Exploring the link between cellular mechanisms and cortical folding in the developing human brain

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Abstract

Brain development is a complex process that involves a precisely orchestrated sequence of genetic, biochemical, and physical events. At the cellular scale, different types of progenitor cells divide to eventually produce neurons that then migrate towards the brain surface to form the cortex. At the organ scale, physical forces play a central role in translating these cellular mechanisms into the complex surface morphology of the human brain. The folding pattern is not only the prerequisite for higher cognitive functions, but also a classical hallmark of diseases such as epilepsy. In this context, computational models are a valuable tool to understand the link between cellular brain development and cortical folding to eventually advance diagnosis and treatment strategies for cortical malformation associated with neurological disorders. Here, we present a computational model that couples advection-diffusion equations representing the behavior of different cell types in the developing brain with the theory of finite growth to describe cortex expansion and cortical folding at the macroscopic scale. The model allows us to explore the link between cellular division and migration at the cell scale and (ab)normal folding patterns at the tissue or organ scale. We calibrate our model based on histological sections of the human fetal brain and prove its validity through comparisons with magnetic resonance images. The presented framework can not only improve our understanding of human brain development but could eventually help diagnose and treat neurological disorders arising from disruptions in cellular development and associated malformations of cortical development.

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