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Exploring the role of different progenitor cell types during human brain development through a physics-based multifield model.

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The cognitive ability of the human brain closely correlates with its complex structure. Cortical folds not only increase the outer surface area but also double the number of cortical neurons. For decades, neuroscientists have studied the evolution of the cortex at a cellular level and have investigated the source of the cortical neurons. However, it remains unknown, how cortical folding relates to these cellular processes. Previous studies have emphasized the role of mechanical forces for the macroscopic process of brain folding. These forces may help to understand the underlying mechanisms of normal and abnormal cortical folding. On the cellular level, the proliferation process determines the number of brain cells. This process starts around the fourth gestational week (GW) with the symmetric division of progenitor cells, i.e., radial glial cells (RGCs). Around GW 5, the RGCs switch to asymmetric division and produce intermediate progenitor cells (IPCs) and neurons. In the gyrencephalic species and around GW 11, RGCs switch to generate a new type of progenitor cells that is called outer radial glial cells (ORGCs). ORGCs also divide asymmetrically later to generate IPCs and neurons, which is the central unit of the nervous system. The different progenitor cell types distribute in two distinct zones in the developing brain, where the RGCs occupy the ventricular zone while the ORGCs occupy the outer subventricular zone [1]. In this work, we establish a multifield computational model that links these cellular processes with cortical folding to assess how both RGCs and ORGCs affect the shape of the human brain. The model couples an advection-diffusion model with the theory of finite growth [2]. The advection-diffusion equation is formulated in such a way to mimic the proliferation process in both regions ventricular and outer subventricular zones. The cell density is introduced as a second field, controlling the anisotropic cortical growth. Our work shows the important role of ORGCs in the outer subventricular zone for the forming of complex convolutions in the gyrencephalic species. Increasing the division rate of ORGCs leads to a doubling in the number of cortical neurons in a relatively shorter time. Furthermore, secondary instabilities and period-doubling patterns are enhanced in the case of including the effect of the ORGCs. The presented framework can not only improve our understanding of cortical folding but could eventually help diagnose and treat neuronal disorders arising from disruptions in cellular development.

REFERENCES

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