Shifting towards a naturalistic paradigm to investigate emotional processing in adolescent depression

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from molecules to mind

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BACKGROUND

- Adolescence is a developmental period that is marked by significant brain plasticity and maturational change[1].
- This sensitive period is associated with increased vulnerability to emotional dysregulation and psychiatric symptoms related to depression, particularly amongst females[2,3].
- Recently, movie-watching fMRI has emerged as a promising naturalistic approach to reveal processes that support emotional regulation and dysregulation as they unfold.
- Here, we build on previous work[4] to investigate cross-participant similarities in emotional processing and regulation during an emotionally evocative movie, using intersubject correlation analysis.
- We hypothesised that intersubject correlations in emotional processing would be modulated by individual differences in depressive symptom severity and emotional regulation.

RESEARCH QUESTION

➢ **Can intersubject correlations during emotional processing be modulated by individual differences in depressive symptom severity and emotional regulation in a sample of neurotypical youths and adolescents with depressive symptoms?**

METHODS

Participants

- 21 adolescents experiencing depressive symptoms (DS) (13-20 years, mean age 16.9 ± 1.9) and 31 age- and gender-matched neurotypical youths (NT) were recruited during which they watched a short emotional evocative movie ("The Present").

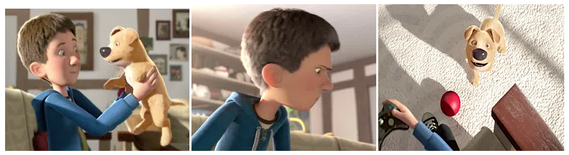


Fig.1. Stills shown from the emotional evocative movie ("The Present").

MRI Data Acquisition

- Functional data was acquired using a Philips Achieva 3T scanner (200 EPI volumes, TR = 2000ms, TE = 30ms, 37 slices, voxel size = 3.2x3x3mm).
- Anatomical T1-weighted images were also acquired with a spatial resolution of 0.9x0.9x0.9mm.

Self-Reported Phenotypic Measures

- The Depressive Inventory from the Beck Youth Inventories[5] (BDI-Y) was completed to assess depressive severity.
- The Cognitive Emotion Regulation Questionnaire[6] (CERQ) was used to measure emotional regulation.

fMRIPrep Preprocessing Pipeline[7]

- Structural: bias field correction, skull stripping, spatial normalisation to the standard MNI152 space and tissue segmentation.
- Functional: slice-timing correction, motion correction, functional-to-anatomical registration, confound regression (motion, WM, CSF, global signal), spatial smoothing with a Gaussian kernel of 6mm FWHM and temporal filtering with a cut-off threshold at $0.01 < f < 0.1$Hz.

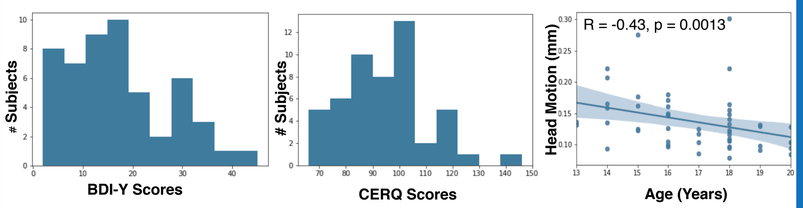
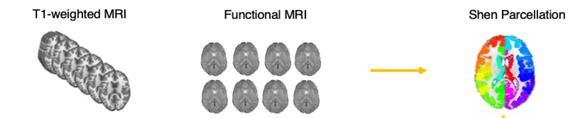


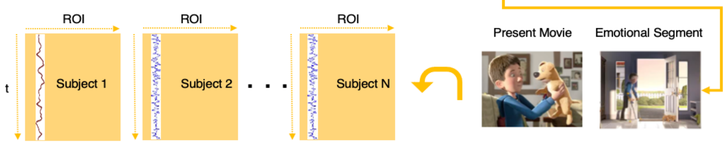
Fig.2. Demographics information derived from 21 DS adolescents and 31 age- and gender-matched NT youths.

ANALYSIS

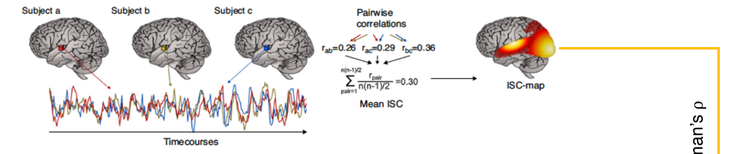
A. fMRIPrep Preprocessing Pipeline



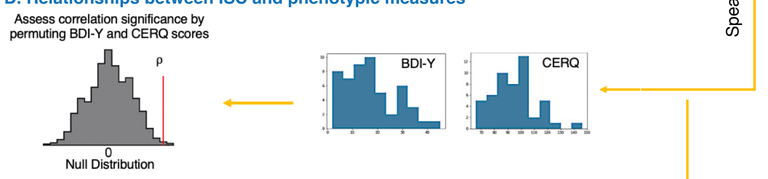
B. Extract fMRI timeseries



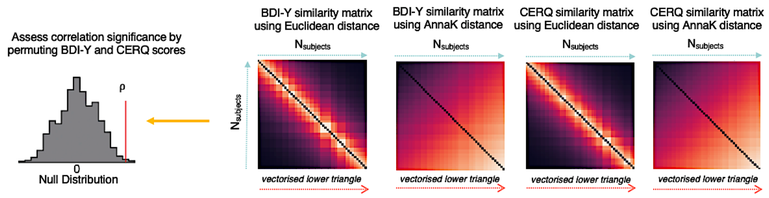
C. Intersubject Correlation (ISC)



D. Relationships between ISC and phenotypic measures



E. Intersubject Representational Similarity Analysis (IRSA)



F. Intersubject Phase Synchronisation (ISPS)

4 frequency bands[8,9]: slow-5 [0.01-0.027Hz], slow-4 [0.027-0.073Hz], 0.04-0.07Hz, slow-3 [0.073-0.198Hz]

RESULTS

Whole-brain synchronisation across NT and DS youths using an emotional evocative movie

- Significant ISC was observed posteriorly in the occipital and parietal lobes, extending to superior temporal gyrus as well as posterior components of the default network ($p < 0.05$ FDR).

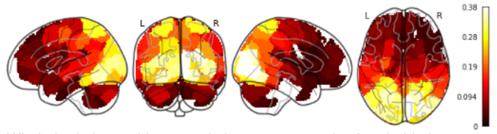


Fig.3. Whole-brain intersubject correlations across youths thresholded at $p < 0.05$ FDR.

Regional synchronisation across NT and DS youths using high emotion segments

- Difference in ISC during low and high emotion segments resulted in relatively increased ISC in the default network, lingual gyrus and fusiform gyri. Relatively decreased ISC was observed in the angular gyrus, primary motor and somatosensory cortices, MTG, SMA and SPL ($p < 0.05$ FDR).

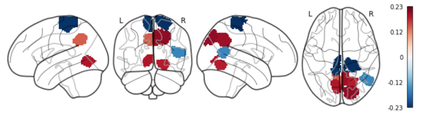


Fig.4. Regional intersubject correlations across youths thresholded at $p < 0.05$ FDR.

Relationships between ISC and phenotypic measures

- Greater severity of depressive symptoms was related to weaker ISC in the basal ganglia, limbic system, insular cortex, frontal pole, MTG and cerebellum, and to stronger ISC in the primary motor and somatosensory cortices in addition to the ITG and TFG ($p < 0.05$ unc).
- Stronger emotional regulation was associated with weaker ISC in the auditory cortex, hippocampus, central opercular cortex, brain stem and cerebellum ($p < 0.05$ unc).

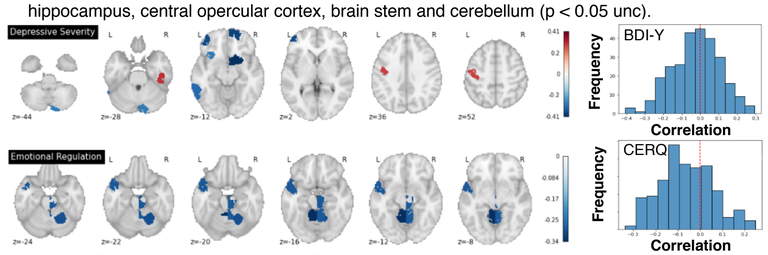


Fig.5. Relationships between ISC and phenotypic measures thresholded at $p < 0.05$ unc.

Intersubject representational similarities between brain and phenotypic measures

- Participants who had similar BDI-Y and CERQ scores shared more similarity across specific brain regions which was captured by the Euclidean model. The AnnaK model captured low-scoring participants on both scales who were less similar to high and low scorers (more idiosyncrasy).
- As was seen for the primary ISC analysis, neither the Euclidean nor the AnnaK models captured significant relationships between brain and phenotypic similarity after applying FDR correction.

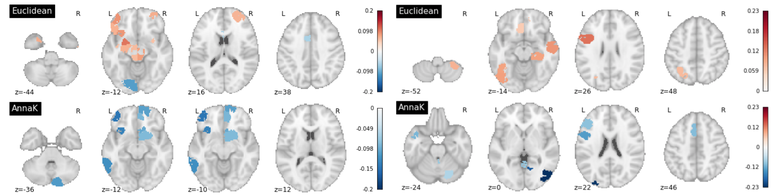


Fig.6. Intersubject representational similarity for BDI-Y (Left) and CERQ (Right) thresholded at $p < 0.05$ unc.

Temporal dynamics of intersubject synchrony across NT and DS adolescents

- All the low and high frequency bands showed reproducible patterns of ISPS in components of the default network, primary motor and somatosensory cortices, lingual gyrus and fusiform gyri ($p < 0.05$ FDR).

Fig.7. Instantaneous intersubject phase synchronisation across youths thresholded at $p < 0.05$ FDR.

CONCLUSIONS

- Naturalistic paradigms that evoke emotional responses may capture changes in brain synchrony and their relationships with emotional processing in depressive adolescents.
- Further analyses will investigate dynamic emotional processing to capture moment-to-moment responses to events that may vary with depressive symptom severity.

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[1]Casey BJ, Getz S, Galvan A. The adolescent brain. Dev Rev. 2008; 28(1):62-77. [2]Kerestes R, Davey C, Stephanou K, Whittle S, Harrison B. Functional brain imaging studies of youth depression: A systematic review. Neuroimage: Clinical. 2014; 4:209-231. [3]Fuhrmann D, Knoll L, Blakemore S. Adolescence as a Sensitive Period of Brain Development. Trends Cogn Sci. 2015; 19(10):558-566. [4]Gruskin D, Rosenberg M, Holmes A. Relationships between depressive symptoms and brain responses during emotional movie viewing emerge in adolescence. Neuroimage. 2020; 216:116217. [5]Beck, JS., Beck, AT., & Jolly, J. Manual for the Beck Youth Inventories of Emotional and Social Impairment. San Antonio, TX: The Psychological Corporation. 2001. [6]Garnefski N, Kraaij V. The Cognitive Emotion Regulation Questionnaire: Psychometric features and prospective relationships with depression and anxiety in adults. European Journal of Psychological Assessment. 2007; 23:141-149. [7]Esteban O, Markiewicz C, Blair R et al. fMRIPrep: a robust preprocessing pipeline for functional MRI. Nat Methods. 2018; 16(1):111-116. [8]Glerean E, Salmi J, Lahnakoski J, Jääskeläinen I, Sams M. Functional Magnetic Resonance Imaging Phase Synchronization as a Measure of Dynamic Functional Connectivity. Brain Connect. 2012; 2(2):91-101. doi:10.1089/brain.2011.0068. [9]Zuo X, Di Martino A, Kelly C et al. The oscillating brain: Complex and reliable. Neuroimage. 2010; 49(2):1432-1445. doi:10.1016/j.neuroimage.2009.09.037.