



XVII Convegno

I CENTRI PER I DISTURBI COGNITIVI E LE DEMENZE E LA GESTIONE INTEGRATA DELLA DEMENZA

Contributo dei biomarcatori nel processo diagnostico di MCI e demenza tra pratica clinica e ricerca

Giovanna Zamboni

13. Considerare l'uso di ulteriori test diagnostici solo nel caso in cui:

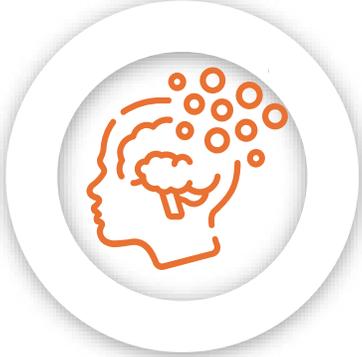
- siano di supporto alla diagnosi del sottotipo e
- la conoscenza della sottocategoria diagnostica modifichi la gestione.

(DEBOLE POSITIVA)

29. Non offrire biomarcatori per la diagnosi e diagnosi differenziale di MCI. **(FORTE NEGATIVA)**

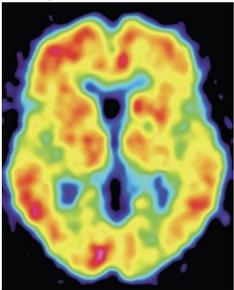


Diagnosi differenziale

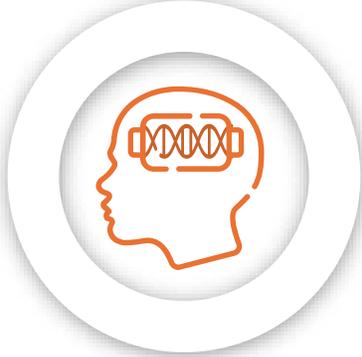


A

amyloid-PET

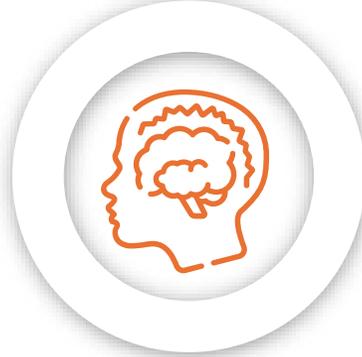


CSF $A\beta_{42/40}$



T

CSF p-tau

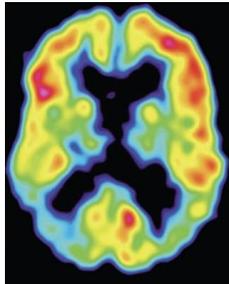


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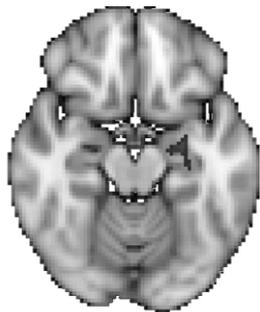
CSF t-tau



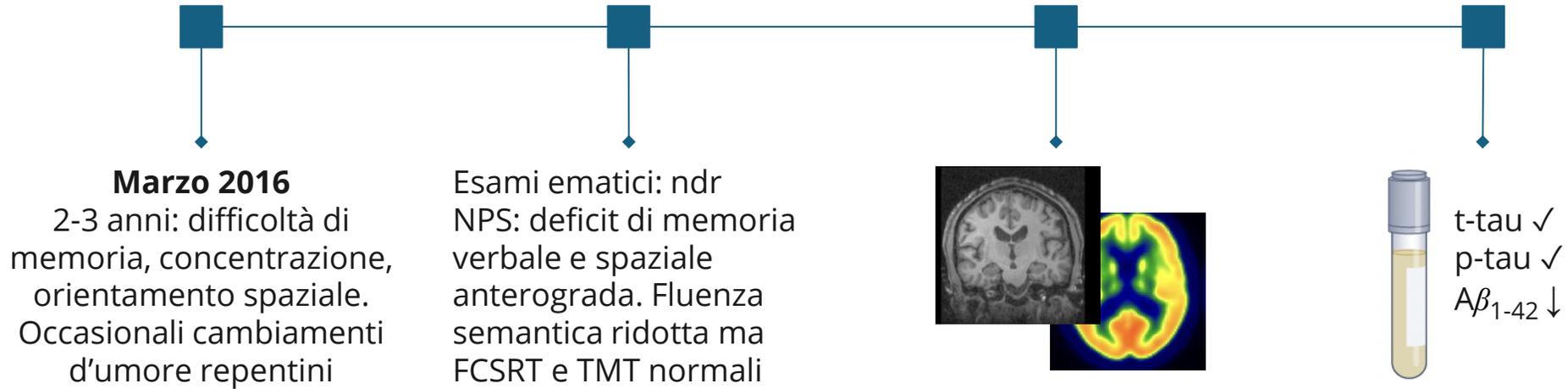
FDG-PET



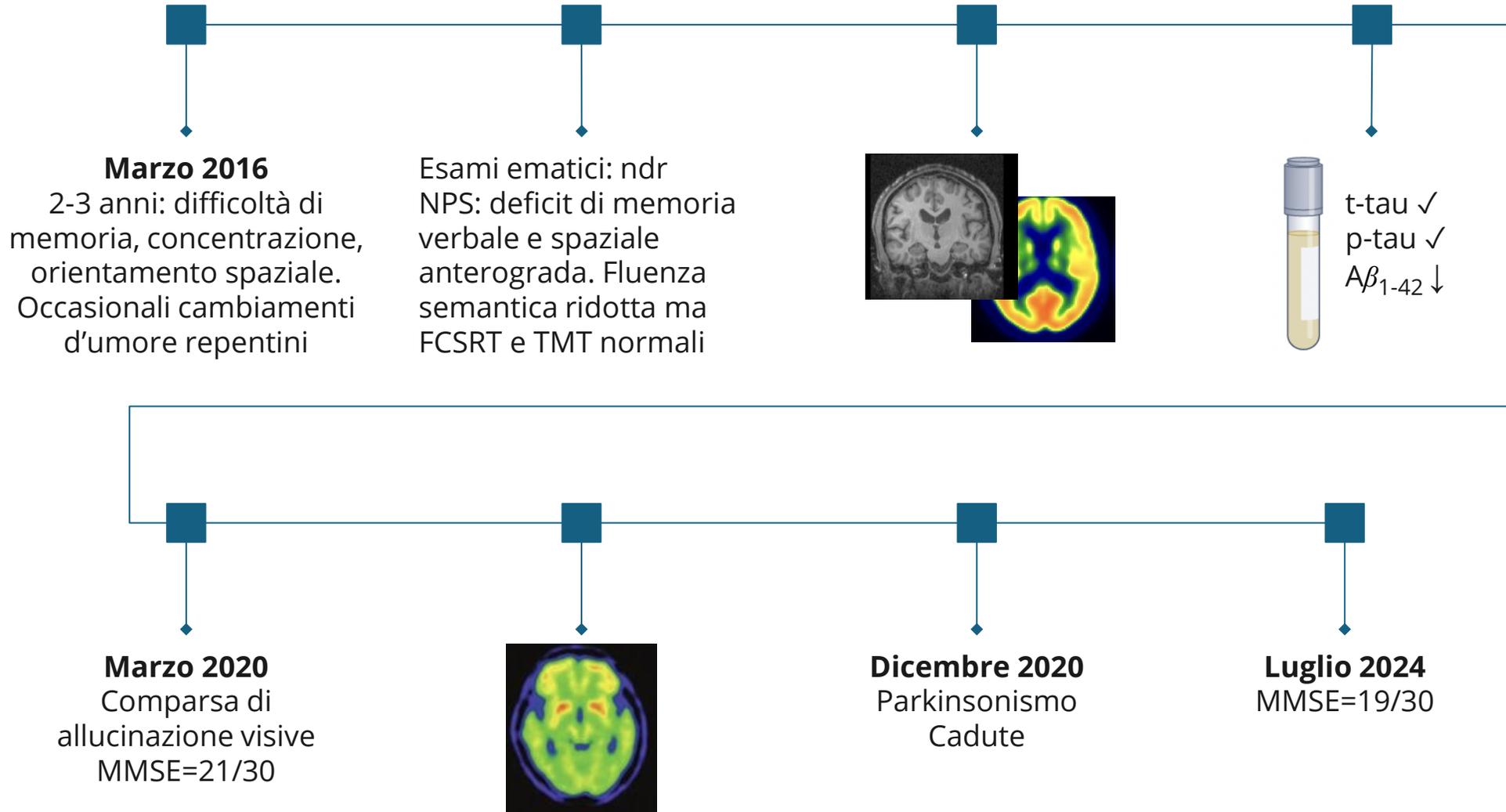
MRI



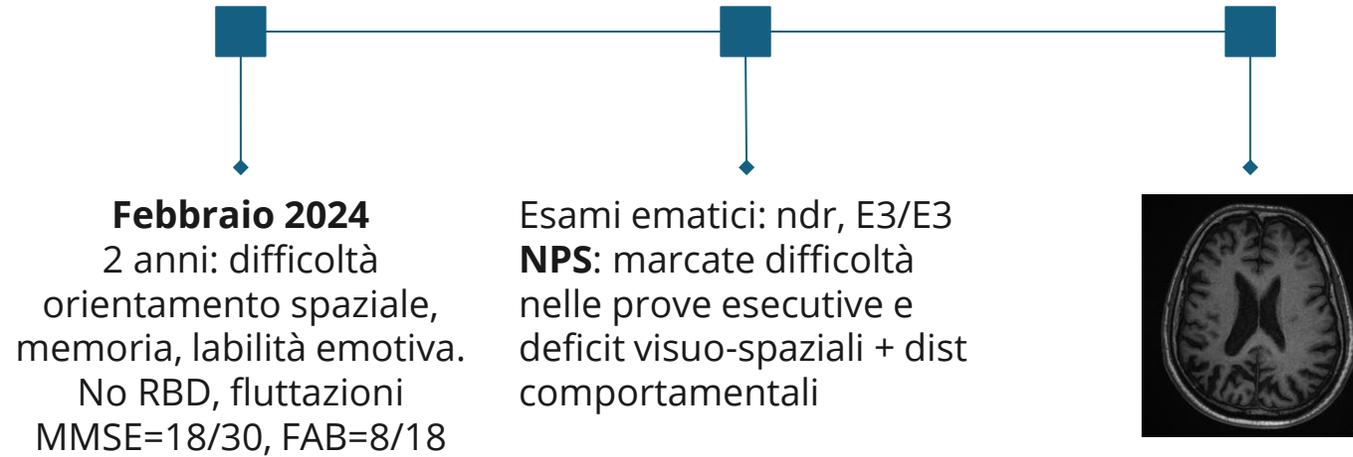
BD, 63 ♂



BD, 63 ♂



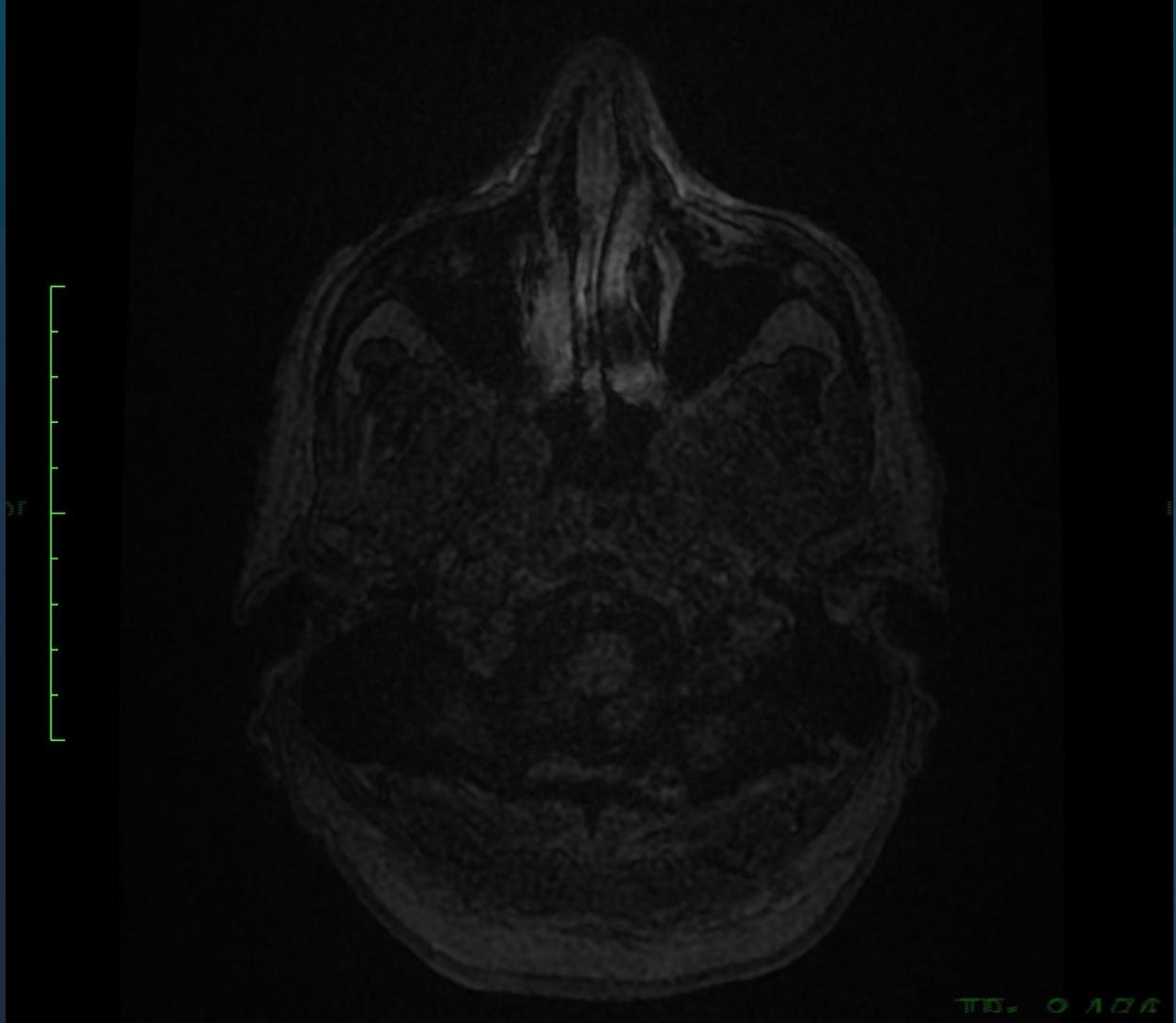
MR, ♂73



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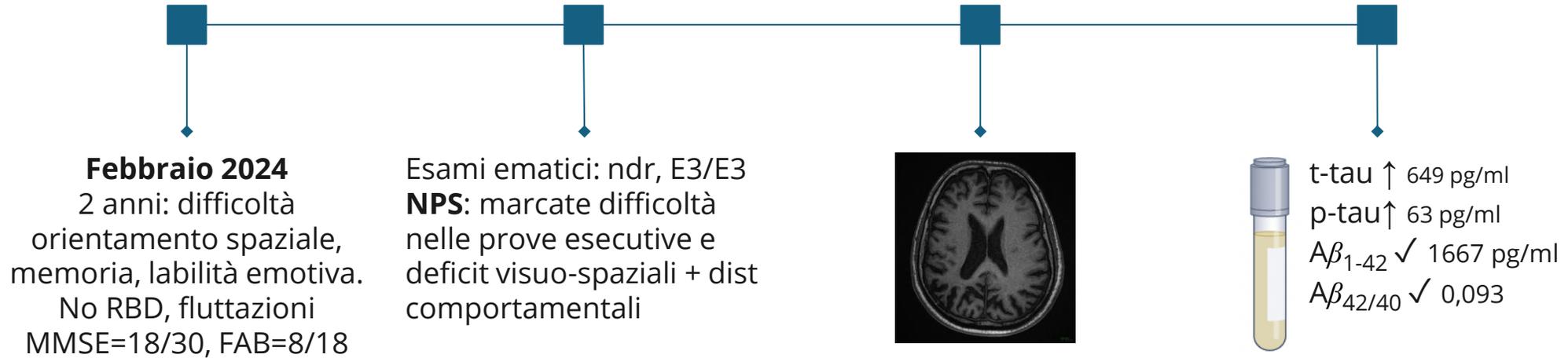
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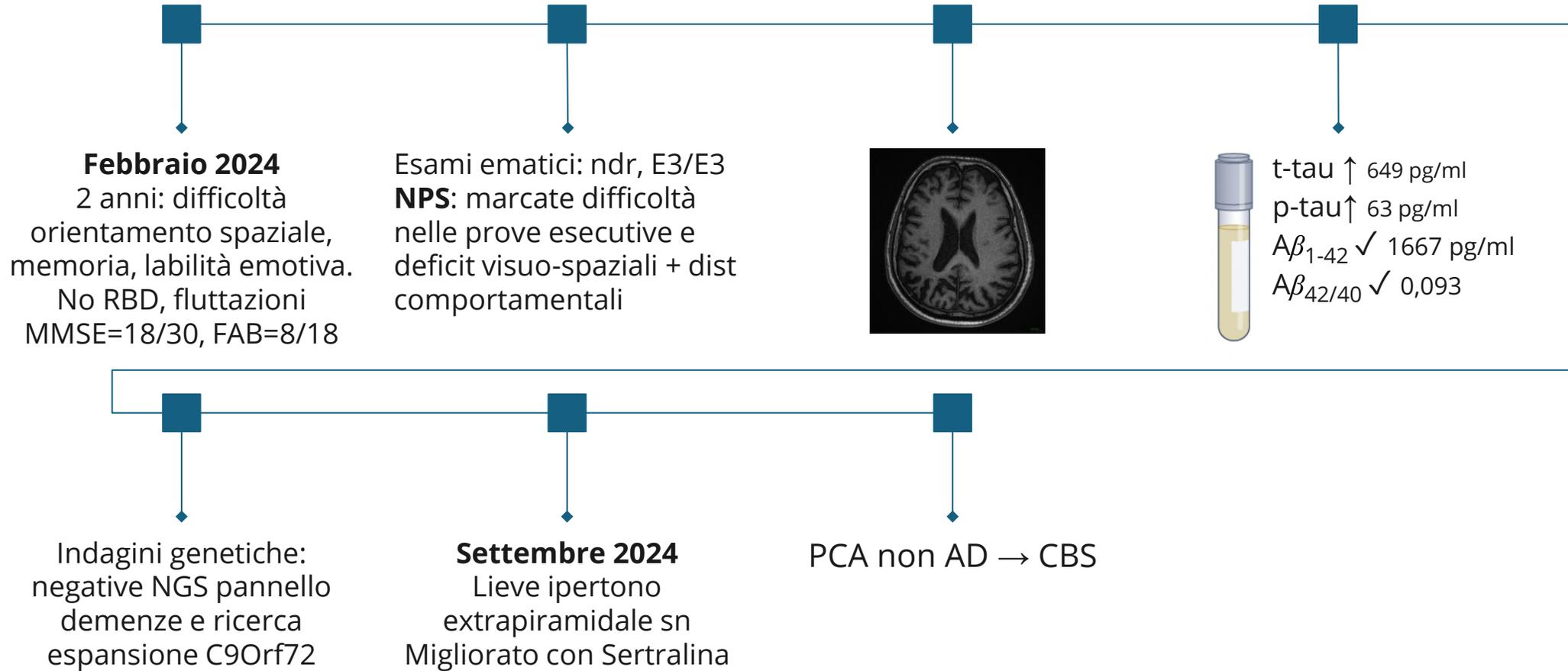
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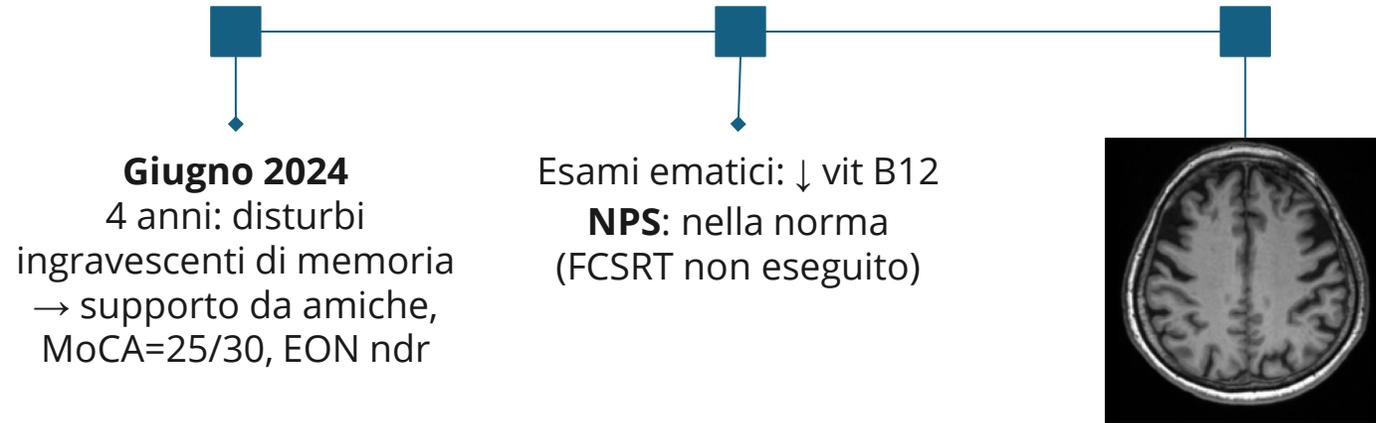
MR, ♂73



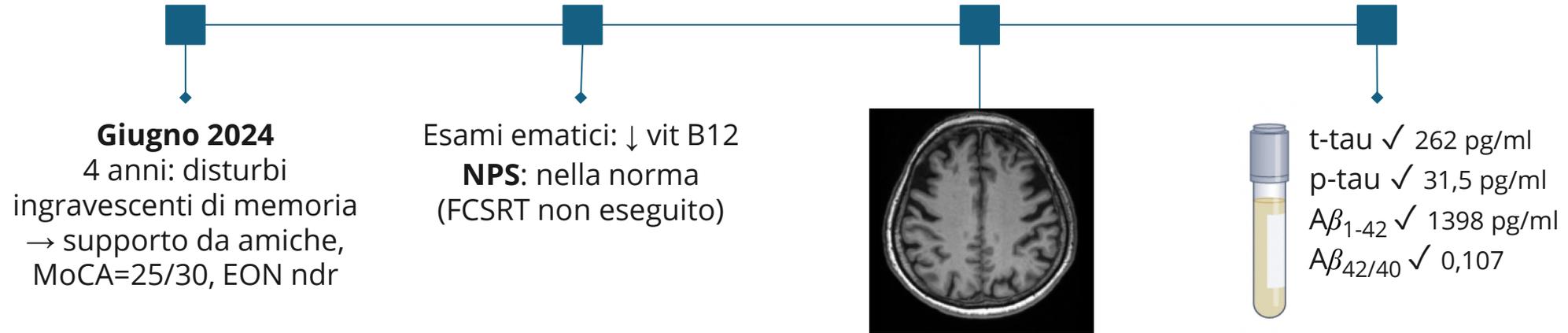
MR, ♂73



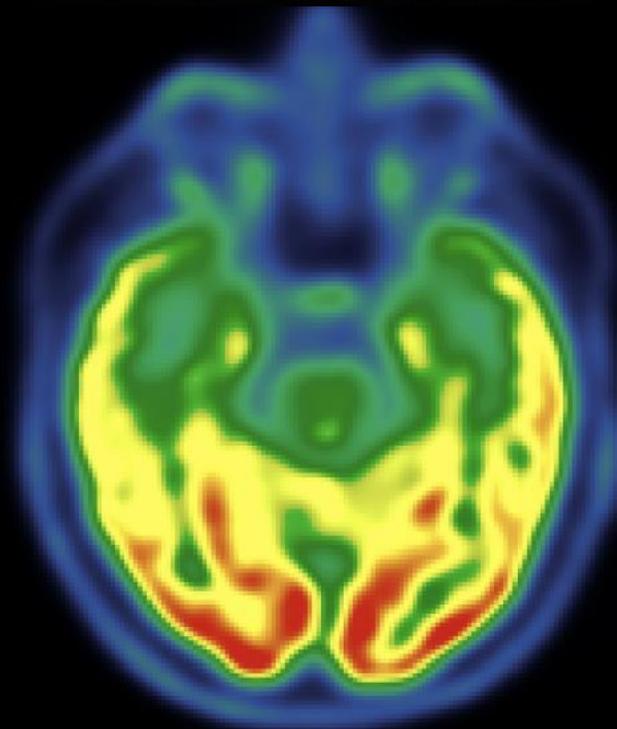
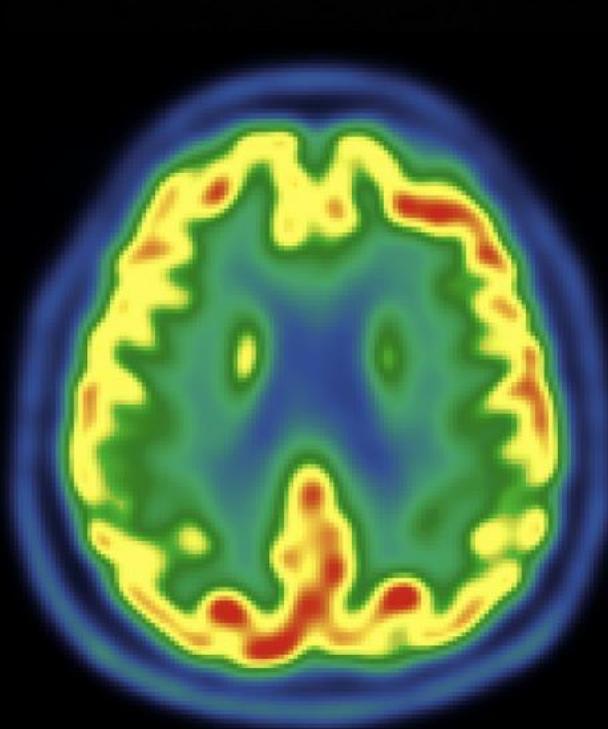
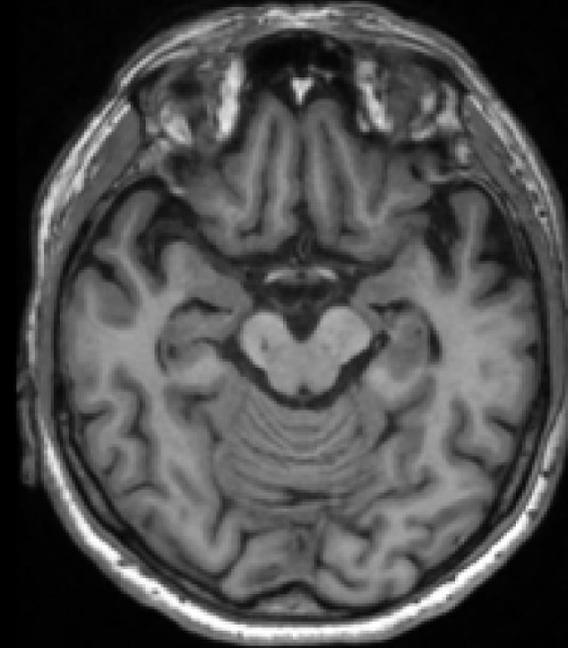
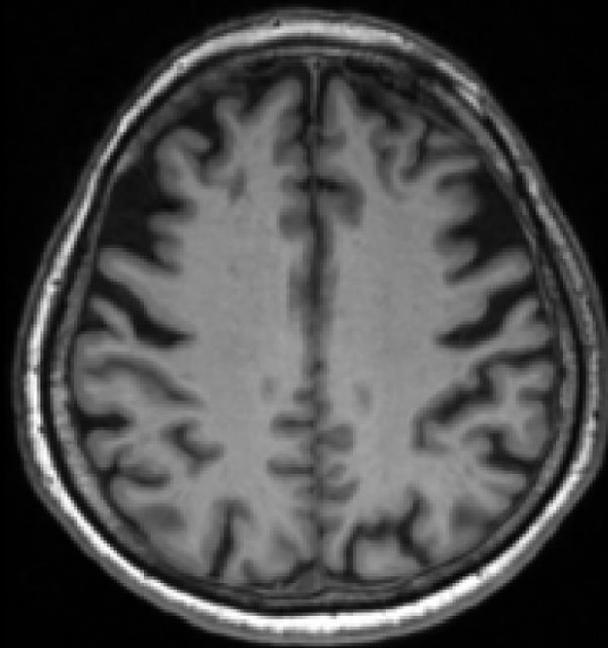
SE, ♀6



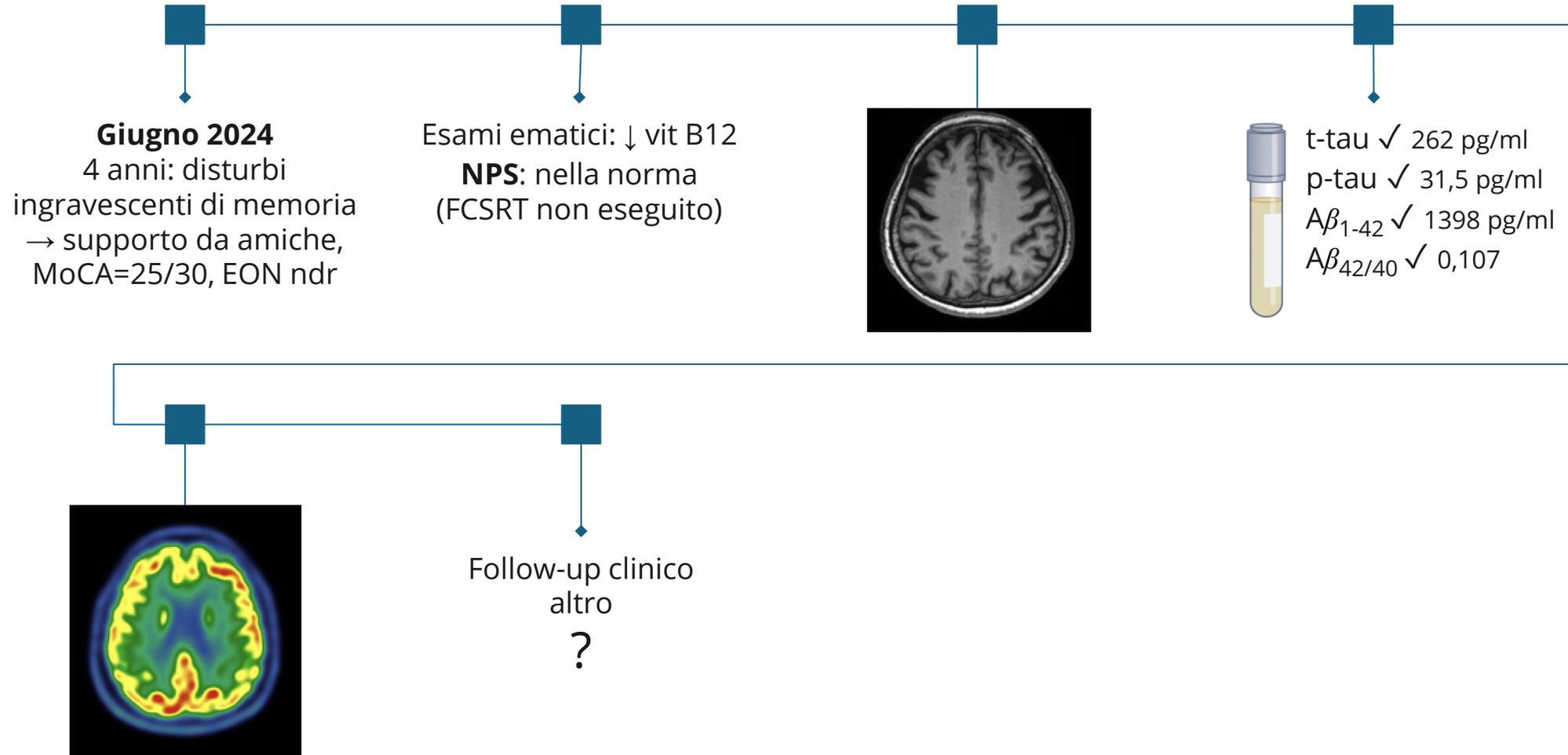
SE, ♀6



SE, ♀6

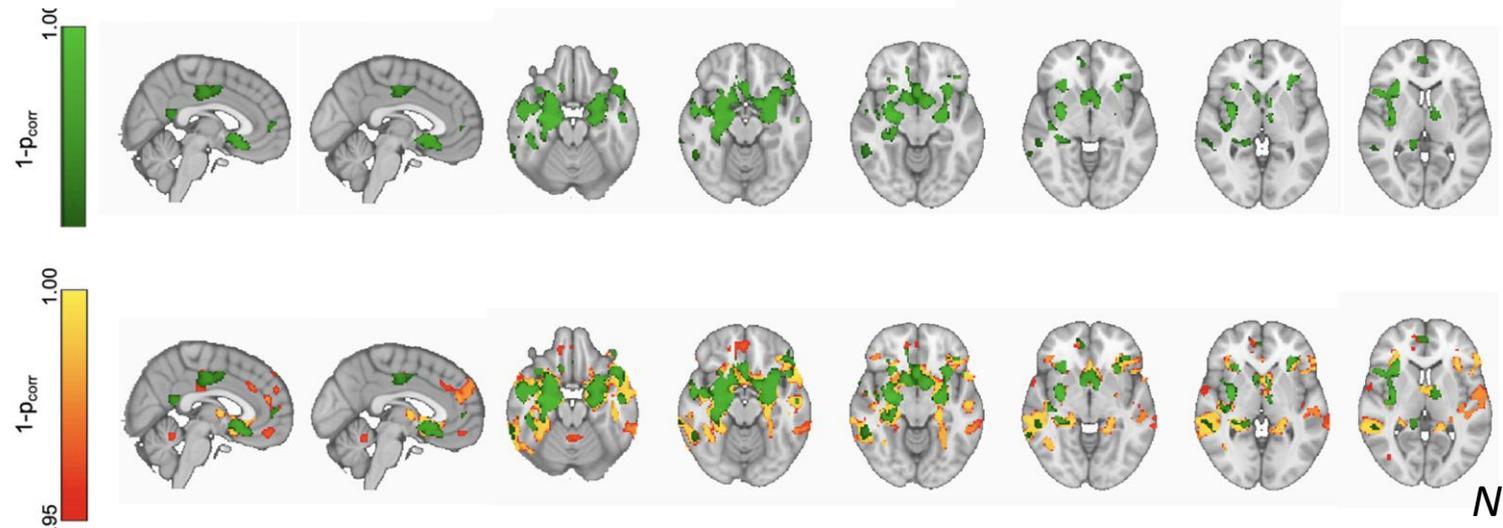
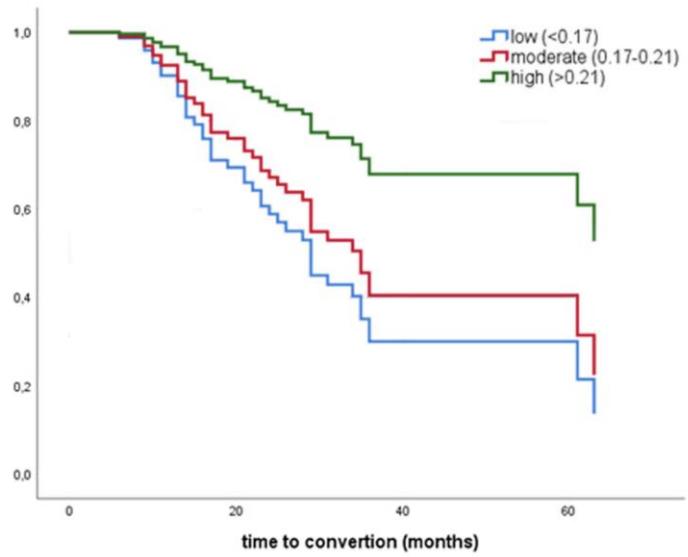
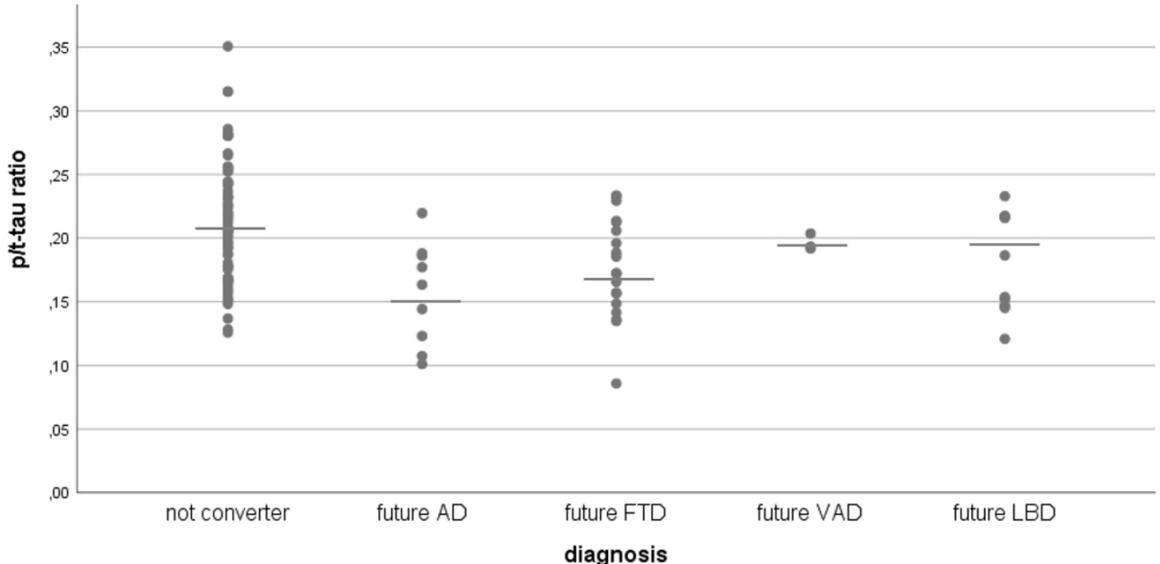


SE, ♀6

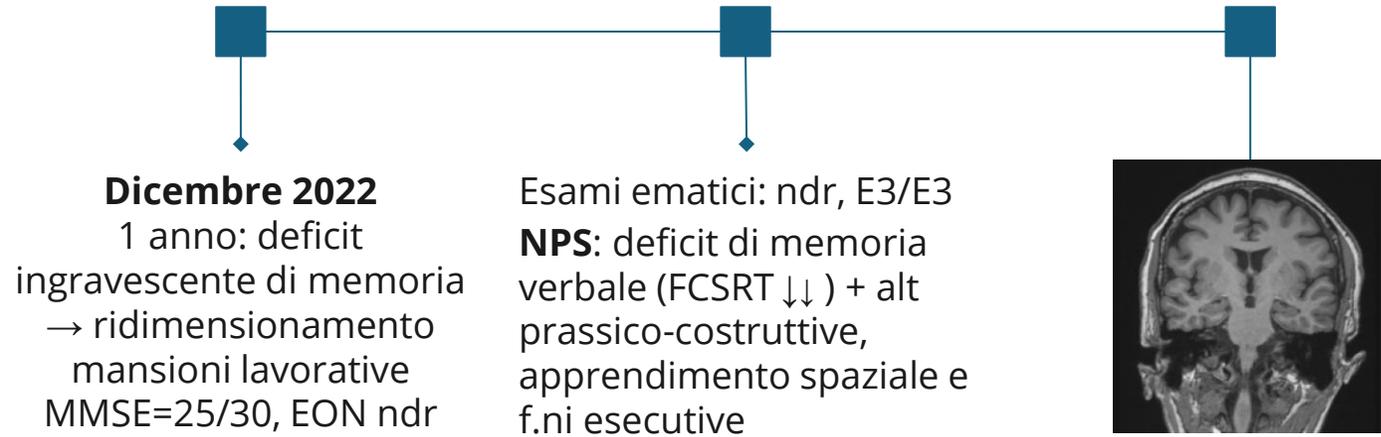


Predictive value of phospho-tau/total-tau ratio in amyloid-negative Mild Cognitive Impairment

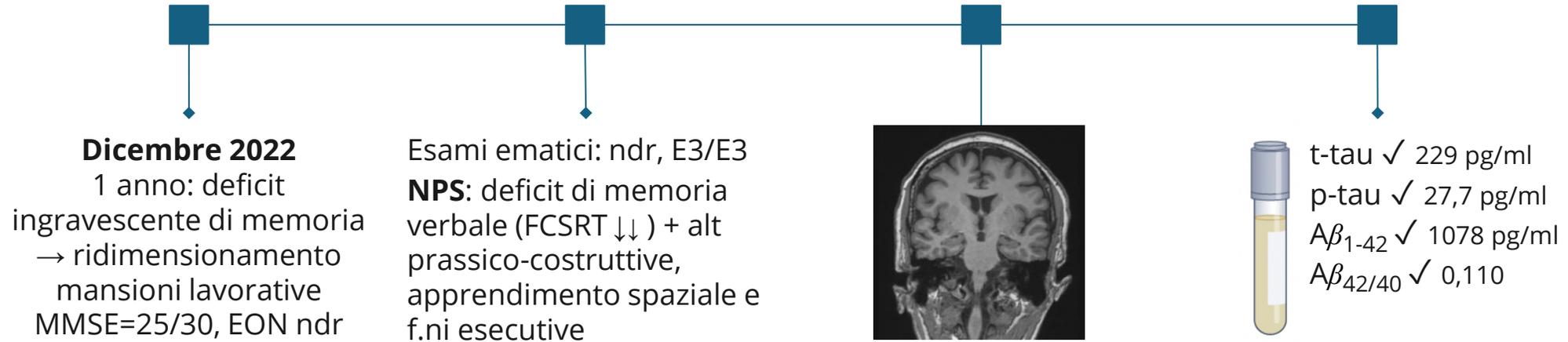
Manuela Tondelli^{a,b}, Simone Salemmè^{a,b}, Giulia Vinceti^{a,b,c}, Roberta Bedin^{a,b}, Tommaso Trenti^d, Maria Angela Molinari^c, Annalisa Chiari^c, Giovanna Zamboni^{a,b,c,e,*}



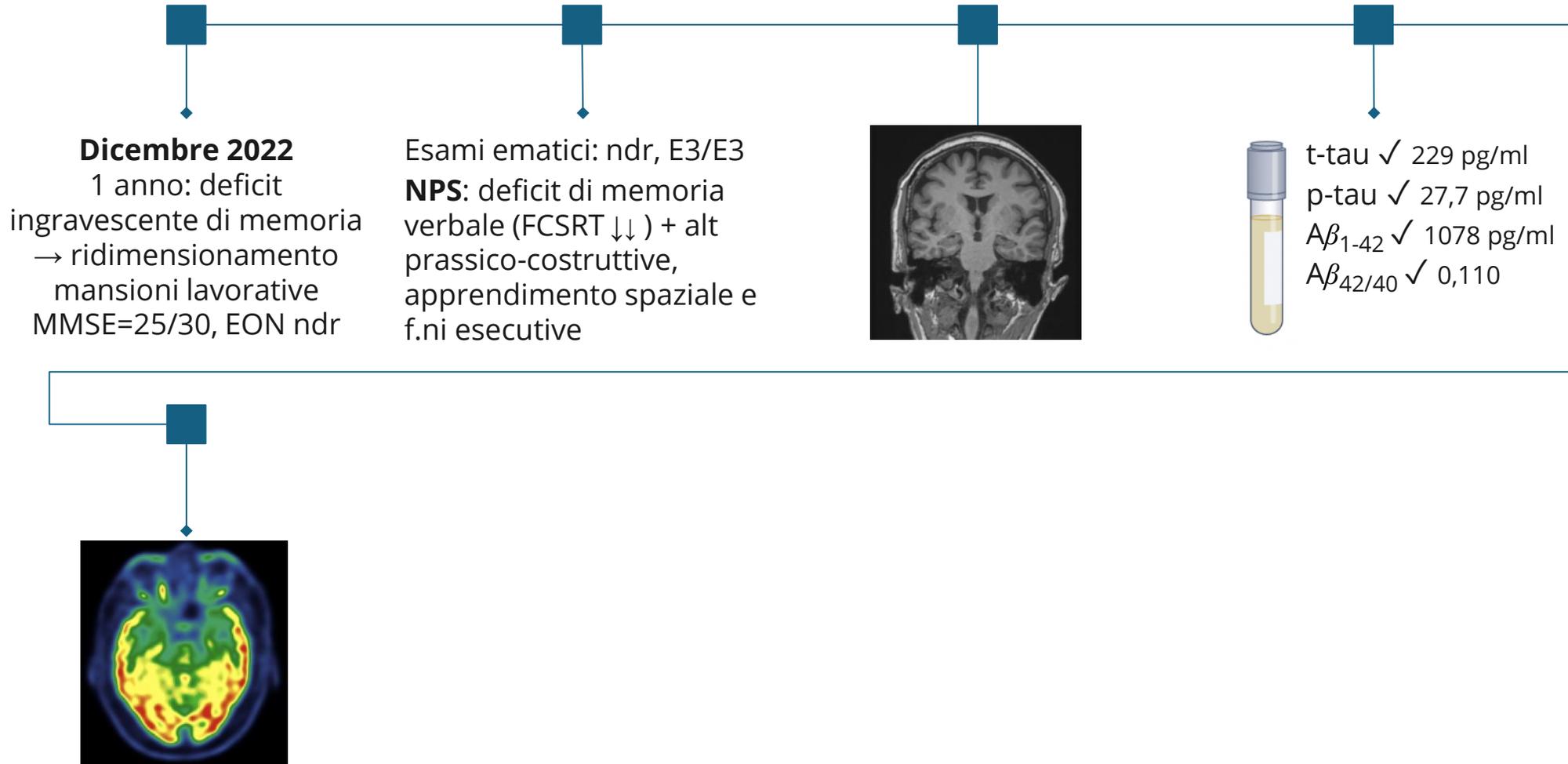
PW, ♀ (;)



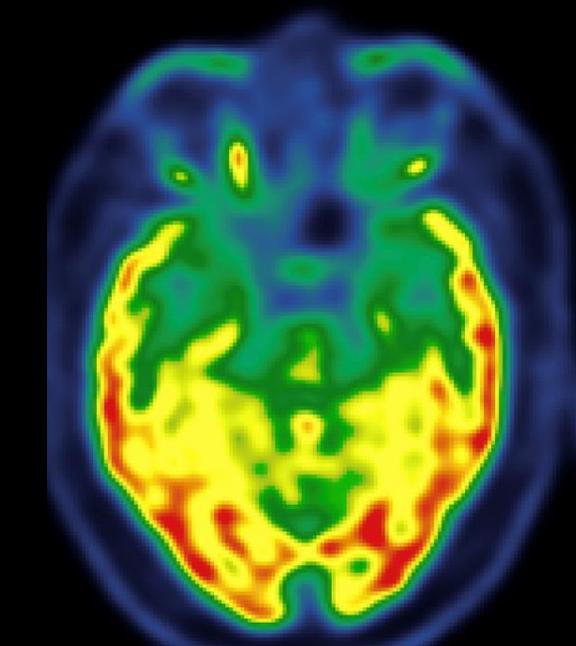
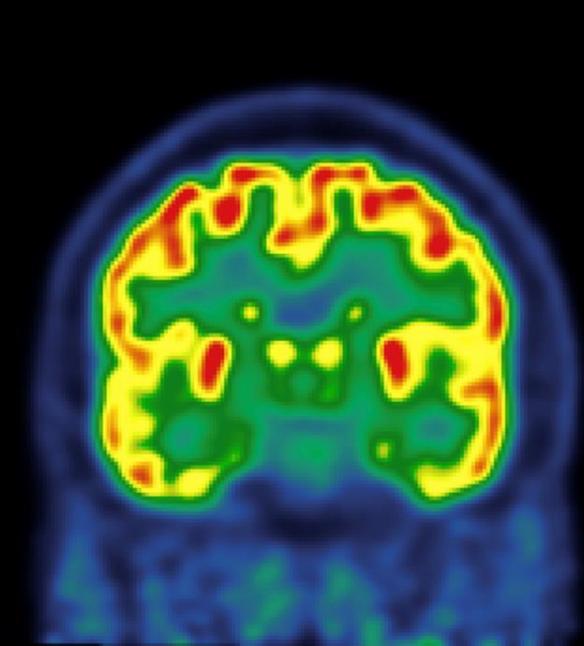
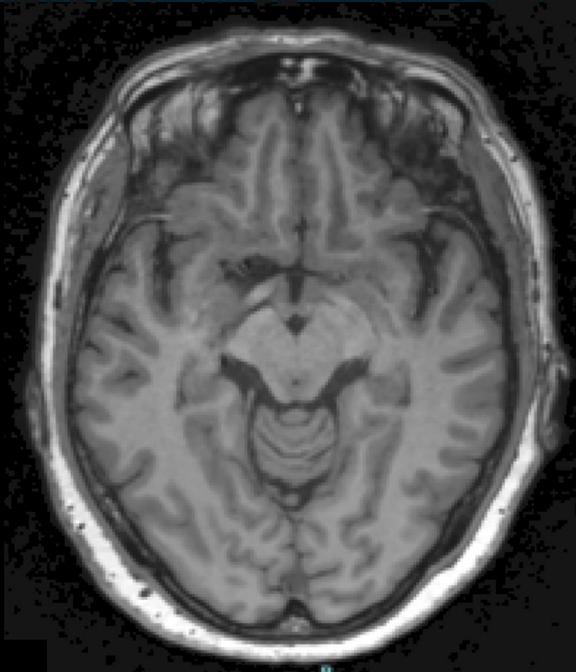
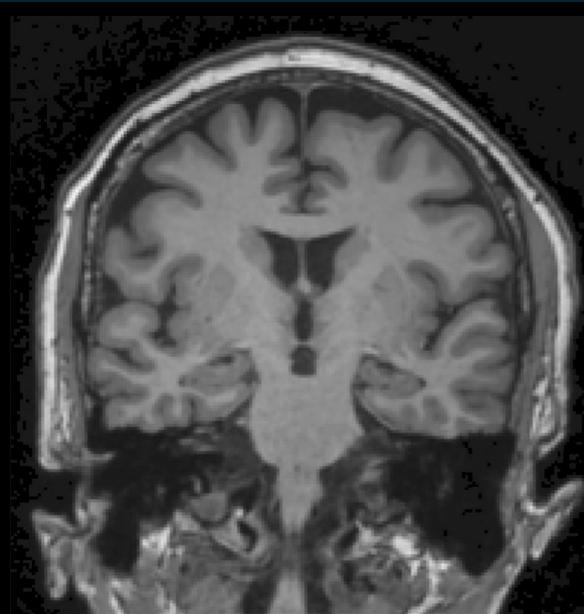
PW, ♀ ()



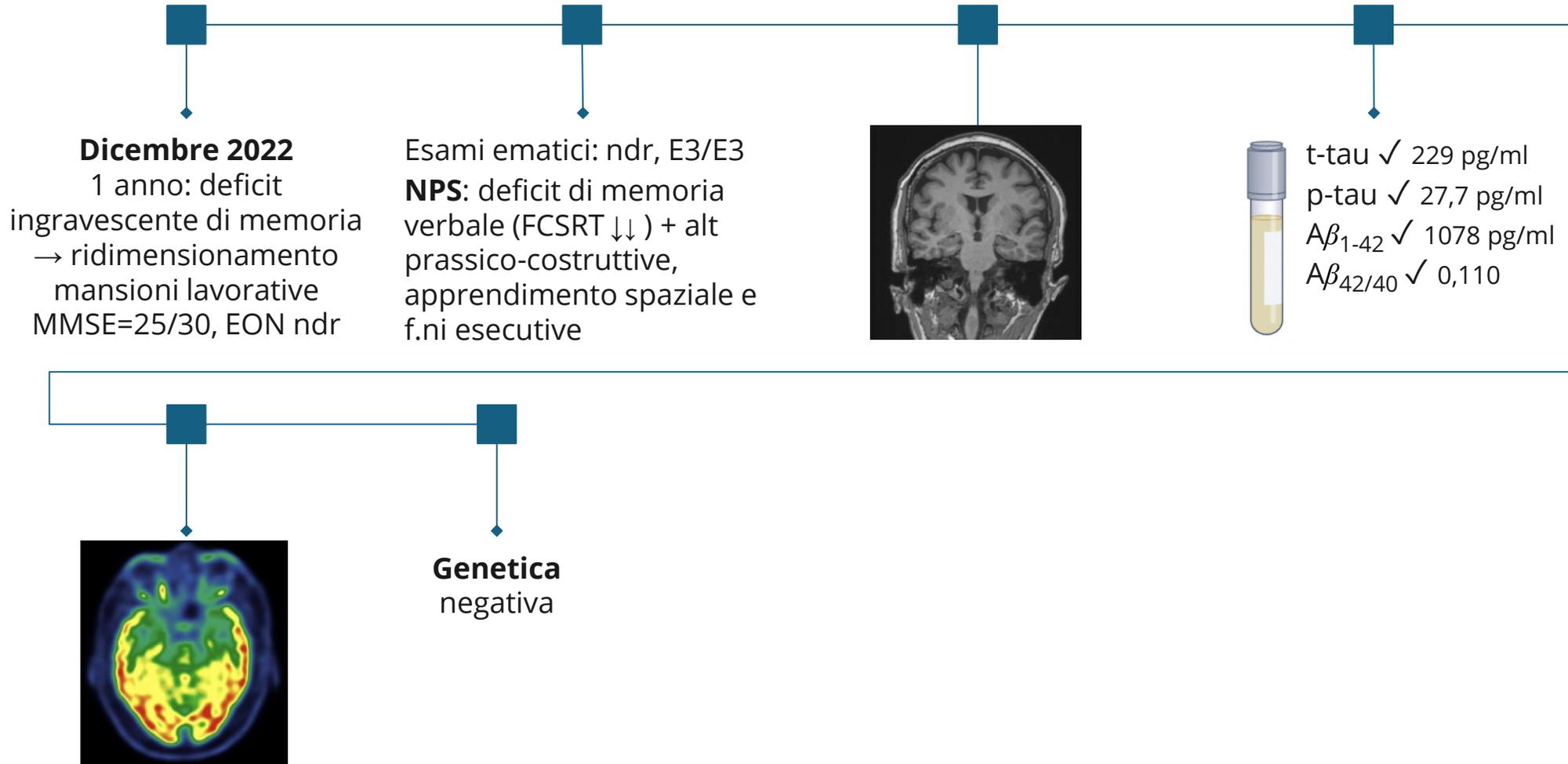
PW, ♀ ()



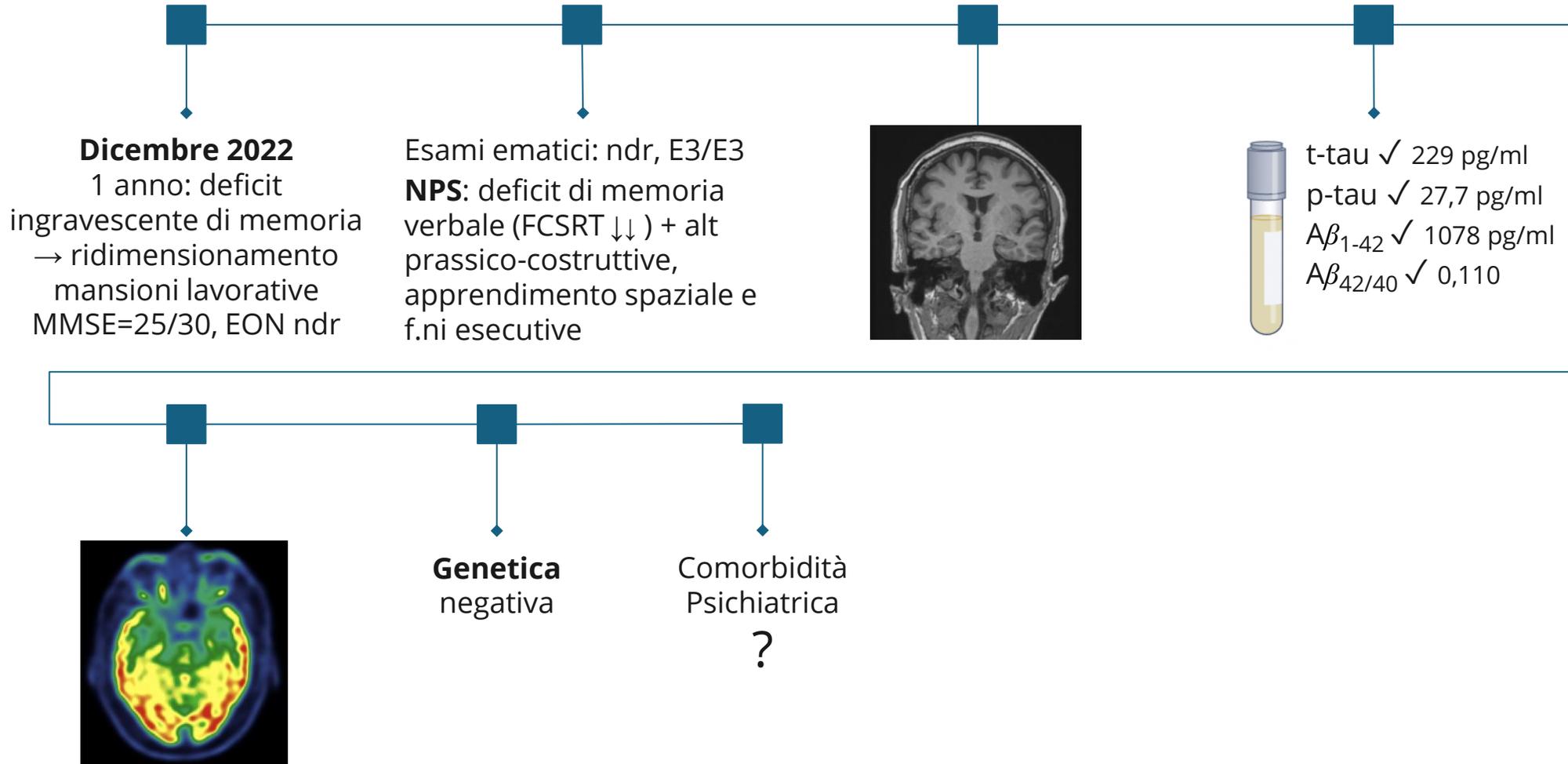
PW, ♀65



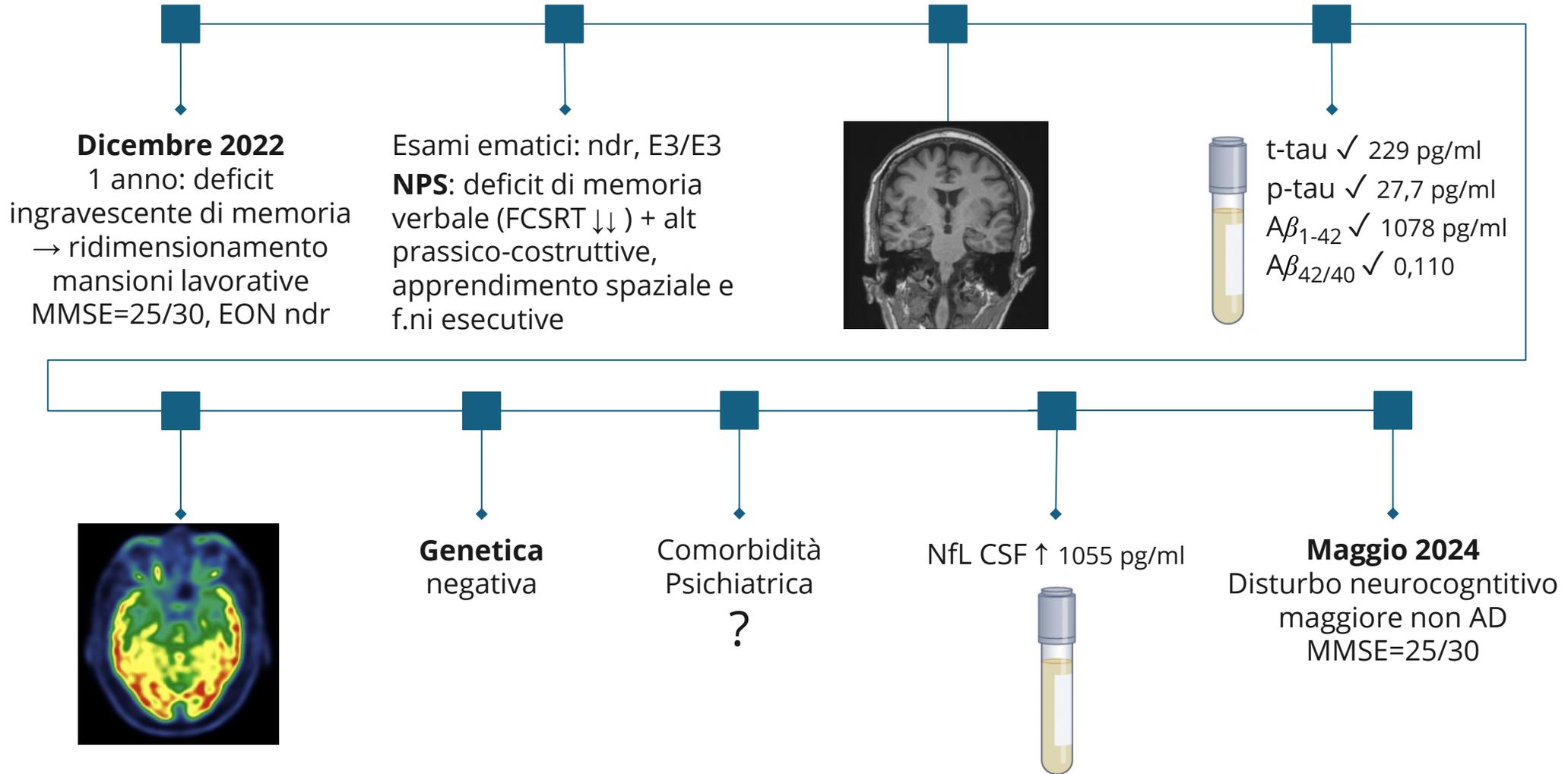
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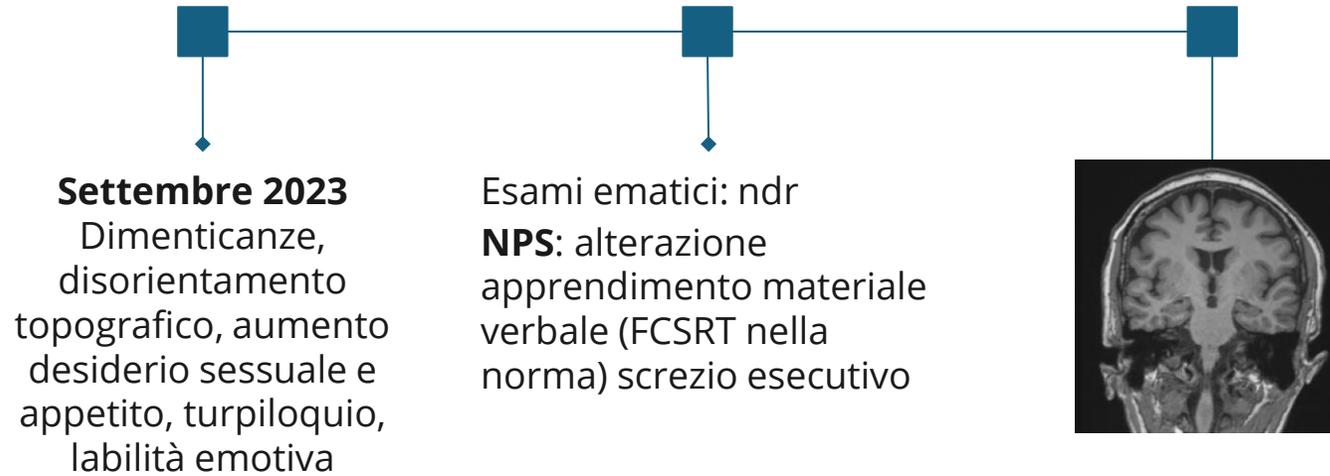
PW, ♀ ()



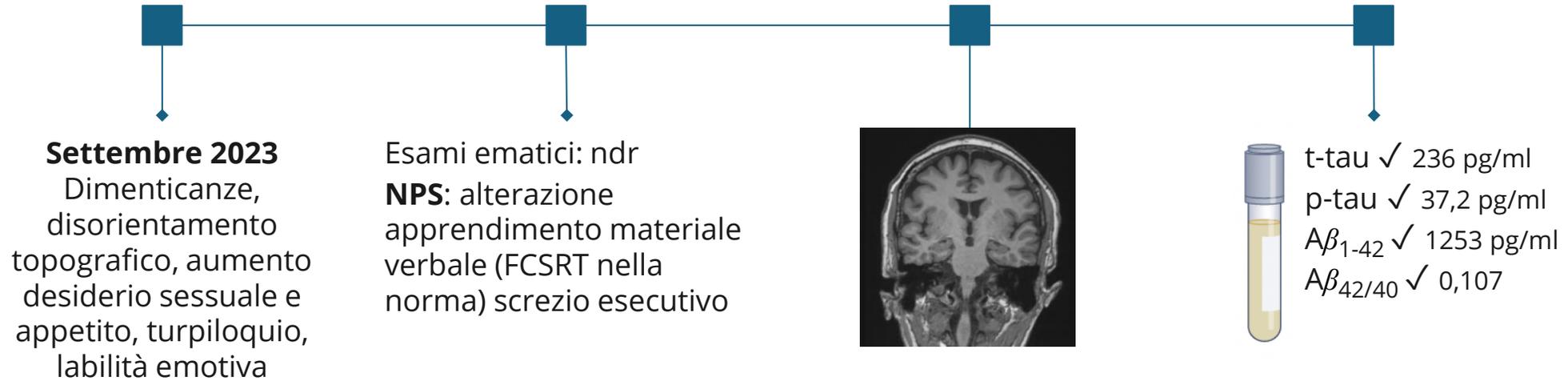
PW, ♀ (;



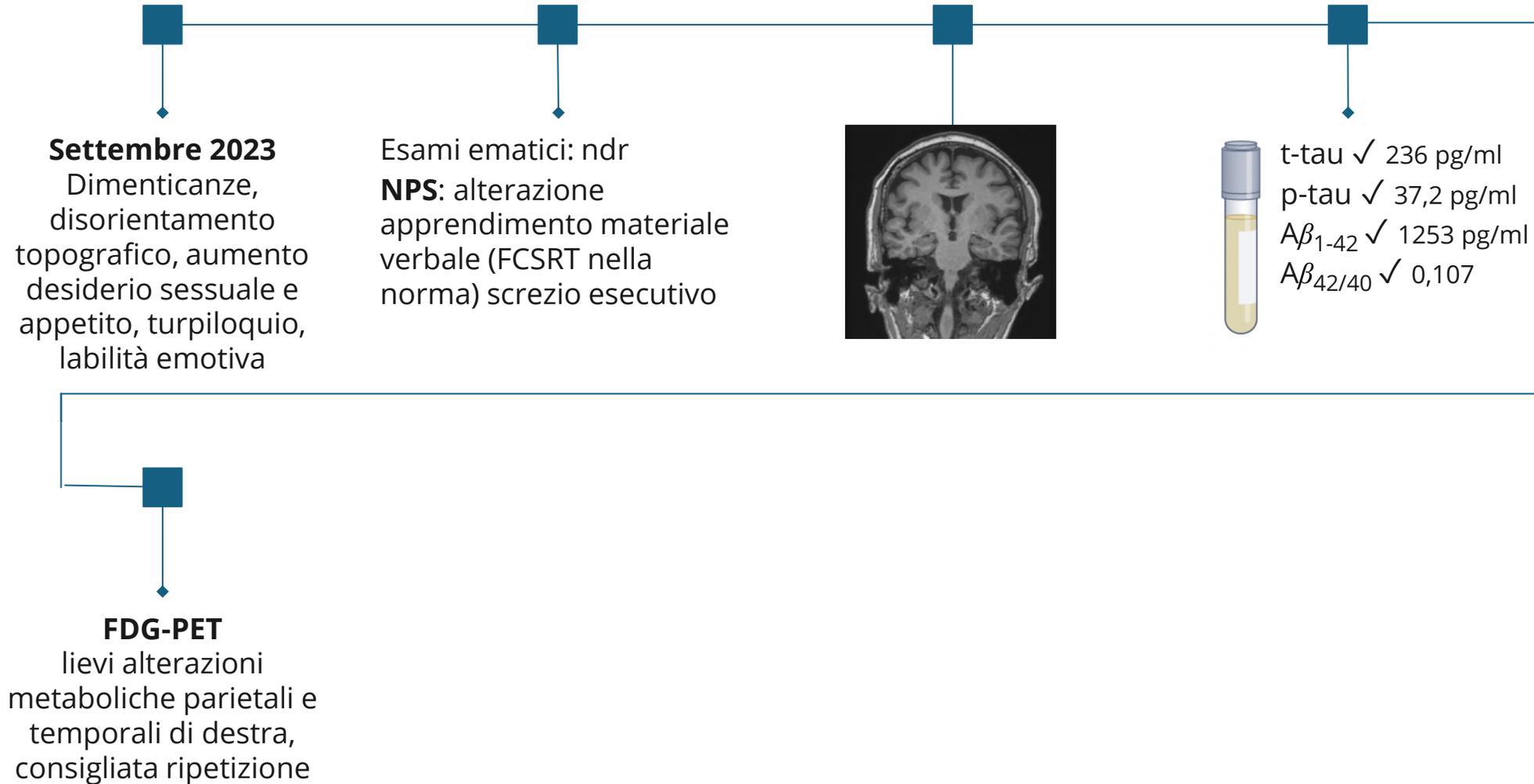
BG, 55



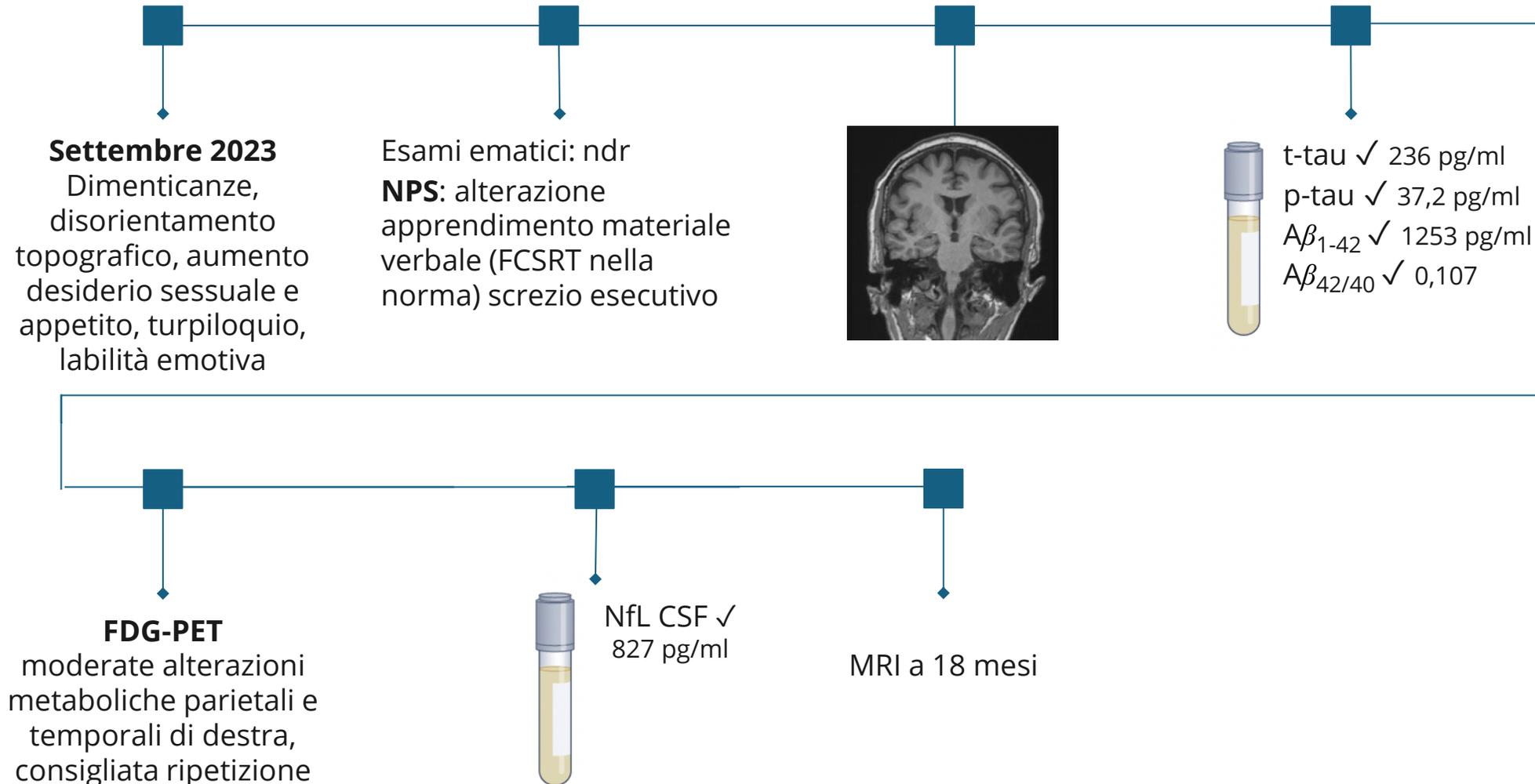
BG, 55



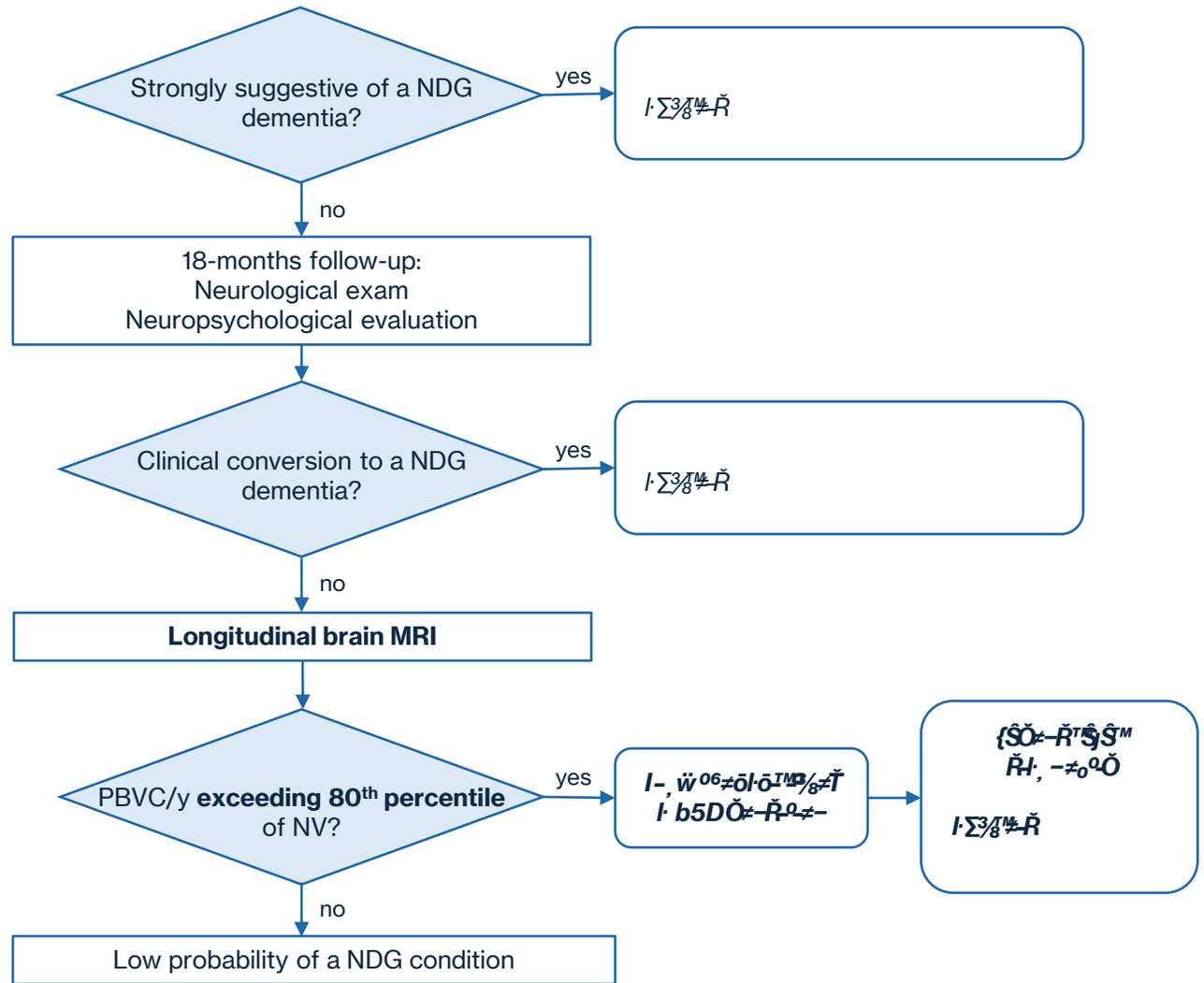
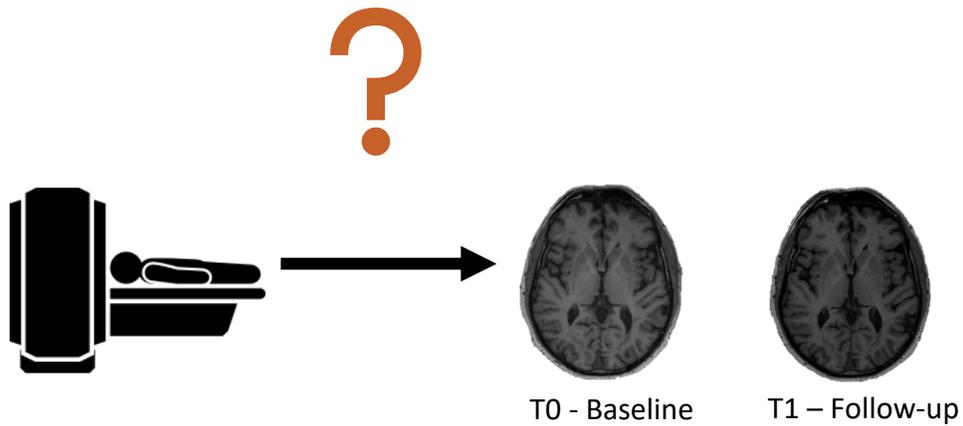
BG, 55

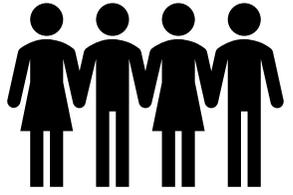


BG, 55



Subtle/subjective cognitive or behavioural complaints





- Dysexecutive profile
- Personality and behavioral changes



bvFTD/PPD/phFTD

Longitudinal MRI



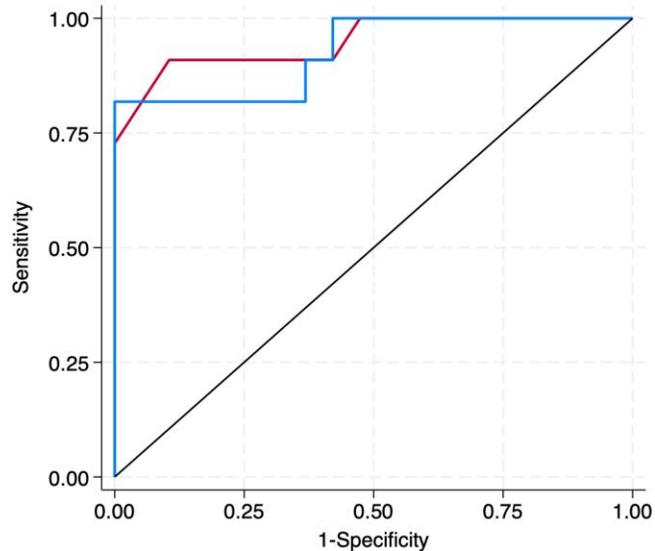
T0 - Baseline T1 - 18 months

Percentage of brain volume change (PBVC/y)

Progressive
Above 95th percentile

cut-off **21.5 pg/ml serum NfLs**
cut-off **972 pg/ml CSF NfLs**

Non-Progressive
Below 95th percentile

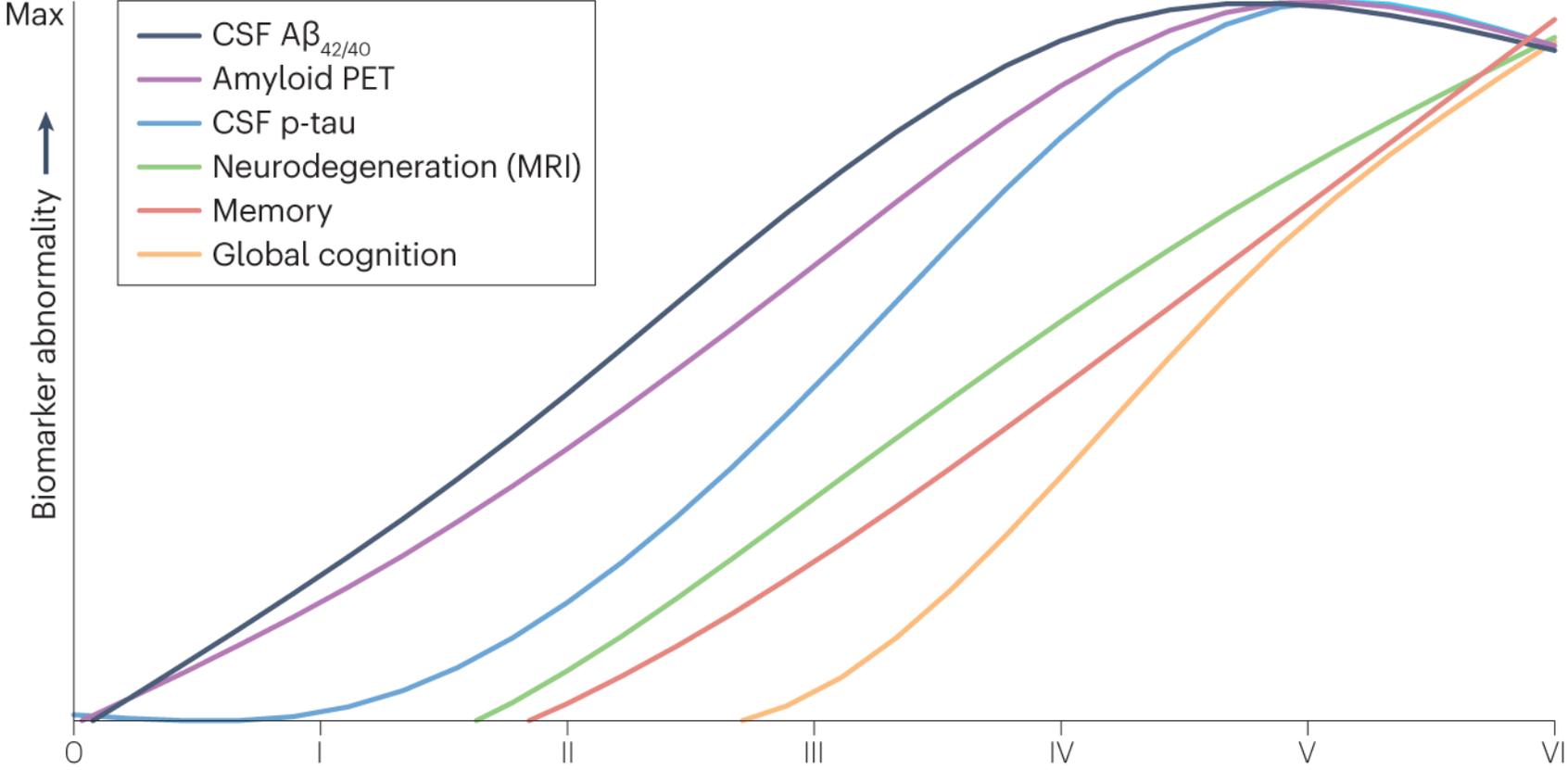


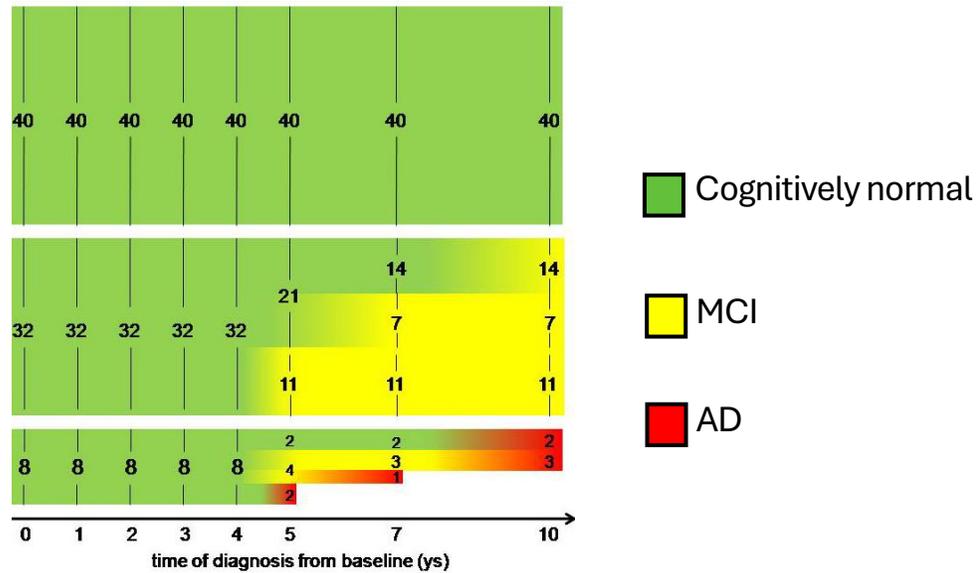
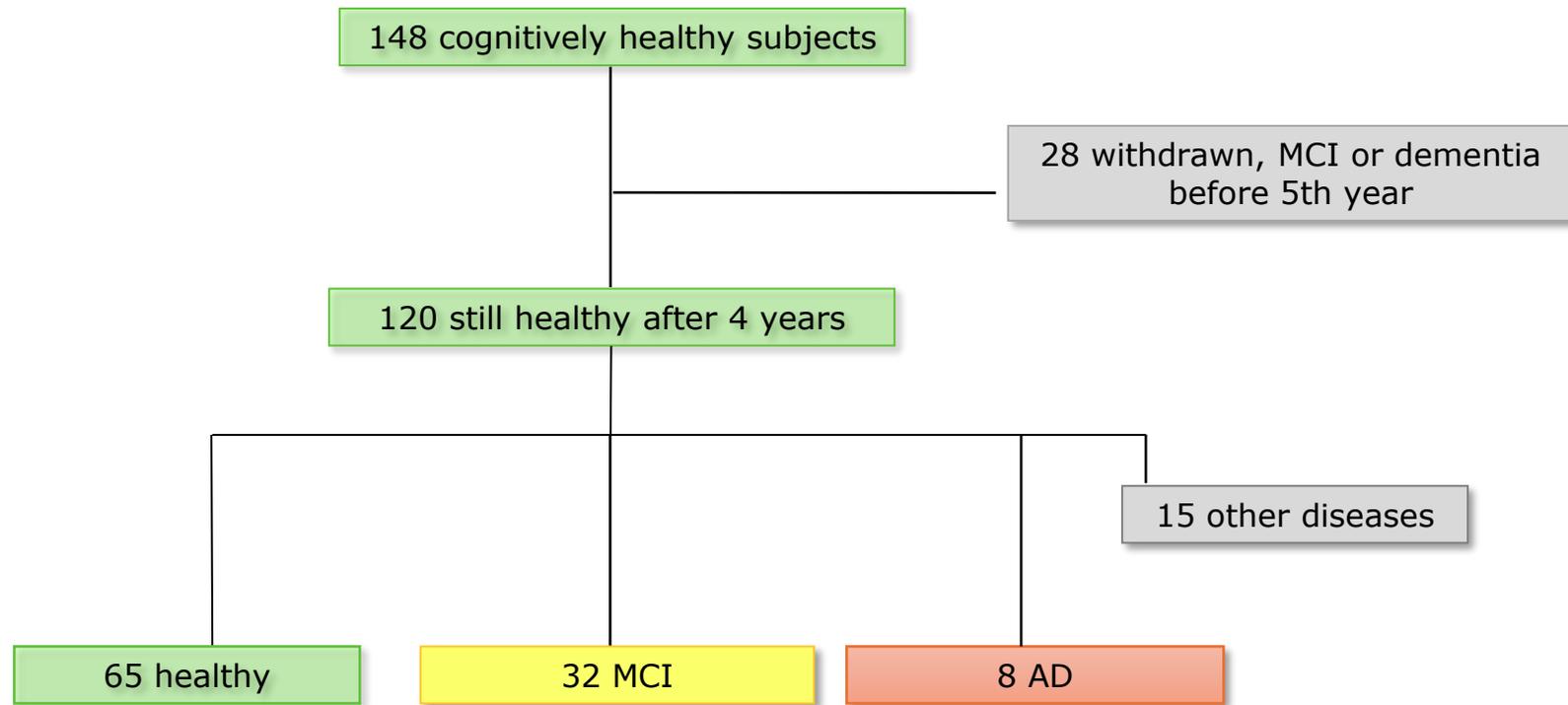
— Serum NfL AUC: 0.949
— CSF NfL AUC: 0.928
— Reference

• **Serum NfLs:** 81.82% sensitivity and 94.74% specificity (AUC = .949)

• **CSF NfLs:** 81.82% sensitivity and 100% specificity (AUC = .928)

Ruolo prognostico

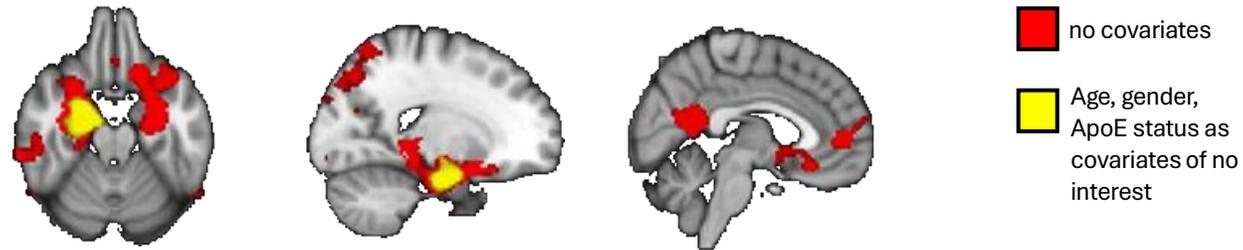




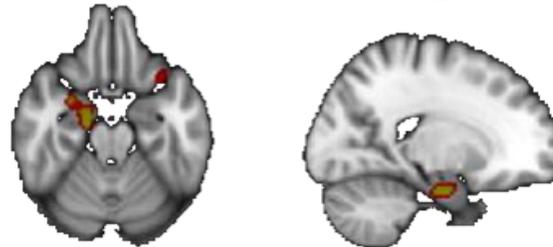
Structural MRI changes detectable up to ten years before clinical Alzheimer's disease

Manuela Tondelli^a, Gordon K. Wilcock^b, Paolo Nichelli^a, Celeste A. De Jager^b,
Mark Jenkinson^c, Giovanna Zamboni^{b,c,*}

Preclinical AD 5-10 years before symptoms < No cognitive decline over 10 years

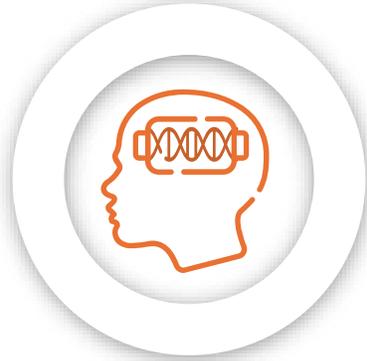
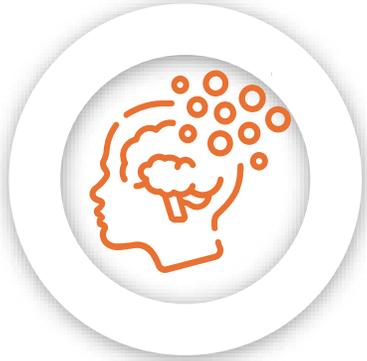


Preclinical AD 7-10 years before symptoms < No cognitive decline over 10 years

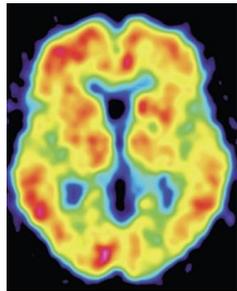


Atrophy is not a late, “downstream” event in AD progression

Il futuro



amyloid-PET



CSF $A\beta_{42/40}$



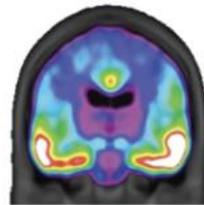
CSF p-tau



CSF p-tau



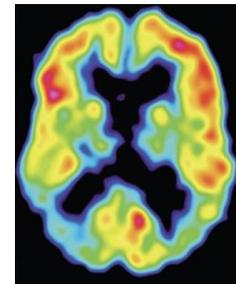
tau-PET



CSF t-tau



FDG-PET



MRI

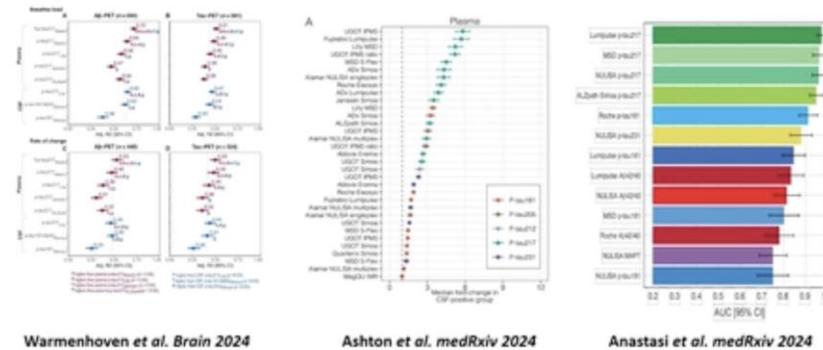


Il futuro è nel plasma

Fra le diverse isoforme di tau, la p-tau217/tau217 è come CSF nel classificare PET A e tau (Barthelemy 2023, 2024)

- Primary care doctor: 61% accurate
- Dementia specialists: 73% accurate
- **High performance BBM test: 91% accurate**

Palmqvist et al. JAMA 2024



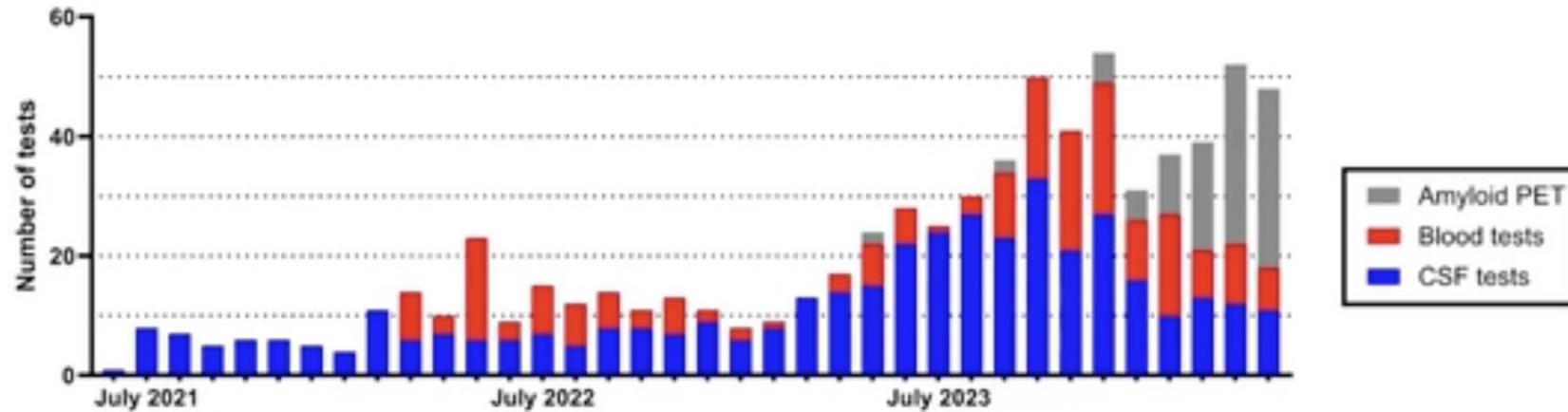
Attenzione ai casi in cui patologia AD non è patologia causa dei sintomi (caso BP)
Attenzione ai casi in cui non c'è patologia AD ma altra causa di demenza

Plasma MTBR-tau275 e MTBR-tau282: CBD, FTLN-MAPT, AD (Horie 2022)

Vescicole plasmatiche extracellulari per TDP-43 e rapporto 3R/4R: FTD e SLA (Chatterjee 2024)

CSF per test di amplificazione alfa-sinucleina

Clinical AD biomarker testing at Washington University Memory Diagnostic Center



Validazione validazione validazione

Performance of Fully-Automated High-Throughput Plasma Biomarker Assays for Alzheimer's Disease in Amnesic Mild Cognitive Impairment Subjects

G.M. Giuffrè¹⁻³, D. Quaranta¹⁻³, M.G. Vita¹, E.M. Costantini¹, S. Citro¹⁻³, C. Carrozza⁴, G. De Ninno⁴, P. Calabresi¹⁻³, C. Marra^{2,3}

Capillary DPS p-tau 217

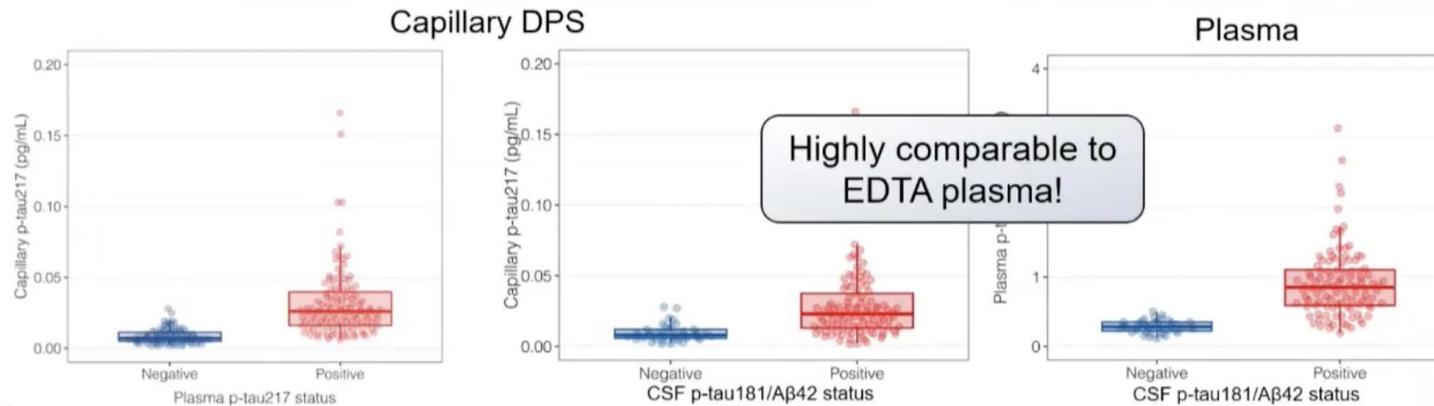
Venous blood sampling requires certain infrastructure and immediate processing

What if there was an even easier method?



Capillary p-tau217 in amyloid positive vs. negative individuals

Capillary DPS p-tau217 levels discriminate A+ vs. A- individuals



Using a binary threshold for plasma p-tau217 positivity:
Fold change: +2.75 or +275% increase
AUC ROC curve: **0.92** (95%CI: 0.89 - 0.96)
n=206

CSF p-tau181/Aβ42 positivity:
Fold change: +2.18 or +218% increase
AUC ROC curve: **0.88** (95%CI: 0.83 - 0.94),
n=151

CSF p-tau181/Aβ42 positivity:
AUC ROC curve: **0.98** (95%CI: 0.97 - 0.98), n=151



21 mm
01:21



GRAZIE

Annalisa Chiari
Manuela Tondelli
Chiara Carbone
Simone Salemme
Chiara Gallingani
Giulia Vinceti
Silvia Cossutti
Najara Iacovino
Davide Salvatori
Riccardo Maramotti
Daniela Ballotta
Roberta Bedin
Teresa Urbano



 SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
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