

## MRI Investigation of Cerebrovascular Reactivity and Neurovascular Coupling in Chronic Hypertension

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**Target Audience:** neuroscientists and hypertension researchers

**PURPOSE** Chronic hypertension could alter cerebrovascular reactivity and neurovascular coupling, increasing susceptibility to brain disorders, such as ischemic stroke and cognitive decline, among others. The goal of this study is to evaluate the effects of chronic hypertension on fMRI responses to hypercapnic (5% CO<sub>2</sub>) challenge and to forepaw stimulation in chronic hypertension in an established animal model, the spontaneous hypertensive rats (SHR).

**METHODS** Male SHR (N=7) and WKY (N=6) rats at 38~40 weeks old were studied. Body weight, heart rate and tail mean-arterial-blood pressure (MABP) in awake conditions were measured before each MRI section.

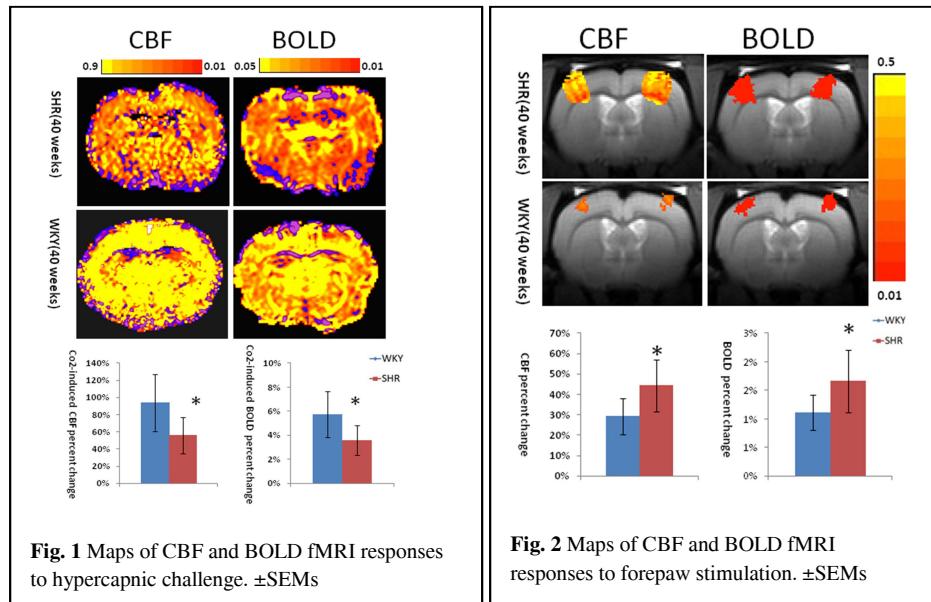
MRI was performed on an 11.7-Tesla Bruker Biospec scanner with a surface coil for brain imaging and a neck coil for arterial-spin labeling. Combined CBF and BOLD measurements were made using the continuous arterial spin-labeling technique with single-shot, gradient-echo, echo-planar-imaging (EPI) acquisition. Paired images were acquired alternately—one with arterial spin labeling and the other without (control). MRI parameters were: TR=3 s, TE=20 ms, matrix=96×96, and FOV=25.6×25.6 mm. Hypercapnic challenge for study used 5% CO<sub>2</sub>. Bilateral forepaw stimulation used 4 epochs (96 s OFF and 30 s ON) of 2 mA, 8 Hz and 1 ms pulse with the two forepaw stimulated. Five repeated trials were made for each condition on each animal. Breaks of 5 min were given between trials. Error bars are ±SEMs.

**RESULTS and DISCUSSION** At 40 weeks, blood pressure was statistically different between WKY and SHR (109 ± 10 versus 180 ± 13 mmHg, P<0.05). Basal WKY CBF was significantly higher than SHR CBF at 40 weeks (0.72±0.13 vs 0.62±0.03 ml/g/min, P<0.05). **Fig. 1** shows the group-averaged maps of CBF and BOLD fMRI responses to 5% CO<sub>2</sub> challenge at SHR and WKY rats. The group-averaged CBF and BOLD fMRI responses to 5% CO<sub>2</sub> challenge from the S1 ROIs were statistically smaller (P<0.05) in SHR than that in WKY. The CBF: BOLD % change ratios of WKY and SHR were 21±7 vs 14±2 (P<0.05). The reduced cerebrovascular reactivity in chronic hypertension suggests that 5% CO<sub>2</sub> challenge might have reached the maximal cerebrovascular reserve.

**Fig. 2** shows the group-averaged maps of CBF and BOLD fMRI responses to forepaw stimulation at SHR and WKY rats. fMRI responses to bilateral forepaw stimulation were localized to forepaw primary somatosensory cortex (S1) as expected. Forepaw-evoked CBF and BOLD responses were statistically greater in SHR than that in WKY rats (P<0.05). This is opposite that of hypercapnic challenge. Our finding is consistent with a previous study that found increased arterial blood pressure is accompanied with an enhanced evoked response (1). It is possible that higher blood pressure yielded greater CBF and BOLD responses when the evoked changes are relatively small and the neurovascular coupling is within the autoregulatory ranges.

The CBF: BOLD % change ratios of WKY and SHR were 27±6 versus 28±9, P>0.05). Both of these ratios are similar to the ratio for 5%CO<sub>2</sub> in WKY, supporting the notion that the neurovascular coupling is still within the autoregulatory ranges with the relatively mild forepaw stimulus.

**In conclusion**, we found that chronic hypertension alters cerebrovascular reactivity and neurovascular coupling, indicative of reduced cerebrovascular reserved.



**REFERENCES:** (1) Tuor UI et al. JCBFM 2007 Nov; 27(11): 1819-29.