Comparison of efficacy of diffusion kurtosis imaging in detection of occult brain damages in neuromyelitis optica and multiple sclerosis

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Target audience: researchers interested in the investigation of neuromyelitis optica (NMO) and multiple sclerosis (MS).

Introduction: NMO and MS are two common types of inflammatory demyelinating diseases of central nervous system. Although NMO was considered to be a variant of MS, recent clinical, immunological and pathological findings suggest distinct aetiology of them, and neuroimaging plays a vital role in both diagnosis. However, to distinguish these two diseases is quite challenging in the early or stable stage when lesions appear ambiguous while conventional MRI suffers low sensitivity and specificity to detect “occult” pathological alterations in both normal-appearing WM and GM (NAWM/NAGM) of patients. Several advanced imaging techniques, such as diffusion tensor imaging (DTI), have been applied to investigate the pathologies and search for useful separation imaging markers. As an extension of conventional DTI, diffusion kurtosis imaging (DKI) estimates all the conventional DTI metrics more accurately while provides additional kurtosis metrics which quantify the changes in tissue heterogeneity or microstructural complexity of both anisotropic and isotropic biological tissues and have been proved to be less sensitive to CSF partial volume effect. In the present study, we performed DKI on the brain of healthy volunteers and patients diagnosed with NMO and MS to test whether DKI-derived metrics are sensitive to subtle changes in NAWM and NAGM tissue microstructures in NMO and whether DKI can be used to distinguish it from MS.

Methods: Subject: 8 NMO patients at stable phase (1M7F, 43.8 ± 13.0 yrs), 18 MS patients (6M12F, 42.1 ± 10.1 yrs) and 18 healthy volunteers (7M11F; 43.4 ± 12.3 yrs) were studied after signed, informed consent.

Image acquisition: All scans were performed on a 3T MRI scanner (Philips Healthcare, Best, The Netherlands) with body coil excitation and 8-channel SENSE head coil for reception. Four averaged minimally weighted (b0) and 2 averaged 32 gradient directions with two b values (1000 and 2000 s/mm2) were acquired using single-shot EPI sequence with following parameters: TR/TE = 2000/69 ms, nominal / reconstruction resolution = 2.55x2.55x3 / 2x2x3 mm3, 44 axial slices with no interslice gap to cover the whole brain, SENSE factor = 2, 3/4 partial Fourier encoding, total scan time = 19 min 39 s. T1w images were acquired using 3D-MPRAGE sequence (TR/TE = 7.0/3.2ms, TI = 800 ms, nominal/reconstruction resolution = 1x1x1 mm3, 167 slices, total scan time = 10 min 41 s). Axial T2w images with the same geometry as the DKI acquisition of the brain were also obtained using multishot-TSE sequence (TR/TE= 3000/80 ms, reconstruction resolution = 0.33x0.33x3 mm3, 44 slices, total scan time = 2 min 48 s).

Data processing and analysis: DKI-derived indices were estimated using Diffusional Kurtosis Estimator (DKE)3. Each T1w hypointense lesion of MS patients in T1w-MPRAGE images was filled up with the mean intensity value of the surrounding NAWM in the same slice, and the newly generated images were used for later volumetric analysis. For each subject, the volumes of GM, peripheral GM and WM were estimated by applying Sienax in FSL with the optimized parameter choice for BET in MS. The MPRAGE images were segmented into WM and GM and then coregistered to b0 images. The NAWM and cortical NAGM masks were checked by an experienced observer with T1w and T2w images to exclude any visible lesions and transferred to all DKI-derived maps for quantification. Independent samples T tests were performed to test group difference of each metric

Results and Discussion: No visible lesions were identified on T1w and T2w images of healthy volunteers and patients with NMO. Although progressive brain atrophy is considered as an important feature of MS pathology and previous studies also observed reduced volumes in both WM and GM of NMO patients volmetric analysis in this study showed no obvious volume changes but trends of decline in both patient groups. However, DKI-derived indices were sensitive to reveal the subtle pathological alterations in the tissue microstructure of NAWM and cortical NAGM. In the upper part of Fig.1, MK in NAWM of NMO patients shows significant decrease when compared to controls, implying reduced microstructural complexity or heterogeneity due to the disease pathology. Meanwhile, all indices except λ4 could differentiate NMO from MS, suggesting more severe demyelination and Wallerian degeneration in NAWM of MS. In the lower part of Fig.1, while the significant difference of most of the indices between NMO and controls indicates the presence of occult damage in cortical NAGM of NMO patients, increased MD and λ4 imply a higher possibility of axonal and dendritic transection in cortical NAGM of MS than NMO.

Conclusion: In this preliminary study, we have demonstrated that the occult brain damages of patients with NMO and MS can be detected and differentiated by applying DKI. With the supplementary information provided by Kurtosis metrics, DKI-derived indices may potentially be a useful biomarker in treatment selection and monitoring disease process in patients with NMO.