Frontal lobe dysfunction correlates with microstructural alteration of cerebral white matter in multiple system atrophy.

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Introduction:

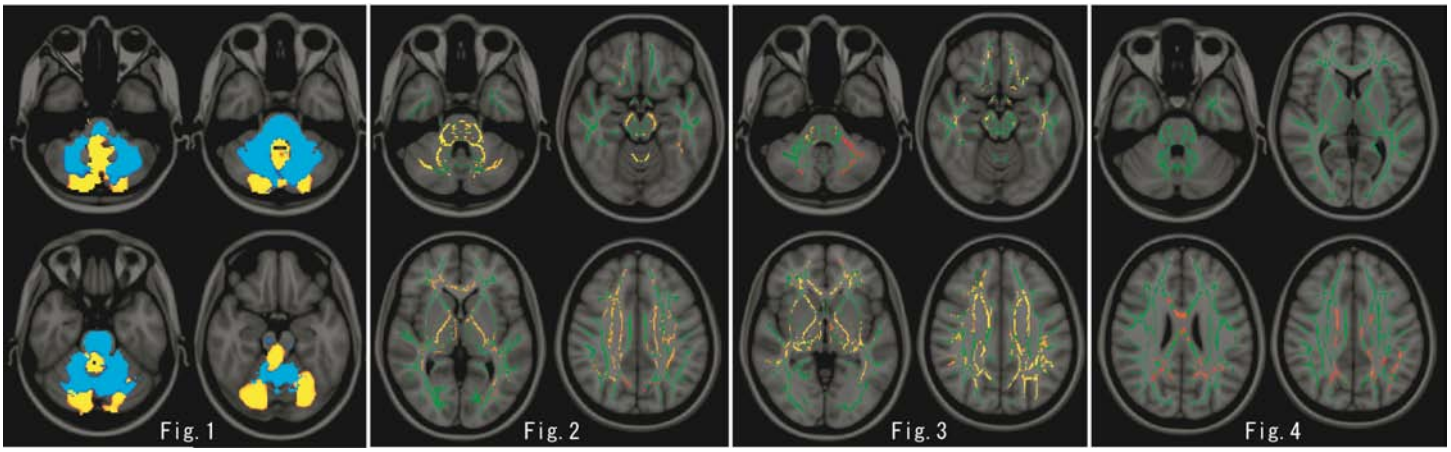
Multiple system atrophy (MSA) is a neurodegenerative disease, which can cause autonomic dysfunction, parkinsonism and ataxia. Pathological hallmark of MSA is glial cell inclusions, which are predominantly found in the cerebral and cerebellar white matter. Recently, several studies have reported that MSA patients also complicate cognitive impairment [1]. However, the underling substrates of cognitive impairment remain to be elucidated. Here, we aimed to elucidate the macro- and micro-structural alteration of brain and neuronal correlates of cognitive impairment in MSA patients by using voxel-based morphometry (VBM) and diffusion tensor imaging (DTI).

Methods:

MSA was diagnosed according to clinical diagnostic criteria [2]. MSA patients and healthy subjects were evaluated by using Mini-Mental State Examination (MMSE), Frontal assessment battery (FAB), word fluency test, the Wechsler Adult Intelligence Scale-III (WAIS-III) letter number sequencing task, Wisconsin Card Sorting Test (WCST) and Trail Making Test (TMT) A and B. Diffusion tensor imaging (DTI, 30 axis of Echo Planner Imaging, 3mm thickness) and 3 dimensional-T1 weighted imaging (sagittal image, 1mm thickness) were obtained by using 3.0T MRI (GE) from all subjects. Structural images were analyzed with VBM implemented in the FMRIB Software Library 4.1.5 (FSL). The segmented white and grey-matter images were compared between MSA patients and control subjects. Voxel-based analysis of the fractional anisotropy (FA) map was carried out using Tract-Based Spatial Statistics (TBSS) analysis implemented in FSL. The mean FA skeleton was thresholded at FA > 0.20. The areas where FA values were correlated with FAB score or number of categories achieved in WCST were explored by using TBSS in MSA patients. Here, age, gender and disease duration were treated as nuisance covariates. The significance criterion was set at the threshold-free cluster-enhancement corrected $P < 0.05$.

Results and Discussion:

We enrolled 16 MSA patients (11 MSA-C and 5 MSA-P) and 10 control subjects. Scores of FAB, word fluency test and WCST were significantly lower and completion time of TMT A and B were significantly longer in MSA patients compared with control subjects. VBM analysis showed significant grey and white matter atrophy which are localized in the brainstem and cerebellum in MSA patients (Fig.1. Blue and yellow areas show atrophied white and grey matter, respectively.). TBSS analysis identified broad areas of white matter where FA values were significantly decreased in MSA patients, including the cerebellum, brainstem, cerebral peduncles, internal capsules, corpus callosum, cingulum and juxtacortical white matter (Fig.2. yellow and orange areas. Green areas show mean FA skeleton). Some of identified areas were also consistent with reported areas in previous DTI study [3]. On the other hand, FAB scores were correlated with FA values in broad cerebral white matter, including temporal lobes, corpus callosum, cingulum and juxtacortical white matter (Fig.3). Scores of WCST were correlated with FA values in part of corpus callosum, cingulum and parietal juxtacortical white matter (Fig.4).



Conclusion:

Out results suggest that there are localized white and grey matter atrophy as well as microstructural alteration in the broad white matter, and the frontal lobe dysfunction correlates with microstructural alteration of cerebral white matter in MSA patients.

References: [1] Kawai et al., Neurology, 2008. [2] Gilman et al., Neurology, 2008. [3] Tha et al., Radiology, 2010.