Relationship of brain and skull more than just packaging

April 13 2006

People usually think of the skull as packaging for the brain and researchers usually investigate them separately, but a team of researchers now thinks that developmentally and evolutionarily that the two are incontrovertibly linked.

The researchers, including biological anthropologists, physicians and a computer scientist, looked at the CT scans and MRIs of infants with particular types of craniosynostosis – a condition where one or more of the sutures -- fibrous bands that connect the bones -- of the baby's skull close too early and deform the skull and brain.

"We are interested in understanding craniosynostosis," says Dr. Joan T Richtsmeier, professor of biological anthropology at Penn State. "We would like to know why it happens, especially when it is not part of a syndrome, but when it occurs alone."

The researchers report in a recent early online publication of the Journal of Experimental Zoology: Molecular and Developmental Evolution: "Our study represents the first empirical evidence of phenotypic integration of brain and skull in 3D, although indirect evidence has been accumulating for years."

The researchers are also interested in understanding how the skull and brain change jointly through evolution. Vertebrate evolution shows a trend toward fewer skull and jaw bones and loss of some intercranial joints. While craniosynostosis is considered a pathology in modern humans, it shares with evolutionary history a reduction in cranial elements and coincident changes in the shape of the skull and brain. The researchers believe that studying craniosynostosis could shed light on the joint evolution of the brain and skull.

The two types of craniosynostosis the researchers studied were early closure of the sagittal suture – the suture that runs down the center of the skull from front to back – and unilateral coronal craniosynostosis, early closure of one side of the suture that runs across the top of the head from ear to ear.

Children with craniosynostosis almost universally have surgery to reopen the sutures and allow normal growth of the boney plates of the skull. Premature closure of sutures causes the skull and the brain beneath to deform. However, the researchers had few CT and MRI images to work with because even if both CT and MRI are acquired for a patient, they are rarely obtained the same day.

"We are extremely conservative in requiring that the two types of images be taken within a 24-hour period," says Richtsmeier. "Early brain and skull growth are so rapid that if the images were taken weeks apart, they would not be an exact fit." T scans record a three-dimensional image of the skull while MRIs provide a three-dimensional brain image.

The researchers caution that the number of infants studied in this way is small at this point, but they found that the brain and skull are strongly integrated.

"We also expected to see higher correlation among those brain and skull measures that were close to each other anatomically, but we did not," says Richtsmeier. "We found that the stronger statistical relationships existed between neural structures located near the top of the brain and boney features at the base of the skull."

To look at the correlations between the skull and the brain, the researchers first had to find locations that could be accurately found again and again. Locating reliable markers was easier on the rigid skull than on the brain. Co-author of the paper, Kristina Aldridge, former postdoctoral researcher at Penn State and now at Washington University, looked at the reproducibility of standard anatomical features on the skull and brain.

"We found that the brain landmarks people often use were highly variable and had the biggest errors in reproducibility," says Richtsmeier. "We eventually chose brain locations that were easier to identify reliably such as the most posterior point or the centroid of small neural structures."

The researchers did not compare one brain to another or one skull to another, nor did they use the data in a coordinate system. Instead, they measured the correlations between measure taken on brain and those taken on skull. Overall, they found that the correlations between brain and skull were very high.

Because normal infants almost never have MRIs and CT scans done at the same time, there are no controls available with which to compare the correlation of skull with brain measurements. Because even infants with craniosynostosis usually do not have both CT scans and MRIs done on the same day, the available study population is small, however, the researchers plan to increase the number of infants studied.

Richtsmeier notes that, from a medical point of view, the researchers want to find genetic mechanism underlying craniosynostosis so that the problem can be prevented or cured. From an evolutionary point of view, researchers focus on the developmental basis for the physical change observed in the fossil record and propose hypotheses about the evolution of the genetic traits responsible for these changes. The researchers propose that the genetic basis of the complex regulatory sequences that cause the changes documented in craniosynostosis infants may also account for the changes observed in the evolution of the vertebrate skull.

The researchers include Richtsmeier; Aldridge; Valerie B. DeLeon and Jayesh Panchal, The Johns Hopkins School of Medicine; Alex A. Kane, Johns Hopkins and Washington University School of Medicine; Jeffrey L. Marsh, St. John's Mercy Medical Center, St. Louis; Peng Yan, computer scientist, Penn State anthropology department; and Theodore M. Cole III, University of Missouri – Kansas City.

Source: Penn State