Enhanced Regional CBF in Patients with Mild Alzheimer's Disease after Three Months of Aricept® Treatment

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Background: Cholinergic inhibitor (Aricept®) has been shown to improve cognitive function in adults with Alzheimer's disease (AD) [1]. Also, it has an effect on improving the cerebral blood flow (CBF) perfusion detected by PET technology [2]. The aim of the current study was to investigate the effects of Aricept® treatment on CBF perfusion in Alzheimer's disease (AD) by using arterial spin-labeling perfusion MRI (ASL-MRI) [3] to measure regional CBF.

Methods: A total of 14 patients (age 77.57 ± 6.57 yrs) with newly diagnosed Alzheimer's disease were enrolled in a 3-month follow-up drug treatment study. Magnetic resonance images were taken both before and after the patients were given donepezil hydrochloride (Aricept®) treatment. ***MRI Protocol:*** All MRI scans were performed on a GE 3T Signa LX scanner. High-resolution anatomical images were acquired, using 3D spoiled gradient echo (SPGR) sequence with 144 continuous axial slices. The functional perfusion scans lasted 6 minutes, acquiring twelve axial slices with 7 mm thickness and 1 mm gap by QUIPSS-II method [4] covering an imaging area of 95mm in thickness. The localization of the imaging area was selected manually from the bottom margin of the inferior temporal lobule to the inferior parietal lobule. The tagging slab was 20cm in length with 1cm space between the distal edge of the tagging area and the imaging slice. A single-shot EPI pulse sequence was employed for image acquisition (FOV/matrix/TR/TE/TI_1/TI_2 = 24cm/64×64/4s/25ms/1.5s/1.75s). The patients were asked to be as still as possible while in the scanner. ***Data Analysis:*** AFNI software was used to process all images. One of the subjects was excluded due to incomplete scans. A 6-direction motion correction was performed to correct artifacts from motion during the scan. Perfusion-weighted CBF images were generated by calculating the difference between the tagged and non-tagged images. The images were then transformed to the Talairach space with a $2 \times 2 \times 2$ mm^3 interpolation. Finally, a paired two-sample *t*-test compared the CBF changes before and after 3-month Aricept® treatment.

Results and Discussion: After the paired group *t*-test between the subject group before and after the drug treatment, we found significantly increased regional CBF in the regions such as bilateral dorsal cingulate cortex (BA 24) and bilateral retrosplenial cortex (BA 29) as a part of posterior cingulate cortex (PCC). Previously PET and SPECT studies using subjects in the resting condition has demonstrated that the hypoperfusion in the early stage of development of AD was most prominent in the parietal associative cortices and cingulate gyri [5]. Especially, as a part of the default mode network, the retrosplenial cortex has been known to cause anterograde amnesia [6] when it is damaged. Therefore, increased CBF in the above regions may be an indication that Aricept can be a potential pharmacological approach to treat AD patients during their early development stage.

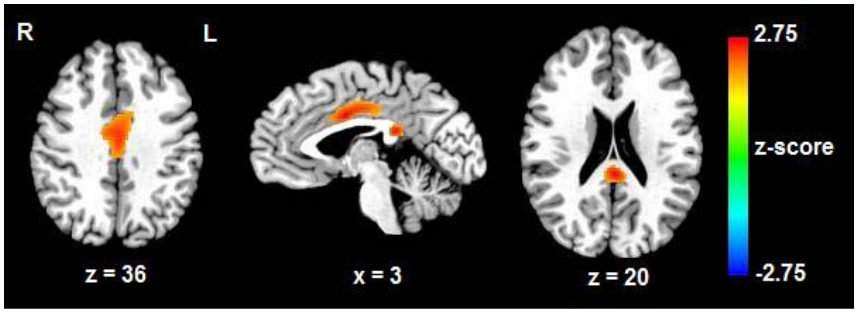

Fig. 1 Increased regional CBF in bilateral dorsal cingulate cortex (BA 24) and bilateral posterior cingulate cortex (PCC) after the cholinergic inhibitor (Aricept) treatment.

References: **1.** Kircher TT. et al. Am J Geriatr Psychiatry 2005. **2.** Ushuijima Y. et al. Ann Nucl Med 2006. **3.** Buxton RB. et al. MRM 1998. **4.** Wong EC. et al. MRM 1998. **5.** Mielke R. et al. J. Neural Transm 1998. **6.** Valenstein E. et al. Brain 1987.

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