Correlation of regional brain tissue loss and disease severity in Relapsing-Remitting Multiple Sclerosis: a VBM study in a large patient population

A. Prinster[1], M. Quarantelli[1,2], R. Lanzillo[3], C. Mollica[2], P. Salvatore[4], G. Orefice[4], B. Alfano[1], V. Brescia Morra[4], A. Brunetti[1,2], and M. Salvatore[2]

[1]Biostructure and Bioimaging Institute, National Research Council, Naples, Italy, [2]Department of Biomorphological and Functional Sciences, University "Federico II", Naples, Italy, [3]Neurology, Hermitage Hospital IDC, Naples, Italy, [4]Department of Neurological Sciences, University "Federico II", Naples, Italy

Introduction:

Global brain atrophy has been demonstrated in multiple sclerosis (MS) patients, correlating with disease severity [Bermel RA and Bakshi R 2006].

Regional assessment of gray matter (GM) loss has shown a preferential involvement of frontal regions [Sailer 2006, Prinster 2005]. However, studies of correlation between disease severity and regional cortical thicknesses, have provided somewhat conflicting results in Relapsing-Remitting MS (RR-MS) patients and in patients with mixed disease subtype [Sailer 2006, Chen 2004, Charil 2007].

Objective

Aim of our study was to investigate possible correlations between brain tissue loss and clinical severity using optimized Voxel.Based Morphometry (VBM [Ashburner 2000]) in a large group of RR-MS patients.

Methods

128 RR-MS patients with clinically defined multiple sclerosis, with a RR course, were enrolled (86 female, mean age 36.07 ± 9.2, mean disease duration 10.14 ± 7.2 years, median EDSS score 2.8, EDSS range 1.0–6.0).

MR studies were performed at 1.5 T (Achieva, Philips Medical Systems) with sequential acquisition of two interleaved sets of oblique axial slices (16 slices per set, thickness 4 mm, slice interval 4 mm).

For each set of slices, two spin echo sequences (TR=600, TE=15; TR=1760, TE=15/90; both with 90° flip angle, 192x256 matrix, 0.89mm pixel size) were acquired sequentially in the same spatial position.

Brain studies were segmented into GM, total white matter (tWM, the sum of normal-appearing and abnormal WM) and CSF using an unsupervised multispectral segmentation method [Alfano 2000].

Resulting GM and tWM volumes were spatially normalized using a site- and study-specific template, and correlations between normalized GM and WM maps and EDSS were assessed using the general linear model. Age, disease duration and total lesion load were included as covariates in the model. Globals for data normalization were derived from total intracranial volume (the sum of GM, tWM and CSF).

Results

Regional GM loss correlated with EDSS in the primary motor and somatosensory areas bilaterally (Brodmann Areas 3 e 4), as well as in the left fusiform gyrus (Fig.1, $p < 0.05$ FWE corrected at cluster level). tWM regional volume correlated with EDSS in the subcortical region near the right primary motor cortex, extending trough the pyramidal tract to the brainsteam (Fig. 2, $p < 0.05$ FWE corrected at cluster level).

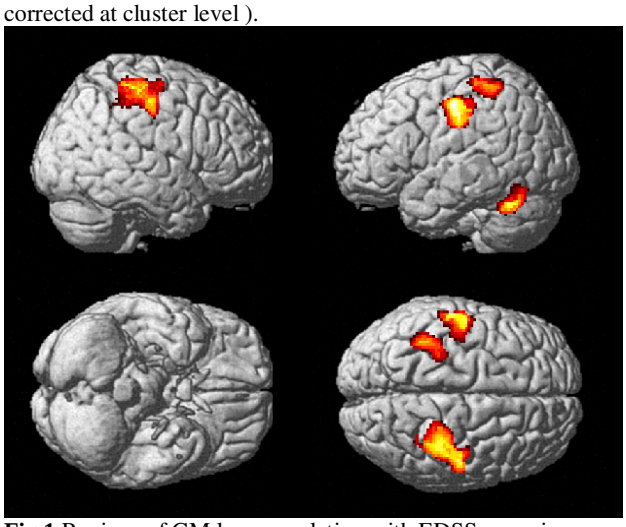

Fig.1 Regions of GM loss correlating with EDSS score in 128 RR-MS patients ($p < 0.05$ corrected at cluster level)

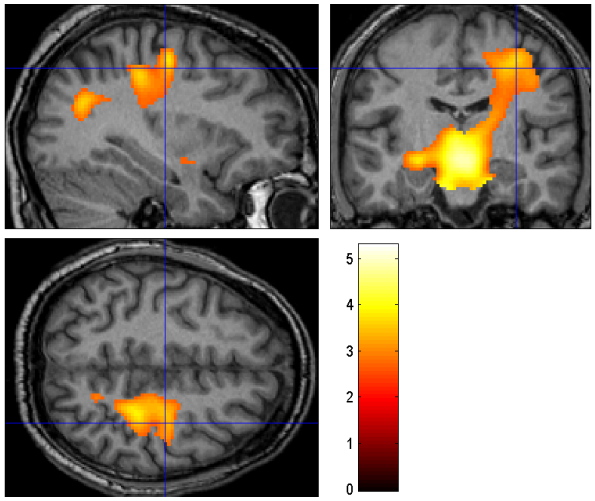

Fig. 2 Maps of tWM loss correlating with EDSS in 128 RR-MS patients ($p < 0.05$ corrected at cluster level)

Discussion and Conclusion

We have shown, in RR- MS patients, a preferential correlation with EDSS of GM volume reduction in the primary motor cortex bilaterally, with an associated preferential right-sided tWM loss in subcortical regions stemming from the rolandic areas and following the pyramidal tract down to the brainsteam.

Longitudinal studies are needed if this correlation is constant throughout the natural history of the disease.

Bibliography

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