Understanding the Abstract
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Understanding the abstract: **Hereditary disorders of connective tissue may present with Chiari I malformation, occipitoatlantoaxial hypermobility, and functional cranial settling.**

For the last several years, three neurosurgeons from The Chiari Institute (TCI) in New York have worked with two geneticists in Baltimore (one from the National Institutes of Health and the other from the Harvey Institute for Human Genetics) to study the connection between Chiari I Malformation (CMI) and hereditary disorders of connective tissue (HDCT). Ehlers-Danlos Syndrome (EDS) and Marfan Syndrome (MS) are two examples of HDCT.

For many years, scientists presumed that Chiari Malformation and connective tissue disorders were unrelated problems arising from different sources, and thus would be very unlikely to appear together in the same person. They estimated that one out of a few thousand people would have Chiari, and another one out of a few thousand people would have a connective tissue disorder. To find the odds of having two unrelated conditions in one person, scientists multiply the separate odds -- so with these numbers, the likelihood of one person having both Chiari and EDS should be one in several million. The chances of a doctor having one patient with both diseases should be very slim, and having more than one should be very rare.

However, that's not how it works. This research team discovered 357 people – representing 12.7% percent of the 2,813 Chiari patients in their study – who have both a hereditary connective tissue disorder and Chiari Malformation. That's a lot more than one in several million, so it means that the two conditions must be linked. This is important new information. The team is publishing its findings in more than one way to reach a wide audience: from the geneticists' point of view (below) and from the neurosurgeons' view (a separate paper) so that doctors and patients in various fields can learn about these discoveries and apply the new Information wherever it is needed.

To promote understanding and to facilitate discussions between patients and their care providers, this article will include the research team's abstract that summarizes their information, broken into small bites and followed by a translation into lay terms. First an explanation, then the abstract with translations.

The title of the team's paper is: “Hereditary disorders of connective tissue may present with Chiari I malformation, occipitoatlantoaxial hypermobility, and functional cranial settling.” This title means that a person with an inherited connective tissue disorder such as EDS may display specific signs that are not

the ones a doctor usually looks for when making the diagnosis of HDCT. If a patient has a Chiari Malformation, or shows signs of looseness, sagging, or mismatch of the joints where the head and neck meet, then the doctor should think of HDCT as a real possibility. The study's authors believe that a patient who shows signs of having the combination HDCT/CMI should have MRIs of the head and spine taken in two positions – lying down as customary, and sitting up, where the effects of being vertical will appear.

Why sitting up? What are the effects of being vertical?

In ordinary healthy humans and in Chiarians who do not have HDCT, the inside of the person's head looks the same whether the person lies down or sits up. A supine (lying down) MRI of the brain accurately shows what it looks like inside the skull, and everything tends to stay that way when the person gets up.

However, in patients who have both HDCT and Chiari (the combo group HDCT/CMI), when the head position changes from horizontal to vertical, there are small but important changes in the placements of key structures inside the lower portion of the skull. Small bones slide around a bit, soft tissues sag, and the spaces between certain structures become more crowded or more spacious. The fluid that surrounds the brain and spinal cord may have trouble moving normally if certain flow spaces are too small or if they are temporarily or permanently blocked by soft or hard tissue. These changes can cause suffering.

The study showed that a combo person's symptoms and signs can become worse when sitting up or standing, and can improve when the person uses traction to hold up the head, or when the patient lies down again.

An additional finding for the combo group is that the small, finger-shaped bone (the C-2 vertebra, or odontoid) at the top of the spine tends to collect pannus or scar tissue on it. Besides being a sign of instability of that bone, pannus in that area also reduces the amount of space between C-2 and the brain stem, making it more likely that the bone may poke into the brain stem when the person moves into certain positions. Since the brain stem controls or influences important body functions, a malfunctioning brain stem can have many negative effects on a person's health. In this study, people with the combination of HDCT and Chiari were more likely to have pannus formations and more likely to have brain stem problems than the plain Chiari group or the healthy control group. They also were far more likely to be female, and to have small mouths and throats.

Now let’s look at the abstract and its translation. The abstract starts with a title, then lists keywords, then gives the title again and tells something about the authors. Then it tells what the researchers did, what they discovered, and why or how the discovery is important. This one offers advice, too.

Article:

Hereditary disorders of connective tissue may present with Chiari I malformation, occipitoatlantoaxial hypermobility, and functional cranial settling.

Keywords: Clinical Genetics, Malformations and Dysmorphology, KW015 - CHARACTERIZATION OF DISORDERS, KW022 - CLINICAL HISTORY, KW099 - NATURAL HISTORY, KW110 - PHENOTYPE, KW131 - SPLICING MECHANISMS

Hereditary disorders of connective tissue may present with Chiari I malformation, occipitoatlantoaxial hypermobility, and functional cranial settling. *C. Francomano[1], T. Milhorat[2], P. Bolognese[2], M. Nishikawa[2], N. McDonnell[3]* 1) Greater Baltimore Med Ctr, Harvey Institute Human Genetics, Baltimore, MD; 2) The Chiari Institute, North Shore-Long Island Jewish Health System, Manhasset, NY; 3) National Institute on Aging, NIH, Baltimore, MD.

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The abstract says: **We report an association of hereditary disorders of connective tissue (HDCT) and Chiari malformation 1 (CM1), presenting with lower brain stem symptoms attributable to occipito-atlantoaxial hypermobility and functional cranial settling.**

Translation: The researchers found that Chiari and hereditary disorders of connective tissue(HDCT) are linked. The person with both diseases shows lower brain stem symptoms not specified in this sentence but explained in detail in the article] that are caused by looseness in the joints at the base of the head and neck, and by sagging of the head down onto the top of the neck.

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Abstract continues: **The prevalence of hereditary disorders of connective tissue (HDCT) was determined in a prospectively collected cohort of 2,813 patients with CM1. All patients underwent a detailed medical and neuroradiological workup that included an assessment of particular mobility.**

Translation continues: The researchers collected 2813 Chiari patients in a row and then figured out how many of them had HDCT. They gave all of the patients detailed medical and neurological tests, looked at the patients' joints to see how they moved, and noted places that were loose.

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Abstract: **Using reconstructed 3D-CT and plain x-ray images, osseus structures comprising the craniocervical junction were investigated**
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morphometrically in 114 patients with HDCT/CM1 and compared to those in patients with CM1 alone (n = 55) and normal controls (n = 55).

Translation: The researchers used three-dimensional CT scans and regular x-rays to look at and measure the sizes, placements and angles of bony structures inside the lower skulls and upper necks of certain people. They looked very closely at 114 of their patients who have both Chiari and HDCT, 55 of their patients who have plain Chiari, and a separate group of 55 people who have neither disease.

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Abstract: **The diagnosis of Ehlers-Danlos syndrome (EDS) or other HDCT was made in 357 of**

2,813 of patients with CM1 (12.7%).

Translation: Out of the whole group of 2,813 Chiari patients, researchers found 357 people who have both Chiari and a hereditary connective tissue disorder (HDCT/CM1). That number equals 12.7% (twelve point seven percent, or between twelve and thirteen percent) of the whole group of Chiarians. [See separate comment about the significance of this number.]

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Abstract: **The clinical features of HDCT/CM1 were distinguished from those of CM1 alone by clinical stigmata of HDCT, a greater female preponderance (7:1 vs. 3:1), and a greater incidence of lower brain stem symptoms (0.43 vs. 0.05), retroodontoid pannus formation (0.71 vs. 0.16), and hypoplasia of the oropharynx (0.45 vs. 0.02).**

Translation: The researchers could tell the difference between patients with the combination of HDCT/CMI and those with plain Chiari and those with neither disorder. The combo patients had symptoms and signs of their connective tissue disease in addition to the symptoms and signs of Chiari. Also, in the combo group, there were 7 times as many females as males. The plain Chiari group had only three times as many females as males. The combo group had other differences, too: they had lower brain stem problems, more incidences of the finger-shaped C-2 vertebra being covered with scar tissue; and more instances of the patient's mouth and throat being small.

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Abstract: **In patients with HDCT/CM1, upon sitting or standing there was reduction of the basal-dens interval (3.6 mm), enlargement of the basal-**
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atlas interval (3.0 mm), and reduction of the clivus-axis angle(10.8°), clivus-atlas angle (5.8°), and atlas-axial angle (5.3°).

Translation: When the combo patients changed position from lying down to sitting up or standing, the positions and relationships of certain bony parts inside their lower skulls changed. The researchers measured those important changes.

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Abstract: **These changes were reducible by cervical traction or returning to the supine position. In normal controls and patients with CM1 alone, these measurements did not change with position.**

Translation: The changes that the researchers noticed in the combo patients could be reversed if the person did one of two things – either use traction to hold up the head to prevent it from sagging onto the neck, or lie down again. In the control group of people without either of these diseases, and in the group of plain Chiarians, the measurements did not change when the person changed position. Only the combo patients were affected.

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Abstract: **Conclusions: The identification of HDCT in 12.7% of patients with CM1 establishes an association between these previously unrelated disorders.**

Translation: Conclusions: Scientists used to believe that these two disorders were unrelated, but the fact that 12.7% of the people in this large group of Chiari patients also have a hereditary disorder of connective tissue means that the two diseases are linked.

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Abstract ends: **[conclusions cont'd:] Patients with HDCT and symptoms suggestive of CM1 should be evaluated with brain MRIs in the supine and upright positions.**

Translation ends: Patients with the combination of HDCT and symptoms that indicate the possibility of Chiari should have brain MRIs in two positions – lying down (as customary), and sitting up.

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