An Investigation of the Neural Underpinnings of Severe Worry and Emotional Anticipation Among Adolescents

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Background

- Worry is a process by which people anticipate uncertain negative emotional events and is present across traditional anxiety and mood disorders[1]
- Previous studies have found activation in the septo-hippocampal system, anterior midcingulate cortex, and anterior insular cortex regions in emotional anticipation[2,3,4]
- However, the majority of previous research in emotional anticipation has been conducted in healthy adults, thus little is known about emotional anticipation neural circuitry in clinical groups or adolescents[1]
- Here we aimed to characterize the pattern of neural activity that occurs in adolescents with and without severe worry when anticipating negative emotion under conditions of uncertainty

Research Hypotheses

Hypothesis 1: Anticipation of negative emotional stimuli will result in heightened activation of the anterior insular cortex and anterior cingulate cortex

Hypothesis 2: Adolescents with greater self-reported worry will have higher levels of activity in brain regions involved in emotional anticipation

Methodology

- n = 23, ages 13-17
- Male: 4, Female: 19; Mean age = 15.5
- The self-report measure Penn State Worry Questionnaire (PSWQ) was used to measure worry in participants
- Participants completed the Emotional Anticipation task[5] described in Figure 1 with neutral, negative, and ambiguous cues. In this study we focused on capturing neural activity following ambiguous cues
- Blood oxygen level dependent (BOLD) fMRI images were collected during the task using a 3.0 T Siemens Skyra MRI scanner
- Data were processed using Statistical Parametric Mapping software (SPM12) and the CONN toolbox in MATLAB version R2017a
- Whole-brain activity following ambiguous cues (prior to viewing the image) was contrasted with activity following neutral cues
- We extracted parameter estimates for all clusters that emerged as significant from the primary contrast, then correlated these values with PSWQ scores

Emotional Anticipation Task

- Emotional anticipation was elicited by presenting participants with a neutral cue (**O**), negative cue (**-**), or ambiguous cue (**?**)
- Neutral cues were followed by neutral images, negative cues were followed by negative images, and ambiguous cues were followed by either negative or neutral images (randomly chosen by the program)
- Following each image, participants were prompted to determine whether the image was negative or not
- This study focused on the contrast between the ambiguous cue situation and neutral cue situation

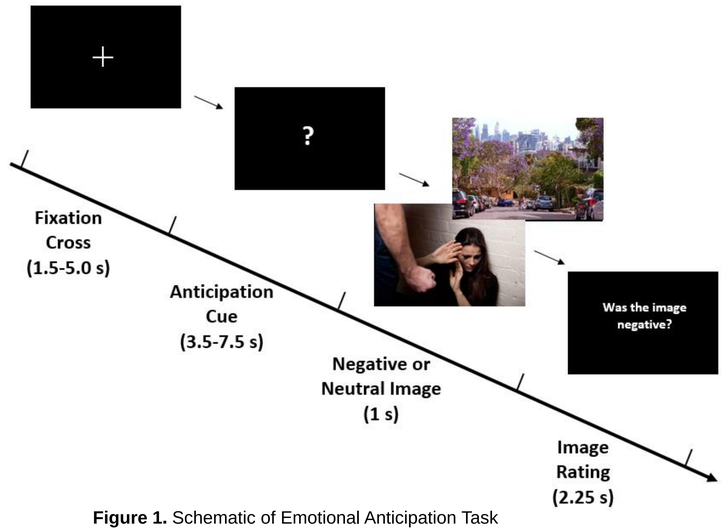

Figure 1. Schematic of Emotional Anticipation Task

Results

Ambiguous cue – Neutral Cue contrast

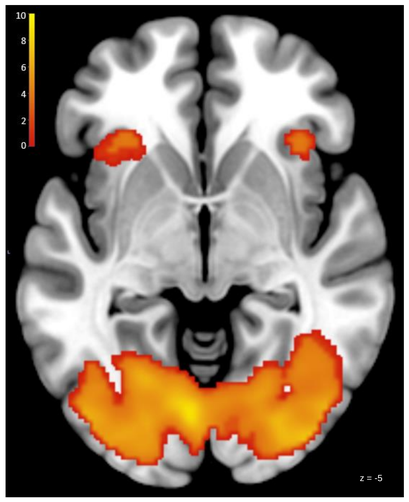

Figure 2. Display of the difference in brain activity in response to ambiguous emotional anticipation cues compared to neutral cues. Voxel threshold: *p<0.001*, extent threshold: *k = 20*

		Montreal Neurological Institute coordinates			
Region	*k*	*x*	*y*	*z*	*t*
Right primary visual cortex	8681	40	-86	4	10.64
Right hypothalamus area	325	4	-22	-18	5.85
Left ventral prefrontal cortex	289	-28	22	-12	4.75
Right dorsal parietal cortex	108	26	-50	62	4.49
Right lateral prefrontal cortex	53	54	28	0	4.41
Dorsal parietal cortex	39	-16	-62	42	4.34
Right anterior insular cortex	43	36	24	-4	4.10

Table 1. Whole brain analysis of activation to ambiguous cues relative to neutral cues

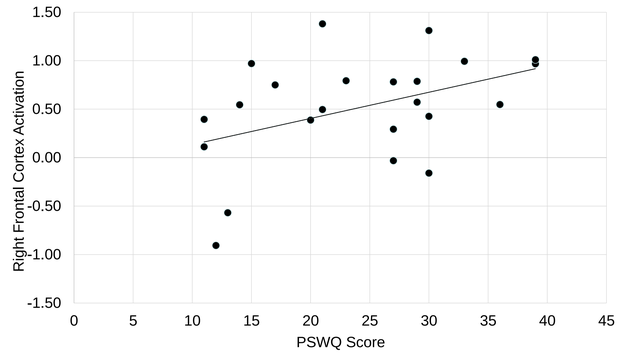

Figure 3. Scatter plot of participant PSWQ scores and difference in right frontal cortex activation in response to ambiguous cues compared to neutral cues, *r = 0.415, p* = 0.049,

Conclusions & Discussion

- Emotional anticipation in response to ambiguous cues is characterized by elevated responses in the left pre-frontal cortex (PFC), bilateral anterior insular cortex, and primary visual cortex (Fig. 2).
- We did not find evidence of activation in the anterior cingulate cortex related to anticipation of negative emotional stimuli. This region has been highlighted in previous research with adults as being central to anticipation.
- Greater activation in the left PFC cluster is significantly positively correlated to experiencing everyday worry in adolescents (Fig. 3).
- Significant primary visual cortex activation in response to emotional anticipation may be due to a preparatory mechanism where adolescents visualize different stimuli possibilities
- These findings are directly applicable to clinical populations, where neural circuitry data can be used to explore possible targets and markers for treatment

Future Directions

- In future analyses, we will examine how conditions of certainty and uncertainty of negative events impacts neural anticipatory processes
- Future research is needed in examining whether successful treatment of worry normalizes the excessive activation of the right prefrontal cortex during anticipation of negative events

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