Cerebral arterial blood volume and blood flow in hypertensive and normotensive rats

Tae Kim[1] and Seong-Gi Kim[1]
[1]*University of Pittsburgh, Pittsburgh, PA, United States*

Introduction

In chronic hypertension, the structure of cerebral arterial vessels becomes altered to cope with increased arterial vessel resistance. It produces a narrowed lumen of *arterial* vessels (1,2), reducing *arterial* cerebral blood volume (CBV_a). These alterations in arterial blood vessels are concurrently associated with cerebrovascular diseases, such as stroke, vascular dementia, and cognitive impairment. Since hypertension most alters the arterial side of vessels, noninvasive imaging assessment of CBV_a is of great clinical relevance for the early diagnosis of hypertensive vascular dysfunction. In this study, we applied magnetization transfer (MT)-varied arterial spin labeling (ASL) technique (3) to a well-established hypertensive animal model (spontaneously hypertensive rats, SHR) and a control model (Wistar Kyoto rats, WKY) to assess quantitative CBV_a and cerebral blood flow (CBF) mapping for regional detection of hypertensive cerebrovascular morphological changes in the baseline condition.

Methods

3 - 5 months old of eight SHR and nine WKY were used. The animals were anesthetized with ~ 1.3 % isoflurane with air supplemented with O_2 to attain a total O_2 level of ~30%. Rectal temperature, blood pressure and blood gases were maintained within normal physiological ranges. Five 2-mm thick coronal slices were acquired on a 9.4 T/31 cm Varian NMR system using the single-shot spin-echo echo planar imaging (EPI) technique with matrix size of 64 (readout) × 32 (phase-encoding) and FOV = 3.0 × 1.5 cm^2. Two actively detunable RF coils were used; a neck coil provided ASL, while a head coil detected image signals and generated MT effects. In each animal, CBV_a and CBF were simultaneously measured by the MT-varied ASL technique (3). Two different targeted MT saturation levels in tissue (S_{sat}/S_0 = 1 and 0.5, where S_{sat} and S_0 are the equilibrium signal in the presence and absence of MT saturation) were achieved by adjusting the power level of MT-inducing RF pulses with +8500 Hz off-resonance frequency to separate tissue and arterial blood signals; pairs of interleaved ASL and MT pulses were repeated during the spin preparation period (2.75s). TR = 3 s and TE of 18 ms were used. CBV_a and CBF were determined from the slope and intercept of the linear fit of normalized ASL ($\Delta S_{sat}/S_0$) vs. control (S_{sat}/S_0) values for results at the two MT levels. Since steady state was not achieved during the relatively short spin preparation period, CBF values were corrected by multiplication with [1-exp(-TR/T_{1app})], where T_{1app} (apparent T_1) = 1.9 s.

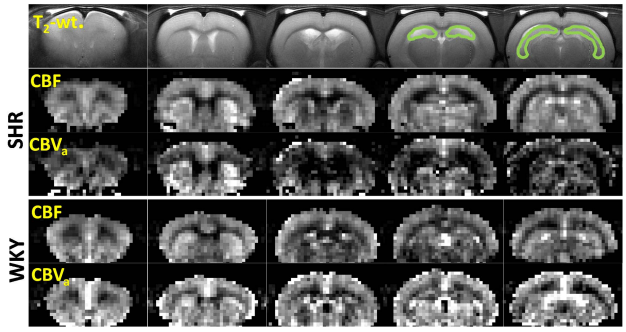

Fig. 1. Multi-slice baseline-condition brain studies at 9.4 T include high-spatial resolution T_2-weighted anatomical images and quantitative maps of CBF and CBV_a from hypertensive (top 3 rows) and control (bottom 2 rows) rats anesthetized with isoflurane. Baseline values for CBF and CBV_a are lower in white vs. gray matter, as expected. Baseline CBV_a is generally lower in hypertensive studies, while baseline CBF is less affected, possibly due to autoregulation. Columns show 5 contiguous 2-mm thick coronal slices. Gray scale: 0-300 ml/100g/min fo r CBF and 0-3 ml/100 g for CBV_a. Green ROI: hippocampus

Results and Discussion

Quantitative multi-slice maps of CBV_a (units of ml / 100 g) and CBF (units of ml / 100 g / min), with T_2-weighted anatomical images were obtained for SHR (MABP ~140 mmHg) and WKY (MABP ~90 mmHg) rats. Fig. 1 shows CBF and CBV_a maps from a representative animal of each group, and Fig.2 shows regional baseline values for SHR vs. WKY. Quantified CBV_a values from SHR were generally smaller than those from WKY, while CBF values were less different agree with previous finding (4). Hippocampal values of CBV_a in SHR are significantly lower than those of SHR (*$p < 0.01$), indicating that region-dependent hypertension-induced cerebrovascular changes may indeed occur. The smaller CBV_a of hippocampus in SHR is possibly related to vascular dementia of this model (5). This study shows CBV_a can be a key indicator to detect regional cerebrovascular impairment in hypertension and follow its progression as hypertension advances.

References: 1. Baumbach and Heistad, Hypertension 1988, 2. Laurent et al., . Hypertension 2005, 3. Kim and Kim, MRM 2006, 4. Leoni et al., Neuroimage 2011, 4. Sabbatini et al., Mech Ageing Dev 2002.

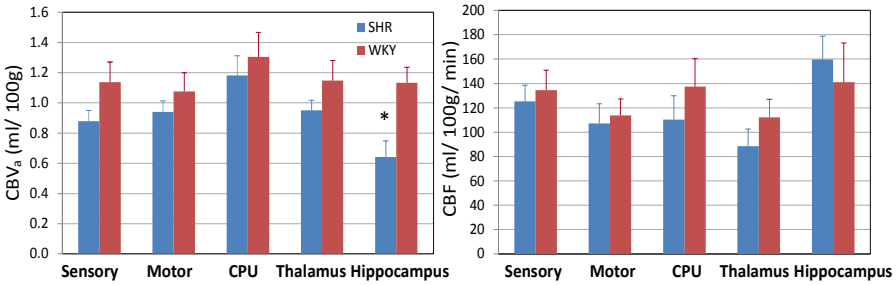

Fig. 2. CBV_a and CBF quantification of multiple tissue regions. CBV_a values of hippocampus region in SHR were significantly lower than WKY (*$p < 0.01$), indicating CBVa is more sensitive biomarker for hypertension. Error bar: SEM. CPU: caudate putamen