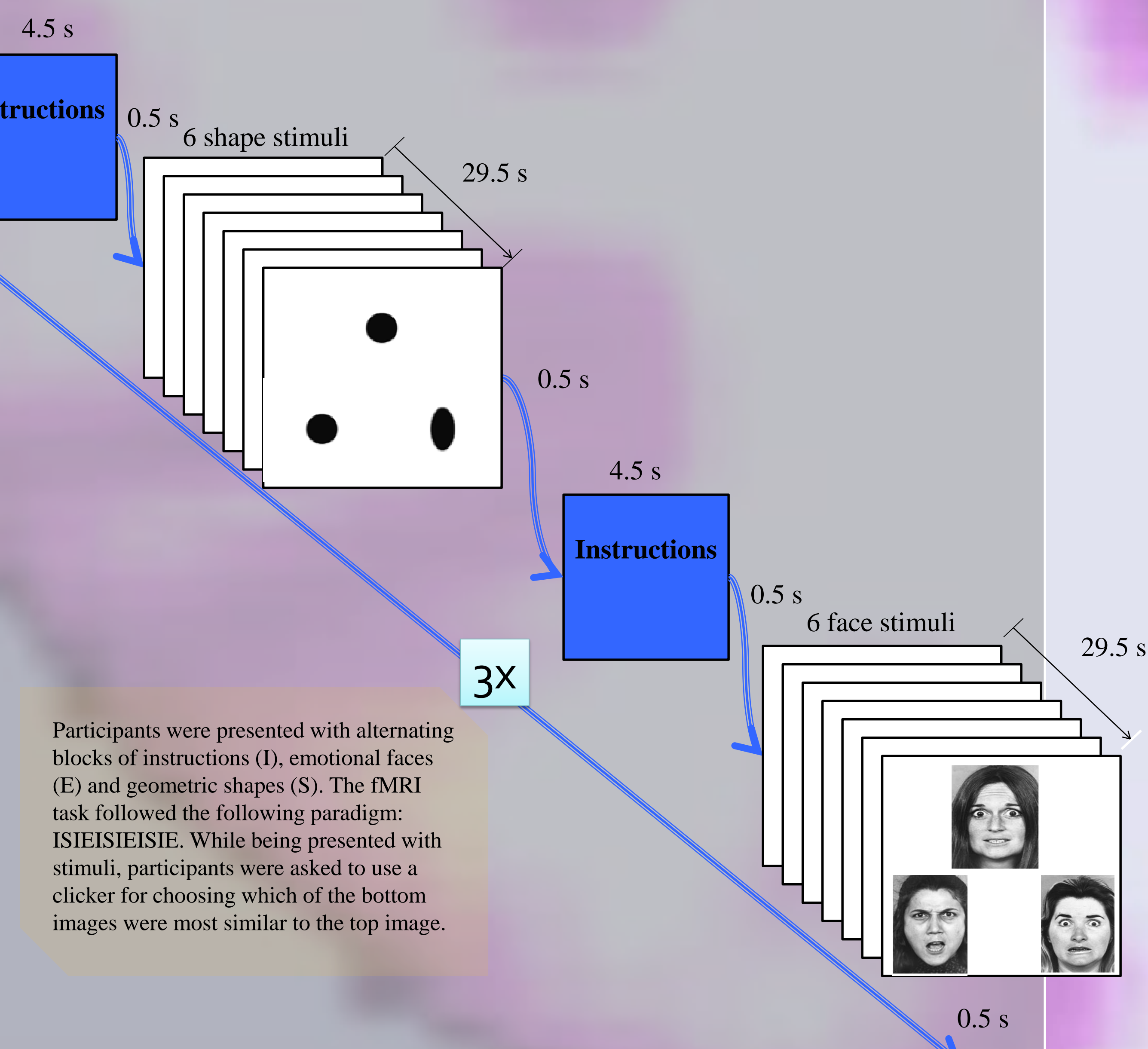
Hypothesis

I hypothesize that when presented with emotionally aversive stimuli (i.e., angry and fearful faces), the ASD group will show a lower correlation between amygdala/vmPFC functional connectivity and social anxiety level.
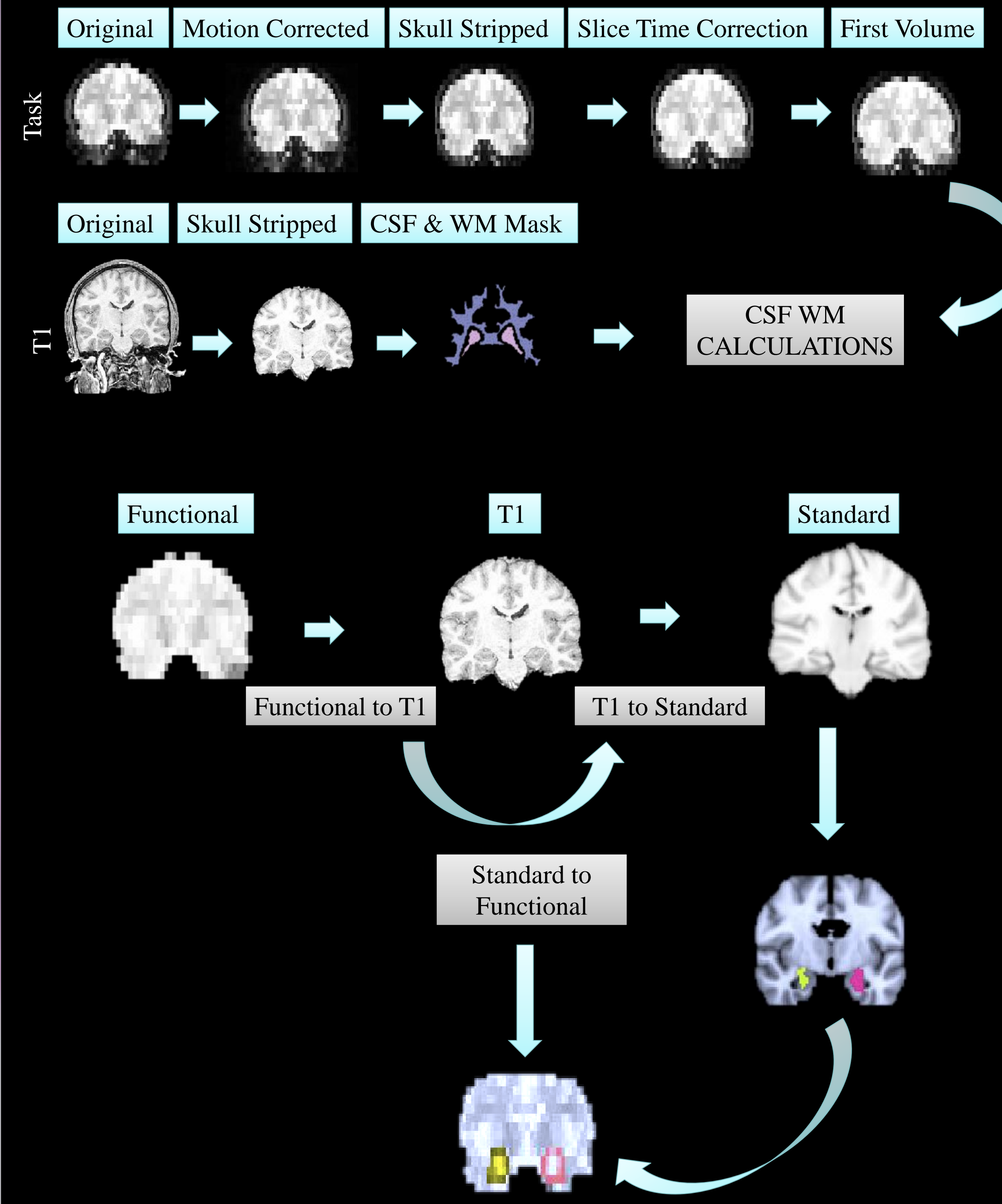
Methods

Participants

- 31 ASD and 25 control adults
- ASD and control groups were matched on IQ and age
- Social anxiety was assessed using the social avoidance and distress scale (SADS)

4.5 s

Instructions

0.5 s

6 shape stimuli

29.5 s

0.5 s

4.5 s

Instructions

0.5 s

6 face stimuli

29.5 s

3x

0.5 s

Participants were presented with alternating blocks of instructions (I), emotional faces (E) and geometric shapes (S). The fMRI task followed the following paradigm: ISIEISIEISIE. While being presented with stimuli, participants were asked to use a clicker for choosing which of the bottom images were most similar to the top image.

Methods (continued)

FMRI Preprocessing

| Original | Motion Corrected | Skull Stripped | Slice Time Correction | First Volume |

Task

| Original | Skull Stripped | CSF & WM Mask |

T1

CSF WM CALCULATIONS

| Functional | T1 | Standard |

Functional to T1

T1 to Standard

Standard to Functional

### Psychophysiological Interaction Analysis

- Psychophysiological interaction analysis (PPI) is a statistical method that extracts an interaction value between two brain regions as their activation is modulated through a task block.
- I will extract the time course of the basolateral amygdala (BLA) and enter this information, along with task block information (i.e., when emotional faces were presented to subjects), into FSL's FEAT. An interaction variable is then calculated by multiplying the task variable and the time course of the BLA.
- I will use the interaction variable to calculate a z-score for how co-activated the BLA and other brain areas are during the task blocks.
- I will correlate the z-score in vmPFC with social anxiety.

Hypothetical Results

Social Anxiety Level as Function of vmPFC/Amygdala Functional Connectivity
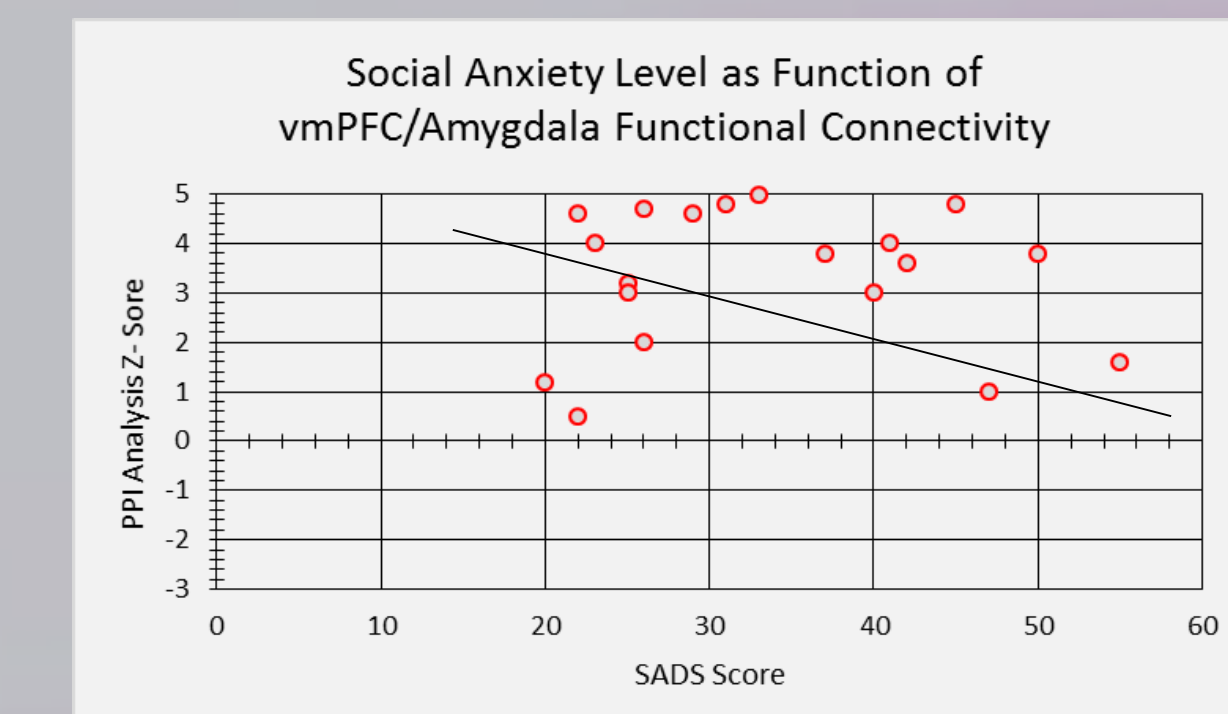
- If the relationship between vmPFC/amydala functional connectivity and social anxiety is negative in the ASD group then, I can inferred that social anxiety in ASD is related to a decreased co-activation of the vmPFC and the amygdala.

Social Anxiety Level as Function of vmPFC/Amygdala Functional Connectivity
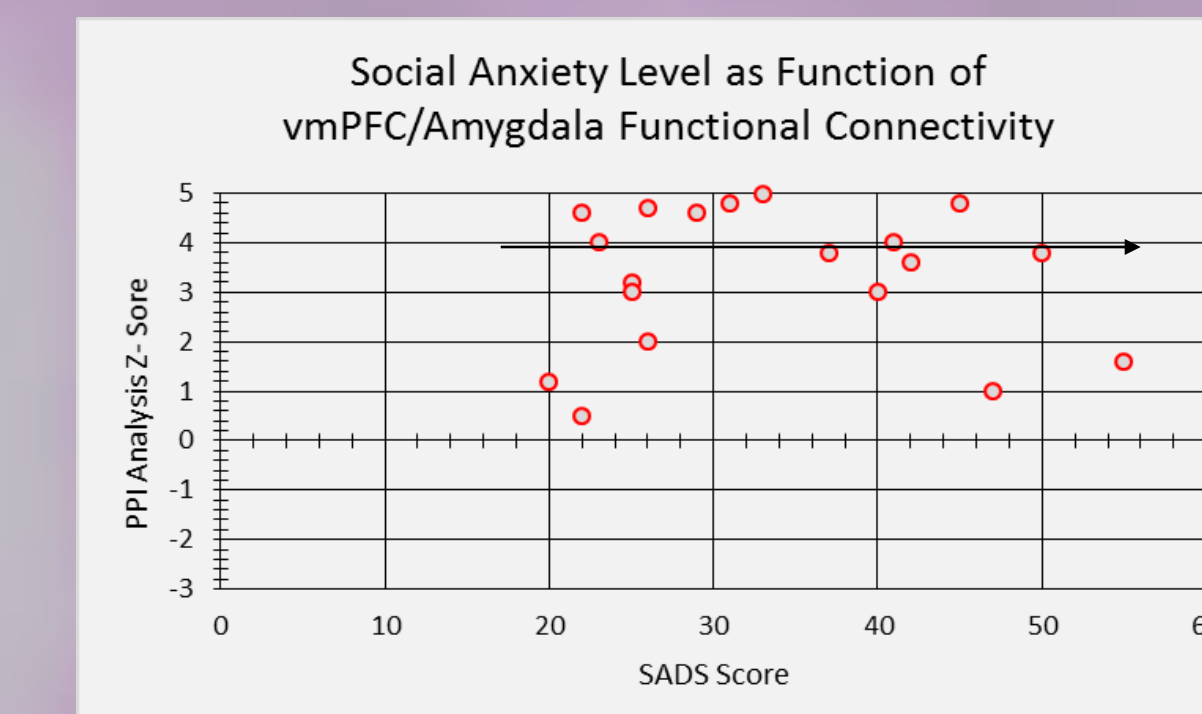
- If there is no relationship, I can infer that the co-activation of the amygdala and the vmPFC may not be related to social anxiety in ASD. In this case, it may be possible that other neural faculties are related to relationship between social anxiety and increased amygdala activation. This may be possible because prior research has demonstrated several abnormal structural and functional characteristics of ASD.

Social Anxiety Level as Function of vmPFC/Amygdala Functional Connectivity
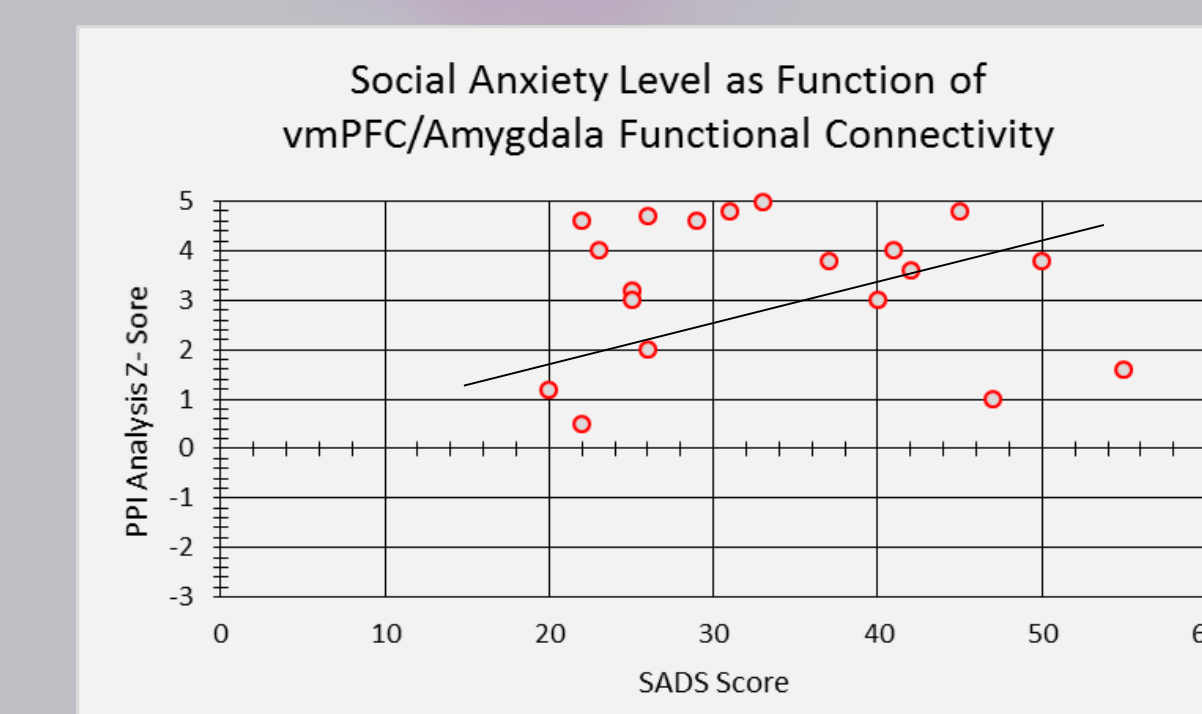
- A positive relationship may be more difficult to explain because that would mean that a stronger co-activation of the amygdala and vmPFC is related to social anxiety in ASD. Further research may be necessary to understand this result.