The effect of cerebrovascular risk factors on regional cerebral blood flow: a population study with arterial spin labeling MRI

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Introduction:

A unique aspect of arterial spin labeling (ASL) MRI is the ability to study the regional cerebral blood flow (rCBF) non-invasively. Thus far, no ASL perfusion measurements have been performed in large population studies. This type of study offers the possibility to correlate rCBF with cerebrovascular risk factors. Knowledge on the influence of cerebrovascular risk factors on rCBF could influence therapeutic interventions in patients having (chronic) low rCBF. Thus far, the methods to measure rCBF in population studies, such as positron emission tomography and single photon emission computed tomography, use radiation or administration of intravenous agents (*Naritomi et al., Arch Neurol 1979; Meyer et al., Stroke 1985; Rodriguez et al., Stroke 1994)*. Consequently, these population studies typically involve small sample sizes and thus have limited value in showing relationships between cerebrovascular risk factors and rCBF. To show these relationships, large patient groups are required. The purpose of our study was to prospectively investigate which cerebrovascular risk factors are related to rCBF, measured non-invasively with ASL MRI, in a large patient group with symptomatic atherosclerotic disease.

Methods:

One-hundred-thirty consecutive patients (107 men and 23 women, age 58 ± 10 years) with symptomatic atherosclerotic disease were included in the study. All patients were classified into four disease categories: cerebrovascular disease, cardiovascular disease, peripheral arterial disease and abdominal aortic aneurysm. Cerebrovascular risk factors were assessed by means of a questionnaire and physical, ultrasonographic and laboratory examination. The control group consisted of ten healthy subjects (8 men, and 2 women, age 58 ± 15 years) matched for age and sex without symptomatic atherosclerosis and without abnormalities on MRI of the brain. The MRI investigations were performed by using a 1.5-T whole body system. Perfusion imaging was achieved with the turbo transfer insensitive labeling technique (*Hendrikse et al., MRM 2003)*. The perfusion imaging slice (slice thickness 10 mm) was positioned above the ventricles through the centrum semi-ovale and aligned to the orbito-meatal angle. The labeling slab (slice thickness 140 mm) was set 10 mm below and parallel to the perfusion imaging slice. For image acquisition a series of thirteen 35° excitation pulses were applied, with increasing delay times from 200 ms to 2600 ms with a constant interval of 200 ms, followed by single shot gradient EPI readout. Other MRI parameters were: TR 3000 ms; TE 5.6 ms; 62% partial Fourier acquisition; field-of-view 240 x 240 mm; matrix 64 x 64; bandwidth per pixel 3336.7 Hz; averages 50; scan time 5 minutes. In the grey matter of the flow territory of the middle cerebral arteries, regions-of-interest CBF quantification was performed on the basis of established kinetic perfusion models (*Buxton et al., MRM 1998; Gunther et al., MRM 2001)*. The $M_{a,0}$ was estimated by fitting the unlabeled signal in the brain tissue to a saturation-recovery curve. The other parameters were fixed and obtained from the literature: R_1 = 1.0 s^{-1}; R_{1a} = 0.71 s^{-1}; λ = 0.9 ml/g. The effect of the individual cerebrovascular risk factors on the rCBF was assessed by using linear regression analysis.

Results:

The baseline characteristics of the study population are given in Table 1. No significant differences were found for the rCBF between the different disease categories (Table 2). After adjustment for age and sex, hypertension (β = 6.5 ml/min/100gr; 95% confidence interval (CI) 1.4; 11.7) and hyperhomocysteinemia (β = -7.4 ml/min/100gr; 95% CI -12.7; -2.1) remained significantly associated with rCBF. Additional adjustment for the presence of cerebrovascular disease did not materially alter the associations between hypertension (β = 6.2 ml/min/100gr; 95% CI 1.0; 11.4) and hyperhomocysteinemia (β = -7.0 ml/min/100gr; 95%CI –12.2; -1.6) with rCBF. The use of anti-hypertensive medication did not affect the relation between hypertension and rCBF. No significant association was found for other cerebrovascular risk factors.

Table 1. Patients characteristics (n = 130)

Age (years)	58 ± 10
Men	107 (82)
Systolic blood pressure (mm Hg)	148 ± 25
Diastolic blood pressure (mm Hg)	86 ± 12
Hypertension	41 (32)
Body Mass Index (kg/m^2)	27 ± 4
Diabetes Mellitus	31 (24)
Hyperlipidemia	51 (39)
Hyperhomocysteinemia	30 (23)
Carotid artery stenosis	17 (13)
Smoking	
never	35 (27)
past	67 (52)
current	26 (20)
Total cholesterol (mmol/L)	5.0 ± 1.0
LDL cholesterol (mmol/L)	2.9 ± 0.9
HDL cholesterol (mmol/L)	1.3 ± 0.4
Triglycerides (mmol/L)	1.8 ± 0.9
Plasma homocysteine (μmol/L)	15.5 ± 4.9
Cerebrovascular disease	32 (25)
Cardiovascular disease	72 (55)
Peripheral vascular disease	20 (15)
Abdominal aortic aneurysm	6 (5)

Data are numbers (percentage) or mean ± standard deviation

Table 2. rCBF for patients (disease categories) and control subjects

Cerebrovascular disease (n = 32)	66 ± 13
Cardiovascular disease (n = 72)	63 ± 12
Peripheral vascular disease (n = 20)	64 ± 17
Abdominal aortic aneurysm (n = 6)	67 ± 13
Control subjects (n = 10)	72 ± 11

Data are mean ± standard deviation (in ml/min/100gr)

Conclusion:

In conclusion, to our knowledge, this is the first study to report the clinical feasibility and utility of non-invasive ASL MRI perfusion measurements in a large patient population study. Our study results show that in patients with symptomatic atherosclerotic disease, hypertension is related to a higher rCBF, possibly due to altered cerebrovascular autoregulatory function. In addition, hyperhomocysteinemia is related to a lower rCBF, possibly due to endothelial cell damage and direct neurotoxic effect.