Introduction. In multiple sclerosis (MS), tissue loss and microscopic disease-related abnormalities in the overall gray matter (GM) have been associated with disability progression.

Objectives. The objective of this study was to assess the value of thalamic damage, taken in isolation, and its short-term changes in predicting the long-term accumulation of disability in MS.

Methods. Conventional and magnetization transfer (MT) MRI scans of the brain were obtained at baseline and after 12 months in 73 patients with relapse-onset MS, who were followed prospectively with clinical visits for 8 years. Volumes of T2-hyperintense lesions, T1-hypointense lesions, GM, thalami, and white matter (WM) were measured at baseline and 12 months. Average lesion MT ratio (MTR) and MTR histograms of the GM, thalami, and WM were also computed. A multivariate analysis, adjusted for follow up duration, was performed to establish which variables were significant predictors of long-term neurological deterioration.

Results. At the end of follow up, 44 patients (60%) showed a significant disability worsening. A multivariable model included baseline thalamic fraction \( [p=0.01, \text{ odds ratio (OR)}=0.62] \), and average lesion MTR percentage change after 12 months \( (p=0.04, \text{ OR}=0.90) \) as independent predictors of disability worsening at 8 years \( (r^2=0.29) \). The discriminating ability of such a model in predicting the individual patients’ outcome was 69%. Baseline thalamic fraction was significantly correlated with T2 \( (r=-0.75, p<0.0001) \) and T1 \( (r=-0.60, p<0.0001) \) lesion volumes.

Interpretation. Thalamic damage predicts the long-term accumulation of disability in MS. Trans-synaptic and Wallerian degeneration are likely to contribute in causing thalamic tissue damage and loss in MS.