Abstract

Clinical course of multiple sclerosis (MS) is heterogenous and white matter lesion count and volume on brain magnetic resonance imaging (MRI) correlate with clinical course only partially. Therefore, there is an urgent need for more reliable prognostic biomarkers. This work explored three imaging markers - spinal cord (SC) imaging (specifically SC volume measurement and assessment of focal and diffuse SC changes), atlas-based model of "disconnectome" (i.e. disruption of brain connectivity due to white matter lesions) and periventricular white matter gradient assessed with T1 relaxometry. For the SC projects, we assessed MRI from 2044 MS patients with a semi-automatic method for SC volume measurement. We confirmed (i) a relationship between diffuse SC changes, SC volume and disability; (ii) a novel finding was that in patients with EDSS ≤ 4.0, diffuse changes contributed to higher disability more than SC volume; (iii) SC volume explains the paradox in patients with dissociation between brain white matter lesion load and disability; (iv) SC focal and/or diffuse changes are present in 75% patients with early MS, of which 43% have diffuse changes that are related to brainstem lesions. In the disconnectome project, we evaluated the disruption of connectivity caused by white mater lesions in 745 patients with MS in three separate cohorts; (i) a comparison of the disconnectome model obtained by classical individual tractography and the disconnectome model based on a freely available tractographic atlas showed a good agreement. Although disconnectome-derived parameters did not overperform conventional MRI parameters in terms of correlations with disability, however, in patients with lower lesion volume, we observed an association of lower EDSS in patients with high global effectivity. For the T1 mapping project, we used MP2RAGE sequence in 99 MS patients. We assessed the T1 abnormalities as z-scores, i.e. deviations from normative values obtained from a study specific atlas based on data from 92 healthy volunteers. The main findings are (i) confirmation of a gradient of tissue damage in normally appearing white matter (NAWM) and lesions obtained with T1 relaxometry; (ii) better correlation of NAWM T1 gradient with disability in early MS compared to lesion load and count and better correlation of lesions´ T1 gradient with disability in progressive MS compared to lesion load and count.