

## Phenotypic Integration of Neurocranium and Brain

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**ABSTRACT** Evolutionary history of Mammalia provides strong evidence that the morphology of skull and brain change jointly in evolution. Formation and development of brain and skull co-occur and are dependent upon a series of morphogenetic and patterning processes driven by genes and their regulatory programs. Our current concept of skull and brain as separate tissues results in distinct analyses of these tissues by most researchers. In this study, we use 3D computed tomography and magnetic resonance images of pediatric individuals diagnosed with premature closure of cranial sutures (craniosynostosis) to investigate phenotypic relationships between the brain and skull. It has been demonstrated previously that the skull and brain acquire characteristic dysmorphologies in isolated craniosynostosis, but relatively little is known of the developmental interactions that produce these anomalies. Our comparative analysis of phenotypic integration of brain and skull in premature closure of the sagittal and the right coronal sutures demonstrates that brain and skull are strongly integrated and that the significant differences in patterns of association do not occur local to the prematurely closed suture. We posit that the current focus on the suture as the basis for this condition may identify a proximate, but not the ultimate cause for these conditions. Given that premature suture closure reduces the number of cranial bones, and that a persistent loss of skull bones is demonstrated over the approximately 150 million years of synapsid evolution, craniosynostosis may serve as an informative model for evolution of the mammalian skull. *J. Exp. Zool. (Mol. Dev. Evol.) 306B:360-378, 2006.* © 2006 Wiley-Liss, Inc.