Machine learning-based combination of the central vein sign, cortical lesions and paramagnetic rim lesions: a web-based tool for the diagnosis of multiple sclerosis

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Abstract

Background:

Multiple sclerosis (MS) diagnostic criteria lack optimal specificity, leading to potential misdiagnosis. Advanced MRI biomarkers like the central vein sign (CVS), cortical lesions (CL), and paramagnetic rim lesions (PRL) are highly MS specific and could potentially improve diagnostic accuracy.

Methods:

We applied machine learning (ML) techniques to a retrospective, multicentric dataset of 364 MS/MS-mimic (204/118) and 42 prodromal MS/non-MS (26/16) adult patients, incorporating CVS, CL, and PRL biomarkers. We compared (5x2CV combined F-test) the diagnostic performance of 71 ML models using full-count and simplified biomarker assessments against the baseline dissemination in space (DIS) McDonald criteria. The aim was to evaluate the MS diagnostic power of combining these biomarkers in an MRI-only diagnostic framework.

Findings:

51 models outperformed the DIS criteria, achieving balanced accuracy improvements of up to 13·0%. Twelve of these models only used simplified biomarker assessments. There was no significant difference between the best full-count and simplified models (p=0·29). Results were confirmed in two out-of-domain test sets, with simplified assessments generalising better than their full-count counterparts.

Interpretation:

Within a non-invasive MRI-only diagnostic framework, we show that the incorporation of advanced imaging biomarkers into the MS-MRI diagnostic criteria significantly enhances the diagnostic accuracy - especially when using simplified CVS, CL and PRL assessments. The study also provides a publicly available online diagnostic tool, facilitating further interaction, validation and clinical support (https://www.msdiagnostictool.org).

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Keywords

Multiple Sclerosis, Machine learning, Diagnosis, MRI, Central vein sign, Paramagnetic rim lesions, Cortical lesions, Susceptibility-weighted MRI, Computer-aided diagnosis

Research in context

Evidence before this study

The current multiple sclerosis (MS) diagnostic criteria aim to detect MS at an early stage and often prioritise sensitivity over specificity, leading to potential misdiagnosis. To improve diagnostic accuracy, previous research has focused on advanced MRI biomarkers like the central vein sign (CVS), paramagnetic rim lesions (PRL), and cortical lesions (CL), which offer high specificity for MS and the potential to reduce misdiagnosis while still allowing early detection. However, full-count assessments of these biomarkers are time-consuming and not always feasible in clinical settings. Furthermore, the diagnostic value of combining these advanced biomarkers with or without existing criteria remains unclear, as does the potential benefit of using simplified assessments. Finally, no prior study has explored the combination of these biomarkers using machine learning (ML) models, especially focusing on simplified assessments.

Added value of this study

This study uses ML to assess the diagnostic potential of different combinations of CVS, PRL, CL, and dissemination in space (DIS) in a non-invasive MRI-only diagnostic framework. We demonstrate that incorporating these biomarkers significantly improves diagnostic accuracy compared to current criteria, with simplified assessments having even more generalisation power than their full-count counterparts. Additionally, we introduce a web-based tool (https://msdiagnostictool.org) that allows users to interact with the trained models discussed herein.

Implications of all the available evidence

The findings of this study indicate that incorporating combinations of CVS, CL, and PRL into diagnostic workflows through a ML framework can substantially improve MS diagnostic accuracy, reduce the need of additional invasive evaluation without compromising clinical practicality. Additionally, our results suggest that the use of simplified assessments of these advanced biomarkers have greater generalisation power, considerably reducing the time-burden in clinical settings. Finally, we make available a web-based diagnostic tool, enabling reproducibility, benchmarking, further validation, and interaction with the trained models of the study.