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# Whole-brain dynamical modeling of the adolescent developing brain

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Regulation of cortical microcircuits is crucial for optimal neural processing. Adolescence involves substantial macro- and microscale changes in the brain, including maturation of cortical microcircuits. Evidence from animal studies suggests a calibration of cortical microcircuits and excitation-to-inhibition (E-I) ratio during adolescence. However, in-vivo measurement of cortical microcircuits in the human developing brain is challenging, and therefore the supporting in-vivo evidence on maturation of E-I ratio in humans is limited. Whole-brain dynamical modeling is a promising approach that enables mechanistic inferences about hidden brain features, such as estimated properties of cortical microcircuits and E-I ratio. Here, we used whole-brain dynamical modeling to study age-related changes of whole-brain model parameters during adolescence.

We simulated cortical activity based on a mean-field model of excitatory and inhibitory neuronal ensembles in regions connected based on subject-specific or group-averaged structural connectomes. The fit of simulations to empirical resting-state functional images of each subject was evaluated based on comparison of simulated and empirical functional connectivity as well as functional connectivity dynamics matrices. We identified optimal model parameters for each subject using covariance matrix adaptation evolution strategy as well as GPU-accelerated grid search of the whole parameter space. Based on the simulations performed with the optimal parameters, we calculated the regional E-I ratios in the simulation as their time-averaged simulated excitatory firing rates. We observed region-specific changes of E-I ratio with age, which was decreased in parietal and frontal regions and increased in occipital regions. In addition, we observed association of grey-white matter contrast with E-I ratio in specifc regions. Following, we aim to increase regional specificity of the simulations by introducing heterogeneity in the model parameters based on biological maps of receptors as well as myelo- and cytoarchitecture.

Overall, we present a whole-brain modeling approach to estimate E-I ratio in developing adolescents which revealed region-specific changes of E-I ratio with age and its links to cortical microstructure.

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