Improving the T1w/FLAIR ratio as a proxy for the myelin content using machine learning

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Synopsis

Motivation: Myelin can be a useful predictor of disease progression and cognitive decline, however it requires dedicated MRI sequences. The T1w/FLAIR-ratio, which is more readily available, has previously been introduced as a proxy for the myelin content.

Goal(s): To assess whether the T1w/FLAIR-ratio can be improved upon using machine learning.

Approach: The T1w/FLAIR-ratio and myelin-water fraction (MWF) are calculated in a prospective (n=13) sample, and a new combination of the T1w and FLAIR ratio is calculated using a multi-layer perceptron (MLP).

Results: The T1w-FLAIR combination from the MLP has a stronger correlation with MWF values in the white matter.

Impact: The T1w/FLAIR-ratio can be used as a proxy for the myelin content. Here, we showed that a more optimal combination of T1w and FLAIR contrasts exist, which relates to the myelin content better.

Introduction

One of the most characteristic components of the white matter is myelin. Myelination of axons is a vital part of healthy neuronal development, therefore quantification of the in vivo myelin content can provide valuable insights into brain maturation and neurodegeneration. Using MRI, the myelin content can be quantified via dedicated scanning techniques such as myelin-water imaging. However, an improved myelin contrast can be obtained by calculating the ratio of T1w and T2w contrasts (i.e. T1w/T2w-ratio[1]). Furthermore, since FLAIR images have become an increasingly popular alternative to T2w for lesion detection, a T1w/FLAIR-ratio was proposed[2]. However, it has not been investigated whether the simple ratio of T1w over FLAIR approximates the myelin content best. A different and more complex combination, e.g. obtained using a neural network approach[3], of both contrast could result in a further improved myelin contrast. Therefore, in this study we explore whether a neural network can improve upon the T1w/FLAIR-ratio with respect to the sensitivity to the myelin content.

Methods

MRI Acquisition

Thirteen volunteers (mean age 38y, 4 females) underwent 3T MR imaging (MAGNETOM Prisma-fit Syngo MR D13D; Siemens Healthcare, Erlangen, Germany) using a 64-element head/neck coil. A 3D T1w magnetization prepared rapid acquisition gradient echo (MPRAGE) sequence (TR/TI/TE 2,300/900/2.98ms, 176 slices, 256×240 matrix size, and 1.00 mm cubic voxel size) and a fluid-attenuated inversion recovery (FLAIR) sequence (TR/TI/TE 5,000/1,800/394ms, 176 slices, 512×512 matrix size, 0.49×0.49×1.0mm reconstructed voxel size) were acquired.
A 3D gradient echo and spin echo (GRASE) sequence was used for quantification of the myelin-water content[4] (TR/TE 1,000/10:10:320ms, flip angle 90°, 48 slices, 2×2×3mm voxel size, EPI-factor 3).

Image Analysis

First, both the T1w and FLAIR images are bias corrected using the N4-ITK bias correction tool[5]. Next, using non-linear histogram calibration the intensity histograms of cerebral tissue (excluding white matter hyperintensities) of the T1w and FLAIR image are matched to the intensity histograms of standard images in MNI-space[2] using mrhistmatch from MRTrix[6]. Next, the T1w and FLAIR images are registered to the GRASE data.
The myelin content was determined from the multi-echo GRASE data using the non-negative least squares (NNLS) algorithm[7]. A basis set of 120 logarithmically spaced relaxation functions (T2-range 10 to 2000ms) was used, and B1 inhomogeneities were modelled using the extended phase graph (EPG)[8,9]. The algorithm was regularized allowing an increased misfit between 2 and 2.5% ($1.020 \leq \chi_{reg}/\chi_{min} \leq 1.025$)[10]. The myelin-water fraction (MWF) was calculated as the ratio of myelin-water associated T2 components (10-40ms) to all T2 components (10-2000ms).
Three ROIs in the white matter, splenium and genu of the corpus callosum and the corona radiata, were defined using the JHU white matter atlas[11], which was registered to the GRASE data.

Machine Learning

A simple multi-layer perceptron (MLP) was used to estimate the myelin content from a T1w- and FLAIR-image in a voxel-wise manner. The hyperparameters of the MLP are; two hidden layers (with 20 neurons); parametric ReLU activation functions, Adam optimizer, a batch size of 10, a learning rate of .0001 and 5 epochs. The inputs of the MLP are normalized (between 0 and 1), and the FLAIR-intensities are inverted.

Statistical Analysis

To assess the sensitivity to the myelin content, the Pearson's correlation coefficient was used. For each subject, the correlation between all white matter voxels of the MWF and the T1w/FLAIR-ratio as well as the T1w-FLAIR-MLP was calculated. The resulting correlation coefficients were transformed using Fisher's r-to-z', and statistically compared using a paired-data t-test. Regional associations between the MWF and both contrasts were visually assessed.

Results

In Figure 1 the T1w and FLAIR image are shown, as well as the calculated MWF map and T1w/FLAIR-ratio and T1w-FLAIR-MLP. The paired t-test revealed that the within-subject correlation with the MWF is significantly improved for the T1w-FLAIR-MLP contrast compared to the T1w/FLAIR ratio (Fisher's z: .28 vs. .32, $p < .001$) (Figure 2).
For visualization, scatter plots are shown of regional MWF values versus the regional T1w/FLAIR-ratio (Figure 3A) and the T1w-FLAIR-MLP (Figure 3B) values. On average, the T1w-FLAIR-MLP has a higher correlation with MWF compared to the traditional T1w/FLAIR-ratio (Fisher's z' value of .532 vs .257).

Discussion & Conclusion

The T1w/FLAIR-ratio can be used as a proxy for the myelin content, however there is likely a more optimal combination of the T1w and FLAIR images to approximate the myelin content. Here, we used an MLP to find a non-linear and complex combination of T1w and FLAIR contrasts to improve the sensitivity to the myelin content. Indeed, the proposed T1w-FLAIR contrast relates better to the myelin-water content in the total white matter, as well as in highly myelinated regions.

Acknowledgements

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Figures

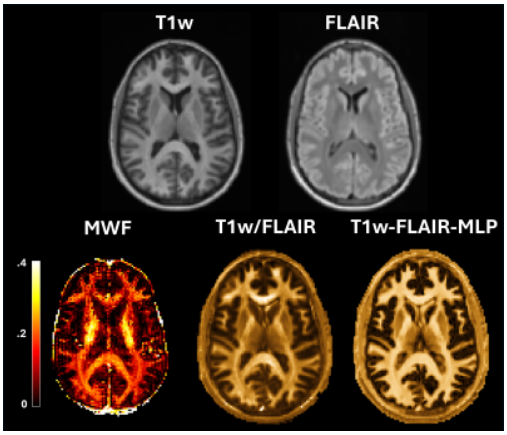


Figure 1: For a representative subject (35 year old male), the T1-weighted and FLAIR images are shown (top row), as well as the myelin-water fraction (MWF) map, traditional T1w/FLAIR-ratio image and the proposed T1w-FLAIR-MLP image (bottom row).

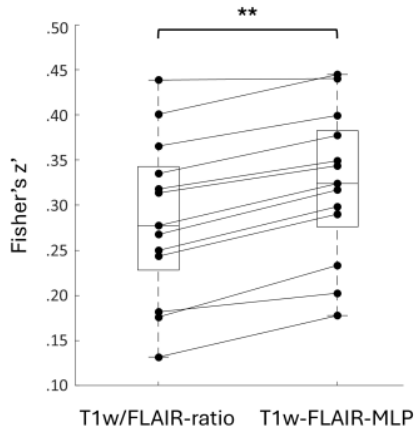


Figure 2: For each subject the strength of the correlation between the MWF and myelin-proxies of all white matter voxels is represented by Fisher's z' values. The T1w-FLAIR-MLP has a significant stronger correlation with MWF compared to T1w/FLAIR-ratio (Fisher's z: .28 vs. .32, **p < .001).

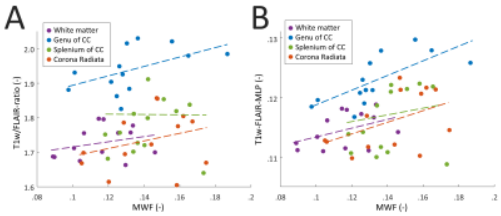


Figure 3: For all subjects the relation between regional MWF values and A) the T1w/FLAIR-ratio, and B) the T1w-FLAIR-MLP is shown. The dashed, least-squares, lines are added for visualization.