Background

- Worry is a process by which people anticipate uncertain negative emotional events and is present across traditional anxiety and mood disorders. Previous studies have found activation in the septo-hippocampal system, anterior midcingulate cortex, and anterior insular cortex regions in emotional anticipation. 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. 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 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.

Results

<table>
<thead>
<tr>
<th>Region</th>
<th>Parameter Estimates</th>
<th>Montreal Neurological Institute coordinates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>k</td>
<td>x</td>
</tr>
<tr>
<td>Right primary visual cortex</td>
<td>8681</td>
<td>40</td>
</tr>
<tr>
<td>Right hypothalamic area</td>
<td>325</td>
<td>4</td>
</tr>
<tr>
<td>Left ventral prefrontal cortex</td>
<td>289</td>
<td>-28</td>
</tr>
<tr>
<td>Right dorsal parietal cortex</td>
<td>108</td>
<td>26</td>
</tr>
<tr>
<td>Right lateral prefrontal cortex</td>
<td>53</td>
<td>54</td>
</tr>
<tr>
<td>Dorsal parietal cortex</td>
<td>39</td>
<td>-16</td>
</tr>
<tr>
<td>Right anterior insular cortex</td>
<td>43</td>
<td>36</td>
</tr>
</tbody>
</table>

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

Conclusions & Discussion

- Emotional anticipation in response to ambiguous cues is characterized by elevated responses in the left prefrontal 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.

Acknowledgements

- 2017 Summer Research Program for Undergraduate Students at the Pediatric Mental Health Institute.
- National Institutes of Mental Health (Grant number: R23MH108640).