Elderly with memory impairment deteriorate to dementia of Alzheimer type (DAT) by way of mild cognitive impairment (MCI) when they show no disability on their daily life. Previous postmortem studies have revealed demyelination in the white matter of DAT. However, little has been reported on microstructural alteration of white matter, compared to a large number of studies on the gray matter. Diffusion Tensor Imaging has an advantage in the evaluation of microstructural alteration in vivo. The aim of this study is to investigate microstructural alteration and its correlations with cognitive functions and behavioral and psychological symptoms of dementia (BPSD).

The subjects consisted of 39 patients with DAT, 21 age- and gender-matched subjects with MCI and 20 normal controls. All participants received clinical evaluation with neurological examinations, the Neuropsychological Test Battery for Alzheimer’s Disease, and the Neuropsychiatric Inventory. Diffusion Tensor Imaging was acquired for all the subjects with 3T Magnetic Resonance Imaging Equipments, and fractional anisotropy (FA) and apparent diffusion coefficient (ADC) maps were generated by conventional methods. All types of images including FA, ADC, and 3D T1 maps in native space were transformed with spatial normalization and their smoothed images were compared by means of voxel-based analysis with a threshold of uncorrected p < 0.001, adjusted for age, gender, and education years. In additional analysis, the values of FA, ADC, and gray matter density in the specific area were extracted by means of the Region-of-Interest analysis method, and their values were examined to have any correlations with cognitive functions and BPSD.

As results, the MCI group showed significant regional reductions of FA compared to normal controls in the subgyral white matter of the right temporal lobe and in the superior longitudinal fasciculus of the left frontal lobe. There was no significant difference of ADC between the two groups in any region. On the contrary, the DAT group showed significant regional reductions of ADC compared to the MCI group in the bilateral parahippocampal gyri. There was no significant difference of FA between the two groups in any region. The FA values of the corpus callosum showed significant positive correlations with gray matter density in temporal lobe in the DAT and MCI group but not in the normal group. The FA values of the right subgyral white matter of the temporal lobe showed significant reductions in the MCI subjects, compared between the normal controls and the MCI subjects who showed preserved gray matter density in the right superior temporal gyrus. General cognitive functions showed positive correlations with the gray matter density of the temporal lobe, but not with the FA values of the temporal and the frontal lobe in the DAT group. DAT with psychosis showed reductions in the FA values of the temporal lobe. Agitation and apathy showed reductions in the FA values of the frontal lobe. Anxiety showed increases in the ADC values of the temporal lobe. However, BPSD showed no significant difference in the gray matter density.

In conclusion, microstructural alteration of white matter occurred in MCI, prior to the development into DAT. It could be an evidence of Wallerian degeneration in the white matter that the MCI group showed decreases in the FA but not in the ADC values, compared with the normal controls, and that the FA values of the corpus callosum showed a significant correlation with gray matter density in the temporal lobe. The microstructural alteration of white matter is associated with behavioral and psychological symptoms of dementia, compared with cognitive functions in dementia of Alzheimer type.

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