# CLINICAL AND NEUROPHYSIOLOGICAL EFFECTS OF PEA-LUT ON FRONTOTEMPORAL DEMENTIA

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## Introduction

**Frontotemporal dementia** (FTD) is a frequent cause of presenile neurodegeneration that still lacks effective pharmacological treatments able to slow its progression. Recently, specific forms of FTD have been linked to **neuroinflammation**, which seems to be an important factor of the disease since its early phases [1]. These information lead to consider new drugs targeting the neuroinflammatory processes. In this direction, we investigated efficacy and safety of **palmitoylethanolamide combined with luteoline** (PEA-LUT), endogenous compounds with anti-inflammatory properties, in a sample of FTD patients.

## Materials and method

We enrolled **17 patients** with a diagnosis of **probable FTD**. We performed **cognitive and neurophysiological evaluations** at baseline **(T0)** and after 4 weeks **(T1)** of **PEA-LUT (Glialia)** at the oral dosage of 700 mg x 2/day.

| Clinical and demographical data | |
|---|---|
| **patients** | 17 |
| **age** | 62.35 ± 9.43 |
| **gender (F/M)** | 11/6 |
| **variant (PPA/BV)** | 9/8 |
| **disease duration (Y)** | 2.62 ± 1.29 |
| **baseline CDR-FTD** | 8.41 ± 4.22 |

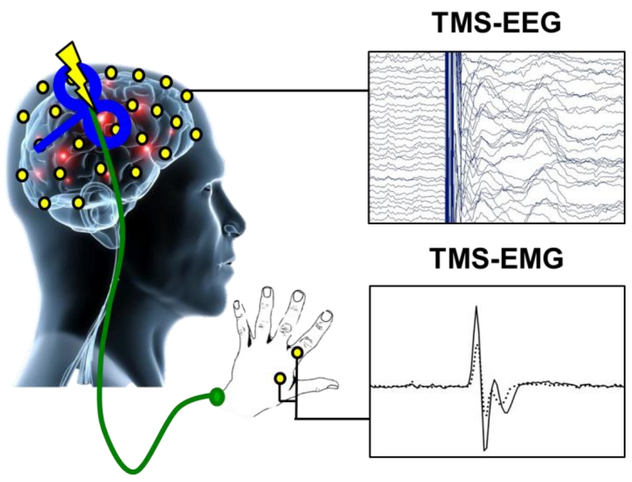
**T0 Evaluation** → **4 weeks PEA-LUT 700 mg x 2** → **T1 Evaluation**

**Neuropsychological evaluation:**

- MMSE, FAB, SAND, NPI, CDR-FTD, ADL/IADL

**Neurophysiological evaluation:**

- TMS-EMG (SICI, ICF, LICI, SAI, LTP)
- TMS-EEG (areas of interest: DLPFC l/r, control areas: PPC l/r)




## Results

**Neuropsychological evaluation** (Fig.1) revealed an improvement in Frontal Assessment Scale (**FAB**) score (p=0.03) and in Neuropsychiatric Inventory (**NPI**) (p=0.02) after 4 weeks of treatment. The neurophysiological **TMS-EMG evaluation** (Fig.2) conducted by means of TMS-EMG showed a significant difference between T0 and T1(p=0.04) in the long-interval intracortical inhibition (**LICI**), in particular at 100ms (p=0.03), suggesting a modulation of GABA(B) activity.

**Fig. 1**

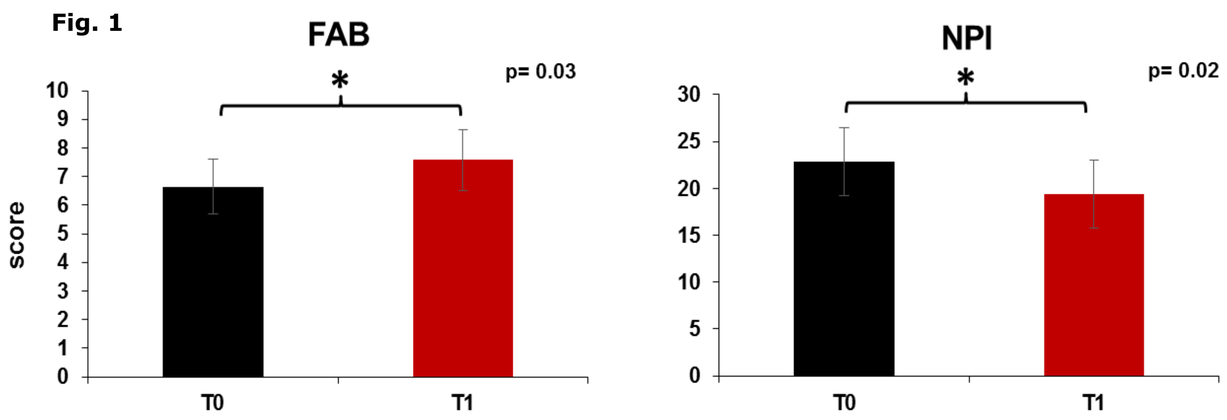
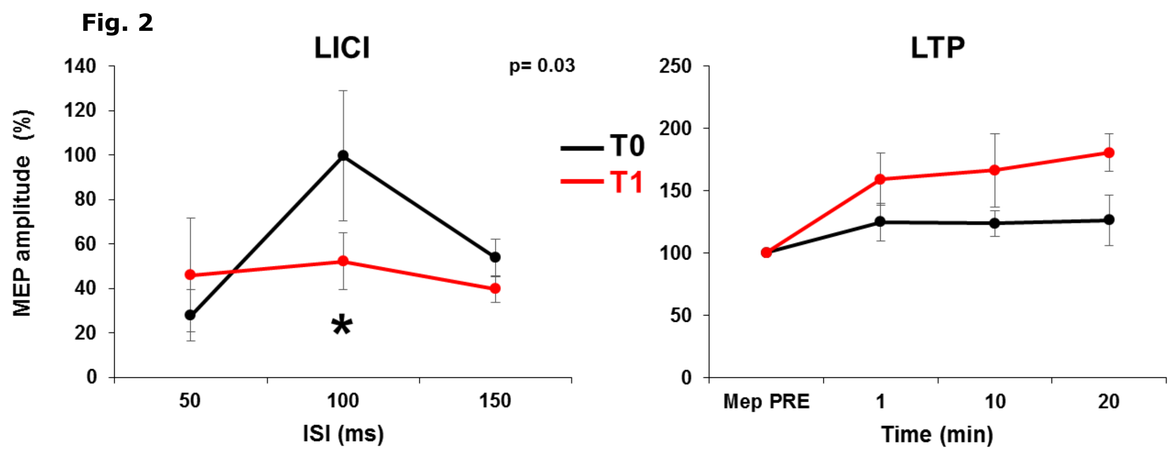



**Fig. 2**




**TMS-EEG evaluation** revealed a specific **increase** in **gamma/beta oscillatory activity** (P=.034) (Fig. 3A) and **cortical activity** (p=.002) (Fig. 3C) in **left DLPFC** after treatment. No significative differences were found when stimulating the control areas (PPC l/r) (Fig.4).

**Fig. 3** LEFT DLPFC — RIGHT DLPFC

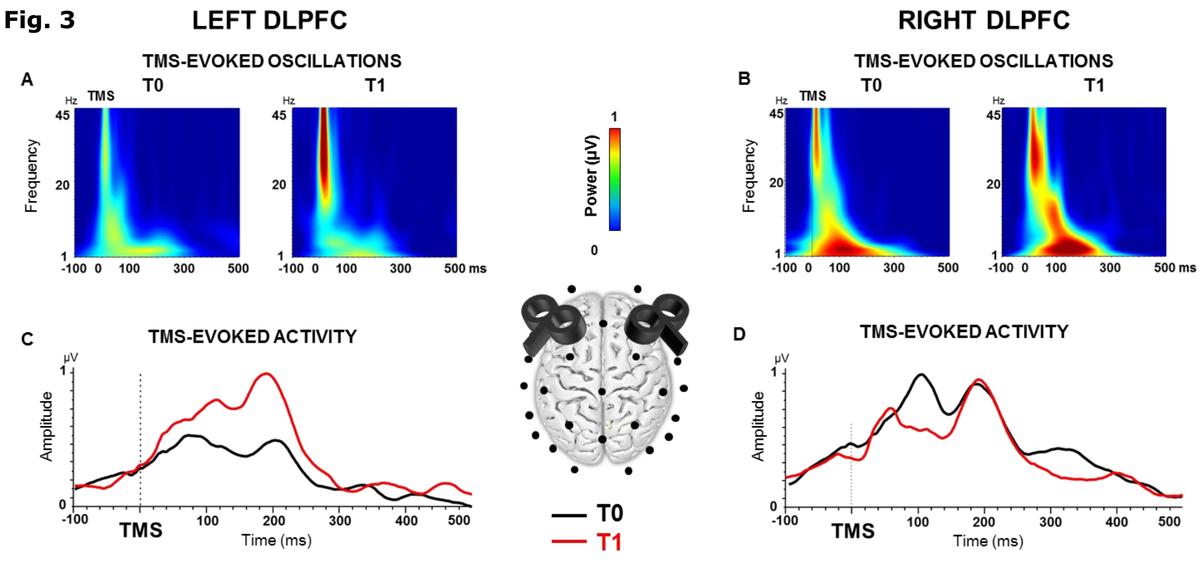
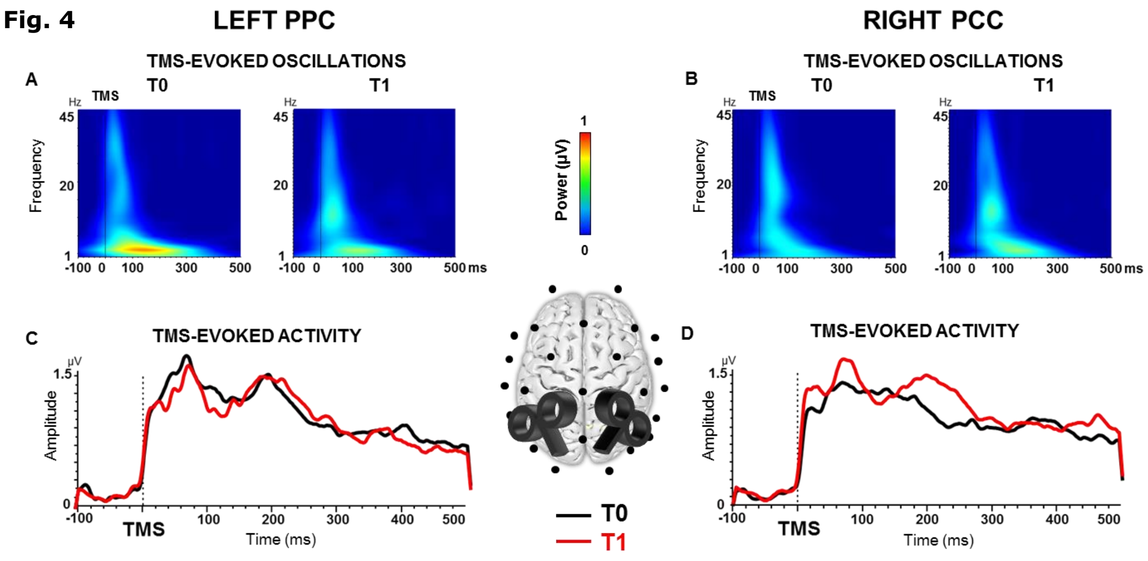



**Fig. 4** LEFT PPC — RIGHT PCC




## Conclusions

**PEA-LUT** improved executive functions and behavioral disturbances. These clinical data were associated with restoration of long-term intracortical inhibition, mediated by GABA-B receptors, which has been found to be altered in FTD [2]. Moreover, the treatment led to an increase in left DLPFC activity and in DLPFC gamma/beta oscillatory activity, which seems to be reduced in **FTD patients** [3]. Thus, PEA-LUT could have a **therapeutic effect** in FTD.

## References

1 Bright, F., Werry, E. L., Dobson-Stone et al., (2019). Neuroinflammation in frontotemporal dementia. Nature reviews Neurology, 15(9), 540-555.

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[3] Murley, A. G., & Rowe, J. B. (2018). Neurotransmitter deficits from frontotemporal lobar degeneration. Brain, 141(5), 1263-1285.

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