Alteration in Cerebral Arterial Haemodynamics in MS

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Abstract
Regional alteration of perfusion has been shown in patients with MS. The aim of this study was to investigate these CBF abnormalities further by concurrently assessing the cerebral arterial haemodynamic measurement of arterial transit time (ATT) along with CBF using an arterial spin labelled MRI sequence.

In addition to the previously reported reduction in perfusion in deep grey matter, we found that ATT was significantly prolonged (921 +/- 140 ms vs. 794 +/- 140 ms, p=0.007). While CBF was not significantly associated with measures of disability, prolonged deep grey matter ATT was, it was higher in patients with EDSS of greater than 3.5 (1002 +/- 143 vs. 846.6 +/- 140ms, p=0.002) and prolongation correlated with decrease in MSFC (r=−0.53, p=0.011).

Cerebral blood flow and arterial transit time in normal appearing white matter (NAWM) in patients with relapsing remitting MS. These haemodynamic abnormalities may reflect altered tissue metabolic activity, and neurodegeneration.

Introduction and Purpose
Cerebral metabolism requires high delivery of oxygen and glucose by cerebral blood flow, in the face of limited space within the skull. This is achieved by high capillary density, low cerebral blood volume and perfusion regulation that anticipates changes in metabolic demand.

Regional alteration in cerebral blood flow (CBF) and prolongation of cerebral transit time have been reported in patients with Multiple Sclerosis (MS). Changes in CBF may suggest alteration in metabolic demand, or could represent pathophysiological alteration in perfusion control.

In order to understand these findings further it is helpful to concurrently study cerebral arterial haemodynamic markers of arterial blood volume (ABV) and arterial transit time (ATT).

QUASAR Arterial Spin Labelling technique

The QUASAR arterial spin labelling technique is a 7 slice, multi-time point MRI technique that can simultaneously quantify CBF, ATT, and ABV non invasively without the need for contrast infusions. The QUASAR arterial spin labelling technique is a 7 slice, multi-time point MRI technique that can simultaneously quantify CBF, ATT, and ABV non invasively without the need for contrast infusions.5

Methods

23 patients with relapsing remitting MS (BM, 11F, mean age 38.6, median EDSS 3.3) and 21 controls (9M, 12F, mean age 36.9) had QUASAR arterial spin labelled perfusion scans, plus T1 and T2 weighted structural scans using a 3 Tesla scanner (Philips, Best, Netherlands) and 32 channel receive head coil.

QUASAR scan parameters were TR 4000ms, TE 23ms, ATT 300ms, 64 x 64 matrix, field of view 240 x 240, voxel size 3.75x3.75x6mm3, slice 7, slice thickness 6mm, slice gap 2mm, flip angle = 35/11.7°, sense=2-5, 84 averages (48 with vascular crusher gradients of 4cm/s, 24 with no vascular crusher gradient, 12 with low flip angle). Scan time 6 minutes.

Using the co-registered T1 and T2 weighted images as a guide, regions of interest were placed in normal appearing white matter (NAWM) and in the caudate and thalamus.

These regions of interest were used as masks to calculate a single mean CBF, ABV and ATT in NAWM and deep grey matter in each subject.

Comparisons were made using univariate analysis of variance with age and gender entered as co-variates. Results are presented as mean +/- standard deviation between subjects.

Results

CBF was reduced and ATT prolonged in deep grey matter in MS

CBF was significantly reduced in the deep grey matter in patients with MS (36.3 +/- 4.2 vs. 10.1 +/- 2.5 ml min-1 100ml-1, p=0.005) (Figure 1 and 3B).

ATT was significantly prolonged (921 +/- 140 ms vs. 794 +/- 140 ms, p=0.007) in deep grey matter in patients with MS (Figure 2 and 3C).

Disability was not significantly associated with deep grey matter CBF, nor with CBF and ATT in NAWM.

CBF was increased in NAWM in MS

CBF was significantly higher in NAWM in MS as compared to controls (13.3 +/- 4.2 vs. 10.1 +/- 2.5 ml min-1 100ml-1, p=0.005). (Figure 5 and 7C)

Conclusion
The reduction in perfusion in deep grey matter and prolongation of ATT could represent a reduction in demand following neuroaxonal loss or mitochondrial dysfunction.

The significant association between disability and prolongation of deep grey matter ATT, but not with CBF suggests that ATT may be more directly responsive to underlying clinically relevant pathophysiology.

Increase in perfusion in NAWM suggests widespread vasodilatation, which could be secondary to increased energy demands from inflammation or dysregulation of perfusion control.

Conclusions

References
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