Using Dynamic Susceptibility Contrast MRI for Cerebral Perfusion while Studying Alzheimer's Disease

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Introduction According to National Institute on Aging up to 4.5 million Americans suffer from Alzheimer's disease (AD), the most common neurodegenerative disease. Blood flow is a candidate marker for detecting early stages of AD because a decrease in cerebral perfusion has already been observed with perfusion MRI in AD using Arterial Spin Labeling (ASL) techniques [1]. However, the ASL perfusion method does not provide complementary information on blood volume and transit time that can help distinguish reduced perfusion due to brain atrophy from vasoregulatory changes. The application of DSC perfusion with intravenous gadolinium contrast injection to investigate perfusion changes in AD has received only limited attention. The DSC technique has the ability to provide cerebral blood flow (CBF), cerebral blood volume (CBV), and mean transit time (MTT) perfusion maps. Also this technique can be performed rapidly and is less sensitive to normal age-dependent reductions in blood flow. Moreover, the clinical workup for dementia `often already includes imaging with gadolinium contrast agents. Despite these advantages, conventional DSC MRI with indicator-dilution modeling techniques have limited accuracy due to inadequate temporal resolution, partial volume artifacts and non-linearity in MR signa ml as a function of contrast agent concentration. Recent approaches have made DSC MRI more quantitative using estimates of blood volume in the steady-state [2,3]. In a previous review, perfusion changes were observed using 13 subjects [4]. The current study will include 7 more subjects. The purpose of this study is to investigate the ability of DSC MRI with hybrid applications that combines bolus and infusion techniques to measure CBV and CBF changes in subjects with AD.

Materials and Methods Ten subjects with AD (mean age = 79 +/- 6.9 years) and ten Control Normal subjects (mean age = 76.1 +/- 9.7 years) were scanned on a GE Signa 1.5T MR. The imaging protocol included two injections of contrast agent (gadolinium). One relatively rapid bolus injection (65 µmol/kg at 3 mL/s) followed by a slow infusion (35 µmol/kg at 1 mL/s). For the bolus technique, the acquisition parameters were optimized for depicting temporal dynamics: TR of 1150 ms, TE of 35 ms, Flip angle of 90°, 12 slices, and thickness of 5 mm with a gap of 1 mm [6]. Slices were angled obliquely parallel to the base of the temporal lobe to maximize coverage. However, the total superior/inferior (S/I) coverage of ~8 cm did not always cover the top of the parietal lobe. The parametric maps were compared for the Control Normal and AD groups for differences in CBV and CBF. The perfusion maps were calculated by first selecting the arterial input function (AIF) followed by deconvolution with block-circulant SVD [5]. The CBF map was generated using the central volume principal, CBF = CBV/MTT. The CBV was derived from the infusion scan while the MTT was derived from the bolus scan. CBV, MTT, and CBF perfusion maps were normalized to standard MNI space and smoothed with a 10mm FWHM Gaussian kernel using SPM5 [The Wellcome Department of Imaging Neuroscience, London, UK]. A two-sample t-test was implemented voxel-by voxel, with a significance threshold of $p<0.005$. Gray matter masking with a dilation of 1 mm was used to improved specificity.

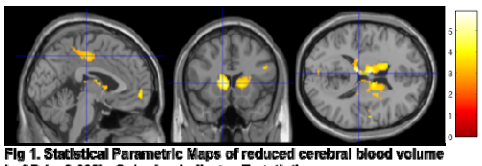

Fig 1. Statistical Parametric Maps of reduced cerebral blood volume in AD (p<0.005). Color bar indicates T-statistic.

Results The statistical maps generated showed perfusion differences among the AD and Control groups for the CBV and CBF. A decrease in perfusion is consistently seen in expected areas, including the Posterior Cingulate (PC), caudate, and thalamus (Fig 1.) AD compared to Control Normals. Both CBV and CBF showed hypoperfusion in the posterior cingulate (PC) and the thalamus (Fig 1 and 2).

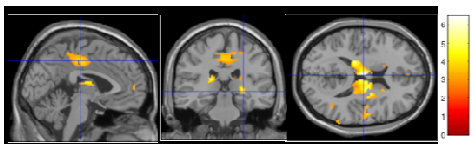

Fig 2. Statistical Parametric Maps of reduced cerebral blood flow in AD (p<0.005). Color bar indicates T-statistic.

Locations of maxima are reported in units of mm. For CBV, the maximum in the reduced blood volume in the PC was located at (2 -20 46), T value = 3.60 and in thalamus the maximum was located at (-6 -24 16), T value = 5.91. Reduced blood volume was also shown bilaterally in the caudate and frontal operculum. Hypoperfusion observed in the CBF maps was also observed in the PC with a maximum located at (2 -22 44), T value = 3.83 nearly identical to that for reduced CBV. For the thalamus the maximum was also highly overlapped the region of reduced blood volume, located at (-4 -14 16), T value = 6.17. Hypoperfusion was also shown in the posterior hippocampus but did not overlap with significant blood volume changes.

ROI Analysis

Both mean blood flow and blood volume are seen to decrease at specific ROIs located in expected areas, including the thalamus, PC, and caudate (Figs 3 and 4). These results are in agreement with prior studies of perfusion changes in AD [1].

Discussion The data support DSC MRI as a viable means for measuring relative perfusion changes in AD. The regions identified as hypoperfusion in AD subjects are consistent with prior studies using ASL and PET perfusion methods [1]. Future work will include MTT perfusion maps and the MTT ROI values. According to the central volume principle, if no significant changes are found in MTT, then most of the CBF reduction is due to reduced blood volume. Thus if most of the CBF reduction is due to reduced blood volume without significant changes in MTT, then it is possible to speculate that perfusion changes are due to reduced vascularity in these regions rather than a anomalous vasoregulatory response.

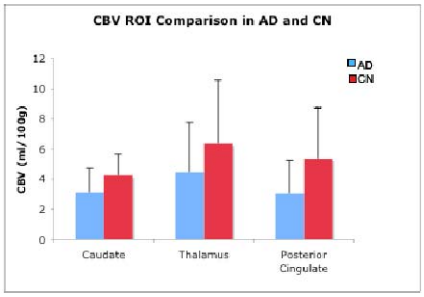

Fig 3. Comparison of the average CBV in the Caudate, Thalamus, and Posterior Cingulate.

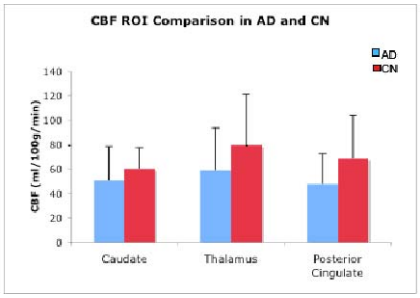

Fig 4. Comparison of the average CBF in the Caudate, Thalamus, and Posterior Cingulate.

References

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