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# Severity of brain and spinal motor tract lesions in multiple sclerosis using quantitative MRI imaging

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**Objectives:** Motor deficits in people with multiple sclerosis (pwMS) are often asymmetrical suggesting a major role of focal lesions affecting the corresponding motor pathways.[1] However, the association between lesion load and physical disability remains modest in pwMS. One hypothesis could be that severe lesions, i.e. heavily demyelinated, along the motor pathways would be associated with functional consequences.

**Material and methods:** Sixty relapsing-remitting pwMS and 33 healthy controls were recruited in 2 centers (NCT04220814). Lesions were segmented on both brain (FLAIR) and whole spinal cord (SC)(axial T2\* and T2) 3T MRI acquisitions. The complete motor tracts were reconstructed, including brain and SC portions, using probabilistic atlases.[2,3] Lesion severity was approximated using magnetization transfer ratio (MTR), computed in different regions along the tracts, and at the voxel level using z-scores based on HC to identify severe lesions (thresholded at 2 SD). Functional motor consequences per limb were assessed using clinical scores and central motor conduction times (CMCT). The analyses were repeated using simultaneous brain and cervical SC MP2RAGE quantitative T1 imaging (qT1).[4]

**Results:** Associations between clinical motor scores and imaging were modest. The CMCT was positively associated with the lesion load and MTR for both upper and lower limbs. Severe lesions were more frequently observed in pwMS with abnormal than with normal CMCT (e.g.: severe lesions in normal/abnormal CMCT in upper limbs: 38.1/80.8%; in lower limbs: 33.3/93.9%; all  $p$ 's<.001), but not in relation with clinical motor score status (all  $p$ 's>.1). Multivariable logistic regression models indicated that the presence of a severe lesion in the SC was associated with an increased risk of having an abnormal CMCT in lower limbs only ( $p$ <.001). Main findings were reproduced using qT1, but to a lesser extent.

**Conclusions:** Motor evaluation in pwMS is challenging and clinical motor scores may lack sensitivity, while CMCT proved to be a reliable reflection of whole CST integrity. The hypothesis that prolonged CMCT of a limb is explained by the presence of at least a severe lesion on the corresponding motor pathway was confirmed for lower limbs only and would need further investigations using more specific biomarkers of myelin content.

**References:** [1] Sechi E. et al., Neurology, 2019; [2] Kerbrat A. et al., 2020, Brain; [3] De Leener B. et al., NeuroImage, 2018; [4] Forodighasemabadi A. et al., Magn Reson Imag, 2021.

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