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Computer-Based 3D MR Imaging Analysis in Amyotrophic Lateral Sclerosis: Common and Specific Factors Among Studies

Computerized MR imaging analysis including automatic measurements of whole-brain atrophy and the use of unbiased analysis techniques for regional atrophy without prior restriction of the search volume (such as voxel-based morphometry [VBM]) is a rapidly growing field in neuroimaging. Recently, Mezzapesa et al[1] reported global brain atrophy (ie, reduced brain parenchymal fraction [BPF]) in a group of 16 patients with amyotrophic lateral sclerosis (ALS); and in the analysis of local brain changes by VBM in the same patients, they reported gray matter reductions in extramotor areas, including the bilateral frontal and temporal lobes. Both with respect to the global brain atrophy measure and to the regional findings, however, additional comparisons with previous 3D MR imaging studies in ALS are necessary beyond those discussed by Mezzapesa et al.

In a previous study of 22 patients with definite ALS,[2] BPF assessment by use of the same technical approach but a different software solution (statistical parametric mapping [available at www.fil.ion.ucl.ac.uk/spm/] versus Structural Image Evaluation, Using Normalization, of Atrophy [available at www.fmrib.ox.ac.uk/analysis/research/siena] in Mezzapesa et al[1]) came to the same result of a highly significant global brain atrophy compared with 22 age-matched controls. Obviously, whole-brain atrophy as assessed by BPF seems to be an ALS-associated feature, as now demonstrated by 2 independent studies in a total of 38 patients. It is remarkable that this effect could only be observed in the analysis of BPF as the size-normalized proportion of brain parenchymal volume to total intracranial volume, whereas neither the calculation of normalized brain volume in the same study[1] nor the absolute volume measurements in non-normalized 3D MR imaging data of ALS patients[3] nor the earlier MR imaging studies cited by Mezzapesa et al[1] led to significant group differences between ALS brains and those of controls. Thus, BPF seems to be the most sensitive MR imaging–based biologic marker in this motor neuron disease and has to be further evaluated in a longitudinal design.

With respect to the regional distribution of this atrophy, the pattern and extent of volume losses particularly in frontal and temporal areas vary widely among studies within the well-known overlap of ALS and frontotemporal lobar degeneration (FTLD). Even if detailed neuropsychological investigations as a conditio sine qua non in patient characterization were performed, the results would be heterogeneous. In agreement with Mezzapesa et al,[1] Grosskreutz et al[4] reported extramotor volume losses in parietal and frontal areas in another recent VBM study of 17 patients with ALS, whereas the results of the VBM analysis by Kassubek et al[2] of patients with ALS without any neuropsychological/behavioral signs of FTLD with only 1 very small frontal area of gray matter loss were apparently at odds with those of Mezzapesa et al[1] and Grosskreutz et al[4]. Even if methodologic factors might be of relevance, such as the smoothing during data preprocessing (the use of 12-mm FWHM[1] versus 6 mm[2] increases the sensitivity and reduces the specificity), the exact patient characterization with respect to the clinical presentation and disease-related factors is of utmost importance. For the white matter, the structural brain alterations along the corticospinal tracts were only observed in 1 study so far.[2]

In summary, the morphologic fingerprint of ALS in motor and extramotor brain areas assessable by in vivo 3D MR imaging analysis awaits further investigations in larger homogeneous patient groups; and for the establishment of BPF as a biologic marker at group level, studies in longitudinal design as far as they may be applicable in this rapidly progressive disorder are required.

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