The relationship between resting-state connectivity alterations and the extent of focal white matter lesion changes in multiple sclerosis

D. Pinter¹, M. Khalil¹, P. Greiner¹, D. Moser¹, M. Koini¹, E. Pirker¹, A. Pichler¹, G. Bachmaier², S. Ropele¹, S. Fuchs¹, F. Fazekas¹, C. Enzinger¹,³

¹Medical University of Graz, Department of Neurology, Graz, Austria
²Medical University of Graz, Institute for Medical Informatics, Statistics and Documentation, Graz, Austria
³Medical University of Graz, Department of Radiology, Division of Neuroradiology, Vascular and Interventional Radiology, Graz, Austria

Background: Multiple sclerosis (MS) is an inflammatory disease, characterized by focal white matter (WM) changes on MRI, and a common cause of disability in young adults. Neurological and cognitive deficits in MS have not only been related to structural damage, but also to functional imbalance in and between brain networks. It has also been assumed that such network changes might at least partially compensate for structural damage. However, the relationship between rfMRI and different amounts of WM changes as evidenced by MRI has rarely been tested in sufficiently large patient samples.

Methods: We here therefore assessed 180 MS patients (mean age= 35.9 yrs, SD=9.7; 63% female) and 65 healthy controls (HC; mean age= 31.0, SD=8.9; 51% female) using T1- and T2-FLAIR-weighted imaging, DTI, and rfMRI at 3T. Disability was measured using the Expanded Disability Status Scale (EDSS; median= 1). Hyperintense T2-lesion load (T2-LL) was assessed by a semi-automated region growing algorithm subsequent to lesion identification by an experienced rater, and normalized by intracranial volume. Resting-state connectivity was assessed for the visual network, anterior (ACC) and posterior default-mode (DM) network (precuneus), and motor network by means of ICA.

Results: T2-LL in MS patients ranged from 1.45 cm³ to 127.61 cm³. We stratified patients by the extent of WM changes into four groups defined by T2-LL quartiles. Global brain and WM damage as evidenced by age-corrected normalized brain volume (HC: 1583.54 cm³, MS-low to high T2-LL: 1537.49, 1539.59, 1525.10, 1473.79 cm³) and white matter integrity (whole brain fractional anisotropy; HC: 0.468, MS-low to high T2-LL: 0.450, 0.451, 0.453, 0.446) were lower in all MS groups compared to HC, and increased with increasing T2-LL. Age-corrected rfMRI connectivity in visual and DM networks were significantly increased in patients with the lowest T2-LL compared to HC and patients with moderate to high lesion load.

Conclusions: In the context of measurable brain tissue damage, MS patients with low T2-LL showed increased rfMRI connectivity in the visual and DM network. However, this relationship got lost with more extensive tissue damage, thus suggesting exhaustion and finally collapse of initial functional network adaption with accumulation of brain tissue damage.