Altered Functional Connectivity in Depressed Adolescents: Using Deep Learning for Neuroimaging Insights

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Introduction

During adolescence and neurodevelopment the brain is highly susceptible to both internal and external factors that can lead to neurological abnormalities. Abnormal brain connectivity is associated with mental disorders in adults but little is known about adolescents. Here, we use the neuroimaging data obtained from the Adolescent Brain Cognitive Development study (ABCD) at the baseline, including structural and functional MRI to study brain connectivity. Our sample consisted of 1429 healthy participants and 353 adolescents diagnosed with depression, all aged 9-10 years.

Fig. 1 The ABCD neuroimaging study

Methods

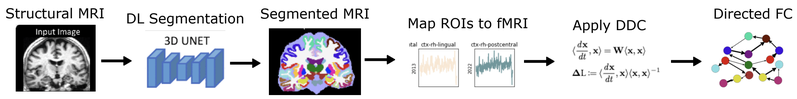


Fig. 2 Overview of automated neuroimaging pipeline for functional connectivity

1. Pre-processing resting state fMRI data

We applied a novel deep learning seed-based segmentation algorithm called SynthSeg+ to each subject's structural MRI, resulting in 98 regions of interest (ROI) defined by the Desikan-Killany brain atlas. The segmentation and cortical parcellation was then applied to the rs-fMRI data to obtain time series data from each ROI (Fig. 2).

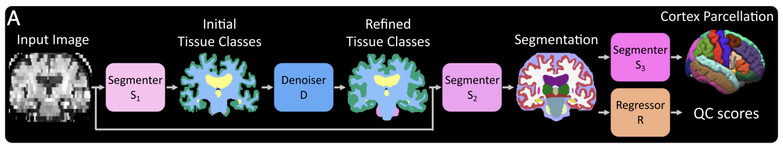


Fig. 3 From B. Billot et al. 2023 Overview of SynthSeg+ inference pipeline

2. Dynamical Differential Covariance (DDC)

Conventional functional connectivity (FC) is often assessed by calculating symmetric pairwise covariance (Cov), which is unable to detect directional interactions and is biased by correlation. We employed a new algorithm called dynamical differential covariance (DDC), a method based on dynamical network models that detects directional interactions with low bias and high noise tolerance under nonstationarity conditions.

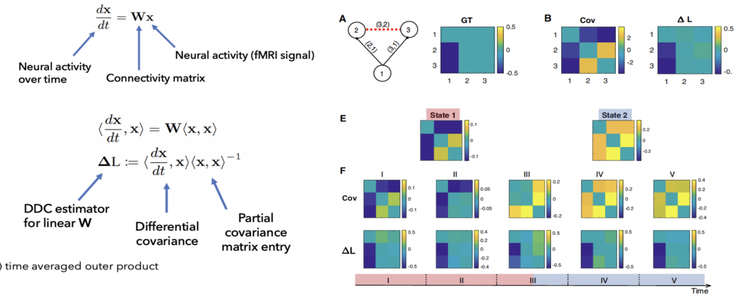


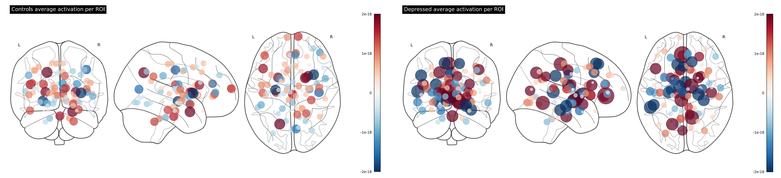
Fig. 4 From Y. Chen et al. 2022. Left: equations of the linear dynamical model defined to compute the DDC estimator. Right: **A** simulated network and its ground thruth connections; **B** comparison between DDC and Cov. **E** Simulation of a two-states dynamical system; **F** Sample covariance estimation shifted between states while ΔL estimation consistently reported the static true connectivity.

References

[1] Volkow, Nora D., et al. "The conception of the ABCD study: From substance use to a broad NIH collaboration." Developmental cognitive neuroscience 32 (2018): 4-7.
[2] Billot, Benjamin, et al. "Robust machine learning segmentation for large-scale analysis of heterogeneous clinical brain MRI datasets." Proceedings of the National Academy of Sciences 120.9 (2023): e2216399120.
[3] Chen, Y., Rosen, B. Q., & Sejnowski, T. J. (2022). Dynamical differential covariance recovers directional network structure in multiscale neural systems. Proceedings of the National Academy of Sciences, 119(24)

Results

Fig. 5 Resting state fMRI recordings show differences in brain activity of adolescentd with MDD (*right*) compared with healthy adolescents (*left*).



Our findings revealed disrupted patterns of functional connectivity in adolescents with MDD compared to the control group (Fig. 5).

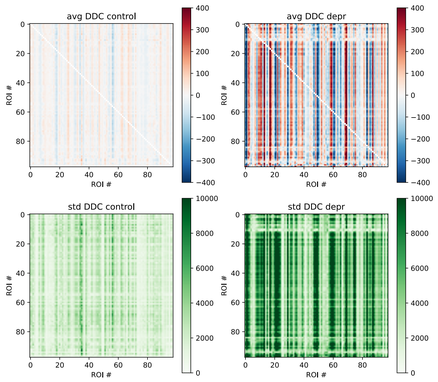


Fig. 5 Mean (*top*) and standard deviation (*bottom*) of whole brain functional connectivity matrices obtained with DDC in healty adolescents (*left*) and adolescents with MDD (*right*)

FC alterations were observed at both the whole brain level (Fig. 6) and within functional subnetworks (Fig. 7) such as the Default Mode Network (DMN), Central Executive Network (CEN), and Salience Network (SN), which aligns with previous studies.

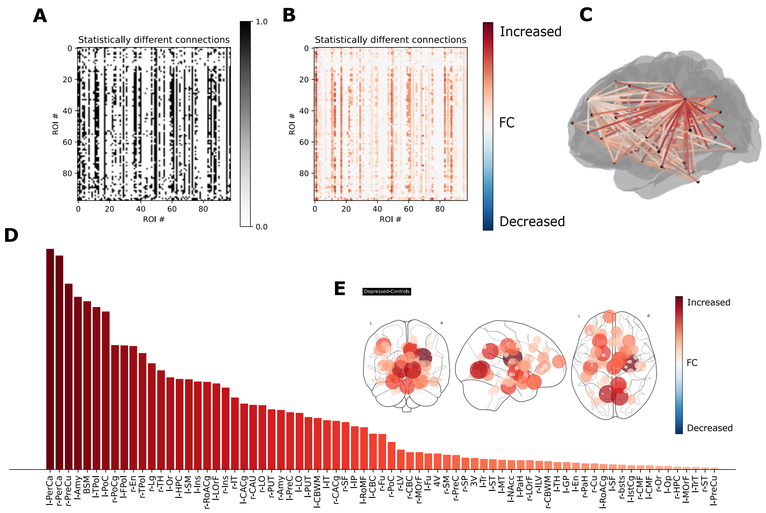
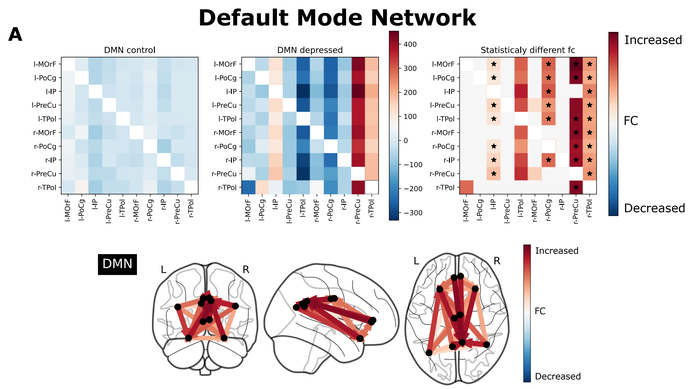


Fig. 6 A: binary matrix of significantly different functional connections ($p<0.05$) at whole brain level. **B**: Functional connectivity is increased in adolescents with MDD. **C:** 3D view of the functional connections increased in MDD adolescents. **D:** barplot of FC change per ROI, and **E:** their location in the brain.

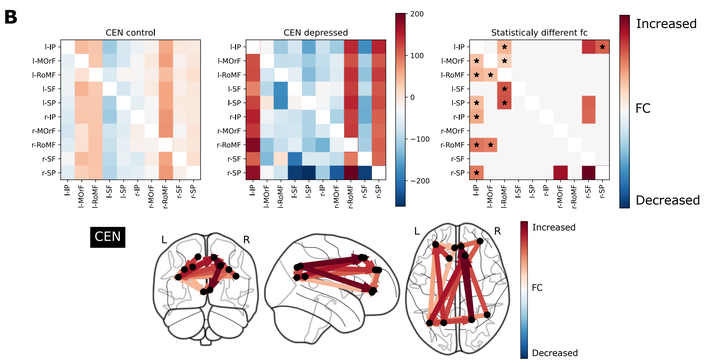
Conclusions

- **Increased connectivity**
  - at whole brain level
  - within DMN and SN
  - between DMN and SN
- Abnormal SN causes abnormal balance between DMN and CEN
- **DMN** changes related to the patient's rumination symptoms
- **CEN** changes related to decreased cognitive performance symptoms

Default Mode Network



Central Executive Network



Salience Network

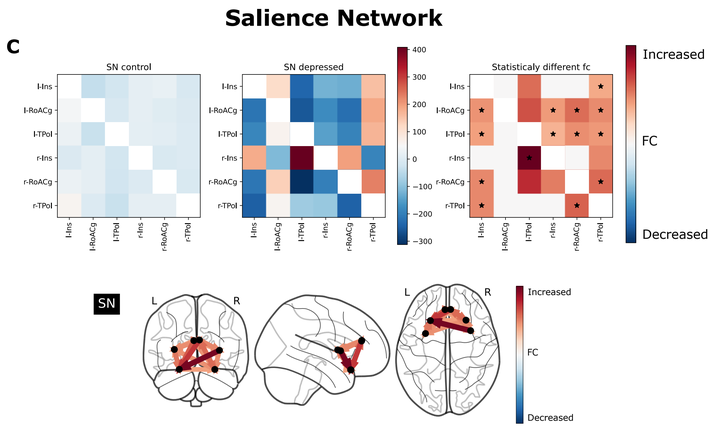


Fig. 7 Significantly different connectivity patterns observed in DMN, CEN and SN between healty and MDD adolescents. We show, from left to right, DDC in controls adolescents, DDC in MDD adolescents, and their difference in the regions that show significant changes ($p<0.05$) as matrices and graphs on the brain surface. Stars mark connections that have opposite sign in the two populations.

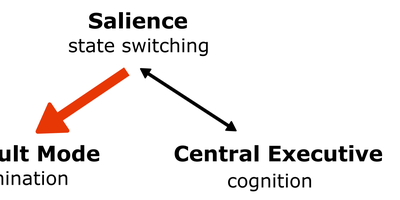


Fig. 8 SN shows increased preference towards DMN vs CEN state in depressed adolescents causing abnormal balance between the two subnetworks.

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