Published in final edited form as:

Neurosurgery. 2015 July ; 77(1): 96–103. doi:10.1227/NEU.0000000000000740.

Imaging-Based Features of Headaches in Chiari Malformation Type I

Noam Alperin, PhD, James R. Loftus, BS, Carlos J. Oliu, BS, Ahmet M. Bagci, PhD, Sang H. Lee, MS, Birgit Ertl-Wagner, MD*, Raymond Sekula, MD**, Terry Lichtor, MD, PhD***, and Barth A. Green, MD****

Department of Radiology, University of Miami, Miami, FL

*Department of Radiology, University of Munich, Munich, Germany

**Neurological Surgery, University of Pittsburgh, Pennsylvania

***Department of Neurosurgery, Rush University, Chicago, IL

****Department of Neurological Surgery, University of Miami, Miami, FL

Abstract

Background—Sub-occipital cough-induced headaches are considered a hallmark symptom of Chiari Malformation Type I (CMI). However, non-Valsalva-related suboccipital headaches and headaches in other locations are also common in CMI. The diagnostic significance and the underlying factors associated with these different headaches types are not well understood.

Objective—This imaging-based study compares cranial morphology and hydrodynamics in three types of headaches in CMI to better understand the pathophysiological basis for the different headache characteristics.

Methods—Twenty-two cranial physiologic and morphologic measures were obtained using specialized MRI scans from 63 symptomatic pretreated CMI patients, 40 with suboccipital-headaches induced by Valsalva maneuvers (34F, 36±10years), 15 with non-Valsalva related suboccipital-headaches (10F, 33±9years), 8 with non-suboccipital non-Valsalva induced headaches (8F, 39±13years), and 37 control subjects (24F, age 36±12years). Group differences were identified using two-tailed Student's t-test.

Results—Posterior cranial fossa markers of CMI were similar among the three headache subtypes. However, the Valsalva-related suboccipital-headaches cohort demonstrated significantly lower intracranial compliance index than the non-Valsalva-related suboccipital-headaches cohort (7.5±3.4 vs. 10.9±4.9), lower intracranial volume change during the cardiac cycle (0.48±0.19 vs. 0.61±0.16mL), and higher MRICP (11.1±4.3 vs. 7.7±2.8mmHg, p=0.02). The Valsalva-related suboccipital-headaches cohort had smaller intracranial and lateral ventricles volumes compared to

Corresponding author: Noam Alperin, Department of Radiology, University of Miami, Professional Arts Center, Suite 713, 1150 N.W. 14th Street, Miami, FL 33136, Phone: 305-243-8098, Fax: 305-243-3405, Nalpeirn@med.miami.edu.

Disclosure: Noam Alperin is a shareholder in Alperin Noninvasive diagnostics, Inc. The other authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

the healthy cohort. The non-Valsalva-related suboccipital-headaches cohort had reduced venous drainage through the jugular veins.

Conclusion—Valsalva-induced worsening of occipital-headaches appears related to a small intracranial volume rather than the smaller posterior cranial fossa. This explains the reduced intracranial compliance and corresponding higher pressure measured in CMI patients with headaches affected by Valsalva maneuvers.

Keywords

Occipital headaches; Valsalva maneuver; Chiari Malformation Type I; Posterior Cranial Fossa Morphology; Intracranial compliance; CSF flow

Introduction

Headaches are a common symptom in neurological problems associated with impaired CSF dynamics. They occur when intracranial pressure (ICP) is elevated, as in idiopathic intracranial hypertension,¹ and when it is too low, as in the presence of a CSF leak.² Headache characteristics often differ between the different neurological problems. In Chiari Malformation type I (CMI), suboccipital headaches that are exacerbated by cough or Valsalva maneuver have been described as the most common symptom.³ McGirt et al found that occipital headache in CMI is more frequently associated with obstructed CSF flow than frontal or general headaches, but noted that CMI patients with the later type of headaches may also respond to decompression surgery.⁴ Another study emphasized the importance of headaches induced or exacerbated by cough as a predictor of good surgical outcome.⁵

Milhorat et al. suggested that the smaller posterior cranial fossa (PCF) found in CMI leads to reduced compliance of the CSF system and thereby the Valsalva-related headaches.⁶ Sansur et al. measured lumbar subarachnoid CSF pressure in 26 CMI patients and 15 healthy subjects and reported that peak intrathecal pressures during cough and at baseline were elevated in patients with cough headaches compared with either patients without cough headaches or healthy volunteers.⁵ They explained the cough headaches due to a sudden increase in the intrathecal pressure caused by an obstruction to the flow of CSF in the subarachnoid space. Chen et al reported that cough headache occurs in CMI patients with overcrowded PCF with or without tonsillar herniation.⁷ A lower intracranial compliance measured noninvasively by MRI was found in a cohort of symptomatic CMI patients with symptoms including severe headaches, neck pain and sensory and motor difficulties, compared to healthy volunteers.⁸ Using the same MRI technique it was shown that patients who underwent decompression surgery with good outcomes had a large increase in intracranial compliance post-surgery.⁹

Diagnosis and treatment decisions for CMI patients with headaches that are not triggered or worsened by Valsalva-related maneuvers or that are not suboccipital are challenging, as these symptoms are considered atypical for CMI.¹⁰ Previous studies have not determined whether the different types of headaches reported in CMI are associated with differences in cranial and/or PCF morphology and CSF physiology. This study addresses this question by using MRI measures of PCF morphology and CSF physiology in three sub-types of

headaches reported in CMI, i.e., suboccipital headaches worsened by Valsalva maneuvers, suboccipital headaches not related to Valsalva maneuvers, and headaches not in the suboccipital region and not related to Valsalva maneuvers. The study further aims to determine if specific morphologic and physiologic characteristics differentiate between the different types of headaches in CMI.

Methods

Subjects

A total of 100 subjects were included in this study. Following approval by the respective institutional review boards and informed consent by study participants, a cohort of 63 symptomatic pretreated patients (52 women, age 36 ± 10 years) with a radiological diagnosis of CMI (i.e., tonsillar herniation of ≥ 5 mm) and a cohort of 37 age and gender-matched healthy control subjects (24 women, age 36 ± 12 years) without a history of neurological problems were included in the study. All patients filled out a detailed questionnaire documenting symptom types, severity, and frequencies. The headache-related details in the questionnaire included the description of the location and nature of their headaches and possible triggers. Patient clinical files were reviewed to ensure consistency between the questionnaire information and physician office visit report. Patients for whom the information was incomplete or inconsistent were excluded from the study. The 63 CMI patients were divided into three sub-cohorts based on the characteristics of their headache symptoms: 1) suboccipital headaches induced or worsened by Valsalva (40 patients (34F) age 36 ± 10) (group 1), 2) suboccipital headache not related to Valsalva (15 patients (10F) age 33 ± 9) (group 2) and, 3) non-suboccipital non-Valsalva related headaches (8 patients (8F) age 39 ± 13) (group 3). Although headache location (suboccipital versus other areas) and the association with Valsalva-related maneuvers were the criteria for dividing into the three sub-cohorts, the CMI patients reported additional symptoms that did not exclude them from sub-cohort selection. For example, a patient in the suboccipital Valsalva-induced headache sub-cohort could have a frontal headache, muscle weakness, and neck pain in addition to the suboccipital headache.

MRI Acquisition and Data Analysis

MR imaging was performed using 1.5T (Signa HDx, GE Healthcare, Milwaukee, WI) and 3T (Magnetom Verio/Trio, Siemens Healthcare, Erlangen, Germany and Signa HDX, GE Healthcare, Milwaukee, WI) scanners. The imaging protocol included a 3-D T1-W scan for the morphological assessment and two cine velocity encoded phase contrast scans, one with high velocity encoding (70–80 cm/s) for imaging the arterial and venous blood flows to and from the cranium, and the second with low velocity encoding (7–8 cm/s) for imaging the CSF flow and cord motion at the upper cervical region. The MPRAGE technique on the Siemens scanner and the equivalent SPGR on the GE scanner were used to acquire the T1-weighted images. Square pixel size was either 0.9 or 1 mm, with a slice thickness of 1–1.5 mm. The voxel dimensions for the phase contrast scans were also similar, using a pixel size of 0.56×0.6 mm and slice thickness of 5–6 mm. The MRI-derived anatomical and physiological parameters were divided into the following classes: linear and volumetric PCF morphology, CSF flow and cord motion dynamics in the cranio-cervical junction (CCJ),

arterial inflow and venous outflow through the jugular veins, and global intracranial hydrodynamic measures as listed in Table 1.

Linear PCF Measures

Linear PCF measures were obtained by a single experienced observer blinded to the patient classification from the mid-sagittal slice of the 3-D T1 weighted image using an in-house image display utility. The clivus was measured from the inferior boundary of the dorsum sellae to the basion, the supraocciput from the opisthion to the internal occipital protuberance, McRae's line from the basion to the opisthion, and Twinning's line from the inferior boundary of the dorsum sellae to the internal occipital protuberance.

Cranial and PCF Volumetric PCF Measures

The automated PCF volumetric data analysis method used has been previously described in detail.¹¹ This method quantifies the volume of the PCF (PCFV), hindbrain (HBV), and 4th ventricle using automated segmentation which is guided by a tailored brain atlas developed from MRI data of CMI patients. A measure of crowdedness is obtained from the ratio of the HBV and PCFV.

CSF Flow and Intracranial Hydrodynamics Measure

The methods used to derive the CSF flow, cord motion and the intracranial hydrodynamics measures, which include the intracranial volume change during the cardiac cycle, intracranial compliance index and pressure, have been previously described in detail.^{8,10,12} In brief, volumetric flow rates through blood vessels and the upper cervical CSF lumen are obtained using the Pulsatility Based Segmentation (PUBS) method for measurement of pulsatile flow, which utilizes the dynamic information throughout the cardiac cycle and a cross correlation method to differentiate lumen from the background pixels and delineates the lumen boundary.¹³ Mean flow rate is then calculated by integrating all pixels within the delineated lumen. Mean velocity is the average velocity within the lumen boundary. Upper cervical CSF stroke volume (SV) is derived by time integration of the absolute values of the CSF volumetric flow rate waveform and division by two after subtraction of the net flow. It represents the CSF volume that moves back and forth between the cranium and spinal canal during one cardiac cycle. Maximal cord displacement during the cardiac cycle is obtained by time integration of the average velocity waveform obtained in a region of interest inside the cord.

The method for derivation of pressure by MR (MRICP) has been also described in detail.¹² Intracranial compliance is first derived from the ratio of intracranial volume and pressure changes during the cardiac cycle. Intracranial volume change (ICVC) is derived from the momentary differences between the total cerebral blood inflow (tCBF), venous blood outflow, and cranio-spinal CSF that enter and leave the cranium during the cardiac cycle. The maximal change in pressure is derived from the change in the CSF pressure gradient, which is calculated using the Navier-Stokes relationship between pressure gradients and temporal and spatial derivatives of the cranio-spinal CSF velocities. The tCBF is derived by summation of the flow through the internal carotid and vertebral arteries. The venous

outflow is derived by summation of the flow through the internal jugular veins and secondary venous channels (e.g., epidural and vertebral veins) when present.

Statistical Analysis

The statistical analyses performed in this study include comparison of the Valsalva-induced suboccipital headache sub-cohort to the other two CMI sub-cohorts as well as the comparison of the three sub-cohorts to the healthy control cohort. Comparisons were performed using two-tailed Student's t-test for unequal variances using MedCalc Software version 14 (MedCalc Software bvba, Ostend, Belgium). Physiologic measures were available in 38 CMI patients with suboccipital headache exacerbated by Valsalva maneuvers, 14 patients with suboccipital headache not related to Valsalva maneuvers, and 7 patients with non-suboccipital headaches not related to Valsalva maneuvers. Volumetric analyses were available in 37, 9, and 6 patients, respectively. All sub-cohorts were also compared to the control cohort, which includes 37 subjects.

Results

Three intracranial hydrodynamic and one hemodynamic measures related to cerebral venous drainage were significantly different between the Valsalva and non-Valsalva-related suboccipital headache cohorts. The hydrodynamics measures were the maximal intracranial volume change (ICVC) during the cardiac cycle, the intracranial compliance index (ICCI), and the MR-derived ICP (MRICP). ICVC and ICCI were lower in the Valsalva-related headache group compared with the non-Valsalva group, $0.47 \pm 0.19 \text{ mL}$ vs. $0.60 \pm 0.16 \text{ mL}$, and 7.5 ± 3.4 vs. 10.9 ± 4.9 , respectively. Consequently, the MRICP, which is inversely related to intracranial compliance, was significantly higher in the Valsalva-related suboccipital headache group, 11.1 ± 4.3 vs. $7.7 \pm 2.8 \text{ mmHg}$, $p < .01$. Examples of velocity encoded MR images used for derivation of the intracranial compliance and pressure are shown in Figure 1a and 1b, respectively. The net arterial minus venous blood flow and the cranio-spinal CSF flow waveforms from CMI patients with and without Valsalva-related suboccipital headaches are shown in Figure 2a and 2b, respectively. The reduced compliance in the CMI patient with Valsalva-related headaches is evident from the more tight proximity between the CSF waveform and the arterial minus venous waveform, which is the driving force for the CSF waveform; the Monro-Kellie principle holds that these waveforms, representing inflow and outflow respectively, should be equal in a non-compliant system. The hemodynamics measure that was significantly different, the venous drainage through the jugular veins, was lower in the non-Valsalva-related cohort (group 2) compared to the Valsalva cohort (group 1), 58 ± 26 vs. $74 \pm 14\%$, respectively. An example of MR venography images of the neck veins from representative CMI patients from group 1 and 2 are shown in Figure 3a and 3b, respectively. Mean and SD of the morphologic and physiologic measures in the control group and in each of the three CMI sub-cohorts, and corresponding p-values are listed in Table 2.

One CSF flow measure was statistically different between the suboccipital-Valsalva-related headaches group (group 1) and the non-sub-occipital non-valsalva-related headaches group (group 3). The cranio-spinal CSF stroke volume (C2SV), i.e., the amount of CSF volume

that moves between the cranium and the spinal canal with every heartbeat, was larger in the Valsalva sub-cohort compared with the non-occipital non Valsalva cohort (0.54 ± 0.20 and 0.40 ± 0.12 mL, p -value=.03). The ICCI and MRICP followed the same trend when comparing group 1 to group 3 (reduced ICCI and higher MRICP in Valsalva induced suboccipital patients). However, only the difference in MRICP reached statistical significance 11.1 ± 4.3 vs. 7.6 ± 2.4 mmHg, $p < .01$. PCF volume, PCF crowdedness and maximal cord displacement at C2, all important markers for CMI, were not significantly different in the three CMI sub-cohorts. For example, the average maximal cord displacement was 302 ± 113 , 275 ± 94 , and 300 ± 129 μ m, respectively. Tonsillar descent below the foramen magnum was also not significantly different between the three CMI sub-cohorts with mean and SD values of 9.4 ± 3.9 mm, 10.1 ± 5.4 mm, and 11.8 ± 6.8 mm, respectively. Comparing the three CMI sub-cohorts to the control cohort, the clivus and supraocciput length, PCFV, HBV/PCFV, 4th ventricle volume, and maximal cord displacement in the CMI groups were all significantly different from the control healthy cohort. Unexpectedly, two measures which are not CMI markers, intracranial volume (ICV) and the lateral ventricles volume, were significantly smaller in group 1 compared to the control cohort (1408 ± 150 vs. 1505 ± 109 ml, $p < .01$, and 13.1 ± 5.0 vs. 16.1 ± 7.2 , $p = .04$), respectively. MRICP was also significantly higher in group 1 compared to the control cohort (11.1 ± 4.3 vs. 8.8 ± 2.3 , $p < .01$).

Discussion

Suboccipital headaches worsened by Valsalva maneuvers are considered a hallmark symptom of CMI. However, many patients with a suspected diagnosis of CMI suffer from suboccipital-headaches that are not exacerbated by Valsalva maneuvers or from non-suboccipital headaches. Comparison of the cranial and PCF morphology, and CSF physiology measures in CMI patients with differences in the symptomatic presentation of their headaches elucidated the diagnostic significance of having suboccipital headaches which are either exacerbated or not exacerbated by Valsalva. Previously identified morphologic markers of CMI, e.g., PCF volume, PCF crowdedness, 4th ventricular volume, and maximal cord displacement during the cardiac cycle¹⁰ were similar among the CMI sub-cohorts. Therefore, these markers are not associated with specific headache characteristics reported in CMI. This observation contradicts previous suggestions that the small PCF in CMI is the primary reason for the cough-induced headaches.⁶ Interestingly, structures which are not CMI markers, i.e., the intracranial volume and the lateral ventricles volume, which were shown to be within the normal range in CMI,¹⁰ were found to be smaller than normal in the subgroup of CMI patients with occipital headache that is worsened by Valsalva. The worsening of headaches with Valsalva maneuvers seems to indeed be due to reduced overall intracranial compliance, which is primarily due to a smaller intracranial volume and only secondary to the smaller PCF. Therefore, presentation of occipital headaches not worsened by cough or Valsalva maneuvers should not exclude the diagnosis of CMI.

Moreover, the difference in cerebral venous drainage pattern between the Valsalva-related and the non-Valsalva-related occipital-headaches further supports the hypothesis that differences in headache characteristics are not CMI specific. Suboccipital-headaches not worsened by Valsalva were associated with reduced cerebral drainage through the jugular

veins. This finding is in agreement with previous reports of reduced primary cerebral drainage in patients with migraine,¹⁴ which are usually also unaffected by Valsalva maneuvers, and in subjects with history of mild traumatic brain injury.¹⁵

The most prominent difference between the Valsalva- and the non-Valsalva-related suboccipital headaches was the MRI measurement of ICP. Mean MRICP in the Valsalva-related headache cohort was 3.4mmHg higher than in the non-Valsalva-related HA cohort. The MRICP values measured in the non-Valsalva-related group were similar to those measured in the healthy cohort. These findings are in excellent agreement with invasive measurements of CSF pressures performed by Sansur et al. in CMI patients with cough and non-cough-induced headaches and healthy subjects. Baseline ICP in the CMI patients with cough headaches was approximately 3 mmHg higher than in patients with no cough headaches.⁵ The higher MRICP found in our cohort of CMI patients with Valsalva-related headaches is an indication of a lower intracranial compliance—a more limited ability of the intracranial space to accommodate the increase in cerebral blood volume during the Valsalva maneuver without a large increase in pressure. The elimination of Valsalva-related occipital headaches following successful posterior fossa decompression surgery can be attributed to the increased intracranial compliance following the expansion of the intracranial compartment.⁹

Similar to previous observations,⁵ the degree of tonsillar herniation in the current study was not significantly different between the cohorts with Valsalva-induced or Valsalva-unaffected suboccipital or non-suboccipital headaches, further pointing to the limitation of tonsillar herniation as a standalone marker of CMI.

The results of this study demonstrate the reliability and the high sensitivity of the MRICP measurement to detect relatively small differences in ICP, 3–4mmHg, between the different headache cohorts. The validity of the MRICP measurements was recently assessed independently by Muehlmann et al who found good agreement between the MRICP measurement and the VP shunt valve opening pressure setting in hydrocephalic patients, with 95% limits of agreements of ± 2.3 mmHg.¹⁶ Association between change in ICP and headaches was also recently reported in a study of acute mountain sickness, where severity of headaches was shown to be proportional to the hypoxia-induced increase in ICP as measured by MRICP.¹⁷

Limitations

There are limitations of the study that need to be taken into account when interpreting the data of the current study. The number of patients included in the sub-cohort of CMI-patients with non-occipital headaches is considerably smaller than the number of subjects in the cohorts with suboccipital headaches. Therefore, statistical analyses and discussion of the results was primarily focused on the suboccipital headache groups and the possible factors associated with the involvement of the Valsalva maneuvers.

Conclusion

This study confirmed previous suggestions that suboccipital headaches worsened by Valsalva maneuvers in CMI patient are related to reduced overall intracranial compliance. However, the likely primary factor that leads to the Valsalva involvement seems to be a smaller overall ICV and not the smaller PCF as, the PCF volume and other CMI markers such as PCF crowdedness and maximal cord displacement were similar in the 3 CMI patient sub-groups. These findings suggest that diagnosis of CMI should not be excluded in patients with suboccipital headaches that are not worsened by Valsalva maneuvers.

Acknowledgments

Funding: Supported by NIH grant no 7R01NS052122

References

1. Wall M. The headache profile of idiopathic intracranial hypertension. *Cephalalgia : an international journal of headache*. Dec; 1990 10(6):331–335. [PubMed: 2289234]
2. Mokri B. Headaches caused by decreased intracranial pressure: diagnosis and management. *Current opinion in neurology*. Jun; 2003 16(3):319–326. [PubMed: 12858068]
3. Mueller DM, Oro JJ. Prospective analysis of presenting symptoms among 265 patients with radiographic evidence of Chiari malformation type I with or without syringomyelia. *Journal of the American Academy of Nurse Practitioners*. Mar; 2004 16(3):134–138. [PubMed: 15130068]
4. McGirt MJ, Nimjee SM, Floyd J, Bulsara KR, George TM. Correlation of cerebrospinal fluid flow dynamics and headache in Chiari I malformation. *Neurosurgery*. Apr; 2005 56(4):716–721. discussion 716–721. [PubMed: 15792510]
5. Sansur CA, Heiss JD, DeVroom HL, Eskioglu E, Ennis R, Oldfield EH. Pathophysiology of headache associated with cough in patients with Chiari I malformation. *Journal of neurosurgery*. Mar; 2003 98(3):453–458. [PubMed: 12650413]
6. Milhorat TH, Chou MW, Trinidad EM, et al. Chiari I malformation redefined: clinical and radiographic findings for 364 symptomatic patients. *Neurosurgery*. May; 1999 44(5):1005–1017. [PubMed: 10232534]
7. Chen YY, Lirng JF, Fuh JL, Chang FC, Cheng HC, Wang SJ. Primary cough headache is associated with posterior fossa crowdedness: a morphometric MRI study. *Cephalalgia : an international journal of headache*. Sep; 2004 24(9):694–699. [PubMed: 15315524]
8. Alperin N, Sivaramakrishnan A, Lichter T. Magnetic resonance imaging-based measurements of cerebrospinal fluid and blood flow as indicators of intracranial compliance in patients with Chiari malformation. *Journal of neurosurgery*. Jul; 2005 103(1):46–52. [PubMed: 16121972]
9. Sivaramakrishnan A, Alperin N, Surapaneni S, Lichter T. Evaluating the effect of decompression surgery on cerebrospinal fluid flow and intracranial compliance in patients with chiari malformation with magnetic resonance imaging flow studies. *Neurosurgery*. Dec; 2004 55(6):1344–1350. discussion 1350–1341. [PubMed: 15574215]
10. Alperin N, Loftus JR, Oliu CJ, et al. Magnetic resonance imaging measures of posterior cranial fossa morphology and cerebrospinal fluid physiology in Chiari malformation type I. *Neurosurgery*. Nov; 2014 75(5):515–522. discussion 522. [PubMed: 25328981]
11. Bagci AM, Lee SH, Nagornaya N, Green BA, Alperin N. Automated posterior cranial fossa volumetry by MRI: applications to Chiari malformation type I. *AJNR. American journal of neuroradiology*. Sep; 2013 34(9):1758–1763. [PubMed: 23493894]
12. Alperin NJ, Lee SH, Loth F, Raksin PB, Lichter T. MR-Intracranial pressure (ICP): a method to measure intracranial elastance and pressure noninvasively by means of MR imaging: baboon and human study. *Radiology*. Dec; 2000 217(3):877–885. [PubMed: 11110957]

13. Alperin N, Lee SH. PUBS: pulsatility-based segmentation of lumens conducting non-steady flow. *Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine/Society of Magnetic Resonance in Medicine*. May; 2003 49(5):934–944.
14. Koerte IK, Schankin CJ, Immler S, et al. Altered cerebrovenous drainage in patients with migraine as assessed by phase-contrast magnetic resonance imaging. *Investigative radiology*. Jul; 2011 46(7):434–440. [PubMed: 21317790]
15. Pomschar A, Koerte I, Lee S, et al. MRI evidence for altered venous drainage and intracranial compliance in mild traumatic brain injury. *PloS one*. 2013; 8(2):e55447. [PubMed: 23405151]
16. Muehlmann M, Koerte IK, Laubender RP, Steffinger D, Lehner M, Peraud A, et al. Magnetic resonance-based estimation of intracranial pressure correlates with ventriculoperitoneal shunt valve opening pressure setting in children with hydrocephalus. *Investigative Radiology*. Jul; 2013 48(7):543–7. [PubMed: 23695081]
17. Lawley JS, Alperin N, Bagci AM, et al. Normobaric hypoxia and symptoms of acute mountain sickness: Elevated brain volume and intracranial hypertension. *Annals of neurology*. Jun; 2014 75(6):890–898. [PubMed: 24788400]

Figure 1.

Examples of velocity encoded phase contrast images used for measurements of blood and CSF flow. A. High velocity encoding image used for measurement of arterial inflow through carotid and vertebral arteries and venous outflow through the internal jugular veins. B. Low velocity encoded phase contrast image used for measurements of the flow through the CSF and other secondary venous channels. The lumen boundaries (red-arteries, blue-veins, and yellow and red-CSF and cord) were automatically identified using the PUBS method.¹³

Figure 2.

Arterial minus venous blood flow and CSF flow waveforms from Valsalva-related headache group which represents the “lower” compliant state (A) where CSF waveform follows closely to A-V waveform, and from non-Valsalva related headache group which represents the “higher” compliant state (B) where CSF does not follow A-V waveform closely.

Figure 3.

MR venography images of the neck veins from representative CMI patients A. Valsalva-related headache patient where internal jugular veins (white arrow heads) are the dominant drainage pathway, and from non-Valsalva-related headache group (B) where there is reduced drainage through the jugular veins and increased drainage through secondary veins the epidural, vertebral and deep cervical veins (white arrows). Axial source images are shown at the top, and MIPs are shown at the bottom.

Table 1

Quantitative morphologic and physiologic measures derived from the MRI scans

Linear PCF	Volumetric PCF	CSF Flow and Cord Movement	Cerebral Blood Flow	Intracranial Hydrodynamics
Clivus	Intracranial Volume (ICV)	CSF Stroke Volume (SV)	Total Cerebral Blood Flow (TCBF)	Intracranial Volume Change (ICVC)
Supraocciput	PCF Volume (PCFV)	Systole CSF Velocity	% Jugular Cerebral Venous Drainage	Pulse Pressure Gradient (PTP-PG)
Twining's Line	Hindbrain Volume	Diastole CSF Velocity		Intracranial Compliance index (ICCI)
McRae's Line	4th Ventricle Lateral Ventricles	Max. Cord Displacement		Intracranial Pressure (MR-ICP)

Table 2

Morphologic and Physiologic measure in the control and CMI patients sub cohorts.

	Control	SO HA w/Valsalva (Group 1)	SO HA w/o Valsalva (Group 2)	Non SO/Valsalva HA (Group 3)	G1:G2	G1:G3	CTR:G1	CTR:G2	CTR:G3
ID Morphology									
Herniation (mm)		9.4±3.9	10.1±5.4	11.8±6.8	.64	.37			
Clivus (mm)	41.0±2.7	35.0±3.3	33.4±4.7	34.6±5.2	.24	.85	<.001	<.001	.01
Supraocciput (mm)	43.0±3.3	38.0±2.9	37.3±8.3	36.4±3.6	.78	.27	<.001	.02	<.001
3D Cranial Morphology									
ICV (mL)	1505±109	1408±150	1489±167	1388±171	.21	.80	.002	.78	.16
Cerebrum GM + WM (mL)	N/A	973±97	1006±95	1004±156	.14	.13			
Cerebrum Crowdedness	N/A	0.783±0.027	0.778±0.031	0.829±0.051	.79	.08			
Lat Vent Vol (mL)	16.1±7.2	13.1±5.0	18.0±8.3	12.9±6.4	.12	.95	.04	.54	.33
3D PCF Morphology									
PCFV (mL)	211±16	184±16	193±21	179±20	.28	.54	<.001	.03	.008
HBV (mL)	168±16	162±13	168±18	161±19	.39	.88	.14	.92	.47
PCFV/ICV	0.141±0.008	0.132±0.010	0.130±0.008	0.129±0.011	.58	.65	<.001	.004	.053
HBV/PCFV (Crowdedness)	0.793±0.036	0.880±0.018	0.873±0.032	0.873±0.019	.58	.50	<.001	<.001	<.001
4 th Ventricle Vol (mL)	2.19±0.69	1.26±0.34	1.51±0.43	1.24±0.35	.15	.91	<.001	.003	<.001
CSF Flow Measurements									
Cord Max Disp (um)	174±47	302±113	275±94	300±129	.41	.97	<.001	.004	.04
C2SV (mL)	0.54±0.18	0.54±0.20	0.47±0.14	0.40±0.12	.19	.03	.96	.20	.03
CSF Sys. Vel. (mm/s)	17.4±5.7	17.9±6.3	18.5±5.2	17.6±9.6	.70	.94	.73	.50	.95
CSF Dia. Vel. (mm/s)	9.4±3.0	9.9±3.1	11.0±3.2	11.7±4.0	.26	.26	.48	.10	.16
Blood Flow Measurements									
TCBF (mL/min)	776±107	783±105	782±123	726±126	.97	.26	.77	.88	.32
Jugular Drainage (%)	70±15	74±14	58±26	82±7	.04	.03	.22	.11	.002
Intracranial Parameters									
PTP-PG (mmHg/cm)	0.035±0.011	0.036±0.012	0.040±0.013	0.039±0.020	.36	.72	.62	.21	.59
ICVC (ml)	0.52±0.16	0.47±0.19	0.60±0.16	0.51±0.18	.02	.63	.19	.15	.83

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

	Control	SO HA w/Valsalva (Group 1)	SO HA w/o Valsalva (Group 2)	Non SO/Valsalva HA (Group 3)	G1:G2	G1:G3	CTR:G1	CTR:G2	CTR:G3
ICC Index	8.7±3.1	7.5±3.4	10.9±4.9	10.3±3.4	.03	.08	.10	.14	.29
MR-ICP (mmHg)	8.8±2.3	11.1±4.3	7.7±2.8	7.6±2.4	.002	.008	.005	.20	.24

SO= Sub-occipital, HA=headaches, G1=Group 1, G2=Group 2, G3=Group 3, and CTR=Control.

No parameters are significantly different between groups 2 & 3