Shifting towards movie-watching fMRI to investigate emotional processing in adolescent depression

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

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from molecules to mind

Jivesh Ramduny[1,3], Clare Kelly[1,2,3]

[1]School of Psychology, Trinity College Dublin, Dublin, Ireland
[2]Department of Psychiatry, School of Medicine, Trinity College Dublin, Dublin, Ireland
[3]Trinity College Institute of Neuroscience, Trinity College Dublin, Dublin, Ireland

IMMA LAB

ramdunyj@tcd.ie
@JRamduny

BACKGROUND

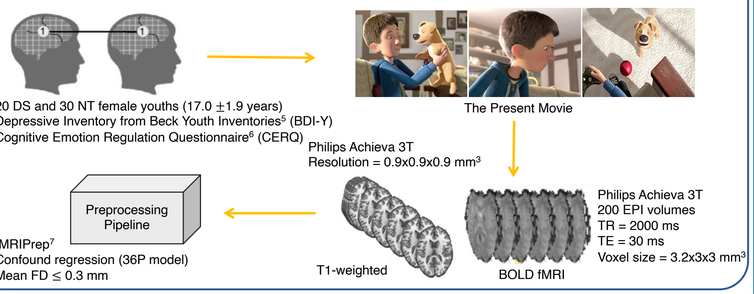
- Adolescence is a developmental period that is marked by significant brain plasticity and maturational change[1].
- This sensitive period is associated with increased vulnerability to emotional dysregulation and psychiatric symptoms related to depression, particularly amongst females[2,3].
- Recently, 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

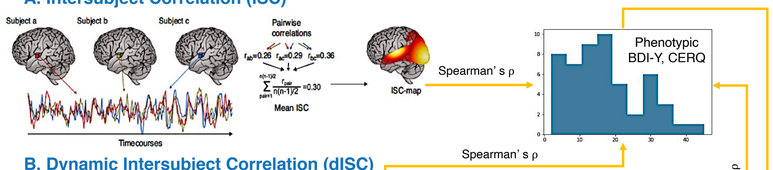
➢ **Are intersubject correlations during emotional processing modulated by individual differences in depressive symptom severity and cognitive emotional regulation styles in a sample of adolescents and young adults?**

METHODS

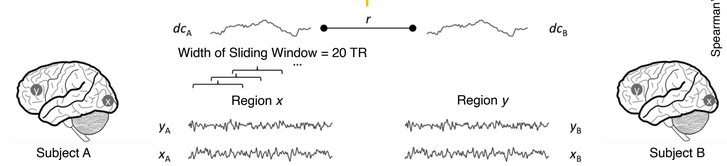
Materials



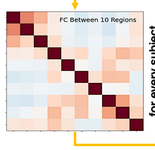
A. Intersubject Correlation (ISC)



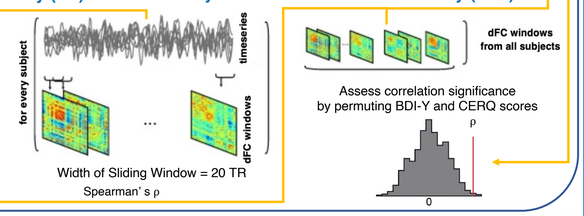
B. Dynamic Intersubject Correlation (dISC)



C. Functional Connectivity (FC)



D. Dynamic Functional Connectivity (dFC)



RESULTS

Whole-brain synchronisation during an emotional evocative movie

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

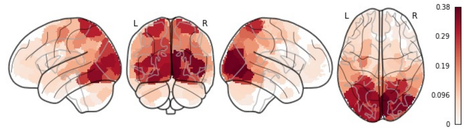


Fig.1. Whole-brain intersubject correlations across youths thresholded at $p < 0.05$ FDR.

Regional synchronisation during low and high emotional segments of the movie

- A direct comparison of ISC during a low- relative to a high-emotional segment revealed that the low-emotional segment was associated with relatively increased ISC in the lateral occipital cortex but relatively decreased ISC in the default network (e.g., angular gyrus, precuneus), primary somatosensory cortex, middle temporal gyrus (MTG) and superior parietal lobule (SPL) ($p < 0.05$ FDR).

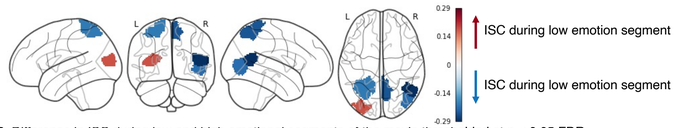


Fig.2. Difference in ISC during low and high emotional segments of the movie thresholded at $p < 0.05$ FDR.

Relationships between ISC and phenotypic measures

- There were no significant relationships between ISC and phenotypic measures (i.e., BDI-Y, adaptive CERQ, maladaptive CERQ) that exceeded thresholds corrected for multiple comparisons (268 nodes).
- At an uncorrected threshold, greater depressive severity was related to weaker ISC in the basal ganglia, limbic system, insular cortex, frontal pole, MTG and inferior temporal gyrus (IFG), and to stronger ISC in the primary motor and somatosensory cortices, angular gyrus, supramarginal gyrus, SPL in addition to the brainstem ($p < 0.05$ unc).
- Stronger adaptive CERQ scores were related to weaker ISC in the parahippocampal gyrus and hippocampus ($p < 0.005$ unc).
- Stronger maladaptive CERQ scores were related to weaker ISC in the occipital fusiform gyrus and several portions of the cerebellum including the right Crus I and right V1 ($p < 0.005$ unc).

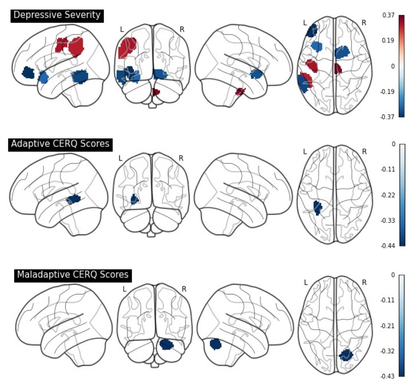


Fig.3. Relationships between ISC and phenotypic measures (i.e., BDI-Y, adaptive CERQ, maladaptive CERQ) thresholded at $p < 0.05$ unc for BDI-Y and $p < 0.005$ unc for the CERQ measures.

Temporal ICA reveals functional networks that capture dynamic intersubject synchrony

- We employed a tapered cosine sliding window approach with a width of TR = 20s (cosine fraction = 0.95) to compute dynamic ISC. This approach aims to reduce the impact of timepoints which are located at the extremes of the sliding window by assigning more weights to the timepoints that are closer to the center of the window.
- Temporal ICA reveals 12 independent (ICs) that captured moment-to-moment ISC in previously identified functional networks with resting-state conditions[9] such as the lateral and medial visual, sensorimotor, cerebellar and subcortical (e.g., thalamic, hippocampal) networks.

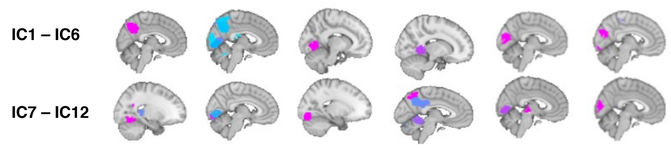


Fig.4. Temporal ICA shows 12 ICs that were identified during an emotional evocative movie.

- The timecourse of the IC maps showed that participants mainly exhibited an idiosyncratic response during the emotional segment of the movie (TR ≥ 67). However, there were no significant relationships between dISC and phenotypic measures (i.e., BDI-Y, adaptive CERQ, maladaptive CERQ).

Functional connectivity (FC) between regions that play a role in emotional regulation

- We performed static and dynamic FC analyses with 10 regions of interest (ROIs) that play an important role in emotional regulation derived from an automated meta-analysis (Neurosynth).
- Static FC did not reveal any significant edge-level associations with the phenotypic measures (i.e., BDI-Y, adaptive CERQ, maladaptive CERQ) after applying FDR corrections for the 45 edges.
- We performed dFC analyses by applying the same tapered cosine sliding window approach as described above. We thresholded the edge-level correlations between the dFC and phenotypic measures at $p < 0.01$ within each sliding window and retained the significant edges which were present in at least 5 consecutive windows (Fig.6).

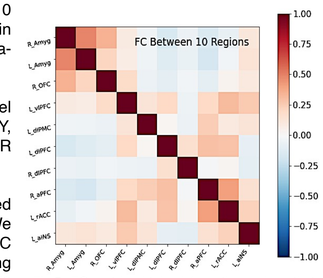


Fig.5. FC matrix obtained from the regions that play an important role in emotional regulation.

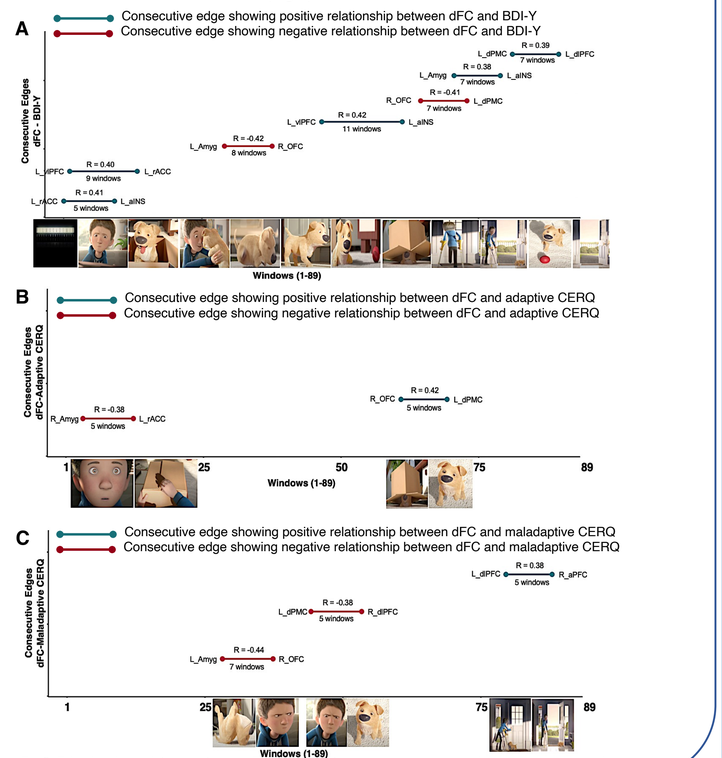


Fig.6. Edge-level correlations between dFC and phenotypic measures using a sliding window approach.

CONCLUSIONS

- Naturalistic paradigms that evoke emotional responses may capture changes in dynamic functional connectivity and their relationships with emotional processing in depressive adolescents.
- However, the lack of significant brain-phenotypic relationships from static and dynamic ISC may be attributed to our limited sample size, short emotional movie (where the high emotional content is at the end of the movie) and non-clinically depressive adolescents.
- Further analyses will investigate whether static and dynamic changes in ISC are driven by changes in the content of another movie with longer duration, and whether such changes are modulated by individual differences in self-reported cognitive emotional regulation styles and depressive symptoms.

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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]Smith S, Fox P, Miller K et al. Correspondence of the brain's functional architecture during activation and rest. Proceedings of the National Academy of Sciences. 2009; 106(31):13040-13045. doi:10.1073/pnas.0905267106.