

Myelin dynamics in the spinal cord predict cord atrophy and disability progression at 5-years in early relapsing-remitting MS

Malo Gaubert^{1,2}, Benoit Combès², Elise Bannier^{1,2}, Arthur Masson², Vivien Caron², Gaëlle Baudron², Jean-Christophe Ferré^{1,2}, Emmanuelle Le Page³, Laure Michel³, Bruno Stankoff^{4,5}, Gilles Edan³, Benedetta Bodini^{4,5} and Anne Kerbrat^{2,3}

1 CHU Rennes , Department of Neuroradiology, Rennes, France

2 University Rennes, Inria, CNRS, Inserm, IRISA UMR 6074, Empenn U1228, Rennes, France

3 CHU Rennes, Department of Neurology, Rennes, France

4 Sorbonne Université, Paris Brain Institute, ICM, CNRS, Inserm, Paris, France

5 St Antoine Hospital, Neurology Department, APHP-Sorbonne, Paris, France

Introduction

Despite the major prognostic value of early spinal cord (SC) damage, the processes of demyelination and remyelination in this structure and their clinical relevance remain to be evaluated. In this longitudinal study, we used magnetization transfer ratio (MTR) changes in the cervical SC to generate patient-specific profiles of myelin content change and investigated their clinical relevance.

Objectives

i) to characterise myelin content changes in the SC over a period of 1 year in early relapsing remitting MS patients (RRMS); ii) to investigate the association between SC myelin content changes with disability and cross-sectional area (CSA) at 5-year.

Methods

After IRB approval (NCT02117375), 37 RRMS patients (disease duration < 1 year; mean EDSS = 0.6 at baseline [BL]) underwent a cervical SC MRI at BL, 1 year and 5 years, and 19 healthy controls (HC) at BL only. SC lesions were manually segmented on T2*w cervical axial images at BL. CSA in C2C3 was computed at BL and 5 years on T1w brain images. Based on HC, SC MTR z-maps were computed for each MS patient at BL and 1 year and binarized at -2.58 ($p = .01$) as a proxy of demyelination. A global index of myelin content change (GIMCC) was calculated as the proportion of voxels classified as normal at BL and identified as demyelinated after 1 year (demyelination over time) minus the proportion of voxels classified as demyelinated at BL but not at 1 year (remyelination over time). Partial correlations between GIMCC and disability scores or CSA at BL and 5 years were calculated, with age and gender as covariates.

Results

We observed a wide variability of GIMCC [-13% to 28%], with 18 patients showing a predominance of demyelination over 1 year ($GIMCC > 0$) and 18 a predominance of remyelination ($GIMCC < 0$). Greater GIMCC, reflecting a predominant process of demyelination over remyelination in the SC, was associated with more severe disability at 5 years (EDSS $p = .007$) and with greater disability progression over the follow-up (EDSS

change over 5 years $p=.012$). Greater GIMCC was associated with reduced CSA at 5 years ($p=.032$) and BL ($p=.023$), but not with lesion volume at BL ($p=.36$).

Conclusion

Patients with early RRMS exhibit heterogeneous profiles of SC myelin loss and repair measured over 1 year. Greater SC remyelination during the first year was significantly associated with lower disability progression and greater SC volume 5 years later. These results highlight the potential of myelin repair in the SC to prevent neurodegeneration and clinical progression in patients with MS.

Malo Gaubert: nothing to disclose

Benoit Combès: nothing to disclose

Elise Bannier: nothing to disclose

Arthur Masson: nothing to disclose

Vivien Caron: nothing to disclose

Gaëlle Baudron: nothing to disclose

Jean-Christophe Ferré: nothing to disclose

Emmanuelle Le Page: consulting or lectures, and invitations for national and international congresses from Biogen, Merck, Teva, Sanofi-Genzyme, Novartis Alexion, research support from Teva and Biogen, academic research grants from PHRC and LFSEP, and travel grant from ARSEP Foundation

Bruno Stankoff: nothing to disclose

Gilles Edan: nothing to disclose

Benedetta Bodini: nothing to disclose

Anne Kerbrat: nothing to disclose