Functional Brain Networks Underlying Anxiety in Youth

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Introduction

- Anxiety is the most prevalent mental disorder, characterized by excessive and persistent worry in the DSM-V. Anxiety is common in children and adolescents, with approximately 9.4% of U.S. youth aged 3-17 experiencing anxiety problems (Bitsko et al., 2022).
- The Triple Brain Network (Menon, 2011) proposes that anxiety disorders are linked to disruptions within and between three core networks: the Default Mode Network (DMN), Frontoparietal Network (FPN) , and the Salience Network (SN).
- In addition to these, the Dorsal Attention Network (DAN), Ventral Attention Network (VAN), and Cingulo-Opercular Network (CON) also play roles in cognitive and emotional processing.
- This study aims to examine how connectivity within and between these networks correlates with anxiety symptoms in pre-adolescents.

Methods

Participants:

- Data sourced from the Adolescent Brain Cognitive Development (ABCD) Study.
- The ABCD study recruited ~11,875 children aged 9-10 from 21 research sites across the U.S.
- The sample reflects sociodemographic diversity representative of the general U.S. population.

Mental Health Data:

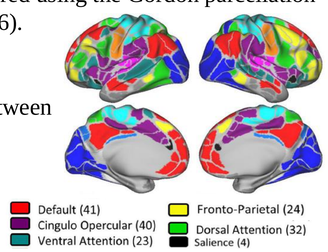
- Anxiety symptoms measured using the Child Behavior Checklist (CBCL) and Brief Problem Monitor (BPM).

rs-fMRI Data Collection:

- Resting-state fMRI (rs-fMRI) used to analyze functional connectivity.
- Participants viewed a fixation crosshair for four 5-minute scans (total of 20 minutes).
- Preprocessing steps included motion correction, distortion correction, and alignment with reference scans.

Functional Connectivity Analysis:

- Connectivity was measured using the Gordon parcellation atlas (Gordon et al., 2016).
- Connectivity strength is calculated as the average correlation within and between network regions.



Statistical Analyses:

- Linear regression was used to predict anxiety symptoms from network connectivity.
- Covariates: child age, sex, and ethnicity included in all models.
- Multiple comparison correction applied using FDR (Benjamini & Hochberg, 1995).

Hypothesis

We hypothesize that disruptions in functional connectivity within and between the DMN, FPN, SN, DAN, VAN, and CON, as observed through rs-fMRI data in youth from the ABCD study will correlate positively with higher levels of anxiety symptoms and disorders. Specifically, we expect that

1. Decreased functional connectivity within each of these six networks
2. Decreased functional connectivity between the DMN and networks overlapping with the SN and FPN
3. Increased functional connectivity between networks overlapping with the SN and FPN will be correlated to anxiety symptoms and disorders.
4. Altered connectivity in attention-related networks (DAN, VAN, CON) may contribute to dysregulated cognitive and emotional processing in anxiety.

Results

After the corrections, the analysis revealed significant correlations between specific CBCL and BPM scores and rs-fMRI connectivity measures:

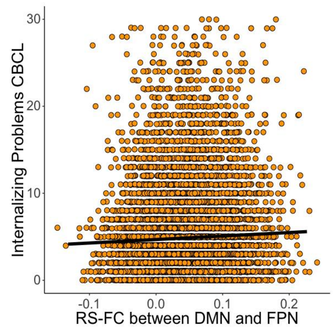


Figure 1. Positive correlation between CBCL internalizing Problems and DMN and FPN Connectivity

- A **positive correlation** between **CBCL internalizing problems** and rs-fMRI connectivity between the **Default Mode Network and Fronto-Parietal Network** (uncorrected-p = 0.002). This suggests that **higher internalizing symptoms** in children, as reported in the CBCL, were associated with **increased functional connectivity** in the Default Mode Network.

- **A positive correlation** was also found between **CBCL anxious/depressed symptoms** and rs-fMRI connectivity within the **Cingulo-Opercular Network** (uncorrected-p = 0.003). This indicates that **greater symptoms of anxiety and depression** predicted **increased connectivity** in these brain networks in children.

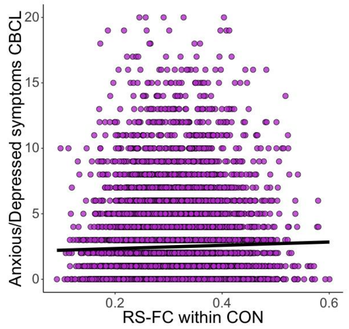


Figure 2. Positive correlation between CBCL anxious/depressed symptoms and CON Connectivity

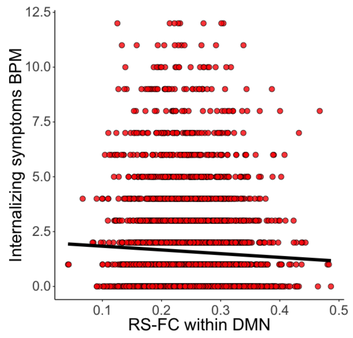


Figure 3. Negative correlation between BPM internalizing problems and DMN Connectivity

- Conversely, **a negative correlation** was found between **BPM internalizing problems** and rs-fMRI connectivity within the **Default Mode Network** (uncorrected-p = 0.006). This indicates that **higher internalizing symptoms** reported in the BPM were associated with **decreased functional connectivity** in this network.

Discussion

Summary

- Results show **both positive and negative correlations** between brain network connectivity and anxiety/internalizing symptoms.

Key Findings

- CBCL internalizing problems **positively correlated** with DMN and FPN connectivity.
- CBCL anxiety/depressed symptoms **positively correlated** with CON connectivity.
- BPM internalizing problems **negatively correlated** with DMN connectivity.

Interpretation

- The DMN and FPN's connectivity being highly correlated with CBCL internalizing problems suggests that excessive interaction between these networks may reflect difficulties in cognitive control over self-focused thoughts, which is a key symptom of anxiety and/or depression.
- The CON's role in cognitive control and error monitoring may explain its positive correlation with anxiety, as hyperactivity in this network could reflect heightened threat sensitivity or difficulty disengaging from negative stimuli.
- On the contrary, the negative correlation between BPM internalizing problems and DMN connectivity suggests that lower DMN function may contribute to reduced self-referential processing, potentially impacting emotional regulation in children.

Future Direction

- Investigate longitudinal changes in connectivity and anxiety symptoms.
- Examine subtypes of anxiety separately to see if connectivity patterns differ.

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