Arterial Spin Labeling Quantification of Cerebral Blood Flow and Cerebrovascular Reactivity to Carbon Dioxide in Normotensive and Hypertensive Rats: A Comparative Study

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INTRODUCTION

Arterial spin labeling (ASL) has evolved into an important tool to obtain quantitative maps of perfusion non-invasively [1, 2] and has become remarkably useful for the diagnosis of cerebrovascular diseases [3]. Following recommendations of the Stroke Therapy Academic Industry Roundtable (STAIR) [4], there has been an increase in the number of studies utilizing experimental animal models more closely associated with patient pathophysiology. In particular, animal models of cerebral ischemia play an important role in the study of stroke and other cerebrovascular diseases. The spontaneously hypertensive rat (SHR) is a strain that exhibits spontaneous elevated blood pressure, resulting in vascular remodeling, that has been widely used as an experimental model of hypertension and stroke [5]. A recent study [6] reported higher cerebral blood flow (CBF) values in this strain when compared to normotensive rats. In the present study, CBF and the cerebrovascular reactivity to carbon dioxide were obtained in normotensive and hypertensive rats using continuous ASL (CASL).

MATERIALS AND METHODS

Sprague-Dawley rats (SDR) (N=6) and SHR (N=6), weighing 250-400g, were anesthetized under isoflurane (2-2.5%) in a 2:2:1 mixture of medical air, nitrogen, and oxygen and scanned in a horizontal 7T/30cm magnet (Bruker-Biospin, Billerica, MA) equipped with gradients capable of 450mT/m amplitude (Resonance Research Inc, Billerica, MA). A home-built, transmit-only birdcage volume RF coil, 12 cm internal diameter, and a commercially-built, receive-only quadrature surface coil (RAPID Biomedical GmbH, Rimpar, Germany), were used for all image acquisition. A small figure-8 shaped labeling coil [7] was positioned under the neck of the animal, approximately 2cm away from isocenter. All coils were equipped with active decoupling circuits to minimize coil-to-coil interferences during the labeling and imaging phases of the experiment, and to avoid off-resonance saturation of water in the acquisition region [7]. For induction of hypercapnia, the inhaled gas composition was changed to 5% and 10% CO_2 in the original mixture. A five minutes adjustment period was allowed before starting the acquisition. Single-shot echo-planar images were obtained during CASL achieved with flow-driven adiabatic inversion using TR/TE=5000/48ms, FOV=2.56x2.56cm, matrix=128x128, slice thickness=2mm, and 30 averages.

RESULTS

Figure 1 shows representative multislice anatomical and CBF maps obtained at normocapnia from an SDR (Fig. 1a-b) and an SHR (Fig. 1c-d). Whole brain CBF values in SHR rats (146±33 ml/100g/min, N=6) were significantly higher than in normotensive rats (113±18 ml/g/min, N=6, $p<0.05$). Fig. 2 shows the variation in CBF in both strains in response to hypercapnia challenges. Both strains had a significant increase in CBF in response to CO_2. Whole brain CBF values in SHR (186±44 ml/100g/min (5% CO_2); 195±44 ml/100g/min (10% CO_2)) were significantly higher than in normotensive rats (147±27 ml/100g/min (5% CO_2), $p<0.05$; 166±29 ml/100g/min (10% CO_2), $p<0.05$) at all conditions. Fig. 3 shows the relative cerebrovascular reactivity to CO_2 for both strains. The CBF reactivity to 5% CO_2 was similar for both strains: 31±7% for SDR and 28±6% for SHR, $p > 0.05$. However, SHR showed a significantly decreased reactivity to 10% CO_2 (34±6%) in comparison to normotensive rats (47±9%), $p<0.05$.

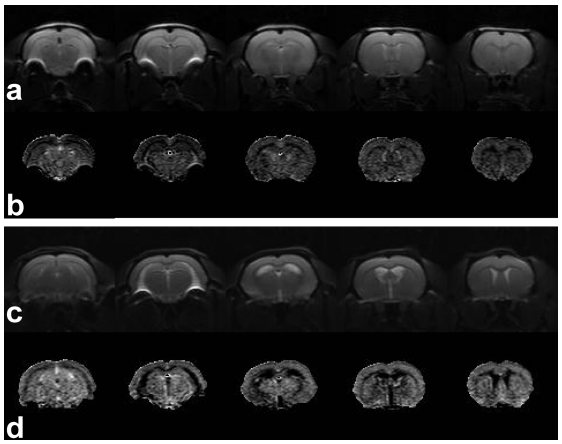

Figure 1: (a) Representative coronal images obtained from a SD rat and its (b) corresponding CBF maps. (c) Representative coronal images obtained from a SHR rat and its (d) corresponding CBF maps.

DISCUSSION AND CONCLUSIONS

The CBF increases obtained for normotensive rats at all CO_2 levels are in good agreement with previously published data [8]. As well, a lower CO_2 reactivity has been reported in SHR rats [9], although anesthesia may significantly influence this property [10]. In summary, continuous arterial spin labeling with a dedicated labeling coil was employed to compare resting and hypercapnic CBF in normotensive and hypertensive rats. The characterization CBF as well as vascular reactivity in SHR rats will allow future detailed studies in this strain of animals.

REFERENCES

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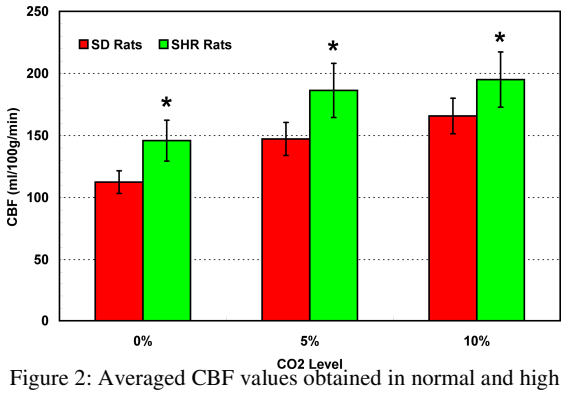

Figure 2: Averaged CBF values obtained in normal and high flow states (5% and 10% CO_2) in normotensive and hypertensive rats.

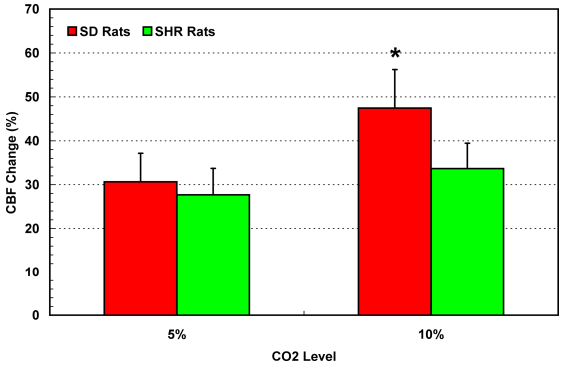

Figure 3: CBF percentage changes during hypercapnic (5% and 10% CO_2) challenge in normotensive and hypertensive rats.