Introduction: Online cognitive assessment allows to efficiently collect large-scale cognitive data and monitor changes in cognition over time. In a previous study, over 3,000 people with Multiple Sclerosis (pwMS) were tested using 22 online cognitive tasks and a randomised study design, proving the feasibility of online cognitive assessment in MS. A reduced battery of online cognitive tasks specific to MS was derived to periodically monitor the observed cognitive impairments.
Objectives/Aims: The current study aimed to validate the robustness of this reduced battery, investigate how cognitive impairments evolve over time in MS, and identify specific cognitive changes in relapsing remitting (RR) individuals transitioning to secondary progressive (SP) MS.
Methods: Data were collected from over 2,500 pwMS using 12 of the original 22 cognitive tasks, with approximately half of the participants having completed the assessment also in the previous study.
Results: Results showed that the selected cognitive tasks were robust, with the same pattern of cognitive deficits observed at both timepoints for pwMS performing the tasks for the first time. Significant changes in performance over one year were detected only in a subset of the tasks, for pwMS having performed the tasks at both timepoints, suggesting that different aspects of cognition deteriorate at different rates. Additionally, the study found that RR individuals progressively worsen across all measured cognitive domains as they transition to SPMS, highlighting the potential use of online cognitive assessment as a digital marker of disease progression.
Conclusion: In conclusion, the reduced battery of online cognitive tasks is a reliable method for measuring cognitive impairments in pwMS and could potentially be used to periodically monitor cognitive changes in MS and make predictions on disease progression.
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Identification of paramagnetic rim lesions using conventional MRI - a deep learning approach

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Introduction: To date, the detection of paramagnetic rim lesions (PRLs) in multiple sclerosis (MS) is based on susceptibility-based MRI sequences, which are not widely implemented in clinical routine. In this work, we exploit a deep learning approach to segment white matter lesions (WML) based on conventional MRI data (FLAIR and T1-weighted images) and then employ saliency maps (SMs) - which are usually generated to understand which parts of a model's input have the highest impact on classification - to characterise PRLs.

Objectives/Aims: To expose significant differences between PRLs and WML in MS using conventional MRI. Exploiting the potential of these findings to classify PRLs.

Methods: FLAIR and MPRAGE were collected in 650 MS patients (age: 45.7±12.3, EDSS median: 2.5 [0-9]) and used to train a U-Net network to segment WML. This model was then tested on an independent set of 20 MS patients presenting PRLs. In both datasets, WML masks were annotated by three expert clinicians, while PRLs in the test set were marked by a neurologist.

With respect to both input modalities, we generated a local SM for each lesion (SmoothGrad), using WML masks as footprint. Confluent lesions were excluded from the study, leading to 47 PRLs and 598 WML. Positive and negative contributions in a SM respectively represent voxels whose increase in intensity would suggest and reject the presence of a lesion. Separating positive and negative values, we observed and reported their distributions across PRLs and WML.

Lastly, we explored the classification of PRLs and WML by setting a threshold at the 90th percentile of positive contributions with respect to (w.r.t.) FLAIR.

Results: On the test set we achieved a normalised Dice score of 0.75. Lower intensity areas in PRLs were not correctly predicted: in SMs they showed lower attention, indicating that the model focuses on hyperintensities. SMs computed w.r.t. FLAIR showed consistently higher values than MPRAGE, i.e., FLAIR features were more relevant. The distribution of positive values in SMs w.r.t. FLAIR for PRLs and WML was different (Mann-Whitney U test, $p<0.0001$). The true positive rate of PRLs and WML was around 70%.

Conclusion: Our investigation supports the feasibility of generating saliency maps to expose and exploit features of PRLs for lesion classification based on conventional MRI sequences.

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Transfer learning on structural brain age models to decode cognition in MS: a federated learning approach

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Introduction: Classical deep learning research requires lots of centralised data. However, data sets are often stored at different clinical centers, and sharing sensitive patient data such as brain images is difficult.
Objectives/Aims: In this manuscript, we investigated the feasibility of federated learning (FL), sending models to the data instead of the other way round, for research on brain magnetic resonant imaging (MRI) of people with multiple sclerosis (MS).
Methods: Using transfer learning on a previously published brain age model, we trained a model to decode performance on the symbol digit modalities test (SDMT) of patients with MS from structural T1 weighted MRI. Three international centers in Brussels, Greifswald and Prague participated in the project. In Brussels, one computer served as the server coordinating the FL project, while the other served as client for model training on local data (n=97). The other two clients were Greifswald (n=104) and Prague (n=100). Each FL round, the server sent a global model to the clients, where its fully connected layer was updated on the local data. After collecting the local models, the server applied a weighted average of two randomly picked clients, yielding a new global model.
Results: After 22 federated learning rounds, the average validation loss across clients reached a minimum. The model appeared to have learned to assign SDMT values close to the mean with a mean absolute error (MAE) of 9.04, 10.59 and 10.71 points between true and predicted SDMT on the test data sets of Brussels, Greifswald and Prague respectively. The overall test MAE across all clients was 10.13 points.
Conclusion: Federated learning is feasible for machine learning research on brain MRI of persons with MS, setting the stage for larger transfer learning studies to investigate the utility of brain age latent representations in cognitive decoding tasks.
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