Adolescent maturation of cortical excitation-inhibition balance based on individualized biophysical network modeling

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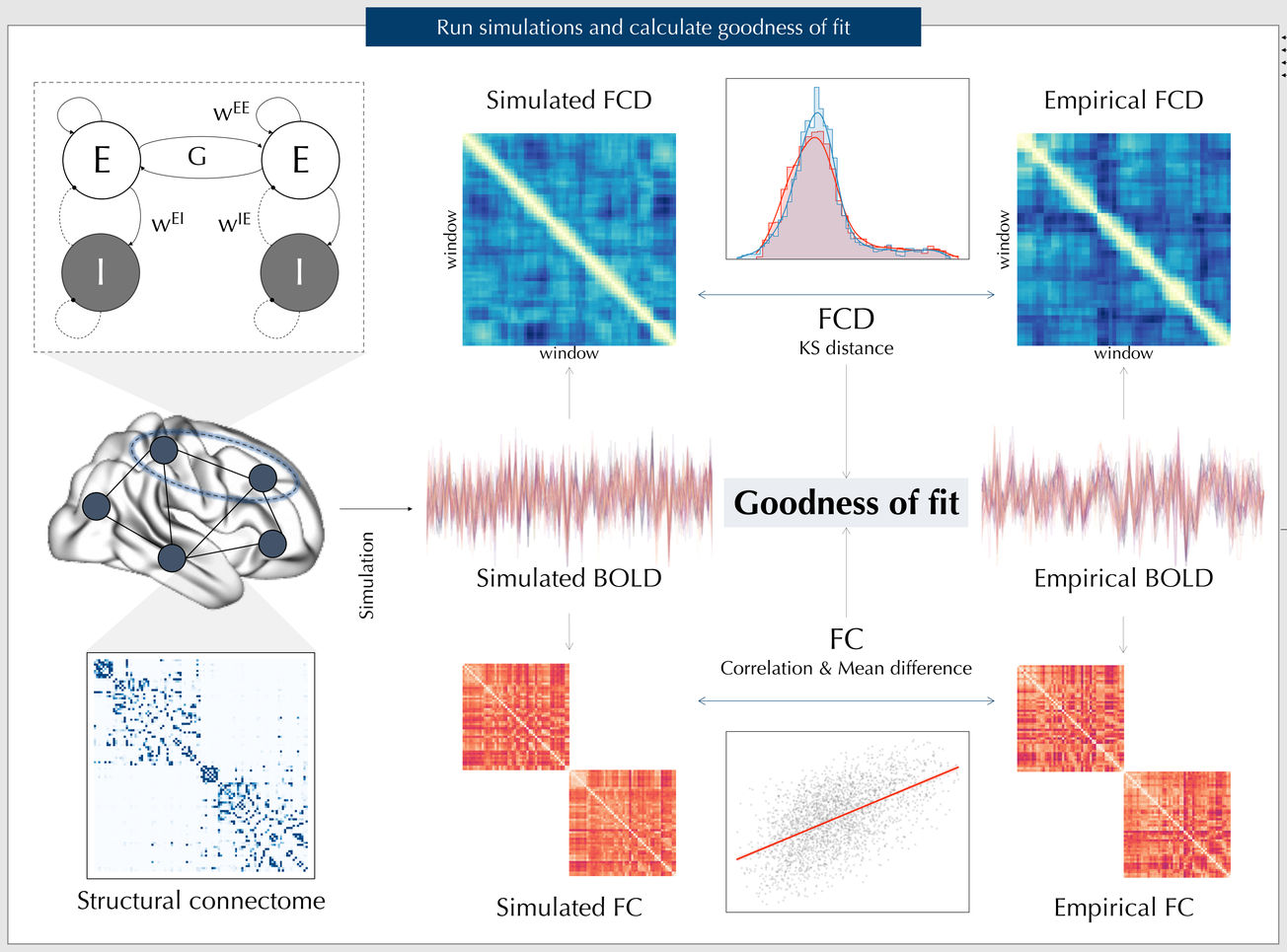
Introduction

- Excitation-inhibtion (E-I) balance is essential for central aspects of cortical functioning, such as the dynamic stability of activity and efficient coding of the information[1].
- Adolescence involves substantial macro- and microscale changes in the brain, including maturation of the E-I balance[2-3].
- Currently available evidence on the in vivo maturation of the E-I balance in humans is limited, as the invasive methods used in animal studies are not feasible in humans.
- Biophysical network modeling (BNM) of the brain is a promising technique that can bridge different scales of investigation at a whole-cortical level, and provides a tool to derive mechanistic inferences about the E-I balance based on the observed (empirical) in vivo imaging data at the macroscale[4-5].
- Recently, this approach was applied to group-averaged cross-sectional data of 29 age groups of adolescents and revealed widespread relative decrease of inhibition across the cortex, most prominently in the sensorimotor areas[6].
- However, an individualized *in vivo* estimation of E-I balance is needed for more precise characterization of E-I maturation based on subject-specific simulations, and enables assessing longitudinal changes.

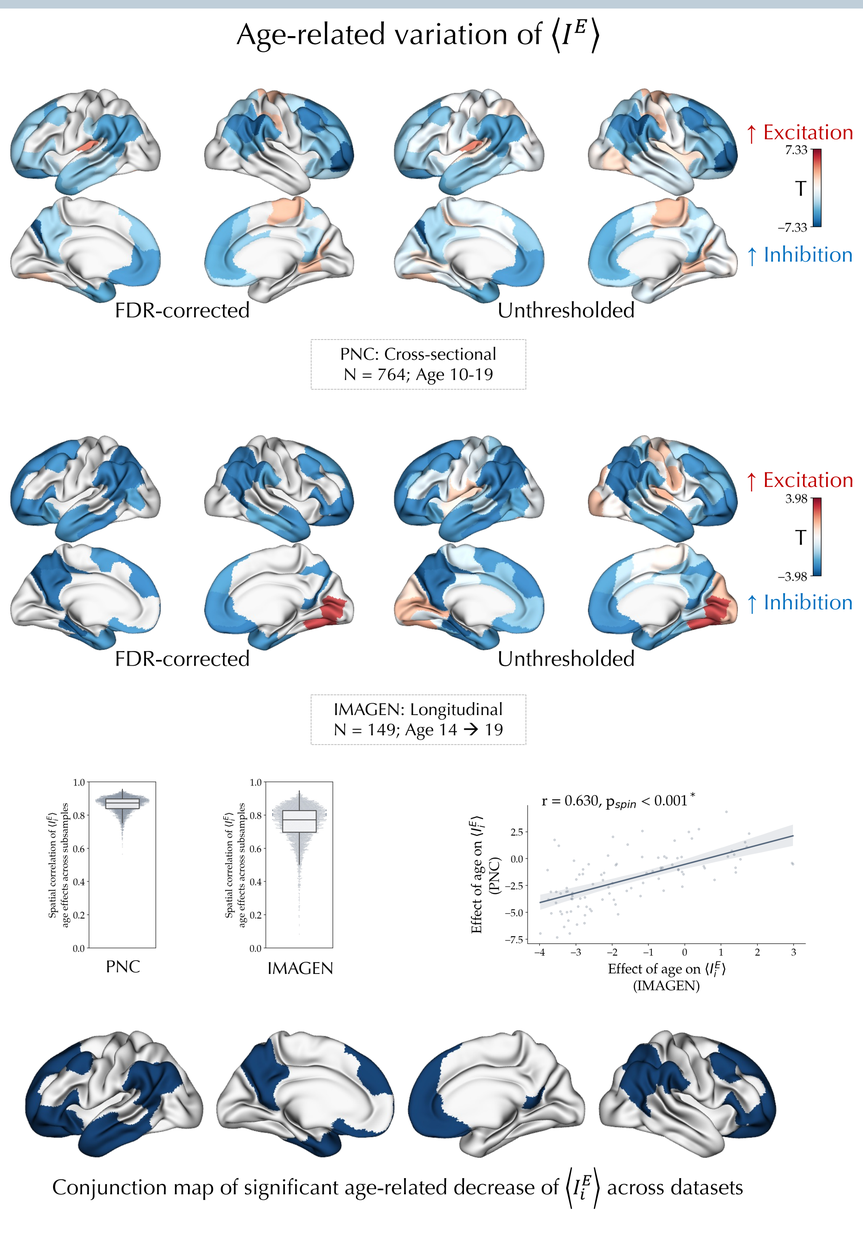
AIM

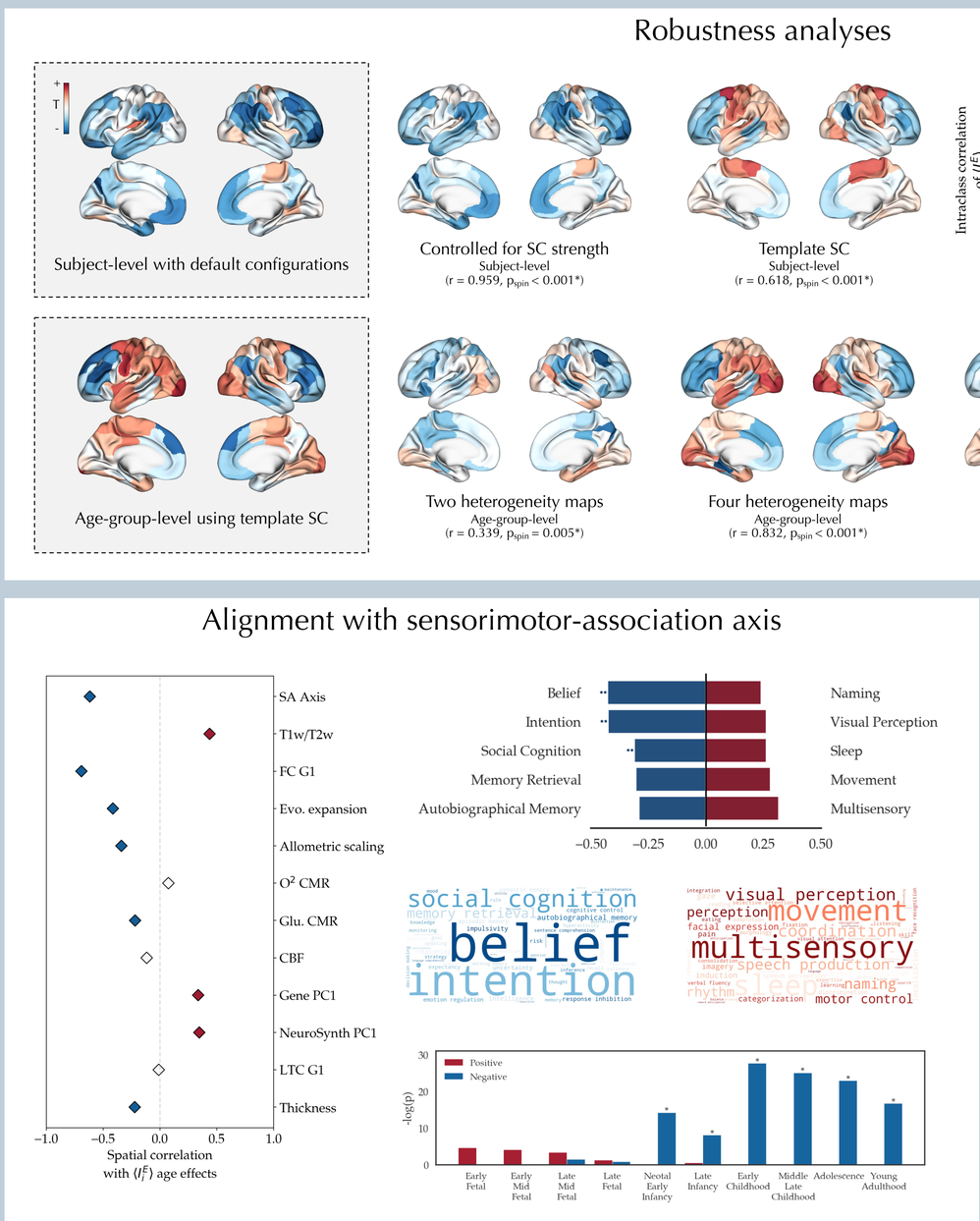
How does excitation-inhibition balance mature during human adolescence at an individual level, cross-sectionally and longitudinally?

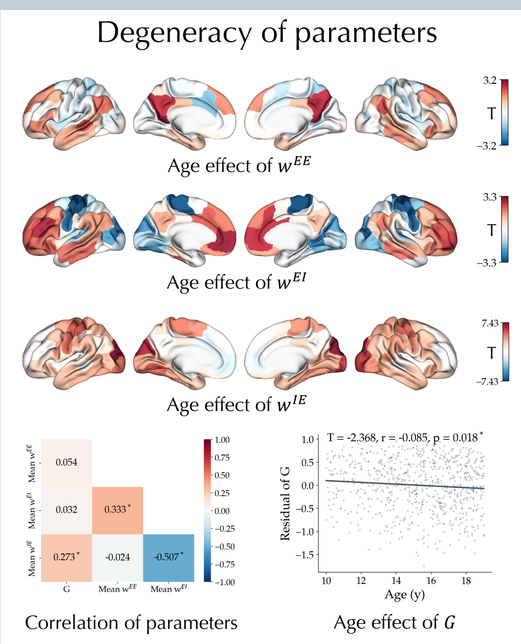
Methods



Results







Take Home

Cross-sectional and longitudinal data showed reliable and robust patterns of E-I balance maturation with:
- Shift towards ↑ inhibition / ↓ excitation in association areas
- Lack of change or shift towards ↓ inhibition / ↑ excitation in sensorimotor areas

The spatial pattern of differential E-I balance maturation across cortical areas co-aligns with the proposed sensorimotor-association axis of neurodevelopment, similar to several other cortical features[2].

There are important methodological considerations with using BNMs for the estimation of E-I balance. For example, inter-dependency of model parameters and the difficulty of interpreting their concurrent changes make them unsuitable for this purpose.

References:
1. Isaacson JS, Scanziani M. How Inhibition Shapes Cortical Activity. Neuron. 2011 Oct 20;72(2):231–43. **2.** Sydnor VJ, Larsen B, Bassett DS, Alexander-Bloch A, Fair DA, Liston C, et al. Neurodevelopment of the association cortices: Patterns, mechanisms, and implications for psychopathology. Neuron. 2021 Jul 15; **3.** Caballero A, Orozco A, Tseng KY. Developmental regulation of excitatory-inhibitory synaptic balance in the prefrontal cortex during adolescence. Semin Cell Dev Biol. 2021 Oct;118:60–3. **4.** Deco G, Kringelbach ML. Great Expectations: Using Whole-Brain Computational Connectomics for Understanding Neuropsychiatric Disorders. Neuron. 2014 Dec 3;84(5):892–905. **5.** Zhang S, Larsen B, Sydnor VJ, Zeng T, An L, Yan X, et al. In vivo whole-cortex marker of excitation-inhibition ratio indexes cortical maturation and cognitive ability in youth. Proceedings of the National Academy of Sciences. 2024 Jun 4;121(23):e2318641121.

Preprint

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