Inspiration drives cerebrospinal fluid flow in humans

Steffi Dreha-Kulaczewski[1], Arun Jospeh[2,3], Klaus-Dietmar Merboldt[2], Hans Ludwig[4], Jutta Gaertner[1], and Jens Frahm[2,3]

[1]Department of Pediatrics and Adolescent Medicine, Division of Pediatric Neurology, University Medical Center, Goettingen, Germany, [2]Biomedizinische NMR Forschungs GmbH am Max-Planck-Institut fuer biophysikalische Chemie, Goettingen, Germany, [3]partner site Goettingen, German Center for Cardiovascular Research, Germany, [4]Department of Neurosurgery, Division of Pediatric Neurosurgery, University Medical Center Goettingen, Germany

Target audience: clinicians in the fields of neuropediatrics, neurology, neuroradiology, as well as clinical MR researchers.

Introduction

The mechanisms behind cerebrospinal fluid (CSF) flow in humans are still not fully known. CSF circulates from its production in the choroid plexus of the lateral ventricles through the ventricular system (Fig. A) until reaching subarachnoid spaces. So far, most studies employed phase-contrast MRI techniques with cardiac gating to determine velocities and stroke volumes of CSF flow, while focusing on the presumed pulsatile nature of CSF flux during cardiac systole and diastole [1]. Only very few MRI studies without cardiac gating confirmed contributions of respiratory rhythms in CSF flow dynamics [2,3,4]. Here, we applied a novel real-time MRI technique at high spatial and temporal resolution in healthy human subjects to investigate CSF flow without limiting technical assumptions.

Subjects and Methods

T1-weighted images of 10 subjects (19–53 yrs, 2 f) were obtained at 50 ms temporal resolution as well as 0.75×0.75 mm^2 in-plane resolution and 5 mm section thickness using highly undersampled radial FLASH with regularized nonlinear inverse (NLINV) reconstruction (15 spokes per frame, TR 3.33 ms, TE 2.10 ms, flip angle 8º) [5,6]. All studies were performed at 3 T using a 32-channel head coil (Tim Trio, Siemens, Germany). Serial images were reconstructed online using a highly parallelized version of the NLINV algorithm on a "bypass" computer fully integrated into the host of the MRI system and equipped with two processors and eight GPUs [7,8]. All subjects were required to follow three protocols; 1) normal breathing, 2) preset rhythm of forced breathing (8 periods of 2.5 s inspiration and 2.5 s expiration), 3) breath hold over 12 s. Because real-time MRI of through-plane CSF flow exploits the inflow phenomenon, it precludes access to absolute velocities and directions. Multiple regions-of-interest (ROI) were placed along the ventricular system (Fig. A, B).

Results

A pulsating CSF flow component at a frequency corresponding to the heart rate was observed in all subjects (Fig. C). In addition, we identified another most significant and indeed dominating component which refers to a much stronger CSF flow. When performing a forced breathing protocol, the results clearly indicated that respiratory cycles drive this major component of CSF flow. Figure D depicts MRI signal intensity time courses for the corresponding protocol and illustrates that exclusively inspiration (black boxes) elicits significant CSF flow. In contrast, the cardiac-related CSF flow pattern constituted only a minor contribution. Conversely, breath-holding completely suppressed the respiratory-related flow component (Fig. E). Normal breathing before and after the breath-hold period yielded variable CSF flow similar to Fig. C. Measurements in the 3rd ventricle (Fig. B) generated the most consistent findings.

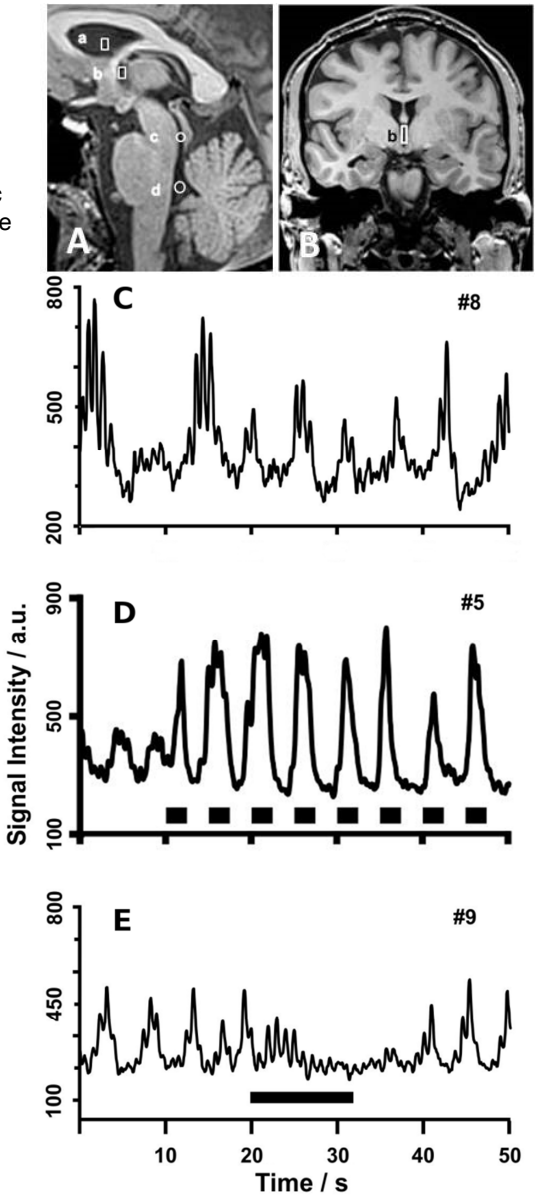

Fig.: A Sagittal T1-w image with ROI in *a)* lateral, *b)* 3rd, and *d)* 4th ventricle, *c)* aqueduct; ***B*** Coronal T1-w image with ROI in 3rd ventricle; ***C*** CSF flow in aqueduct during normal breathing (subject #6); ***D*** CSF flow in 3rd ventricel during forced breathing (black bars = 2.5 s inspiration, subject #5); ***E*** CSF flow in 3rd ventricle during 12 s breathhold (black bar, subject #9).

Discussion and Conclusion

The results provide unambiguous evidence that inspiration is the main driving force for CSF dynamics in healthy human subjects, in particular during forced breathing. Consistent with previous studies we also found a cardiac-related CSF flow component at higher frequency though at much lower amplitude. Our identification of inspiration as the main mechanism behind CSF flow is in contrast to studies which determined cardiac-related pulsations as the most important regulator. This is of no surprise because electrocardiogram-synchronized MRI acquisitions are unable to detect any non-periodic processes which are not synchronous to the heart beat which particularly refers to slower respiratory modulations. Inspiratory thoracic pressure reductions have been shown to affect the intracranial CSF dynamics by direct exposure of the veins around the thoracic vertebral column which transmit the pressure changes via abundant anastomoses into the epidural venous system of the spinal canal [9]. In conclusion, the approach will enable us to study the pathophysiology of various forms of hydrocephalus and to design appropriate therapeutic strategies.

References: 1. Enzmann *Radiology* 1991:178:467; 2. Schroth *Neuroradiology* 1992:35:10; 3. Bhadelia *AJNR* 2013:34:1857; 4. Yamada *Fluid and Barriers of the CSF* 2013:10:36; 5. Uecker *NMR Biomed* 2010:23:986; 6. Zhang *Quant Imaging Med Surg* 2014:10; 7. Frahm *The Open Med Imaging J* 2014:8:1; 8. Schaetz *Lect Notes Comp Sci* 2012:7439:114; 9. Williams *Acta Neurochir* 1981:58:167.