

Vasospasm and phlebotasia following subarachnoid hemorrhage

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Target Audience: neurologists and researchers interested in subarachnoid hemorrhage and its effects on artery and veins

PURPOSE: Subarachnoid hemorrhage (SAH) is a medical emergency. Vasospasm is a hallmark of human SAH and needs to be promptly treated¹. Similar animal MRI studies of vasospasm in SAH are sparse. Moreover, SAH's effects on veins remain unknown in both SAH patients and animal models of SAH. This study investigated the effects of SAH on cerebral arteries and veins in an established rat model of SAH using MR angiography (MRA) and venography (MRV).

METHODS: Male Sprague-Dawley rats (n=6 for SAH, n=4 for control, 350-400 g) were studied under 1.2% isoflurane anesthesia. SAH model was created using a modified intracisern autologous blood infusion method². PE-10 tubing with artificial CSF/blood pre-loaded was inserted into and positioned within the cistern magna. MRI was performed on a Bruker 11.7-T/16-cm scanner before and again 1hr, 3hrs, 2 days and 7 days after 300 μ L of artificial CSF (ACSF) or blood injected remotely without taking the animal out of the scanner.

For MRA, a 3D FLASH sequence was used with TE/TR=2.125/15ms, FA=25°, band width=100kHz, FOV=25.6×20.8×12.8mm, matrix=256×256×256 (100×80×50 μ m). Horizontal angiograms were generated by maximum intensity projections. Horizontal angiograms were reconstructed into 50×50 μ m before running a customized MATLAB code to measure the artery diameter.

For MRV, a 3D FLASH sequence was used with TE/TR=12/40 ms, FA=20°, band width=20kHz, FOV=25.6×25.6×12.8mm, matrix=256×256×128 (100×100×100 μ m). Axial venograms were generated by minimum intensity projections every 15 slices. Regions of interest (ROIs) were drawn in cortex across multiple slice images. Vein volume change was measured by calculating the proportion of low-density pixels against pre-injection condition.

RESULTS: Figure 1 shows MRA before and after SAH, and the group arterial diameter differences from pre SAH. Vasospasm is apparent immediately after SAH compared to controls, normalized at 150mins, but returned on day 2 in some animals.

Figure 2 shows the MRV before and after SAH, and the group venous volume differences from pre SAH. SAH also markedly affected the veins. Venous volume and diameters markedly increased compared to controls.

Note that artificial CSF (control) group did not significantly change arterial diameters but increase venous volume slightly.

DISCUSSION & CONCLUSION: In acute phase, autologous blood spilled into subarachnoid space led to severe arterial vasospasm. Its effects appeared transient and biphasic. Arterial vasospasm was not a result of potential increase in intracranial pressure given that equal amount of artificial CSF did not cause significant vasospasm. By contrast, autologous blood induced venous volume change in both control and SAH model, suggesting potential increased intracranial pressure could be an important factor for early brain injury by impeding vein reflux.

Furthermore, the vein morphological dilation potentially induced by blockage of venous reflux may participate in the pathogenesis associated with high intracranial pressure in the brain³. Blockage of venous reflux is commonly thought to exert its deleterious effect on the brain by a simple reduction in cerebral perfusion pressure resulting in cerebral ischemia, increased blood-brain barrier permeability and brain edema⁴. Our studies point to an additional and underappreciated set of physiologic effects that are caused by subarachnoid hemorrhage.

REFERENCE: 1) Connolly ES Jr, et al. Stroke. 2012; 43:1711. 2) Barry KJ, et al. Stroke. 1979; 10:538. 3) Nedelmann M, et al. J Neurol. 2009; 256:964. 4) Bragin DE, et al. Stroke. 2013; 44:177.

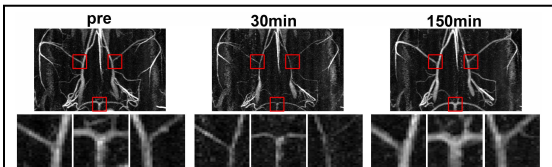


Figure 1A. MRA pre-, 30min, 150min after artificial CSF (control) and blood injection (SAH). ROI showed bilateral middle cerebral artery and basilar artery.

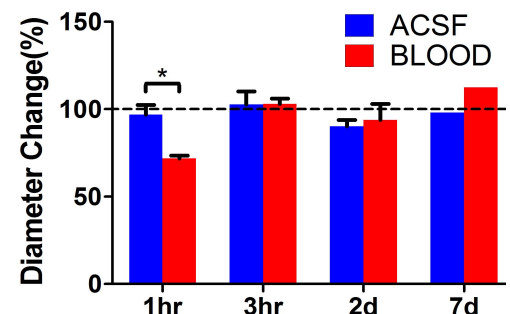


Figure 1B. Group-averaged arterial diameter differences from pre artificial CSF and blood injection.

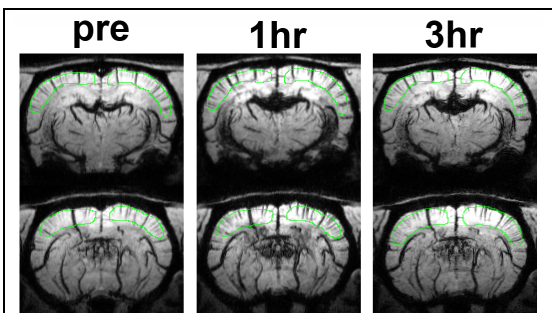


Figure 2A. MRV pre, 1hr after artificial CSF (control) and blood injection (SAH).

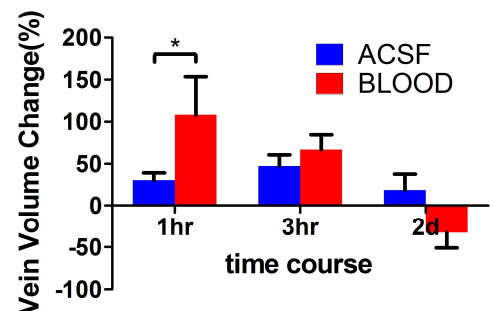


Figure 2B. Group venous volume difference from pre artificial CSF and blood injection.