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BIOMARKERS

POSTER PRESENTATIONS

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Biomarkers (non-neuroimaging) / Novel biomarkers

Cortical plasticity assessment predicts decline in patients with mild cognitive impairment

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Abstract

Background: Alzheimer's disease (AD) is characterized by loss of synaptic connections, cell death and disruption of structural and functional networks. One of the most consistent findings is the impairment of cortical plasticity, especially Long Term Potentiation (LTP) mechanisms. Recently, the use of new diagnostic criteria allowed to considered AD as a clinico-biological entity identifiable in vivo on the presence of biomarkers. In light of these new criteria, aim of the current work is to investigate cortical plasticity in patients with hippocampal type memory impairment admitted for the first time in the memory clinic and stratified according to CSF biomarkers profile; moreover we followed patients up to a period of three years to explore the relationship between neurophysiological, neuropsychological and CSF biomarkers and clinical progression.

Method: Seventy-three patients were recruited and followed up for 36 months. They underwent CSF sampling and Transcranial Magnetic Stimulation to investigate LTP and intracortical circuits. According to the new AD criteria we divided patients in three groups: 1) Mild Cognitive Impaired (MCI) patients (n=21); Prodromal AD (PROAD) patients (n=24); AD Dementia (ADD) patients (n=28).

Result: In neurophysiological evaluations only iTBS protocol was different among the different groups showing a paradoxical reversal of LTP for ADD and PROAD and a poor response for MCI patients. ProAD worsened faster than MCI. Regression analyses showed that LTP impairment was related to clinical progression. Kaplan-Meyer analyses showed that patients expressing the worst LTP values were the ones to progress faster in a 3 year time.

Conclusion: The new criteria based on the presence of biomarkers and dementia allow us to identify patients at a prodromal stage that will develop dementia due to AD. LTP impairment drives the clinical progression in patients at prodromal stages confirming its pivotal role in determining cognitive decline. These results pave the way for the identification of new therapeutic targets such as synaptic plasticity modulators.

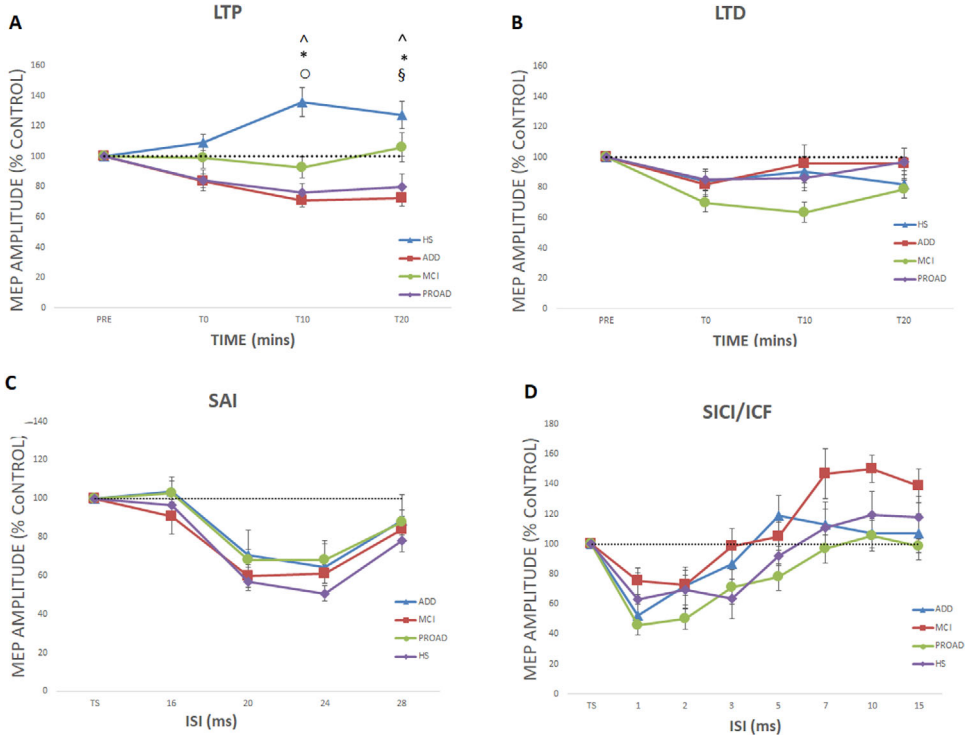

FIGURE 1

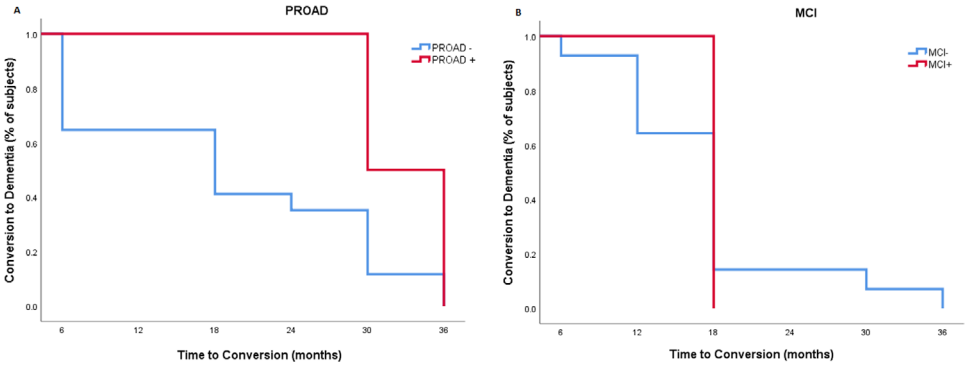

FIGURE 2

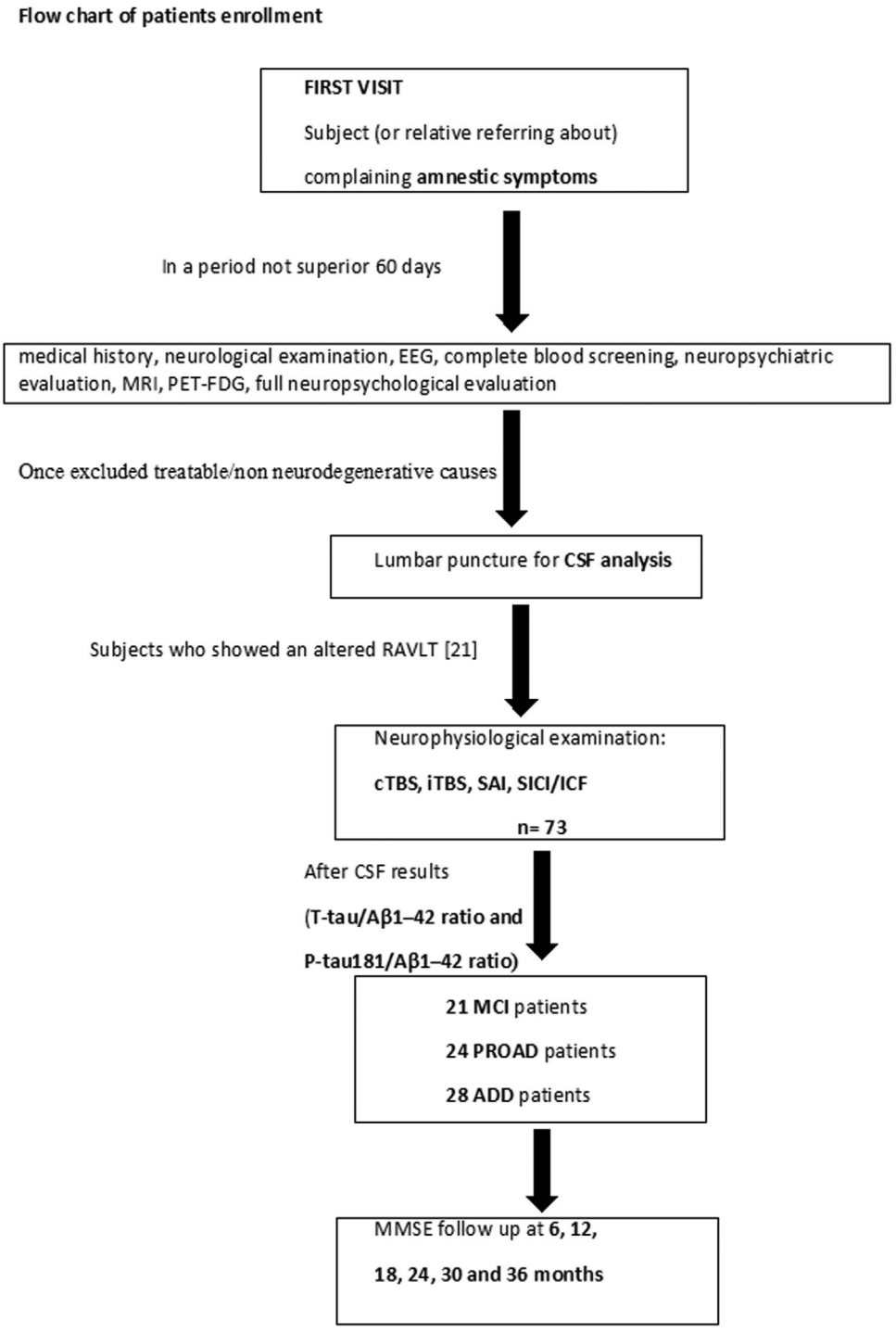
Flow chart of patients enrollment
FIRST VISIT
Subject (or relative referring about)
complaining amnestic symptoms
In a period not superior 60 days
medical history, neurological examination, EEG, complete blood screening, neuropsychiatric evaluation, MRI, PET-FDG, full neuropsychological evaluation
Once excluded treatable/non neurodegenerative causes
Lumbar puncture for CSF analysis
Subjects who showed an altered RAVLT [21]
Neurophysiological examination:
cTBS, iTBS, SAI, SICI/ICF
n= 73
After CSF results
(T-tau/Aβ1–42 ratio and
P-tau181/Aβ1–42 ratio)
21 MCI patients
24 PROAD patients
28 ADD patients
MMSE follow up at 6, 12,
18, 24, 30 and 36 months

FIGURE 3