

Effects of Palmitoylethanolamide Combined with Luteoline on High Frequency Oscillations and GABAergic Transmission in Patients with Frontotemporal Dementia

Francesco Di Lorenzo, Martina Assogna, Elias Casula, Ilaria Borghi, Sonia Bonni, Caterina Motta, Alessandro Martorana, Giacomo Koch

Introduction: Frontotemporal dementia (FTD) is a presenile neurodegenerative disease for which there is no effective pharmacological treatment. Recently, a link has been proposed between neuroinflammation and FTD. Objective: Here, we aim to investigate the effects of palmitoylethanolamide (PEA) combined with luteoline (PEA-LUT), an endocannabinoid with anti-inflammatory and neuroprotective effects, on behavior, cognition, and cortical activity in a sample of FTD patients. Methods: 52 patients with a diagnosis of probable FTD were enrolled. Cognitive and neurophysiological evaluations were performed at baseline and after 4 weeks of PEA-LUT 700mgx2/day. Cognitive effects were assessed by Neuropsychiatric Inventory (NPI), Mini-Mental State Examination, Frontal Assessment Battery (FAB), Screening for Aphasia in Neurodegeneration (SAND), Activities of Daily Living-Instrumental Activities of Daily Living (ADL-IADL), and Frontotemporal Lobar Degeneration-modified Clinical Dementia Rating (FTD-CDR) scale. To investigate in vivo neurophysiological effects of PEA-LUT, we used repetitive and paired-pulse transcranial magnetic stimulation (TMS) protocols assessing LTP-like cortical plasticity, short-interval intracortical inhibition, long-interval intracortical inhibition (LICI), and short-latency afferent inhibition. Moreover, we used TMS combined with EEG to evaluate the effects on frontal lobe cortical oscillatory activity. Results: Treatment with PEA-LUT was associated with an improvement in SAND, FTD-CDR and ADL/IADL scores. Neurophysiological evaluation showed a restoration of LICI, in particular at ISI 100ms, suggesting a modulation of GABA(B) activity. TMS-EEG showed a remarkable increase of TMS-evoked frontal lobe activity and of high-frequency oscillations in the beta/gamma range. Conclusion: PEA-LUT could improve functional impairment s in FTD patients through the modulation of cortical oscillatory activity and GABA(B)ergic transmission

Conflicts of interest

Nothing to disclose