Characterizing diffuse and focal grey matter damage with soma and neurite density image metrics in multiple sclerosis

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BACKGROUND AND AIMS

Different models based on diffusion MRI techniques have been implemented to study the microstructural properties of white matter (WM). Recently, the Soma and Neurite Density Imaging (SANDI) model has been proposed to investigate microstructural information in gray matter (GM).

Based on SANDI metrics, in this study, we aimed to characterize the tissue damage parameters between the normal-appearing grey matter (NAGM), the cortical lesions (CLs), atrophic and non-atrophic brain areas in people with multiple sclerosis (PwMS) compared to the GM of the healthy control subjects (HCs). Moreover, we compared the microstructural parameters within the CLs of PwMS with their non-damaged regional counterparts in contralateral GM (cCLs).

METHODS

40 PwMS (43.6±12.9 years, 26 females) and 14 HCs (36.1±12.8 years, 8 females) underwent the same MRI protocol on a 3T Siemens Magnetom Prisma, which comprised: 3D T1-MPRAGE (TR=2300ms, TE=2.96ms, 1mm isotropic voxel, flip Angle=8°); Diffusion-weighted PGSE sequence (TR=2600ms, TE=80ms, δ=24.66ms, Δ=39.07ms, 2mm isotropic voxel, 213 gradient directions, bvalue=0/500/1000/2000/3000/4000/6000 s/mm^2), with an additional bvalue=0 s/mm^2 acquired with reverse phase encoding direction. A 3D-DIR sequence (TR=5500ms, TE=2500ms, TI=2500 and 450 ms, 1.2mm isotropic voxel) was acquired in PwMS. WM lesions and CLs were manually identified on T1 and DIR images in PwMS, respectively. For each PwMS, T1 images were then filled using a T1-hypointense lesion mask and FSL . The non-damaged contralateral GM regions of CLs were extracted using in-house software.

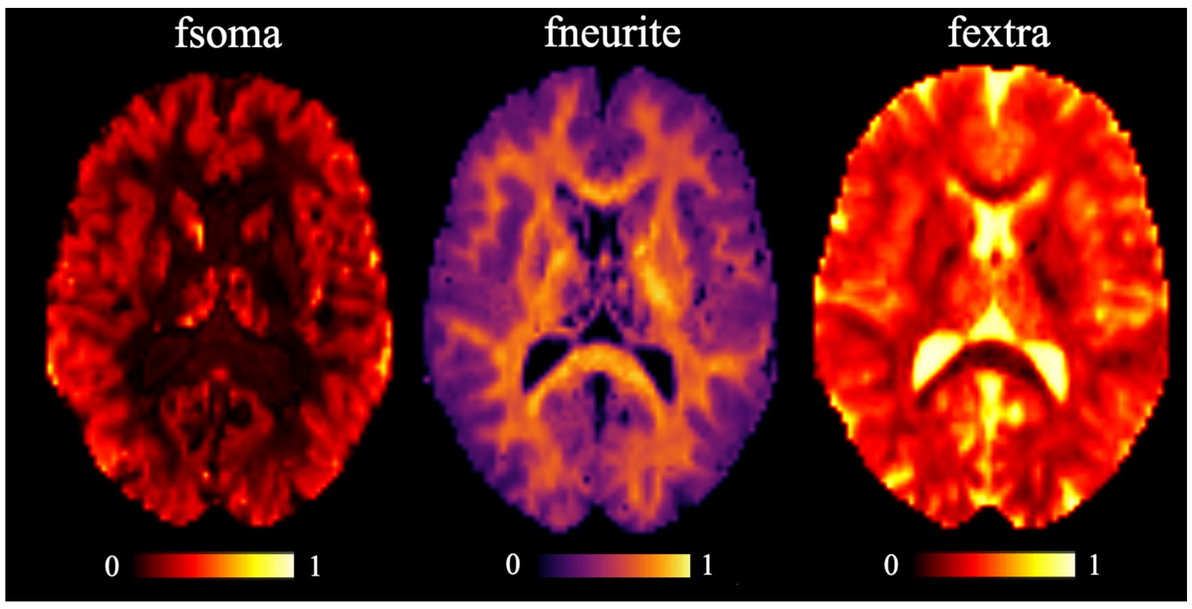
GM volumes for both PwMS and HCs were computed from T1 images using FreeSurfer. Voxel-Based Morphometry (VBM) analysis was performed using SPM to identify atrophic GM areas of PwMS with respect to HCs while controlling for age and gender (uncorrected p< 0.001).

Diffusion images were pre-processed via DESIGNER, including coregistration, eddy current correction, geometric distortion correction, and registration to anatomical data.

Microstructural metrics of SANDI (fsoma, fneurite, fextra) computed with the AMICO toolbox were extracted within cortical GM in HCs, atrophic and non-atrophic cortical GM areas, NAGM, CLs, and their cCLs in PwMS. **Figure 1** shows an example of SANDI maps.

Statistical analyses were performed using Python (v.3.8.13). Two-sided p-values<0.05 were considered significant. ANCOVA analysis adjusted for age and gender was used to compare GM volumes and SANDI metrics across the groups.

FIG. 1



RESULTS

149 CLs were globally detected (range for patient 0-28). **PwMS showed GM atrophy with respect to HC** (530.6±72.4 ml vs 581.8±75.6 ml, p<0.001). VMB analysis resulted in different cortical atrophy GM areas of PwMS compared to HCs: right precental gyrus, precunes cortex and parahippocampal cortex; left superior frontal gyrus and paracingulate cortex; insular cortex and temporal pole for both hemispheres.

PwMS CLs presented a higher degree of tissue disruption both compared to HC GM (lower fneurite: 0.27±0.09 vs 0.38±0.02 and higher fextra: 0.58±0.08 vs 0.42±0.03, p<0.00001 for both) **and PwMS NAGM** (lower fneurite: 0.27±0.09 vs 0.37±0.01 and higher fextra: 0.58±0.08 vs 0.44±0.03, p<0.00001 for both). **Microstructural damages were also observed in the PwMS NAGM with respect to HCs GM** (higher fextra: 0.44±0.03 vs 0.42±0.03, p=0.008) (**Figure 2**). **Compared to HCs GM, microstructural changes were detected in atrophic cortical GM** (lower fneurite: 0.2±0.04 vs 0.38±0.02 and higher fextra 0.50±0.03 vs 0.42±0.03, p<0.00001 for both), **but also within non-atrophic cortical GM** (higher fextra: 0.44±0.03 vs 0.42±0.03, p=0.03) of PwMS. **A worsening of the microstructural properties resulted between PwMS CLs and their regional counterparts in the contralateral GM** (lower fsoma: 0.19±0.09 vs 0.24±0.08, lower fneurite: 0.27±0.09 vs 0.31 ±0.07 and higher fextra: 0.58±0.08 vs 0.45±0.03, p=0.009, p=0.02 and p=0.00003 respectively) (**Figure 3**)

FIG. 2

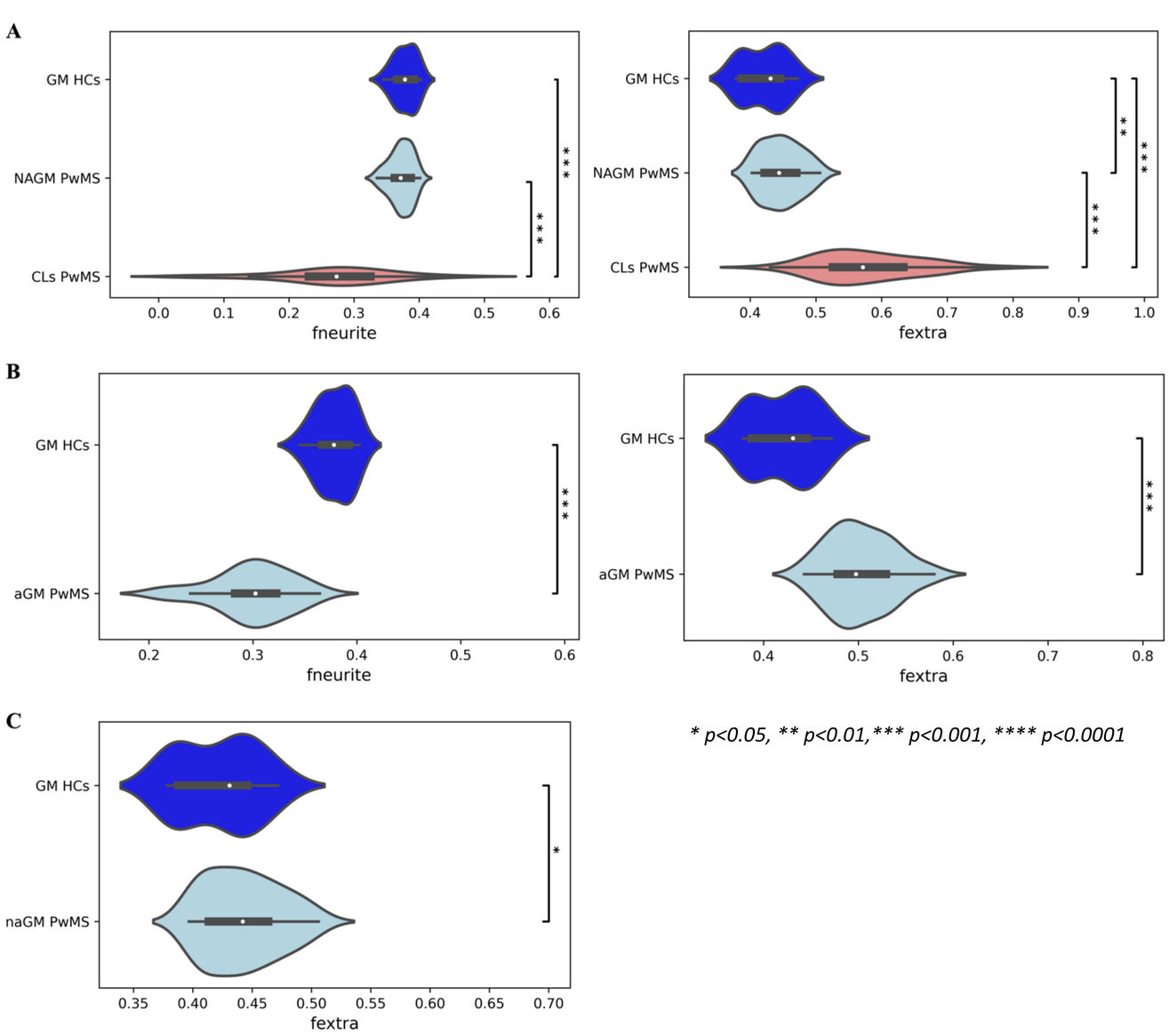
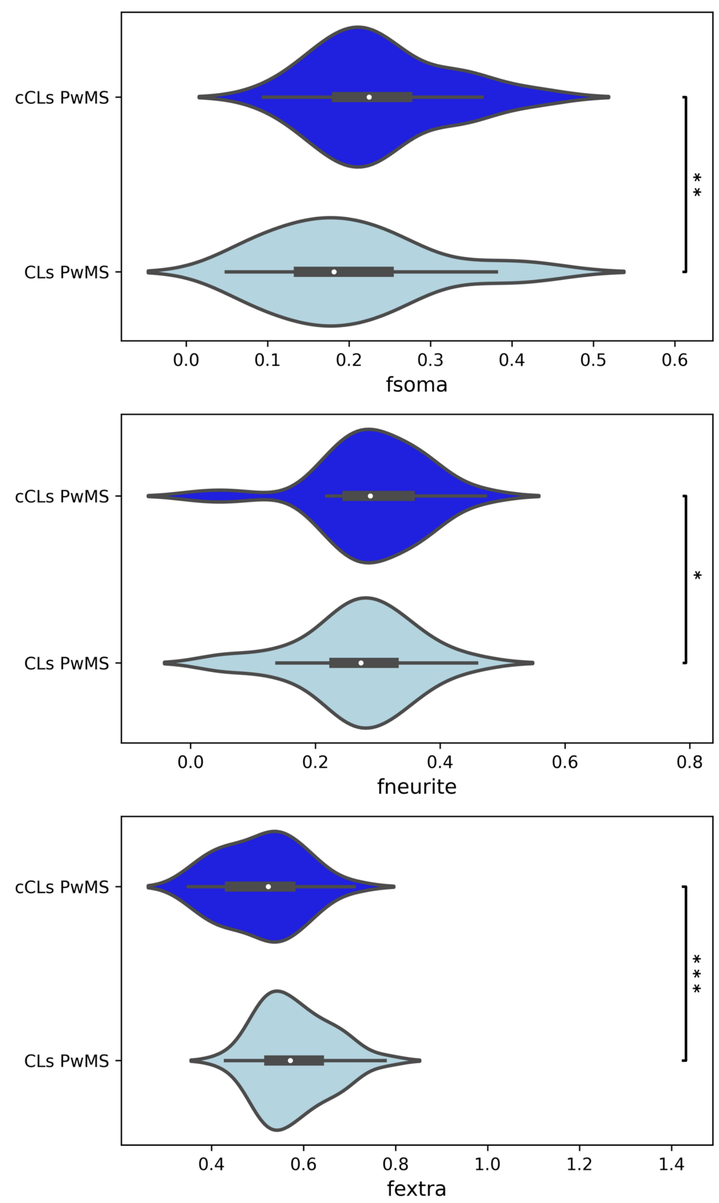


FIG. 3



CONCLUSION

We assessed the differences in microstructural properties based on SANDI metrics between PwMS and HCs. Tissue destruction was observed in the PwMS atrophic cortical GM compared to HCs GM. However, the **CLs exhibited the highest degree of tissue damage within cortical GM. On the other hand, diffuse microstructural damage also seemed to be present in non-atrophic cortical GM and in NAGM tissue**. **These findings suggest that the SANDI technique may be more sensitive to microstructural changes compared to conventional atrophy measure**s. In conclusion, SANDI may be very useful to investigate in vivo the pathophysiology of focal and diffuse GM damage in MS and its temporal relationship with atrophy and WM involvement.

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