Different MRI measures predict clinical deterioration and cognitive impairment in MS: a 5 year longitudinal study

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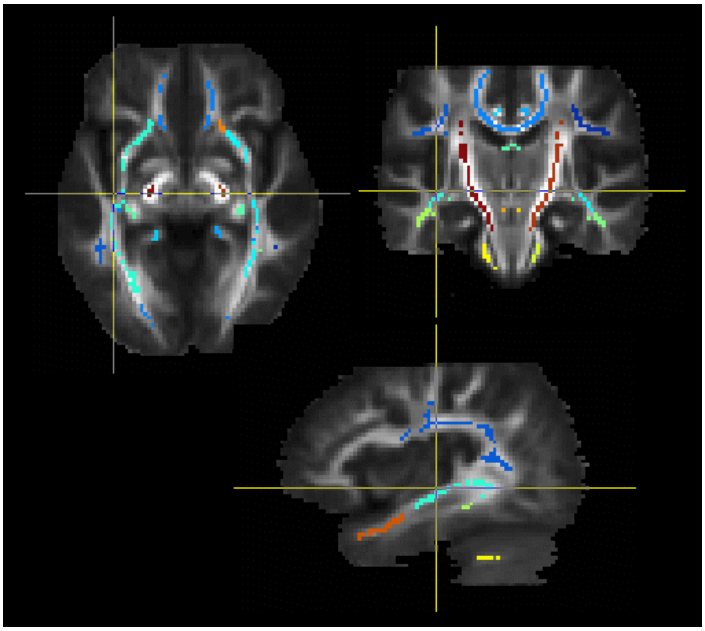
Target audience. Neuroradiologists, radiologists, neurologists.

Background. The identification of imaging biomarkers for monitoring disease progression in multiple sclerosis (MS) is an unmet need.

Purpose. To assess the value of conventional and quantitative MRI measures of brain and spinal cord in predicting disability and cognitive worsening in MS patients after 5 years.



Methods. Brain dual-echo, 3D T1-weighted and diffusion tensor [DT] MRI and cervical cord T2-weighted, 3D T1-weighted and magnetization transfer [MT] MRI scans were obtained at baseline (T0) and after 5 years (Y5) in 76 MS patients and 7 controls, who were followed prospectively with clinical (EDSS and phenotype changes) and neuropsychological evaluation (Rao's battery). At T0 and Y5, measures of lesion load, brain and cord atrophy were obtained. Brain DT MRI measures of white matter (WM) tracts (Figure 1), normal appearing WM and gray matter (GM) as well as cord MT ratio were also assessed. A random forest analysis was performed to identify predictors of neurologic deterioration, phenotype modification and cognitive worsening at Y5.

Figure 1. Color coded map of WM matter fiber bundles included in the analysis.

Results. At Y5, 46/76 (61%) MS patients showed a significant disability worsening (death=9 patients), 23/76 (30%) evolved to a worse clinical phenotype and 15/61 (25%) had a worsening of cognitive functions. At Y5, MS patients had a significant accumulation of brain T2 lesions, brain atrophy (most pronounced for the GM), diffusivity abnormalities of WM tracts and spinal cord atrophy. At random forest analysis, baseline diffusivity measures of WM tract integrity predicted worsening of clinical disability (classification [C]-index=70%) and phenotype modification (C-index=78%), whereas baseline brain volume, GM diffusivity and diffusivity abnormalities of cognitive-related WM tracts predicted cognitive worsening (C-index=78%).

Conclusions. Different mechanisms are likely to contribute to clinical and cognitive worsening in MS patients after 5 years. While disability deterioration seems mainly due to disruption of WM integrity, cognitive dysfunction is the result of a complex interplay between WM and GM damage.