Cerebral Blood Perfusion Dynamics in Alzheimer's Disease and Mild Cognitive Impairment Using Discrete Modeling of Arterial Spin Labeling MRI

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INTRODUCTION: Reductions in regional cerebral blood flow (rCBF) and blood volume (rCBV) in Alzheimer's disease (AD) and mild cognitive impairment (MCI), a potential precursor of AD, are generally attributed to diminished brain function. However, vascular factors, restricting blood supply, may exacerbate the problem [1]. To study the vascular aspects of cerebral perfusion in AD and MCI, we used a four phase two compartment discrete model for quantifying arterial spin labeling (ASL) MRI [2] that provides estimates of bolus arrival time (BAT), intrinsic arterial-arteriole transit time (aaTT), and time to peak (TP), in addition to rCBF and rCBV. In this study, we tested the hypothesis that BAT, aaTT, and TP are prolonged in AD and MCI relative to normal aging, in addition to reductions in rCBF and rCBV..

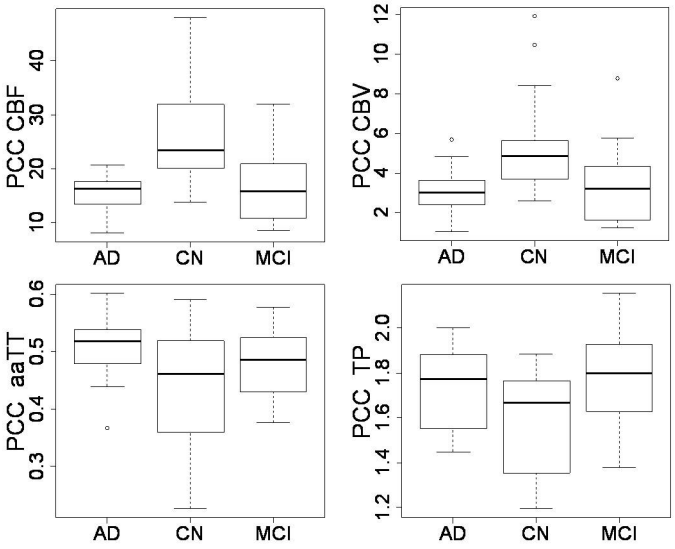

Figure 2: Comparison of averaged CBF, CBV, aaTT and TP in PCC across AD, CN and MCI subjects.

METHODS: Fourteen cognitively normal (CN) subjects (7 men, 7 women, mean age 70.7 ± 7.2; mini mental state exam (MMSE) 29±1.2), eleven patients with AD (6 men, 5 women, mean age 69.4 ± 11.4; MMSE 22.7±4.9) and thirteen subjects with mild cognitive impairment (MCI) (7 men, 6 women, mean age73.6 ± 4.8, MMSE 27.6±3.1) were studied on a 4 Tesla MRI scanner. A dynamic ASL-MRI was performed, consisting of 12 serial 3D image frames with variable post-labeling delays [3]. The dynamics of the ASL signal was evaluated and perfusion parameters estimated using a discrete four-phase model for blood flow[2]. Perfusion was evaluated globally for grey matter (GM) as well as regionally for posterior cingulate cortex (PCC) and precuneous (PRE), which are known for their early involvement in AD pathology. Group differences were evaluated using t-tests.

RESULTS: AD and MCI subjects had up to 30% lower rCBF values of global GM, PCC ($p = 0.01$) and PRE ($p = 0.05$) when compared to CN and similar rCBV reductions, as expected. In addition, AD and MCI subjects had up to 16.4% longer aaTT values in PCC, 14.1% in PRE, and 9.6% in GM in comparison to CN subjects. Similar to aaTT, TP was also longer in AD and MCI patients by 13.2% in PCC, 14.9% in PRE, and 9.4% in GM compared to CN subjects. BAT was also longer in AD and MCI patients by 21% in PCC, 20.5% in PRE, and 15.2% in GM. The most prominent differences in perfusion dynamics between the groups were seen in the PCC (**Figure 1**). Results of the analysis of perfusion dynamics are summarized in **Table 1**.

	CN (mean±sd)	MCI (mean±sd)	AD (mean±sd)	AD vs CN	MCI vs CN	AD vs MCI
GM CBF(mL/100mL/min)	21.60±5.11	17.27±4.46	17.57±3.61	|t|=2.21 *	|t|=2.34 *	|t|=0.18
PCC CBF	24.54±9.18	17.04±6.89	15.38±3.74	|t|=3.73 ***	|t|=2.97 **	|t|=0.53
PRE CBF	13.16±4.81	10.91±3.71	10.32±3.33	|t|=2.05 *	|t|=1.85 •	|t|=0.40
GM CBV (mL/100mL)	5.04±1.29	3.71±1.06	4.06±1.20	|t|=1.94 •	|t|=2.90 **	|t|=0.75
PCC CBV	5.60±2.77	3.55±2.19	3.13±1.32	|t|=2.91 **	|t|=2.48 *	|t|=0.55
PRE CBV	2.90±1.09	2.05±1.10	2.19±1.07	|t|=1.87 •	|t|=2.27 *	|t|=0.32
GM BAT (seconds)	0.54±0.10	0.62±0.10	0.59±0.12	|t|=1.25	|t|=1.95 •	|t|=0.59
PCC BAT	0.67±0.18	0.81±0.19	0.75±0.17	|t|=1.49	|t|=2.42 *	|t|=0.83
PRE BAT	0.49±0.11	0.59±0.16	0.50±0.12	|t|=0.36	|t|=2.33 *	|t|=1.55
GM aaTT (seconds)	0.45±0.05	0.49±0.05	0.46±0.04	|t|=0.83	|t|=2.42 *	|t|=1.57
PCC aaTT	0.43±0.10	0.48±0.06	0.50±0.06	|t|=2.57 •	|t|=1.84 •	|t|=0.64
PRE aaTT	0.34±0.07	0.38±0.07	0.36±0.04	|t|=0.52	|t|=1.62	|t|=1.16
GM TP (seconds)	1.35±0.13	1.48±0.12	1.44±0.14	|t|=1.68	|t|=2.71 *	|t|=0.69
PCC TP	1.57±0.24	1.77±0.24	1.73±0.20	|t|=2.21 *	|t|=2.34 *	|t|=0.18
PRE TP	1.14±0.19	1.31±0.23	1.17±0.14	|t|=3.73 ***	|t|=2.97 **	|t|=0.53

Significant code: < 0.001 '***'; 0.001 '**'; 0.01 '*'; 0.05 '•'; 0.1 ''

CONCLUSION:The findings demonstrate that vascular aspects contribute to rCBF and rCBV reductions in AD and MCI. Evaluating vascular factors of perfusion and rCBF/CBV together should improve the classification of AD and MCI from normal aging.

REFERENCE: [1] Farkes E, et al., Progress in Neurobiology 64:575–611(2001). [2] Li, et al., Magnetic Resonance in Medicine 53:511–518 (2005). [3] Gunther, et al., Magnetic Resonance in Medicine 54:491-498 (200