Deficits in Memory and Spatial Cognition Correlate With Regional Hippocampal Atrophy in Multiple Sclerosis

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Introduction. The hippocampus has a critical role in episodic memory and visuospatial abilities, which are frequently affected in multiple sclerosis (MS).

Objective. To assess the patterns of whole and regional hippocampal atrophy in a large group of MS patients, and their correlations with neuropsychological impairment.

Methods. From 103 MS patients (22 relapsing remitting [RR], 33 secondary progressive [SP], 23 primary progressive [PP], and 25 benign [B] MS) and 28 healthy controls (HC), 3D T1-weighted images were acquired using a 3.0 Tesla scanner. All subjects underwent neuropsychological evaluation, including word-list (WL), short-story (SS), delayed recall of Rey-Osterrieth Complex Figure (ROCF-recall) and ROCF-copy. The hippocampi were manually segmented and volumes derived. From contours, radial atrophy was calculated for assessment of regional atrophy distribution. Correlations between regional hippocampal atrophy and clinical, neuropsychological and T2 lesion metrics were assessed.

Results. Right and left hippocampal volumes differed significantly between groups ($p<0.001$). Significant differences were found, for the right and left hippocampus respectively, in: RRMS *vs*. HC ($p=0.03$, $p=0.004$), SPMS *vs.* PPMS ($p=0.01$, ns), BMS *vs.* RR (ns, $p=0.04$). In MS patients, radial atrophy was detected in the lateral portion of the body and tail (CA1 subfield) and the subiculum, bilaterally. The ventral surface of the subiculum was also affected (Figure 1). Significant correlations ($p<0.01$) were found between performance at: 1) WL *vs*. tail (CA1 subfield) of the left hippocampus atrophy; 2) ROCF-recall *vs*. tail (CA1 subfield) of the right hippocampus atrophy; and 3) ROCF-copy *vs*. body of the left hippocampus atrophy (Figure 2). Regional hippocampal atrophy correlated with brain T2 lesion volumes, while no correlation was found with global clinical disability.

Conclusions. Hippocampal subregions have a different vulnerability to MS-related damage, with a relative sparing of the head. The assessment of hippocampal atrophy at a regional level may contribute explaining deficits in specific cognitive functions, including memory and spatial cognition.

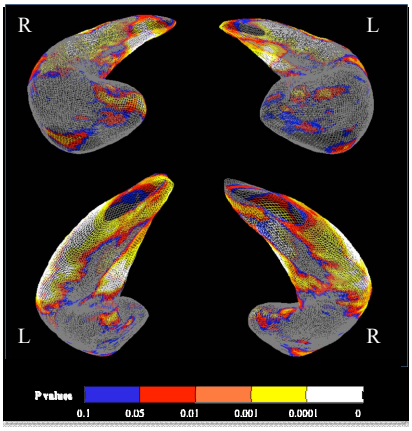

Figure 1. A. Topographic distribution of atrophy of hippocampal formation in MS patients compared to healthy controls. R=right; L=left hippocampus. Top row: anterior view, dorsal aspect. Bottom row: posterior view, ventral aspect.

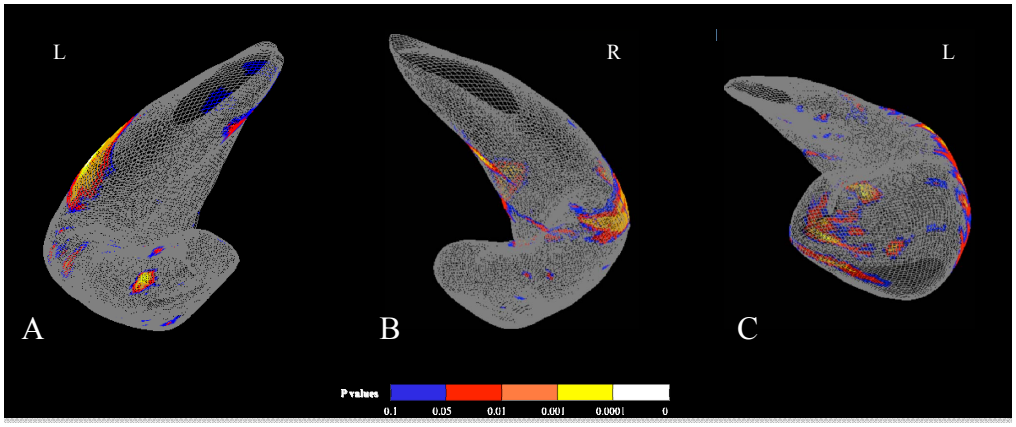

Figure 2. Correlation between performance at **A.**WL *vs*. CA1 subfield atrophy of the left hippocampus; **B.** ROCF-recall *vs*. CA1 subfield atrophy of the right hippocampus; **C.** ROCF-copy *vs*. CA1 subfield atrophy of the left hippocampus.
R=right; L=left hippocampus.