Diffusion Tensor Imaging and Voxel-based Morphometry Study in Mild Alzheimer's Disease

Q. Chen[1], L. Zou[2], Q. Yuan[1], Z-Y. Li[2], L. Ou-Yang[3], W-W. Zhang[2], L-J. Jiang[4], D. Zhou[1], and Q-Y. Gong[2,5]

[1]Department of Neurology, West China Hospital of Sichuan University, Chengdu, Sichuan, China, People's Republic of, [2]Huaxi MR Research Center (HMRRC), Department of Radiology, West China Hospital of Sichuan University, [3]Department of Phychology, Southwest University, [4]Psychiatric Center, West China Hospital of Sichuan University, [5]Division of Medical Imaging, University of Liverpool

Introduction

Over the past few years, various neuroimaging techniques have been proposed to study Alzheimer's disease (AD) for diagnostic purpose(1). Despite many efforts to draw a clear cut picture of the disease, a comprehensive characterization of grey and whiter matter changes in mild Alzheimer disease (AD) is still not available. In this study, we aimed to characterize the brain changes in mild AD by the combined used of VBM and DTI, two unbiased neuroimaging techniques which have recently been introduced for structural evaluation of the brain in neurological disorders (2).

Subjects and Methods

The study was approved by the local ethical committee and written informed consent was obtained from all subjects. Twelve right handed patients (mean age=72±5.1 years, 7 males and 5 females) who met the criteria of the National Institute of Neurological and Communicative Disease and Stroke (NINDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA) for a diagnosis of mild AD were recruited. Eleven age- and sex-matched healthy volunteers (mean age=69±6.3 years, 5 males and 6 females) were recruited as control group. Magnetic resonance imaging (MRI) was undertaken on a 3.0T MR scanner (GE EXCITE, Milwaukee, USA). For VBM analysis, three dimensional SPGR T1 weighted images were acquired (TR/TE =8.5/3.4ms, flip angle =12°, FOV = 240 mm, matrix=256×256, slice thickness = 1 mm). DTI was acquired using a spin echo single-shot EPI sequence with 15 directions (TR/TE =10000/70.8ms, FOV = 24cm2, matrix=128×128, slice thickness =3.0mm, b value = 0, 1000s/mm^2). Analyses were run on Matlab 7.0 (MathWorks, Natick, Massachusetts, USA) and SPM2 (http://www.fil.ion.ucl.ac.uk/spm/software/). Customized a priori and template image creation and preprossing analysis were carried out using an optimized VBM protocol (3). FA maps were generated from each participant's DTI scan using DTI-Studio software (http://www. cmrm.med.jhmi.edu). Prior to the voxel-based analysis, FA maps were normalized using the parameters determined from the normalization of the b =0 image to MNI EPI template and then smoothed with an 8-mm FWHM kernel. A white matter mask derived from the averaged, normalized WM segment of SPGR image was used on FA maps to restrict the analysis to the white matter tracts. Voxel-based analysis of grey matter and FA maps were carried out using two-sample t tests. A p value (two-tailed) lower than 0.001 (uncorrected) in voxel difference with a cluster size greater than 50 voxels were considered to be statistically significant.

Results

Compared with controls, in AD patients VBM analysis showed a significant clusters of reduced grey matter in hippocampus, amygdale, cingulate gyrus, caudate nuclei, middle temporal gyrus and precentral gyrus, bilaterally, as well as the right insula and right frontal cortex (Figure 1). With regard to white matter alterations, bilateral reduced FA in corpus callosum, cingulum, white matter in parietal lobe and frontal lobe was present in AD patients (Figure 2).

Discussion

In our study, a combination of two different technique and structural brain imaging, VBM and DTI, was adopted in attempt to shed light on the relation between grey matter and white matter abnormalities in mild AD patients. These data provide evidence for both grey and white matter degeneration in brains of mild AD patients from the early disease stage, suggesting that atrophy of cortical and subcortical structures and nerurodegeneration of specific fibre tracts contribute to neurological deficits in AD. This approach provide a completely new way of gaining direct in vivo information on brain tissue loss, and may guide future research investigating the relation between the brain areas involved and the clinical features in different phases of the disease.

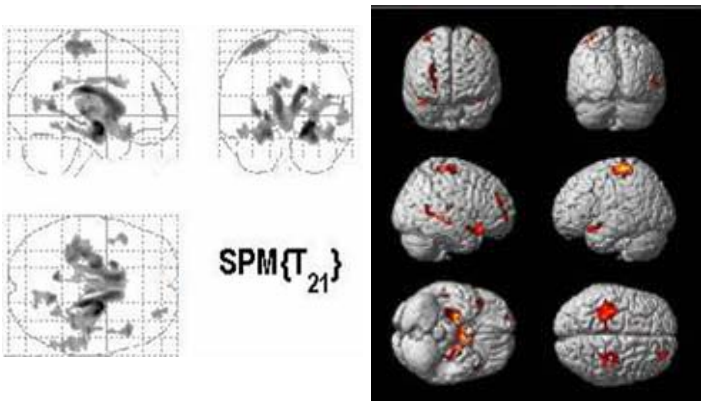

Figure 1. Patterns of grey matter atrophy in AD compared with controls. The results are shown on the SPM glass brain template (left panel) and a 3D surface render (right panel).

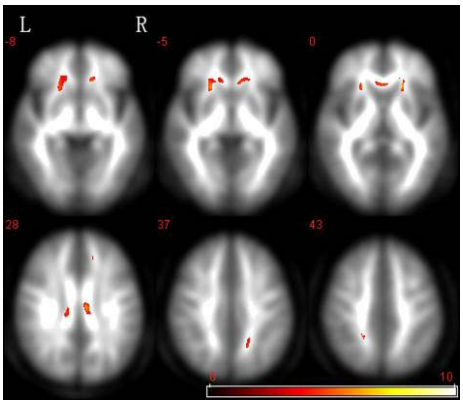

Figure 2. Voxels that showed significant reduction in white matter fractional anisotropy in AD patients compared with controls, mapping onto an average FA image of controls and AD patients.

Reference.

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3 Good CD, et al. Neuroimage, 2001;14:21-36.