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The Epigenetic Funnel and the Cranial Base: how cranial bone growth helps integrate interactions between the face and the brain to constrain overall skull shape

Daniel E. Lieberman, Benedikt Hallgrimsson, W. Liu

Abstract:
Understanding the developmental and genetic bases for evolutionarily important variations in complex phenotypes such as the skull is a challenge because of the complexity of the factors involved. We hypothesize that even in this complex system, the expression of phenotypic variation is structured by interactions among a limited set developmental processes. One such process may be cranial base flexion. It has long been hypothesized that the growth of the brain and the face have opposite influences on the midline angle of the intervening cranial base so that constraints on cranial base flexion and elongation can modulate many aspects of the overall skull shape. This hypothesis has been difficult to test using comparative or longitudinal studies in which other covarying factors also influence cranial shape. Here we experimentally tested several hypotheses about interactions of the cranial base using mouse mutants from the same genetic background but with specific, independent developmental perturbations that affect brain size. Geometric morphometric comparisons of these mutants, their wildtypes, and their F2 crosses show that increased brain size and decreased face size both act to flex the cranial base, but with comparable overall effects on skull shape. The results indicate that vastly different mutations can have similar effects on overall cranial shape because key processes such as cranial base flexion funnel their effects in similar ways.