How does the human brain develop to the right size and shape? The role of the extracellular matrix.

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Understanding how our own brains develop is a vital step in understanding how they perform the many higher cognitive functions that make us human, such as our memory, speech and advanced learning. Although these are clearly important functions, we still understand very little about how the neocortex controls them. Evidence from patients with neurodevelopmental disorders suggests that this relies on the correct development of the neocortex, as defects in the size, shape or organisation of the neocortex can lead to cognitive impairment. In spite of this importance, how these processes are regulated during development remains elusive. This is especially true for certain aspects, such as the formation of the folds on the surface of the neocortex. A better understanding of these processes will broaden our perspective of and offer new insights into the neurodevelopmental disorders that affect neocortex function.

Our research focuses on how the human neocortex develops with the correct size, shape and organisation, and the role of the extracellular matrix in these processes. Extracellular matrix is highly abundant in the developing human neocortex, but its function in neocortex development is not yet fully understood. To address this we use an interdisciplinary approach to look at the cellular and mechanical mechanisms by which the extracellular matrix drives the development of the human neocortex, including the formation of the folds present on the surface of the neocortex, and how dysregulation of these functions can lead to neurodevelopmental disorders. We have shown that manipulating the extracellular matrix can both induce and reverse cortical folding in human fetal neocortex slice cultures, providing a novel model in which to study the mechanisms that drive folding in the human brain.