Acute hypotension reduces venous cerebral blood volume

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Introduction:
The changes in cerebral blood volume (CBV) under hemorrhagic hypotension remain controversial. Studies using a variety of methods, including autoradiography, x-ray fluorescence and microscopy have generally demonstrated either increases in CBV or constant CBV within autoregulatory conditions. [1]. Most of these studies have focused on total or arterial CBV, as it is more straightforward to measure these parameters. Based on the signal model proposed by Yablonskiy [2] and imaging methods developed by An and Lin [3], venous blood volume measurements can be performed in-vivo. Thus, we sought to explore the behavior of the venous CBV under the conditions of severe hemorrhagic hypotension (SHH) and labetalol induced hypotension.

Methods:
The Institutional Animal Care Committee approved all protocols. The femoral artery was cannulated in each of five female Long Evans Rats (300 +/- 25 grams). The animal was ventilated with medical air through a tracheotomy. Pancuronium bromide (1 ml/kg) was utilized to prevent the animal's own respiration drive. Animals were imaged on a Siemens 3.0T Allegra, with a custom birdcage coil (4.3 cm diameter). A multi-echo sequence with a SE-TE of 10msec and 22 additional gradient echoes following the SE was used to acquire 23 images. Hereafter, this sequence will be referred to as SEFID. A ΔTE of 4.0 msec was used between two adjacent echoes. Imaging parameters was as follows: TR=1.5 sec, 10 averages, FOV=43 x 43 mm with a matrix size of 64x64 and 1 mm slice thickness.

Prior to manipulations, a baseline CBV measurement was performed using the SEFID sequence. Two different models of hypotension were used, labetalol (2.5 mg/kg) administration (4 animals) with blood withdrawal and acute blood withdrawal (1 animal). For the labetalol administration, a high dose of labetalol was administered immediately after baseline CBV measurements. Blood (1cc) was then withdrawn from the femoral artery at a rate of 0.5 ml/min, immediately after which the SEFID images were acquired. This was repeated twice for each animal, with a total of 2cc's of blood removed. For the SHH model, 3cc of blood were acutely withdrawn, followed by the SEFID acquisition. A small dose 0.25mg/kg of labetalol was administered to maintain cardiac output. Blood pressure measurements were available for two animals of the labetalol and the SHH animal using a second femoral artery cannulation. A region of interest encompassing both hemispheres in the subcortical area was drawn on the image slice from each animal. Based on the signal model, the CBV is the difference between the actual acquired SE signal and the signal extrapolated from the R2* decay back to the time of the SE. In other words, the log of the signal was fit to a curve where $\ln S(t)=a - R2^*(t)$ using the last 15 points of the decay curve. CBV is then equal to the difference between extrapolated and actual signal, or $CBV= a - \ln S(0)$.

Results
Mean baseline venous CBV for all of the animals was 2.8% +/- 0.54%. Mean blood pressure (MBP) for two of the labetalol animals was 111.7 +/- 7.5 mmHg at baseline, and 116 for the SHH animal. The average MBP after labetalol administration was 70 +/- 5.7 mmHg and stayed relatively constant throughout the experiment. The SSH animal with 3cc of blood removed had a MBP of 40.1 mmHg after blood removal. Results for the individual animals are located in Figure 1 with vCBV plotted against blood removed.

Table 1. Labetalol hypotension model		
Model	Blood Withdrawn (cc)	Mean CBV (%)
Labetalol	0	2.8 +/-0.54
Labetalol	1	2.5 +/- 0.77
Labetalol	2	1.9 +/- 0.20

Table 2. Severe hemorrhagic hypotension model		
Model	Blood Withdrawn (cc)	Mean CBV (%)
SHH	0	3.4 %
SHH	3	0.45 %

Discussion and Conclusion
The physiological reaction of the cerebral vasculature to hypotension remains controversial. We utilized two different hypotension models to examine the behavior of the venous vasculature in response to hypoxia. Both the labetalol and acute blood withdrawal act to reduce blood pressure, through pharmacological and physiological means. Based on these results, it appears that the drop in blood pressure causes a reduction of venous cerebral blood volume, while total CBV increases. This may be due to the collapse of venous blood vessels, generally considered to be capacitance vessels under the low blood pressure. Combined with the results of Zaharchuck et al, [1], this would suggest that the arterial vasculature under hypotension must be dilated to account for the lack of total blood volume changes. Further work is needed to fully explore this behavior under these pathophysiological conditions, but the measurement of vCBV should be able to greatly contribute to our overall understanding of the cerebral vasculature.

References: 1. Zaharchuck G, et al. Stroke 1999; 30: 2197-2205. 2. Yablonskiy DA, MRM. 1998 Mar;39(3):417-28. 3. An H and Lin W MRM. 2002 Oct;48(4):583-8.