Perfusion and structural characteristics in the grey & white matter of young and elderly adults with white matter disease: a pseudo-continuous ASL and VBM study

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Introduction: Structural brain changes including grey matter atrophy and white matter disease (WMD) are commonly assessed with MRI as markers of aging and disease. This study seeks to extend our understanding of these structural changes by examining cerebral perfusion of elderly patients and healthy young adults. In the elderly participants, WM regions were differentiated as normal appearing white matter (NAWM) or WMD using fluid-attenuated inversion recovery (FLAIR) images and a semi-automated algorithm performing WMD classification. WMD was of interest in this study because it is associated with pathological aging and reported to be the most common neurological disease [1]. Cerebral Blood Flow (CBF) was measured with Arterial Spin Labeling (ASL), an ideal perfusion technique for aging and/or longitudinal studies. ASL relies on the magnetically labeled blood water as an endogeneous contrast agent but the relatively short half-life ($T_{1,artery}$ = 1.65 s at 3 T) is thought to preclude reliable perfusion estimates in cases where the transit time is prolonged. White matter (WM), for example, is fed by long penetrating arteries and consequently estimating perfusion is challenging. Van Osch et al argue that upwards of 60 difference images are required to achieve a non-zero WM signal [2]. In the current study we use pseudo-continuous ASL (pc-ASL) and evaluate the ability to measure perfusion in different tissue types and as a function of aging.

Methods: Structural and perfusion pc-ASL data were collected in two groups of adults: 1) young healthy adults (N=16; 9/7 W/M, mean age: 27 ±4 years) and 2) elderly adults (N=35, 17/18 W/M, mean age 75 ±8 years) selected for moderate-severe WMD burden. Imaging sequences included: T1-weighted anatomical (TR/TE/TI=9.5/2.3/1400ms, 140 slices, FA=8deg, 256x164 matrix, 1x1.2x1.2mm^3 voxels), FLAIR (TR/TE/TI=9000/125/2800ms, 52 slices, 240x217 matrix, 1x1.1x3mm^3 voxels) pc-ASL (TR/TE=4000/9.7ms, 18 slices, 64x64 matrix, 3x3x5mm^3 voxels, label offset=80mm, delay /duration=1600/1650, 35 EPI volumes, duration=4:48), and a reference ASL scan for absolute quantification. MRI was performed on a 3 Tesla Philips Achieva MRI system using body coil transmission and an 8 channel head receive coil. The local ethics committee approved this study. FLAIR images were used to quantify the WMD burden as a percentage of the total white matter. VBM was performed on T1-images using FSL, after masking regions identified as WMD, to identify GM atrophy that is correlated with WMD burden. CBF maps were calculated according to [2], and using the M_0 reference image to correct for image inhomogeneity. In the elderly cohort phase-contrast angiography was collected at the level of carotid and vertebral arteries as a means to estimate pc-ASL label efficiency (in N=19) [3]. Temporal mean and standard deviation values for the ASL data were used to calculate each voxel's SNR. Voxels with a threshold SNR>1 were considered reliable. ASL images were coregistered to a template atlas using the FMRIB Software Library (FSL) non-linear registration tool. T1-images were segmented into GM, WM and WMD (the latter for the elderly only) using FAST as part of FSL.

Results: In the elderly cohort, the VBM analysis showed a negative correlation between grey matter density and WMD in bilateral posterior hippocampus, after correction for multiple comparisons with TFCE (Figure 1, p<0.05). An analysis of perfusion reliability in the elderly cohort revealed 51 ±20% of GM and 26 ±15% of WM voxels met a threshold level for detectability (Figure 2). In the young cohort, 73 ±17% of GM and 37 ±15% of WM voxels met a threshold level for detectability. There was a significant cohort difference for GM (P<0.001) and WM (P<0.02) and this effect did not remain significant after accounting for age as a covariate (P>0.5, Figure 3).

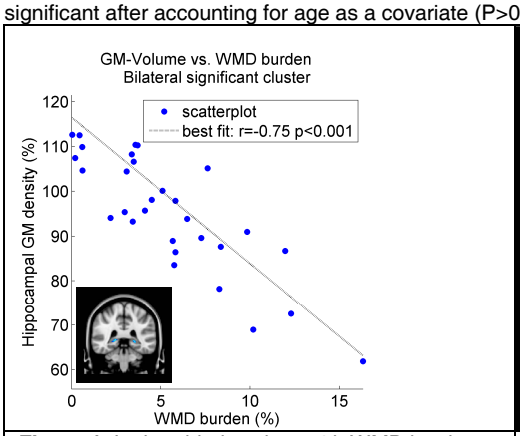

Figure 1. In the elderly cohort with WMD burden, hippocampal GM density was correlated with WMD, expressed as a % of total WM. Significant hippocampal voxels are shown (inset).

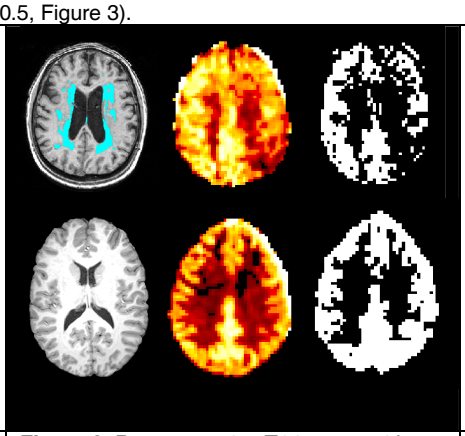

Figure 2. Representative T1 images with WMH segmentation in young and elderly adults. Corresponding ASL images and SNR mask (i.e. SNR>1) are shown.

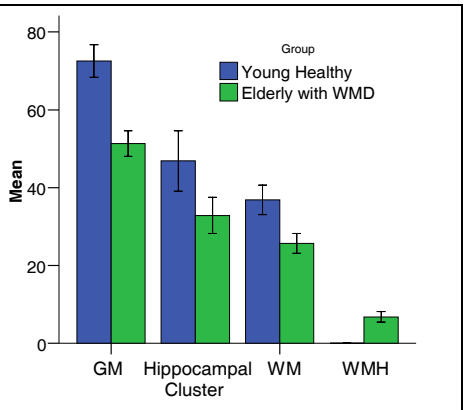

Figure 2. % of CBF voxels that met an SNR threshold criteria for young (blue) and elderly (green) cohorts. GM had the higher proportion and there was a significant aging effect.

Discussion: We have demonstrated that the proportion of ASL voxels that meet an SNR threshold is influenced by tissue type and age. Both cohorts showed that between 20 and 40% of WM voxels could be estimated, which provides support for previous studies reporting WM perfusion. In the elderly cohort the degree of WMD did not influence the proportion of WM or GM voxels. VBM results indicate a relationship between WMD and posterior hippocampal atrophy. The SNR analysis found that hippocampal hemodynamics are less reliable than other GM regions. However, insula perfusion was found to correlate with degree of WMD (data not shown). We have found that head motion during ASL was correlated with standard deviation of CBF difference images and future work will explore criteria for excluding aberrant difference pairs. Others have proposed ways to improve the reliability of WM perfusion with ASL [4], which may be a useful area of work given that WMD is common in elderly and the etiology of this disease remains poorly understood. Relatively few studies have investigated perfusion characteristics in elderly adults with WMD.

References:

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