Key Points

1. Researchers studying the evolutionary development of the neck and shoulder may have identified the origin of Chiari malformations
2. Used fate mapping to study what embryo cells eventually become the bones and muscles in the neck and shoulder
3. Found that cells from both the neural crest and mesoderm compose specific regions of bone and muscle in this area
4. Since neural crest cells can develop into bone, muscle, or connective tissue, they are prone to malformation if they develop into the wrong thing
5. Authors hypothesize that Chiari may be due to a bone in the skull base, the clivus, not developing properly
6. The muscles of the larynx and pharynx attach to the clivus, which would help explain why Chiari people have trouble swallowing

Definitions

clivus - one of the bones that make up the skull base

connective tissue - body parts, like cartilage, which provide structure to the body and connect other parts

fate mapping - a technique which is used to track where an individual cell moves and what it becomes during embryological development

germ layers - three initial layers of cells which form in an embryo: ectoderm, mesoderm, endoderm

Klippel-Feil Syndrome - congenital condition of the spine resulting in a short neck, limited mobility, and sometimes neurological problems

mesoderm - middle germ cell layer, from which the musculo-skeletal and vascular systems

Tracing The Origins Of Chiari

November 15, 2005 -- Scientists studying the evolutionary history of the neck and shoulder region in vertebrates have come across what may be significant finding related to Chiari. In the July 21st issue of the prestigious journal Nature, an international team led by Toshiyuki Matsuoka from the Wolfson Institute For Biomedical Research reported on their efforts to track the cellular development of the neck and shoulder in genetically engineered mice.

The neck/shoulder region in animals with backbones (including people) has undergone a complex evolutionary development, which is not yet completely understood. In order to study this process in more detail, the researchers used a technique known as fate mapping. In fate mapping, the movement and development of specific cells can be tracked from their embryonic origins. In this case, the scientists used genetically engineered mice to trace the origins of the bones and muscles in the neck and shoulder.

To understand what they found when they did this, it is necessary to understand some basics of embryology. When an embryo first develops, three distinct cell layers form, the ectoderm, mesoderm, and endoderm. In general, cells in the mesoderm develop into muscle, bone, blood vessels, and connective tissue. The ectoderm, or outer layer, forms into the skin and nerve tissues. During this process, the neural tube forms - which is actually a tube - and eventually turns into the brain, spinal cord, and nerves of the body. Another structure that develops from the ectoderm is the neural crest. The neural crest is collection of cells which essentially form a ridge at the top of the neural tube and eventually breaks away from the tube itself. The final inner layer of germs cells, the endoderm, turns into internal structures such as the digestive tract, lungs, etc.

Matsuoka's team found that rather than the neck and shoulder region being comprised solely of mesodermal cells (as was believed to be the case), the region developed as a specific mapping of a combination of neural crest cells and mesodermal cells. In other words, the neural crest developed into specific muscles and bones, and so did the mesoderm. While this finding has profound implications for people who study the evolution of animals, obviously by itself, it doesn't mean much for the average Chiari patient.

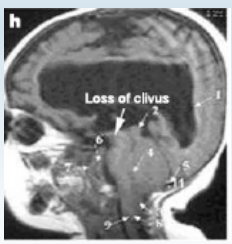
However, neural crest cells are known to be prone to errors as they develop. Because they need to travel, or migrate, across the body and can develop into several different types of tissue, they are prone to what is known as transcription errors. In fact, neural crest defects are well known to cause a variety of problems. With this in mind, the research team began to look for conditions which would involve only the neural crest developed regions they had identified.

They found several, including Klippel-Feil and Chiari. With Chiari, they postulate that the clivus - one of the bones in the skull base - forms as connective tissue instead of bone. Interestingly, the clivus is where the muscles of the larynx and pharynx attach, so this might explain the swallowing and voice problems associated with Chiari. With Klippel-Feil, they hypothesize that the opposite happens and that what should be connective tissue forms as bone, and thus limits mobility.

Unfortunately, the authors do not go into great detail regarding their specific theory on Chiari, but do state they will explain it further in a later publication. It is unclear, for example, whether what they propose can be easily verified on a number of Chiari patients, or even fits in with the existing data regarding a small posterior fossa.

If they are right however, it would provide another place to look for the genetic source of Chiari. Because Chiari patients on average have smaller posterior fossas, many researchers believe that Chiari is a defect of the mesoderm. If it involves the neural crest, or both the mesoderm and neural crest, maybe we are one step closer to really understanding the roots of the problem.

Figure 1
Possible Origin of Chiari Malformation



develop

neural crest - specific group of cells which arise from the ectoderm; neural crest cells migrate all over the body and develop into a variety of different types

pharynx - upper part of the throat

transcription factor - a protein which acts to regulate the function of a gene and influences how that gene is expressed

vertebrates - animals with backbones

cerebellar tonsils - portion of the cerebellum located at the bottom, so named because of their shape

Source

Matsuoka T, Ahlberg PE, Kessaris N, Iannarelli P, Dennehy U, Richardson WD, McMahon AP, Koentges G. Neural crest origins of the neck and shoulder. Nature. 2005 Jul 21;436(7049):347-55.

Note: Matsuoka found that the clivus, one of the bones of the skull base, develops from neural crest cells. He proposes that in Chiari, the clivus, instead of forming as bone, forms as connective tissue. Since this is where the muscles of the larynx and pharynx connect, it causes the swallowing problems common in Chiari.

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