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Neuroimaging / Optimal neuroimaging measures for tracking disease progression

Impact of cortical and subcortical atrophy in the diagnosis and prognosis of bvFTD: A multicenter longitudinal study

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Abstract

Background: The behavioral variant of frontotemporal dementia (bvFTD) presents with variable patterns of cortical and subcortical atrophy on Magnetic Resonance Imaging (MRI). We aimed to assess the clinical utility of two reproducible measure-

ments of cerebral atrophy (Harper's visual atrophy scale [HVAS], and the Magnetic Resonance Parkinsonism Index [MRPI]) in a large multicenter sample of bvFTD with longitudinal follow-up.

Methods: We included 466 participants from three centers: 241 bvFTD (according to the International bvFTD Criteria Consortium), and 225 healthy controls (HC). Clinical deterioration was assessed with Mini-Mental State Examination (MMSE) and the Clinical Deterioration Scale Sum-of-boxes (CDR-sb). bvFTD participants were considered to have an increased certainty of underlying Frontotemporal Lobar Degeneration (+FTLD) when: (i) FTLD was confirmed at autopsy (n=72); (ii) a secondary FTLD-related phenotype was identified during follow-up (n=47) or (iii) a FTLD-related mutation was found (n=49). Six raters blinded to clinical data were first asked to dichotomize participants according to the presence of "a clear pattern of atrophy suggestive of probable bvFTD", and then applied the HVAS (ICC(2,k)=.86 to .96). The MRPI was calculated with a fully automated algorithm.

Results: Mean age of bvFTD participants was 63.3 ± 10, 68% were male (MMSE=23 ± 7 and CDR-sb=6.7 ± 3.5). Blinded raters had 52% sensitivity and 97% specificity for the identification of bvFTD participants (AUC=.74, p=.001). All HVAS measures with the exception of posterior atrophy discriminated between bvFTD and HC (AUC=.77 to .83, p<.001). The composite bvFTD score (average score of orbitofrontal, anterior cingulate, anterior temporal, medial temporal lobe and frontal insula regions) showed the best diagnostic accuracy for the differentiation of bvFTD from HC (AUC=.91, p<.001 in +FTLD). This composite score also differentiated between bvFTD participants that were not considered to have a clear pattern of atrophy suggestive of probable bvFTD (blinded raters) and HC (p<.001). We hypothesized that HVAS and MRPI scores may be independent predictors of clinical deterioration and survival in bvFTD (definitive results pending).

Conclusion: The combination of HVAS and MRPI may provide valuable diagnostic and prognostic information in the behavioral syndromes verifying bvFTD criteria. These measures represent reliable, reproducible and affordable imaging biomarkers.