Cerebral autoregulation impairment measured at the brain tissue level with arterial spin labeling MRI in patients with a symptomatic carotid artery stenosis

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Introduction

Patients with a symptomatic stenosis of the carotid artery have a high risk of ischemic stroke. In these patients, impairment of the vasodilatory capacity of the cerebral vasculature is an important measure of the degree of hemodynamic compromise (1). There are two basic strategies for measuring cerebral vasodilatory capacity. In the first, the flow velocity in a major cerebral artery is measured before and after a vasodilatory stimulus and in the second strategy, cerebral perfusion is measured at brain tissue level with techniques such as PET, CT or dynamic susceptibility contrast MRI. A disadvantage of these imaging methods is that they are invasive and require ionizing radiation and / or contrast agents. Furthermore, a steno-occlusive lesion in one of the brain feeding arteries may lead to a shift in the perfusion territories of these arteries, making it difficult to measure vasodilatory capacity in the complete territory of an individual artery. Recently arterial spin labeling (ASL) MRI in combination with a vascular challenge has been introduced as an alternative non-invasive technique for measuring cerebrovascular reactivity throughout the brain (2). The aim of our study was to measure the cerebral autoregulatory status of the brain tissue supplied by the individual brain feeding arteries in patients with symptomatic internal carotid artery (ICA) stenosis using arterial spin labeling (ASL) MRI and to compare this to healthy controls.

Methods and materials

Twenty-three patients (13 men; mean age ± standard deviation (SD), 69±8 years) with a recently symptomatic unilateral ICA stenosis ≥ 50% and 20 healthy control volunteers (12 men; mean age ± SD, 67±6 years were investigated on a 3 Tesla MRI scanner. All patients had suffered a transient ischemic attack (TIA) or non-disabling ischemic stroke ipsilateral to the ICA stenosis. The MR protocol consisted of a pseudo-continuous (3) and a regional perfusion imaging (RPI) ASL sequence (4;5) before and 15 minutes after administration of an intravenous bolus of 14 mg/kg acetazolamide. RPI perfusion images were acquired to determine the flow territories of the basilar and internal carotid arteries. The pseudo-continuous ASL parameters were: FOV 240x240 mm^2; 17 slices; background suppression; SENSE 2.5; label duration 1650 ms, TR 825ms; TE 14ms. For M_0 and segmentation purposes an inversion recovery sequence was acquired. For the placement of the regions of interest throughout all slices, three preprocessing steps were performed (Fig 1): first, the flow-territories of the basilar and ICAs were manually segmented on the RPI images. Second, a T_1 image was calculated from the inversion recovery sequence and segmented with SPM5 into gray and white matter probabilistic maps. Thresholding of the gray matter maps was applied to avoid partial voluming of white matter. The final step was to combine the flow territory masks with the gray matter mask. All images were co registered to correct for motion. Differences between pre and post acetazolamide CBF were tested using paired *t* test. Differences between gray and white matter CVR were evaluated with an independent *t* test.

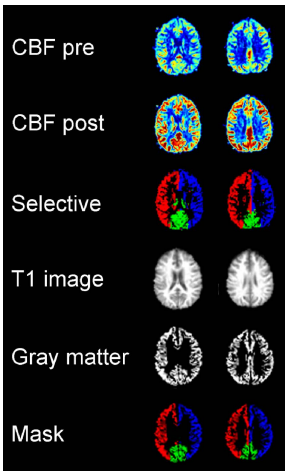

Figure 1. *Pictorial description of the pre-processing steps in a healthy 56-year old female.*

Results

Table 1 summarizes the CBF values before and after administration of acetazolamide in the flow territories of the ICAs ipsilateral and contralateral to the symptomatic stenosis, and of the basilar artery. There was a significant ($p<0.01$) increase in CBF at brain tissue level in all perfusion territories in both healthy controls and patients. In all flow territories, CBF was lower in patients than in the control group, but a reduced cerebrovascular reactivity as compared to controls was observed only in the territory of the symptomatic ICA (mean difference, -12.0%; 95 CI, -20.7 – -3.3). The cerebrovascular reactivity was lower ($p<0.01$) in the flow territory of the symptomatic ICA when compared to the contralateral unaffected ICA (mean difference, - 8.7%; 95 CI, -12.5 – -4.8). No difference in reactivity was observed between the unaffected ICA and healthy controls (mean difference, 4.7%; 95 CI, -12.9 – 6.3).

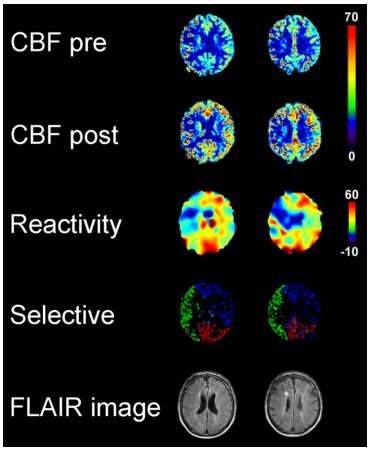

Figure 2. *Representative CBF maps pre and post acetazolamide in a 69-year old man with a symptomatic stenosis of the right internal carotid artery.*

Conclusion

The results of this study show that in patients with a symptomatic ICA stenosis, the vasodilatory capacity in the flow territories of the major cerebral arteries can be visualized and quantified at the brain tissue level with ASL MRI.

	Pre-ACZ mL·100mL^{-1}·min^{-1}	**Post-ACZ** mL·100mL^{-1}·min^{-1}	**Reactivity** (% increase)
Healthy controls			
ICA	52.2 ± 1.8	77.4 ± 3.2 *	47.9 ± 3.1
Basilar artery	48.7 ± 2.6	82.6 ± 4.8 *	69.9 ± 4.8
Patients			
Symptomatic ICA	44.7 ± 1.9	60.9 ± 3.0 *	35.9 ± 3.0 ** †
Contralateral ICA	43.1 ± 2.4	61.5 ± 3.1 *	44.6 ± 3.5
Basilar artery	42.9 ± 2.5	66.5 ± 3.7 *	56.7 ± 3.9

Table 1. *Cerebral blood flow in mL·100mL^{-1}·min^{-1} pre and post acetazolamide and the reactivity (percent CBF increase) in the territories of the basilar and ICAs.*

References

[1] Derdeyn, Brain ‘02;125:595.
[2] Detre, jMRI ‘99;10:870-875.
[3] Dai, MRM ‘08;60:1488-1497.
[4] Gevers, ISMRM ‘09;1524.
[5] Wong. MRM ‘07;58:1086-1091.