Objective: To assess the value of structural and functional network MRI measures in predicting clinical deterioration over a 6.5-year follow-up in patients with multiple sclerosis (MS).

Background: In patients with definite MS, no reliable markers to predict medium- and long-term disease evolution are currently available. The analysis of brain structural and functional network architecture might improve the prediction of long-term MS prognosis.

Design/Methods: Conventional, 3D T1-weighted, diffusion-weighted MRI and resting state (RS) fMRI scans were obtained at baseline from 233 MS patients and 77 healthy controls. Patients underwent a neurologic evaluation at baseline and after a median follow-up of 6.5 years. At follow-up, patients were classified as clinically stable or worsened according to Expanded Disability Status Scale (EDSS) score change. In relapsing-remitting (RR) MS, conversion to secondary progressive (SP) MS was also evaluated. Spatial independent component analysis was applied to RS fMRI data to derive the main large-scale RS functional connectivity (FC) networks and to grey matter (GM) probability maps and fractional anisotropy maps, to identify the corresponding structural GM and white matter networks.

Results: At follow-up, 105/233 (45%) MS patients showed significant EDSS worsening and 26/157 (16%) RRMS patients evolved to SPMS. The multivariable model, adjusted for follow-up duration, identified baseline EDSS (odds ratio [OR]=1.59, p<0.001), normalized GM volume (OR=0.99, p=0.001) and abnormally high baseline RS FC of the left precentral gyrus in the sensorimotor network (OR=1.67, p=0.03) as predictors of EDSS worsening (C-index=0.80). Such variables survived also when adjusting for treatment effect. Baseline EDSS (OR=2.8, p<0.001) and atrophy of GM networks associated with sensory (OR=0.5, p=0.01) and motor (OR=0.4, p=0.03) functions were independent variables associated with conversion to SPMS (C-index=0.89).

Conclusions: Structural and functional network measures improved the prediction of long-term clinical worsening in MS patients.