



Get Clarity On Generics

Cost-Effective CT & MRI Contrast Agents



FRESENIUS
KABI

WATCH VIDEO

AJNR

Reply:

D.M. Mezzapesa and I.L. Simone

AJNR Am J Neuroradiol 2007, 28 (9) 1627

doi: <https://doi.org/10.3174/ajnr.A0684>

<http://www.ajnr.org/content/28/9/1627>

This information is current as
of August 12, 2025.

Reply:

The recent development of advanced automated 3D MR imaging analysis provides new tools aimed at defining the entity and topography of brain tissue loss in neurodegenerative diseases. The application of voxel-based analysis in amyotrophic lateral sclerosis (ALS) has recently produced several reports of evidence of a brain involvement beyond the motor areas.¹⁻⁵ Moreover, discordant results emerge from the comparison of these studies. In particular, the pattern and extent of volume loss in frontal and temporal areas vary widely among studies. Also 2 studies did not show atrophy in the primary motor cortex.^{1,5}

The main explanation of these discrepancies could derive from the combination of 2 factors: the heterogeneity of ALS-related brain pathology and the high sensitivity of the voxel-based analysis (in particular voxel-based morphometry [VBM]). The presence of regional atrophy in the frontal and temporal lobes supports the current opinion of a continuum between ALS and frontotemporal dementia. Each single subject could belong to a wide range of combinations of pathology inside this continuum. Unfortunately VBM is not able to depict tissue loss in individual brains but only recognizes differences among groups of subjects. Despite the effort to select homogeneous subjects in the study groups, particularly considering the neuropsychological profile, the relatively rapid course of ALS could prevent the appearance of extramotor symptoms and mask an understanding subclinical heterogeneity.

On the other hand, VBM seems extremely sensitive and could depict a small amount of intergroup difference in terms of regional volume loss, especially in gray matter, even in the presence of very low global brain atrophy. Indeed, only brain parenchymal fraction (BPF) was able to discover global brain atrophy in ALS, as detected in 2 studies.^{4,5} Therefore, we agree with the opinion that among whole-brain measures, BPF is the most sensitive as a biologic marker in neurodegenerative diseases. Again, the high sensitivity of automated

3D MR imaging analysis calls for a selection of homogeneous patient groups to provide compelling results.

Another aspect that must be kept in mind when volumetric analyses are performed is that brain pathology in neurodegenerative diseases is not reducible exclusively to volume loss. For example, reactive gliosis may occur to mask tissue loss, particularly in the primary motor cortex, as speculated by Filippi et al.⁶

For all these reasons, further longitudinal studies are required with a multiparametric MR imaging approach, adding MR spectroscopy and diffusion tensor imaging, to investigate both tissue volume and tissue attenuation.⁶ In addition, an intriguing finding, which was not investigated enough, is the hemispheric asymmetry of atrophy in ALS subjects, with a right lateralization reported by 2 studies.^{4,5}

References

1. Ellis CM, Suckling J, Amaro E Jr, et al. **Volumetric analysis reveals corticospinal tract degeneration and extramotor involvement in ALS.** *Neurology* 2001;57:1571-78
2. Chang JL, Lomen-Hoerth C, Murphy J, et al. **A voxel-based morphometry study of patterns of brain atrophy in ALS and ALS/FTLD.** *Neurology* 2005;65:75-80
3. Abrahams S, Goldstein LH, Suckling J, et al. **Frontotemporal white matter changes in amyotrophic lateral sclerosis.** *J Neurol* 2005;252:321-31
4. Kassubek J, Unrath A, Huppertz HJ, et al. **Global brain atrophy and corticospinal tract alterations in ALS, as investigated by voxel-based morphometry of 3-D MRI.** *Amyotroph Lateral Scler Other Motor Neuron Disord* 2005;6:213-20
5. Mezzapesa DM, Ceccarelli A, Dicuonzo F, et al. **Whole-brain and regional brain atrophy in amyotrophic lateral sclerosis.** *AJNR Am J Neuroradiol* 2007;28:255-59
6. Filippi M, Agosta F, Rocca MA. **Regional assessment of brain atrophy: a novel approach to achieve a more complete picture of tissue damage associated with central nervous system disorders?** *AJNR Am J Neuroradiol* 2007;28:260-61

D.M. Mezzapesa

I.L. Simone

Department of Neurological and Psychiatric Sciences

University of Bari

Bari, Italy

DOI 10.3174/ajnr.A0684