Differentiation of Early-Stage Parkinsonisms with Diffusion Kurtosis Imaging Using The Diffusion Magnetic Resonance Parkinsonism Index

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Target audience: Researchers interested in the application of diffusion kurtosis imaging and/or investigations of parkinsonisms

Purpose: It is often difficult to differentially diagnose Parkinson's disease (PD) and related disorders, such as multiple system atrophy (MSA) and progressive supranuclear palsy (PSP), in their early stages because the clinical symptoms and neurological signs of all these disorders are similar. In addition, magnetic resonance imaging (MRI) findings only show small differences between these disorders. Therefore, several quantitative metrics have recently been proposed. These include the magnetic resonance parkinsonism index (MRPI) for T1-weighted images. The MRPI has been reported to distinguish between patients with PD, MSA, and PSP.[1] However, the diagnostic performance of these indices remains suboptimal in the early stages of these disorders. Diffusion kurtosis imaging (DKI), which is an extension of the conventional diffusion tensor imaging, is thought to detect minute microstructural alterations in the non-Gaussian water diffusion of cerebral white matter (WM) and gray matter (GM). DKI has been applied in various neurological disorders.[2,3] In this study, we investigated whether DKI detected subtle pathological changes that occur in early-stage parkinsonisms and differentiated these disorders, particularly when the newly proposed diffusion MRPI (dMRPI), which is a DKI-equivalent for MRPI, was used.

Methods: ***Subjects*:** We examined 31 patients with PD, 10 patients with MSA (6 with predominant parkinsonism [MSA-P] and 4 with predominant cerebellar ataxia [MSA-C]), 9 patients with PSP, and 10 control subjects; the median durations of the disease were 1.5, 1.9, 1.5, and 1.5 years, respectively. ***Image Acquisition*:** DKI images were obtained with a 3-Tesla scanner (Discovery MR750, GE Healthcare) with a single-shot spin echo-echo planar imaging sequence with the following parameters: TR/TE, 4,000/110 ms; averages, 4; resolution, 0.94 × 0.94 × 3 mm^3; *b*-values, 1,000 and 2,500 s/mm^2; and diffusion encoding directions, 20. ***Quantitative Measurements*:** We calculated diffusion metrics, including the mean kurtosis (MK), fractional anisotropy (FA), and mean diffusivity (MD), with an in-house software program.[4] The images were nonlinearly registered to the Johns Hopkins University (JHU) template with Advanced Normalization Tools.[5] Regions of interest (ROIs), including the midbrain tegmentum (MT), the pontine-crossing tract (PCT), the superior cerebellar peduncle (SCP), and the middle cerebellar peduncle (MCP), were defined based on the JHU_EvePM atlas (Fig. 1).[6] The mean MK, FA, and MD values within these ROIs were calculated, and the dMRPI of these metrics was then obtained with the equation (PCT/MT)·(MCP/SCP). These values were compared among the groups and with conventional indices, such as the MRPI and early/late heart/mediastinum (H/M) ratios of ^{123}I-metaiodobenzylguanidine (MIBG) scintigraphy with Steel-Dwass tests. In addition, receiver operating characteristic (ROC) analyses were performed to determine the sensitivities and specificities of dMRPI, MRPI, and MIBG scintigraphy.

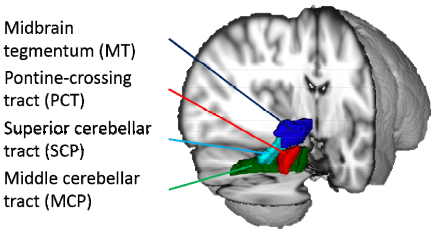

Fig. 1 Atlas-based Regions of Interest.

Results: Among the indices, only the dMRPI-MK values significantly differed among the 3 patient groups, while the dMRPI-MD values and early H/M ratios did not differ between the PD and MSA groups and between the MSA and PSP groups. The dMRPI-FA and MRPI values significantly differed only between the PD and MSA groups and between the MSA and PSP groups (Fig. 2). The areas under the ROC curve of dMRPI-MK were 0.81–0.90, and the sensitivities and specificities were 80%–100% and 80%–93%, respectively, for differentiating patients with early PD, MSA, and PSP (Table 1).

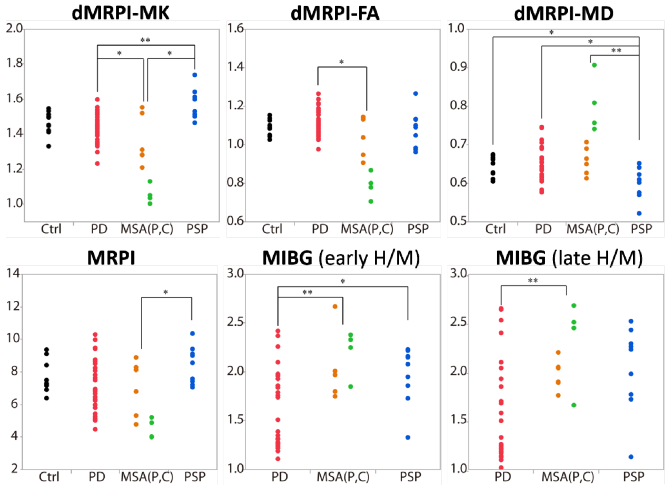

Fig. 2 Scatterplots of dMRPI-MK/FA/MD, MRPI, and early/late H/M values among the groups. *$p < 0.05$, **$p < 0.01$

Discussion and Conclusion: In this study, we detected significant differences in the brainstem and cerebellar peduncle structures in patients with early-stage parkinsonisms with dMRPI, a newly proposed quantitative index. In particular, we found that only dMRPI-MK values significantly differed among patients with early PD, MSA, and PSP, suggesting that MK can more efficiently detect subtle pathological changes in the GM and WM, including neuronal loss, gliosis, axonal degeneration, and demyelination, compared to FA, MD, conventional MRI, and MIBG scintigraphy. The sensitivities and specificities of dMRPI-MK for distinguishing between patients with early PD, MSA, and PSP were both over 80%, indicating that this new index can potentially be used for the early differential diagnosis of these disorders. In conclusion, quantitative DKI analyses with dMRPI-MK can differentiate patients with early-stage parkinsonisms with high sensitivities and specificities and may be beneficial for the early differential diagnoses of these disorders.

Table 1 ROC analysis of dMRPI, MRPI, and MIBG scintigraphy for discriminating between patients with early PD, MSA, and PSP.

		PD vs. MSA			PD vs. PSP			MSA vs. PSP		
		AUC	Sensitivity (%)	Specificity (%)	AUC	Sensitivity (%)	Specificity (%)	AUC	Sensitivity (%)	Specificity (%)
dMRPI	FA	0.78	70	90	–	–	–	–	–	–
	MD	–	–	–	0.80	67	80	0.93	100	70
	MK	0.81	80	93	0.89	89	80	0.90	100	80
MRPI		–	–	–	–	–	–	0.86	100	70
MIBG	Early	0.83	100	59	0.77	78	69	–	–	–
	Late	0.82	90	72	–	–	–	–	–	–

References: [1] Quattrone A et al., Radiology 2008;246:214–221. [2] Wang JJ et al., Radiology 2011;261:210–217. [3] Van Cauter S et al., Radiology 2012;263:492–501. [4] Yokosawa S et al., ISMRM 2014;2581. [5] Klein A et al., Neuroimage 2009;46:786–802. [6] Lim IA et al., Neuroimage 2013;82:449–469