Hemodynamic Characterization of Dementias via Pseudo Continuous ASL

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Introduction Dementias span a broad range of neurodegenerative diseases that presently afflict over 30 million people worldwide.[1] Progressive neurodegeneration is frequently associated with and likely exacerbated by an impairment in cerebral microvascular functioning.[2] However, the current understanding of the hemodynamic profiles of various dementias is incomplete and the literature to date suggests spatially and temporally varying changes in brain hemodynamics. The current study employs pseudo continuous ASL, [3, 4] a highly efficient technique for rapid multiple-delay time sampling of the labeled spins' passage through the cerebral microvasculature, and a two-compartment signal model to produce quantitative measurements of cerebral hemodynamics in a small cohort of dementia patients and a group of healthy, age-matched volunteers.

Methods Twelve subjects participated in the study: 4 were healthy elderly volunteers; 2 were diagnosed with mild cognitive impairment; 5 were early to mild AD and one was diagnosed with Lewy body dementia. The scanning protocol included a 3D fast spoiled gradient-echo sequence for anatomical reference (0.86x0.86x0.86 mm3), followed by a 3D time-of-flight MRA scan to facilitate PCASL label prescription. Between 4 and 6 different inversion times (from 100 to 1700ms) were sampled, with at least 12 repetitions of each, using a pseudo continuous arterial spin labelling sequence, with a TE/TR of 17ms/3.5-5s, for a total PCASL scan time of under 10 minutes. Seventeen 4.2-mm thick slices were acquired at a slice gap of 1.4-mm with a 3.4x3.4mm in-plane resolution. The 5mm labeling plane was positioned perpendicular to the internal carotid arteries, just superior to the carotid bifurcation to allow whole-brain coverage. The labeling comprised a series of 1000 slice-selective Hanning-shaped RF-pulses with a flip angle of 35° and a spacing of 1.5-ms for optimal difference image SNR while maintaining SAR level compatible with continuous scanning. Examinations were completed on a GE 3T MR-750 system using an 8-channel head phased array coil. The PCASL data were motion corrected using AFNI's 3dvolreg software and spatially smoothed in plane by half the voxel size. At each TI the signal difference between control and tag was averaged across all repetitions and resulting data were fitted, voxel-wise using a non-linear least-squares optimization, to the slow solution of the two compartment model described in Parkes et al.[5] so as to arrive at images of absolute cerebral blood flow (CBF) and arterial transit time (t_A). Permeability surface area product and longitudinal relaxation times for water in the different compartments were taken from the literature, whereas equilibrium magnetization of arterial blood and inversion efficiency of labeling were estimated from independent experiments focused on isolation of the internal carotid arterial blood signal superior and inferior to the labeling plane, respectively. To allow the analysis of hemodynamic changes in the regions of interest known to be affected by the disease process, the anatomical scans were manually parcelated, identifying medial temporal lobe (MTL), lateral temporal lobe (LTL), posterior cingulate (PC), and anterior cingulate (AC), and prefrontal regions (PR).

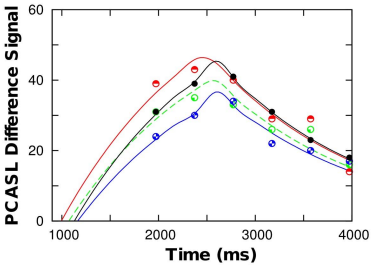

Fig.1. Perfusion data and corresponding voxel fits in 4 voxels of a healthy volunteer.

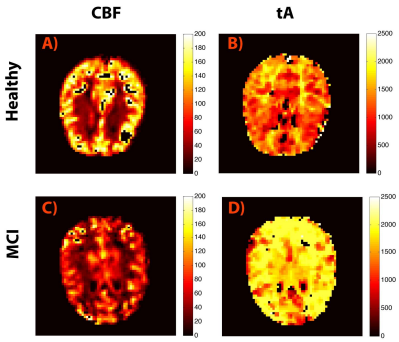

Fig.2. Perfusion and tA maps in a healthy volunteer (A,B) and a patient with MCI (C,D).

Results Fig. 1 displays sample voxel wise model fits to data from 4 different voxels at 6 different inversion times. Fig. 2 shows sample maps of absolute perfusion (ml blood/100g tissue/min) and arterial transit time (ms) estimates in a healthy, elderly volunteer (A, B) and a patient diagnosed with mild cognitive impairment (MCI) (C, D). In accordance with the existing data from SPECT, ASL MRI, and ^{15}O PET, the neurodegeneration is associated with pronounced hypoperfusion. In contrast to some recent work,[2] however, the arterial transit time (reflecting the transit time from labelling plane to the imaged voxel; a metric that is correlated with the mean transit time[6]) appears prolonged, as well, likely indicating compensatory vasodilatation in the affected tissue. The table lists average CBF estimates in each ROI of interest. Across all subjects, CBF showed a trend toward decrease in MCI and a statistically significant reduction in AD ($p<0.05$).

ROI		MTL	LTL	PC	AC	PR
Cond.	NC	77±16	71±17	56±15	68±16	71±18
	MCI	69±20	64±18	39±10	69±15	47±17
	AD	59±16	46±13	43±11	48±12	46±13

Discussion Current study demonstrates the ability of PCASL to provide sensitive, whole brain mapping of perfusion and arterial transit time in elderly population and in dementias in clinically relevant time. Future work will focus on scanning a larger population of subjects, allowing a finer categorization of the stages of dementia in the subject pool as well as per-subject estimation of inversion efficiency and T1 relaxometry to increase the accuracy of the resulting hemodynamic estimates. Such quantitative imaging of cerebral hemodynamics will provide key insight into the temporal evolution and spatial selectivity of the highly complex changes in the brain vascular state during progressive neurodegeneration.

References

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