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Reply:

S.A. Sajjadi and P.J. Nestor

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REPLY:

We thank Dr Matias-Guiu et al for their interest in our study on the role of MR imaging in the syndromic classification of primary progressive aphasia (PPA).[1] Their proposal that FDG-PET might be a more sensitive method than structural MR imaging is highly plausible. We also agree with Matias-Guiu et al that direct comparison would be necessary to definitively resolve the issue. For instance, both structural MR imaging and FDG-PET measure neurodegeneration. The greater the degree of neurodegeneration, therefore, the more likely it is to be detectable with these types of imaging. In other words, the sensitivity of any technique that operates through detecting degeneration is also a function of disease severity. To this end, it is possibly relevant that their PPA group as a whole was more advanced than those with PPA in our series—mean Mini-Mental State Examination and Addenbrookes cognitive examination scores of 18.5 ± 8.1 and 46.1 ± 22.0,[2] respectively, compared with scores of 22.1 ± 3.9 and 56.4 ± 14.1.[1] Whether this confounder offers a credible explanation for the apparent increased sensitivity of FDG-PET of Matias-Guiu et al is perhaps debatable, but nonetheless important to address with a direct comparison.

A further methodologic feature that we would strongly advocate in designing a future study is the inclusion of a good number of negative (healthy age-matched) and positive (non-PPA degenerative dementia) controls. If raters know a priori that the scans they are evaluating come from a few predefined groups, the rating essentially becomes a forced-choice paradigm; this, in turn, may artificially inflate the accuracy compared with a real-world clinical environment in which the differential diagnosis is more open-ended.

Finally, as noted by Matias-Guiu et al, a new study could also assess the potential benefit of the combination of FDG-PET and MR imaging. To this end, we would add the possibility that the decision of whether to combine them is likely to vary according to the precise clinical question. For instance, our study showed that MR imaging returns near-perfect accuracy in detecting the lesions of semantic-variant PPA, making FDG-PET redundant in this scenario. In contrast, the terrible sensitivity yet good specificity for nonfluent and logopenic PPA with MR imaging suggest that a hierarchic algorithm in which one proceeds to FDG-PET if the MR imaging is nonspecific might be sensible.

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S.A. Sajjadi
Department of Neurology
University of California, Irvine
Irvine, California
P.J. Nestor
German Center for Neurodegenerative diseases
Magdeburg, Germany