

Flow and Perfusion in the Evolution of Dementia: Preliminary Findings

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Introduction: A four-year study of elderly subjects is being conducted at the University of Pittsburgh to identify markers for Alzheimer's disease (AD) dementia. Preliminary results are currently being generated from the first year (2002-2003) of the dementia study. Blood flow velocities, perfusion rates, and T_1 relaxation were measured using phase contrast (PC) Cine, multislice continuous arterial spin labeling (CASL), and saturation recovery MRI, respectively, for patients diagnosed as normal, mild cognitive impaired (MCI), and early dementia.

Methods: To date, 160 elderly volunteers (aged 55 and older) have been scanned using a 1.5 T GE Signa system after providing informed consent either directly or through their caregiver (i.e., for some dementia patients). Subjects were classified based on neuropsychological testing and clinical evaluation. The MRI protocol acquired structural images using T_1 weighted RF spoiled gradient recalled echoes (SPGR), T_1 maps using saturation recovery echo-planar imaging (EPI), B_1 maps using variable nutation EPI, perfusion using CASL with DAI with multislice EPI, and velocimetry of the internal carotids using fast phase contrast (PC) Cine gradient recalled echoes. The CASL labeling plane was located 10 cm inferior to the center of the 20 x 20 x 9 cm imaging volume. The velocity measurements were obtained at the labeling plane, contingent on the orientation of the arteries.

Structural images for 124 of the studies were reviewed by a board-certified radiologist to identify disease and exclusionary criteria. Functional images for 25 of the studies have been reconstructed and analyzed offline to date. Gray and white matter were segmented using Statistical Parametric Mapping (SPM, Wellcome Department of Imaging Neuroscience) and the high-resolution SPGRs. SPM was also used to perform motion correction and co-registration of the functional images (T_1 , B_1 , and CASL images). Matlab (The MathWorks Inc.) routines were used to calculate T_1 , B_1 , and CASL data based on model fitting.

Results & Discussion: Dementia subjects pose several imaging challenges (Table 1) compared to age-matched subjects including: 1) the increased incidence of cerebrovascular disease, and 2) excessive patient motion. Subjects with cerebrovascular disease were not included in the subsequent functional analyses. The ability to tolerate the 1 hour scans (i.e., rate of claustrophobia or discomfort) was consistent between subject groups and other MR studies (e.g., young healthy subjects).

Table 1. Radiologic Findings

Preliminary Classification	Radiologic Evidence of Cerebrovascular Disease	Excessive Patient Motion	Claustrophobia
Normals (N=30)	6 (20%)	1 (3%)	3 (10%)
MCI (N=67)	10 (15%)	3 (4%)	7 (10%)
Early Dementia (N=27)	9 (33%)	3 (11%)	3 (11%)

We found no significant differences in the internal carotid velocities among the three subject groups (Table 2). However, the carotid velocities were significantly lower than those we measured in healthy young (aged 18-45, N=8) volunteers (30 +/- 1.5 cm/s). White matter T_1 values were significantly lower in MCIs than in normal or early dementia subjects.

Table 2: Functional Results

Subject Classification	$T_{1\text{obs}}$ (ms)		Velocity (cm/s)		Perfusion (ml/100g-min)			
	Gray Matter	White Matter	IC Right	IC Left	Gray Matter Hemispheres		White Matter Hemispheres	
			Right	Left	Right	Left	Right	Left
Normals (N=9)	1223 +/- 54	927 +/- 17	18.3 +/- 1.1	19.1 +/- 1.6	58.8 +/- 8.2	63.9 +/- 8.7	49.5 +/- 5.8	52.5 +/- 5.5
MCI (N=9)	1175 +/- 33	858 +/- 16	19.9 +/- 1.8	20.4 +/- 1.2	62.0 +/- 7.0	62.4 +/- 7.0	47.9 +/- 5.9	52.9 +/- 6.9
Early Dementia (N=6)	1217 +/- 36	928 +/- 26	17.4 +/- 2.2	18.4 +/- 1.3	55.1 +/- 3.8	58.4 +/- 3.4	50.4 +/- 5.5	49.8 +/- 4.1

The gray matter perfusion rates were generally consistent with previous studies [1]. Although the raw CASL difference signals for white matter were half that of gray matter for all three groups, normalization with their respective T_1 's caused the perfusion rates to be uncharacteristically high. The differences in perfusion rates between subject groups were not statistically significant due to the low number of subjects analyzed to date. However, we observed that the CASL signals and perfusion rates for early dementia subjects were consistently lower than MCIs and normals. Future work will involve the continued analysis of study data to enhance statistical sensitivity, and enhancement of the kinetic models used in calculating the perfusion rates from the CASL difference signals.

References: 1. Alsop, D.C., J.A. Detre, and M. Grossman, Annals of Neurology, 2000. **47**(1): p. 93-100.