

**LE DEMENZE: SINERGIE TRA OSPEDALE E
TERRITORIO**
MAPPA DEI SERVIZI DELLA REGIONE VENETO
Mirano, 5 ottobre 2019

Ruolo della diagnostica SPET e PET



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Servizio di Medicina Nucleare
Ospedale dell'Angelo Mestre (Ve)

Sommario

- **Imaging funzionale delle demenze**
- **FDG-PET: patterns di diagnosi differenziale**
 - **Alzheimer Disease**
 - **Fronto-Temporal Dementia**
 - **Lewy Body Dementia**
- **Datscan SPET**
- **PET con tracciante per amiloide: indicazioni**
- **Utilità clinica della dgn nel paziente con MCI**

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Main dementias

A β -amyloid

α -sinucleino-pathies

tau-pathies

Alzheimer

Lewy-body

PDD

PSP

CBD

Fronto-temporal

Frontal degeneration

Non fluent aphasia

ALS-FTD Complex

Semantic dementia

Vascular

Mixed

Ischemic-hypoperf.

Hemorrhagic

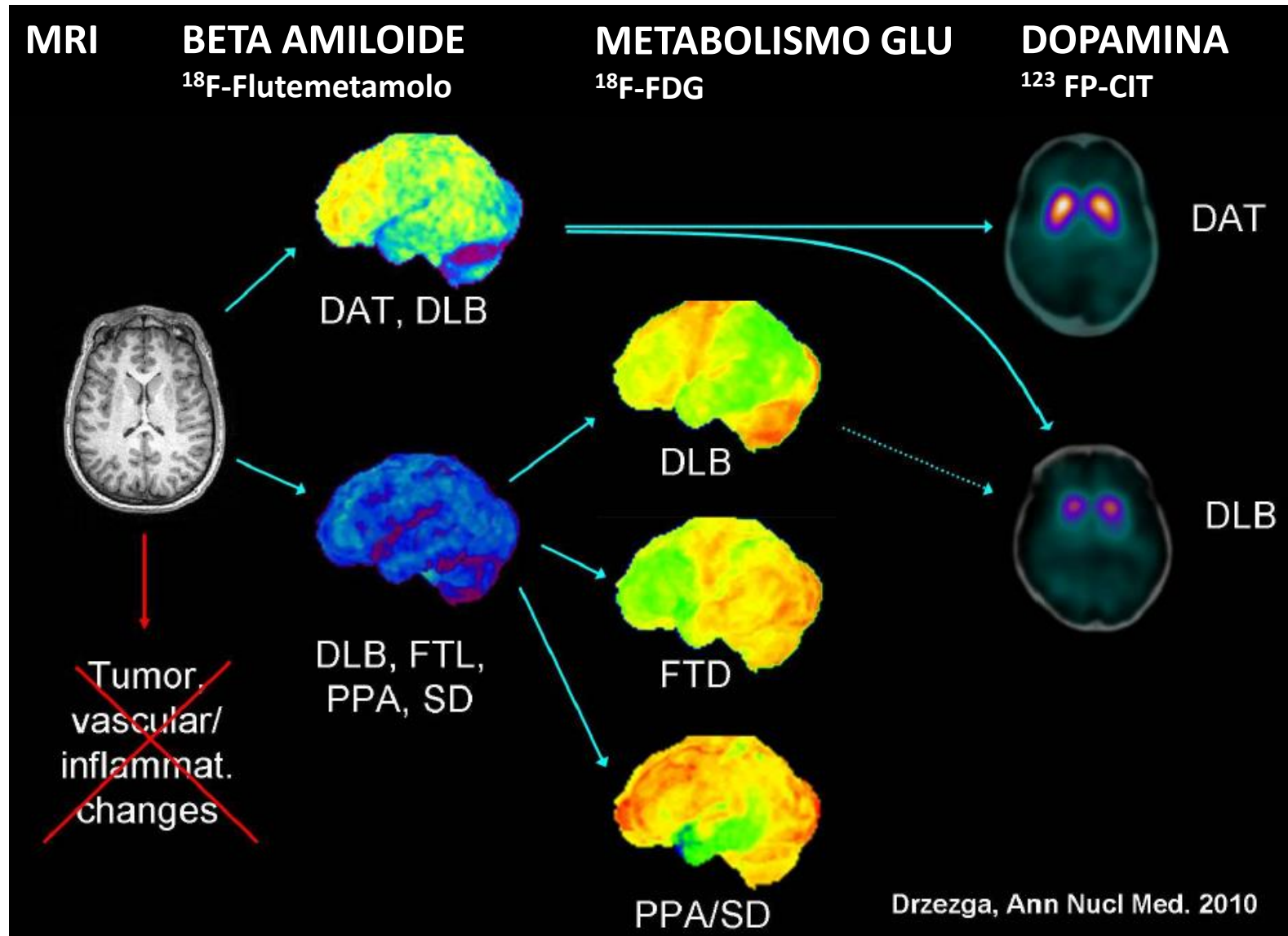
Small-vessels Large-vessels

Ischemia

Demenze: diagnosi clinica

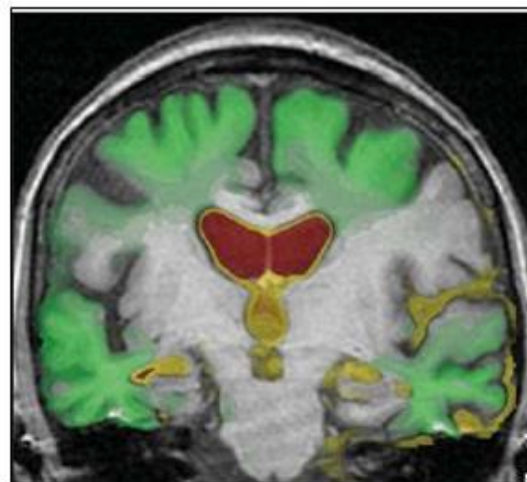
- Malattie complesse (geni+ambiente)
- Eterogeneità /variabilità (esordio-durata- evoluzione)
- Overlapping sintomatologico
- Diagnosi complessa e comunque probabilistica (100% solo autoptica)

Multimodal differential diagnosis of dementias



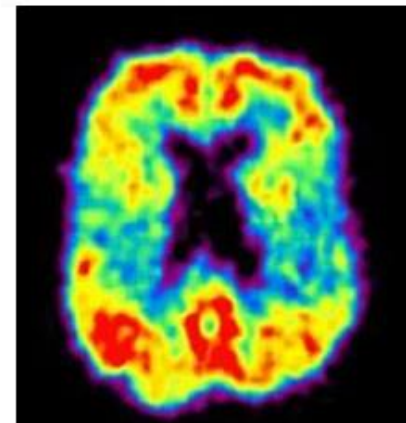
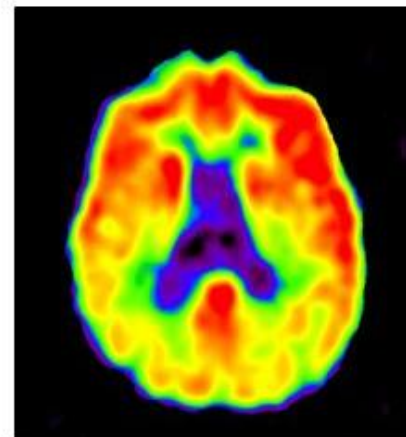
Evolution of neuroimaging in AD

- Computed Tomography
- MRI
- Volumetric MRI
- Co-registration of MRI
- Functional MRI
- FDG Glucose PET
- Amyloid Imaging
- P-Tau imaging



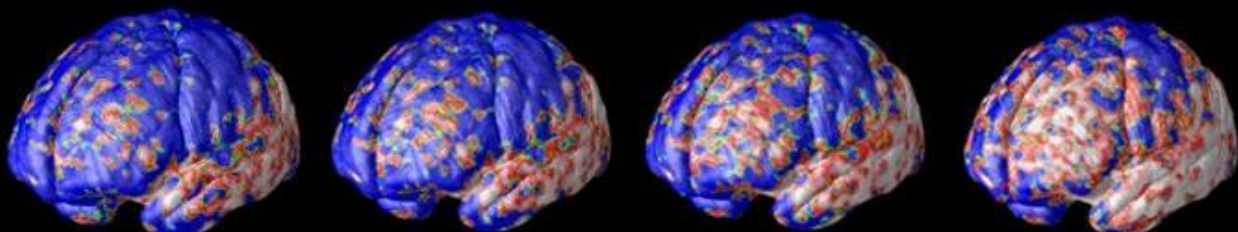
Helmuth L. *Science*.
2002;297:1260-1262.

FDG Glucose PET



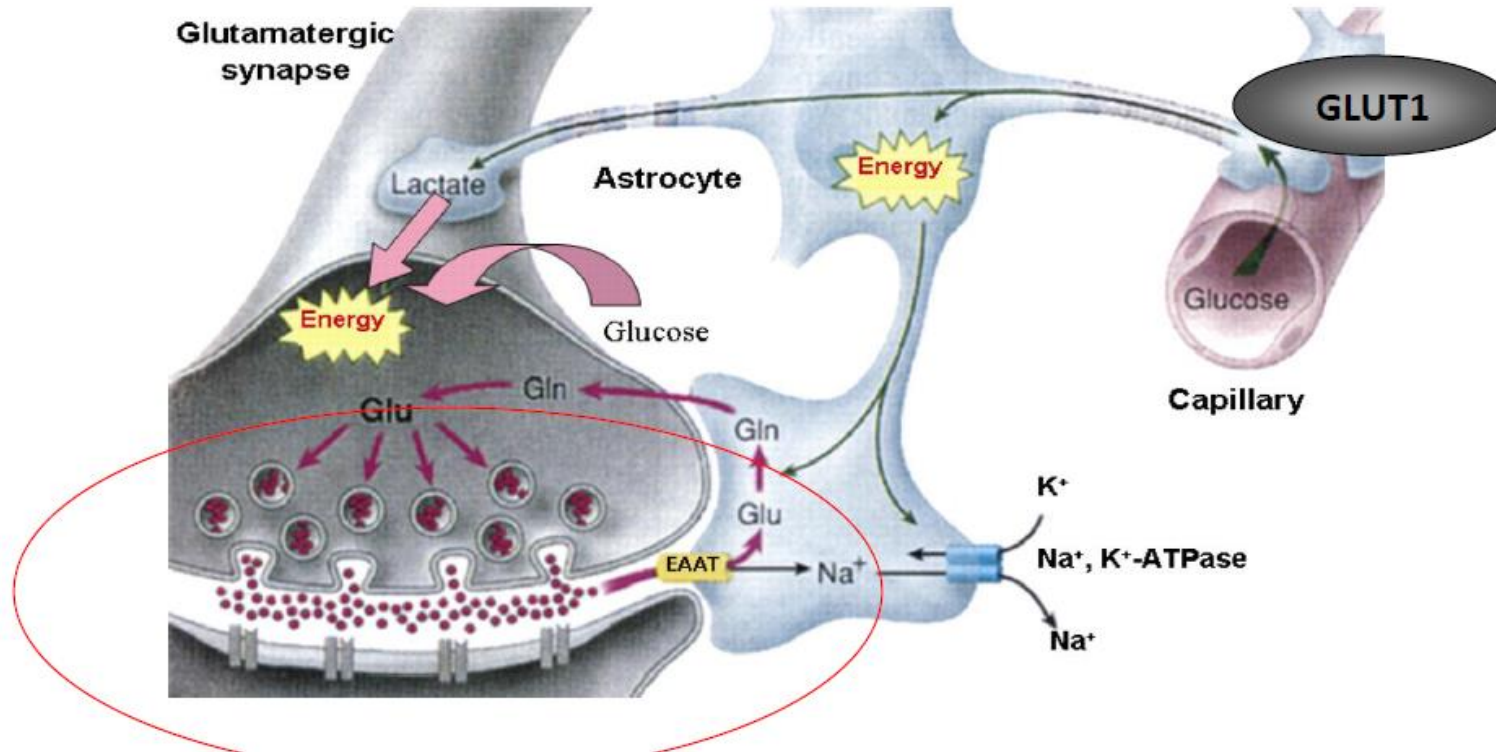
Alzheimer Disease Forum.
<http://www.alzforum.org/new/detail.asp?id=948>.

Brain Maps: Alzheimer's Disease Spreading

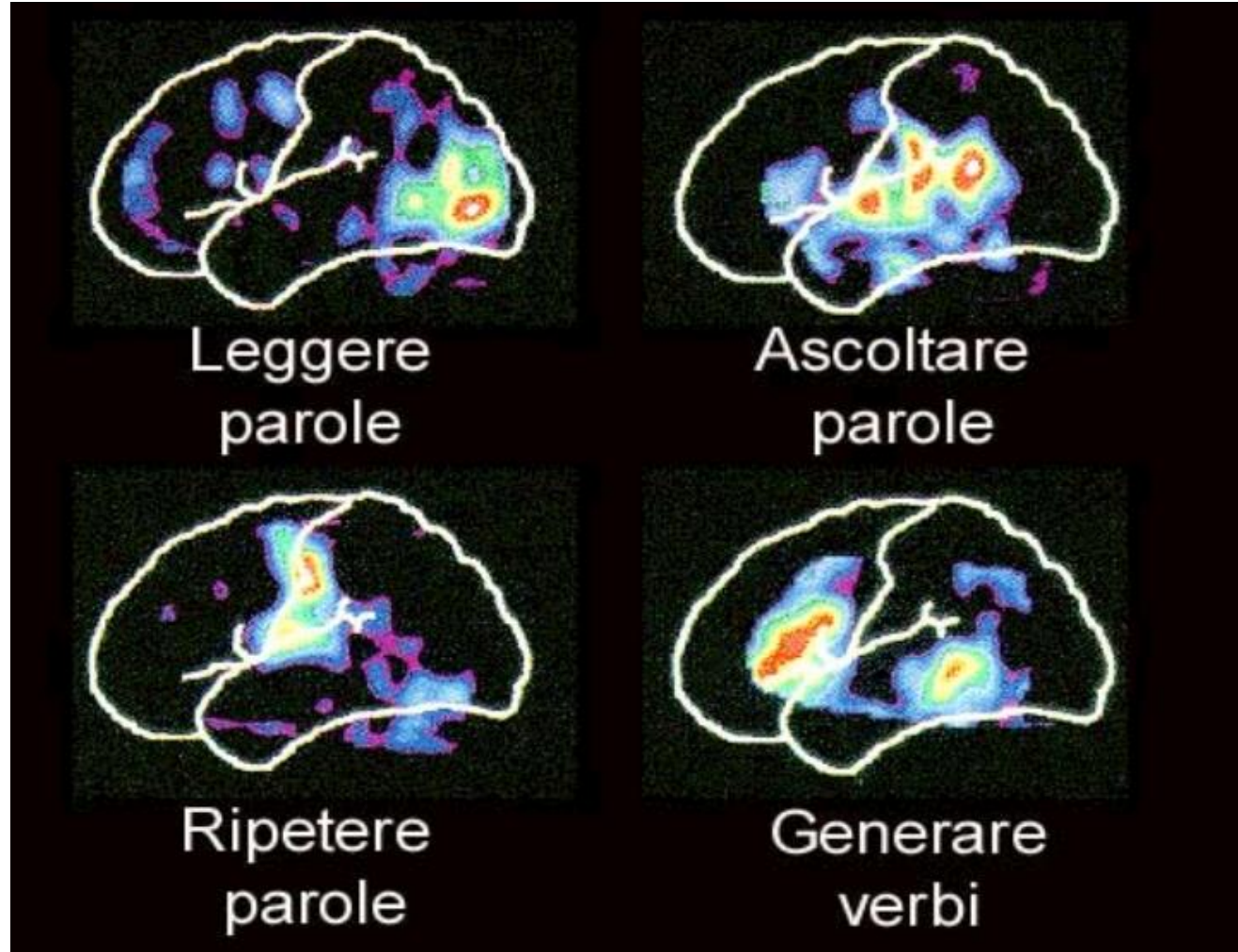


Lab of Neuro Imaging UCLA School of Medicine. www.loni.ucla.edu/~thompson/AD_4D/dynamic.html.

Brain energy metabolism



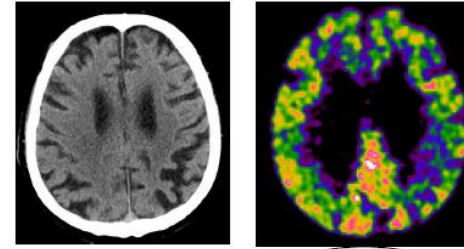
Functional imaging



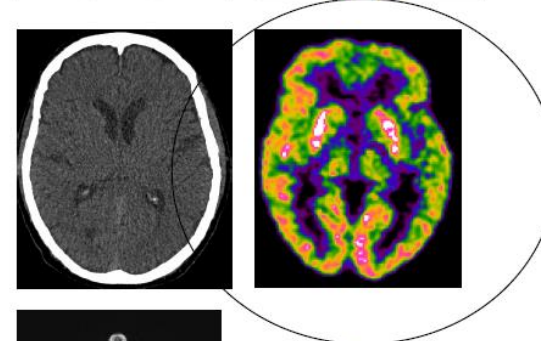
Functional imaging

What does reduced signal correspond to?

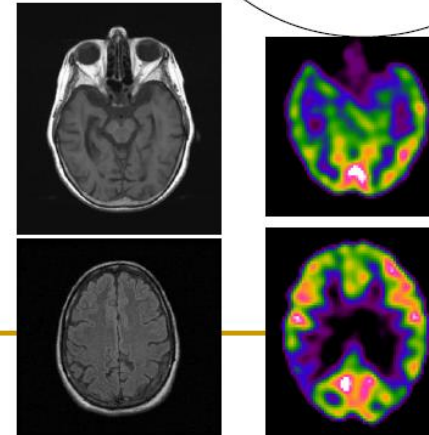
1. Atrophy



2. Reduced CMRGlu due to reduction of local synapses (cortico-cortical neurons)



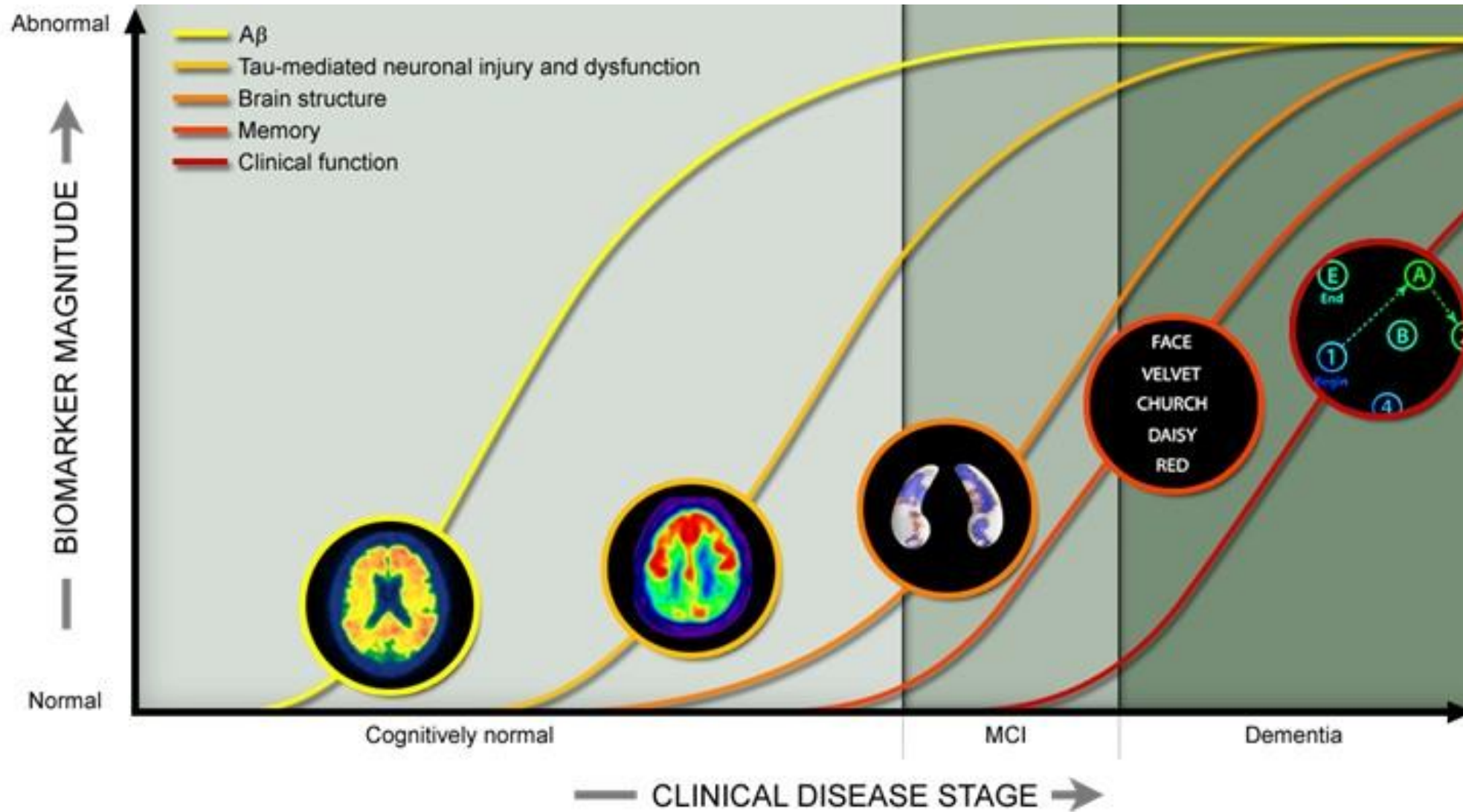
3. Reduced CMRGlu due to reduction of distant synapses (deafferentation/diaschisis)



Rodriguez-Vieitez E et al. Methods Biol Mol, 2018

Imaging Neuroinflammation: Quantification of Astrocytosis in a Multitracer PET Approach.

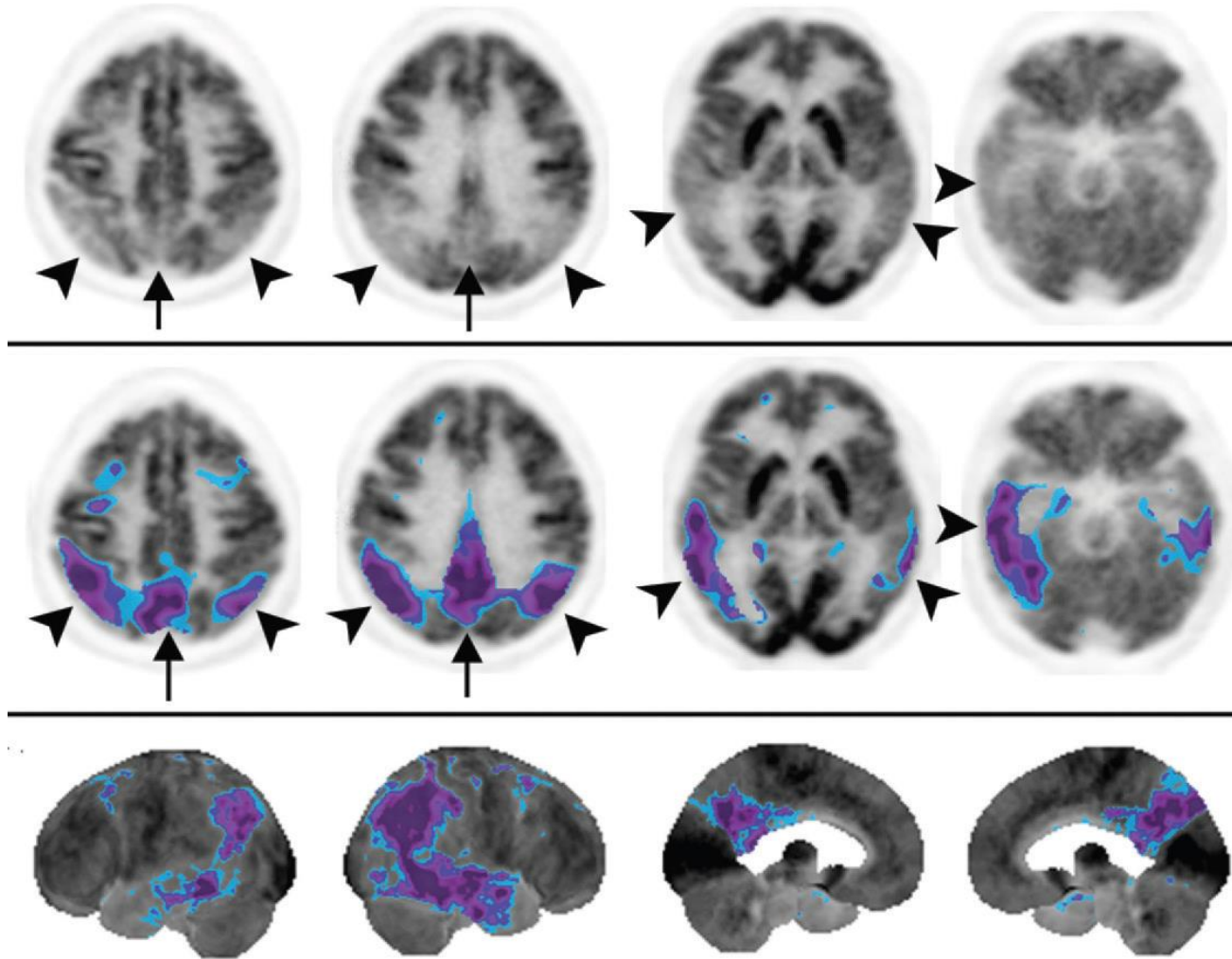
Biomarkers



Sommario

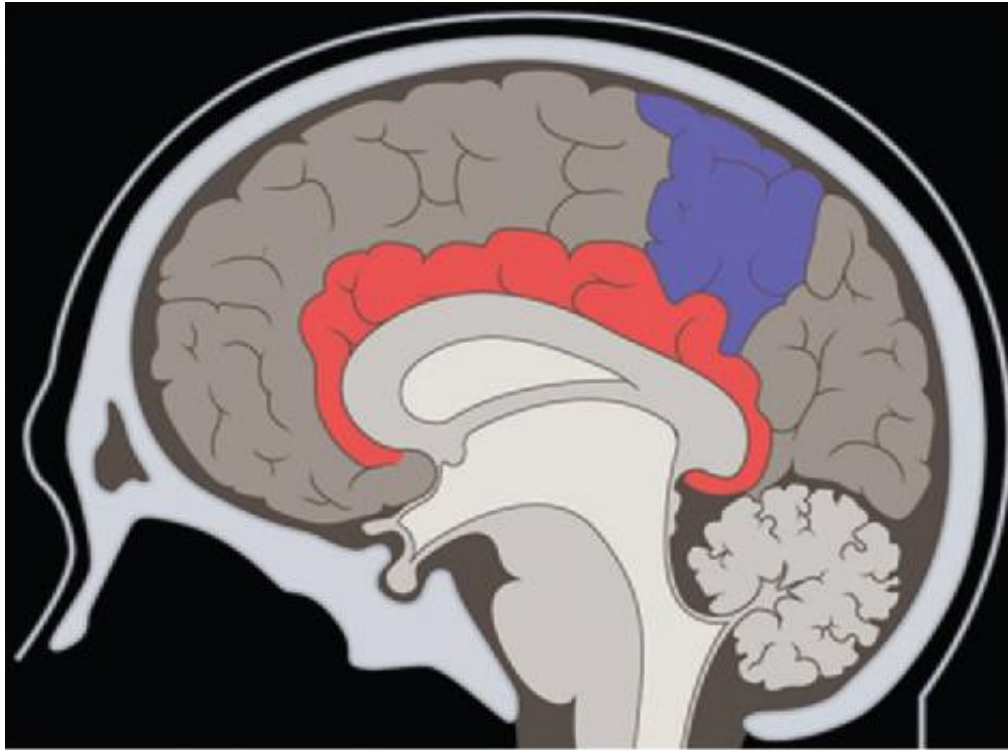
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18FDG-PET: Characteristic patterns of AD

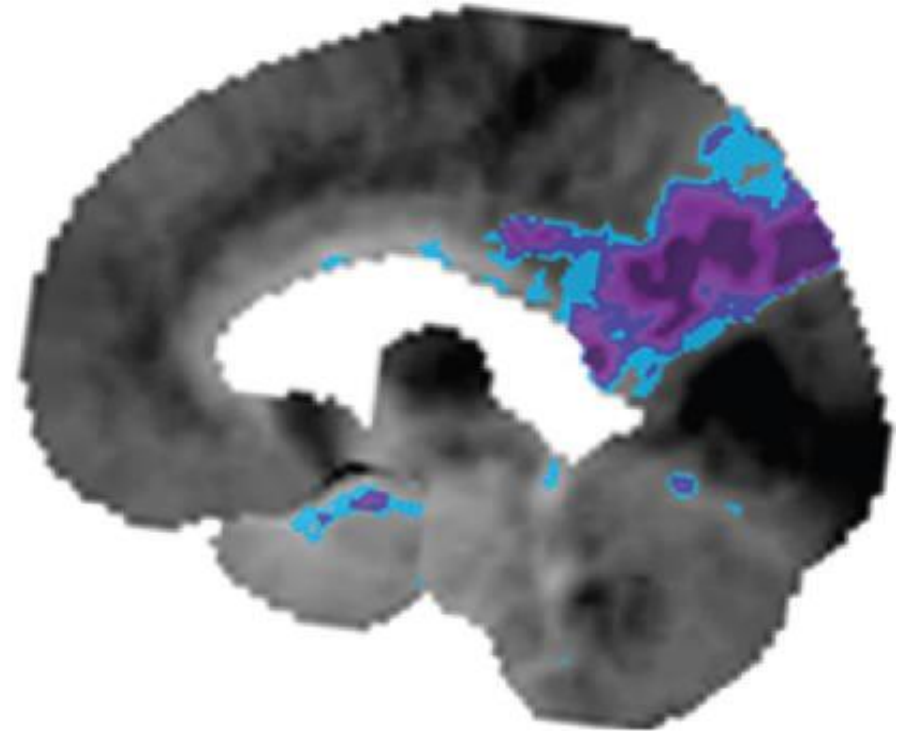


Parietal-temporal
Posterior cingulate
Precuneus
Medial temporal lobe

18FDG-PET: Characteristic patterns of AD



a.

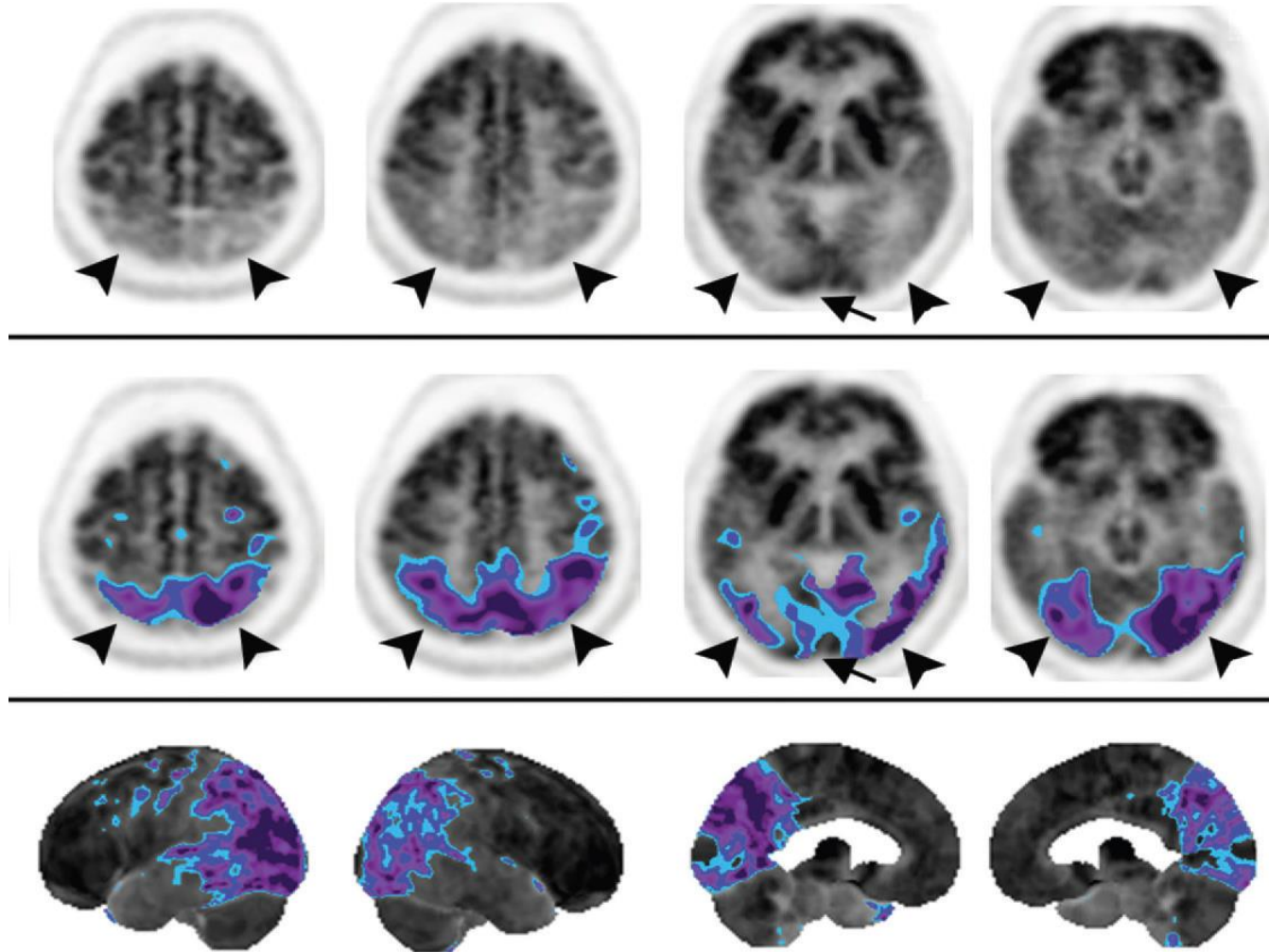


b.

Surface-rendered image shows FDG hypometabolism in the posterior cingulate and precuneus cortices. Blue = -2 SDs, purple = -3 SDs. The cingulate gyrus and precuneus are important structures to identify and analyze when reviewing brain FDG PET images obtained in patients with cognitive impairment.

Minoshima, 2014

Posterior cerebral atrophy (PCA)

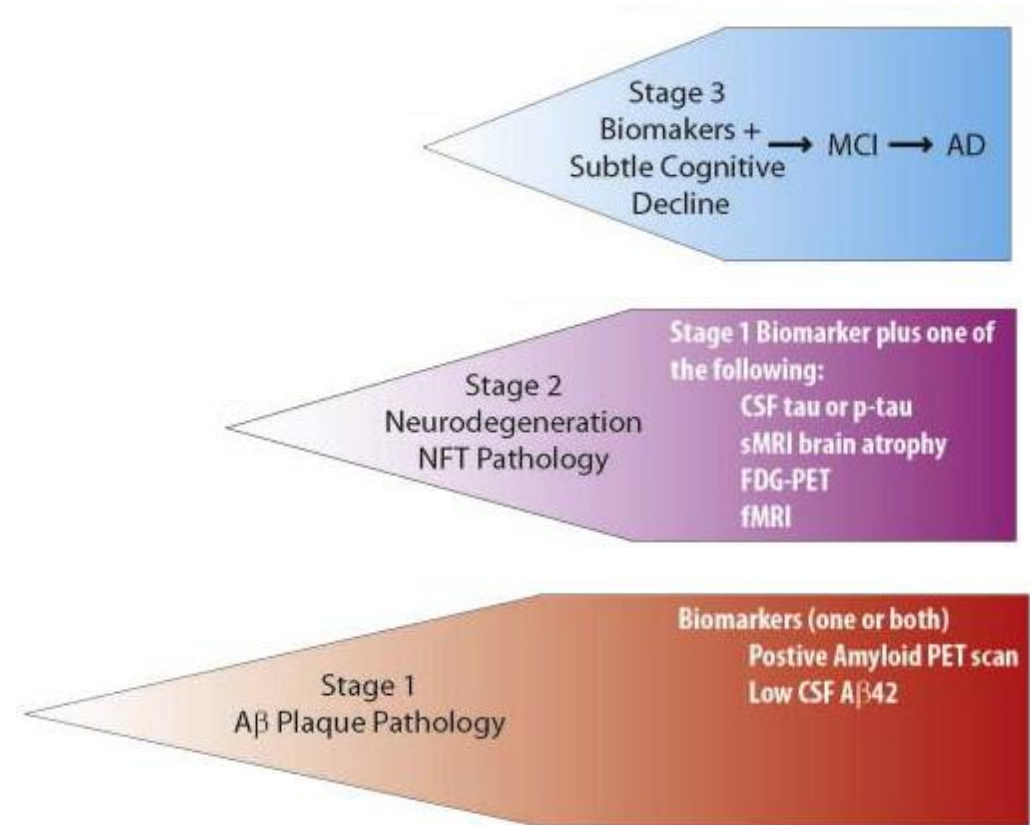
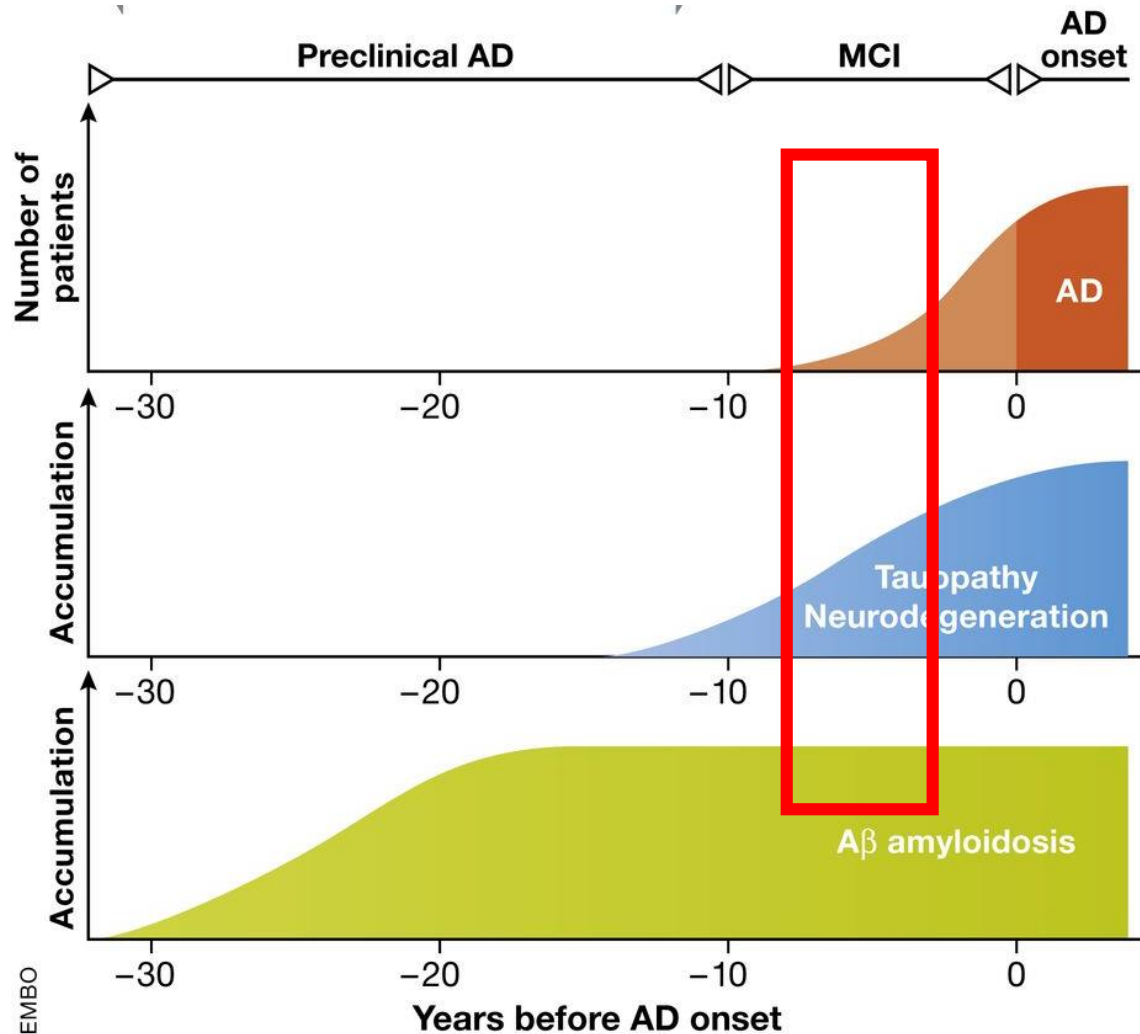


Posterior cortical
hypometabolism of AD

+

involvement of the
lateral occipital
association cortex

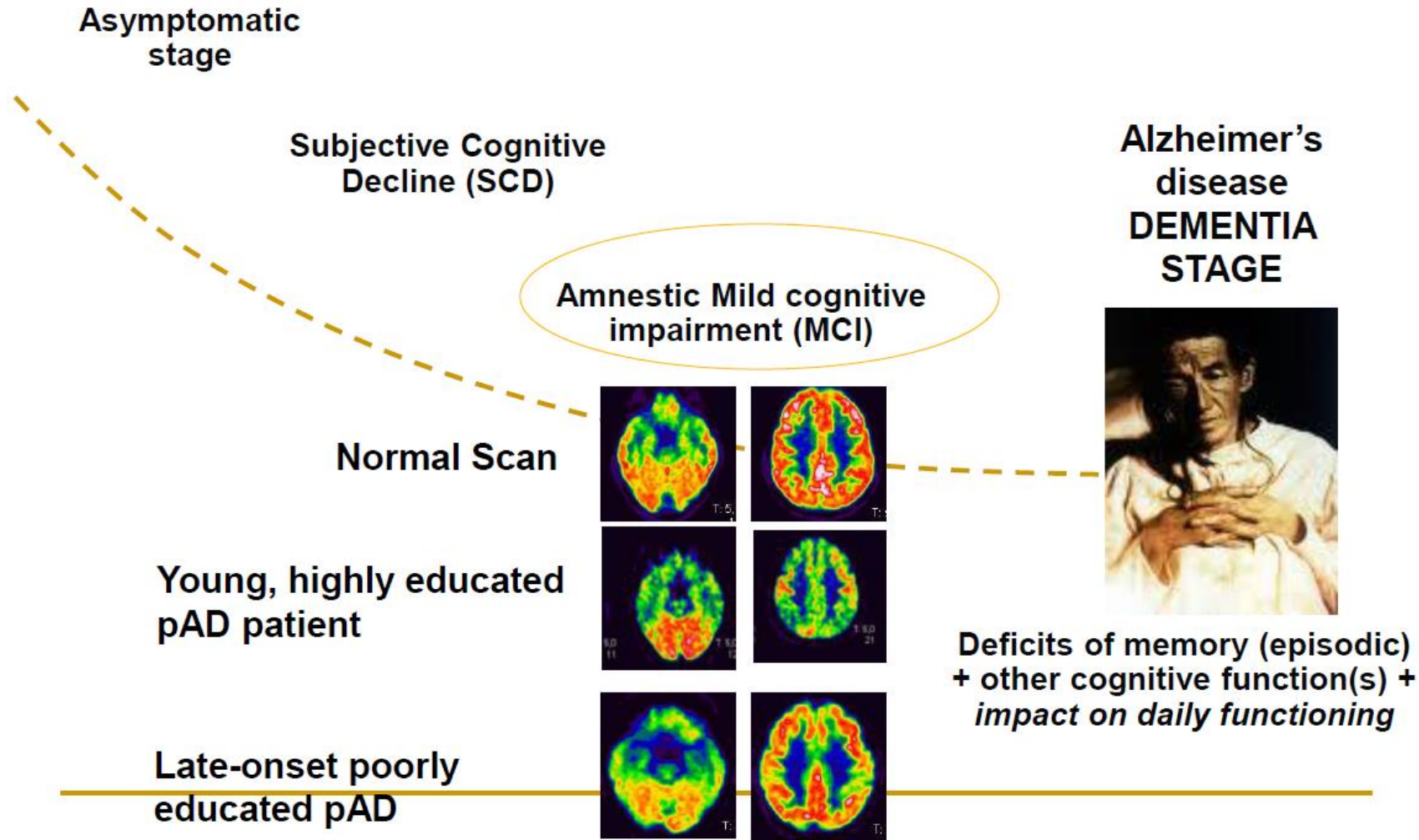
Window for AD prevention



Sasaguri H et al, EMBO 2017

Golde et al, 2011

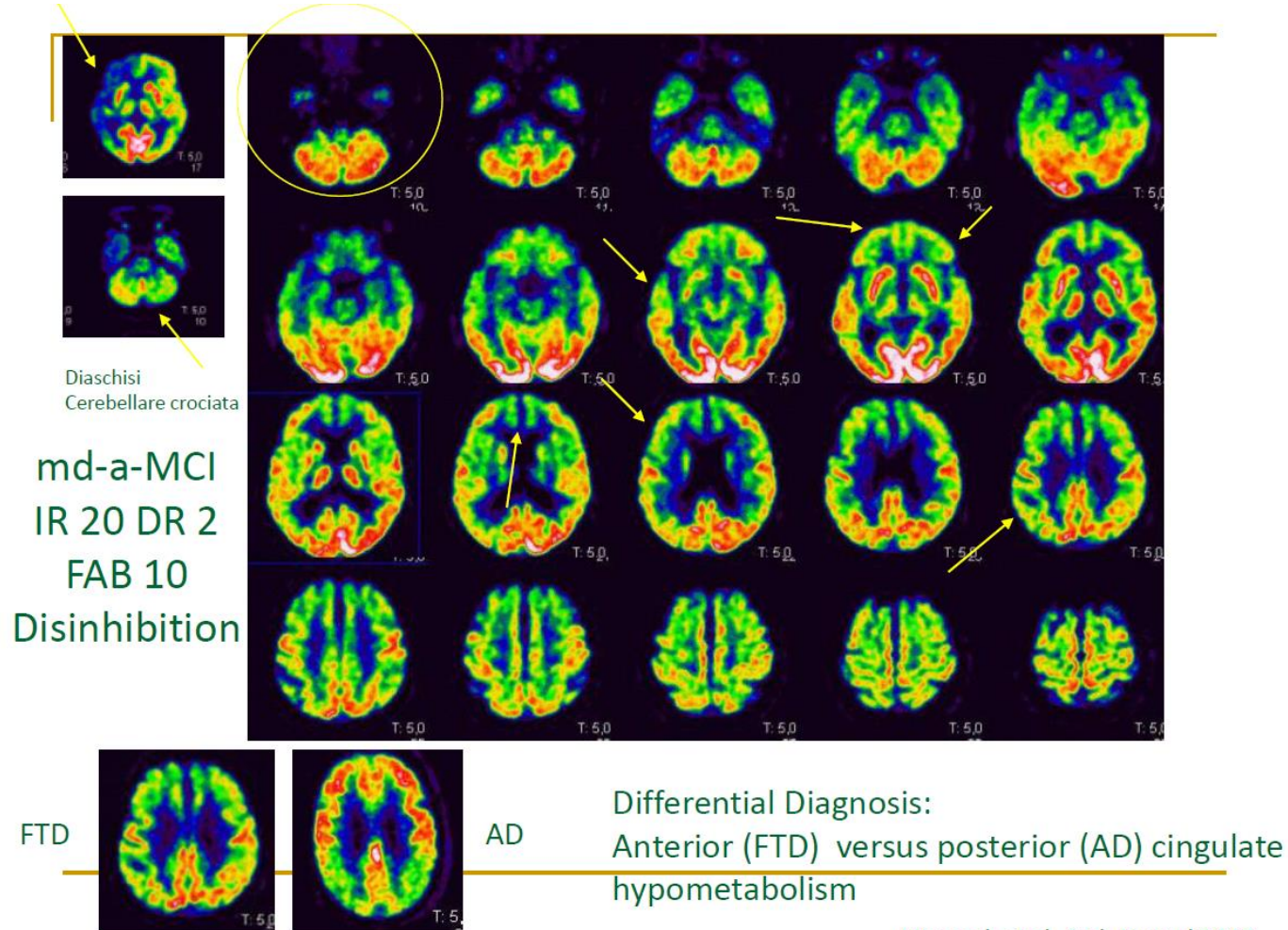
Pre-dementia stage



Ewers M. et al, Neurology 2013

Cognitive reserve associated with FDG-PET in preclinical Alzheimer disease.

MCI Differential Diagnosis: AD vs FTD

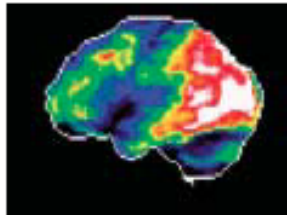


Caminiti SP et al. Neuroimage Clin, 2018
FDG-PET and CSF biomarker accuracy in prediction of conversion to different dementias in a large multicentre MCI cohort.

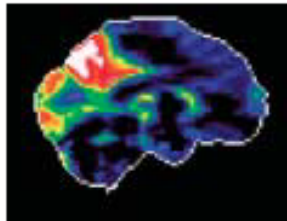
Differential diagnosis: AD vs FTD

Maggior fonte di errore: ipometabolismo temporo-parietale

AD



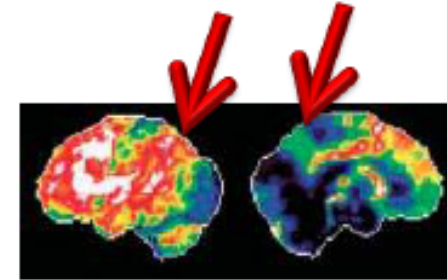
Ipometabolismo
parieto-temporale
più sensibile



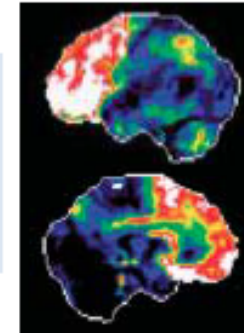
Ipometabolismo
PCC/precuneo
più specifico

FTD

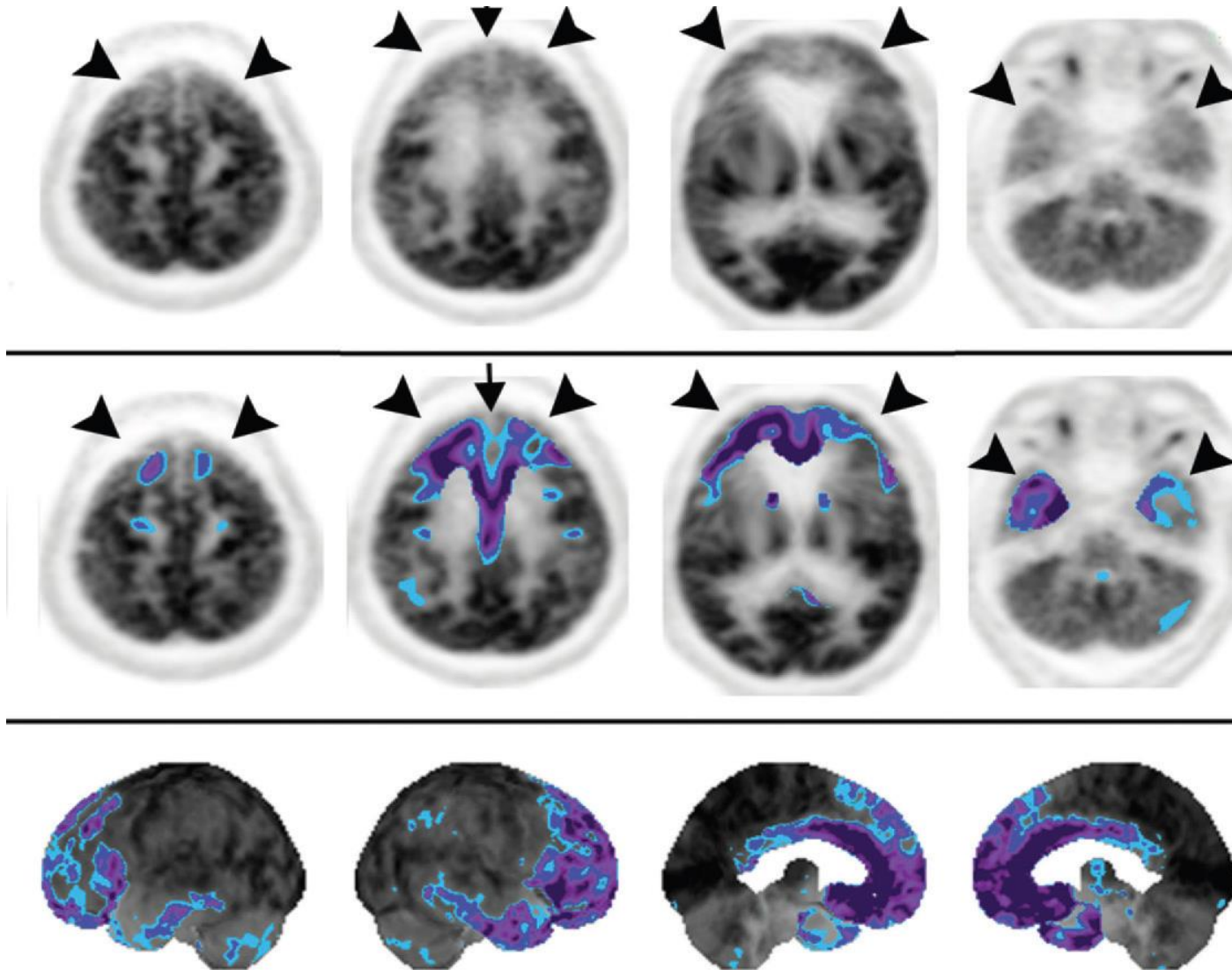
50% FTD
ipometabolismo
parieto-temporale



Ipometabolismo
ACC e temporale anteriore
più specifico
(anche in presenza di ipo parieto-temporale)



Characteristic metabolic patterns of FTD

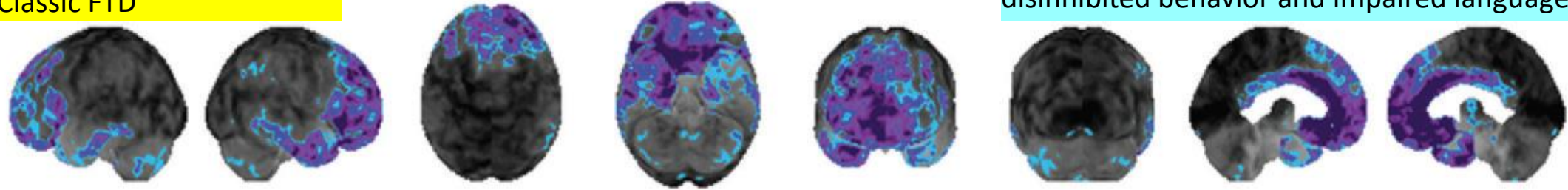


Frontal
Anterior temporal
Anterior cingulate

Relatively preserved
PCC /precuneus

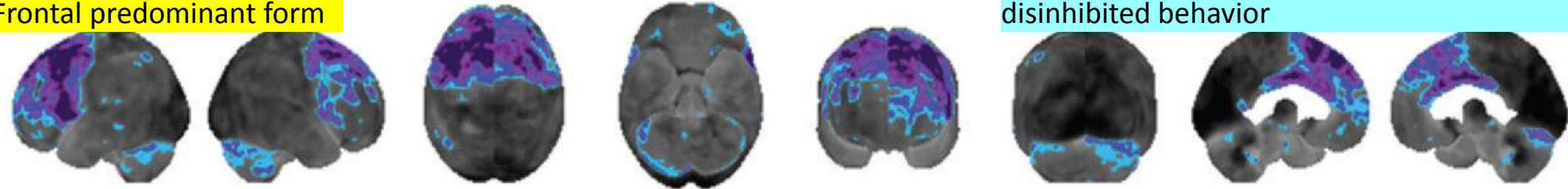
Fronto-Temporal Dementia Variants

Classic FTD



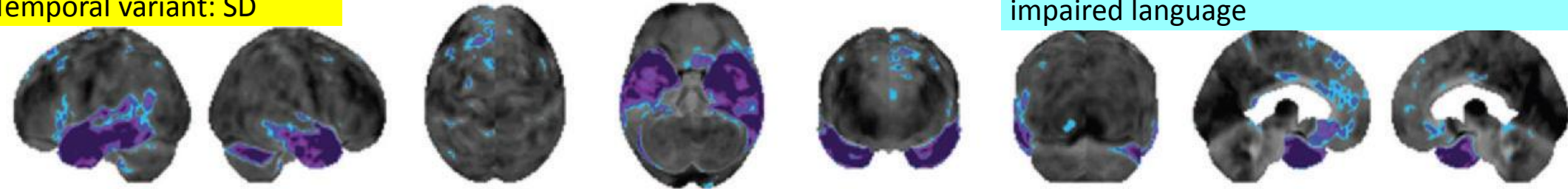
disinhibited behavior and impaired language

Frontal predominant form



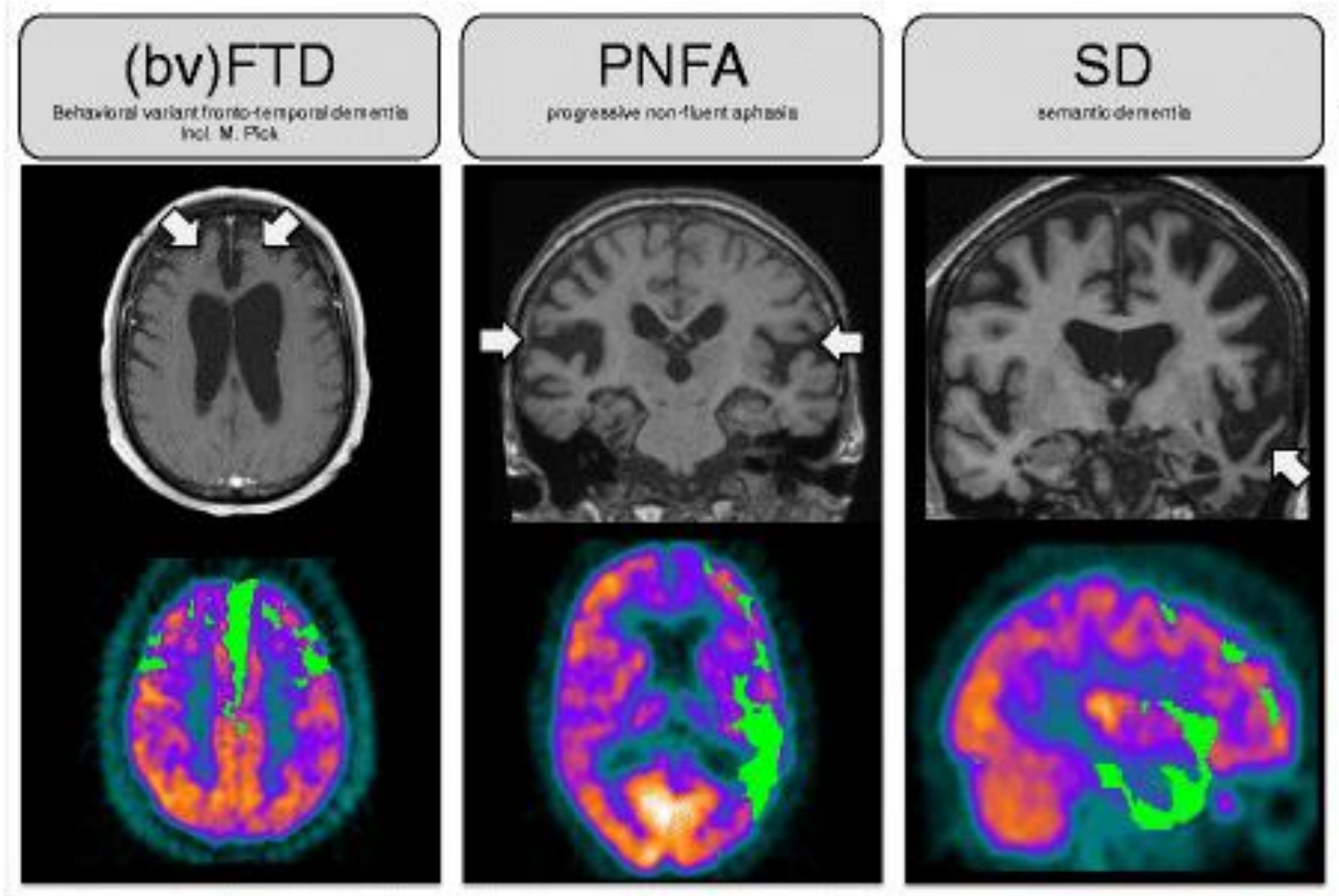
disinhibited behavior

Temporal variant: SD



impaired language

Fronto-Temporal Dementia Variants



^{18}F FDG-PET: bv FTD

Pazienti con **apatia**

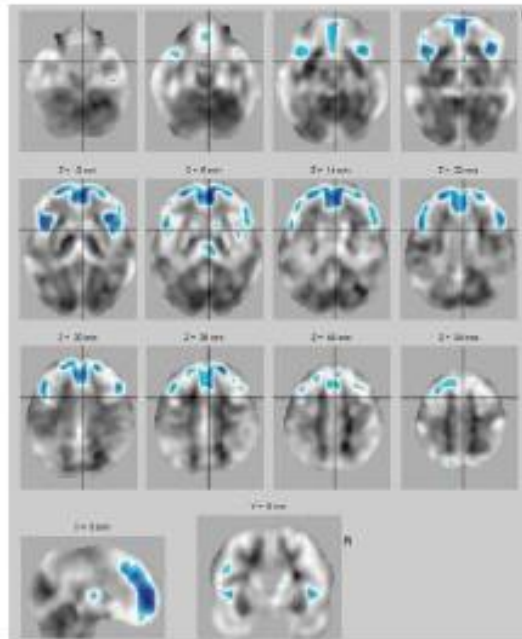
Ipometabolismo

Corteccia frontale mediale

Frontale polare

DLPFC

Parte anteriore di OFC



Pazienti con **disinibizione**

Ipometabolismo

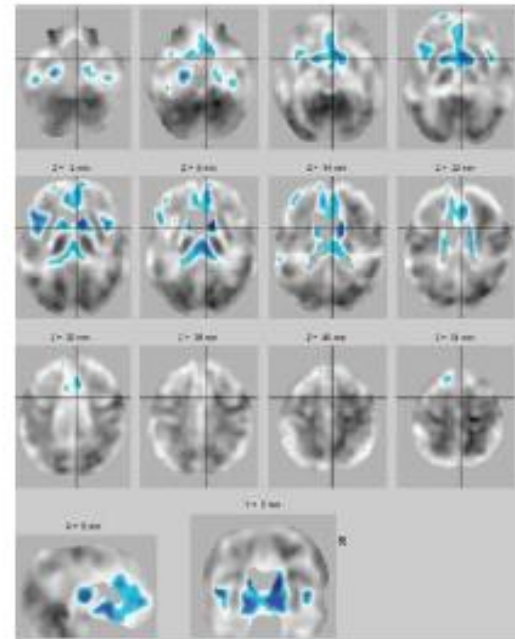
Regione posteriore di OFC

ACC

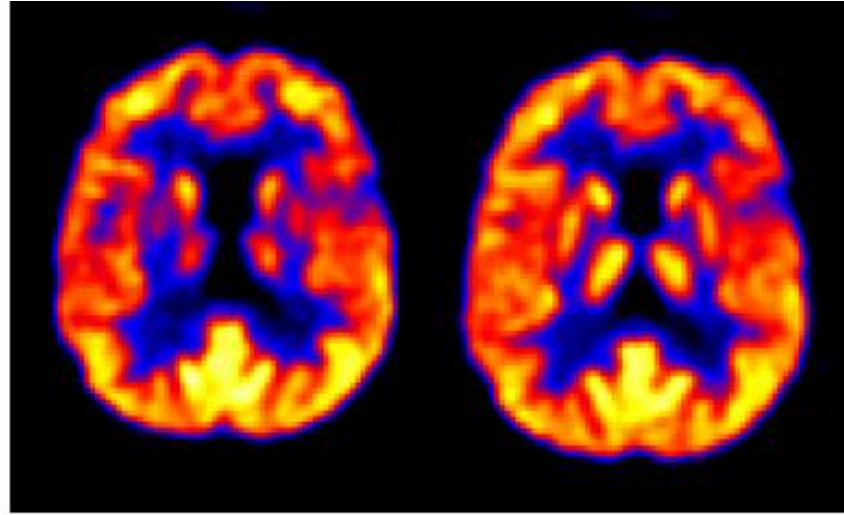
Lobo temporale inferiore

Ippocampo/amigdala

Nucleus accumbens

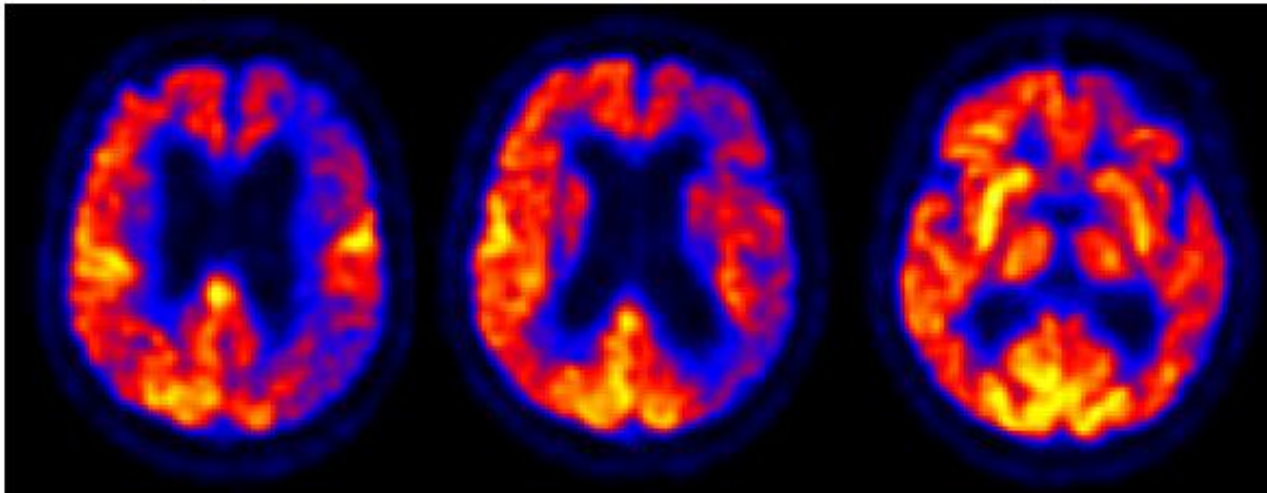


Broca's area hypometabolism: PNFA



Asimmetry: LEFT LOBE

Inferior frontal gyrus
Inferior temporal lobe
Anterior insula



Nestor PJ et al. 2003

International consensus criteria for bv FTD

III. Probable bv FTD

All of the following behavioral/cognitive symptoms (A-C) must be present:

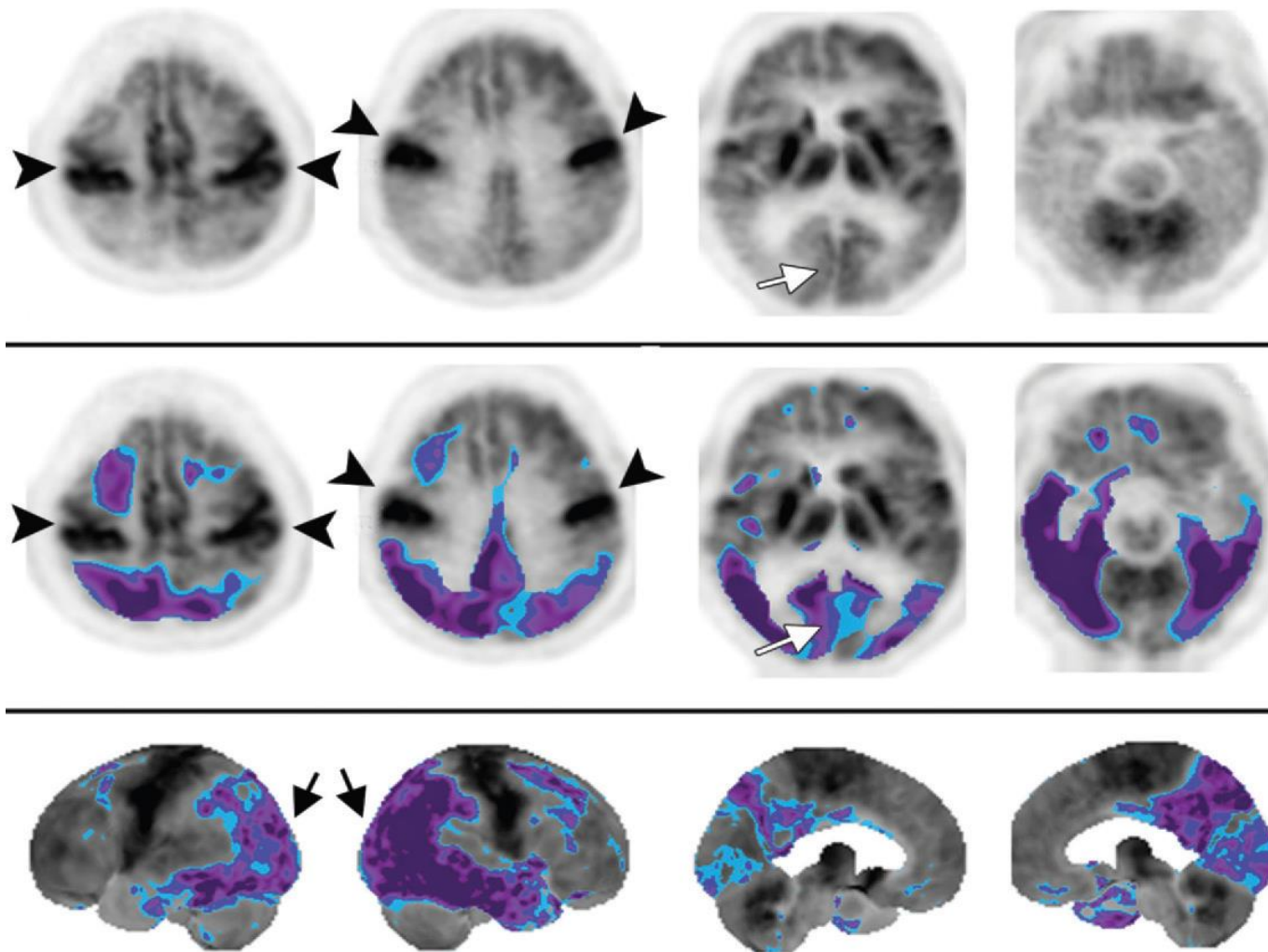
- A. Meets criteria for possible FTD
- B. Shows significant functional decline (by caregiver report or as evidenced by CDR)
- C. Consistent Imaging
≥ 1 between frontal and/or anterior temporal atrophy on MRI or CT and frontal and/or anterior temporal hypoperfusion/hypometabolism on SPECT/PET

IV. Definite bvFTD

All of the following behavioral/cognitive symptoms (A-C) must be present:

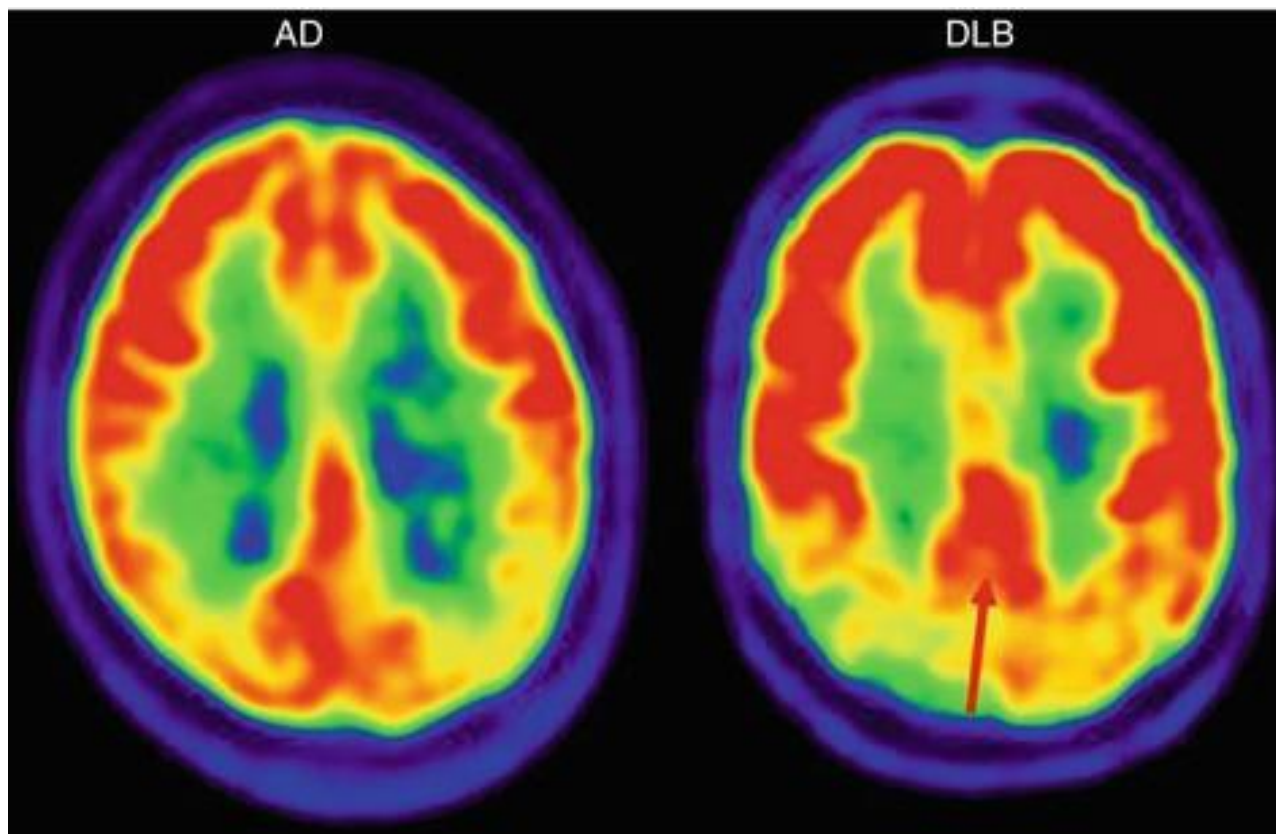
- A. Meets criteria for probable bvFTD (A+either B or C)
- B. Histopathologic evidence on biopsy or autopsy
- C. Presence of a known pathogenic mutation

Characteristic Metabolic patterns of LBD



Ventrolaterale frontale
Parietal-temporal
Precuneus
Occipital
Visual cortex

^{18}F FDG-PET Cingulate Island Sign (CIS)



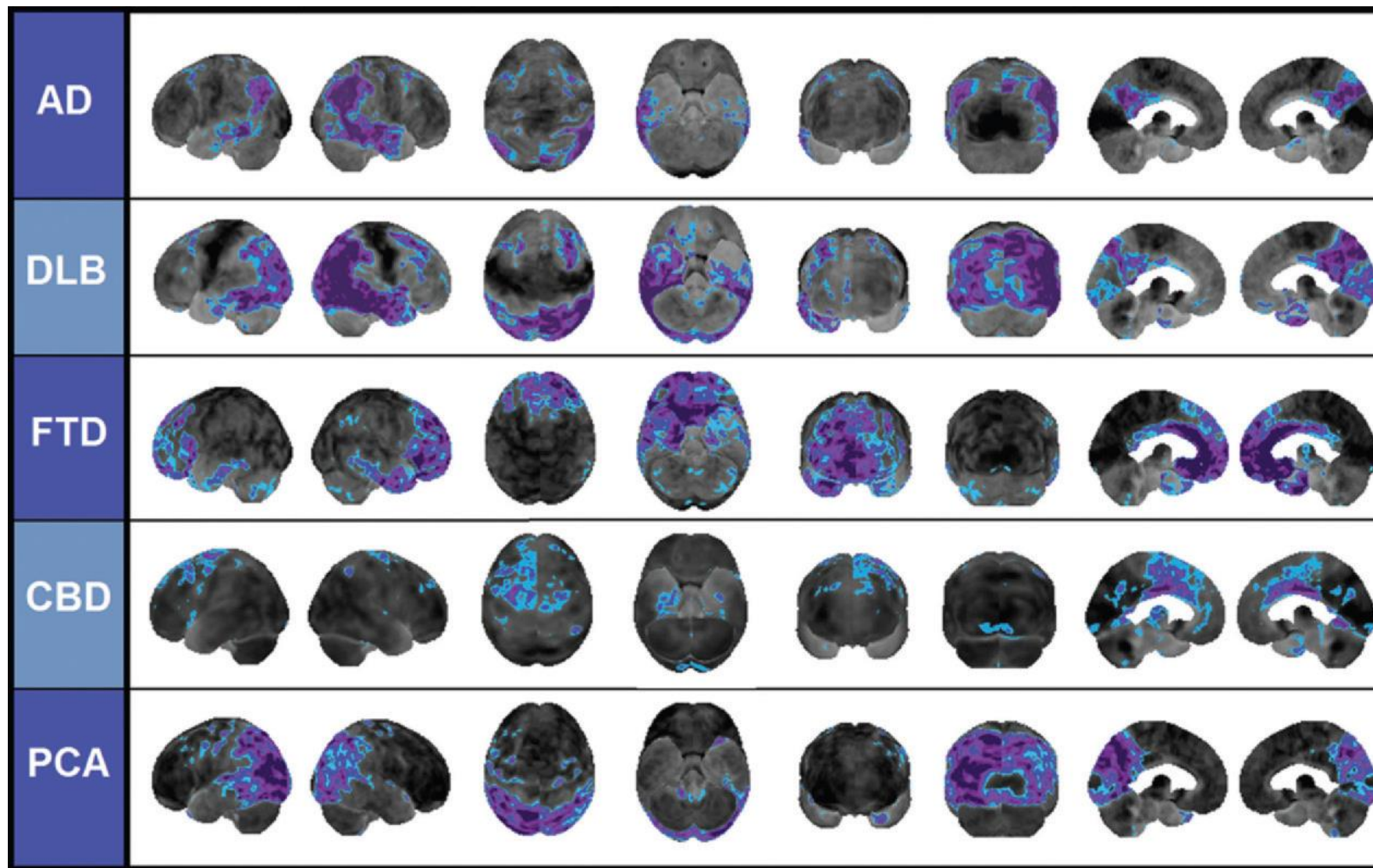
Ratio: PCC/precuneus + cuneus

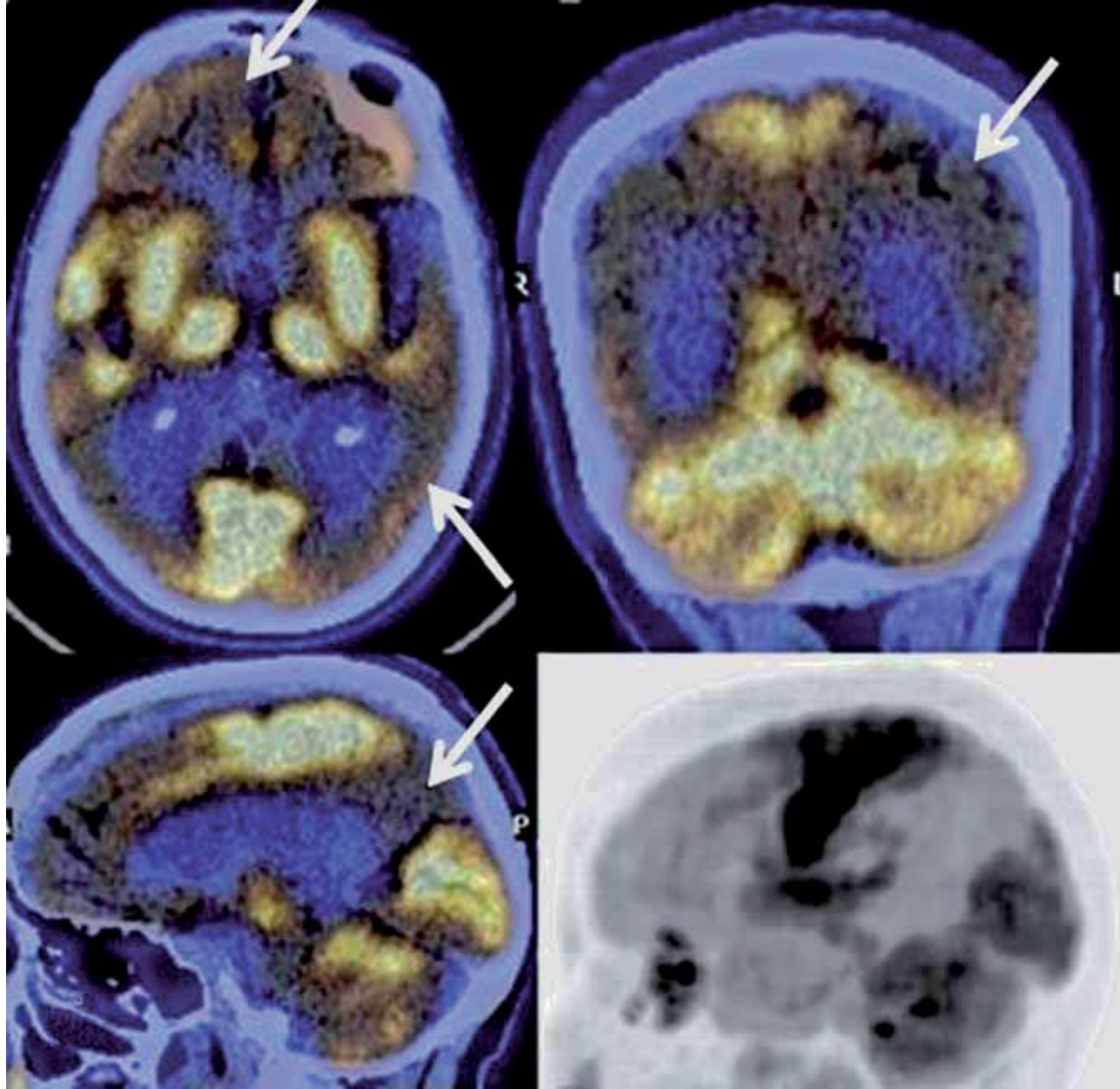
Attenzione:

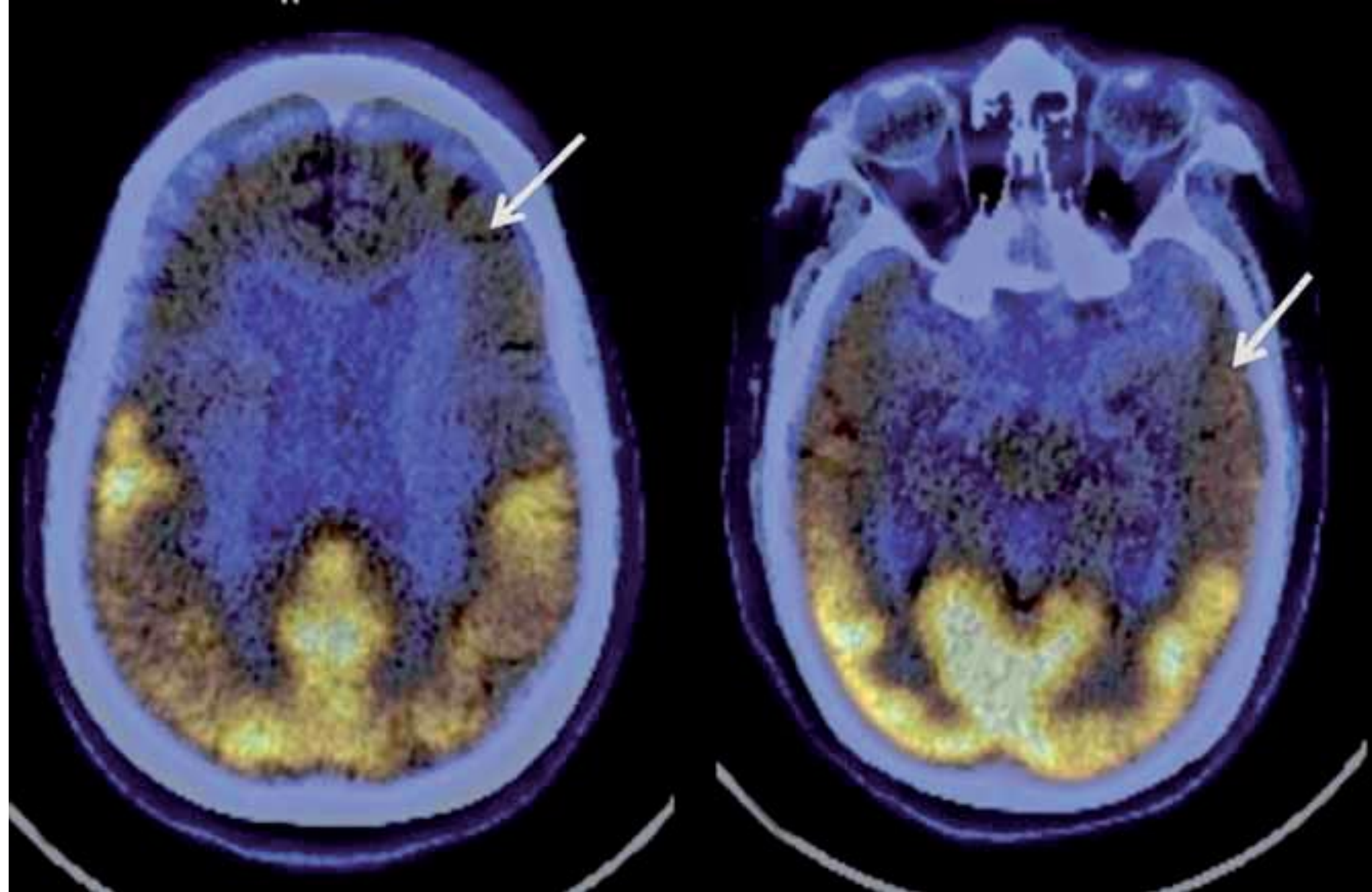
è presente anche nella PDD e PCA

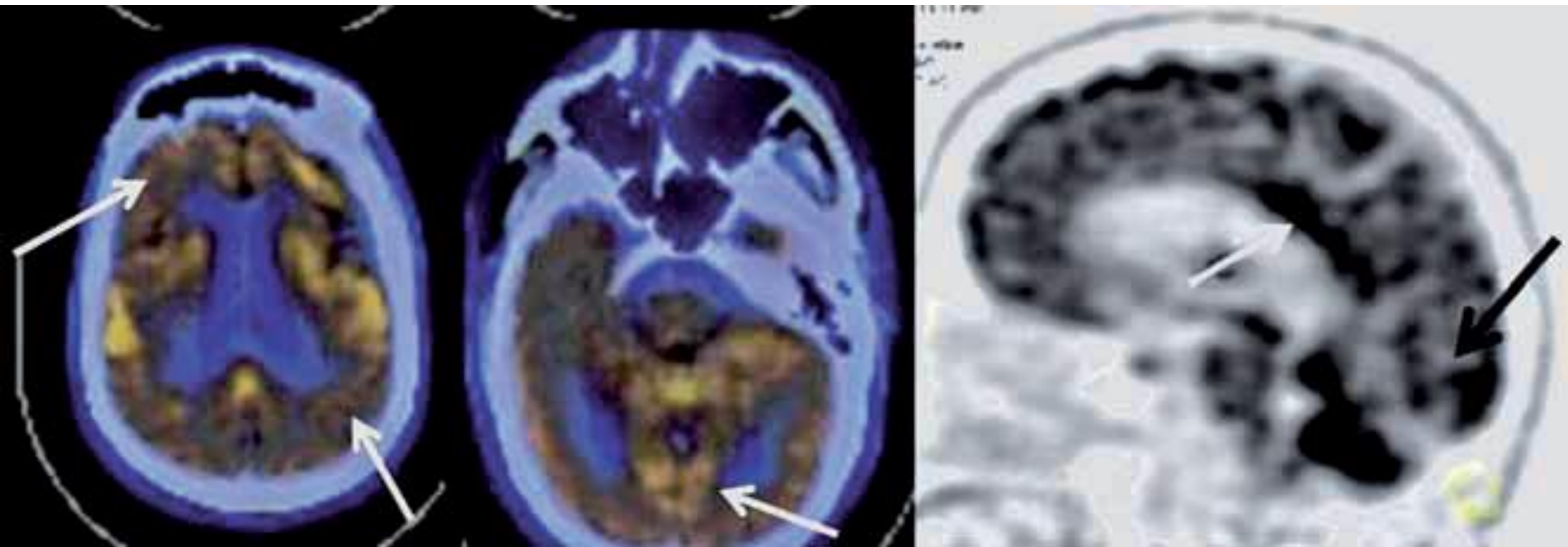
Lim SM et al. JNM 2009

18 FDG-PET differential diagnosis of dementias





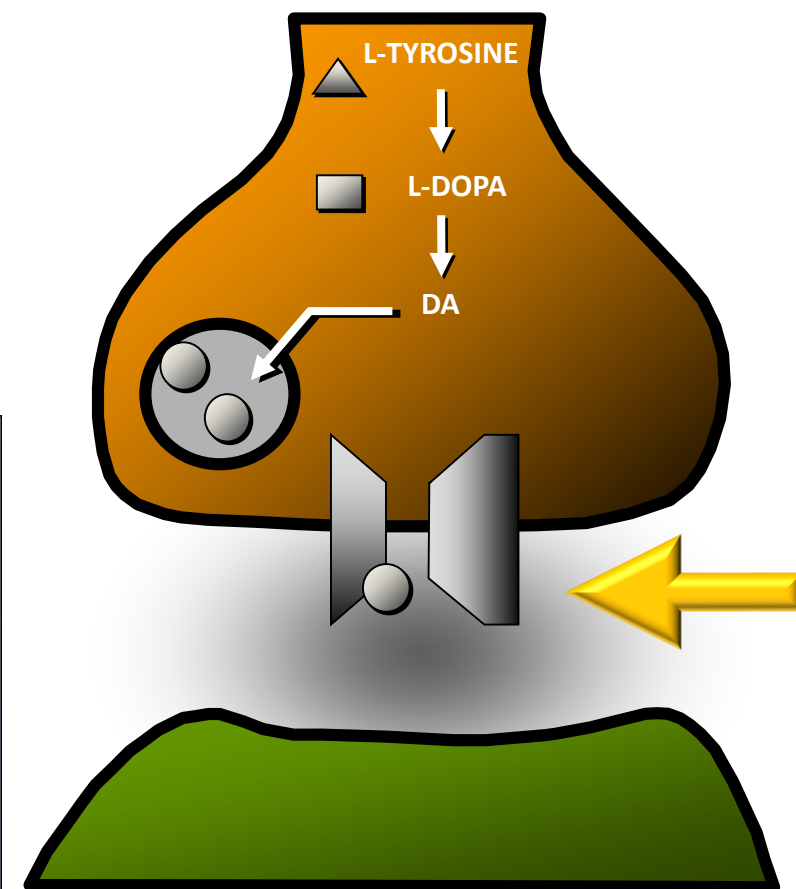
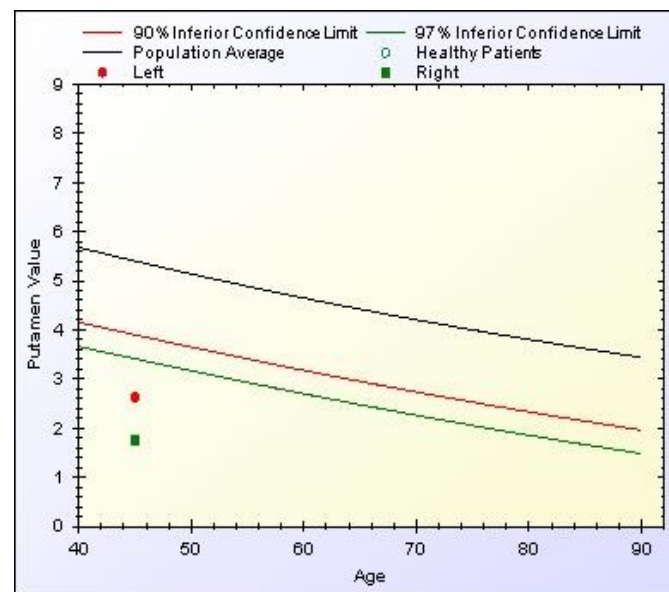
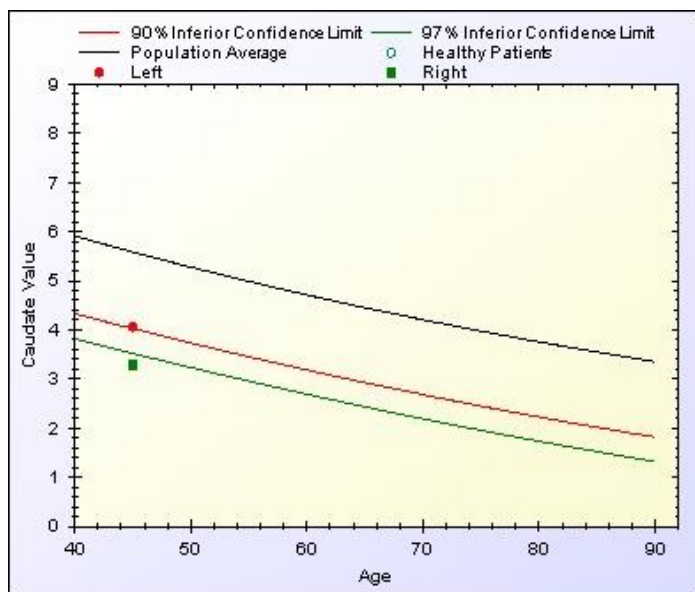
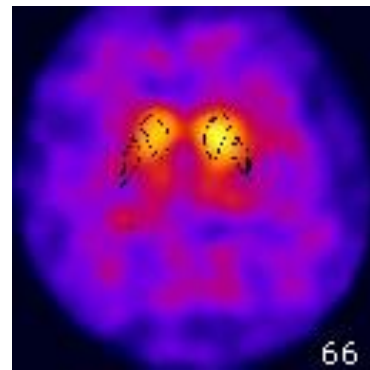
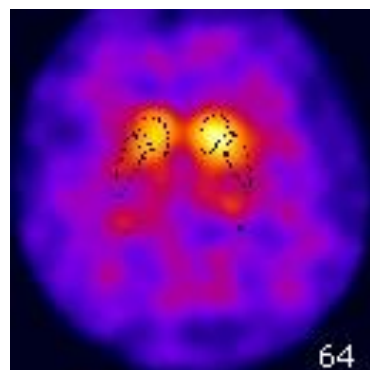
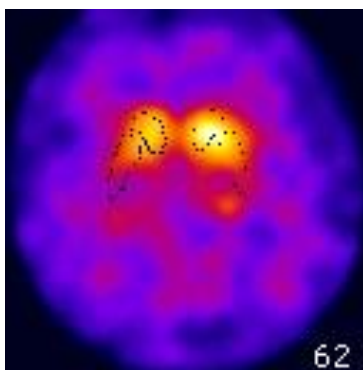




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 - Lewy Body Dementia
- **Datscan e MIBG SPET**
- PET con tracciante per amiloide: indicazioni

123I-Ioflupane (Datscan): LBD



FDG-PET e Datscan-SPET: Indicazioni

E' consigliato l'uso della **PET con ^{18}F -FDG**:

nella **diagnosi precoce** dell'**AD** e nella dd tra **AD** e **VD** e tra **AD** e **FTD**

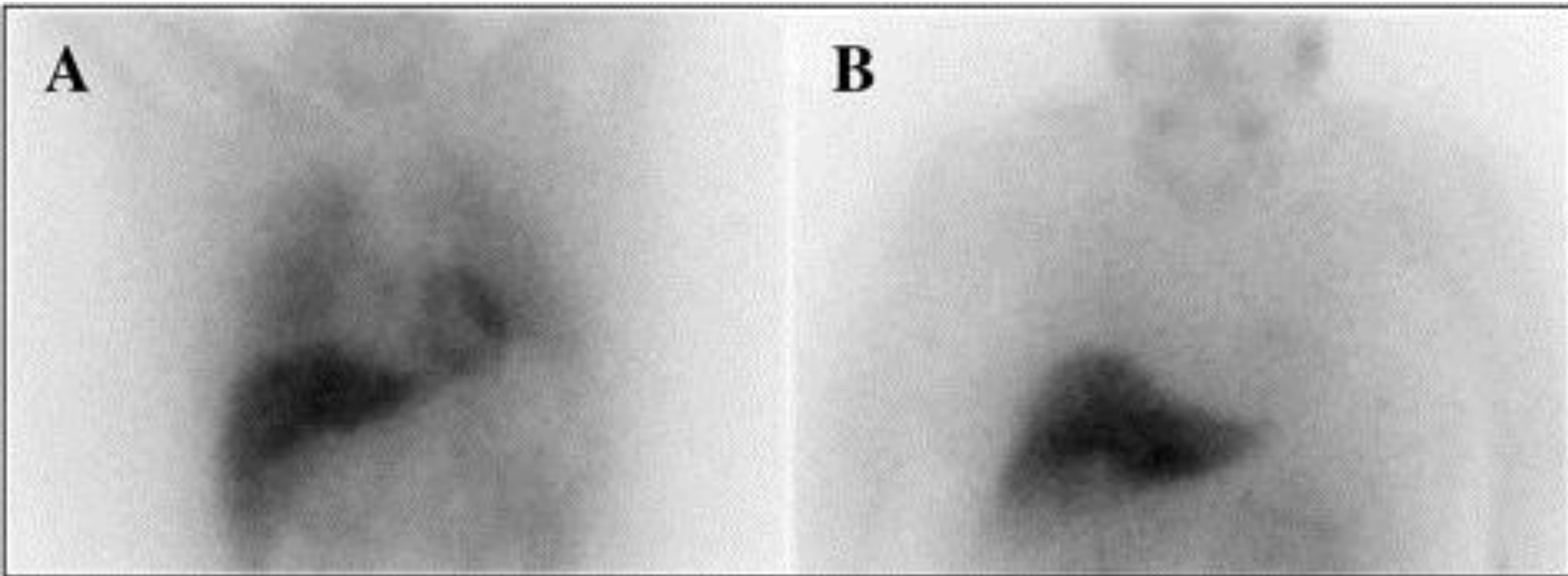
E' consigliato l'uso della **SPECT con ^{123}I -FP-CIT**

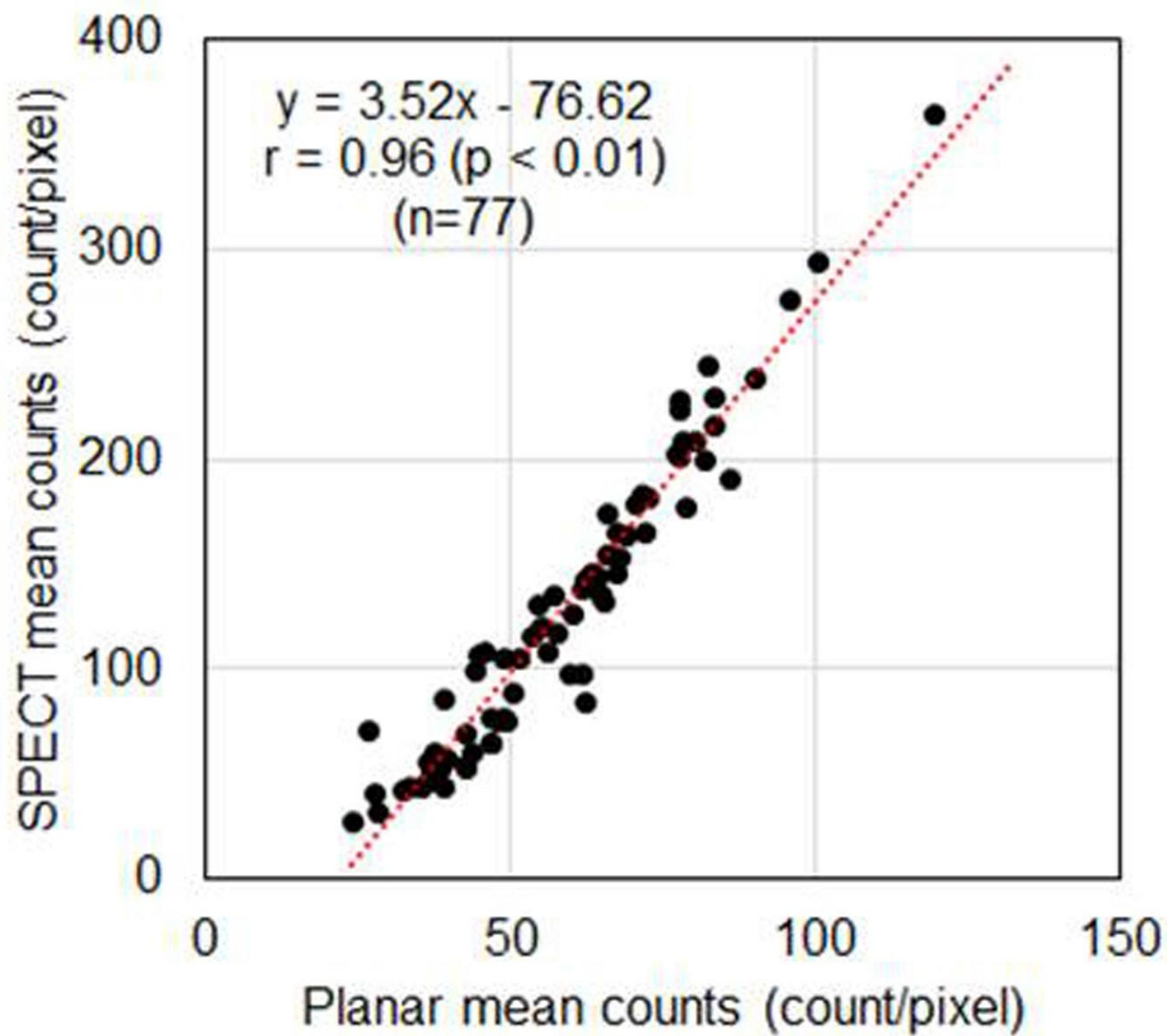
nella dd tra **AD** e **LBD**



Morbelli et al. ELNMI 2015

^{123}I -MIBG: AD vs LBD

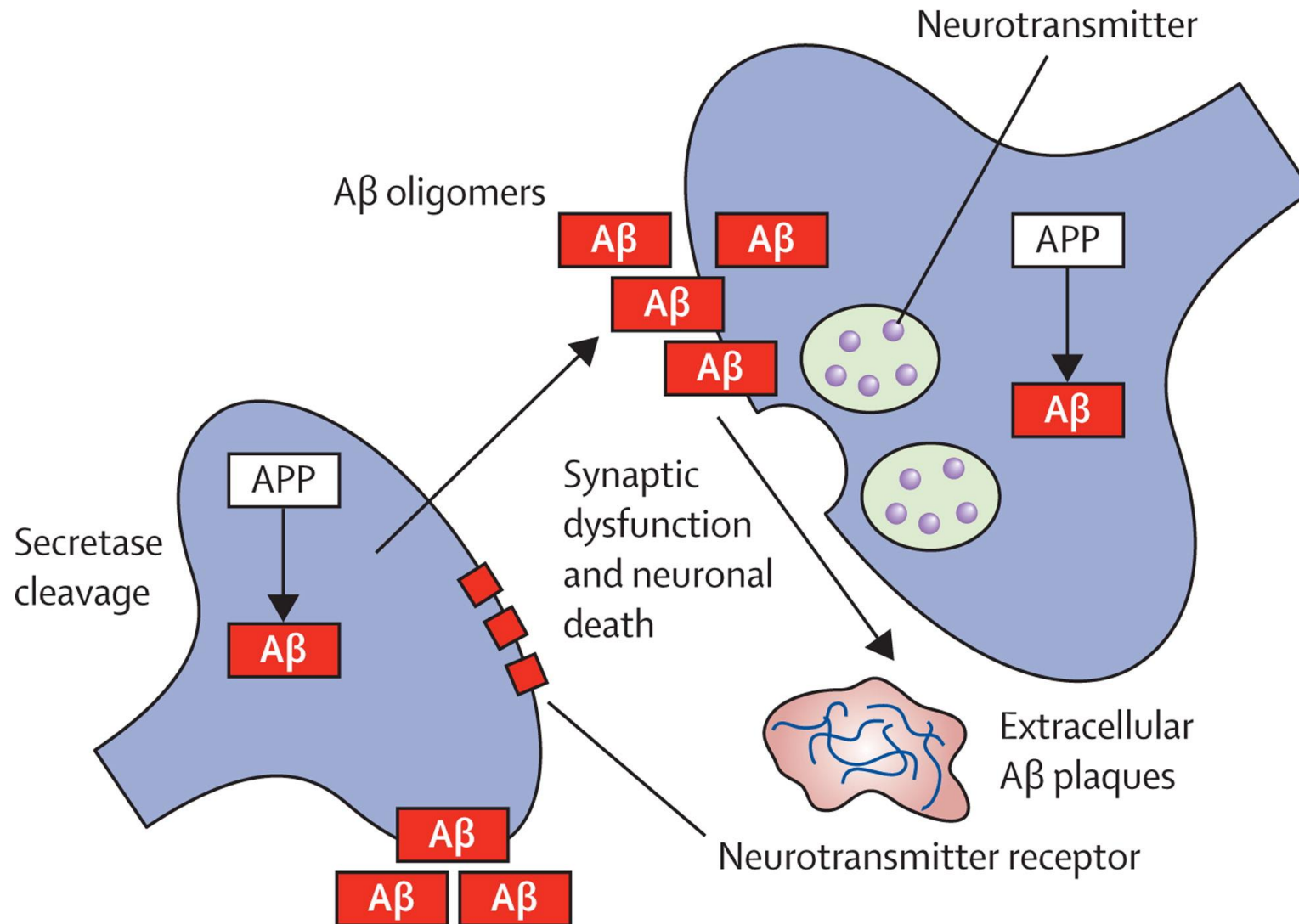




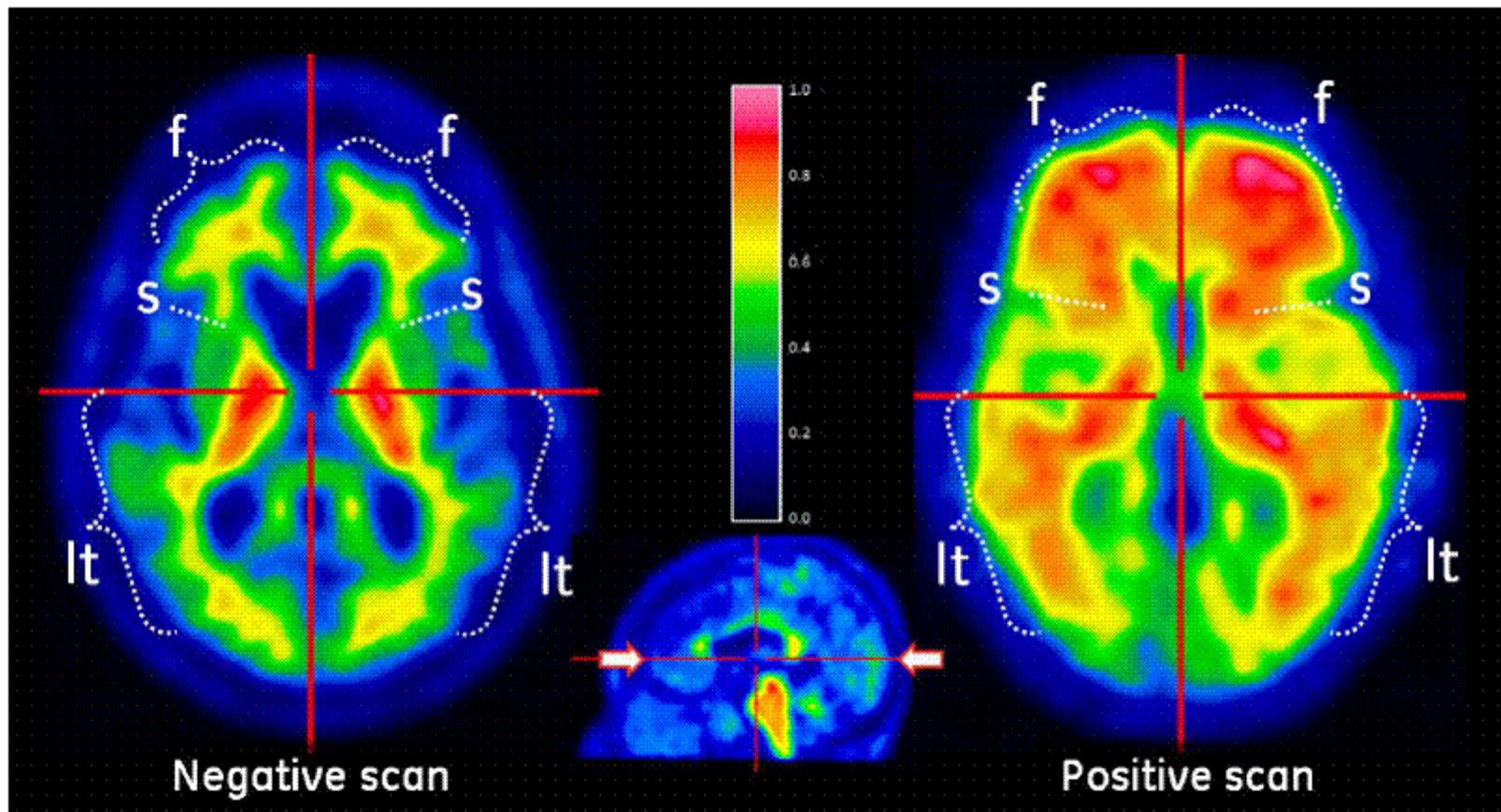
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Amyloid-PET



Amyloid-PET



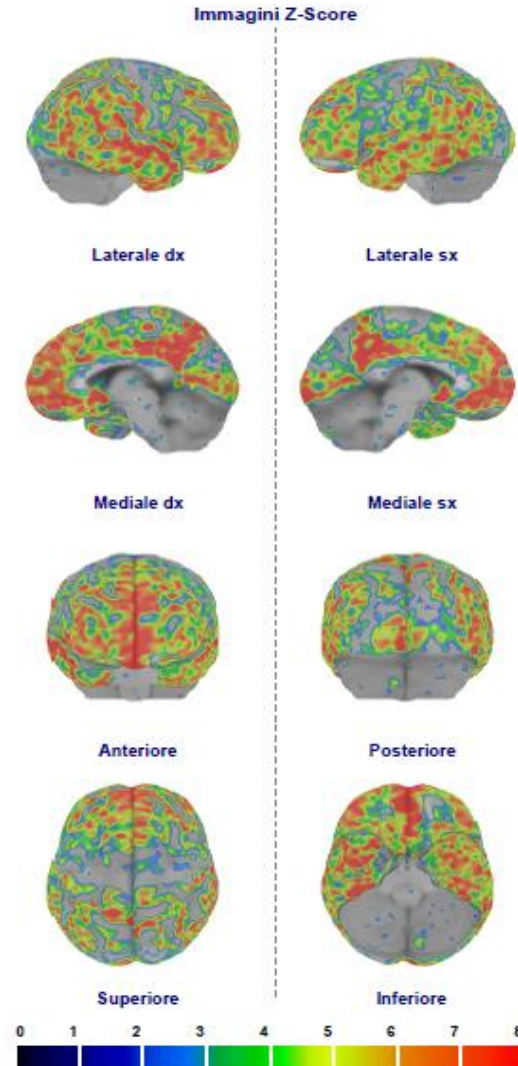
Perani D. et al. Biomed Res Int 2014

A Survey of FDG- and Amyloid-PET Imaging in Dementia and GRADE Analysis

Amyloid-PET

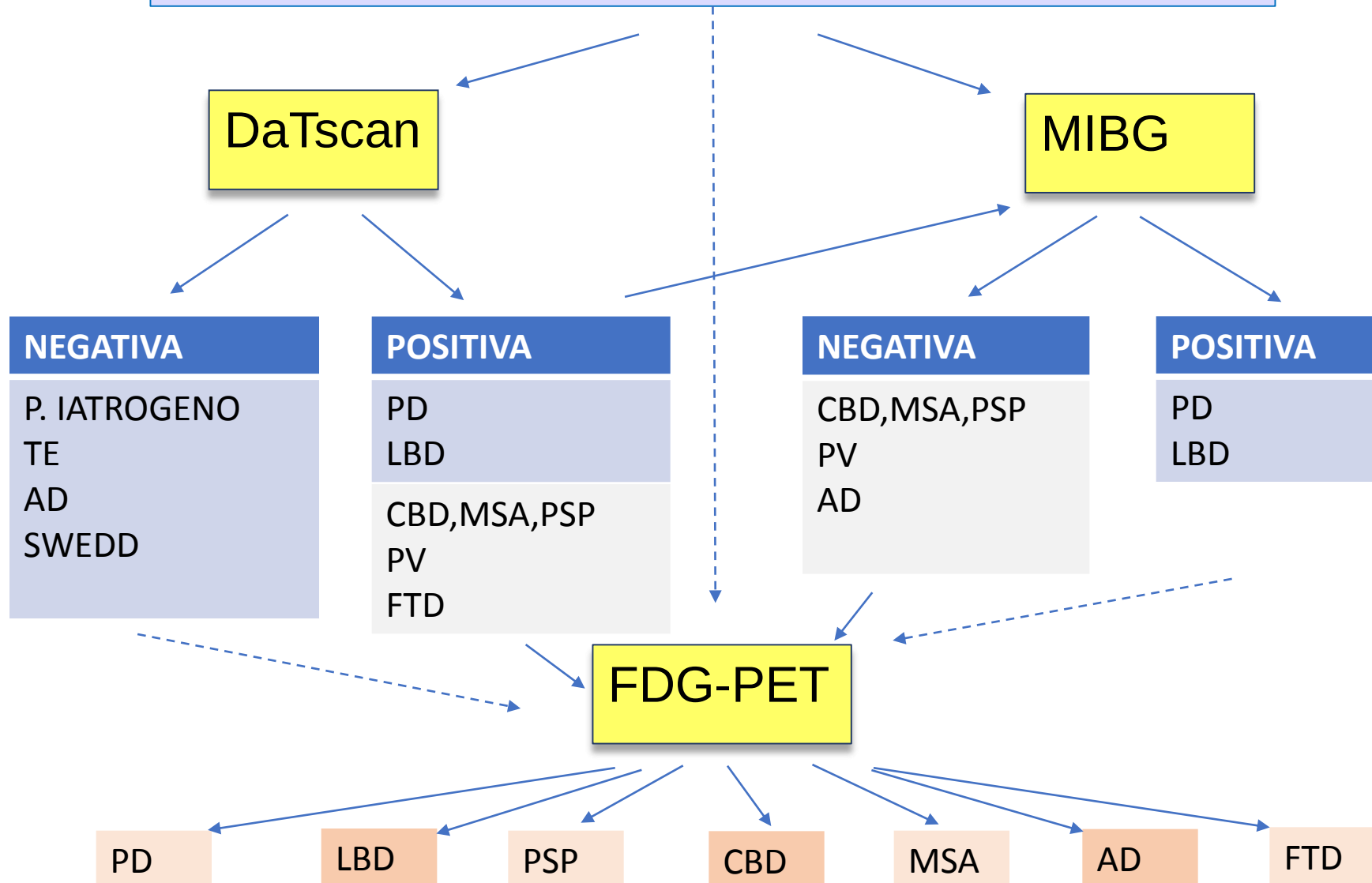
Regione	Rapporto di assorbimento	Z-Score
Composite	0,91	9,19
Prefrontal R	0,88	7,81
Prefrontal L	0,91	8,12
Anterior Cingulate R	0,94	7,29
Anterior Cingulate L	1,00	7,28
Precuneus PostCing R	0,95	8,69
Precuneus PostCing L	0,93	7,81
Parietal R	0,86	7,35
Parietal L	0,87	7,63
Temporal Lateral R	0,93	9,69
Temporal Lateral L	0,93	9,92
Occipital R	0,79	5,85
Occipital L	0,82	6,61
Sensorimotor R	0,75	4,49
Sensorimotor L	0,73	4,16
Temporal Mesial R	0,68	4,49
Temporal Mesial L	0,66	3,68
Cerebellum Grey	0,35	-1,56
Cerebellum Whole	0,41	-2,34
Pons	1,00	0,00

Regione di riferimento: Pons

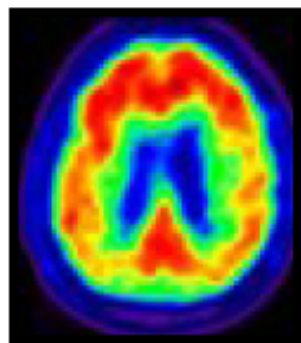


Regione	Z-score
Prefrontal R	7.81
Prefrontal L	8.12
Temporal Lateral R	9.69
Temporal lateral R	9.92
Precuneus PostCing R	8.69
Precuneus PostCing L	7.81

Paziente con sdr extrapiramidale/deficit cognitivi



Utilizzo clinico dei traccianti PET per amiloide



AmyPET +



Diagnosi di AD

Presenza di amiloidosi cerebrale

Questioni irrisolte

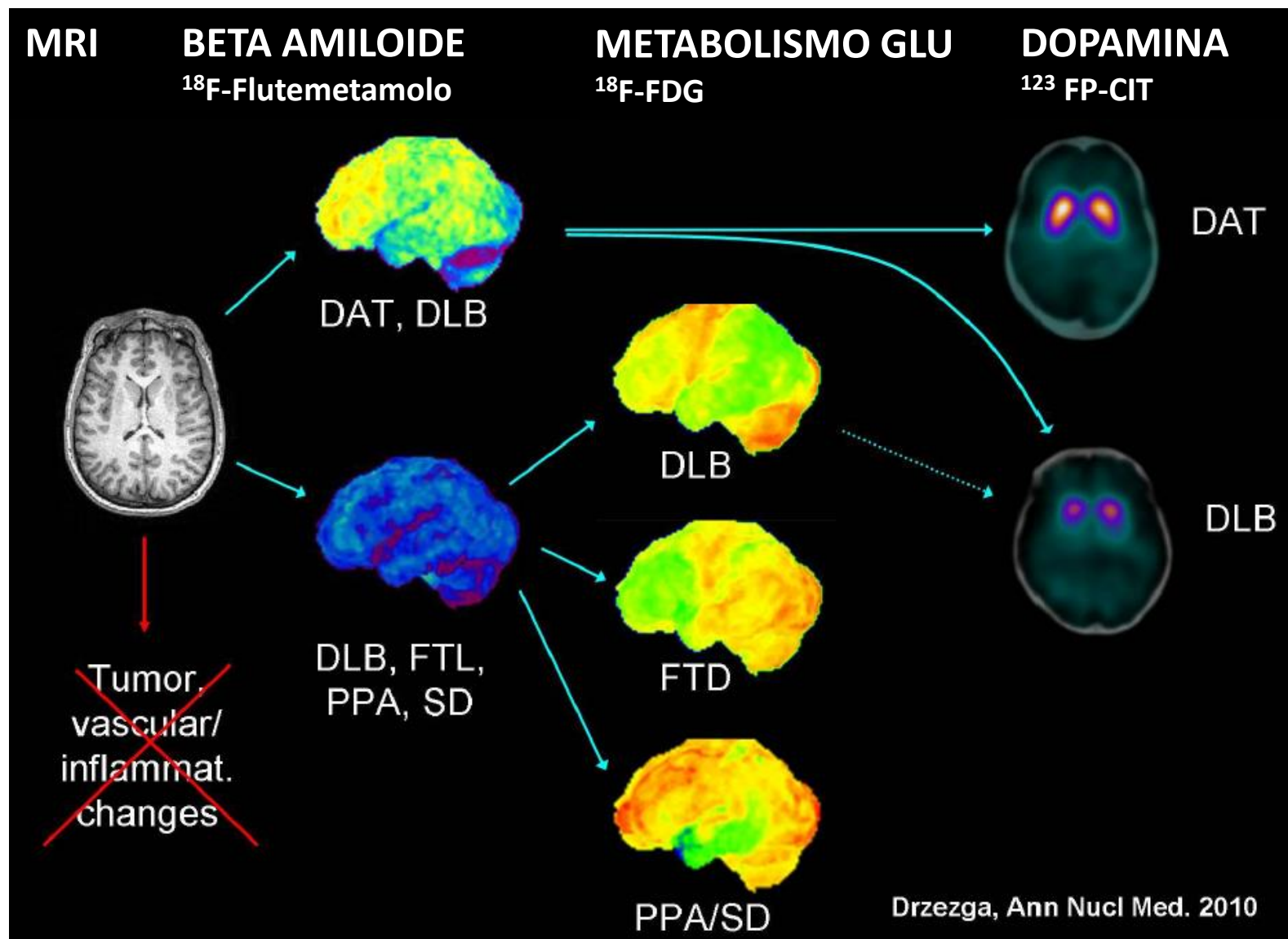
- Alta prevalenza (20%) di individui cognitivamente normali amiloide-positivi (età-correlata)
 - 50-60 aa < 5%
 - 60-70aa 10%
 - 79-80aa 25%
 - 80-90aa >50%
- AmyPET positiva anche in altre condizioni patologiche
 - DLB
 - angiopatia amiloidea cerebrale

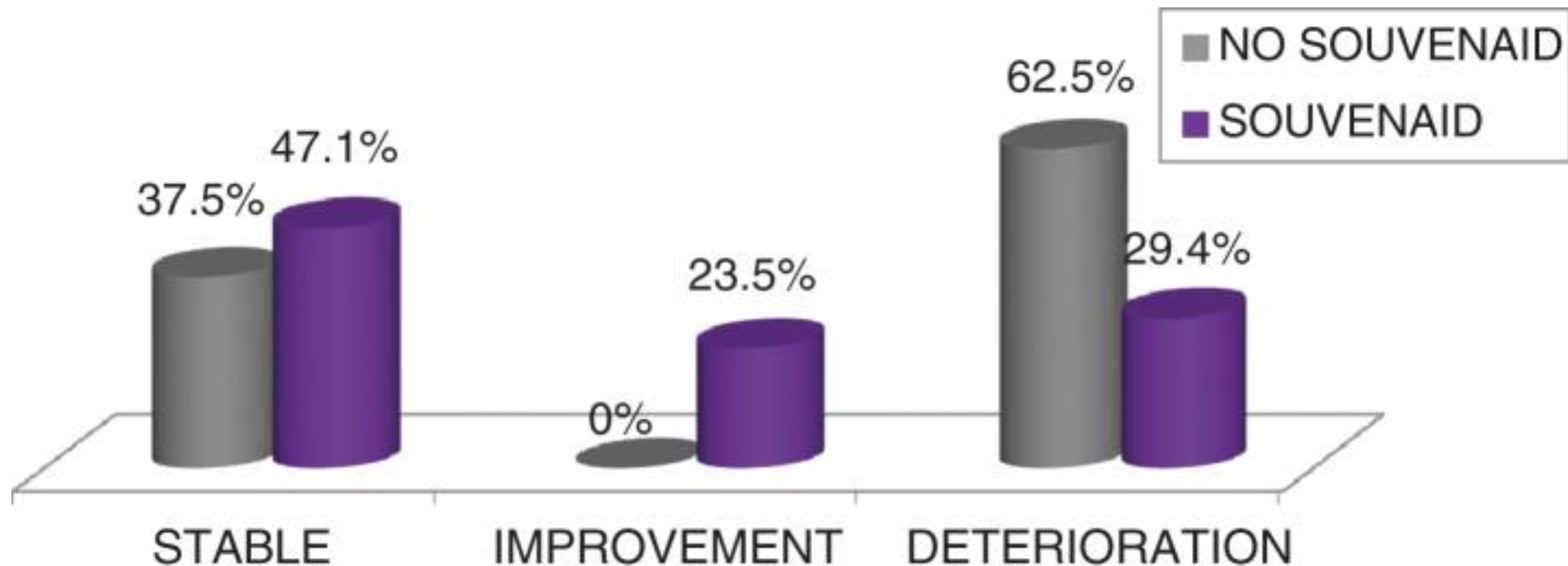


“Criteri ad uso interno AULSS3” AUC +

- ✓ **MCI >6 mesi con diagnosi dubbia** dopo PET FDG e MRI
- ✓ **MCI dubbio:**
Esordio atipico
Comorbidità e fattori confondenti
- ✓ **AD possibile (NIA-AA 2011) con diagnosi dubbia** dopo PET FDG e MRI per **(solo se < 75 aa?)**
Presentazione atipica
Progressione atipica
Comorbidità confondenti
- ✓ **Decadimento cognitivo < 65 anni con diagnosi dubbia** dopo PET FDG e MRI
- ✓ **Sdr focali con diagnosi dubbia** dopo PET FDG e MRI

Multimodal differential diagnosis of dementias

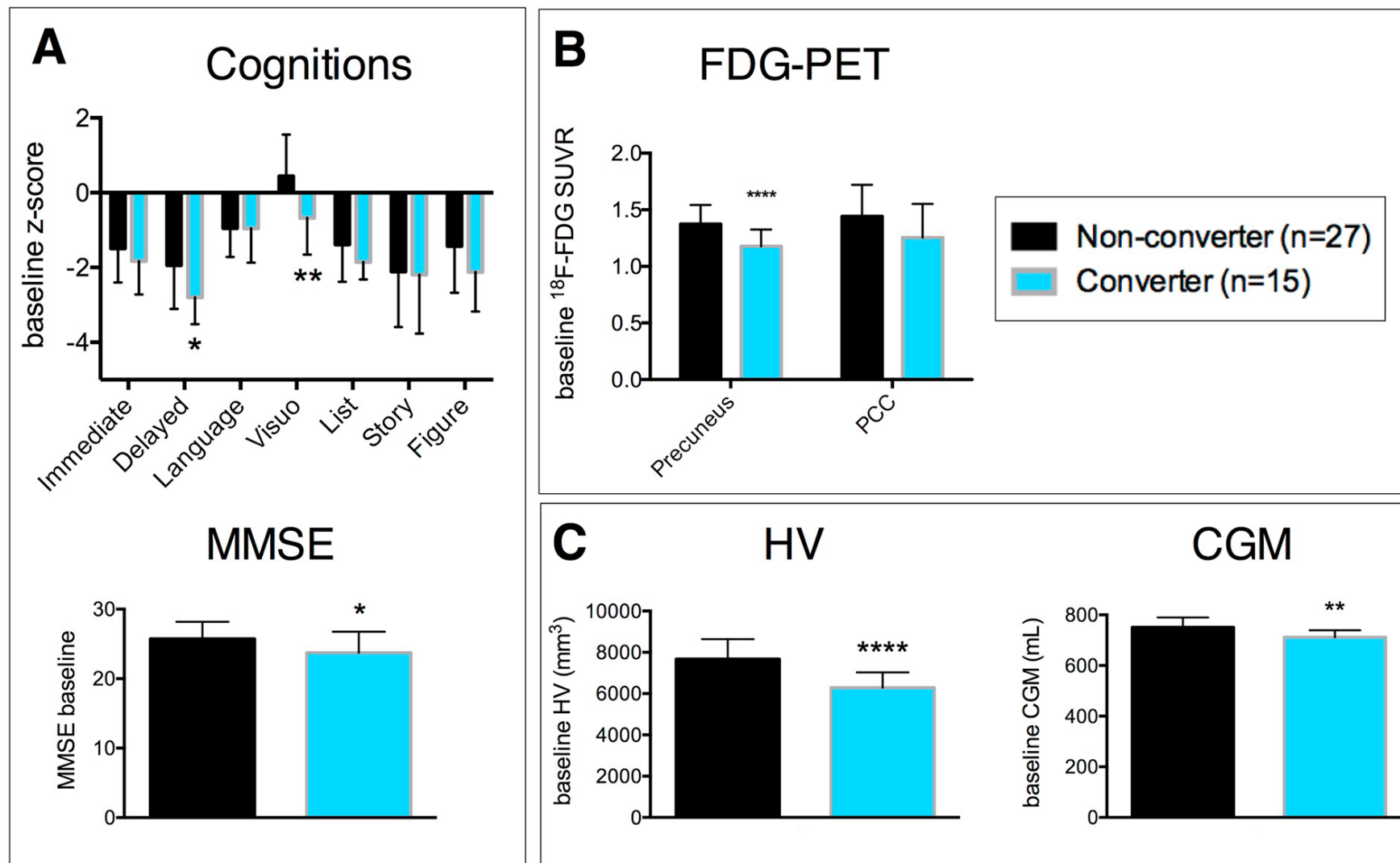




[J Alzheimers Dis Rep. 2019; 3\(1\): 95–102.](#)

Mild Cognitive Impairment with a High Risk of Progression to Alzheimer's Disease Dementia (MCI-HR-AD): Effect of Souvenaid® Treatment on Cognition and ^{18}F -FDG PET Scans 2019 Apr 29.

Baseline cognitive scores (A), regional ^{18}F -FDG uptake (B), and MRI-based HV hippocampal volume and CGM (C) in MCI-to-AD dementia converters (blue) versus non-converters (black) after 1 year follow-up.



[Neuroimage Clin.](#) Mar 2019

Association of short-term cognitive decline and MCI-to-AD dementia conversion with CSF, MRI, amy and ^{18}F -FDG-PET imaging

[Julie Ottoy](#) et al.

Conclusioni:

1. La diagnosi di demenza è eminentemente **clinica**.
2. La ^{18}F FDG-PET presenta patterns caratteristici e **precoci**, che nella maggior parte dei casi differenziano con sufficiente sensibilità e specificità: **AD, VD, FTD, LBD**.
3. La ^{123}I -Datscan-SPET ha altissima specificità nella dd tra **AD e LBD**.
4. La PET con traccianti per amiloide ha un alto VPN, dovrebbe essere usata solo in alcune **categorie di pazienti** e solo se la dgn rimane incerta **dopo** FDG-PET e/o Datscan-SPET.

Grazie!

*Se riuscire a dimenticare è segno di sanità mentale,
Ricordare senza posa è ossessione e follia.*

Jack London

