Biomarkers (non-neuroimaging) / Multi-modal comparisons

Late-onset epilepsy with unknown etiology: A pilot study on neuropsychological profile, cerebrospinal fluid biomarkers, and quantitative EEG characteristics

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Abstract

Background: Despite epilepsy has been associated with cognitive decline, neuropsychological, neurobiological and neurophysiological features in patients with late-onset epilepsy of unknown etiology (LOEU) are still unknown. This cross-sectional study aims at investigating neuropsychological profile, cerebrospinal fluid (CSF) biomarkers of Alzheimer’s disease (AD), and resting-state quantitative electroencephalographic (qEEG) cortical rhythms in LOEU patients with mild cognitive impairment (LOEU-MCI) and with normal cognition (LOEU-CN), compared to non-epileptic MCI (NE-MCI) and cognitively normal (CN) controls.

Method: Consecutive patients in two clinical Units diagnosed with LOEU-CN (19), LOEU-MCI (27), and NE-MCI (21) were enrolled, and compared to age and sex-matched cognitively normal subjects (CN, 11). Patients underwent standardized comprehensive neuropsychological evaluation and CSF core AD biomarkers assessment (i.e., CSF Aβ42, phospho-tau and total tau, classified through A/T/(N) system). Recordings of resting-state eyes-closed electroencephalographic (EEG) rhythms were collected and cortical source estimation of delta (<4 Hz) to gamma (>30 Hz) bands with exact Low Resolution Electromagnetic Tomography (eLORETA) was performed.

Result: Most of LOEU patients had MCI status at seizure onset (59%). Patients with LOEU-MCI performed significantly worse on measures of global cognition, visuospatial abilities and executive functions compared to NE-MCI patients (p<0.05). Regarding MCI subtype, multiple-domain MCI was 3-fold more frequent in the LOEU-MCI than in the NE-MCI patients (OR 3.14, 95%CI 0.93-10.58, p=0.06). CSF Aβ42 levels were lower in the LOEU-MCI compared with the LOEU-CN group. Finally, parietal and occipital sources of alpha (8-12 Hz) rhythms were less active in the LOEU-MCI than NE-MCI and CN groups, and the opposite was true for frontal and temporal cortical delta sources.
**Conclusion:** MCI status was relatively frequent in LOEU patients, involved multiple cognitive domains, and might have been driven by amyloidosis according to CSF biomarkers. LOEU-MCI status was associated with abnormalities in cortical sources of EEG rhythms related to quiet vigilance. Future longitudinal studies should cross-validate our findings and test the predictive value of CSF and EEG variables.