

Voxel-based analysis of cerebral perfusion changes in Alzheimer disease and mild cognitive impairment measured with a novel 3D arterial spin labeling technique

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Purpose: Alzheimer's disease (AD) is a neurodegenerative disorder characterized by gradual onset and progressive deterioration. Recent studies revealed cerebral perfusion deficiencies were present from the very early pre-clinical phases of AD (i.e., during mild cognitive impairment (MCI)) and persist into the latest stages of the disease [1]. For perfusion measurement, traditional arterial spin labeling (ASL) techniques were developed based on gradient echo (GRE) sequences and suffered from susceptibility distortion, which hindered the accurate voxel-wise comparison between groups. A novel pulsed-continuous 3D ASL technique has been developed within the fast spin echo (FSE) framework to minimize the susceptibility artifacts and improve the signal-to-noise ratio (SNR) [2]. In this preliminary study, a voxel-based comparison was performed to investigate the perfusion changes measured with this newly-developed 3D ASL technique in AD and MCI patients as compared to cognitively normal (CN) subjects.

Methods: The study was approved by the local ethical committee and written informed consent was obtained from all the participants. Twenty-four AD patients (aged 74.6 ± 6.7 years) and seventeen MCI patients (aged 71.4 ± 7.6 years) were recruited according to the criteria of NINCDS-ADRDA, PADCs and Mini-Mental State Examination (MMSE) scores. Twenty-one age-, gender-, and education-matched healthy controls (aged 69.6 ± 5.9 years) were selected for group comparison. Two sets of ASL images were acquired using a 3.0-T GE Signa MR scanner (GE Healthcare, Milwaukee, WI) with an 8-channel phase array head coil, with and without the spatially selective inversion (tagging) pulse (TR/TE 1350/5 ms, flip angle 155° , labeling duration 1 s, post label delay 1.5 s, matrix = 128×128 , FOV 24 cm, thickness/gap 4/0 mm). The difference maps between tag and control pairs were averaged for each subject and quantitative CBF maps were calculate with the vendor provided toolbox. Voxel-based analysis was performed using SPM8 (<http://www.fil.ion.ucl.ac.uk/spm>). Spatial transformation included a three-dimensional rigid body registration to correct for head motion, followed by a nonlinear warping to spatially normalized CBF maps into a standard stereotaxic space using the Montreal Neurological Institute (MNI) template. The final CBF maps were resampled to $2 \times 2 \times 2$ mm³ isotropic voxel size and smoothed with a 6 mm isotropic Gaussian kernel. A second-level one-way ANOVA analysis was performed to identify the perfusion differences among AD, MCI and NC groups. For multiple comparison correction, the AlphaSim program implemented in AFNI (<http://afni.nih.gov/afni/docpdf/AlphaSim.pdf>) was used to control the false positive rate (corrected $p < 0.05$).

Results: As compared to the CN group, AD patients showed decreased CBF in bilateral temporo-parieto-occipital cortex and left limbic lobe but increased perfusion in bilateral thalamus, right caudate nucleus, putamen, temporal lobe and paracentral lobule (Fig. 1). MCI patients showed lower CBF than the normal controls in right posterior cingulate, middle temporal cortex, superior parietal lobe and left superior occipital lobe but elevated perfusion in bilateral frontal lobes and right temporal lobe (Fig. 2). For the comparison between the MCI and AD groups, AD patients showed decreased perfusion in bilateral frontal lobes, left side of anterior cingulate gyrus and inferior parietal lobule as well as the right middle temporo-occipital lobe but increased perfusion in the right thalamus, caudate nucleus, putamen, posterior cingulate and paracentral lobule (Fig. 3).

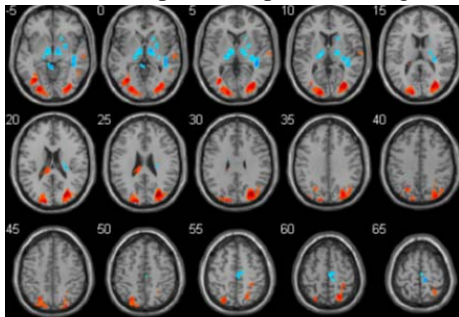


Fig. 1. CBF Comparison (Red: CN>AD, Blue: CN<AD, $p < 0.05$, corrected)

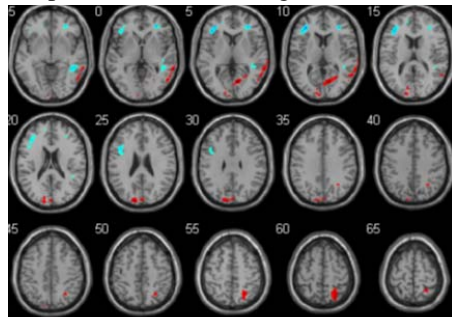


Fig. 2. CBF Comparison (Red: CN>MCI, Blue: CN<MCI, $p < 0.05$, corrected)

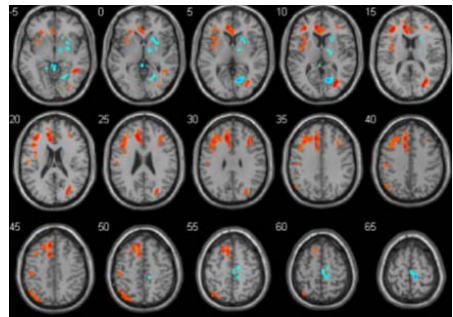


Fig. 3. CBF Comparison (Red: MCI>AD, Blue: MCI<AD, $p < 0.05$, corrected)

Discussion and Conclusion: In this preliminary study, we performed a voxel-based comparison of cerebral perfusion measured with a novel 3D ASL technique. We observed hyperperfusion regions in the MCI and AD groups in addition to hypoperfusion results reported by previous studies. Our results suggested the existence of the different patterns of hyperperfusion in different stages of the disease, which could provide interesting insight into the mechanism of the disease evolution.

References:

- [1] Mazza M, Marano G, Traversi G, et al. J Alzheimers Dis 2011; 23:375-389.
- [2] Dai W, Garcia D, deBazelaire C, et al. Magn Reson Med 2008; 60:1488-1497.