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Determinants driving evolution of newly formed MS lesion into chronic active, chronic demyelinated and remyelinated lesions

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Introduction:

Following the acute inflammatory demyelinating phase at lesion onset, MS lesions may undergo several fates over time.

Objectives/Aims:

To assess the determinants driving the transformation of newly formed MS lesions into chronic active lesions, chronic inactive demyelinated lesions and remyelinated lesions.

Methods:

We analyzed all contrast enhancing lesions (CELs) detected in a longitudinal research MRI protocol and categorized them according to their appearance on QSM at 12-month from lesion onset into paramagnetic rim lesions (PRLs), hyperintese lesions (HYPER) reflecting chronic inactive demyelinated lesions and iso/hypointense lesions (ISO-HYPO) reflecting remyelinated lesions. We analyzed baseline CELs volume, topography, enhancement pattern and diffusion MRI metrics of microstructural integrity. Age at lesion onset, sex, disease duration and therapy were collected. For classification, after random splitting of the dataset into a 80-20 stratified proportion for training and testing, the machine-learning XGBoost algorithms were used (implementing a class weighting strategy based on QSM lesion phenotypes' frequency). For each random split of the dataset (iterated 100 times), the best model was selected according to the area under the Receiver Operating Characteristic Curve (ROC-AUC) and used for SHAP analysis. SHAP is a feature importance tool, which identify the most relevant features that contribute to the model's predictions by calculating SHAP values for each (with higher SHAP values representing more influential variables).

Results:

We assessed 173 CELs from 44 patients. 43 CELs were excluded because they were not evaluable on QSM because of air-tissue interface artifacts. At 12 months, 13% of CELs were classified as PRLs, 42% as HYPER and 46% as ISO-HYPO. SHAP analysis on the overall best classification model including all lesion-specific and patient-specific features (ROC-AUC= 0.91) showed that CELs' volume and patient's age were the most relevant features in predicting the 3 QSM-based phenotypes, being selected within the best 3 discriminant features for every lesion phenotype. Younger age and smaller volume favored ISO-HYPO, while older age and bigger CELs' volume favored HYPER and PRLs. For PRLs prediction, there was an additional substantial contribution of lower ICVF and of ring-like pattern of enhancement and, to a minor extent, of a periventricular localization.

Conclusion:

Age at lesion onset and lesion's volume strongly influence the chance of remyelination and suppression of the inflammatory process.

Disclosures:

GB, DVB, EC, CR, EG, MC, NC, CT, MI have no disclosures related to the present work,