Whole-brain dynamical modeling of the adolescent developing brain

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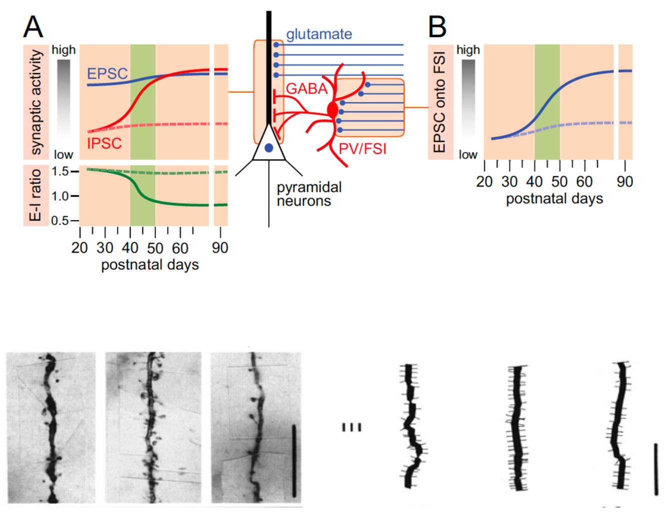
Supplements

Introduction

- Regulation of cortical microcircuits is crucial for optimal neural processing[1]
- Adolescence involves substantial macro- and microscale changes in the brain, including maturation of cortical microcircuits[2]
- Evidence from animal studies suggests a calibration of cortical microcircuits and excitation-to-inhibition (E-I) ratio, including:
  - Reduction in the density of excitatory synapses by ~40-50%[3]
  - Maturation of PV+ interneurons, changes in subunit composition of GABA receptors, and strengthening of inhibitory-to-excitatory synapses[4]



- Evidence on maturation of microcircuits in the human cortex is limited and indicate developmental changes of:
  - Synaptic density and gene expression of neuronal markers based on post-mortem studies[5]
  - Concentration of GABA and Glu neurotransmitters in MRS[6]
  - Gamma oscillations in M/EEG[7]
  - Similarity of rs-fMRI FC to benzodiazepine effects on adult brains[8]

Aim

Based on whole-brain dynamical modeling of resting-state fMRI, how do cortical microcircuits develop during human adolescence?

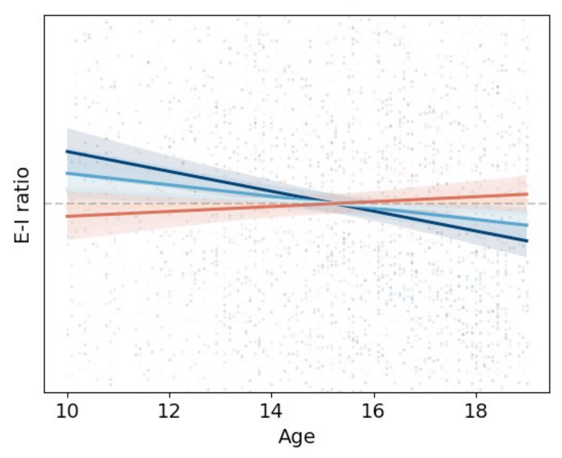
Methods

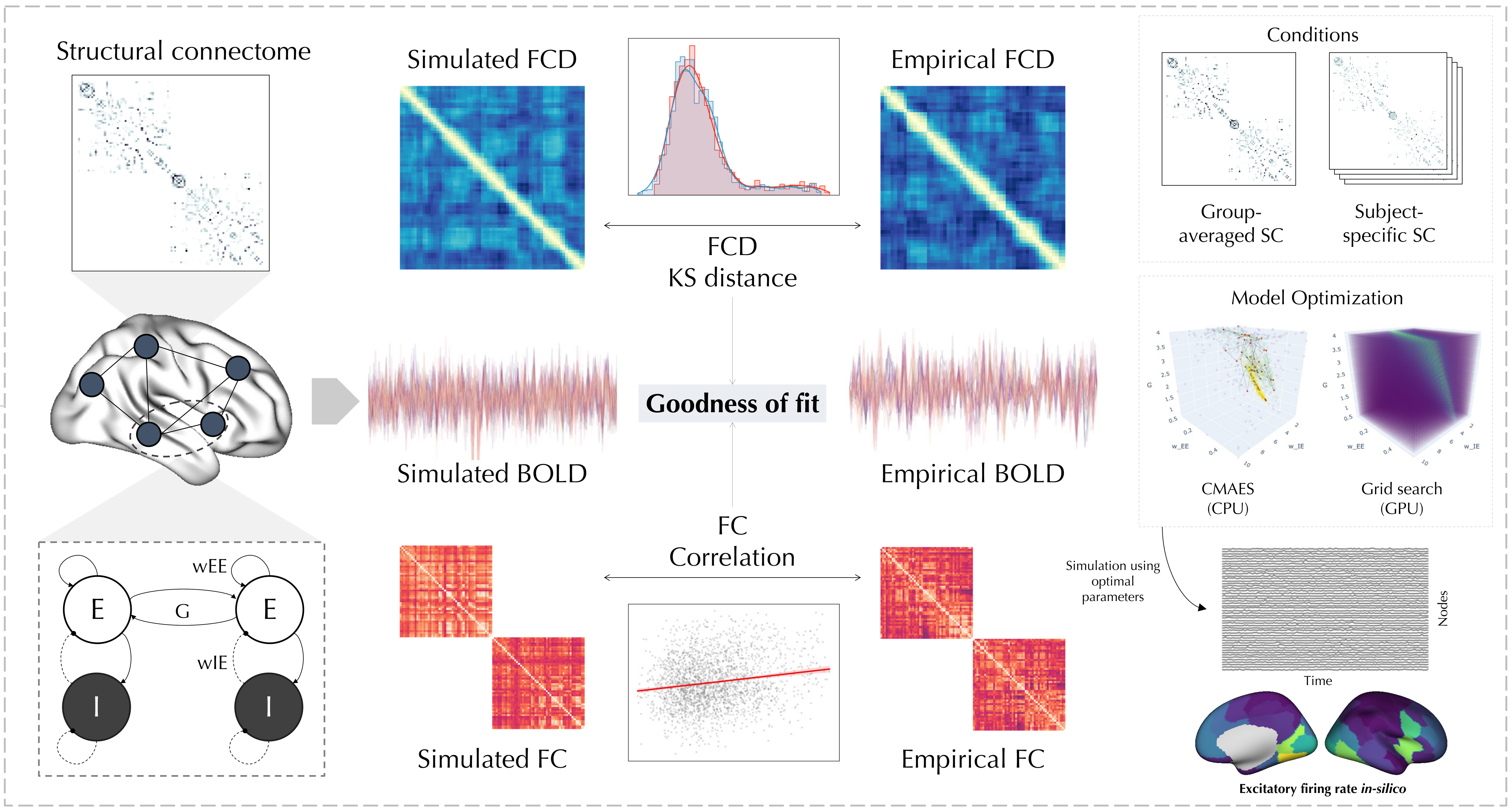
Subjects
- Philadelphia Neurodevelopmental Cohort
- N = 627 (364 Female, 263 Male)
- Age 10-19 (15.2 ± 2.4)

Image processing
- T1w: FreeSurfer
- rs-fMRI: fmriprep, nilearn
- DWI: micapipe

Whole-brain model simulation-optimization

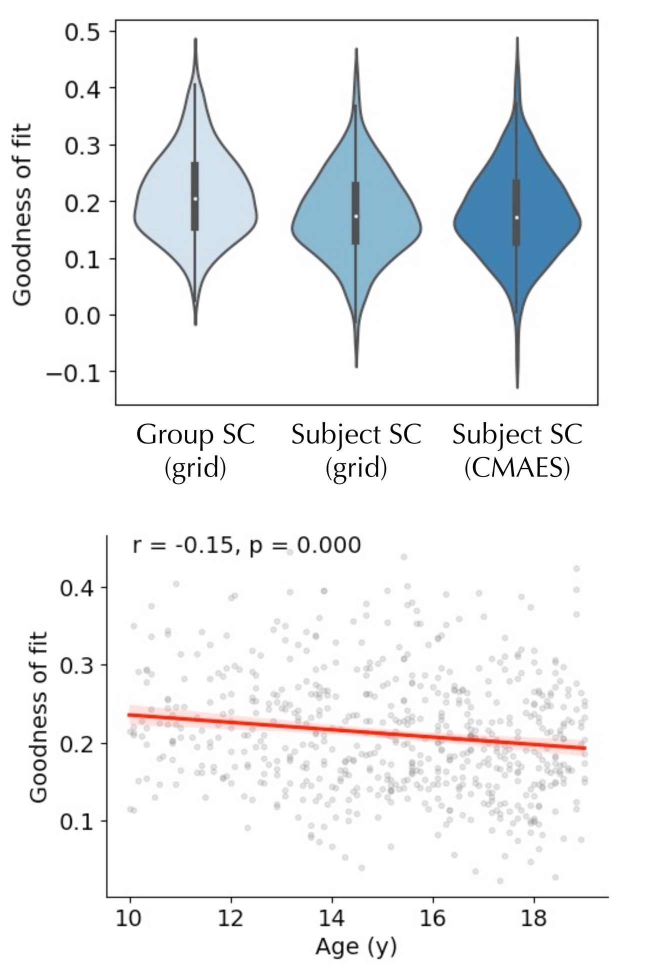
Age variation of estimated E-I ratio



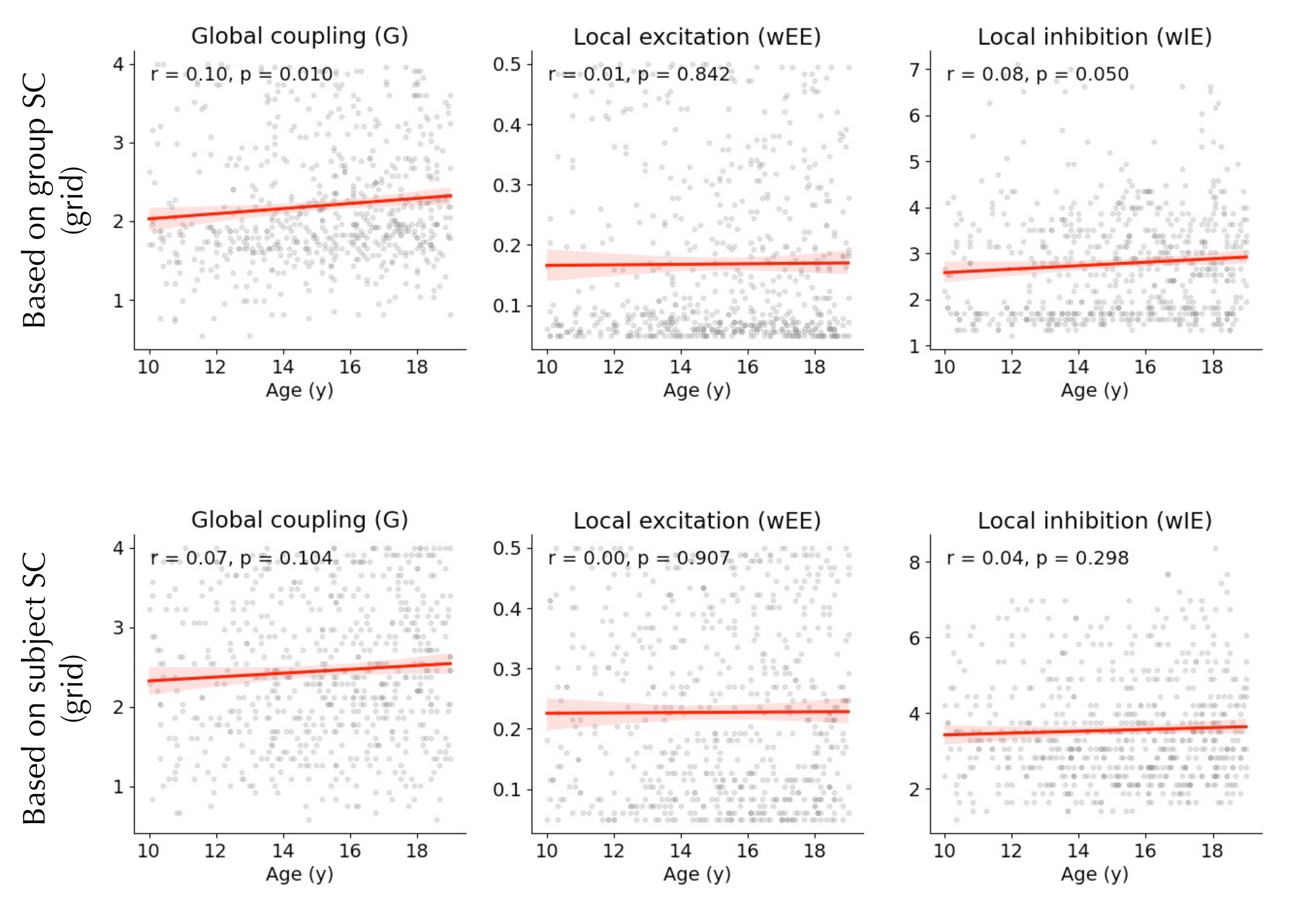


Results

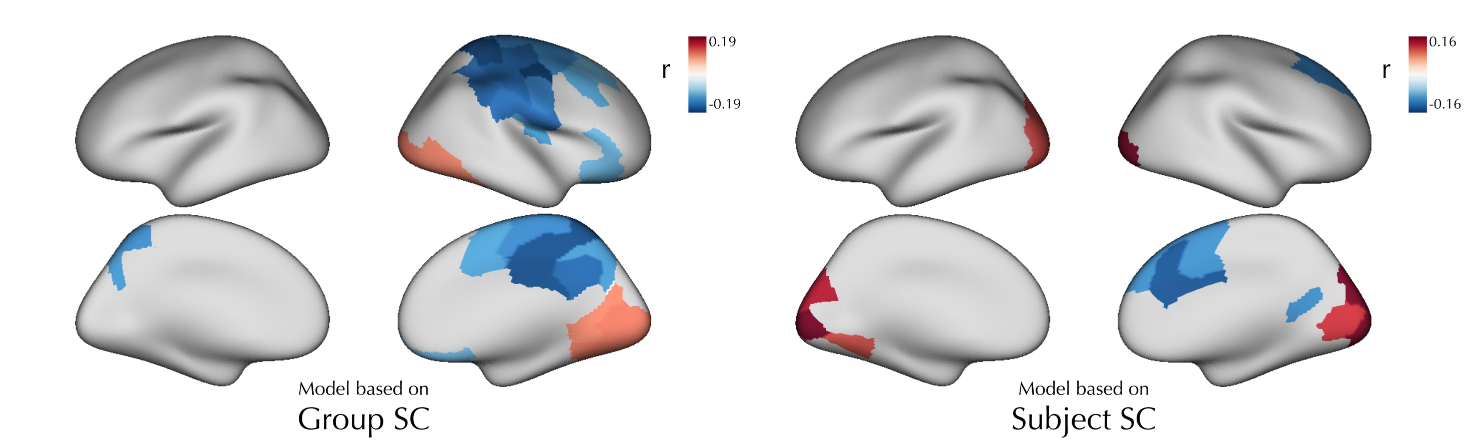
Goodness of fit was higher using group SC and decreased with age



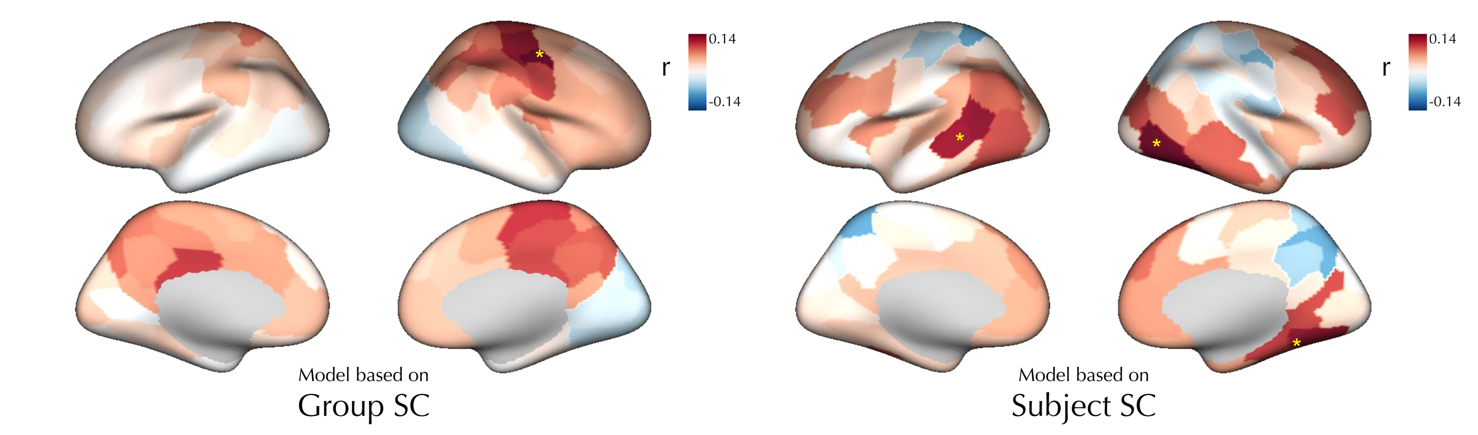
Global coupling increased during adolescence using group SC but showed no significant change using subject SC



Region-specific age-related changes of *in silico* excitatory firing rate



Association of *in silico* excitatory firing rate with grey-white matter contrast



Discussion

- We observed age-related increase of global coupling when group SC was used. However, given the interdependency of model parameters, age-related variation of parameters cannot be interpreted in isolation. Therefore, here we focused on *in silico* activity of regions as an aggregate function of interdependent parameters.
- The *in silico* excitatory firing rate, as a marker of E-I ratio, shows region-specific changes with age during adolescence. We observed decreased E-I ratio in frontal and parietal regions while it increased in occipital regions. This was in line with previous studies indicating decreased E-I ratio predominantly in association regions.[2,8]
- Intracortical myelination, as estimated by grey-white matter contrast, was significantly correlated with *in silico* excitatory firing rate in certain regions. Specifically, increased myelination was correlated with decreased E-I ratio, in line with previous research on the effects of myelination on inhibitory activity and maturation.[9]
- Future work is needed to
  - Investigate age-related changes of cortical microcircuitry in a longitudinal developmental dataset and assess correspondence to cross-sectional age association
  - Use higher-dimensional models which allow regional variation of model parameters
  - Estimate cortical microcircuit parameters by fitting the model to M/EEG data with higher temporal resolution

References
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