Measurement of Cerebrospinal Fluid Flow in the Aqueduct of a Rat Model of Hydrocephalus

R. D. Hazel[1], E. J. McCormack[2], J. Miller[3], J. Li[3], M. Yu[4], H. Benveniste[5], J. P. McAllister II[3], M. Egnor[6], M. E. Wagshul[7]

[1]Department of Neurological Surgery, Stony Brook University, Stony Brook, New Yory, United States, [2]Department of Biomedical Engineering, Stony Brook University, Stony Brook, New York, United States, [3]Department of Neurological Surgery, Wayne State University School of Medicine, Detroit, Michigan, United States, [4]Medical Department, Brookhaven National Laboratory, Brookhaven, New York, United States, [5]Department of Anesthesiology, Stony Brook University, Stony Brook, New York, United States, [6]Department of Neurological Surgery, Stony Brook University, Stony Brook, New York, United States, [7]Department of Radiology, Stony Brook University, Stony Brook, New York, United States

Abstract:

We present the first demonstration of cardiac-gated MRI measurements of pulsatile cerebrospinal fluid (CSF) flow in both control rats and in a new rat model of communicating hydrocephalus (HC). Such measurements are extremely valuable as a non-invasive tool for monitoring functional changes in intracranial dynamics over the course of the development and progression of HC. Images were taken using a fully balanced steady state free precession phase contrast (PC-bSSFP) sequence to visualize CSF flow in the cerebral aqueduct of the rat. While flow could not be detected using a standard spoiled gradient echo sequence, it was easily seen using PC-bSSFP. Peak velocity measured was 0.4 cm/s in a control rat and 0.9 cm/s in the HC rat. Net stroke volume in the control rat was 9.9 nanoliters, while net stroke volume in the HC rat was 54.6 nanoliters. These stroke volumes are approximately 1000 times smaller than those seen in humans. The ability to obtain quantitative measures of CSF flow in the rat will be a tremendous advantage in developing and studying induced hydrocephalus and in using these animals to test theoretical models of intracranial dynamics.

Introduction:

For many years, research, clinical evaluation and the treatment of hydrocephalus has been dominated by the CSF bulk flow model. However, MRI flow techniques have elucidated the importance of pulsatile CSF in intracranial dynamics and measurement of CSF pulsatility in the cerebral aqueduct is often used to evaluate these patients. The study of bulk flow in experimental animal models of HC has been used for many years and has allowed us to gain much knowledge and understanding of this disease. Two major components have been lacking from these animal studies. First, the majority of experimental models of HC, even models involving kaolin injections into the cisternum magnum, are basically non-communicating HC models because of either complete or partial blockage of the fourth ventricular outflow. Secondly, there has been no technique for measuring pulsatile CSF flow properties in these models.

The best example of the use of quantitative measurement in communicating HC is in the evaluation of aqueductal stroke volume in normal pressure HC in order to predict the probability of shunt success. Bradley [1], for example, has established a threshold of 42 µl, above which the likelihood of success for shunting is deemed high. Alperin has developed a measure of net intracranial compliance through measurements of CSF and blood flow at the craniocervical junction [2]. However, no one has rigorously tested these types of quantitative measures in an experimental animal model where the HC and flow parameters can be assessed regularly, and non-invasively, over the course of the progression of the disease. In this study, we have demonstrated that CSF flow can be measured in a rat, and present preliminary flow measures in a control and a hydrocephalic rat.

Methods:

Images were acquired on a 9.4T Bruker Avance MRI system (Bruker Biospin MRI, Inc.) The PC-bSSFP sequence (V_{enc} = 2.0 cm/s, TE/TR = 5.5/11 ms) was calibrated using a steady flow phantom. Adult Sprague-Dawley rats were anesthetized with Nembutal (40 mg/kg), and Glycopyrulate (0.1 mg/kg) to reduce salivation, and allowed to breath spontaneously while anesthesia was maintained with isoflurane (1- 2 %). Heart rate, body temperature and respiration were monitored with a small animal monitoring and gating system (SA Instruments, Inc.). Each rat was immobilized supine with its head resisting on a 3 cm diameter surface coil. ECG-gated cine images (FOV = 4cm, 192 x 256, slice = 1mm, 16 frames/cycle) were acquired over a cardiac cycle. Images were processed using Matlab (The MathWorks Inc., Natick, MA) to produce velocity maps.

Hydrocephalus was induced in the rats with two methods, using 25% kaolin into the sub-arachnoid space (SAS). Method 1: Basal cisterns injections: After anterior exposure of the C1-clivus interval, a blunt 30-36 gauge needle was advanced into the SAS and 20-50µl of kaolin was injected. Method 2: Cortical injections: A craniotomy was created over both cerebral hemispheres, and a curved, blunt tip 25G needle was advanced gently into the SAS. After separating the partitions in the SAS, a total of 50-60µl of kaolin was injected.

Results:

All rats undergoing kaolin injection maintained normal behavioral activity. In rats with basal injections, kaolin was observed grossly in the basal cisterns but not in the cerebello-pontine angle, indicating that communicating - not obstructive - hydrocephalus had been induced. Ventricular dilation was confirmed by measurement of an increased Evan's ratio (mean 0.43).

The aqueduct was clearly distinguishable in PC-bSSFP images (Figure 1) compared to regular gradient echo images where it is not visible due to poor CSF signal-to-noise ratio. Figure 2 shows the CSF flow velocity profile measured over one cardiac cycle in a normal rat. The peak velocity in the control rat was 0.4 cm/s, while in the HC animal it was 0.9 cm/s. The stroke volume in the control HC rat was 9.9 nanoliters, and 54.6 nanoliters in the hydrocephalic animal.

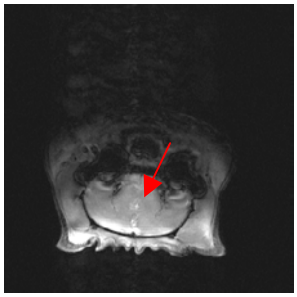

Figure 1: PC-bSSFP image of an axial slice of the brain showing the aqueduct near the center, in a control rat.

Discussion:

Egnor *et al* [3] have suggested that communicating hydrocephalus is primarily the result of redistribution of intracranial CSF and arterial pulsatility. They propose that the normal ratio between the subarachnoid and ventricular pulsatility is altered by increased impedance in the subarachnoid space, which redirects the arterial pulsations entering the cerebrovascular tree away from the subarachnoid CSF and into the ventricular CSF. Validation of this theory depends on the ability to measure pulsatility in the intracranial vascular and CSF spaces.

We have developed a rat model to reproducibly create communicating hydrocephalus using basal kaolin injections, and demonstrated the ability to measure pulsatility in the aqueduct. Increased pulsatility in the hydrocephalus model, as predicted by the theory, was observed in this preliminary study. Improvements in our technique will allow accurate measurements of the distribution of CSF pulses throughout the cranium in the rat model.

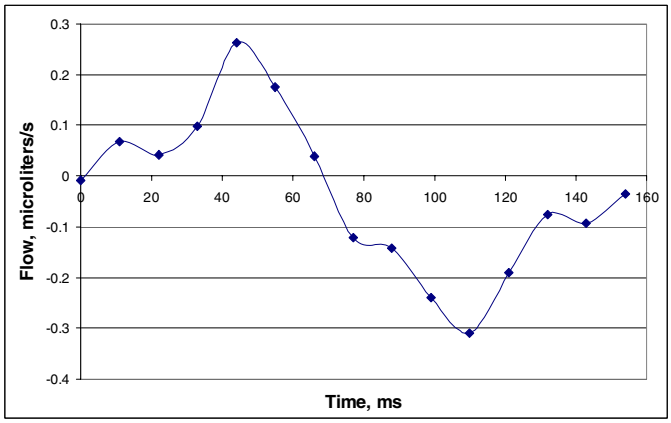

Figure 2: Measured CSF flow velocity in the aqueduct of a control rat.

References:

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