The Influence of Surgical Correction on White Matter Microstructural Integrity in Rabbits with Familial Coronal Suture Craniosynostosis

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Introduction

Craniosynostosis is the premature fusion of one or more cranial sutures during the vulnerable period of rapid brain growth and development. The overall incidence of craniosynostosis is estimated to be 1 out of 2500 live births. Craniosynostosis causes an abnormal head shape, and may result in tissue ischemia and white matter injury, if brain growth is restricted, even in the absence of overt clinical symptoms and signs of elevated intracranial pressure (ICP)[1]. In order to mitigate the risk of brain injury, corrective surgery is often performed shortly after diagnosis.

The aim of this study was to analyze white matter microarchitectural changes seen with craniosynostosis, both before and after surgical correction.

Material and Methods

Rabbits were diagnosed at 10 days, from a colony of rabbits with naturally occurring craniosynostosis, and were assigned to one of nine groups, wild type (WT) at 12, 25 or 42 days of age, complete fusion of the coronal suture (BC) at 12, 25 or 42 days, and those that have undergone surgical correction (BC-SU) at 12, 25 or 42 days. Corrective surgery was performed immediately following diagnosis.

MR studies were performed on a 4.7 Tesla, 40 cm bore Bruker Biospec system. DTI data for the fixed brains was obtained using a 3D spin echo sequence with the following parameters: TR = 1200 ms, TE = 32 ms, 256 x 192 x 192 matrix, FOV = 51.2 x 51.2 x 51.2, 6 diffusion directions, Δ = 16 ms, δ = 8 ms, and a b-value of 2000 s/mm^2.

We used DSI studio (http://dsi-studio.labsolver.org/) to analyze the DTI data. Regions within each hemisphere (corpus callosum, cinglum, internal capsule, fimbria, anterior commissure, guided by assignments from a rabbit brain atlas[2]) were analyzed for FA, ADC, axial and radial diffusivity.

DTI parameters were compared between groups at each age and significant differences were assessed using one-way ANOVA. All differences were considered significant at $p < 0.05$. Individual classification was performed using linear support vector machine classifiers with fixed c = 1 using the LIBSVM package for MATLAB (http://www.csie.ntu.edu.tw/~cjlin/libsvm/). Accuracy was determined by 5-fold cross-validation, and significance was determined by permutation testing with T = 200 tests.

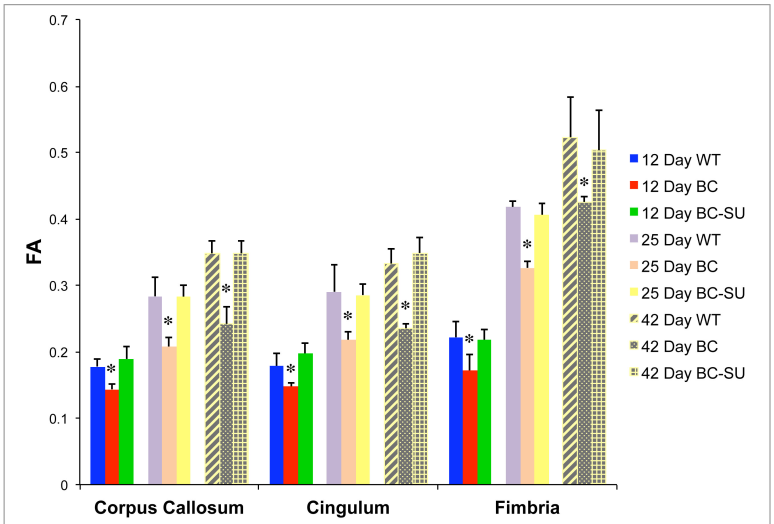

Figure 1: FA of white matter tracts including the cingulum, corpus callosum and fimbria for 12 day old (solid colors), 25 day old (pastel colors) and 42 day old (pattern fill) rabbits. *p<0.05.

Results and Discussion

Figure 1 shows the natural progression of an overall increase in FA with age. Significant differences were found in the corpus callosum, cingulum and fimbriae of BC animals which appears to resolve following suturectomy surgery.

Previous studies have shown that there is a significant increase in intracranial pressure at 25 days in the BC animals as well as a significant increase in pial artery blood flow at the same age, both of which are back to WT levels by 42 days of age[3,4]. This study shows that without surgical correction white matter injury persists past 25 days of age as seen by the decrease in FA and the increase in radial diffusivity (data not shown). In particular, those tracts that are close to the fused coronal suture such as the corpus callosum, cingulum and fimbria.

Individual classification is possible on the basis of anatomical differences alone, with more distinct differences between the WT, BC and BC + WT groups with increasing time after surgery. WT and BC-SU groups seem to be more similar to each other and more distinct from BC.

In conclusion corrective surgery leads to improvement of the neurophysiology of white matter tracts in terms of FA, radial diffusivity and ADC.

References

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