Changes in Cortical Composition during Gyrification in the Developing Brain

Sarah Doherty[1], Kara E. Garcia[1,2]

[1]Indiana University School of Medicine, Evansville, IN; [2]Department of Radiology and Imaging Sciences, Indianapolis, IN

Background and Hypothesis

Abnormal brain folding has been implicated in neurodivergent conditions such as schizophrenia and autism, yet the mechanical and biological processes responsible for this process are not well understood. One current hypothesis is that cortex growth outpaces growth of the underlying white matter to drive mechanical buckling. However, mechanical stresses, such as those resulting from buckling, can also influence cellular behavior. In this study, we hypothesized that mechanical stresses from cortical folding influence processes of biological growth within the cortex, such as dendrite arborization within the neuropil and neuronal differentiation.

Methods

To quantify change in cell body size and neuropil over the period of cortical folding, sections of the developing ferret brain (postnatal days 20, 26, 32, and 38) were stained with FluoroNissl dye, imaged with confocal microscopy, and analyzed using Fiji software. Change in percent neuropil, cell area, cell density, and overall length were quantified at upper, middle, and lower thirds of the cortex to assess the influence of bending stresses within gyri and sulci during development.

Results

Preliminary analysis revealed a substantial increase in neuropil over time in the upper layers of the cortex. However, gyral regions expected to experience mechanical tension and increased expansion did not exhibit the hypothesized differences in neuropil or cell size. Though there was an overall increase in neuropil volume fraction and cell body size over time, throughout all layers of the cortex, these factors only accounted for roughly 2/3 of the physical growth quantified throughout these cortical layers.

Potential Impact

Findings indicate that neuropil and cell body expansion are insufficient to fully explain the growth observed during cortical folding. These results highlight a potential role for alternative cellular processes, such as the migration of other cell types into the cortex, to induce cortical growth and folding in gyrencephalic species.