Differentiation of Early-Stage Parkinsonisms using Diffusion Kurtosis/Tensor Imaging

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Target audience: Researchers interested in the application of diffusion kurtosis/tensor imaging or the investigation of parkinsonisms

Purpose: Differential diagnosis in Parkinson's disease (PD) and related disorders such as multiple system atrophy (MSA) and progressive supranuclear palsy (PSP) is often difficult at the early stage, because the clinical symptoms and neurological signs are similar, and MRI shows only minimal differences between these disorders. Diffusion kurtosis imaging (DKI), an extension of conventional diffusion tensor imaging (DTI), is speculated to detect minute microstructural alterations in the non-Gaussian water diffusion of cerebral white matter (WM) and gray matter (GM), and has been applied to various neurological disorders [1,2]. In this study, we investigated whether DKI can detect subtle pathological changes occurring in early-stage parkinsonisms, and whether it can differentiate these disorders.

Methods: ***Subjects:*** We examined 14 patients with PD, 6 patients with MSA (4 with predominant parkinsonism [MSA-P], 2 with predominant cerebellar ataxia [MSA-C]), 7 patients with PSP, and 5 control subjects (Ctrl). ***Image Acquisition:*** DKI was performed using a 3 Tesla MRI scanner (Discovery MR750, GE Healthcare) with a single-shot SE-EPI sequence with the following parameters: TR/TE: 4000/110 ms; averages: 4; resolution: $0.94 \times 0.94 \times 3$ mm^3; *b*-values: 1000 and 2500 s/mm^2; and diffusion encoding directions: 20. ***Quantitative Measurements:*** We calculated diffusion metrics such as the mean kurtosis (MK), fractional anisotropy (FA), and mean diffusivity (MD) using an in-house software program [3]. Each map, for all subjects, was non-linearly registered to the JHU_MNI_SS_FA-1-mm template using the FSL FNIRT tool. Regions of interest (ROIs) such as the limbic (LB), executive (EC), and sensorimotor (SM) parts of the putamen, midbrain (MB), superior cerebellar peduncle (SCP), pontine crossing tract (PCT), middle cerebellar peduncle (MCP), cerebellar WM, and cerebellar GM were defined based on the Striatal Connectivity Atlas [4] and JHU_MNI_SS_EvePM atlas [5] using FSL (Fig.1). The mean MK, FA, and MD values within these ROIs were calculated and were compared between the groups by using a Steel-Dwass test.

Results: There were significant changes in MK, FA, and/or MD values of the ROIs in the patient groups when compared with the controls. In addition, the MK values of SM, MB, and cerebellar GM as well as FA values of SCP and cerebellar WM were significantly decreased in patients with PSP, while the MD values of PCT and MCP were significantly increased in patients with MSA-C, when compared with the patients with PD (Fig.2). There were no significant differences in other comparisons, including the diffusional metrics between the PD and MSA-P groups.

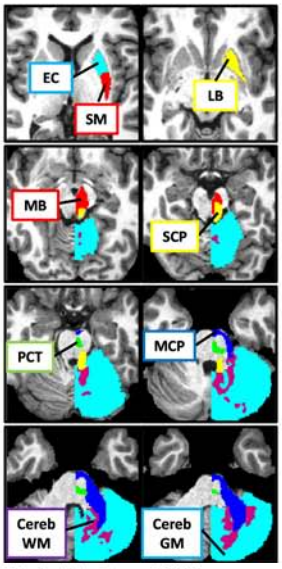

Fig.1 Atlas-based ROIs.

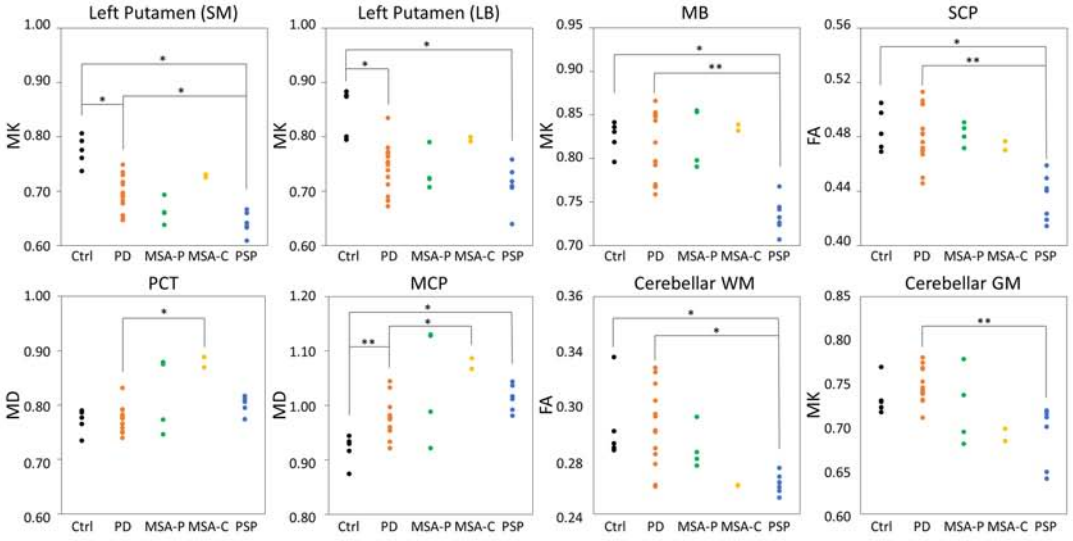

Fig.2 MK, FA, and MD values in the ROIs in which there were significant differences between the groups. **p*<0.05, ***p*<0.01

Discussion: In this study, there were substantial changes in the diffusion metrics of various structures in the basal ganglia, brain stem, and cerebellum of the early-stage parkinsonisms. Further, we successfully revealed that only MK values were significantly different between patients with PD and patients with PSP in the SM of the putamen, MB, and cerebellar GM, suggesting that DKI can detect subtle pathological changes in the GM and complex GM/WM structures, which MD and FA do not. In contrast, MD and FA values, not MK, were significantly different between PD and PSP or MSA-C in the WM structures such as the SCP, PCT, and cerebellar WM, suggesting that DKI can provide little advantage in detecting minute changes in the uniform WM tracts when compared with DTI metrics. In conclusion, combined DKI/DTI analyses can detect significant differences in, and alterations of, various GM/WM structures among patients with early-stage parkinsonisms and can contribute to the early differential diagnosis of these disorders.

References: [1] Hui ES et al., Stroke, 2012. [2] Zhuo J et al., Neuroimage, 2012. [3] Yokosawa S et al., ISMRM, 2013. [4] Tziortzi A et al., Cereb Cortex, 2013. [5] Lim I et al., Neuroimage, 2013.