Evidence for Larger Extra Ventricular Cranial CSF Volume in Idiopathic Intracranial Hypertension

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Introduction
Idiopathic intracranial hypertension (IIH), also known as pseudotumor cerebri, is characterized by elevated intracranial pressure (ICP) of unknown cause [1]. This condition occurs at higher frequency in obese young women of childbearing age. Symptoms include debilitating headaches and visual disturbances, and papilledema is a common finding in IIH. At present, the medical treatment for IIH patients is with acetazolamide, a carbonic anhydrase inhibitor. The lack of understanding of the pathophysiology involved limits our ability to diagnose the disease early and treat it effectively. It is widely accepted that IIH is associated with impaired absorption of CSF [2], which could potentially result with increased CSF volume leading to reduced compliance and increased ICP. Impaired CSF absorption is also the assumed cause for normal pressure hydrocephalous in the elderly. However, unlike hydrocephalous, brain ventricles remain small in IIH. Therefore, if IIH is indeed associated with impaired absorption, an increased extra ventricular CSF volume is expected in IIH. This study measures total cranial, ventricular and extra-ventricular CSF volumes in IIH patients and in healthy subjects of similar age, gender and BMI.

Methods
MRI scans of 11 healthy women (age range 22-50 years, mean ± SD 31 ± 9) and 14 women newly diagnosed with IIH (age range 17-44 years, mean ± SD 27 ± 9) were acquired with a 3T Siemens Trio scanner and a 1.5T Siemens Symphony Tim scanner. The scans included whole brain T1-weighted (MPRAGE) images acquired with the following scan parameters: FOV 25.6x22.4 cm, slice thickness 1 mm, acquisition matrix 256x224, flip angle 15°, TR/TE 1900/2.36 ms, and inversion time 1100 ms. Quantification of intracranial CSF volumes was achieved using the FSL software package (ver 4.1.5) [3]. The brain was extracted from T1-weighted images using the brain extraction tool (BET) based on an optimum threshold and manually input coordinates for the center of the brain. The FAST function was utilized to automatically segment the brain into GM, WM and CSF voles. The intra-ventricular CSF volumes were measured using the 3D Slicer software program (ver 3.6.3 1.0) [4]. A region-growing algorithm initially enabled identification of ventricular CSF spaces on the T1-weighted images. The resulting mask was manually edited to accurately delineate the lateral, third, and fourth ventricles and the cerebral aqueduct. The extra-ventricular CSF volume in the brain was calculated as the numerical difference between the intracranial and intra-ventricular CSF volumes. A two tail t-test was used to assess statistical significant of differences between the two cohorts.

Results
An example of the delineated intracranial and intraventricular CSF spaces from one of the subjects is shown in Figure 1. The 3D volume rendering of the delineated ventricular system is shown in Fig1B. Mean and SD values of the age, body mass index (BMI), intracranial CSF volume, intra-ventricular CSF volume and extra-ventricular CSF volume for the healthy and the patient cohorts are shown in Table 1. Mean intracranial CSF volume of the IIH patient cohort was significantly greater compared to the control subjects (P < 0.01). Specifically, the extra-ventricular CSF space was significantly larger in the patient group (P < 0.01) compared to the healthy cohort. The ventricular sizes were similar between the two groups (P=0.735), in agreement with recent reports in literature [5, 6].

Conclusions
Quantitations of global cranial CSF volumes demonstrate larger CSF volume in the IIH cohort compared to a carefully matched control cohorts. This finding supports the current belief that IIH is associated with impaired CSF absorption. The extra ventricular accumulation of CSF is consistent with findings of CSF accumulation in the optic nerves sheath often seen in IIH. The expansion of extra-ventricular CSF space explains the visual alterations and the papilledema often seen in IIH due to the transmission of the CSF pressure to the globe region. This fining is also consistent with recently reported lower spinal canal compliance in IIH [7], which explains why the increased CSF volume accumulates in the cranial compartment.

References