



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:

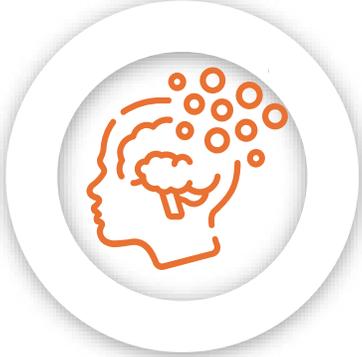
- siano di supporto alla diagnosi del sottotipo e
- la conoscenza della sottocategoria diagnostica modifichi la gestione.

(DEBOLE POSITIVA)

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

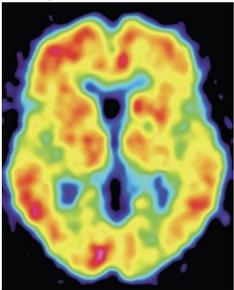


Diagnosi differenziale

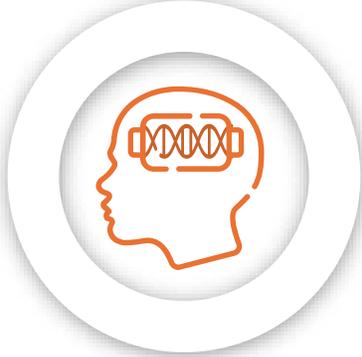


A

amyloid-PET

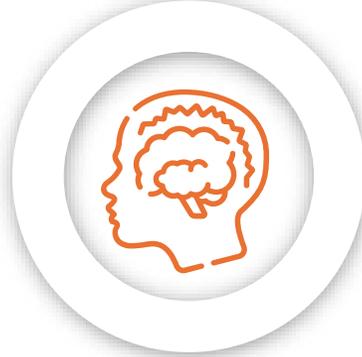


CSF $A\beta_{42/40}$



T

CSF p-tau

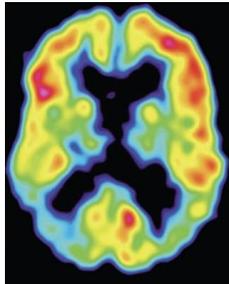


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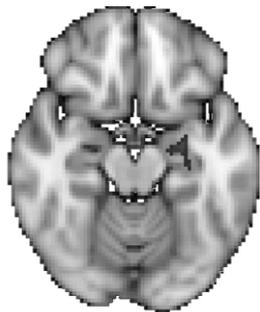
CSF t-tau



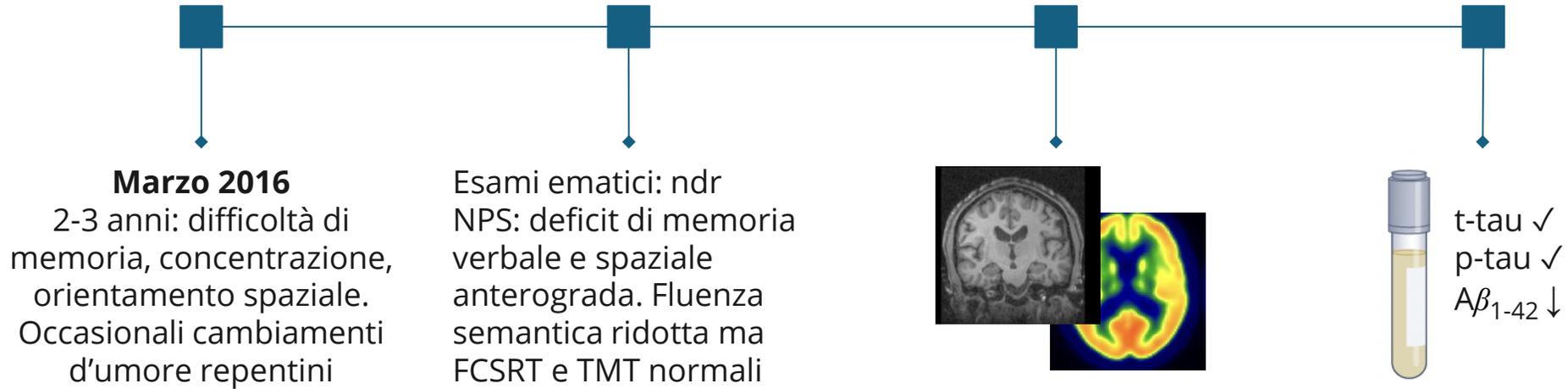
FDG-PET



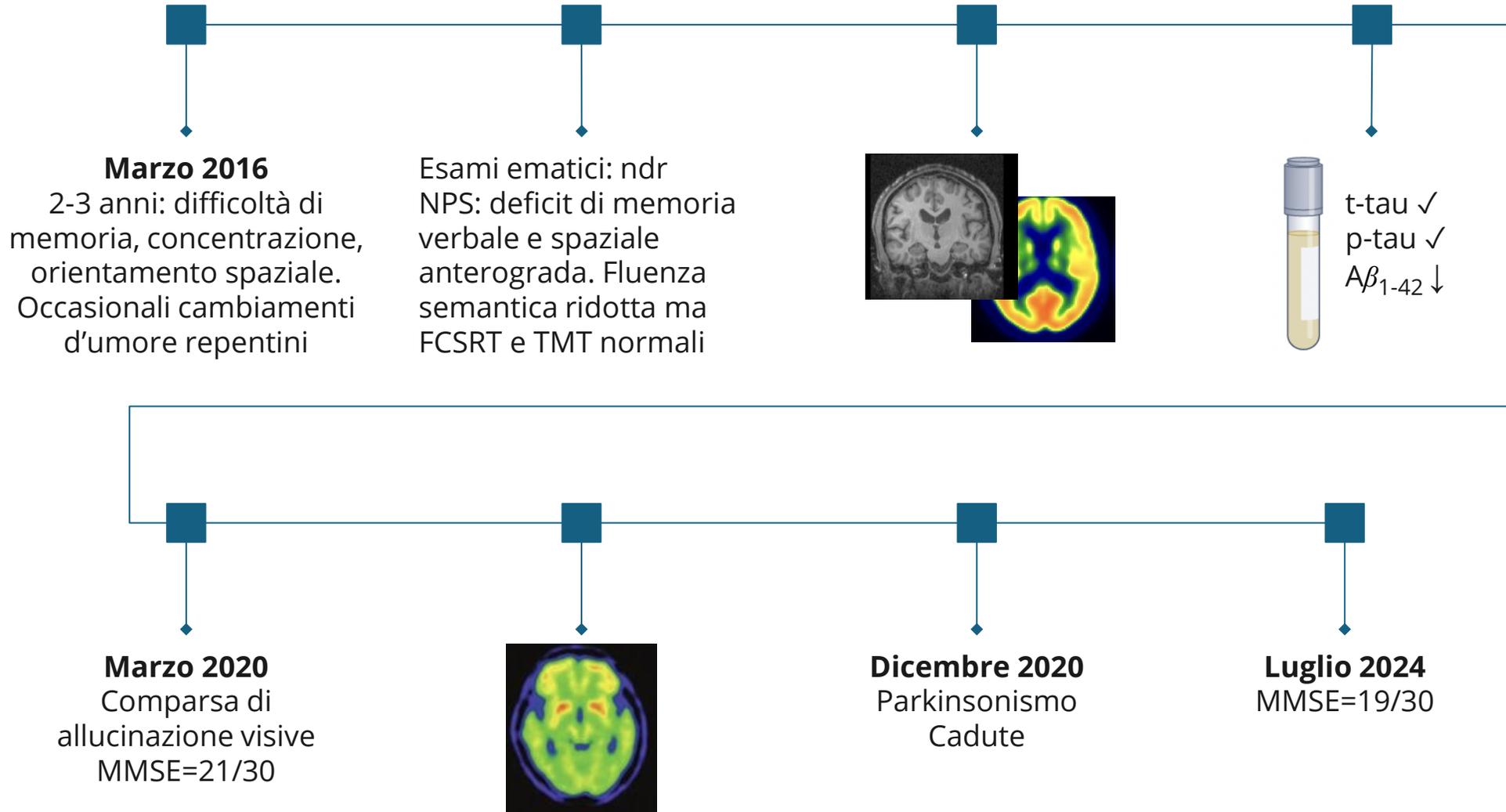
MRI



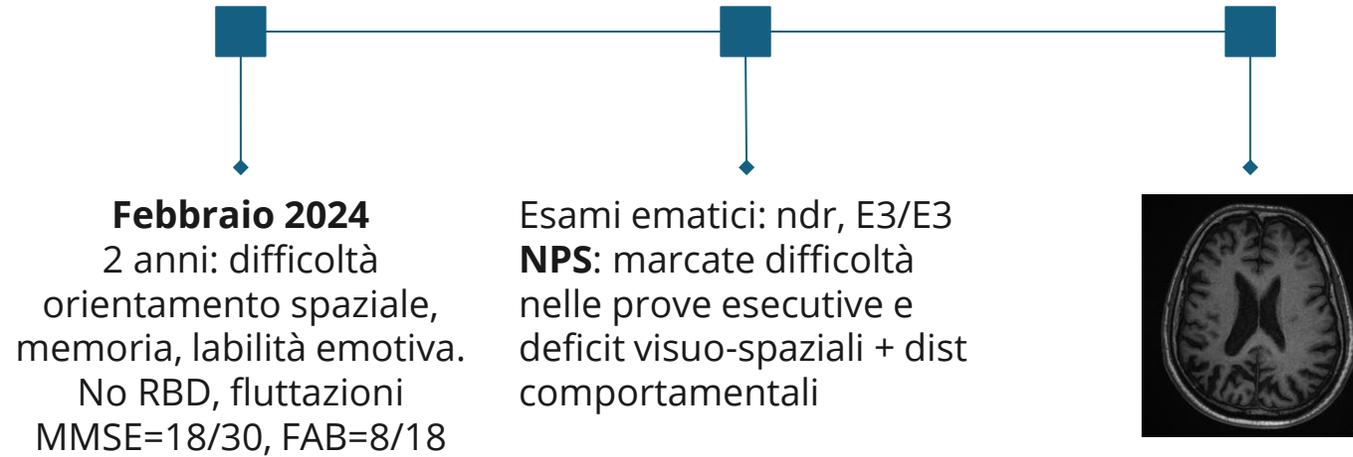
BD, 63 ♂



BD, 63 ♂



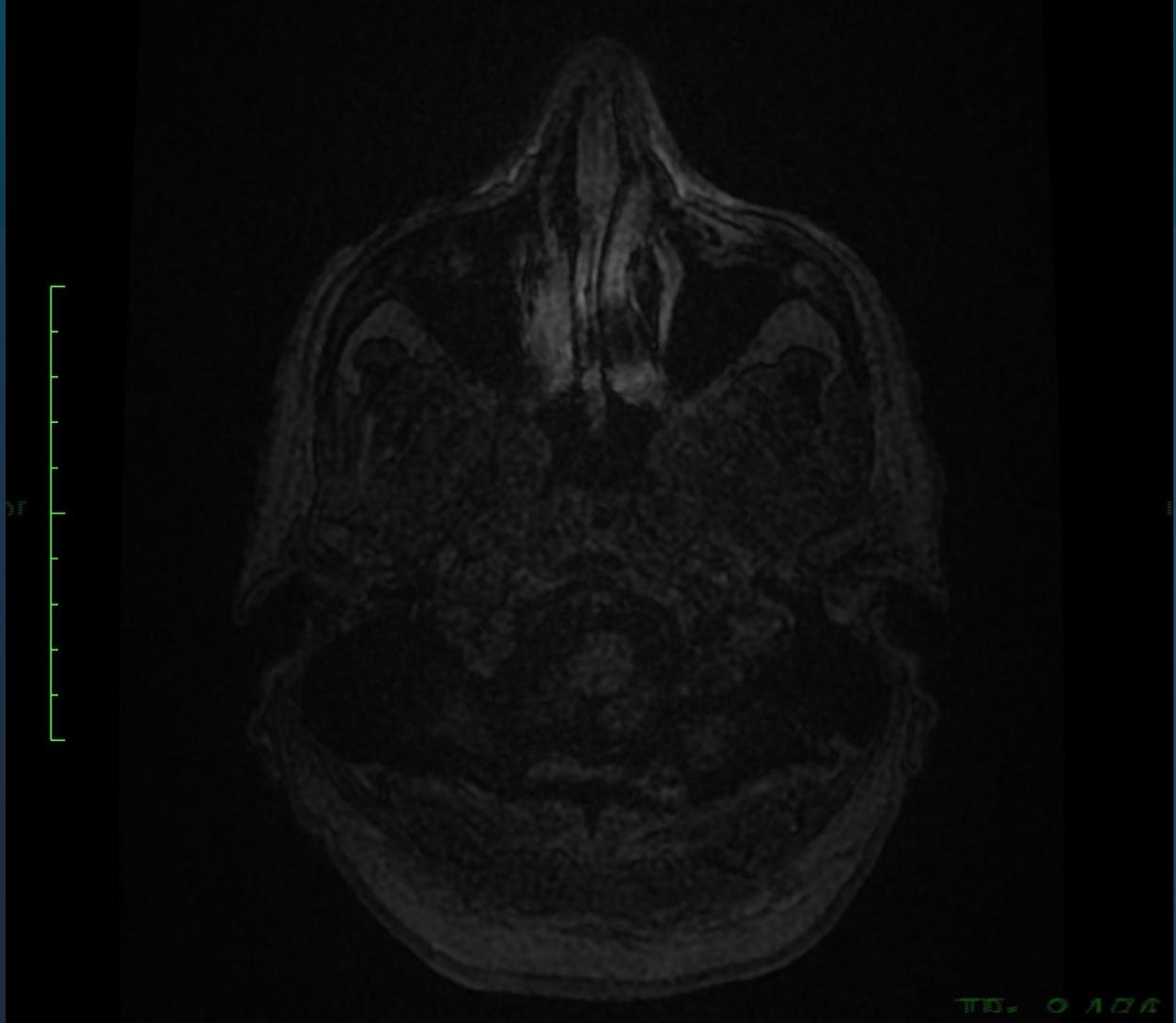
MR, ♂73



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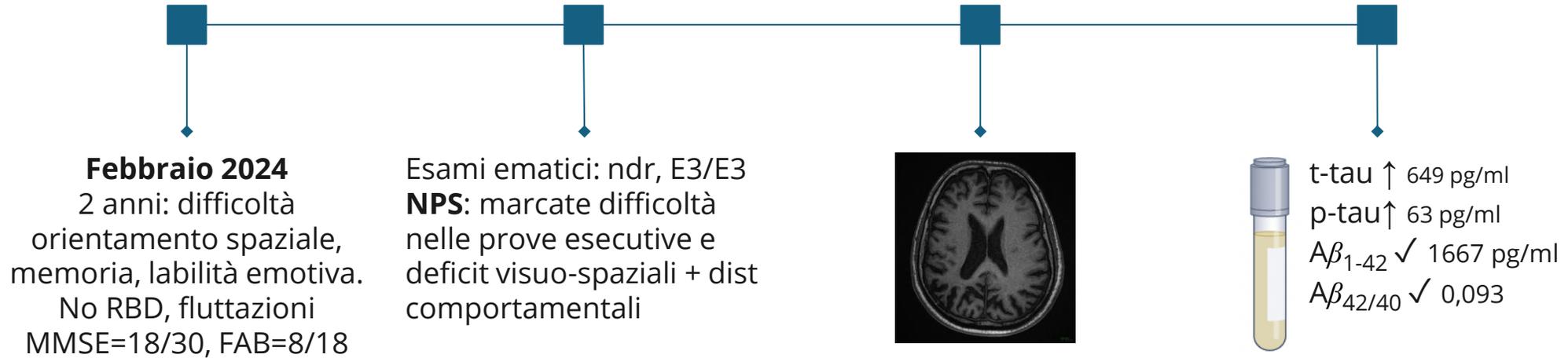
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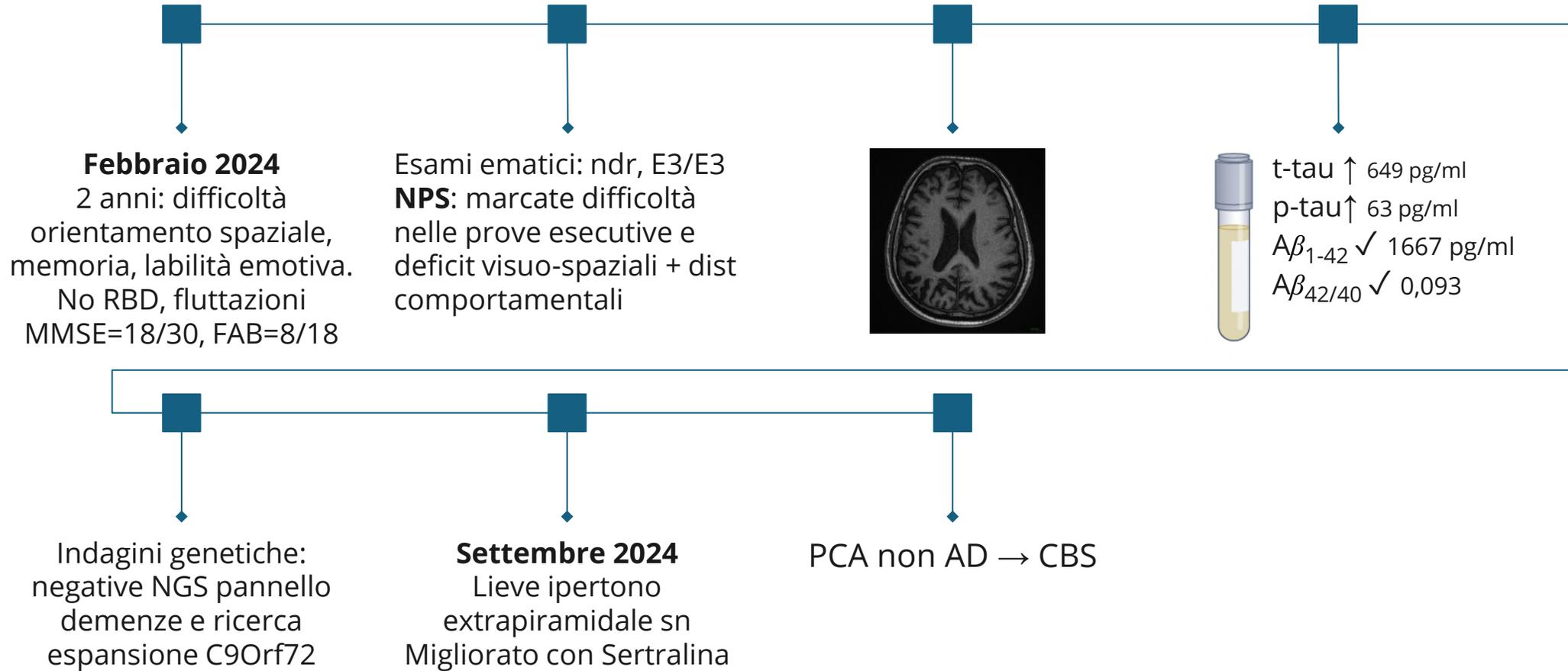
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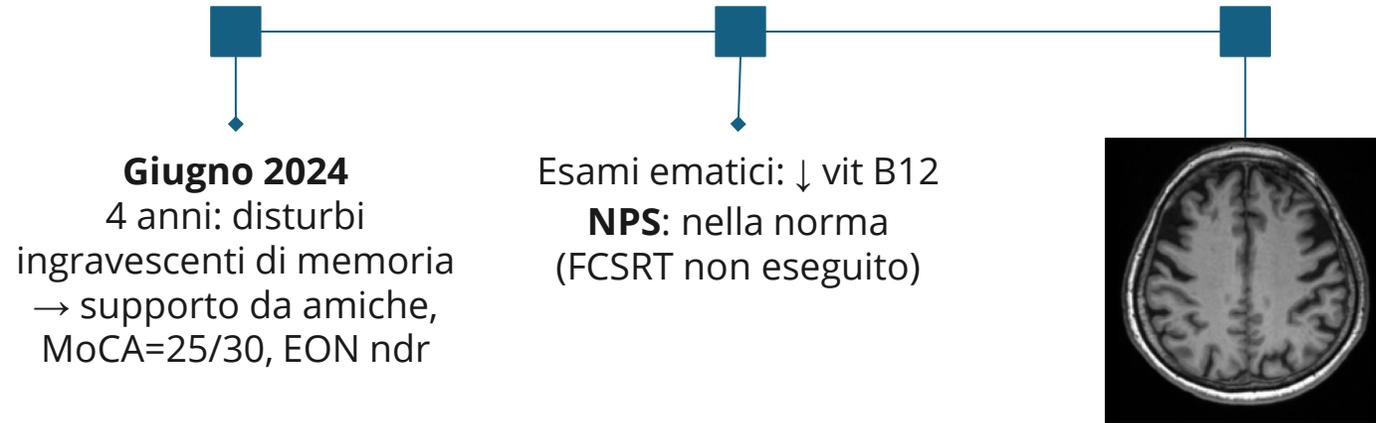
MR, ♂73



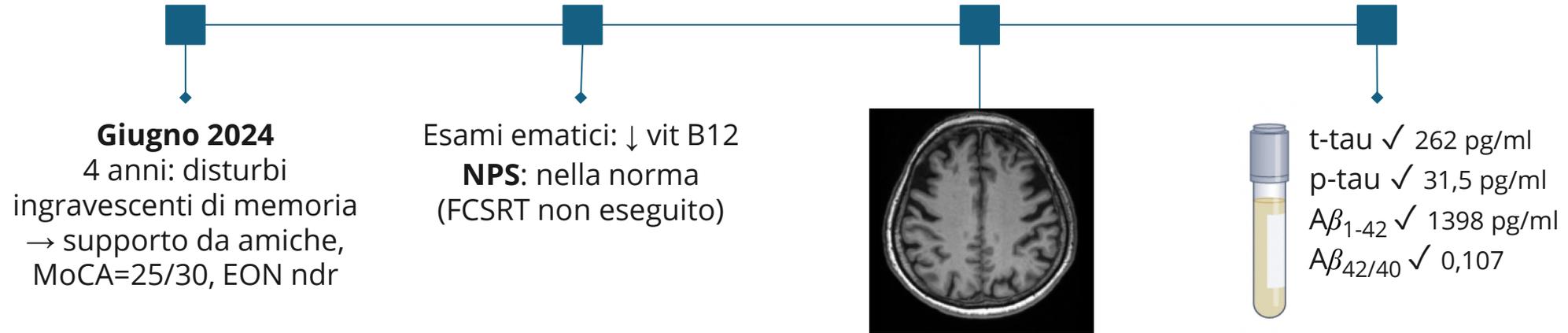
MR, ♂73



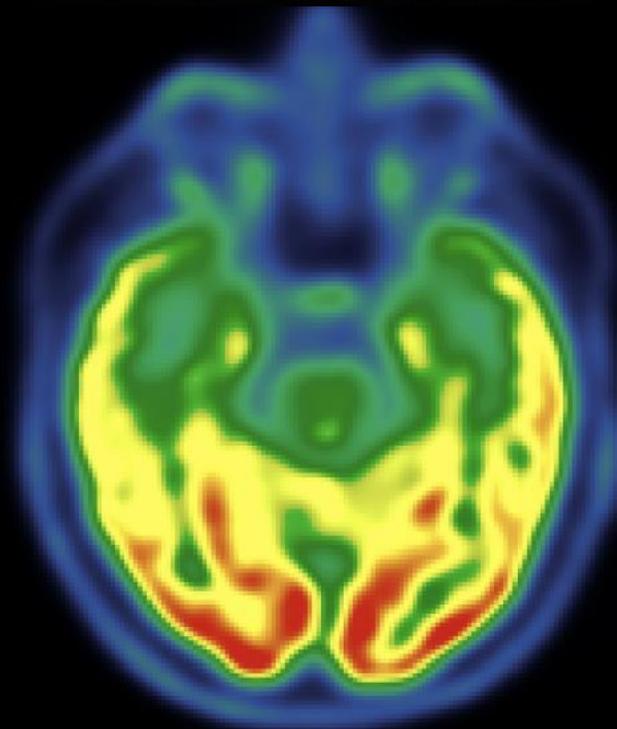
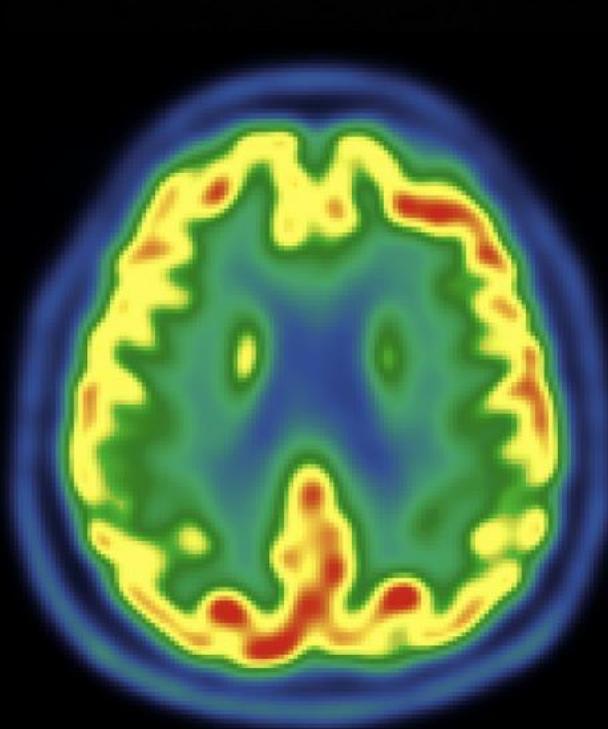
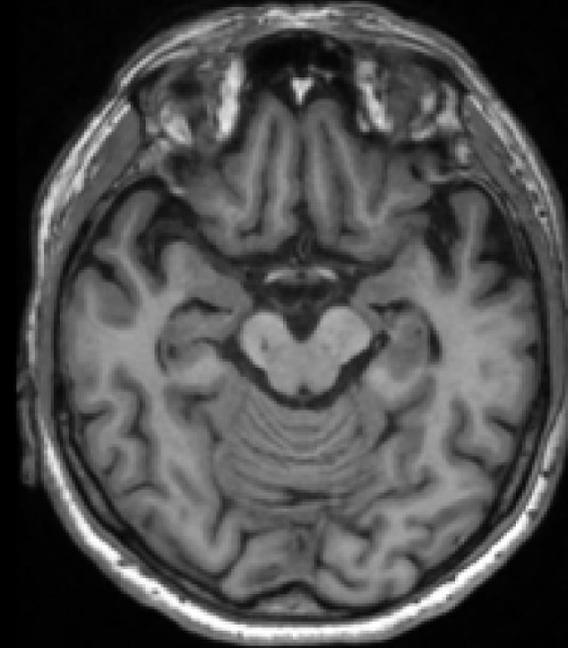
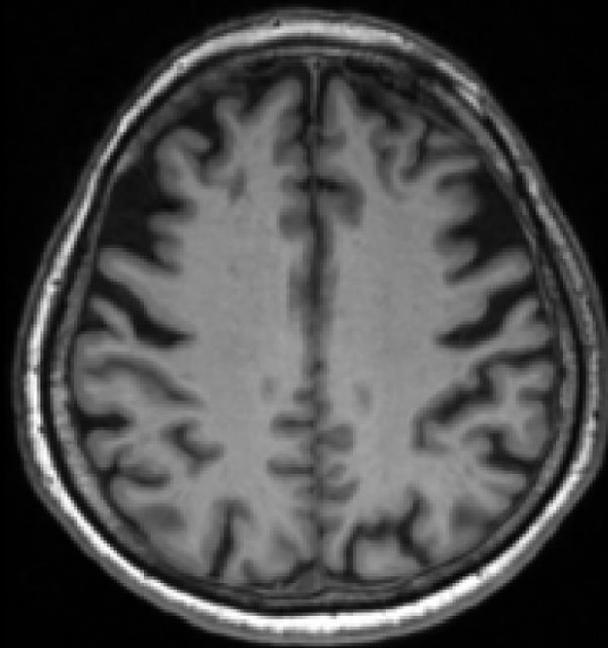
SE, ♀6



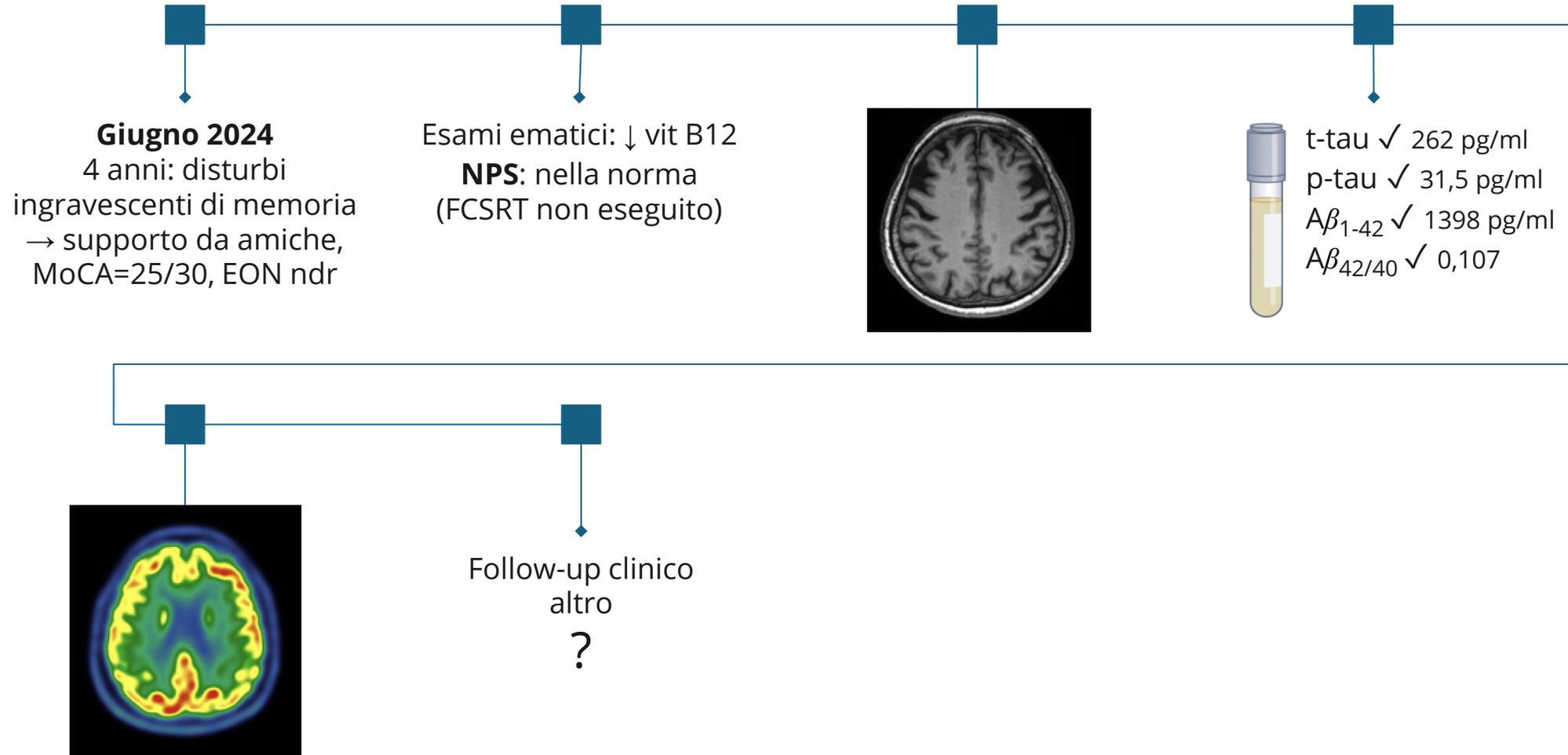
SE, ♀6



SE, ♀6

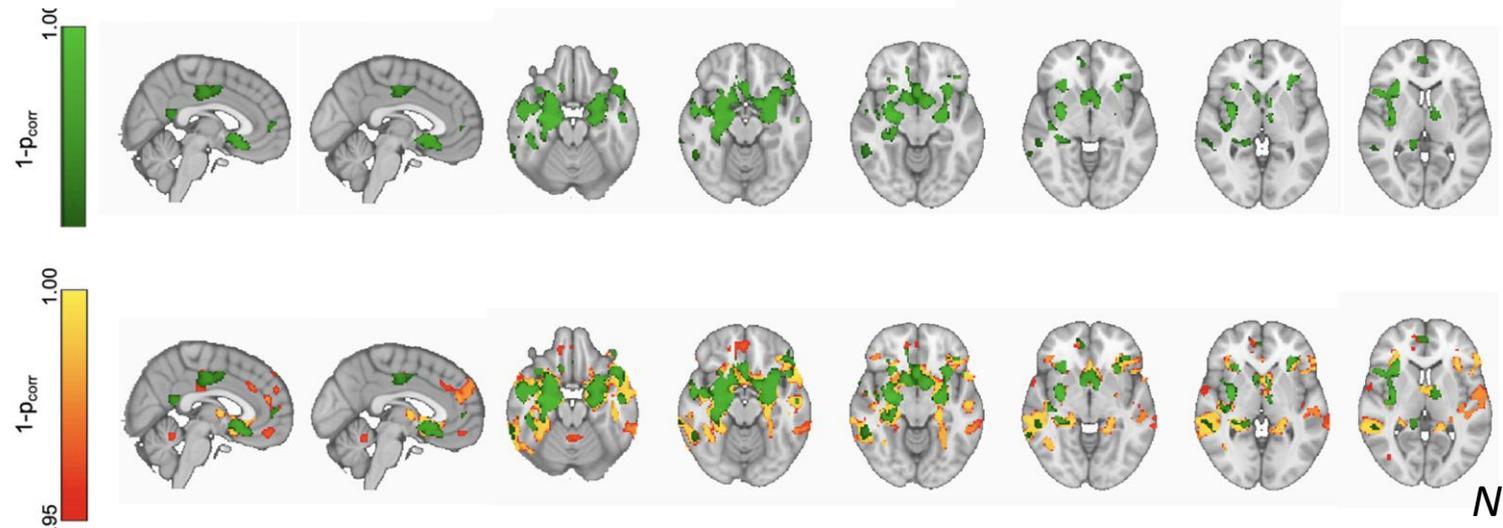
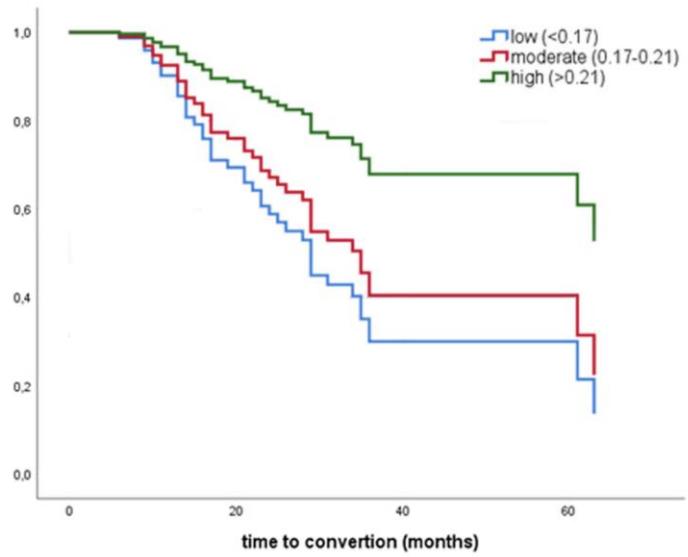
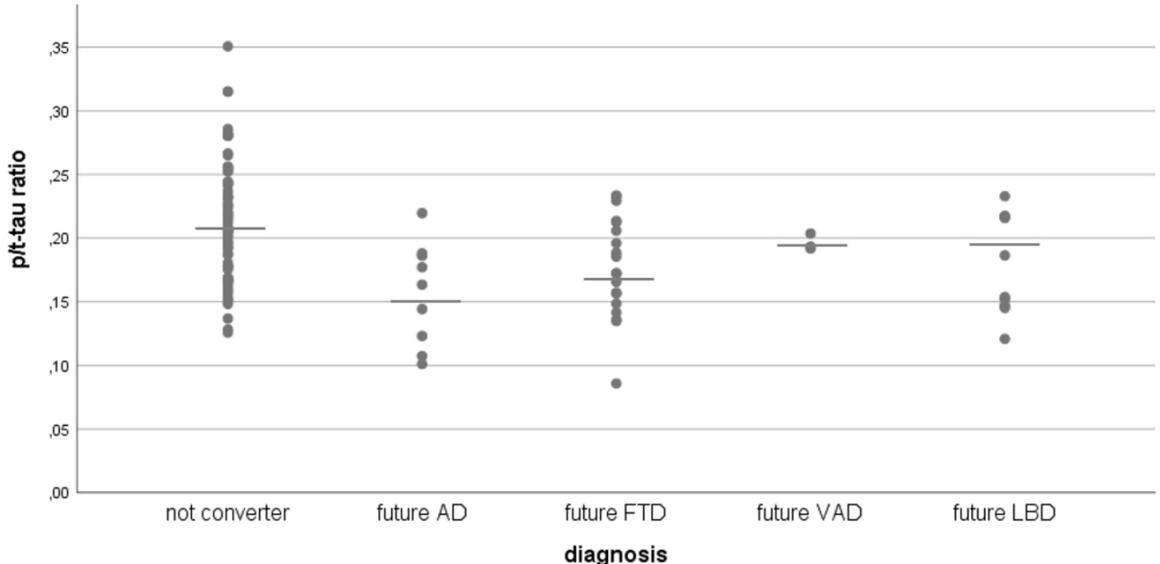


SE, ♀6

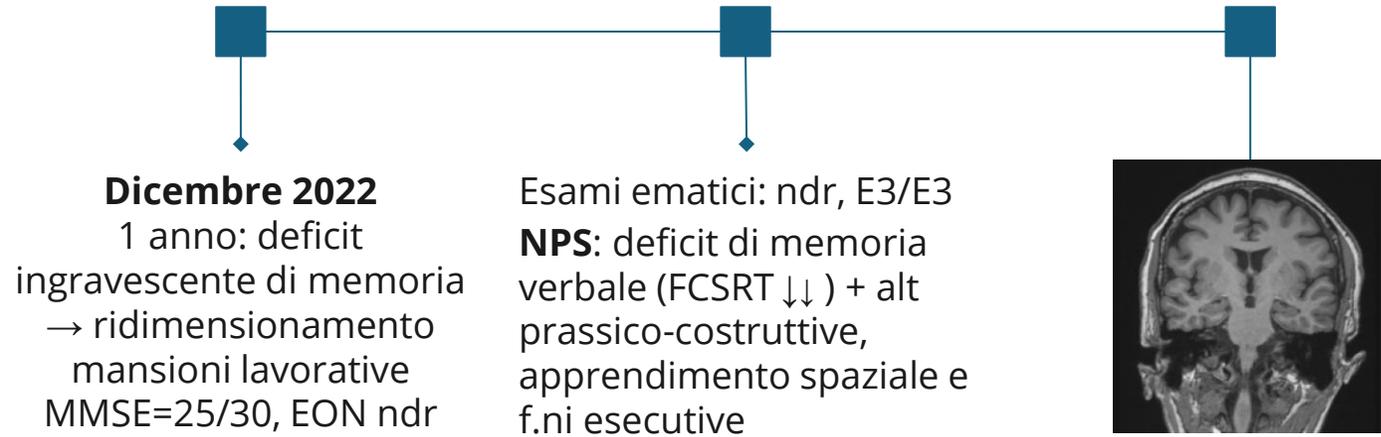


Predictive value of phospho-tau/total-tau ratio in amyloid-negative Mild Cognitive Impairment

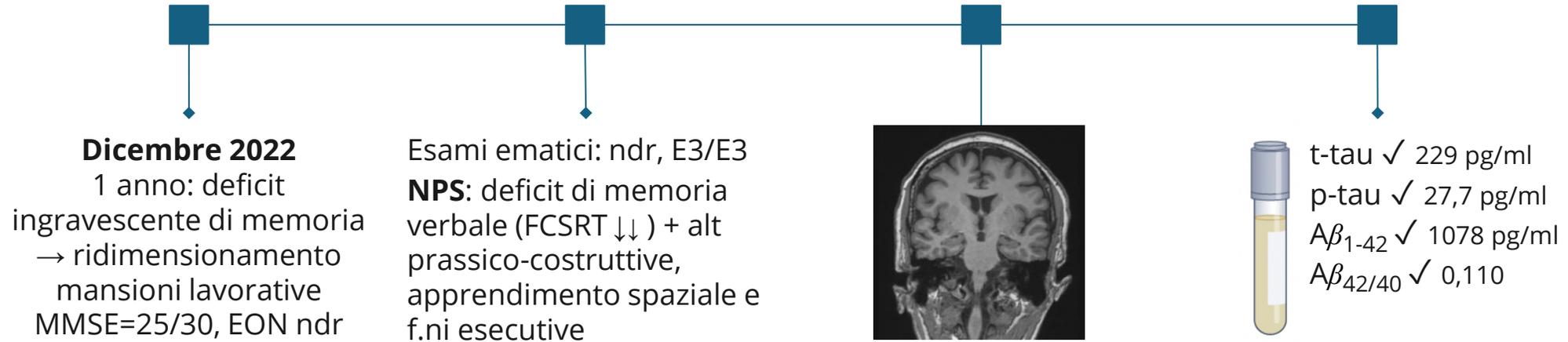
Manuela Tondelli^{a,b}, Simone Salemmè^{a,b}, Giulia Vinceti^{a,b,c}, Roberta Bedin^{a,b}, Tommaso Trenti^d, Maria Angela Molinari^c, Annalisa Chiari^c, Giovanna Zamboni^{a,b,c,e,*}



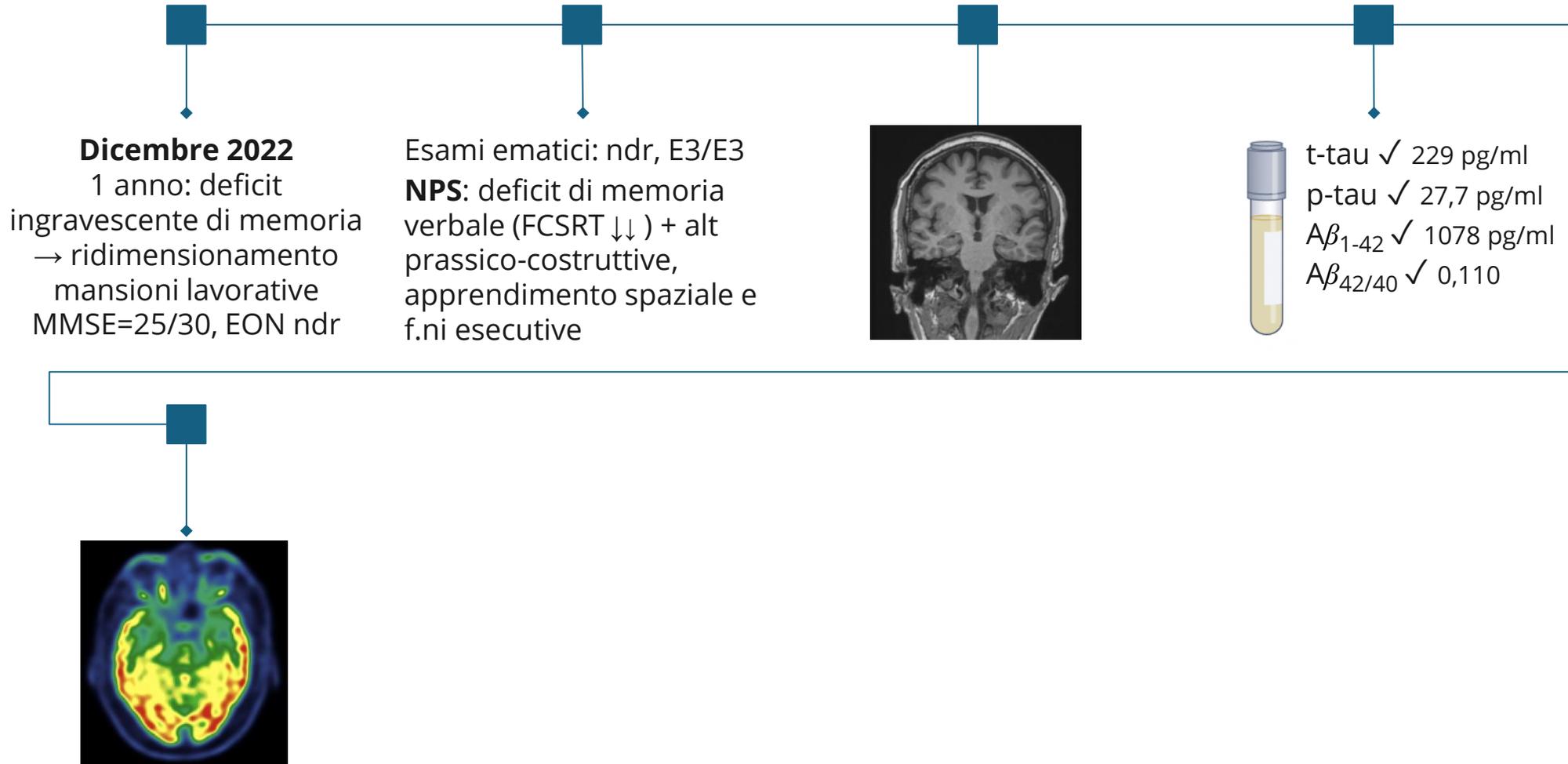
PW, ♀ (;)



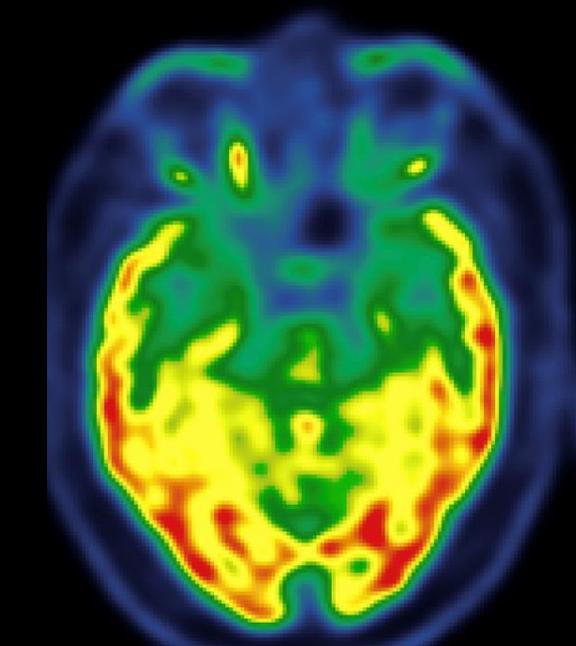
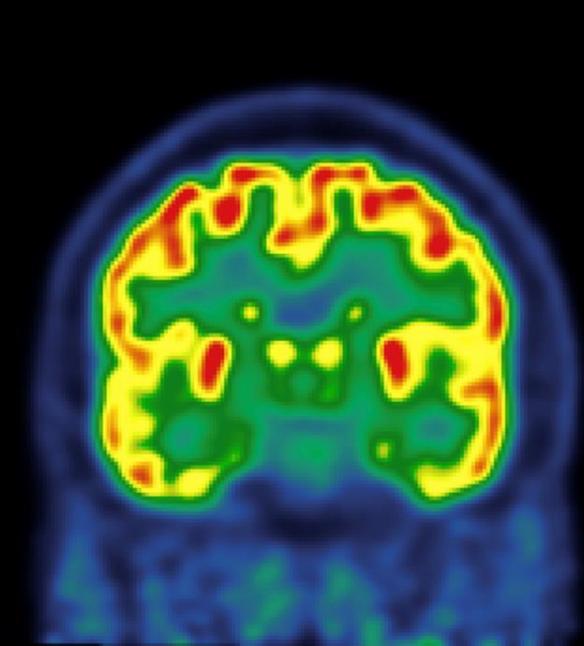
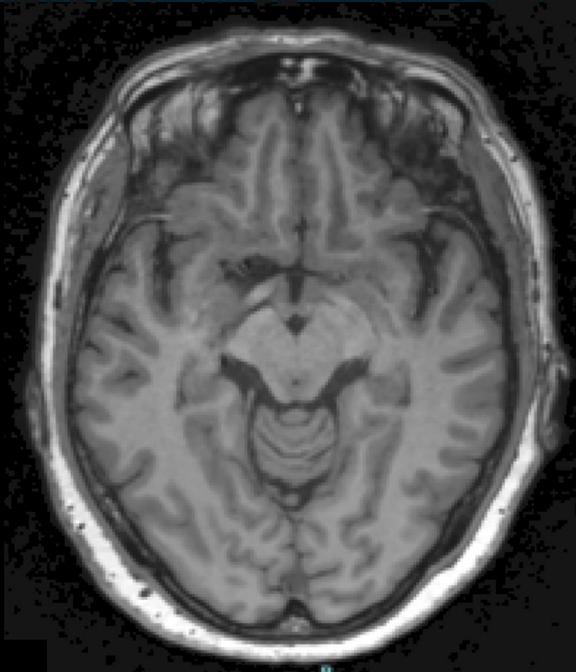
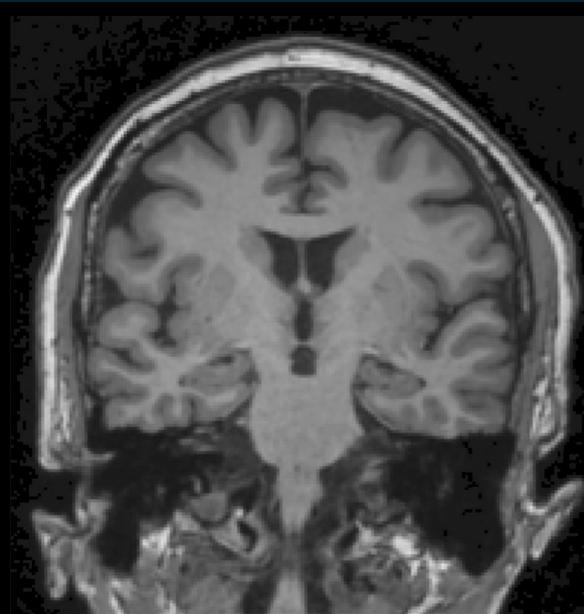
PW, ♀ ()



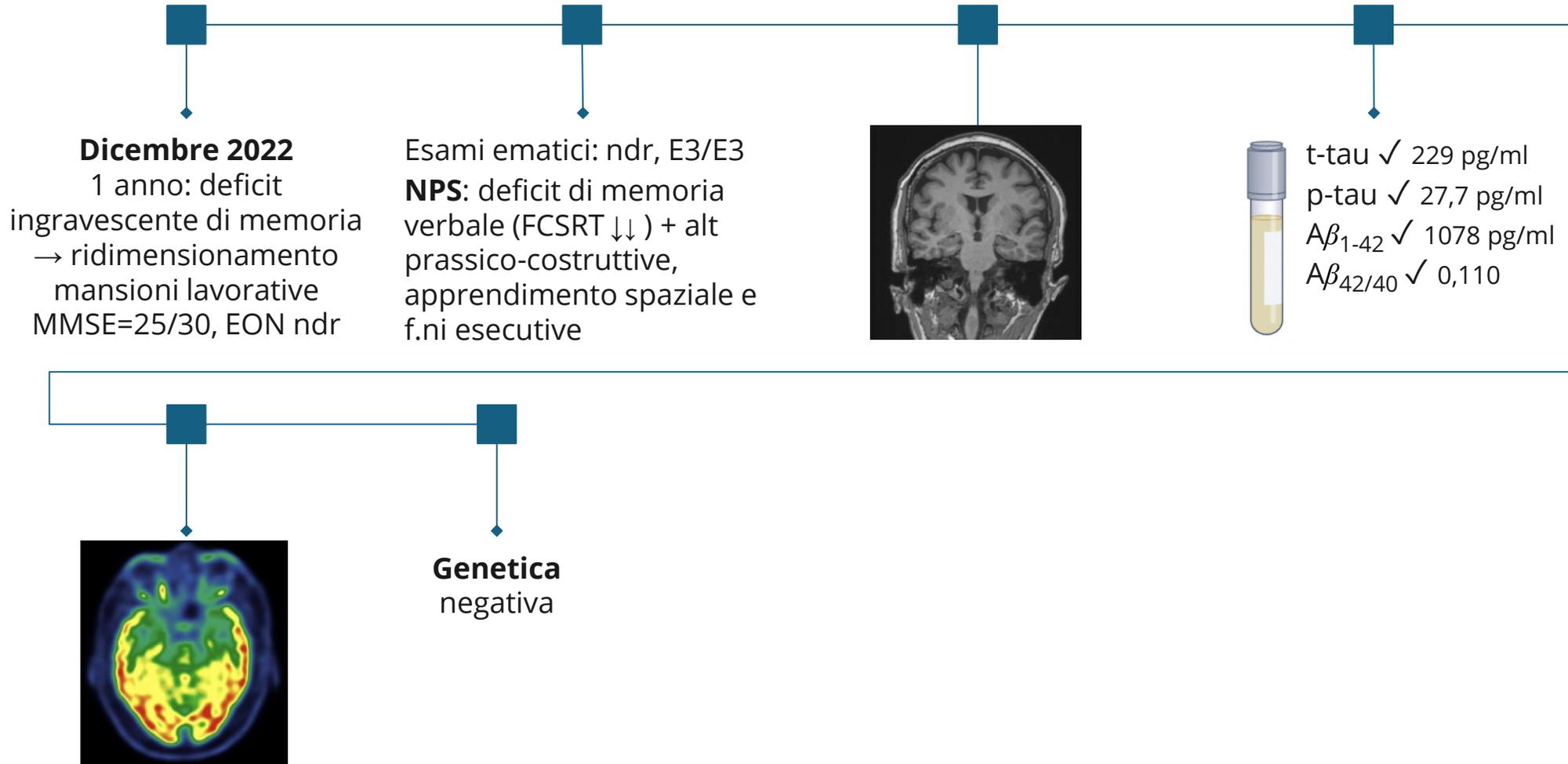
PW, ♀ ()



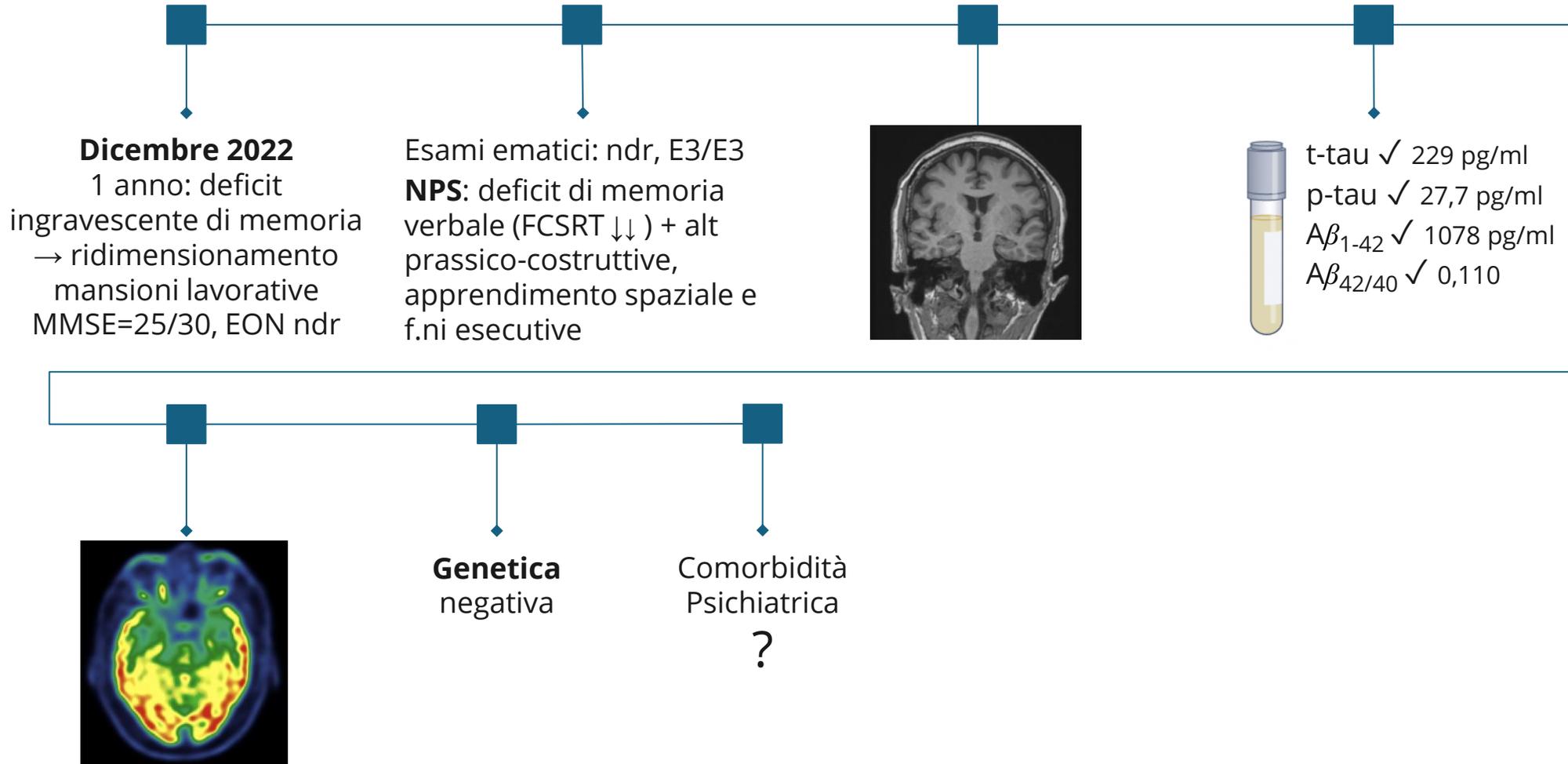
PW, ♀65



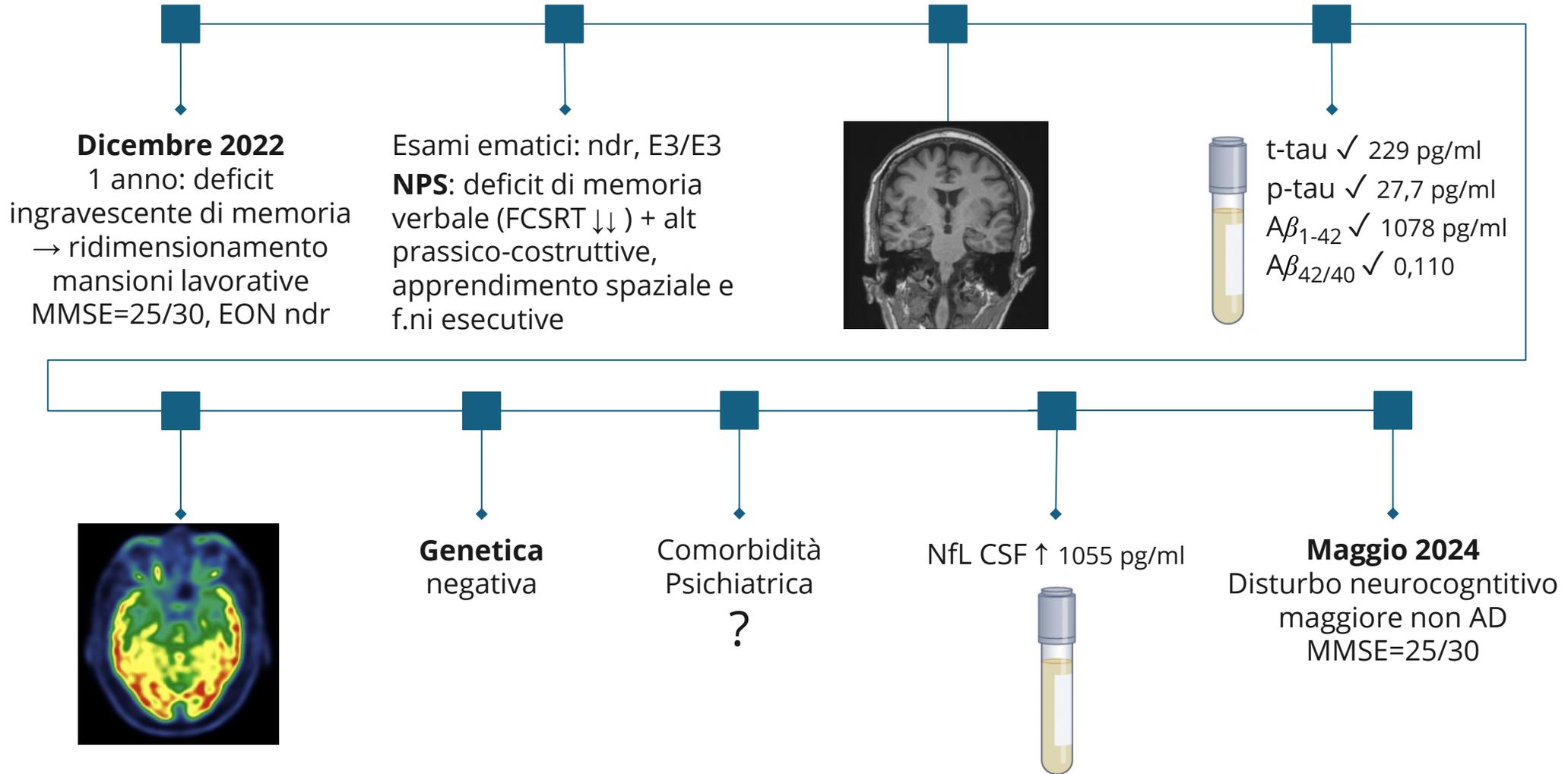
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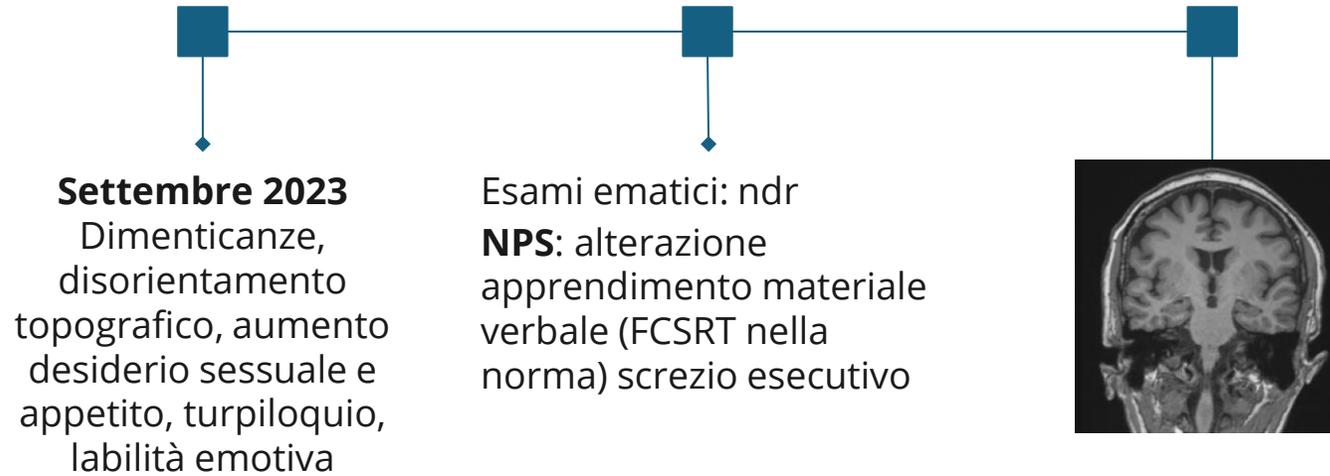
PW, ♀ ()



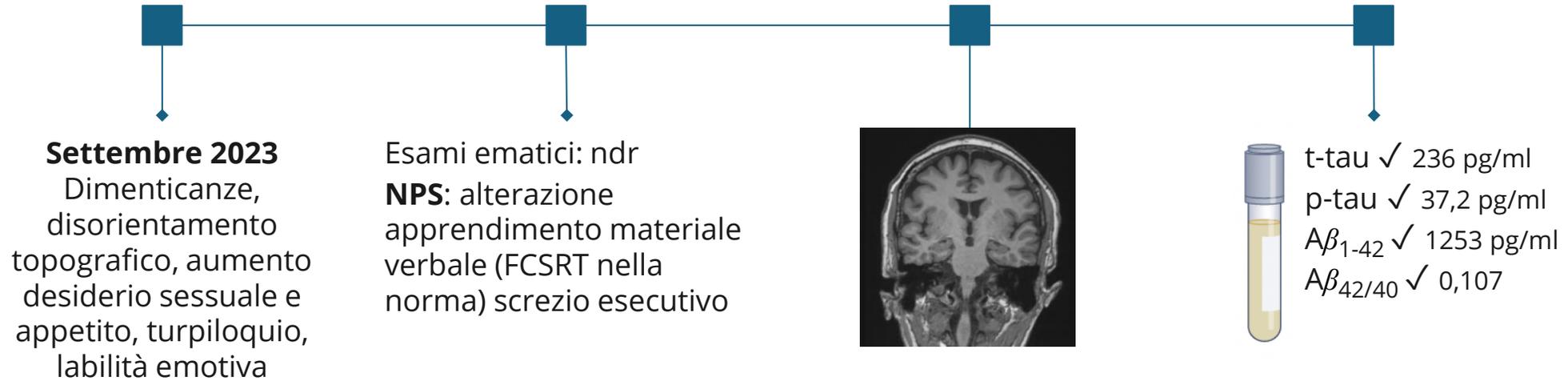
PW, ♀ (;



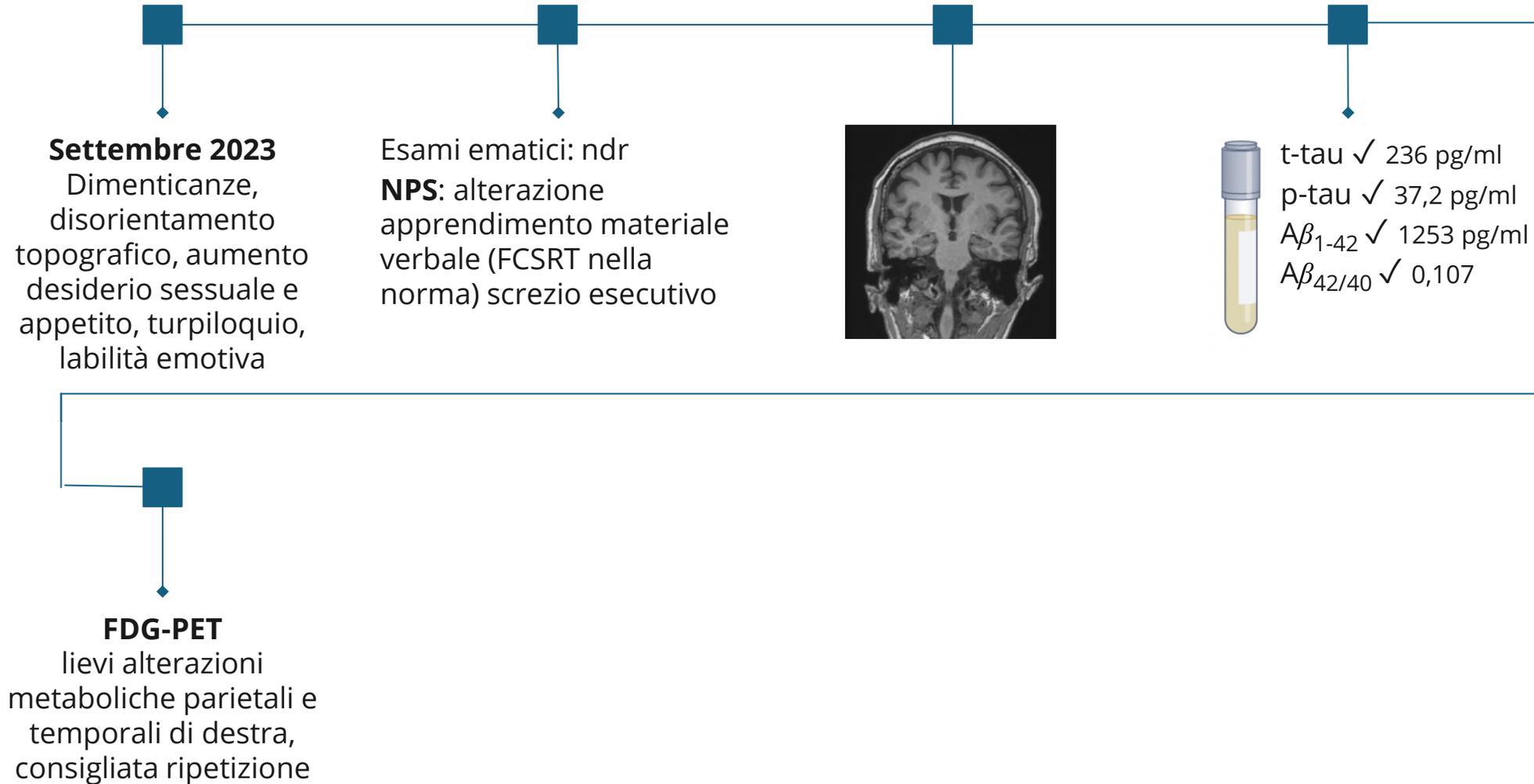
BG, 55



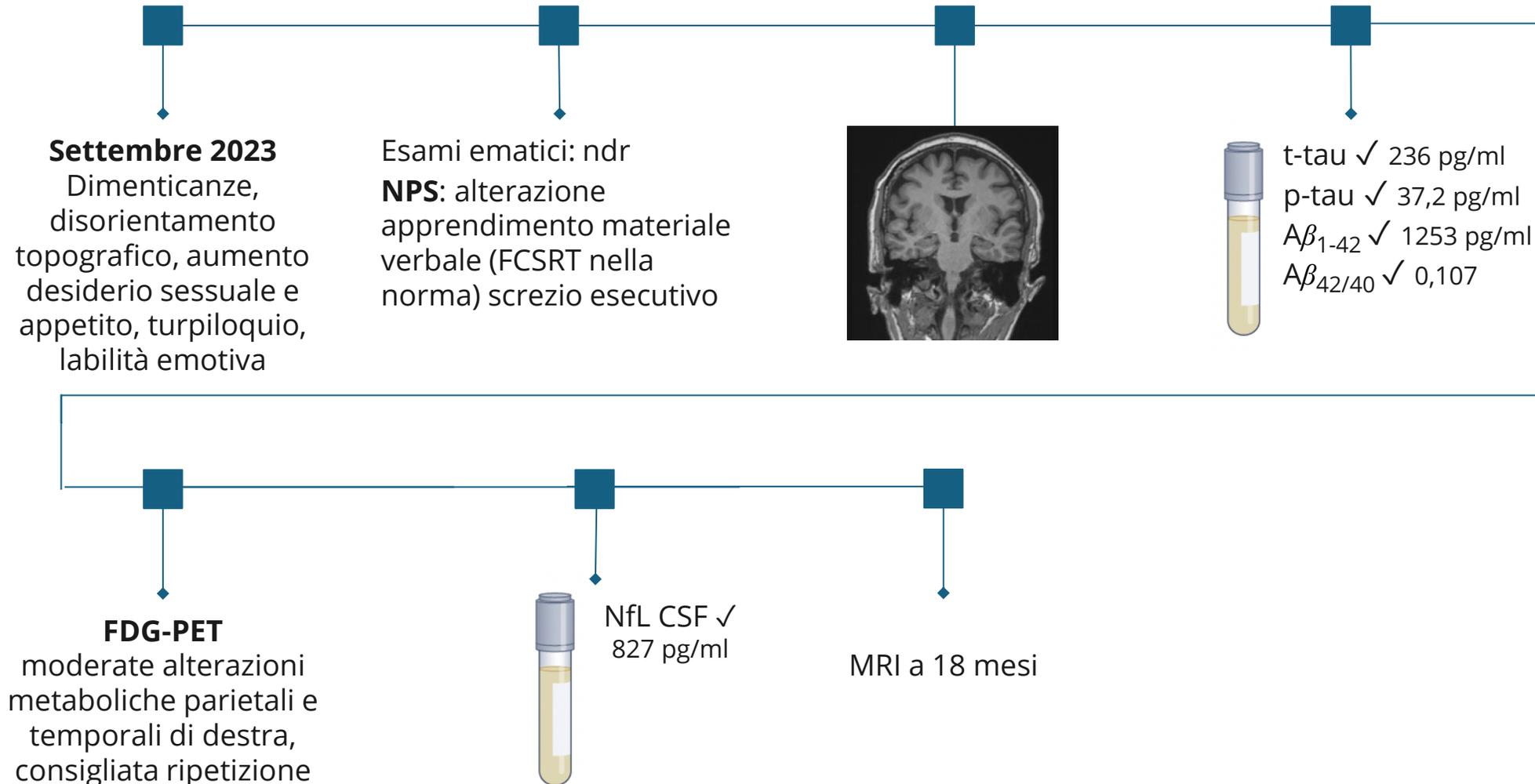
BG, 55



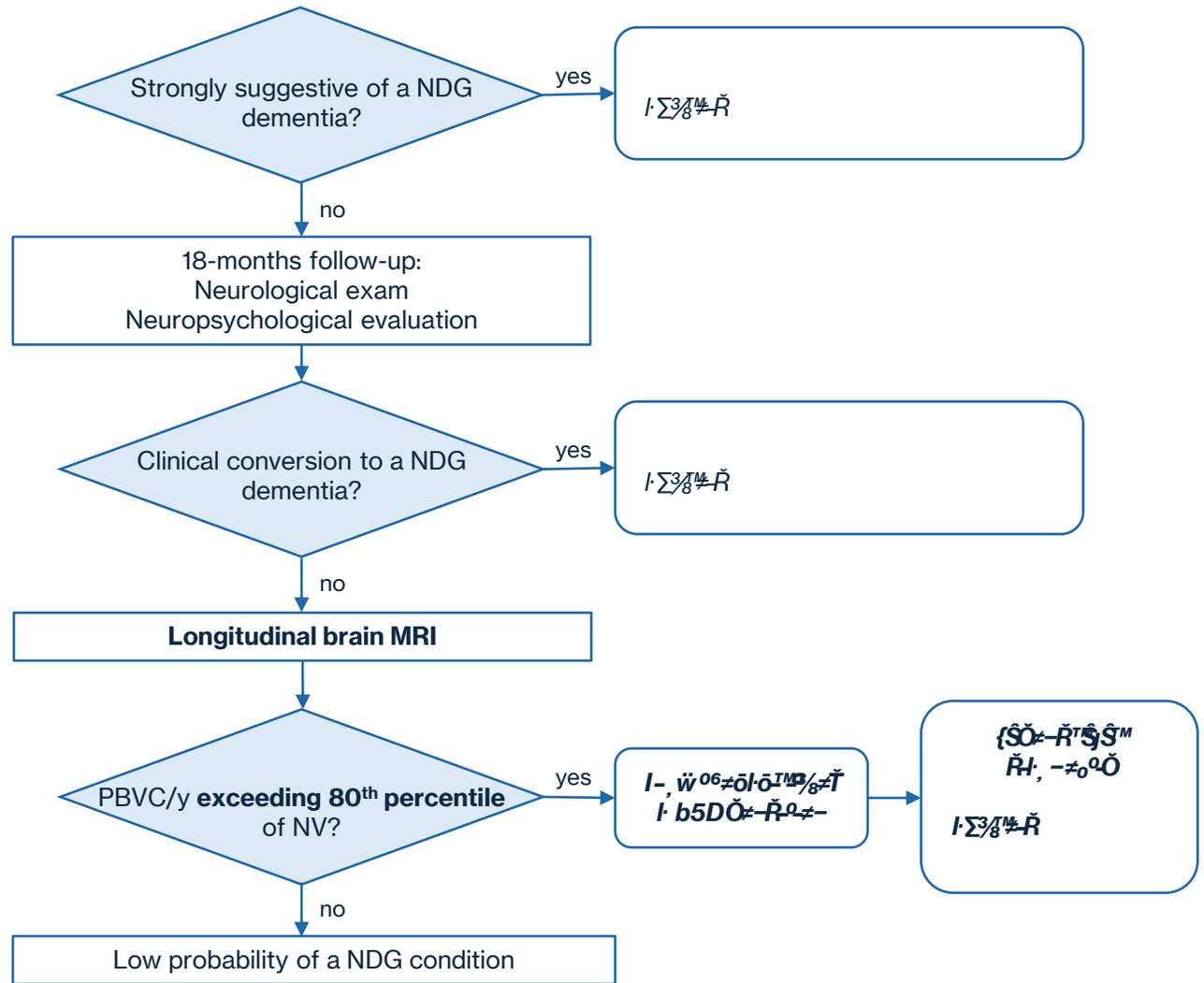
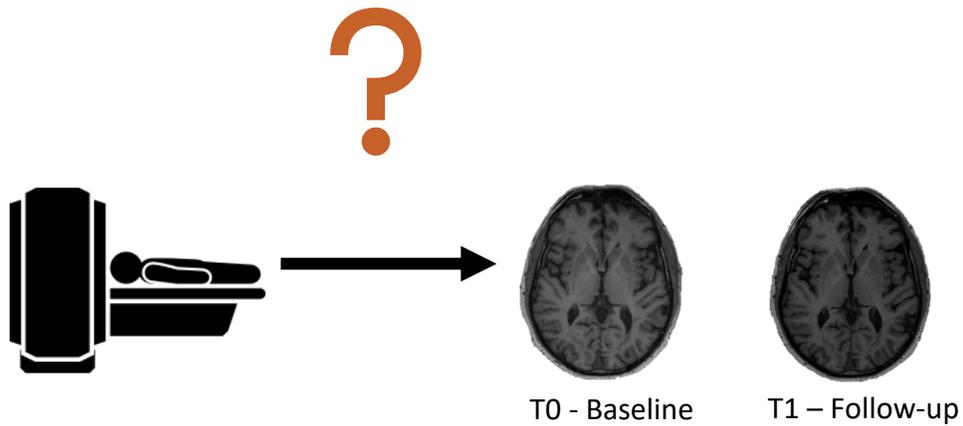
BG, 55

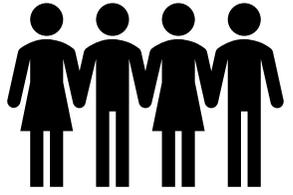


BG, 55



Subtle/subjective cognitive or behavioural complaints





- Dysexecutive profile
- Personality and behavioral changes



bvFTD/PPD/phFTD

Longitudinal MRI



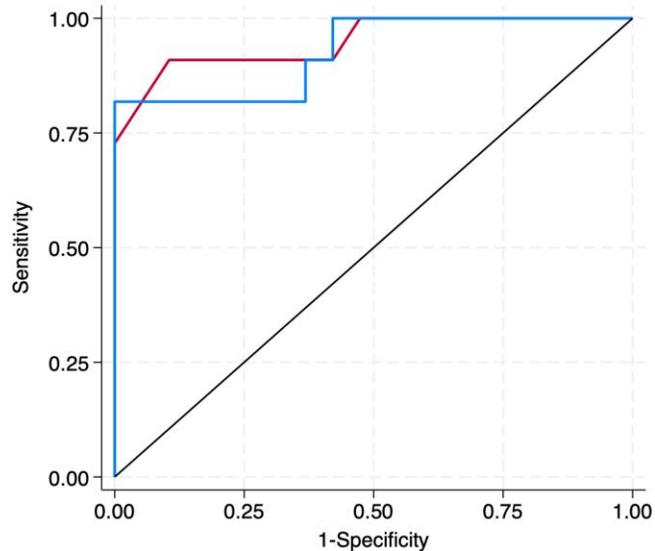
T0 - Baseline T1 - 18 months

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

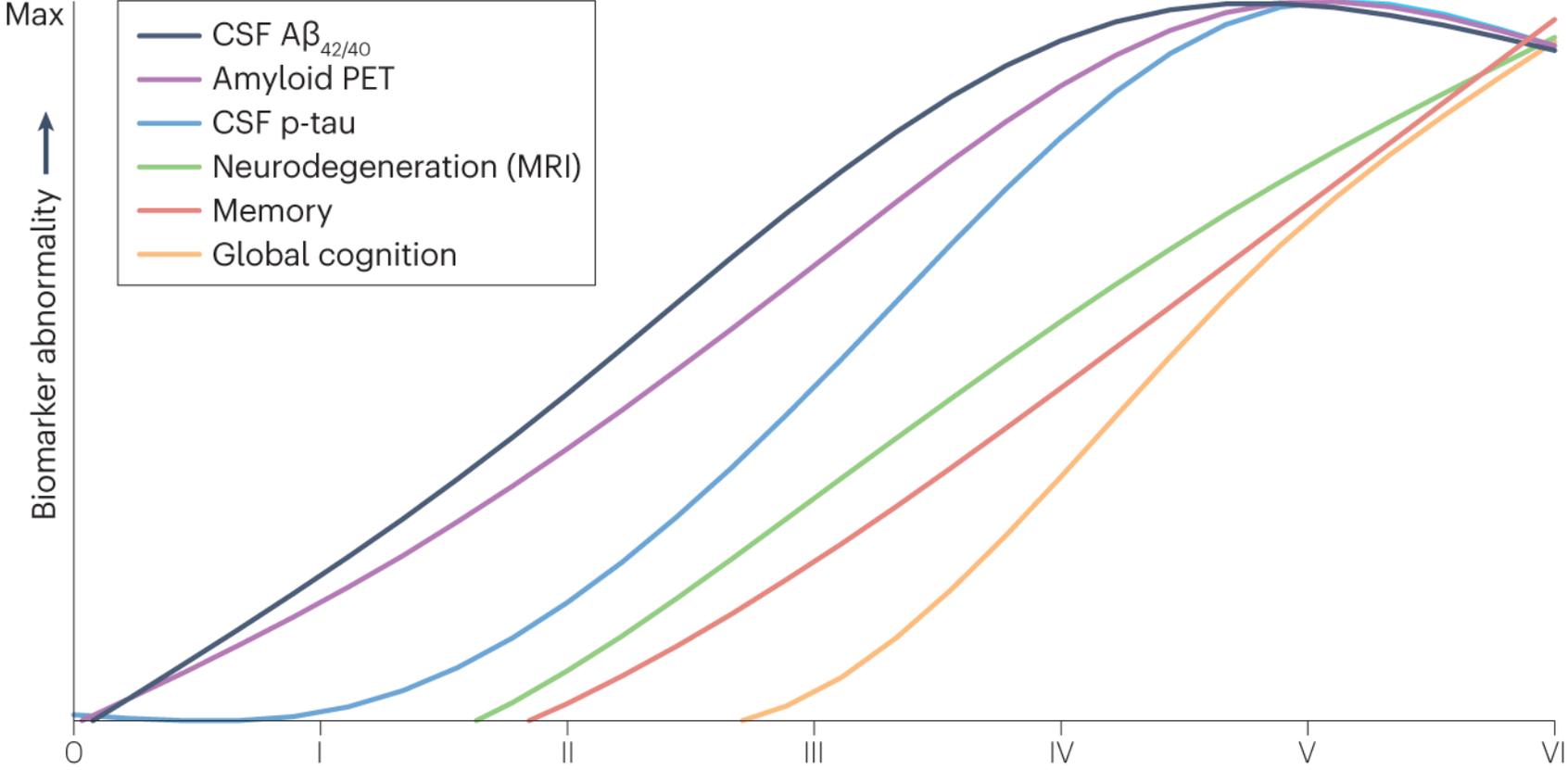


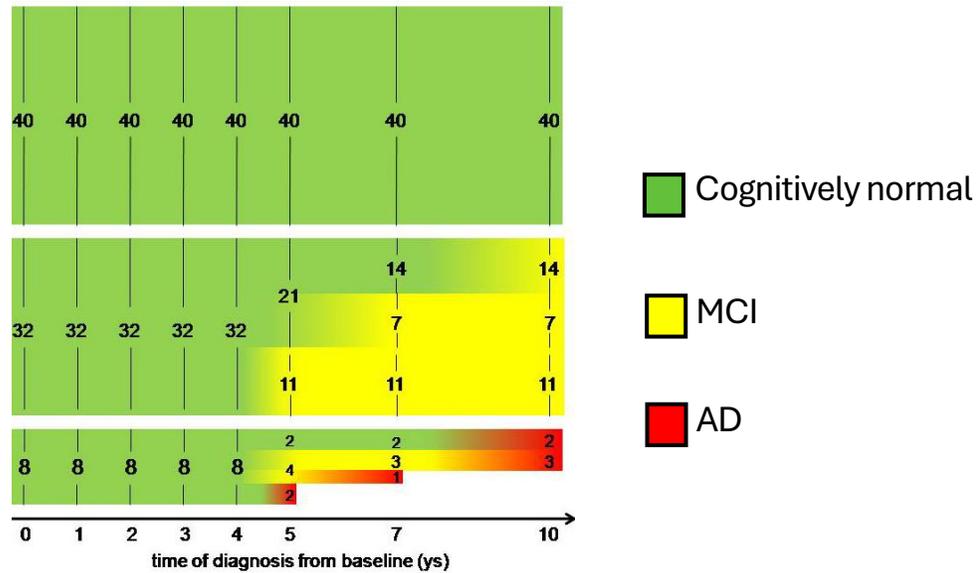
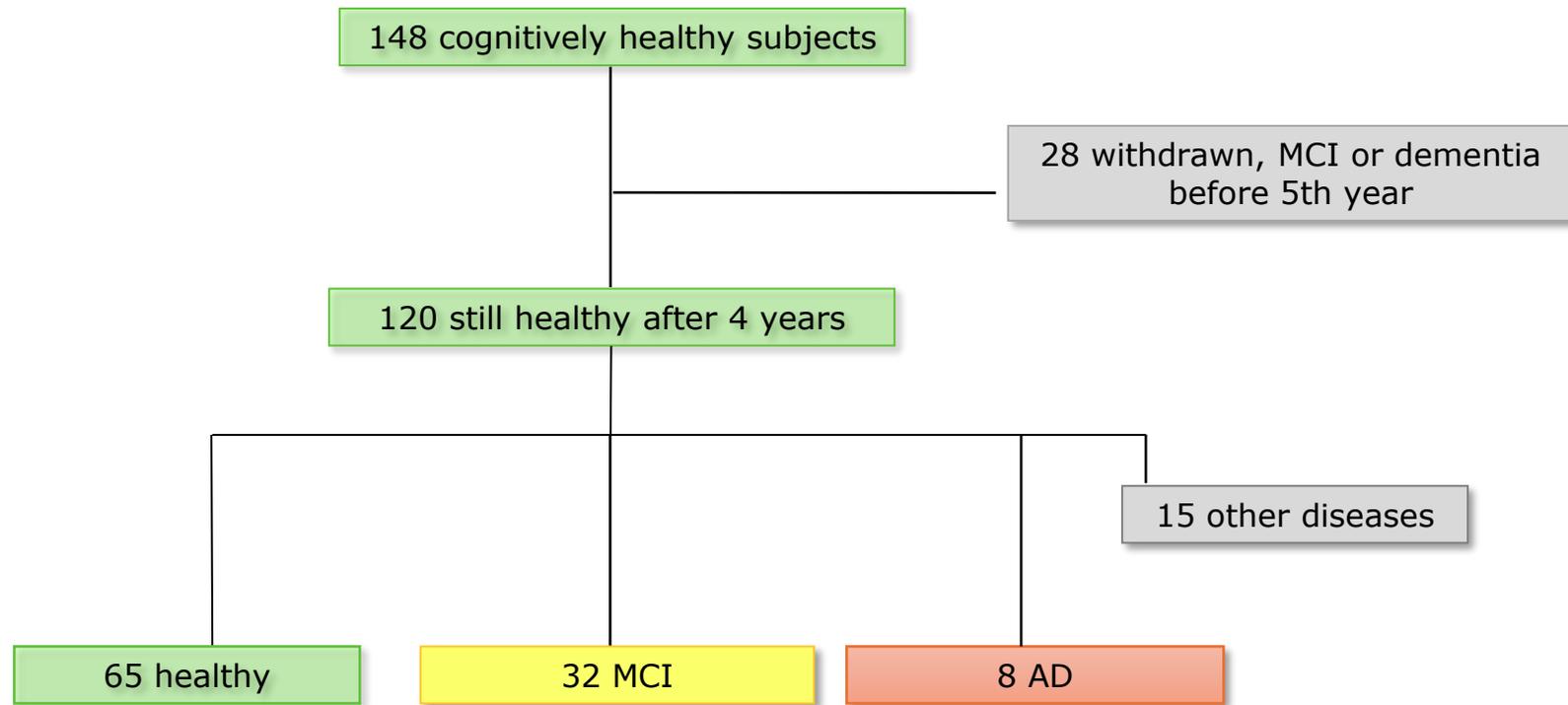
— Serum NfL AUC: 0.949
— CSF NfL AUC: 0.928
— Reference

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

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

Ruolo prognostico

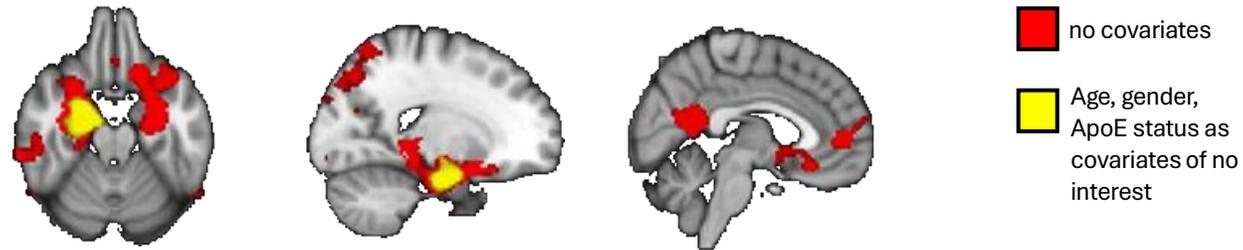




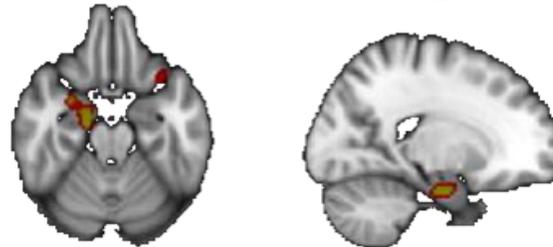
Structural MRI changes detectable up to ten years before clinical Alzheimer's disease

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

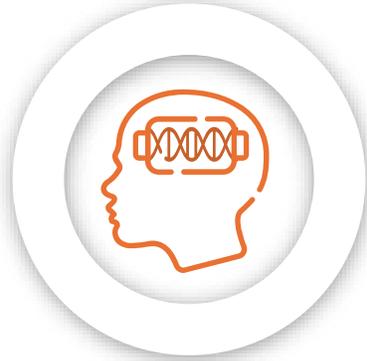
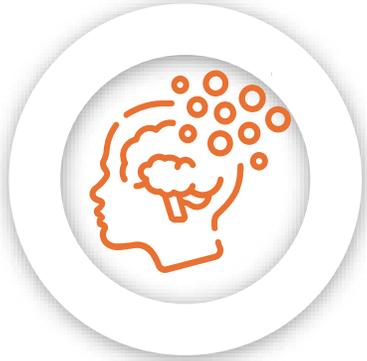


Preclinical AD 7-10 years before symptoms < No cognitive decline over 10 years

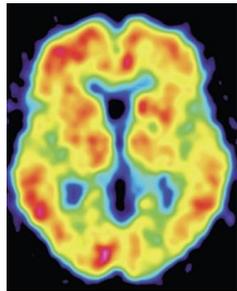


Atrophy is not a late, “downstream” event in AD progression

Il futuro



amyloid-PET



CSF $A\beta_{42/40}$



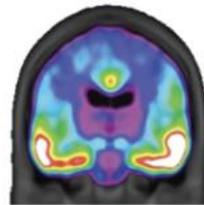
CSF p-tau



CSF p-tau



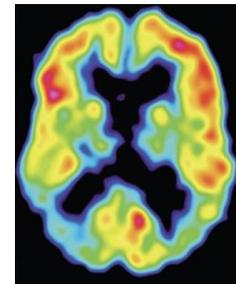
tau-PET



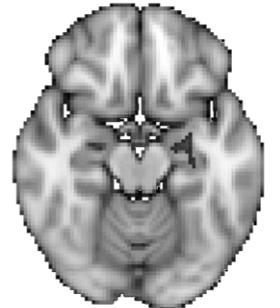
CSF t-tau



FDG-PET



MRI

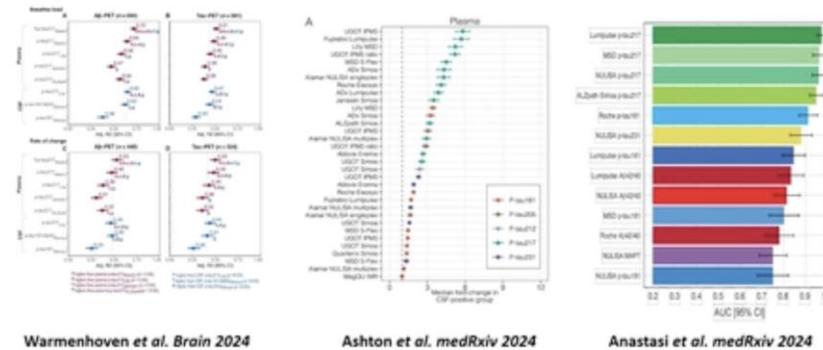


Il futuro è nel plasma

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



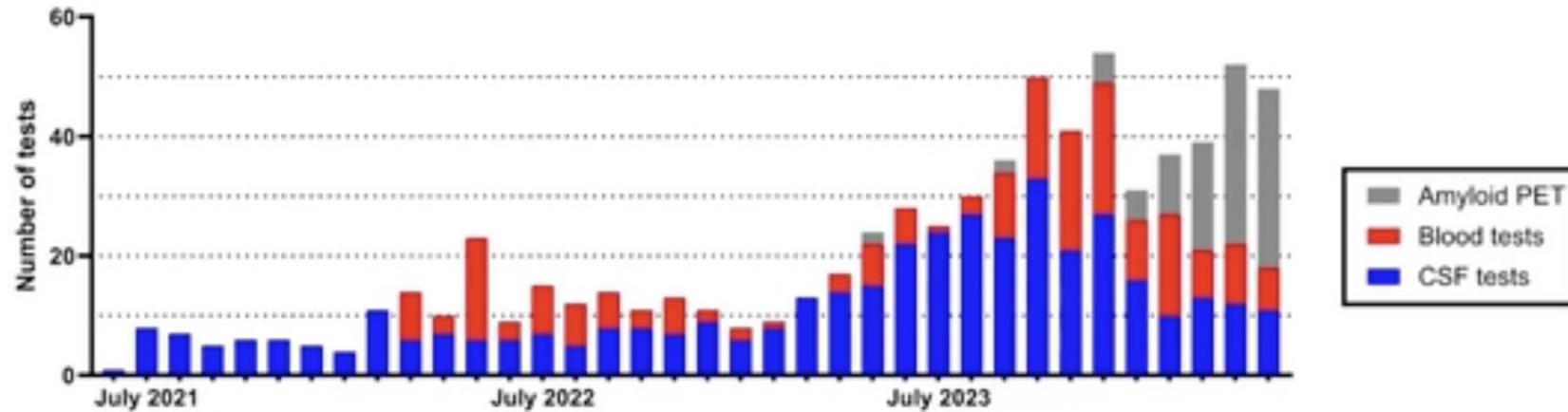
Attenzione ai casi in cui patologia AD non è patologia causa dei sintomi (caso BP)
Attenzione ai casi in cui non c'è patologia AD ma altra causa di demenza

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

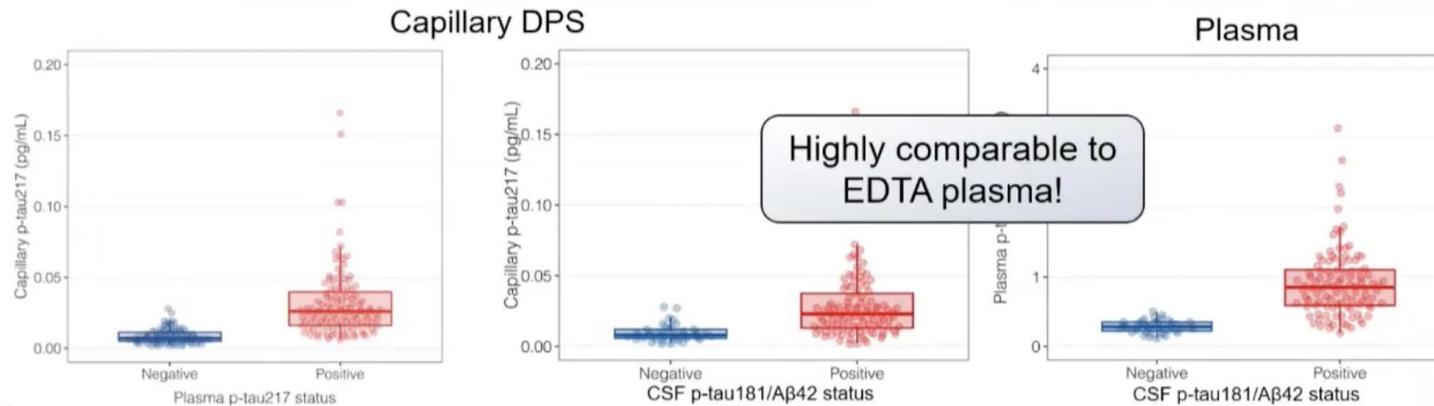
Venous blood sampling requires certain infrastructure and immediate processing

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



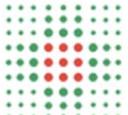
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GRAZIE

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



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EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Modena



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