A New Hypothesis for the Pathophysiology of Symptomatic Adult CMI

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Background

Current theories about Chiari can't explain why many people have tonsillar herniations greater than 5mm but don't have symptoms, or why the amount of herniation is not strongly related to symptom severity. This is a new theory that is built on a substantial number of existing publications, plus preliminary evidence developed at the CCRC.

Hypothesis

The new theory has several parts:

1) In addition to tonsillar herniation (which is more common than originally believed), CMI patients have structural abnormalities of the atlanto-occipital (skull-spine) and atlanto-axial (top two spine vertebrae) joints which leads to subtle, but chronic instability
2) This instability causes the sub-occipital muscles in the neck to be overworked as they constantly engage in order to provide support
3) This leads to mechanical failure of the *Myodural Bridge Complex (MDBC).* The MDBC is a group of connective tissues that link the sub-occipital muscles to the dura covering the upper spine.
4) The failure of the MDBC causes the dura to become stiff and less *compliant* (see diagram).
5) The combination of tonsillar herniation and reduced compliance creates an abnormal pressure environment where during the normal cardiac cycle, and especially during Valsalva or exertion, there is a pressure spike in the brain compared to the spine.
6) This leads to strain on the cerebellum, brainstem, and cervical spinal cord causing many of the common Chiari symptoms.

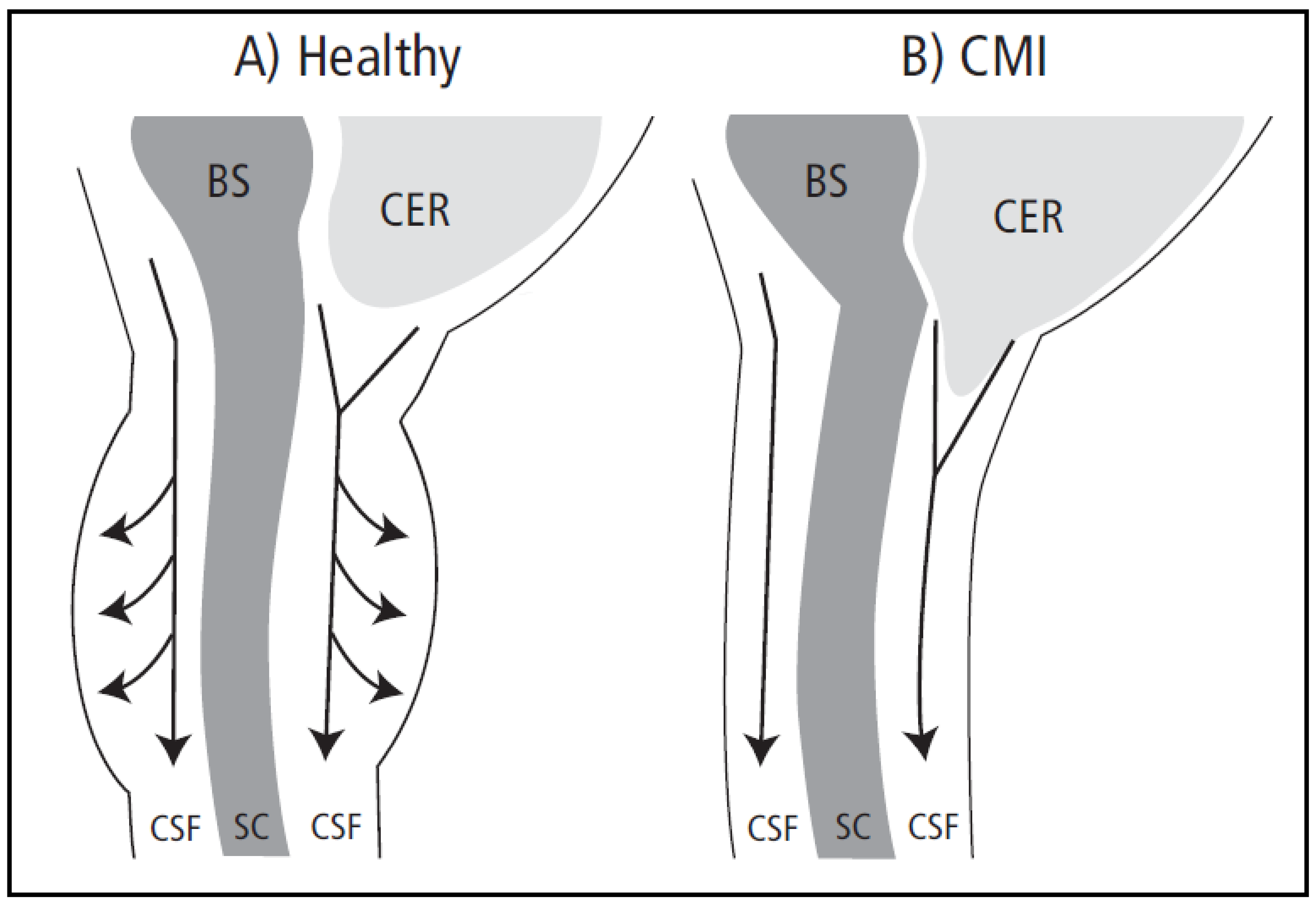
Support

There is substantial support for this theory in the existing literature (see Table). This includes studies that have shown that CMI patients have abnormal bones and ligaments that can lead to instability; preliminary CCRC data that shows reduced cervical compliance in CMI patients; pressure measurements that show abnormal pressure spikes in CMI patients; and imaging which shows strain on, and damage to, the cerebellum, brainstem, and spine of CMI patients.

Testing the Theory

The CCRC, along with partners at Emory, Brown, and Harvard, are currently testing the key aspects of this theory using advanced imaging to measure compliance and buy examining MDBC samples taken from patients during surgery. Hopefully, we'll know more in the next 12-18 months.

CSF Flow During Systole, Healthy vs CMI



In a healthy person (A), spinal fluid (CSF) flows freely across the skull-spine junction when the heart beats and a compliant dura in the cervical region expands to accommodate the increase of fluid. In a CMI patient (B), herniated tonsils cause resistance to CSF flow and increase the pressure required to push the CSF across the junction. In addition, a stiff, less compliant dura can't accommodate the extra CSF volume in the cervical region, which also increases the pressure (similar to how stiff arteries increase blood pressure).

Summary of Supporting Research

	Researcher	**Year**
Subclinical AO Joint Instability	Wan et al.	2020
	Wan et al.	2021
	Karaaslan et al.	2019
	El-Khouri et al.	2014
MDBC	Enix et al.	2014
	Jiang et al.	2020
	Klinge et al.	2021
Reduced Cervical Compliance	Loth et al.	Prelim Data
Elevated Pulse ICP	Fric et al.	2015
	Dyson et al.	2020
	O'Rourke et al.	2001
Increased Tissue Motion & Strain	Nwotchouang et	2021
	Martin et al.	2018
Cerebellum, Brainstem, Spinal Cord Damage	Houston et al.	2020
	Krishna et al.	2016
	Gok et al.	2020