T2 Hypointensity at 3 T Correlates with Expanded Disability Status Scale in Multiple Sclerosis

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Introduction

Abnormally decreased signal intensity (SI) on T2-weighted MR images (T2 hypointensity) has been observed in some deep grey matter (GM) structures of patients with multiple sclerosis (MS). Deep GM (caudate) T2 hypointensity at 1.5 T correlates with disease duration and Expanded Disability Status Scale (EDSS) score in MS[1]. The T2 hypointensity is believed to be due to abnormal iron deposition[1,2]. We have shown that 3 T has greater sensitivity to iron detection than 1.5 T in MS patients[3]. Therefore, we hypothesize that T2 hypointensity measured at 3 T correlates with clinical outcomes in MS. Here, we investigate the relationship of EDSS and T2 hypointensity at 3 T in patients with MS.

Methods

Sixteen relapsing remitting MS patients (mean age of 42 years, range 28 - 59 years, mean EDSS of 3.5, range 1.5 - 7.5, mean disease duration of 7 years, range 1 - 24 years) were scanned with 3 Tesla MRI (GE Healthcare, Waukesha, WI). T2-weighted MR data were acquired using a dual echo fast spin echo pulse sequence (TR/TE1/TE2 = 4000ms/15ms/80ms, FOV = 22 cm, ETL = 8, NEX = 1, matrix size = 256 X192, and slice thickness/gap = 3mm.)

All MR images were non-uniformity corrected using the N3 algorithm[4] before any subsequent processing. The following deep GM structures were identified: head of caudate, thalamus, globus pallidus, putamen, red nucleus and substantia nigra. ImageJ (NIH Image) was used to manually draw ROIs in each deep GM structure on both sides of the brain on slices showing the greatest cross section. An ROI in ventricular CSF was also drawn on the same slice as that of putamen. The T2 hypointensity of each deep GM structure was calculated by averaging signal intensities from every measured ROI in the structure. The mean SI was normalized for analysis by dividing it by the mean SI of CSF in the patient. The same measurement process was repeated three times for each patient.

Initially, linear correlation between EDSS and T2 hypointensity in individual deep GM structures was examined. Next, an inductive modeling algorithm was used to examine nonlinear relationships between deep GM T2 hypointensity and EDSS. This algorithm starts with many simply polynomials (models) then randomly divides the data into training and test subsets. The training set is used to determine model coefficients, and the test set is used to evaluate the goodness-of-fit. The algorithm iterates building more complex models from simpler ones. In this process better fit is rewarded but increased model complexity penalized. The process stops when these competing factors reach a balance. The objective is to find the simplest model best able to predict unseen data[5].

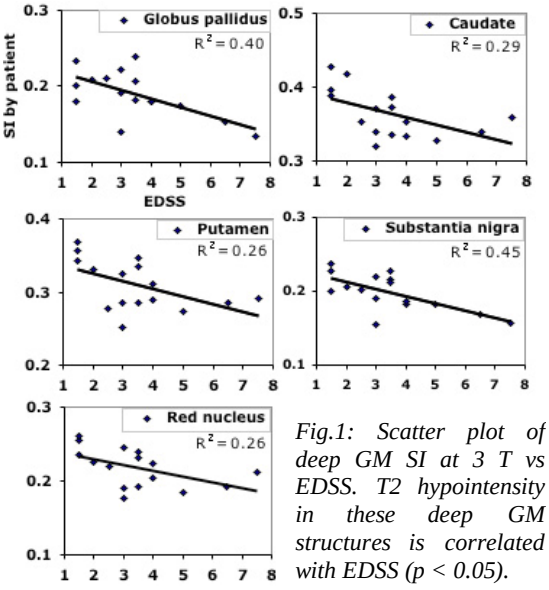

Fig.1: Scatter plot of deep GM SI at 3 T vs EDSS. T2 hypointensity in these deep GM structures is correlated with EDSS ($p < 0.05$).

Results

EDSS score was significantly negatively correlated with 3 T T2 hypointensity in head of caudate ($R^2 = 0.29$, $p < 0.05$), globus pallidus ($R^2 = 0.40$, $p < 0.01$), putamen ($R^2 = 0.26$, $p < 0.05$), red nucleus ($R^2 = 0.26$, $p < 0.05$) and substantia nigra ($R^2 = 0.45$, $p < 0.01$) (Fig.1). Inductive modeling revealed that T2 hypointensity in the globus pallidus and putamen were the most relevant variables in predicting EDSS. The predicted EDSS was highly correlated with the true EDSS score ($R^2 = 0.86$) (Fig. 2). No significant difference was found between the three repeated measurements.

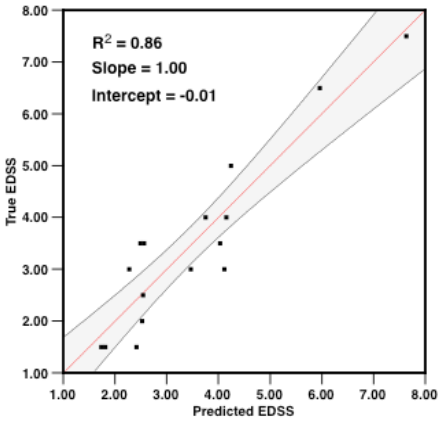

Fig.2: Predicted EDSS vs true EDSS. Nonlinear inductive modeling revealed that only normalized 3T SI from the globus pallidus and putamen were needed to predict the patient EDSS in MS.

Discussions and Conclusions

3 T T2 hypointensity in each deep GM structure, except thalamus, was significantly linearly correlated with the MS patient's EDSS score. Nonlinear inductive modeling revealed that T2 hypointensity in the globus pallidus and putamen were most highly correlated with EDSS. These results suggest that deep GM T2 hypointensity at 3 T could be a surrogate marker for disability in MS. However, further analysis on a larger patient sample is needed to confirm these observations.

References

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