Background In Multiple Sclerosis (MS), demyelination and neuronal loss occur in the brain grey matter (GM) and are associated with a progressive disease course. Using MRI measures of atrophy and GM magnetization transfer ratio (MTR), we investigated the regional localisation of consistent volume loss (reflecting neuronal loss) and intrinsic tissue abnormalities (particularly demyelination) in MS clinical subgroups.

Objective To map regions of consistent GM atrophy and MTR reduction in relapsing-remitting (RR), secondary progressive (SP) and primary progressive (PP) MS.

Methods 102 patients (51 RRMS, 30 SPMS, 21 PPMS) and 32 controls had T1-weighted volumetric and magnetization transfer scans, both acquired at 1x1x1mm3. MTR maps were calculated using MTon and off sequences. MTR in grey matter was extracted by segmenting grey matter on T1-weighted images and binarising the resulting tissue maps with a conservative threshold of 90%. Using SPM8, T1 scans were non-linearly registered to create a DARTEL template, registered to MNI space using affine transformation, and smoothed with an 8 mm full-width half maximum Gaussian kernel. Voxel-based morphometry (VBM) was used to compare regional differences in GM atrophy and a VBM-type analysis was carried out on the grey matter MTR of MS patient subgroups versus controls, adjusting for age and gender, using family wise error (FWE) correction at p<0.05.

Results Compared with controls, PPMS and SPMS groups exhibited more areas of MTR reduction than atrophy while RRMS subjects showed more areas of atrophy than reduced MTR. Co-localisation of atrophy and reduced MTR was most evident in the thalamus in all MS subtypes. There were more areas of cortical MTR reduction and atrophy than where both were co-localised. Compared to controls, there were more areas of cortical MTR reduction in SPMS and PPMS than in RRMS.

Conclusions Assuming that reduced GM MTR implies demyelination and atrophy reflects neuronal loss, the results suggest that: (i) in progressive (SP and PP) MS there is overall more extensive GM demyelination than neuronal loss; (ii) in RRMS there is overall more extensive GM neuronal loss with less noticeable demyelination, (iii) cortical demyelination occurs in more regions in SPMS and PPMS than RRMS; (iv) demyelination and neuronal loss often occur in different locations in the cortex, and (v) co-existent demyelination and neuronal loss is most evident in the thalamus. The variation in regional abnormalities argue against a single common mechanism for demyelination and neuronal loss in MS GM.
REGIONAL PATTERNS OF GREY MATTER ATROPHY AND MAGNETISATION TRANSFER RATIO ABNORMALITIES IN MULTIPLE SCLEROSIS CLINICAL SUBGROUPS

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