

Oral presentation

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Measurement of capillary pulsations in the rat neocortex with two-photon laser scanning confocal microscopy

James P McAllister*, Mark E Wagshul, Shams Rashid and Jie Li

Address: Department of Neurosurgery, Primary Children's Medical Center, Salt Lake City, Utah, 84132, USA

Email: James P McAllister* - pat.mcallister@hsc.utah.edu

* Corresponding author

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Background

Hydrocephalus is associated with increased pulsations in the cerebral aqueduct, as demonstrated by cine MRI, as well as increased pulse pressure, as demonstrated by invasive intracranial pressure monitoring. What has yet to be elucidated is the relationship between increased pulsations and the pathophysiology of hydrocephalus. Are increased pulsations an important component of the pathophysiology, or simply an artefact of decreased intracranial compliance? We have shown that under normal circumstances, the transmission of arterial pulsations into the cranium is minimized (the so-called Windkessel effect). In this paper, we sought to demonstrate this effect directly by measuring capillary pulsations with two-photon laser scanning confocal microscopy.

Materials and methods

Sprague-Dawley rats (4) were anesthetized and a cranial window was created. The dura was left intact and the craniotomy sealed with a coverslip to maintain intracranial physiology. Imaging was performed with a custom-built microscope (Olympus FV300 confocal microscope with a 1.5 W Ti: Sapphire laser, externally mounted Hamamatsu PMT's and an NA 0.9, 60× water immersion objective). A fluorescent dye (70 KDa Dextran fluorescein) was injected into the tail vein. Fluorescent vessels with diameters from 5-15 μm and depths of 50-300 μm below the pial surface were chosen. Flow was measured by repeatedly scanning a vessel and observing the dark unlabeled red blood cells flowing through the bright labelled

plasma background. Flow pulsatility was defined by the pulsatility index, i.e. peak to peak flow (over each cardiac cycle) divided by mean velocity.

Results

Reliable flow waveforms were detected in approximately 100 vessels with a mean diameter of 10.96 ± 2.54 μm, and at a mean depth of 175.62 ± 56.58 μm from the pial surface. Mean flow velocity was 0.75 ± 0.55 mm/sec and mean pulsatility index was $21.2 \pm 13.2\%$. Data from ongoing experiments in hydrocephalic animals will also be presented.

Conclusion

We have demonstrated the feasibility of measuring intracranial capillary pulsatility within the neocortex of healthy rats. These preliminary measurements show that pulsations are transmitted from the macrovascular arterial flow into the microvasculature. However, the amplitude of these flow pulsations is small compared to the mean blood flow velocity. As a comparison, pulsatility is commonly measured in humans within the intracranial macrovasculature (e.g. MCA) using transcranial ultrasound Doppler studies and is found to be 80-90% of the mean flow. This technique will enable the study of changes in capillary pulsatility in rat models of hydrocephalus and its relationship to disease pathophysiology.