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TMS EVALUATION IN COGNITIVE IMPAIRED PATIENTS ACCORDING TO NEW CRITERIA OF AD: A 36 MONTHS FOLLOW-UP STUDY

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Background

Methods

Results

Conclusions

First approach at memory clinic with Cognitive Impaired (CI) patients is usually full of questions from caregivers and patients

Which is the diagnosis?
Which is the progression?

Position Paper

Lancet Neurol 2010; 9: 1118–27

Revising the definition of Alzheimer's disease: a new lexicon

Bruno Dubois, Howard H Feldman, Claudia Jacova, Jeffrey L Cummings, Steven T DeKosky, Pascale Barberger-Gateau, André Delacourte, Giovanni Frisoni, Nick C Fox, Douglas Galasko, Serge Gauthier, Harald Hampel, Gregory A Jicha, Kenichi Meguro, John O'Brien, Florence Pasquier, Philippe Robert, Martin Rossor, Steven Salloway, Marie Sarazin, Leonardo C de Souza, Yaakov Stern, Pieter J Visser, Philip Scheltens

NEW CRITERIA AND CLASSIFICATIONS FOR AD DIAGNOSIS

PROGRESSION?

Categorization of the current most validated biomarkers

	Pathophysiological markers	Topographical markers
Cerebrospinal fluid		
Amyloid β_{42}	Yes	No
Total tau, phospho-tau	Yes	No
PET		
Amyloid tracer uptake	Yes	No
Fluorodeoxyglucose	No	Yes
Structural MRI		
Medial temporal atrophy	No	Yes

Comparative features of different conditions according to the new lexicon

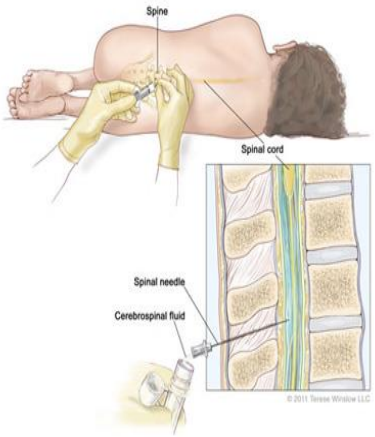
	AD diagnosis	Presence of impairment on specified memory tests	Evidence of biomarkers in vivo
[illegible] AD	Yes	Required	Required
[illegible] AD	Yes	Not required	Required
[illegible]	Yes	Required	Required
[illegible]	Yes	Required	Required
[illegible] AD	Yes	Required	Required
Predi[illegible]AD			
Asympto[illegible] for AD	No	Not present	Required
Presymptomat[illegible]D	No	Not present	Not required
Mild cognitive impair[illegible]		Not required	Not required

Prodromal AD (PROAD)
cognitive impairment **not affecting** daily activity **with evidence** of AD biomarkers

Mild Cognitive Impriment (MCI)
cognitive impairment **not affecting** daily activities **without evidence** of AD biomarkers

AD Dementia
cognitive impairment **affecting** daily activity **with evidence** of AD biomarkers

73 CI patients



CSF withdrawal

Biomarker evidence

T-tau/Aβ1–42 ratio (Maddalena 2003)

P-tau181/Aβ1–42 ratio (Fagan 2007)

	AD	PROAD	MCI	HS	p value
Age at baseline ,y (mean ± SD)[a]	36.8 ± 5.7	70,2 ± 6.2	66 ± 6.4	66.2 ± 5.1	n.s.
Female (%)[b]	50%	54%	59%	44%	n.s.
Disease duration, m (mean ± SD)[a]	13.1 ± 3.5	13.2 ± 2.9	15.1 4.1	/	n.s
Education, y (mean ± SD)[a]	8.3 ± 3.7	8.3 ± 3.1	9.4 ± 4.6	8.2 ± 3.4	n.s
CSF total-tau pg/ml (mean ± SD)	830.1 ± 372	794.1 ± 245	296.5 ± 118	/	< 0.001
CSF p-tau pg/ml (mean ± SD)	98.3 ± 52	84.2 ± 36	49.1 ± 21	/	< 0.001
CSF beta 1-42 pg/ml (mean ± SD)	315.6±114	276.7 ± 136.1	605.2 ± 272	/	< 0.001
APOE4 (E3/E4 + E4/E4) (%)[b]	35%	30%	30%	/	n.s
MMSE baseline (mean ± SD)	18.9 ± 2.5	25.4 ± 1.2	25.8 ± 2.09	29.5 ± 0.5	< 0.001

According to the new criteria for AD proposed patients with CI were divided in three groups:

21 MCI patients

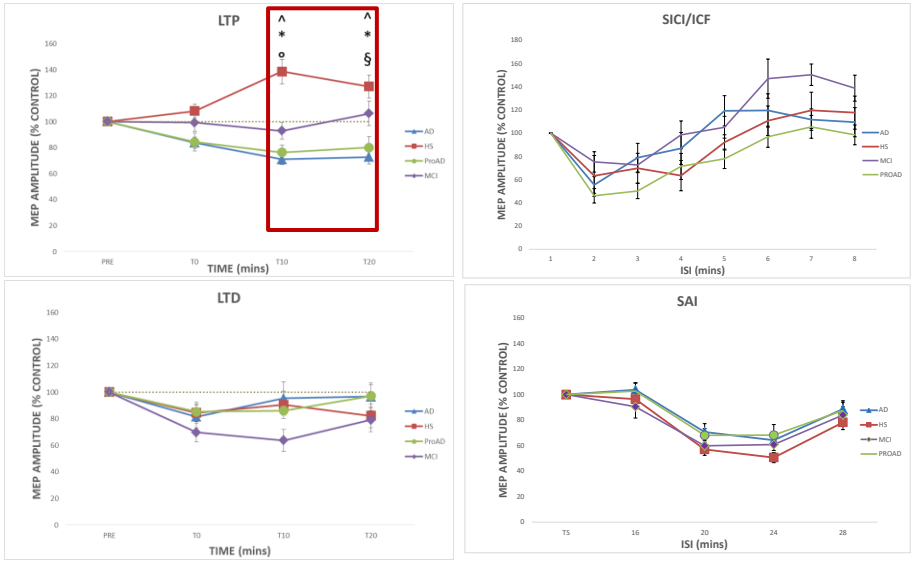
24 PROAD patients

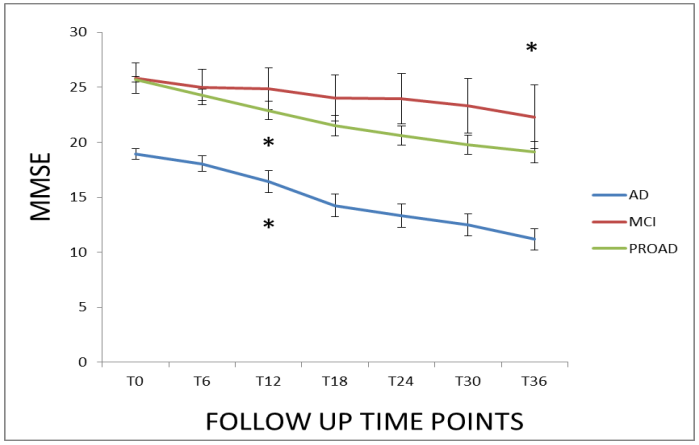
28 ADD patients

TMS EVALUATION
LTP/LTD
SAI
SICI/ICF

MMSE

Baseline **6 months** **12 months** **18 months** **24 months** **30 months** **36 months**





ADD and PROAD patients progressed faster than MCI patients

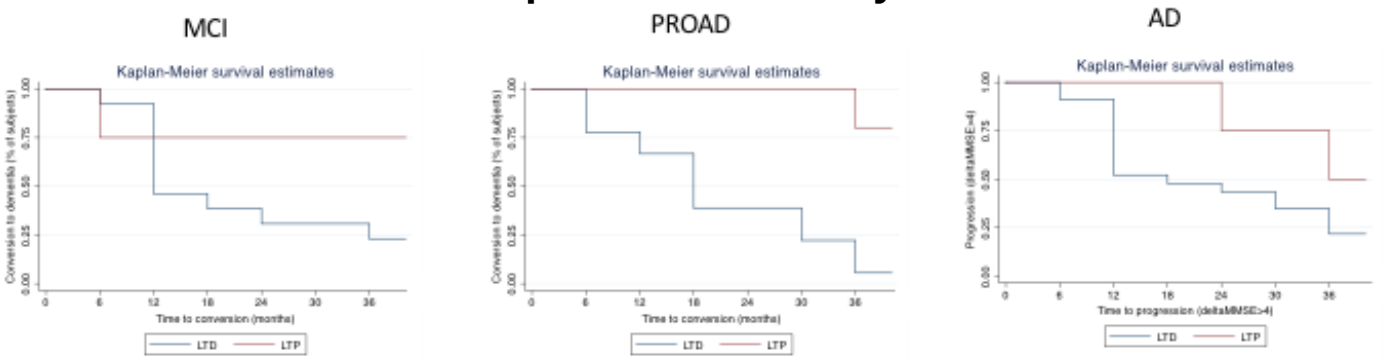
Conversion rate to dementia in PROAD and MCI

79.1% (19 patients on 24) of PROAD patients and

57,1% (11 patients on 21) of MCI patients converted to a state of dementia.

LTP impairment differences converters from non converters in both groups

Kaplan Meier Analisys



In each group (ADD, PROAD, and MCI) the patients who exhibited an impaired LTP plasticity had a more aggressive clinical course (log-rank test, **p < 0.001**)

- Our neurophisiological evaluation is in line with the new classification of AD. **ADD and PROAD showed the same alterations typical of AD, consisting in an impairment of LTP mechanisms**. MCI patients instead showed «half-way» neurophysiological characteristics between HS and AD patients.

- The follow up analysis allowed us to identify the characteristic of PROAD and MCI patients who converted to a state of dementia: **the common point in both groups for converters againts non converters was the impairment of LTP mechanisms**

- **LTP impairment appears as a key element in driving cognitive impairment** and especially **clinical progression** in all the patients complaining memory impairment **apart from evidence of AD pathology biomarkers**

- Our result suggest that **LTP evaluation** can be an useful in **clinical setting** not just as **pathophisiologycal biomarker of the disease** but also a **biomarker of clinical progression in all patients complaining cognitive impairment**

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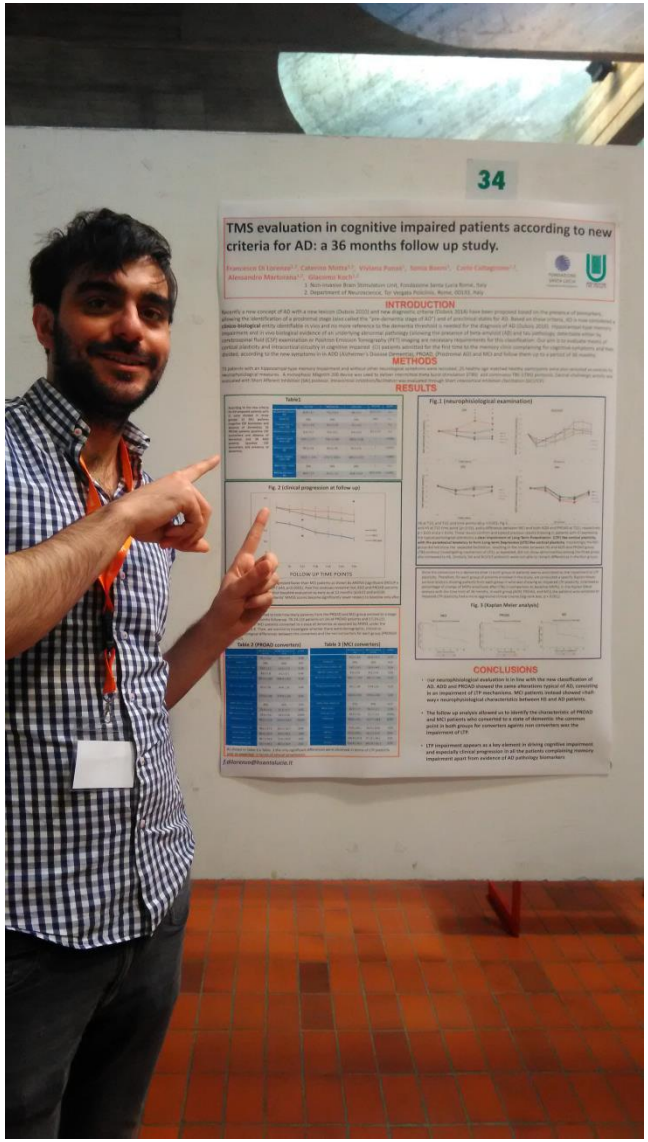

Thanks for your attention

For further discussion come to Poster n° 34