Grey matter perfusion is inversely correlated to T2 lesion load in MS patients - a 3D GRASE arterial spin labeling study at 1.5T

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Introduction

Multiple sclerosis (MS) is a chronic inflammatory-demyelinating disease of the central nervous system, which is accompanied by axonal loss and brain atrophy. PET and MRI studies in MS patients (e.g. [1,2]) have shown reduced cerebral blood flow in cortical grey matter (GM). One hypothesis was that the perfusion reduction might be secondary to decreased metabolic demand in the GM. In the study presented here, we investigated the influence of different clinical and MRI factors, including lesion load, GM atrophy, and disease onset onto GM perfusion. To assess cerebral blood flow, we applied a pulsed arterial spin labeling (ASL) technique combined with single-shot 3D GRASE (gradient-spin echo) readout [3].

Subjects and Methods

A cohort of 177 carefully clinically characterised MS patients (123 RRMS, 42 SPMS, 7 PPMS, and 5 CIS) was recruited over 12 months in this study. Mean age was 45.6 years (range 20y-68y) and the mean disease duration was 13.8 years (range 1y-48y). Only patients without an acute relapse in the preceding four weeks were included in the study. All patients underwent a comprehensive MR examination on a 1.5 T MR-scanner (Magnetom Avanto, Siemens Medical, Germany) including PDw and T2w sequences, a volumetric 3D-T1w scan (MPRAGE, spatial resolution 1x1x1 mm^3), the ASL sequence and a T1w Gd-enhanced scan. The ASL sequence uses the FAIR spin labeling scheme [4] combined with single-shot 3D GRASE readout (26 slices, interpolated spatial resolution 2.3x2.3x4 mm^3, TE/TR/BW = 36 ms/3000 ms/2700 Hz/Px) with a total echo train length of 528 echoes [3]. For the quantification of the cerebral blood flow (CBF), a time series with 10 different TI (300 ms to 3000 ms at 300 ms increments) was acquired. For each TI, five repetitions were applied at an overall measurement time of 6 minutes.

The ASL data sets were realigned to the anatomical volumes and perfusion was estimated by fitting of a stepwise defined model [5] to the ASL time series. The MPRAGE data sets were segmented with FAST (part of the FSL software library [6]), and a GM mask was obtained and further corrected by manually excluding misclassified white matter lesions. According to the GM mask, the mean GM CBF in each patient was calculated for 10 supratentorial slices above the circle of Willis. GM atrophy was related to the fraction of GM in the intracranial volume.

Multiple linear regression (MLR) models were calculated to investigate the relationship between different factor sets and mean CBF. Based on the model with the highest R^2, post-hoc analyses were performed to explore which factors had significant influence to the observed perfusion changes in MS patients.

Results

Part of a representative ASL time series and the respective CBF map is shown in Figure 1. The mean GM CBF of our MS patients varied in a range from 19.2 ml/100g/min to 62.1 ml/100g/min (mean CBF: 40.8 ml/100g/min; SD: 8.4 ml/100g/min). In the MLR analysis, a model including T2 lesion load, age, GM atrophy, and disease duration could explain 23% of variance (adjusted R^2). Post-hoc Spearman rank correlation revealed significant correlation of adjusted CBF with T2 lesion load ($\rho=-0.35$, $p=2*10^{-6}$) and with age ($\rho=-0.23$, $p=0.002$), but not with atrophy ($\rho=0.06$, $p=0.4$); correlation with disease duration was borderline significant ($\rho=0.14$, $p=0.06$). Figure 2 shows the partial regression plot of GM CBF with lesion load; adjusted for age, disease duration, and GM atrophy.

Discussion

The large number of MS patients in this study allowed testing for the potentially determining or associated factors of reduced GM perfusion. We were able to show that GM perfusion is not closely correlated with grey matter atrophy, but that focal white matter damage is the strongest relating factor to GM perfusion reduction. We speculate that white matter damage is associated with changes in the grey matter that lead to less metabolic demand. Findings of MR proton spectroscopy confirm our observations that GM changes may be present in the absence of (or preceding) tissue atrophy. Reduced GM perfusion in MS patients now needs to be explored in more detail to understand its pathophysiology and the consequences of these findings.

References

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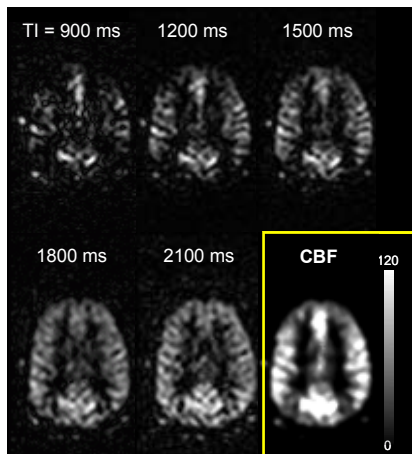[6] Smith SM et al., NeuroImage, 23(S1): 208-219, 2004.

Fig.1: ASL time series for different inflow times TI. The scale of the CBF map is in units of ml/100g/min.
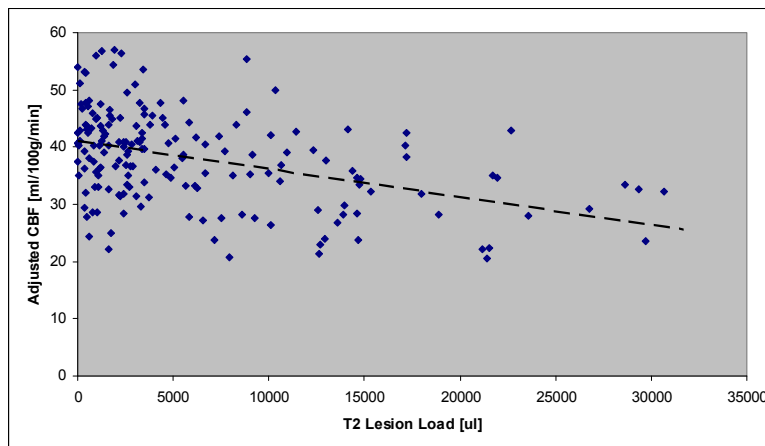

Fig. 2: Partial regression of mean GM-CBF as a function of T2 lesion load; adjusted for age, disease duration, and GM atrophy.