Further Evidence for Arterial Spin Labeling Measurement of White Matter Perfusion Using a Multi-Delay Vessel-Encoded Approach

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Introduction: There has been some debate regarding the ability of arterial spin labeling (ASL) to measure white matter (WM) perfusion. Low cerebral blood flow (CBF) and delayed blood arrival make this measurement challenging for a technique with intrinsically low signal-to-noise ratio (SNR) and limited spatial resolution[1]. However, using recent developments such as pseudocontinuous ASL (PCASL) and background suppression it was demonstrated that WM perfusion measurements are possible, although it was suggested that measurement using a multi-postlabeling delay (PLD) approach would be problematic[2]. Here we provide further evidence for the ability of ASL to measure WM perfusion using a multi post-labeling delay vessel-encoded[3] approach[4].

Methods: Seven healthy volunteers were scanned at 3T under a technical development protocol approved by local ethical and institutional committees. Multi-postlabeling delay vessel-encoded PCASL (VEPCASL) was performed as described previously[4] to generate CBF and bolus arrival time (BAT) maps arising from each major brain feeding artery (the right and left internal carotid arteries, ICAs, and vertebral arteries, VAs): voxel size 3.4x3.4x4.5mm, 24 slices, six post-labeling delays (0.25-1.5s), 96 volumes, 6.5mins. Additional calibration scans were performed to allow quantification of CBF in absolute units. BAT maps were weighted by the relative voxelwise CBF contribution from each feeding artery before being summed to generate a single, combined BAT map for the whole brain. T1-weighted structural images were also acquired for registration and segmentation. Grey matter (GM) and WM partial volume estimates were transformed into ASL space and thresholded at 50% and 99%, respectively. To ensure no contamination of WM signals by GM, the derived WM mask was further eroded using a sphere of radius 4 mm. This eroded WM mask was further split into WM regions supplied by the RICA and LICA. BAT analysis was restricted to voxels where the CBF could be reliably estimated (mean CBF > 2.3 × CBF uncertainty).

Results: Example results in Fig. 1a show delayed BAT in WM relative to GM. Averaging over WM and GM masks across all subjects confirmed that this difference was significant ($p = 10^{-5}$, Fig. 1b). In addition, the estimated CBF of WM in the ICA territories was dominated by the ipsilateral ICA, which would not be the case if the signal were dominated by noise. Across all subjects this difference is also significant ($p < 10^{-3}$, Fig. 1b). The average WM CBF across subjects (17 ± 5 ml/100g/min) agrees well with the literature[1,2].

Discussion: The results obtained in this study provide further evidence for the ability of ASL to measure WM perfusion. It has been suggested that PCASL does not provide sufficient SNR to obtain accurate estimates of BAT in WM[5]. However, here we demonstrate a statistically significant delay in WM blood arrival compared to GM. This delay also shows that the signal being measured is not simply due to partial volume effects with GM. The ability to detect extended BATs was aided by the use of PCASL: the total time available for the labeled bolus to reach the tissue and still be detectable is the sum of the labeling duration (1.4s), the maximum PLD (1.5s) and the delay before the slice was acquired (0-1.1s), which is up to 4s for these experiments. In addition, if the ASL signal in WM were dominated by noise then the CBF estimates would be randomly distributed across the four feeding arteries. This is not the case, with the ipsilateral ICA dominating the CBF estimates within the ICA WM masks, with less than 2 ml/100g/min contributed by the other arteries. The average WM CBF also agrees well with previous estimates, suggesting that GM contamination was minimal. The extended BAT in WM found here agrees with recent results utilizing a high temporal resolution approach[6], although only limited brain coverage is possible with that technique. Further work is required to confirm these findings, ideally using a higher spatial resolution to ensure minimal partial volume effects. In addition, GM and WM CBF could be estimated separately, accounting for partial volume effects directly[7].

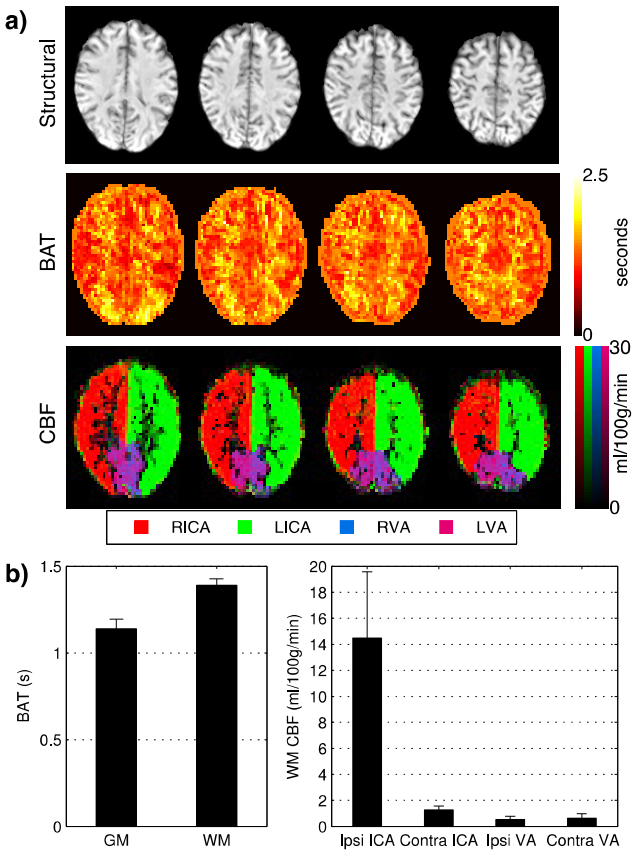

Figure 1: a) Structural, BAT and CBF maps (color-coded according to the legend and windowed to WM perfusion levels) in consecutive slices from one subject. b) Plots showing significantly delayed BAT in WM relative to GM and contributions to the derived CBF values in WM within the ICA territories from the ipsilateral (Ipsi) and contralateral (Contra) feeding arteries. Values are averaged across all subjects (mean ± standard deviation).

References

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