Cerebrovascular reactivity measured with arterial spin labeling MRI in the caudate nucleus, lentiform nucleus, and thalamus in patients with steno-occlusive internal carotid artery disease

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Introduction

Up to one-fourth of all first-presenting ischemic infarcts are lacunar (1). These infarcts are small lesions in the deep white matter, basal ganglia or brainstem, resulting from the occlusion of one of the deep brain structure perforating arteries (2). The lacunar hypothesis states that this is a manifestation of small vessel disease and has a different pathogenesis than cortical stroke (2). Small vessel disease has been suggested to be associated with thickened vessel walls, endothelial dysfunction and impaired hemodynamic autoregulation (3). However, studies have also shown that steno-occlusive carotid artery disease leads to hemodynamic impairement of the brain, significantly increasing the risk of stroke (4). This effect is potentially also present in the deep brain structures and may play a role in the occurrence of sub-cortical infarcts. It has been suggested that endothelial dysfunction is not specific only to small vessel stroke. (5) The aim of our study was to further disentangle small vessel disease and the impact of large vessel disease upon the autoregulative hemodynamics in the deep brain structures by investigating cerebrovascular reactivity (CVR) in subcortical regions in patients with steno-occlusive ICA disease and compare this with healthy control subjects.

Methods

Fifteen patients (13 men; mean age ± standard deviation (SD), 67±9 years) with a recently symptomatic unilateral internal carotid artery (ICA) stenosis and 18 patients (11 men; 56±16 years) with a symptomatic unilateral ICA occlusion and 21 age-matched healthy control subjects (9 men; 62±8 years) were investigated on a 3 Tesla MRI scanner (Philips Medical Systems). All patients had suffered a transient ischemic attack (TIA) or non-disabling ischemic stroke ipsilateral to the ICA stenosis or occlusion. The MR protocol consisted of pseudo-continuous perfusion ASL imaging (6) before and 15 minutes after administration of an intravenous bolus of 14 mg/kg acetazolamide. The pseudo-continuous ASL parameters were: FOV 240x240 mm^2; 17 slices; SENSE 2.5; background suppression; label duration 1650 ms, TR 4000 ms; TE 14 ms. An inversion recovery (IR) sequence was acquired for M_0-determination and segmentation purposes. For the placement of the regions of interest (ROI), three preprocessing steps were performed: first, ROIs were drawn within territory of the medial cerebral artery (MCA), and the caudate nucleus, lentiform nucleus and thalamus. Second, a T1 image was calculated from the IR sequence and segmented into gray (GM) and white (WM) matter probabilistic maps. Thresholding of the GM maps was applied to avoid partial voluming of WM. In the final step the ROIs were combined with the GM mask and the CVR was calculated from the cerebral blood flow (CBF) before and after administration of acetazolamide for the MCA territory and each nuclei.

	Reactivity			
Group and hemisphere	MCA (%)	Caudate (%)	Lentiform (%)	Thalamus (%)
Healthy controls				
Both sides	44.9 ± 2.1	54.9 ± 3.6	42.1 ± 2.3	63.5 ± 4.3
Stenosis patients				
Asymptomatic side	40.1 ± 4.9	38.7 ± 7.3	39.6 ± 3.5	64.4 ± 6.5
Symptomatic side	37.6 ± 3.8	40.1 ± 6.3	34.9 ± 4.6	59.3 ± 5.4
Occlusion patients				
Asymptomatic side	17.9 ± 4.8*†	12.3 ± 8.0*†	6.4 ± 7.0*†	41.8 ± 9.3*†‡
Symptomatic side	19.3 ± 5.0*†	12.5 ± 7.8*†	13.3 ± 6.0*†	38.1 ± 7.3*†‡

Table 1. Cerebrovascular reactivity (percent CBF increase) in the MCA territory, caudate nucleus, lentiform nucleus and thalamus.
** compared to the control group, p<0.05 (independent-t test).*
† compared to the stenosis group, p<0.05 (independent-t test).
‡ compared to the caudate and lentiform nucleus, p<0.05 (paired-t test).

Results

Table 1 summarizes the CVR values in the regions of the MCA territory, caudate nucleus, lentiform nucleus, and thalamus for the control subjects and each patient group. Figure 1 shows the perfusion images before and after administration of acetazolamide and the resulting reactivity image. For the occlusion patients the CVR was significantly reduced in the symptomatic hemisphere as well as in the asymptomatic hemisphere for the regions of the MCA, caudate nucleus, lentiform nucleus, and thalamus when compared to the healthy controls and stenosis patients. No significant differences in CVR where found between the stenosis patients and healthy controls. There were no significant differences found in CVR between the asymptomatic and symptomatic hemisphere in stenosis or occlusion patients. A non-significant trend for decreased CVR was found in the caudate and lentiform nucleus in the stenosis patients and the CVR of the thalamus was comparable to healthy controls. In the occlusion patients the CVR of the thalamus was significantly higher than in the caudate and lentiform nucleus.

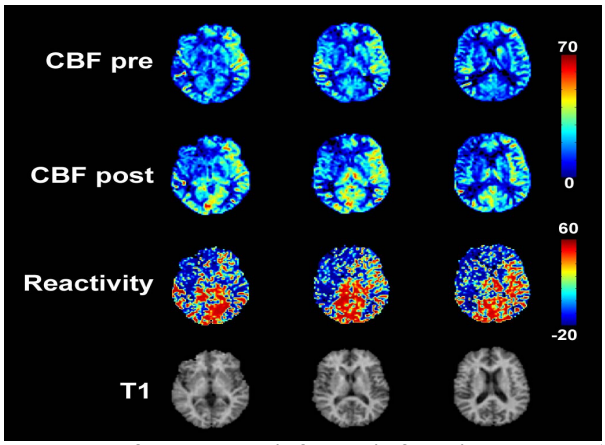

Figure 1. Perfusion images before and after administration of acetazolamide together with the reactivity images and T1 anatomical images from a patient with a right unilateral internal carotid artery occlusion. A subtle increase may be seen between the pre- and post- perfusion on the contralateral side of the occlusion, while the perfusion on the ipsilateral side remains relatively the same.

Conclusions

The results of our study show that the cerebral autoregulation of the deep brain structures is impaired in patients with steno-occlusive large-vessel disease. CVR was the most decreased in the caudate and lentiform nucleus on the side of the steno-occlusive carotid artery disease. While CVR was less impaired in the thalamus, which is fed from the posterior circulation (i.e. basilar artery). This shows that large vessel disease leads to hemodynamic impairment in the deep brain structures and may possibly cause sub-cortical ischemic infarcts. Furthermore this is of great importance when using functional measures for endothelial dysfunction such as cerebral autoregulation for imaging small vessel disease. In conclusion our study shows large vessel disease influences sub-cortical autoregulation and should be taken into account when using function measures to image small vessel disease.

References

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