Biomechanics of craniofacial development in mice

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Introduction

Our understanding of the biomechanical changes that occur during normal mouse skull growth is still limited. The aim of this study was a comprehensive characterization of normal mouse skull growth in terms of its morphology, intracranial pressure, bone and cranial joint (suture) mechanical properties, and the biomechanical strain experienced by the cranial joints during development.

Materials and Methods

A series of *in vivo*, *in vitro* and *in silico* studies was carried out on wild type mice (*Mus musculus*, C57BL) at postnatal (P) day 3–70, with the main focus being up to P20 when calvarial development is completed. First, intracranial pressure was measured in a total of 73 mice (over 5 age ranges) using a differential pressure sensor connected to a custom program written in LabVIEW. Second, the mechanical properties of calvarial bone (frontal and parietal) and suture (posterior frontal, coronal and sagittal) were characterized in a total of 11 mice (over 3 age ranges). This was carried out using a Berkovich diamond tip mounted on a CSM nanoindenter. Third, finite element (FE) analysis was used to develop a FE model of calvarial growth from P3–10. The model was used to estimate the mechanical strain experienced by the cranial sutures during development, and to develop a bone formation algorithm at the cranial joints.

Results

Intracranial pressure was 1.33±0.87 mmHg at P3, increasing to 1.92±0.78 mmHg at P10, 3.60±1.08 mmHg at P20, 3.81±1.14 mmHg at P31 and 4.11± 0.83 mmHg at P70. The elastic modulus of the frontal and parietal bones gradually increased during development from 5.32±0.68 and 4.33±0.18 GPa at P10 to 7.14±0.79 and 6.30±0.47 GPa at P20, and then to 9.4 and 8.7 GPa at P70 respectively (indentation was carried out on one specimen at P70). The suture elastic modulus measurements at P10 lay within the range of 0.008–0.066 GPa with an average of 0.028 GPa with no statistically significant differences between the sutures examined. The FE models predicted the radial expansion of the skull from P3 to P10. The models demonstrated that the sutures experience hydrostatic strain in the range of 1.25–2.5% during early postnatal growth. The FE models could also predict the pattern of bone formation at the cranial sutures from P3–10.

Discussion

Taken together, these data suggest that expansion of the brain, intracranial volume (ICV), intracranial pressure (ICP), bone formation at the sutures, and bone mechanical properties are integrated. The changes occur synchronously until the brain reaches adult size at P20, whereupon ICV and ICP plateau, while bone properties increasingly stiffness the skull. This study provides a strong foundation for future studies on the biomechanics of both normal and abnormal craniofacial development in conditions such as craniosynostosis.

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