Growth Charting of Brain Connectivity Networks and the Identification of Attention Impairment in Youth

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Outline

Motivation

Pediatric Growth Charts

- Long history for height, weight, etc

Intrinsic Connectivity Networks

- Attention & ADHD connection
- DMN vs TPN balance

Background

Focus today: processing pipeline, modeling, and analysis

Sample

- Philadelphia Neurodevelopmental Cohort
- Resting state fMRI
- Penn Continuous Performance Task
- N = 519 (after QC & exclusions)

Task: PCPT

- Penn Continuous Performance Test
- 180 trials
- 1s to respond
- "Go" on digit/letter (varies by phase)
- Measure: Acc (corrected for age with quadratic model)

Clinical Interview

- Assesses psychopathology dimensions
- ADHD Module
- Symptom endorsement -> pseudo ADHD "diagnosis"

MRI Measures

- T1-weighted image (structural contrast)
- Resting State fMRI

T1 Image

- Structural contrast
- Ventricles are black, "gray matter" is darker, "white matter" is brither

Resting state fMRI

- 4D Image (Multiple "Volumes"): X*Y*Z*time
- T2* contrast captures BOLD (blood oxygenation, coupled to neural activity)

fMRI Prepocessing Overview

Lots of quality-control steps throughout

1. Slice-time Correction
2. Motion Correction
3. Normalization
4. Smoothing

Preproc: Slice-time Correction

- Each fMRI volume is acquired sequentially in slices
- Volume not acquired simultaneously
- Correct (through interpolation) s.t. all slices w/in volume temporally aligned

Prepoc: Motion Correction

- Participants move their head over the scan
- Estimate affine realignment to common volume (e.g. V_0)
- Alignment is progressive (rigid body transforms)
  - realign V_1 to V_0 using affine matrix A_1
  - align V_2 to V_0, initialize solution with A_1
  - and so on
- Store A_i
- Process A_i's to capture summary displacement information for each frame
  - this will be used later in preproccessing

Preproc: Normalization

- Everybody's brain is unique
- This is problematic for group analyses
- Standard Brain/Space: MNI (Montreal Neurological Institute)
- Steps
  1. Rigid body registration of T1 scan to T2* scan
  2. Estimate nonlinear warp (affine + splines) b/w T1 and MNI template
  3. Apply estimated warp to each volume of T2* scan

Preproc: Smoothing

- Normalization isn't perfect
- Brain's are plastic and diverse even when perfectly aligned anyway
- Smooth with Gaussian kernel (3D, 8mm FWHM)

Resting Processing & Connectome Generation

Processing

- Linearly detrended
- COMPCor: PCA-based nuisance regression (CSF & WM)
- Bandpass Filtering (0.01 to 0.1 Hz)
- Motion Scrubbing: Delete volumes with large displacement/motion

Connectome Generation

- Isomorphic grid, 12mm spacing
- 1068 Regions of Interest (ROIs)
- Calculate pairwise correlation, then R-to-Z transform
- Vector embedding: Each participant contributes $\binom{1068}{2}$ edges

Data Cleansing

- Intersubject nuisance effects may manifest at edge level
- e.g.: left handers have > connectivity at edge i
- Concatenate vector embeddings into matrix X
- estimate with OLS $X = Y\hat{\beta} + \hat{\epsilon}$
- Reestimate data as $X^{\dagger} = Y^{\dagger}\hat{\beta}$
- Y is ideal design matrix where nuisance fx are flat
- Induce eigenvector selection through augmentation: add $hat\beta$ for fx of interest at each edge

Independent Components Analysis

- reduce rows of $X^{\dagger}$ through PCA (DX) (retain top 15 eigenvectors)
- ICA-decomposition using FastICA $X = AS$
- A: mixing matrix 15 by 15
- S: source matrix: 15 by $\binom{1068}{2}$
- Unreduce $A^{\dagger} = D^{-1}A$
- $A^{\dagger}$ is # of subjects by 15
- The i,j element indicates the expression of component j for subject i

Network Growth Charting Analyses

- Growth charts obtained from OLS population-level estimates
- Predict each column of A with OLS $A_i^{\dagger} = age + age^2$
- Residuals from these models are deviation scores reflecting over- or under- expression of a component relative to age
- Use deviation scores to predict
    - Accuracy on PCPT (age-corrected)
    - ADHD status

Network Growth Charting to Predict Task Accuracy

Shifting DMN-TPN Architecture Among Maturing Components

Shallow vs Lagged Dysmaturation and Task Accuracy

Biomarker of Attention Dysfunction from Network Growth Charting

Biomarker of ADHD from Network Growth Charting

Unraveling miswired connectomes

ICN interplay

Dysmaturation Predicts Dysfunction

Differential Dysmaturation

Conclusions

Brain network growth charting predicts attention functioning.