A Sliding-Window Based Clustering Method to Decode Age-Specific Changes in Brain Functional Connectivity

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INTRODUCTION

- Major advances in neuroimaging methodologies during the past two decades permit detailed study of the maturation of the human brain.
- Investigating the functional neural circuits in normal development can
  - Identify when development abnormalities arise
  - Determine where, when, and how to intervene and thereby prevent illness persistence.
  - Help generate hypotheses regarding the neural bases of developmental psychopathologies
  - Help to improve diagnosis and treatment
- Maturation of functional connectivity (FC) can be examined by quantifying age-related changes in the strength and spatial distribution of intrinsic brain networks
- Problems:
  - The developmental evolution of FC is not following a linear trend over the adolescent period,
  - The onset and the duration of the changes may vary from regions to regions

METHODS

Goal:
- Identify various age-period-specific FC developing patterns

Main Idea:
- Describe the nonlinear developing curves
- Find various clusters of developing patterns

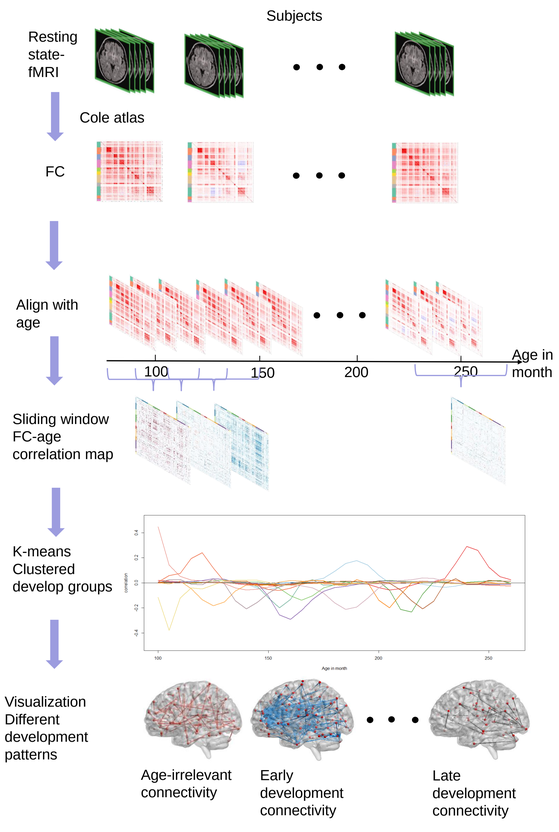

Fig 1: The flowchart of detecting age-specific development patterns.

STATISTICAL MODELS

Notation: N subjects, p ROIs

FC matrices $\{\Sigma_{p\times p}\}_{n=1}^{N}$

- $\Sigma_{p\times p}$ is calculated using Pearson correlation

Step 1. Capture each FC's developing trend along age

- Sliding-widow correlation $\rho_{ij,t}$
  - $\forall\ \{\Sigma_{ij}\}_{n=1}^{N}$, $\forall\ t \in T$, the FC-age correlation

$$\rho_{ij,t} = corr\left(\Sigma_{ij}^{t}, age^{t}\right),$$

    where $age^{t} \in [t-w, t+w]$, w is the half window size, and Σ_{ij}^{t} is the corresponding subset of the FC in $[t-w, t+w]$
  - Spearman rank correlation
- $\rho_{ij,t}$ Meaning
  - Positive: the FC value increases as the age increases within the age interval $[t-w, t+w]$
  - Negative: vice versa,
  - Zero value: the FC value is not related with age

Step 2. Identify the age-period-specific developing patterns

- Clusters that containing the FC's with similar changing curves
  - FC-age correlation sequence $\boldsymbol{\rho}_{ij} = \left(\rho_{ij,1}, \rho_{ij,2}, \ldots, \rho_{ij,T}\right)$
  - K-means clustering on the $\boldsymbol{\rho}_{ij}$ by minimizing the within-cluster sum of squares

$$arg\ \min_{S} \sum_{k=1}^{K} \sum_{\boldsymbol{\rho}_{ij}\in S_k} ||\boldsymbol{\rho}_{ij} - \boldsymbol{\mu}_{\boldsymbol{k}}||.$$

Each cluster $\boldsymbol{\mu}_{\boldsymbol{k}} = (\mu_{k1}, \mu_{k2}, \ldots, \mu_{kT})$ represents one type of FC-age changing curve.

- b-spline regression: $\mu_{kt} = \sum_{m=1}^{M} \alpha_m B_{m,h}(t) + \epsilon_{kt}$,

$$\epsilon_{kt} \sim i.i.d.\ N(0, \sigma^2)$$

MATERIALS

- Dataset: human connectome project-development (HCP-D) [1]
- Subjects

Number of subjects: 528
Age range: 5-21

	F (N=290)	M (N=238)	Total (N=528)
Age in month			
Mean	177.452	181.437	179.248
Min	76.000	67.000	67.000
Q1, Q3	140.250, 217.750	146.000, 221.000	144.000, 218.250
Max	263.000	263.000	263.000

- Brain image: resting-state fMRI (rs-fMRI)

rs-fMRI
- Participants were instructed to stay still, stay awake, and blink normally while looking at the fixation crosshair.
- The total scan duration

age>8, 26 min (4 runs in 2 consecutive days)
age<8, 21 min (6 runs in 2 consecutive days)
- 3T Siemens Prisma platform

HCP minimal preprocessing pipelines [2]
- Several covariates are regressed out: mean cerebral-spinal fluid signal, mean white matter signal, and overall global signal
- Bandpass filtering: 0.008 - 0.12 Hz
- Mean framewise displacement (FD) > 0.3 mm is removed

- Cole parcellation [3]
  - 718 cortical and subcortical regions of interest (ROIs)
- We concatenate the runs acquired at the same day, respectively.
  - First-day dataset for analysis
  - Second-day dataset for validation.

RESULTS

- The development curves show gender differences and are consistent over measures.
- Females matured earlier than males in functional development , but males had higher development rate.

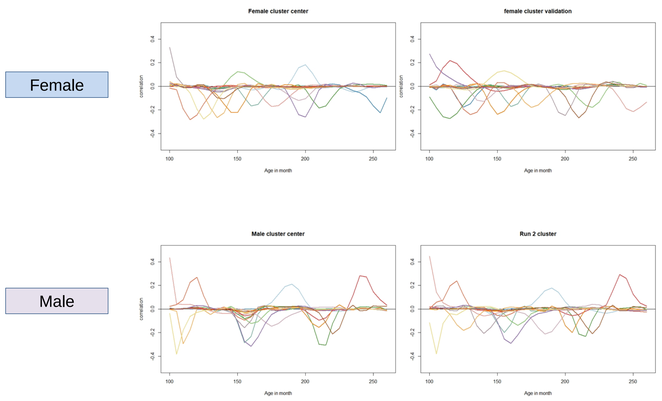

Fig 2: The various developing curves clustered by K-means shown by gender. The left column shows the result from first-day data and the right column is the result from second day

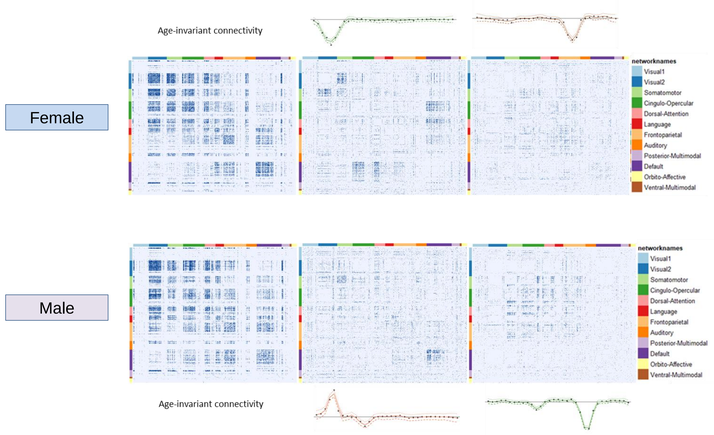

Fig 3: The FC entries of each selected developing patterns.

CONCLUSIONS

- We employ the rolling regression/correlation techniques to delineate the curves with dynamic parameters.
- Main Advantages:
  - Reveal the nonlinear relationship between age and FC.
  - The interpretation of the parameters is straightforward.
  - Flexible enough to expand and compare with other development studies.

ACKNOWLEDGEMENT

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