

## A new pathogenetic explanation of human chiari malformations

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Chiari malformations are a heterogeneous group of congenital disorders that are defined by anatomic anomalies of the cerebellum, brainstem, and craniocervical junction, with downward displacement of the cerebellum, either alone or together with the lower medulla, into the spinal canal.<sup>1</sup> The major categories of symptoms of Chiari malformations are those related to obstructive hydrocephalus, abnormal eye movements, cerebellar deficits, and spinal myelomeningocele.<sup>1</sup> Patients with Chiari malformations are spared the latter, as they do not have neural tube defects such as a myelomeningocele.

The pathogenesis of congenital Chiari malformations remains the subject of debate. Multiple theories have been proposed, though none explains all the features. The molecular genetic theory postulates that Chiari malformations result from primary defects in the genetic programming of hindbrain segmentation and of growth of associated bone and cranial structures.<sup>2</sup> The hydrodynamic pulsion theory suggests that early progressive foetal hydrocephalus pushes down on the brainstem and cerebellum.<sup>3</sup> And the oligocerebrospinal fluid theory proposes that defective closure of the neural tube in early foetal development results in leakage of cerebrospinal fluid, and thus insufficient cerebrospinal volume to fully distend the embryonic ventricular system, which leads to a small posterior fossa and cerebral disorganization.<sup>4</sup>

The pathogenesis of Chiari malformations has always been the subject of debate. However, one of the interesting things is that we have never heard that any animals of Subphylum Vertebrata once suffered from Chiari malformation and there is indeed no literature reporting that. We cannot help wondering such disturbing problems: What are on earth the unique features of human that make us have frustration with Chiari malformations?

Let's shift our sights back to the abnormal anatomic

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features of Chiari malformation. In most cases, the posterior fossa is small, and neural elements are crowded and impacted at the foramen magnum.<sup>1</sup> There was a time when lots of scholars acknowledging the crowding theory which postulated that restricted growth of the posterior fossa causes compression of neural tissue, which is then squeezed through the foramen magnum like toothpaste through a tube.<sup>5</sup> In support of this theory, the posterior fossa is abnormally small and the torcula is displaced downward in patients with Chiari malformations.<sup>6</sup> This is a kind of naive materialism and simple and dialectical view on the pathological theory of Chiari malformation. Nevertheless, this point of view is yet the closest one to the essence of our hypothesis.

Scientists claim that walking on two legs was one of the keys to humans' development from ancient ape-like ancestors. Walking on two legs saved energy and allowed the arms to be used for activities like hunting, crafting simple tools and interacting with objects. Charles Darwin proposed long ago that having two limbs free to use tools constituted a key element of advanced intelligence. A study published in the July 2007 issue of Proceedings of the National Academy of Sciences found that the humans used 75 percent less energy walking upright than the chimps used walking on all fours. Human bodies have a number of adaptations to walking upright.<sup>7</sup> In vertebrates, the foramen magnum, literally meaning "big hole," is a hole in the occipital bone in the base of the skull, through which the medulla oblongata extends from the braincase. In most mammals, including apes, the foramen magnum is situated behind the skull, as the head extends forward from the body. In humans the foramen magnum is situated beneath the skull, as the head is ballanced atop an erect bipedal body.<sup>8</sup> In paleontology the foramen magnum is used to determine whether an animal was bipedal. Taung Child found in South Africa in 1920s had a small brain and many researchers thought the approximately three-million-year-old Taung was merely an ape. But her foramen magnum was positioned further forward under the skull than an ape's, indicating that Taung held its head erect and therefore likely walked upright.<sup>9</sup> Among the primates observed, humans exhibit the most anteriorly positioned foramina magna.<sup>8</sup>

As discussed above, we cannot help but link up foramen

magnum position with the anatomic basis of an increased risk of chiari malformation in humans. It is just this "foramen magnum position" underneath human skulls that give cerebellar tonsil and even medulla oblongata the chance to herniate downward out of the foramen magnum powered by gravity.

In addition, much has been said about braincase size increase during hominid evolution.<sup>10</sup> There is no doubt that the general trend is towards a considerable increase in cranial capacity. With statistics in hand, cranial capacity ranges from 282 to 454 cm<sup>3</sup> in adult chimpanzees, from 350 to 752 cm<sup>3</sup> in adult gorillas (Schultz, 1960, 1965), from 400 to 550 cm<sup>3</sup> in adult australopithecines, from 510 to 1300 cm<sup>3</sup> in adults of earliest Homo, and from 1100 to 2000 cm<sup>3</sup> in adults of modern Homo.<sup>11</sup> Accordingly, the relative weight of brain increases with the process of evolution. This further aggravates the risk of tonsillar hernia malformation through foramen magnum right below the skull.

In fact, there are important adaptations to walking upright and evolution. Overall, every part and aspect about human evolution is coordinated and not isolated. For instance, our foot is specialized as a weight-bearing platform, with an arch that acts as a shock absorber. Our spines have a characteristic double curve, which brings our head and torso into a vertical line above our feet. However, we are by no means perfectly adapted to our gorgeous evolution. In some incidental place and time, the developments of different organs or systems might not match each other. There may be some traits of individual organs, structures or anatomical features don't coordinate with the general one of human population. There is even "atavism" as a case of this mismatching.<sup>12</sup> If the increased brain size and posterior fossa volume

mismatches each other, anatomic anomalies of the cerebellum, brainstem, and craniocervical junction, with downward displacement of the cerebellum, either alone or together with the lower medulla, into the spinal canal will happen. The authors call it "evolutional mismatch" or "evolutional inconformity". With the addition of the brain through foramen magnum in the special position, chiari malformation could be regarded as a kind of disease, related to evolution.

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