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The Mechanical Mechanism of Cortical Folding on 3D Cerebral Organoids

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Abstract: An expansion of the cerebral neocortex is thought to be the foundation for the unique intellectual abilities of humans. The cortical folding has been implicated in neurodevelopmental disorders and yet its origins remain unknown. *In vitro* culture of 3D cerebral organoids from human pluripotent stem cells has been used to study the fundamental mechanisms of mammalian neurodevelopment and characteristics of human brain development. Here, we explores the mechanism of boundary limitation on the formation of gyri and sulci through the self-organization of human brain organoids. The structure of cerebral organoids was analyzed by morphology observation, pathology and immunofluorescence. The different hardness of matrigel and topological structure were mechanically loaded the cerebral organoids, and then the cortical growth, fold index and neuron distribution were analyzed. The parameters of microfluidic cultured cerebral organoids were investigated by parameter optimization, and the effects of pore volume, mechanical strength and surface roughness on cortical layer growth and sulcus formation were observed. The characteristic differentially expressed gene clusters were identified by transcriptome analysis for screen molecular markers for the formation of gyri and sulci combined with human sulcular gyrus formation and clinical features. Our study for the first time explored the mechanism of cortical folding at the biomechanical level, and provides new insights into the mechanisms regulating the structure and organization of the human cortex.

Keywords: Cerebral organoids; cortical folding; topological structure; microfluidic

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