Monitoring Cerebrovascular Reserve Capacity Following Bilateral Carotid Artery Occlusion In Rat Using Arterial Spin Tagging Perfusion Imaging

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Introduction
Information on the cerebrovascular reserve capacity has significant prognostic implications for the treatment of cerebrovascular disease. The cerebrovascular reserve capacity can be measured by evaluating the change of cerebral blood flow (CBF) stimulated by vasodilators such as CO2 or acetazolamide (ACZ), an inhibitor of carbonic anhydrase. In previous studies, the CBF was monitored with laser-Doppler flowmetry[1], [14C]iodoantipyrine / [14C]dextran autoradiography[2] or bolus-tracking MRI[3]. Each of these CBF measurement methods is invasive, has potential risks for the experimental subject or is terminal. Arterial spin tagging (AST) perfusion imaging is a non-invasive MRI technique for CBF quantification[4]. However, when a single coil is used for both labeling the flowing spins in the blood vessels of the neck and obtaining the perfusion images of the brain, inherent magnetic transfer (MT) effects substantially reduce the signal-to-noise ratio. In this work, a dual coil system was used for continuously monitoring the cerebrovascular reserve capacity, with a separate coil for magnetically tagging the blood spins in the neck region to avoid MT effects.

Methods
20 male Sprague-Dawley rats 180-200 g were divided into 5 groups of 4 rats each examined at 4 times (2 days, 2 weeks, 1 month and 2 months) post surgery and a control group. For surgery, the animals were anesthetized (pentobarbital, 50mg/kg). Additional anesthesia was supplemented as needed and O2 and N2O (30:70) supplied via nosecone. The common carotid arteries were exposed and separated from the cervical vago-sympathetic trunks and bilateral arterial occlusion was performed proximal to the bifurcation by double ligation with 6-0 silk suture. For MR imaging, the rat was anesthetized with halothane delivered via a nose-cone by a rodent ventilator. A polyethylene catheter was inserted into the tail artery for continuous monitoring of arterial blood pressure and blood gas analysis and a intraperitoneal tube was inserted for administration of ACZ. Rectal temperature and blood pressure were monitored continuously. Stroke volume and rate were adjusted to establish normal PCO2 at the start of the measurement.

A dual coil system was used with a butterfly labeling coil (7 mm OD). This size is larger than that used previously [5] in order to ensure full labeling of the vertebral arteries. The position of the butterfly coil was adjusted to optimize the spin tagging efficiency, α=0.8. For brain imaging a capacitively driven five-element ladder head coil (half birdcage) 40 mm long and 32 mm in inner diameter was employed. Decoupling of the two coils was achieved using PIN diodes inserted into the head coil and controlled by TTL signal from the spectrometer. Isolation was checked with a network analyzer and found to be about 40 dB.

MR images were acquired with a Bruker Biospec/3 7T/21 cm spectrometer. Perfusion imaging was done using a SNAPSHOT sequence with a TE of 2.3ms, 5 x 5 cm2 field of view, 2 mm thick slice and 128 x 128 matrix size. Labeling was done with a decoupler for a time of 3s. 16 signal averages were acquired. Control images were acquired with the labeling turned off. At each time point, after stable CBF was obtained, ACZ was injected.

Statistical analysis of the effect of ACZ was carried out using repeated measures with factors of brain region and time after surgery. Comparison of absolute CBF post surgery to that in sham-operated rats was carried out using ANOVA and LSD post-hoc comparisons.

Results
CBF changes at different times after carotid artery occlusion before and after ACZ administration along with baseline data for shams are shown in Fig. 1 and Fig. 2 for forebrain and cerebellum, respectively. Within two days CBF in the forebrain and cerebellum was significantly reduced by 52% (p<0.001) and 33% (p<0.05), resp. After two weeks the CBF was still significantly depressed by 34% (p<0.001) and 28% (p<0.05) resp., while after two months, CBF had rebounded to control level. With stimulation of ACZ, at 2 days post-surgery there was a slight CBF increase of 9±9% in the forebrain, and 37%±18% in cerebellum. Repeated measures analysis showed a significant difference between brain regions (p<0.001) but no significant change in this difference with time after surgery.

Discussion
Permanent bilateral carotid artery occlusion causes complicated CBF responses, including a rapid drop shortly after surgery and a rebound to normal level after a long recovery. The results reported here for the forebrain are consistent with the literature [2]. With ACZ stimulation, the failure of CBF to increase significantly was also reported in both animal [1] and human [3] subjects. This may be attributed to the fact that the vascular territories obtain their blood supply by way of small collateral vessels. Although the collateral vessels increase in size with time post surgery, the ACZ stimulation of flow continues to be effective only in the original perfusion territory and not in the newly supplied territory i.e. the forebrain. This could be considered to be a type of steal phenomenon [3].

References