Regional hippocampal involvement differs across multiple sclerosis clinical phenotypes: a radial mapping MR-based study

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Target audience. Neuroradiologists, radiologists, neurologists.

Purpose. Emerging data support the notion of a hippocampal demyelination and neurodegeneration early and throughout the course of MS [1]. Aim of our work was to localize and compare the patterns of regional hippocampal atrophy associated to the main multiple sclerosis (MS) clinical phenotypes.

Methods. Brain dual-echo and 3D T1-weighted scans were acquired from 115 MS patients (28 relapsing remitting [RR], 34 secondary progressive [SP], 27 primary progressive [PP], 26 benign [B] MS) and 28 healthy controls (HC). Hippocampal segmentation was performed manually according to standardized procedures [2], and global volumes derived. From contours, radial atrophy distribution was assessed using three-dimensional parametric surface mesh models.

Figure 1. Estimation of the location of hippocampal subfields superimposed on the average hippocampus obtained from the HC group. Abbreviations: CA = cornu ammonis; DG:H = hilus of the dentate gyrus; DG:SM = stratum moleculare of the dentate gyrus; R = right; L = left. Subfields are mapped basing on [3] and [4].

Results. Right and left hippocampal volumes differed significantly between groups (p<0.001 and p=0.001 respectively). Significant differences were found, for the right and left hippocampus respectively, in: RRMS vs. HC (p=0.002, p=0.01) and SPMS vs. PPMS (p=0.031, n.s.). When compared to HC, RRMS patients showed significant radial atrophy (p<0.001) involving the CA1 subfield and the subiculum of the left posterior hippocampus, and the right hippocampal head. Compared to HC, PPMS patients had a significant volume loss affecting lateral CA1, bilaterally, and right tail subicular region, with mild involvement of the right hippocampal head. Compared to RRMS and PPMS, SPMS patients showed atrophy of the left hippocampal head. Compared to RRMS, BMS patients had focal atrophy of the left hippocampal head. Significant correlations (r ranging from -0.2 to -0.5; p<0.001) were found between T2 and T1 lesion load and atrophy of subiculum and CA1 of posterior hippocampus and CA1 subregion of hippocampal head, bilaterally.

Figure 2. Surface distribution of regions of significant local atrophy among study groups. P value ranges are shown in the color bar.

Discussion. Our data support previous findings of selective and progressive CA1 atrophy in patients with MS [5], and provide evidence of a substantial involvement of the subiculum, the major efferent of hippocampal pathways, even in the early phases of the disease. PPMS patients, in whom inflammation is relatively modest, showed a relative sparing of hippocampal formation.

Conclusions. Collectively, these data suggest that hippocampal regional vulnerability to damage might differ across the main MS clinical phenotypes, possibly reflecting differential susceptibility to inflammatory insults and neurodegenerative processes of the hippocampal subfields. The regional pattern of hippocampal damage associated to each MS phenotype could reflect the complex interplay of inflammatory and neurodegenerative processes on histological sectors with different susceptibility characteristics. Further understanding of these processes could provide targets for therapeutic interventions including neuroprotective treatments and cognitive rehabilitation.