Differences of regional cerebral blood flow in mild cognitive impairment and early Alzheimer's disease measured with CASL

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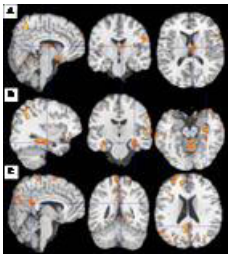
Introduction: Perfusion studies of dementia using MRI, SPECT, and PET imaging have generally reported hypoperfusion in the temporoparietal and frontal regions, and the posterior cingulate. A four-year study of elderly subjects is being conducted at the University of Pittsburgh to identify markers for Alzheimer's disease (AD) dementia. Preliminary results are being generated from the first two years (2002-2003) of the dementia studies. CBF was measured in 59 elderly volunteers (21 healthy controls, 15 MCIs, and 23 early ADs) who satisfied the inclusion criteria (e.g., absence of cerebrovascular disease, able to complete MRI exam, and effective labeling of both hemispheres).

Methods: After providing informed consent, blood flow velocities, perfusion rates, and T_1 relaxation times were measured in each elderly volunteer using phase contrast (PC) Cine, multi-slice continuous arterial spin labeling (CASL), and saturation recovery MRI, respectively on a 1.5 T GE Signa scanner. Multi-slice CASL used *A*lternating *S*ingle and *D*ouble adiabatic inversions (ASD)[1] (3.7 s pulse train at 92% duty cycle) and ramp-sampled echo-planar imaging (EPI) to acquire 19 contiguous axial slices (64×64 matrix, 20 cm FOV, 5 mm thick, 0 spacing, TE: MinFull 21 ms, 76kHz effective receiver bandwidth, TR_{acq}: 1 s, 700 ms transit delay, flip angle: 90^0), with a sequential superior to inferior slice acquisition order to minimize residual magnetization transfer (MT) effects. The pulse sequence was repeated 50 times to permit signal averaging. The inversion efficiencies in the internal carotid arteries were calculated for each subject using B_1 maps and phase-contrast cine velocimetry of the label plane[2]. Coronal T_1-weighted spoiled gradient-recalled echo (SPGR) images covering the whole brain were acquired for gray and white matter segmentation.

Table 1: Demographics

Class	Total	Female	Age
Normals	21	13	82.6 +/- 0.8
MCIs	15	8	84.3 +/- 0.9
Early ADs	23	15	84.3 +/- 0.6

Absolute CBF maps of gray matter were calculated using the kinetic model of CASL[3] and the assumption that gray matter CBF was a global constant. A deformable atrophy-corrected registration method[4] was used to warp the CBF maps to the standard colin27 brain space. The warped CBF maps were smoothed with a 6 mm Gaussian kernel. Image-based voxel-by-voxel t-tests were performed between groups using Statistical Parametric Mapping (SPM2, Welcome Department of Cognitive Neurology) and customized to correct for differences in the functional volumes scanned in the different subjects. Voxels that were shared by at least 8 subjects were counted in the t-test analyses.



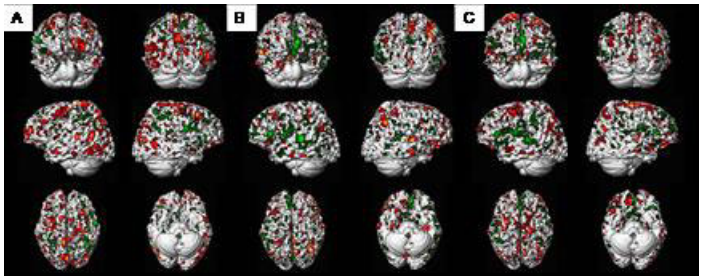


Figure 1: CBF t-test results using SPM2 ($p < 0.05$). Left images: A) $CBF_{MCI} > CBF_{normals}$; B) $CBF_{normals} > CBF_{AD}$; and C) $CBF_{normals} > CBF_{MCI}$. Right images: A). Normal – MCI; B). MCI – AD; and C). Normal – AD. Yellow > orange > red for positive difference (left and right), while light green > dark green for negative difference (right only).

Table 2. Primary Findings

Comparison	Finding (p<0.05)
$CBF_{normals} > CBF_{MCI}$	Posterior cingulate gyrus, superior parietal region
$CBF_{MCI} > CBF_{normals}$	Left Thalamus
$CBF_{normals} > CBF_{AD}$	Right posterior cingulate gyrus, left superior parietal & orbital frontal
$CBF_{AD} > CBF_{normals}$	Anterior cingulate gyrus
$CBF_{MCI} > CBF_{AD}$	Left superior parietal, bilateral hippocampi
$CBF_{AD} > CBF_{MCI}$	Anterior cingulate gyrus

Results & Discussion: The results of separate t-tests between groups were overlaid on the surface section of our standard brain (Fig. 1 left). The statistically significant differences between groups from our customized SPM analysis were overlaid on our standard rendered brain (Fig. 1 right). The regional findings are summarized in Table 2.

Generally, we observed hypoperfusion in MCIs and early ADs, relative to normal controls. However, hyperperfusion was observed in the left thalamus (MCIs) and anterior cingulate (ADs), compared to normals. We also observed hippocampi hyperperfusion in MCIs compared to early ADs. Hyperperfusion was previously reported in the hippocampi (using MRI[5]) and anterior cingulate gyrus (using SPECT[6]) for ADs compared to normals.

References: 1). D. C. Alsop, J. A. Detre. *Radiology* 208:410-416(1998). 2). H. M. Gach, W. Dai. *Magn Reson Med*: **52**:941-946 (2004). 3). R. B. Buxton, et. al. *Magn Reson Med* **40**:383-396 (1998). 4). M. Chen. doctoral dissertation, Carnegie Mellon University, October, 1999. 5). D.C. Alsop et. al., Neurobiology of Aging 25(S2):S296 (2004). 6). K. A. Johnson et. al., Neurobiology of Aging 25(S2):S300 (2004).