The importance of partial volume correction in ASL based studies of cerebral perfusion in Mild Cognitive Impairment: a quantitative comparison

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Target audience: Physicians, psychologists, radiologists and MR researchers.

Purpose:

Arterial Spin Labeling (ASL) is increasingly used in clinical studies of cerebral perfusion and has shown its validity in measuring perfusion changes in several neurodegenerative diseases including Alzheimer Disease (AD) and mild cognitive impairment (MCI)[1,2], which is considered as a transitory stage between a normal cognitive function and AD. Partial volume effects (PVE) are a consequence of limited spatial resolution in ASL, where the low signal-to-noise ratio leads to the need to employ large voxels (aprox. 3x3x6mm), thus a voxel value would have its origins in the sum of the contributions of grey matter (GM), white matter (WM) and CSF rather than a single tissue. As an example grey matter (GM) CBF is approximately two times higher than white matter CBF, significant underestimation of GM CBF can occur. Although the need for PVE correction for ASL applications in AD has been well established; in this work, we quantitatively demonstrate the effect of PVE correction in a well-characterised MCI cohort.

Methods:

MRI examinations were conducted on 36 subjects (11 male and 25 female, 73.7±5.6 years) using a MR scan on a 3T Signa HDx MR scanner (GE Healthcare, Waukesha, WI) using an eight-channel phased array coil. Subjects were classified into: 20 healthy participants and 16 multi-domain MCI (MCIm) patients. Approval from the local ethics committee was obtained and all patients provided informed consent to take part. The MRI protocol included a full brain spoiled gradient echo 3D T1-weighted (3DT1w) volumetric scan with a TR=9.24ms, TE=4.148ms, TI=650ms, NEX=1, acquisition matrix=512x512, resolution=0.47x0.47x1mm, flip angle=12. ASL CBF maps were acquired using a 3D pCASL pulse sequence with full brain coverage, matrix size= 128x128, resolution=1.875x1.875x4mm, flip angle = 155, transit time 2s, TR=4.847s, TE=4.906ms, NEX=3. An interleaved 3D stack of spiral readout was used, employing 8 arms and 512 points per arm. All 3DT1w weighted images and CBF maps were processed using the software ASAP[3] (Automatic Software for ASL Processing). ASAP includes processing functions from both SPM-8 library and FSL software like skull stripping, co-registration, PVE correction, normalisation and smoothing and produces perfusion data that is ready for statistical group analysis. Normalized and smoothed (FWHM=4x4x4mm Gaussian kernel) CBF maps produced by ASAP were employed for the voxel-based statistical analysis. Prior to MNI normalization, two different pipelines were applied to the perfusion maps: no PVE correction and Asllani's[4] PVE correction. For Asllani's PVE correction the perfusion maps were corrected using the partial volumes estimates from the 3DT1w (down-sampled to the ASL space) and a linear regression method within a regression-kernel of size 5x5x1voxels. Therefore, for each subject, original CBF maps and Asllani's PVE-corrected CBF maps were obtained. Also, 3DT1w images were processed with the standard SPM DARTEL pipeline to study GM atrophy. Statistical comparison between control and MCIm groups were generated by means of a two-sample t-test analysis within the General Linear Model as implemented in the SPM8 software suite (with gender, age and intracranial volume as covariates for the study of GM atrophy and, for the CBF hypoperfusion study, gender and age as covariates and mean CBF value of each subject as a regressor).

Results:

Figs.1 and 2 show uncorrected and corrected hypoperfusion patterns in the MCIm group compared to the control group (p_{unc}<0.05), respectively, in the parietal areas. In both cases, areas of hypoperfusion include the posterior cingulate and the precuneus, which agree with earlier studies reported in the literature[5]. Fig.3 shows GM changes using VBM-DARTEL based comparison between control and MCIm groups (p_{unc}<0.05) in the parietal areas, also including changes in areas of the posterior cingulate and the precuneus. Figs. 4 and 5 show uncorrected and corrected perfusion changes in the MCIm group compared to the control group (p_{unc}<0.05), respectively, in the medial temporal lobe. While no perfusion changes were found with PVE-uncorrected CBF maps in the medial temporal lobe, the PVE-corrected results show hypoperfusion in MCIm patients in the left hippocampus and parahippocampal gyrus, which are two of the key regions associated with neurodegenerative atrophy in AD and MCI[6]. Fig.6 shows GM loss in the MCIm group in the medial temporal lobe using VBM-DARTEL (p_{unc}<0.05), depicting GM atrophy in left and right hippocampi and parahippocampal gyrus.

Fig1.MCIm hypoperfusion – parietal areas (PVE-uncorr)

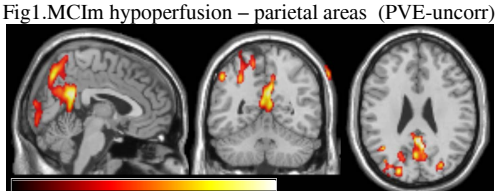


Fig2.MCIm hypoperfusion – parietal areas (PVE-corr)

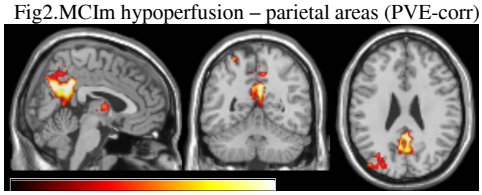


Fig3. MCIm GM loss – parietal areas

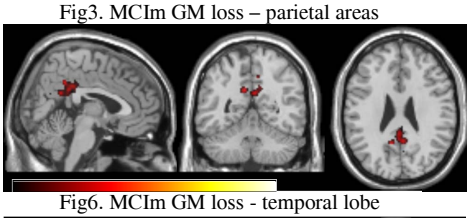


Fig4.MCIm hypoperfusion - temporal lobe (PVE-uncorr)

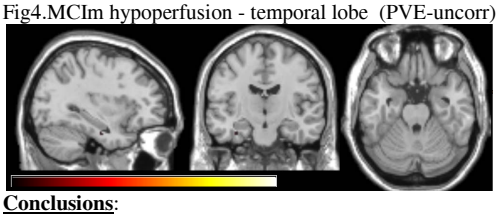


Fig5.MCIm hypoperfusion - temporal lobe (PVE-corr)

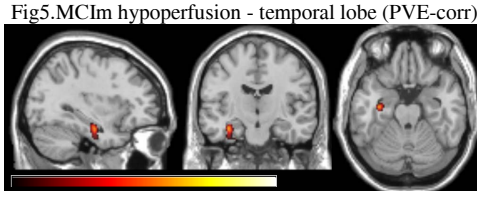
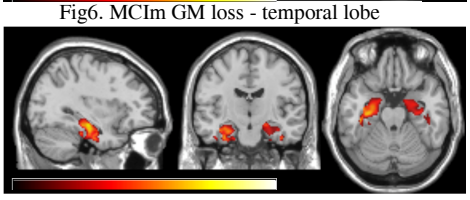


Fig6. MCIm GM loss - temporal lobe



Conclusions:

Our investigation demonstrates that the absence of PVE correction in ASL studies in MCI patients leads to both false positive and false negative findings. By and large, these are present in parietal and temporal regions respectively. This is particularly true in relevant regions of the medial temporal lobe areas such as left hippocampus and parahippocampal gyrus. Given that it has been recently shown that CBF changes may be more sensitive than volumetric ones for predicting the onset of AD[7], our results highlight that PVE correction is essential to maximise the predictive value of ASL in this field of research.

References:

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Acknowledgements: COST Action "Arterial Spin Labelling Initiative in Dementia" (BM1103) and the DEMCAM project of the Community of Madrid. This work has been partially granted by the project TEC2012-39095-C03-01 of the Spanish Ministry of Economy and Competiveness.