A quantification of myelin and axonal damage across multiple sclerosis lesions and clinical subtypes with myelin and diffusion MRI

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SUMMARY

The interplay between axonal and myelin damage in multiple sclerosis (MS) is poorly understood. This study aimed to evaluate the concomitant presence of axonal and myelin injury in living MS patients by using multi-shell diffusion MRI. Concomitant neuroanatomical biomarkers, our results show that axonal and myelin damage coexist in MS lesions in a largely normal-appearing white matter (NAWM) and in combination with myelin damage. Confirming neuropathological findings, our study shows that axonal and myelin damage exists in RRMS and PMS patients: (i) in white matter lesions as well as in normal appearing white matter; (ii) in cortical and sub-cortical white matter; (iii) in WM and GM in HC (WM-HC and GM-HC) and paramagnetic rim lesions; (iv) in PV and JC lesions; (v) in WMLs in RRMS and PMS patients. In addition, we found that axonal damage in lesions with rims is higher than in lesions without rim. Our data also provide new knowledge about myelin and axonal damage in RRMS and PMS patients: (i) axonal and paramagnetic damage in PV lesions is higher than in JC lesions; (ii) axonal damage in CMLs is higher than in LLMs; (iii) axonal and myelin damage differs among lesion subtypes and between PVLs and JCLs. Confirming neuropathological findings, our study shows that axonal and myelin damage coexist in living MS patients in small-sized relapsing-remitting MS (RRMS) cohorts.

METHODS

Diffusion-weighted imaging was obtained in 1310 MS lesions (WMLs: 1106, CLs: 204) and in 3600 voxels of healthy control (HC) cortex and subcortical white matter (WM). Myelin and axonal damage were determined in two consecutive 2-voxel layers of peri-plaque WM (denoted as PP-1 and PP-2) and in non-lesional WM and GM (WM-HC and GM-HC). Lesions were automatically segmented in (i) WMLs, CLs; (ii) two consecutive 2-voxel layers of peri-plaque WM (denoted as PP-1 and PP-2) and non-lesional WM and GM (WM-HC and GM-HC); (iii) WMLs in RRMS and PMS patients. NDI and MWF were extracted in (i) WMLs, CLs; (ii) two consecutive 2-voxel layers of peri-plaque WM (denoted as PP-1 and PP-2) and non-lesional WM and GM (WM-HC and GM-HC); (iii) WMLs in RRMS and PMS patients. Statistical analysis was performed by using nonparametric Mann-Whitney test (for two-group unpaired analyses) and Kruskal-Wallis test with Dunn’s multiple comparisons test. All results were corrected for multiple comparisons with the Benjamini-Hochberg false-discovery rate correction.

RESULTS

We analyzed 1310 MS lesions (WMLs: 1106, CLs: 204) and 3600 HC voxels. NDI and MWF were reduced compared to HC in WMLs and CLs (p< 0.001) (Figure 1 A-D). We found that NDI was lower in WMLs and CLs compared to normal-appearing control tissue (NAWM and WM-HC) (p< 0.001). MWF was extracted in the same lesions (WMLs and CLs) and was lower compared to normal-appearing control tissue (NAWM and WM-HC) (p< 0.001). NDI and MWF were extracted in (i) WMLs, CLs; (ii) two consecutive 2-voxel layers of peri-plaque WM (denoted as PP-1 and PP-2) and non-lesional WM and GM (WM-HC and GM-HC); (iii) WMLs in RRMS and PMS patients. In addition, we found that axonal damage in lesions with rims is higher than in lesions without rim. Our data also provide new knowledge about myelin and axonal damage in RRMS and PMS patients: (i) axonal and paramagnetic damage in PV lesions is higher than in JC lesions; (ii) axonal damage in CMLs is higher than in LLMs; (iii) axonal and myelin damage differs among lesion subtypes and between PVLs and JCLs. Confirming neuropathological findings, our study shows that axonal and myelin damage coexist in living MS patients in small-sized relapsing-remitting MS (RRMS) cohorts.

DISCUSSION

Concomitant neuroanatomical biomarkers, our study showed that NDA and CDA significantly reduced axonal and myelin damage in normal appearing white matter compared to normal appearing grey matter. In addition, we found that axonal damage was not significantly affected in non-lesional white matter compared to normal appearing grey matter.

CONCLUSION

Concomitant neuroanatomical biomarkers, our results show the existence of intra- and inter-lesional differences in axonal and myelin damage in a largely normal-appearing white matter (NAWM) and in combination with myelin damage. Our study shows that axonal and myelin damage coexist in living MS patients in small-sized relapsing-remitting MS (RRMS) cohorts.