Regional Decline of Brain Perfusion in Healthy Aging Detected with Arterial Spin Labeling at 4T

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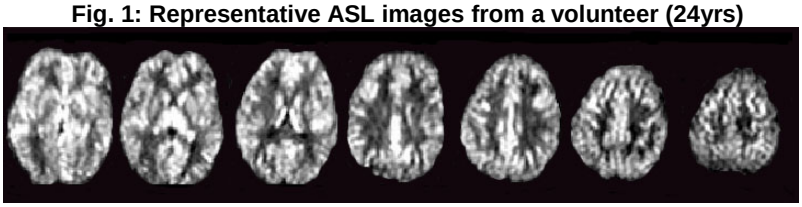
Introduction: Healthy aging is associated with gradual but progressive decline of cognitive function, but the underlying mechanisms remain obscure. Anatomical MRI studies of aging report gray and white matter loss, especially in the frontal, temporal, and parietal lobes (1, 2). On the other hand, whether cerebral perfusion also declines with healthy aging remains controversial (3). Moreover, failure to correct for brain atrophy may have confounded previous findings of perfusion changes with age (3). Using arterial spin labeling (ASL) MRI at 1.5T, we previously found a weak inverse relationship between brain perfusion and age, after correction for brain atrophy (4). However, the sensitivity to measure perfusion was limited by poor signal-to-noise of ASL at 1.5T. Since ASL sensitivity increases substantially at higher magnetic fields (5), we performed an ASL pilot study at 4T on aging. Specifically, our goal was to explore if ASL-MRI at 4T detects a regional pattern of diminished brain perfusion with age.

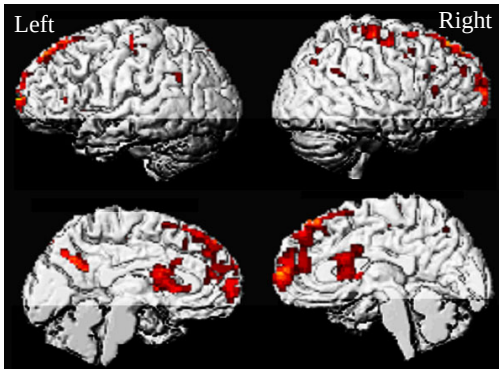
Methods: Twelve healthy volunteers between 22 and 77 years old were studied at 4T (Bruker/Medspec). Perfusion weighted images (PWI) were acquired using a pulsed ASL method (QUIPPS-II (6), TR/TE =2500/40 ms, 9 slices, each 9 mm thick, 2.5 x 2.5 mm^2 in plane resolution), covering the cerebrum superior to the Circle of Willis. In addition, T1-weighted structural images were acquired using an MPRAGE sequence (TR/TI/TE=3000/1200/3.4ms, FA=10°, 1mm^3 isotropic resolution) and FLAIR. MPRAGE images were used to measure brain tissue loss and to account for partial volume effects in ASL data. FLAIR was used to determine if subjects had white matter lesions or other major neuropathologies. Perfusion images were registered to structural images, corrected for partial volume effects and spatially normalized to a study-specific brain template. Systematic effects of group on perfusion and GM density were tested voxel-wise using Statistical Parametric Mapping (SPM2).

Fig. 1: Representative ASL images from a volunteer (24yrs)



Results: Figure 1 depicts representative ASL perfusion images from a 24 year old volunteer. Figure 2 shows regions with a significant relationship between reduced perfusion and increasing age. The light gray areas indicate brain coverage by ASL-MRI. The most prominent reductions of perfusion with age were found in the right superior and frontal gyrus (both $p<0.001$), the caudate nucleus ($p<0.001$), bilaterally in the anterior cingulate ($p<0.01$), and in the precentral gyrus ($p<0.05$), while most of posterior brain regions were spared with the exception of the left precuneus ($p<0.05$). Using perfusion of motor cortex as reference to eliminate global variations of perfusion did not substantially alter the pattern.

Fig. 2: Hypoperfusion as a function of age



Discussion: We observed a regional pattern of age-related decline in brain perfusion, using ASL, consistent with imaging studies using SPECT and PET. Furthermore, since we accounted for partial volume effects, these results cannot be due to underlying brain atrophy. This sharply contrasts with the pattern seen in mild cognitive impairments or Alzheimer's disease, which involves parietal lobe, including the posterior cingulate while sparing frontal lobe regions (7). This would suggest that cognitive decline in healthy aging is a different entity than the progressive cognitive decline seen in mild cognitive impairments and Alzheimer's disease. If these patterns were confirmed, this would establish a key role for ASL-MRI in differentiating between changes in brain function, which might indicate incipient dementia and those related to normal aging. However, these results need to be confirmed on a larger number of subjects and perfusion needs to be quantified. Nevertheless, the data demonstrate the sensitivity of 4T ASL-MRI to detect changes of brain perfusion in aging.

References:

1. Good CD, Johnsrude IS, Ashburner J, Henson RN, Friston KJ, Frackowiak RS. A voxel-based morphometric study of ageing in 465 normal adult human brains. Neuroimage 2001;14(1 Pt 1):21-36.
2. Thompson PM, Moussai J, Zohoori S, Goldkorn A, Khan AA, Mega MS, et al. Cortical variability and asymmetry in normal aging and Alzheimer's disease. Cereb Cortex 1998;8(6):492-509.
3. Meltzer CC, Cantwell MN, Greer PJ, Ben-Eliezer D, Smith G, Frank G, et al. Does cerebral blood flow decline in healthy aging? A PET study with partial-volume correction. J Nucl Med 2000;41(11):1842-1848.
4. Schuff N, Jahng G-H, Zhu X-P, Li K-L, Weiner MW. Age-related Changes of Brain Perfusion by Arterial Spin Labeled MRI. Neurobiology of Aging 2004;25(S2):274.
5. Wang J, Alsop DC, Li L, Listerud J, Gonzalez-At JB, Schnall MD, et al. Comparison of quantitative perfusion imaging using arterial spin labeling at 1.5 and 4.0 Tesla. Magn Reson Med 2002;48(2):242-254.
6. Luh WM, Wong EC, Bandettini PA, Hyde JS. QUIPSS II with thin-slice TI1 periodic saturation: a method for improving accuracy of quantitative perfusion imaging using pulsed arterial spin labeling. Magn Reson Med 1999;41(6):1246-1254.
7. Johnson NA, Jahng G-H, Weiner MW, Miller BL, Chui HC, Jagust WL, et al. Pattern of Cerebral Hypoperfusion in Alzheimer's Disease and Mild Cognitive Impairment Measured With Arterial Spin Labeled MRI. Radiology 2004;in press.