Age-dependent impairment of the cerebrovascular reactivity to CO2 in spontaneously hypertensive rats: an ASL study

R. F. Leoni1,2, F. F. Paiva1, D. B. de Araujo2, and A. C. Silva1
1Cerebral Microcirculation Unit, NINDS, NIH, Bethesda, MD, United States, 2Departamento de Fisica e Matematica, FFCLRP, Universidade de Sao Paulo, Ribeirao Preto, SP, Brazil

INTRODUCTION

Arterial spin labeling (ASL) has been used to measure cerebral blood flow (CBF) noninvasively, by using arterial water as an endogenous tracer [1], and has become a valuable tool for the diagnosis of cerebrovascular diseases. Since hypertension is an important risk factor for stroke, it is crucial to understand its effect on cerebrovascular autoregulation [2]. Although altered cerebral autoregulation has been observed in both human and animal hypertensive models, it is useful to investigate the age relation with this problem. In the present study, CBF maps and the left and right perfusion territories were obtained in two groups of spontaneously hypertensive rats (SHR), differing in age, under normo- and hypercapnia using continuous ASL (CASL).

MATERIALS AND METHODS

Two SHR (8-9 month old), weighing 430g and 456g, were anesthetized under isoflurane (5% induction, 1.5% maintenance), orally intubated and mechanically ventilated in a 2:2:1 mixture of medical air, nitrogen, and oxygen. A PE-50 catheter was inserted into the right femoral artery for sampling of blood gases. Experiments were performed 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 4-element surface coil array (Bruker-Biospin, Billerica, MA), were used for all image acquisition. A small home-built figure-8 shaped labeling coil [3] was positioned under the neck of the animal. For induction of hypercapnia, 1.5%, 3%, 4.5%, 6% and 10% CO2 was added in the inhaled gas composition. Single-shot echo-planar images were obtained during CASL achieved with flow-driven adiabatic inversion using TR/TE=10000/28ms, FOV=3.2x3.2cm, matrix=64x64, slice thickness=2mm, labeling time = 8800ms, and postlabeling delay = 994ms. Arterial blood gases were sampled at the end of each CO2 level. Results were compared to those obtained previously with younger SHR (2 month old, N=6) at the same high field system, but adding 5% and 10% CO2 in the inhaled gas composition for induction of hypercapnia [4].

RESULTS AND DISCUSSION

Figure 1 shows representative coronal images from a SHR (fig.1a) and corresponding CBF maps obtained for normocapnia (fig.1b) and hypercapnia (fig.1c). At normocapnia whole brain CBF in young SHR (147±24 ml/100g/min, N=6) were significantly higher than in old SHR (93±17 ml/g/min, N=2, p<0.05). The same was found for 10% CO2, where whole brain CBF values were 195±42 ml/100g/min and 118±11 ml/100g/min in young and old SHR, respectively (p<0.01). Since hypercapnia was induced in five different levels for the older SHR group, it was possible to observe CBF as a function of PaCO2 (fig.2), which shows a saturation for high CO2 levels, consistent with the literature [5]. The percentage CBF changes to CO2 is also shown (fig.3). Reduced CBF and cerebral CO2 reactivity has been observed in older SHR [6,7], due to the progressive impairment in vasomotor response induced by age, mainly when combined with hypertension [8]. For both groups, right and left perfusion territories were complementary, but not completely symmetric (fig. 4). Some rats showed right (fig. 4a), while others showed left dominance (fig. 4b). These asymmetries may occur due to anatomic variations of the Circle of Willis (COW), which have been observed in healthy animals [4].

CONCLUSIONS

With the combination of CASL and a dedicated labeling coil, we have successfully investigated cerebral perfusion in hypertensive rats of different ages under normo- and hypercapnia, and observed that age can influence the ability of the cerebrovascular system to autoregulate. Findings were also reported regarding the asymmetric perfusion between brain hemispheres and they will be correlated with anatomical formation of the COW obtained by angiograms to help understanding of regional cerebral hemodynamics.

REFERENCES