IL CERVELLO CHE CAMBIA 7
Sabato 11 novembre 2017
Genova, Aula Magna Clinica Neurologica

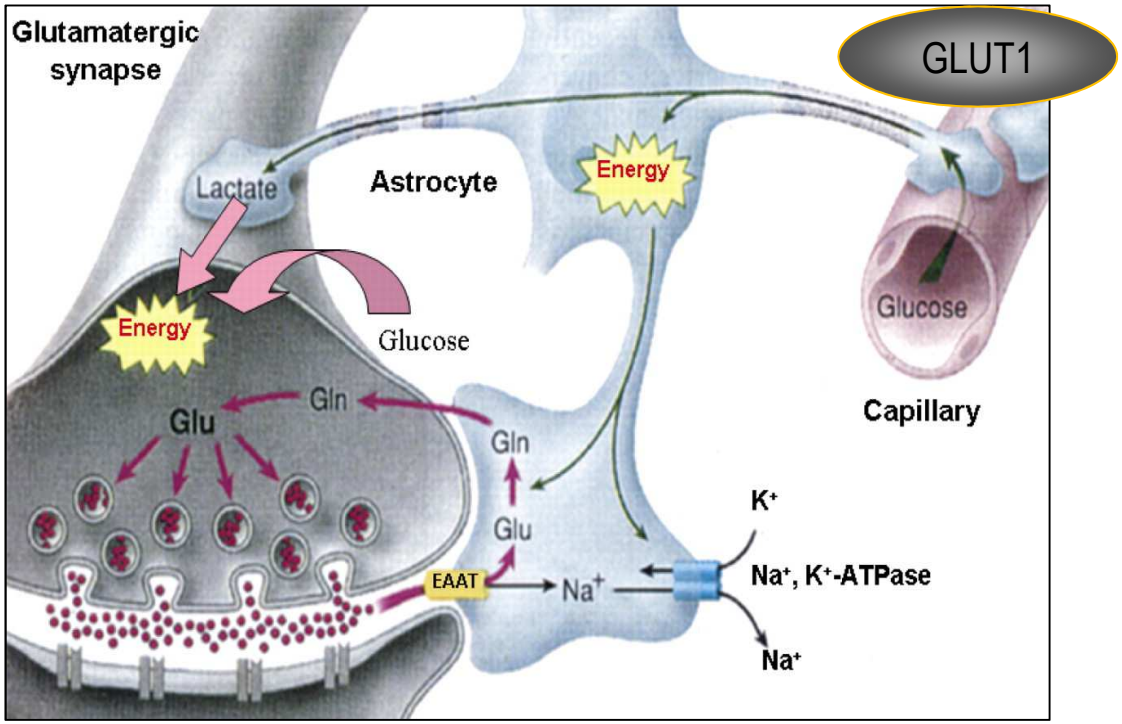
QUEST'ANNO HO LETTO
UN ARTICOLO CHE MI HA
APERTO GLI OCCHI SU…

OSPEDALE POLICLINICO SAN MARTINO
Sistema Sanitario Regione Liguria

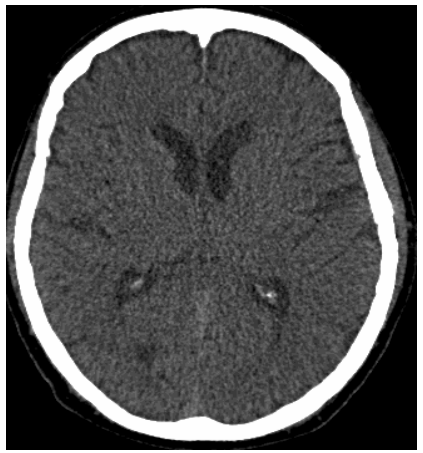
^{18}F-FDG PET

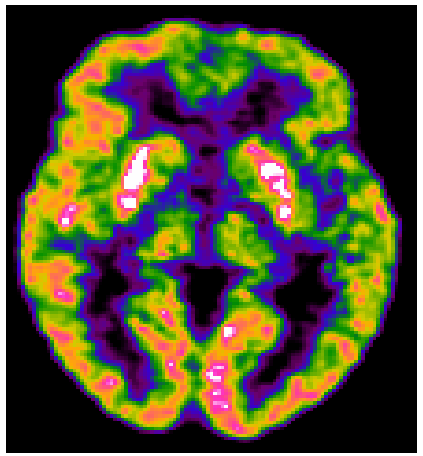
Matteo Bauckneht

U.O. Medicina Nucleare
Ospedale Policlinico San Martino, Genova



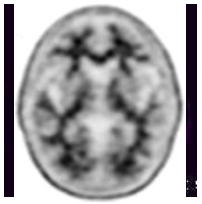
Magistretti P J , Pellerin L Physiology 1999



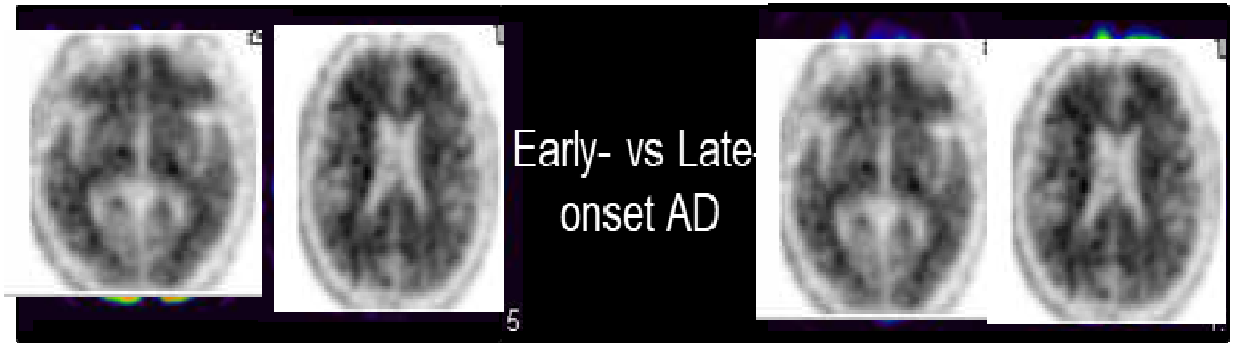


In AD synaptic degeneration precedes neuronal death for a substantial period of time

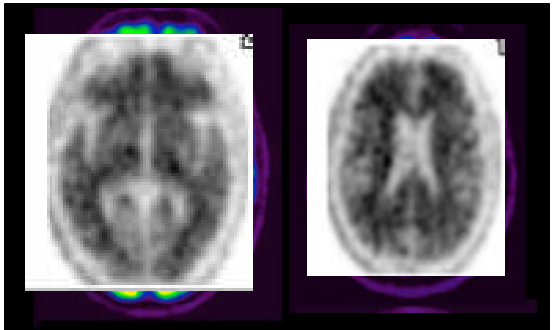
Price et al Ann Neurol 1999



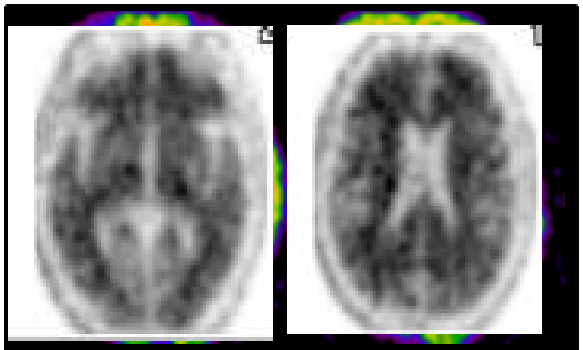
Healthy control



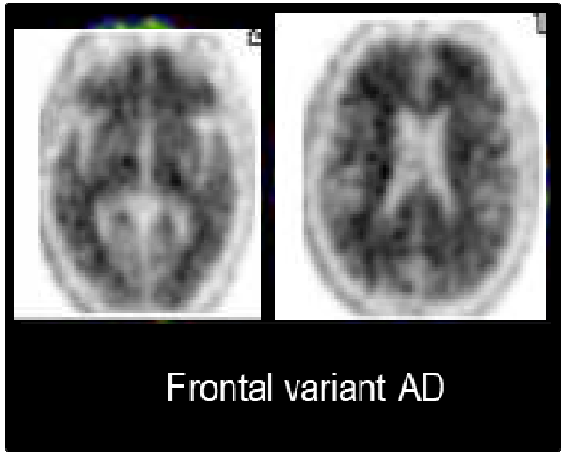
Early- vs Late-onset AD



ApoE ε4+ vs ApoE ε4 - AD

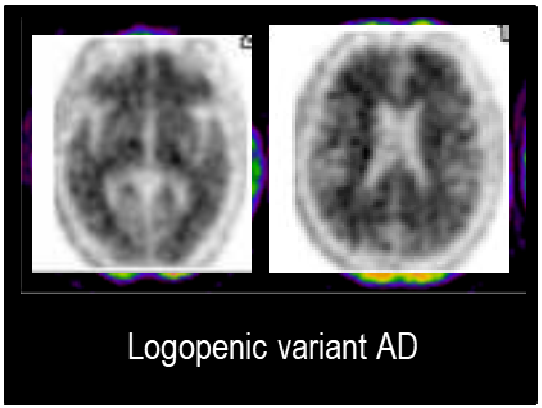


Posterior variant AD

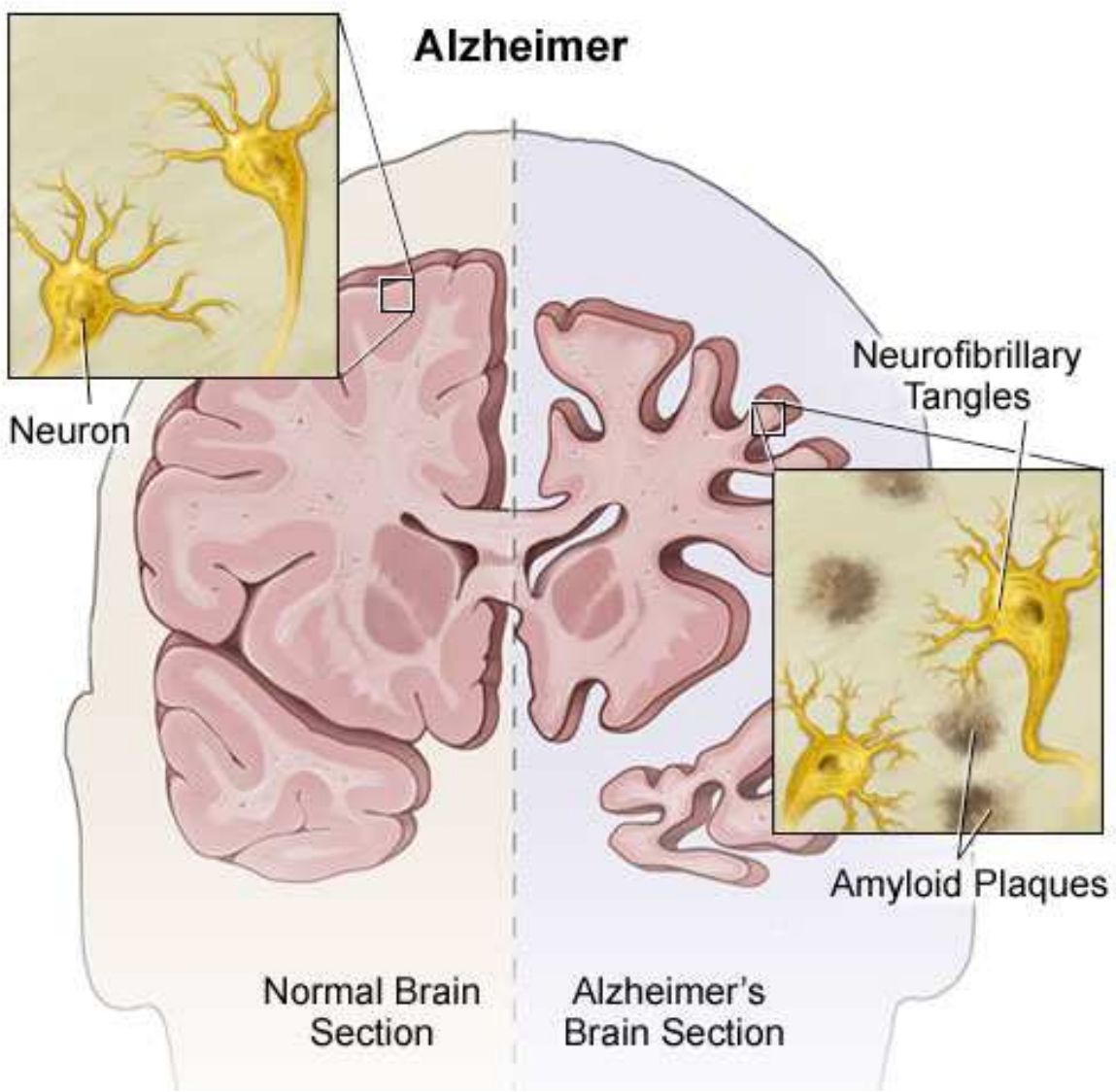


Frontal variant AD

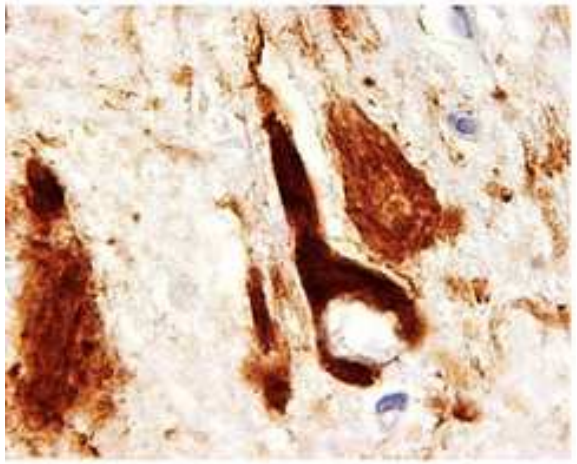
High- vs Low-educated AD



Logopenic variant AD



Neurofibrillary Tangles



TAU PET tracers:

^{8}F-AV-1451
^{18}F-THK5351
^{11}C-PBB3
^{18}F-MK-6240
^{18}F-RO6958948
^{18}F-PI-2620
^{18}F-JNJ64349311

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doi:10.1093/brain/aww027 BRAIN 2016: 139; 1551–1567 | 1551

BRAIN
A JOURNAL OF NEUROLOGY

Tau PET patterns mirror clinical and neuroanatomical variability in Alzheimer's disease

Rik Ossenkoppele,[1,2,3,*] Daniel R. Schonhaut,[1,2,*] Michael Schöll,[2,4] Samuel N. Lockhart,[2] Nagehan Ayakta,[1,2] Suzanne L. Baker,[5] James P. O'Neil,[5] Mustafa Janabi,[5] Andreas Lazaris,[1] Averill Cantwell,[1] Jacob Vogel,[2] Miguel Santos,[1] Zachary A. Miller,[1] Brianne M. Bettcher,[1,6] Keith A. Vossel,[1] Joel H. Kramer,[1] Maria L. Gorno-Tempini,[1] Bruce L. Miller,[1] William J. Jagust[2,5] and Gil D. Rabinovici[1,2]

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Ossenkoppele R et al. Brain 2016, 139:1551-1567

20 probable AD / MCI due to AD

- 7 PCA
- 5 logopenic variant PPA
- 5 amnestic MCI
- 1 corticobasal syndrome
- 1 behavioural/dysexecutive variant
- 1 patient 'non-amnestic'

15 Amyloid negative cognitively normal subjects

MRI
^{18}F-FDG
^{11}C-PiB
^{18}F-AV1451 (Tau tracer)
ApoE genotype
Neuropsycological testing

Study of the Tau tracer uptake in:

- clinical variants of Alzheimer's disease
- early-onset versus late-onset Alzheimer's disease
- APOE e4 carriers versus noncarriers;

Assessment of the correlation between Tau tracer retention and neuropsychological profile.

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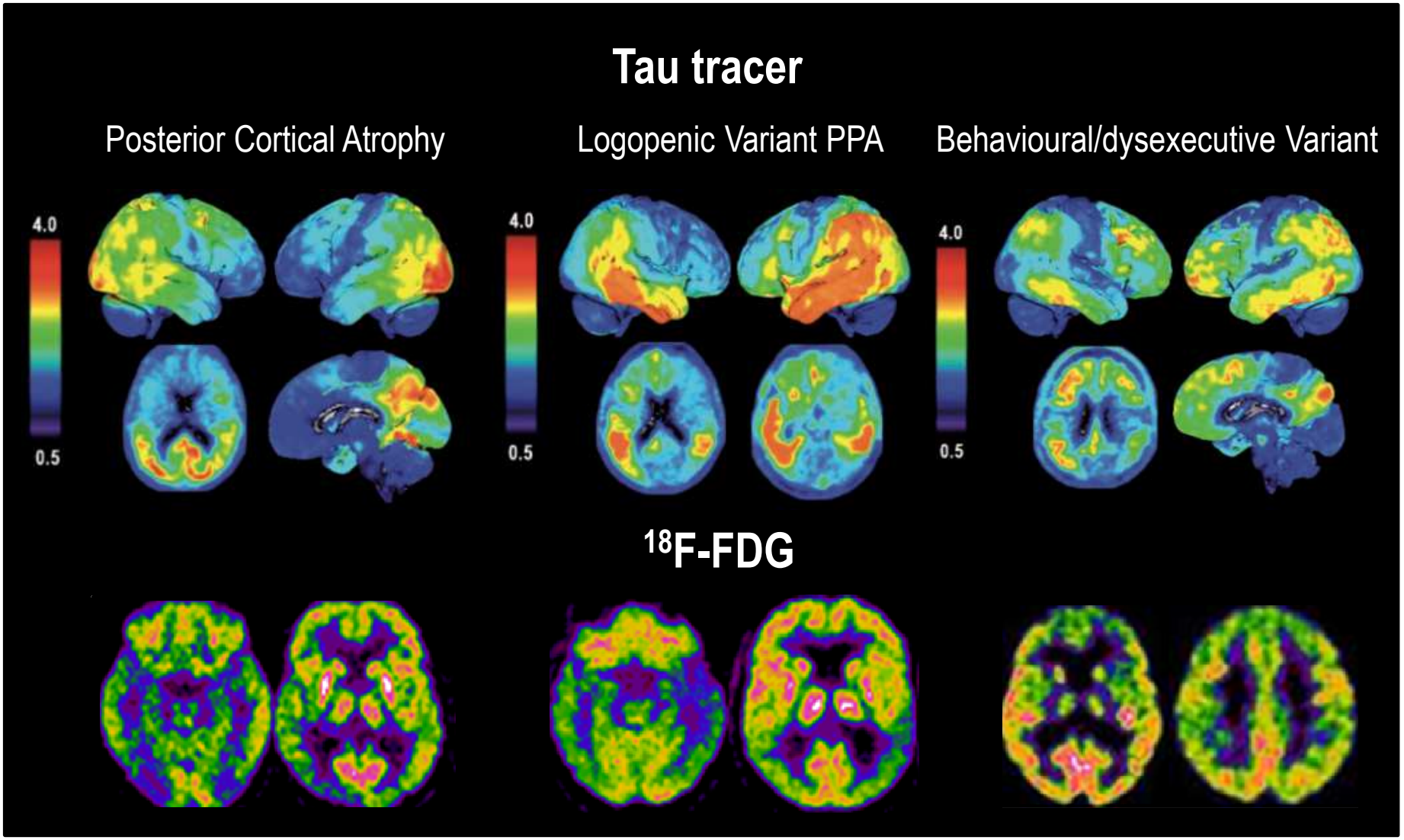

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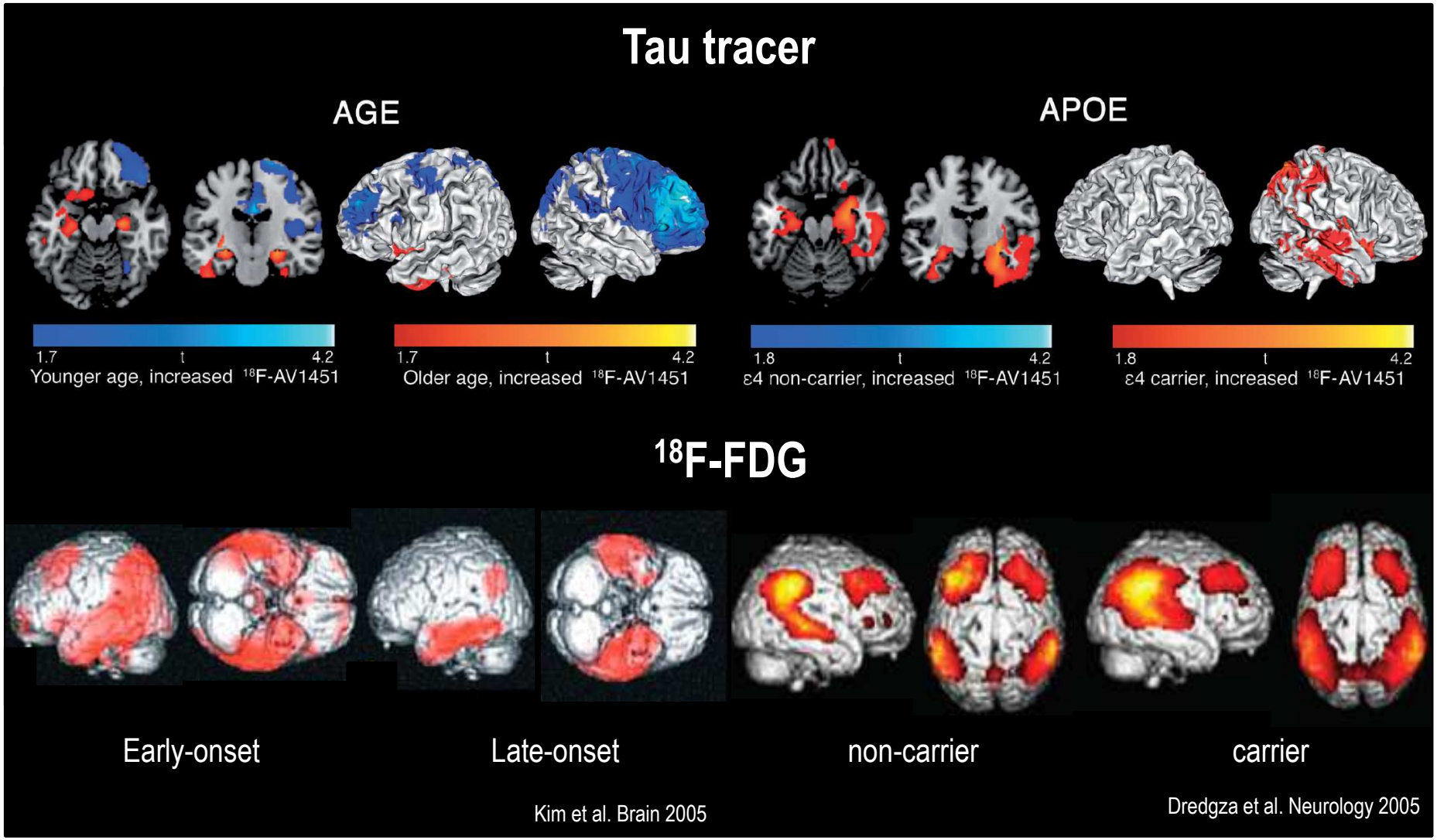

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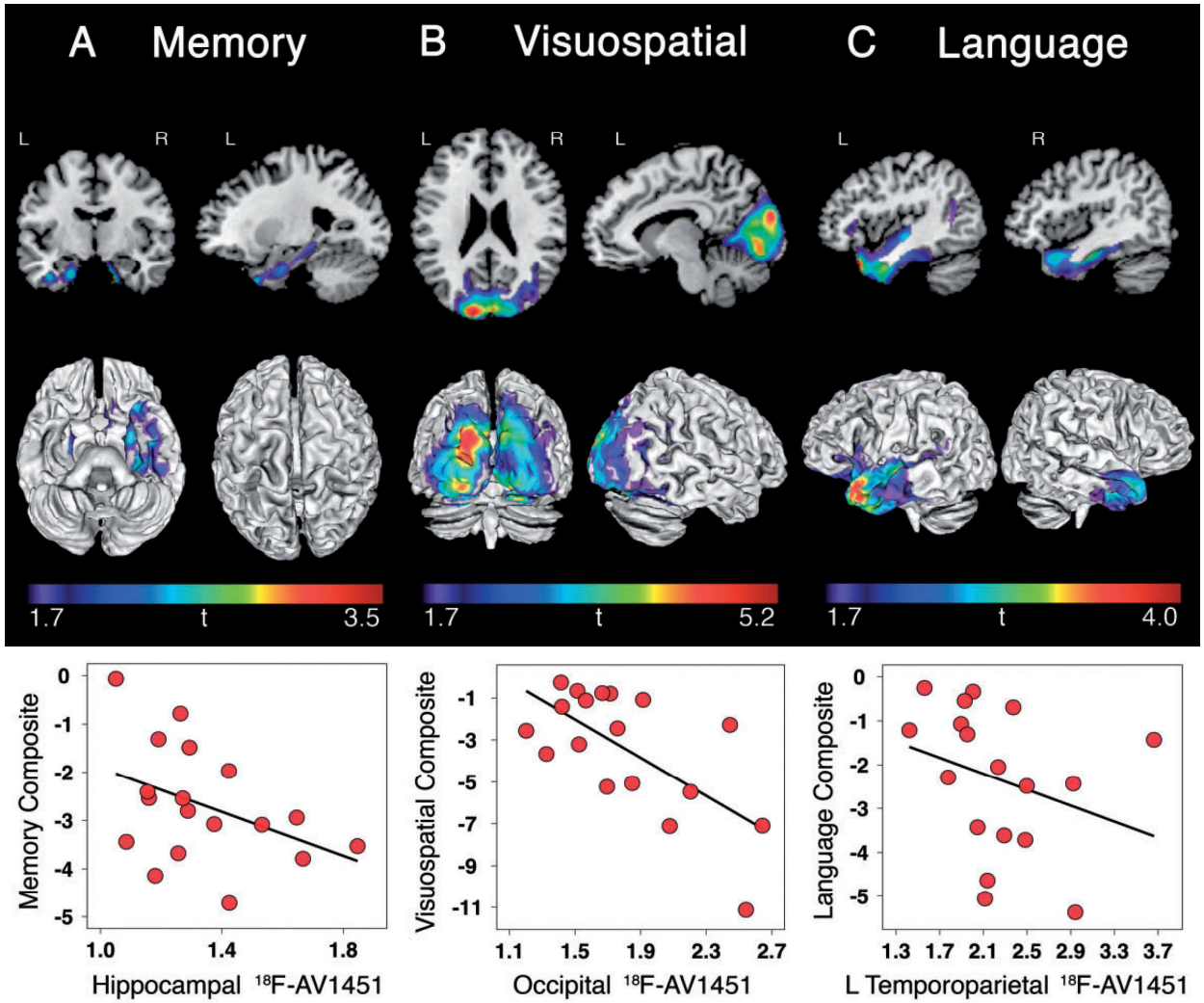
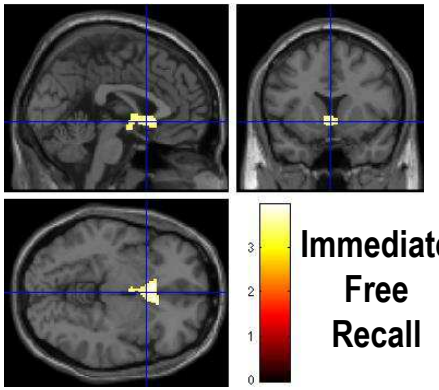


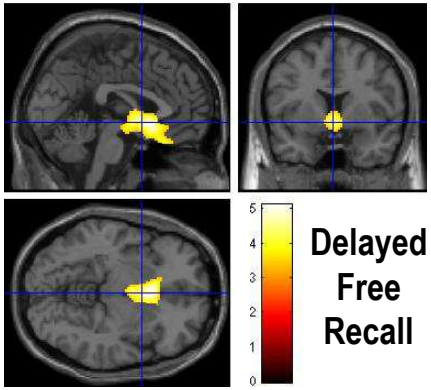
Association between Tau tracer uptake and cognitive performance.

Brain Metabolism Correlates of The Free and Cued Selective Reminding Test in Mild Cognitive Impairment



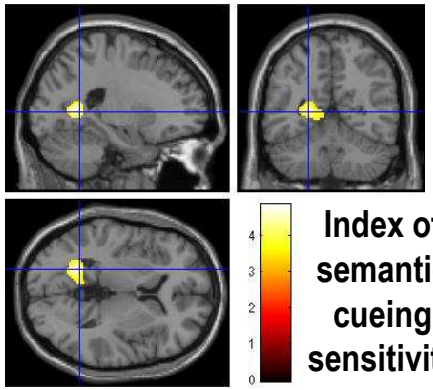
Immediate Free Recall

Bilateral ant.cing



Delayed Free Recall

L ant.ant.cing Medio-frontal

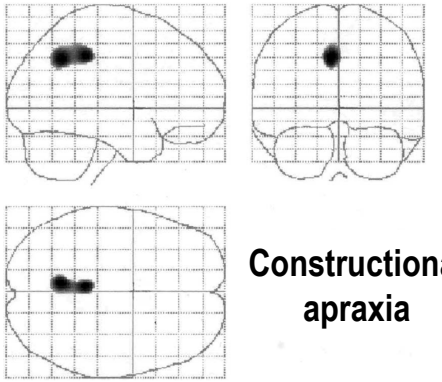


Index of semantic cueing sensitivity

L post.cing

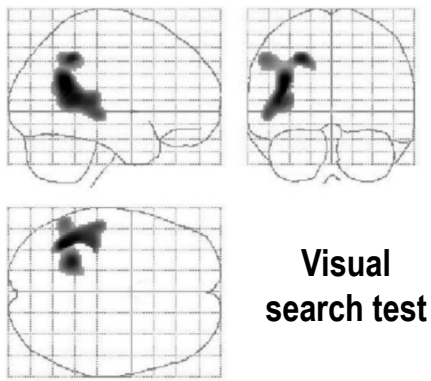
Caffarra P et al. JAD 2016

Resting SPECT-neuropsychology correlation in very mild Alzheimer's disease



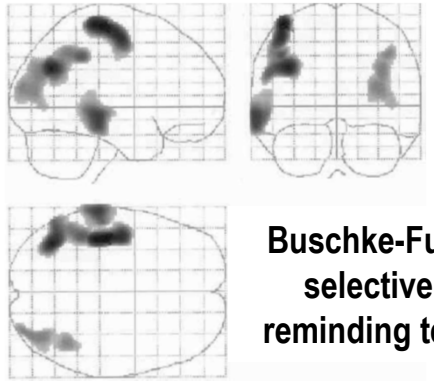
Constructional apraxia

Posterior cingulate and precuneus



Visual search test

L par precuneus and sup temp gyrus.



Buschke-Fuld selective reminding test

L post-central gyrus, par precuneus, inf par lobule and mid temp gyrus. R mid temp and mid occip gyri.

Nobili F et al. Clin Neurophysiol 2005

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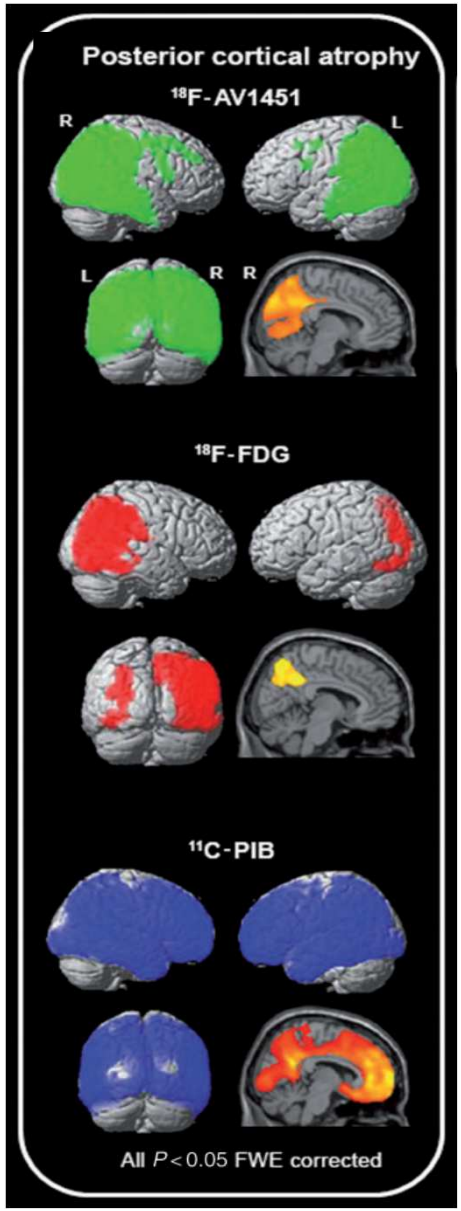
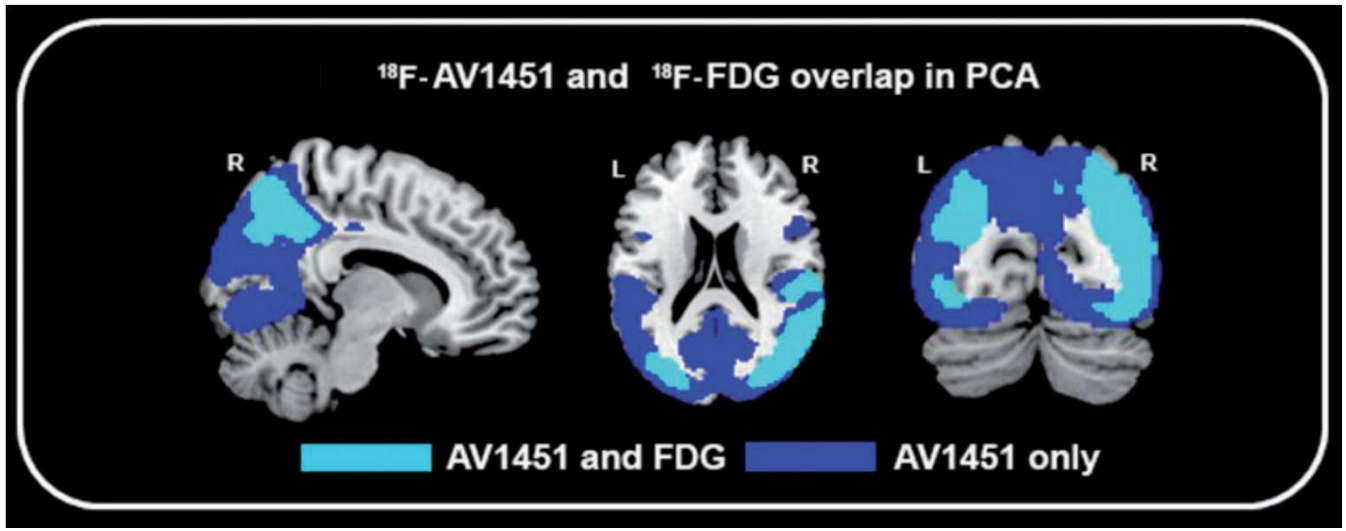
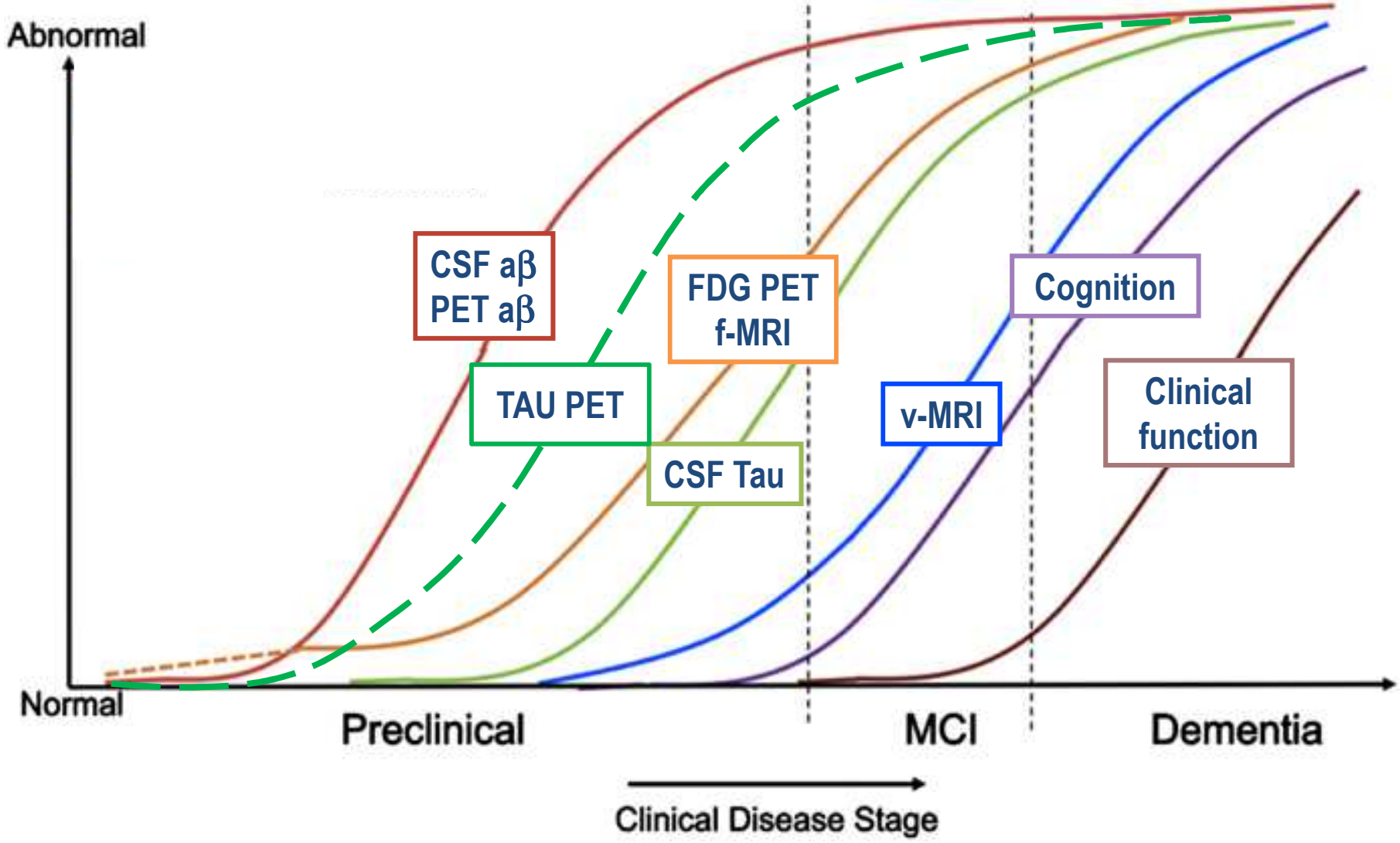


Spatial overlap between Tau tracer and ^{18}F-FDG in PCA

Tau tracer accumulation was elevated in several brain regions where ^{18}F-FDG uptake did not differ from controls.



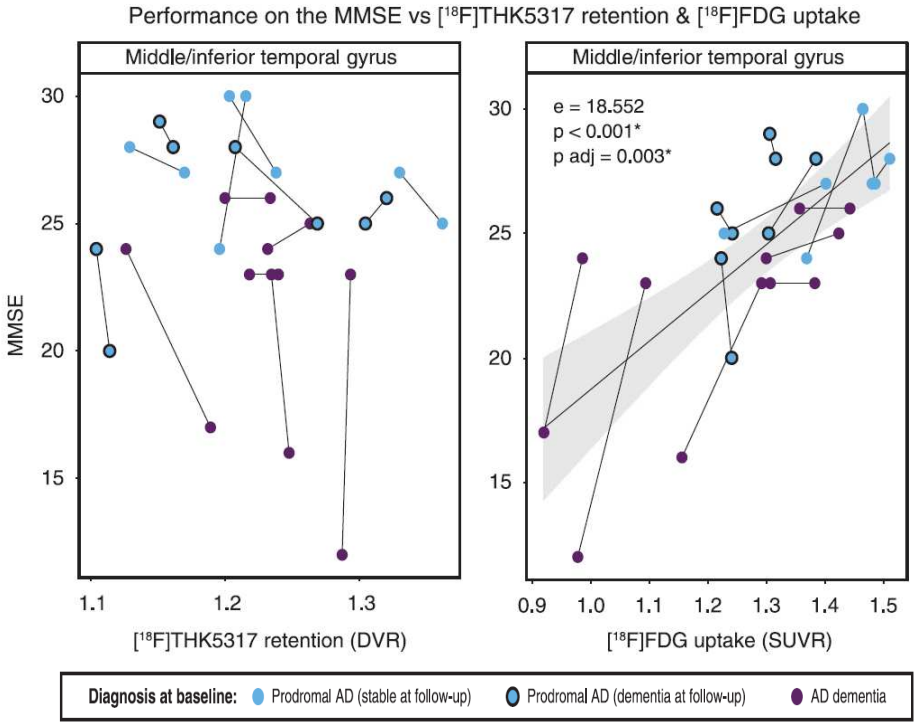


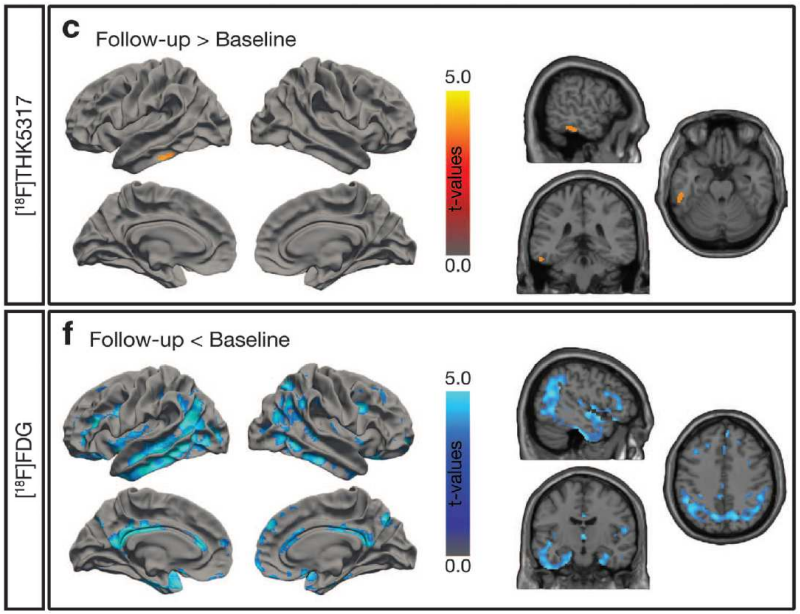
adapted from Sperling et al Alzheimer and Dementia 2011

TAU, FDG and clinical progression

Longitudinal, multimodal follow-up study after a median of 17 months from baseline in 18 AD (prodromal or dementia) patients.

Patients with AD showed **unchanged Tau tracer retention over time**, in contrast to **significant decreases in FDG uptake in temporoparietal areas**.





Global cognition decline correlated with decreased FDG uptake but not with changes in Tau tracer retention over time.

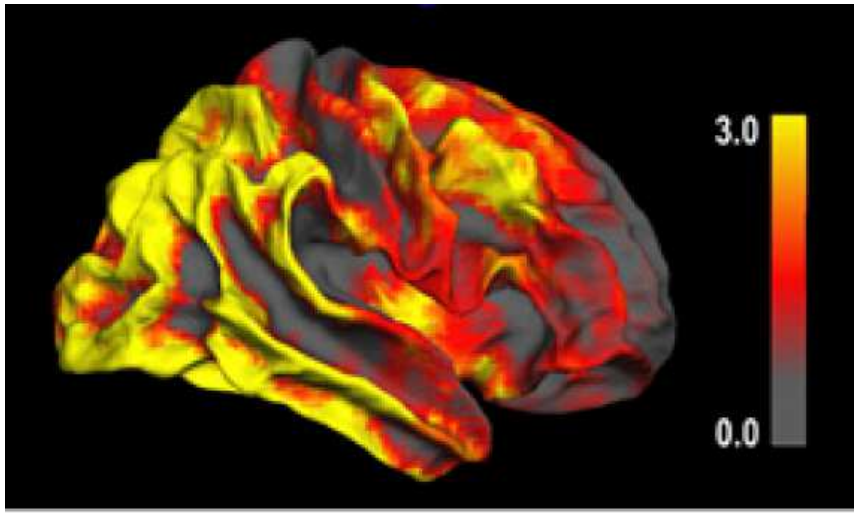
Chiotis et al Molecular Psychiatry 2017

JNM The Journal of NUCLEAR MEDICINE
HOT TOPICS

Is Tau Imaging More Than Just Upside-Down ^{18}F-FDG Imaging?

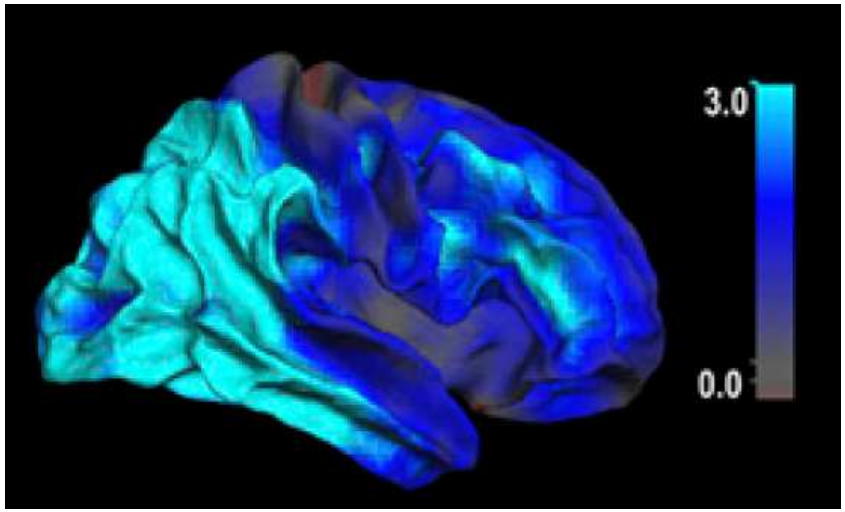
Thilo van Eimeren, Gérard N. Bischof and Alexander Drzezga

TAU tracers



Precede and magnify ipometabolism
Differential diagnosis with non tauopthies
More direct surrogate endpoint for clinical trials

FDG



Clinical validation and standardization
High availability
Low costs
Better assessment of disease progression?

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Grazie a tutti per l'attenzione e soprattutto grazie a:

Medicina Nucleare
Silvia Morbelli
Gianmario Sambuceti
Roberta Piva
Ambra Buschiazzo
Hulya Efeturk
Chiara Ghersi
Nikola Josifov
Infermieri
Tecnici

Neurologia
Flavio Nobili
Dario Arnaldi
Matteo Pardini
Agnese Picco
Federico Massa
Matteo Grazzini
Francesco Famà
Andrea Brugnolo
Nicola Girtler

Post-processing e Statistica
Andrea Chincarini (INFN, Genova)
Fabrizio De Carli (CNR, Genova)
Marco Pagani (CNR, Roma)

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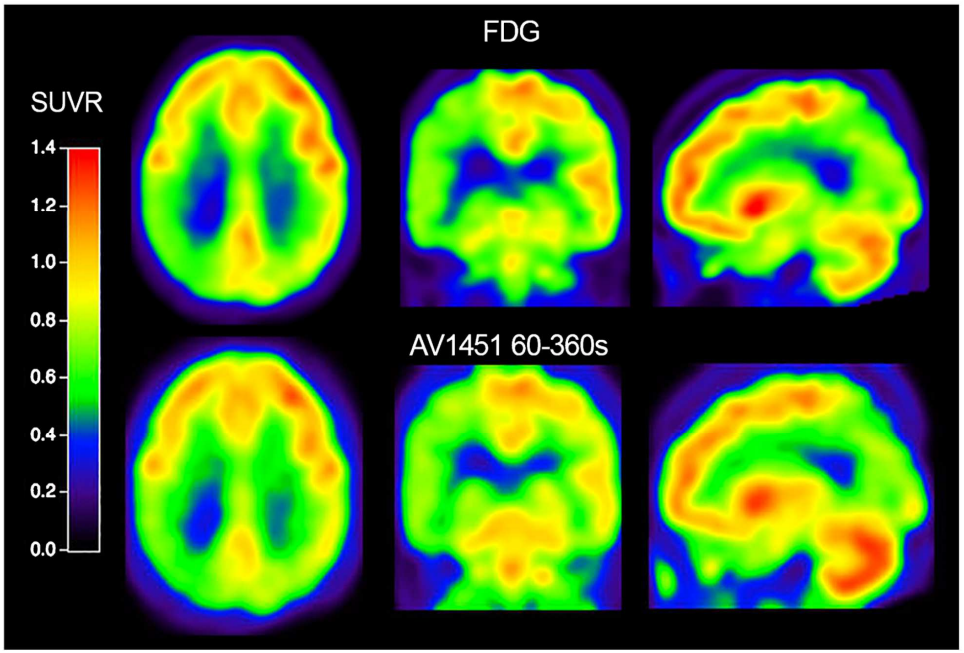
Eur J Nucl Med Mol Imaging

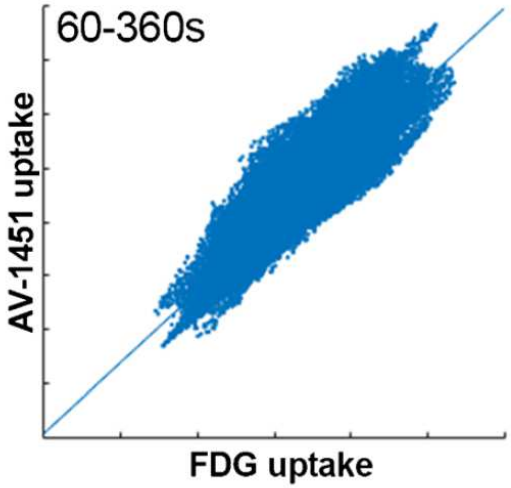
Published online: 12 October 2017

Multimodal correlation of dynamic [^{18}F]-AV-1451 perfusion PET and neuronal hypometabolism in [^{18}F]-FDG PET

Jochen Hammes[1] · Isabel Leuwer[1] · Gérard N. Bischof[1,2] · Alexander Drzezga[1,3] · Thilo van Eimeren[1,2,3]

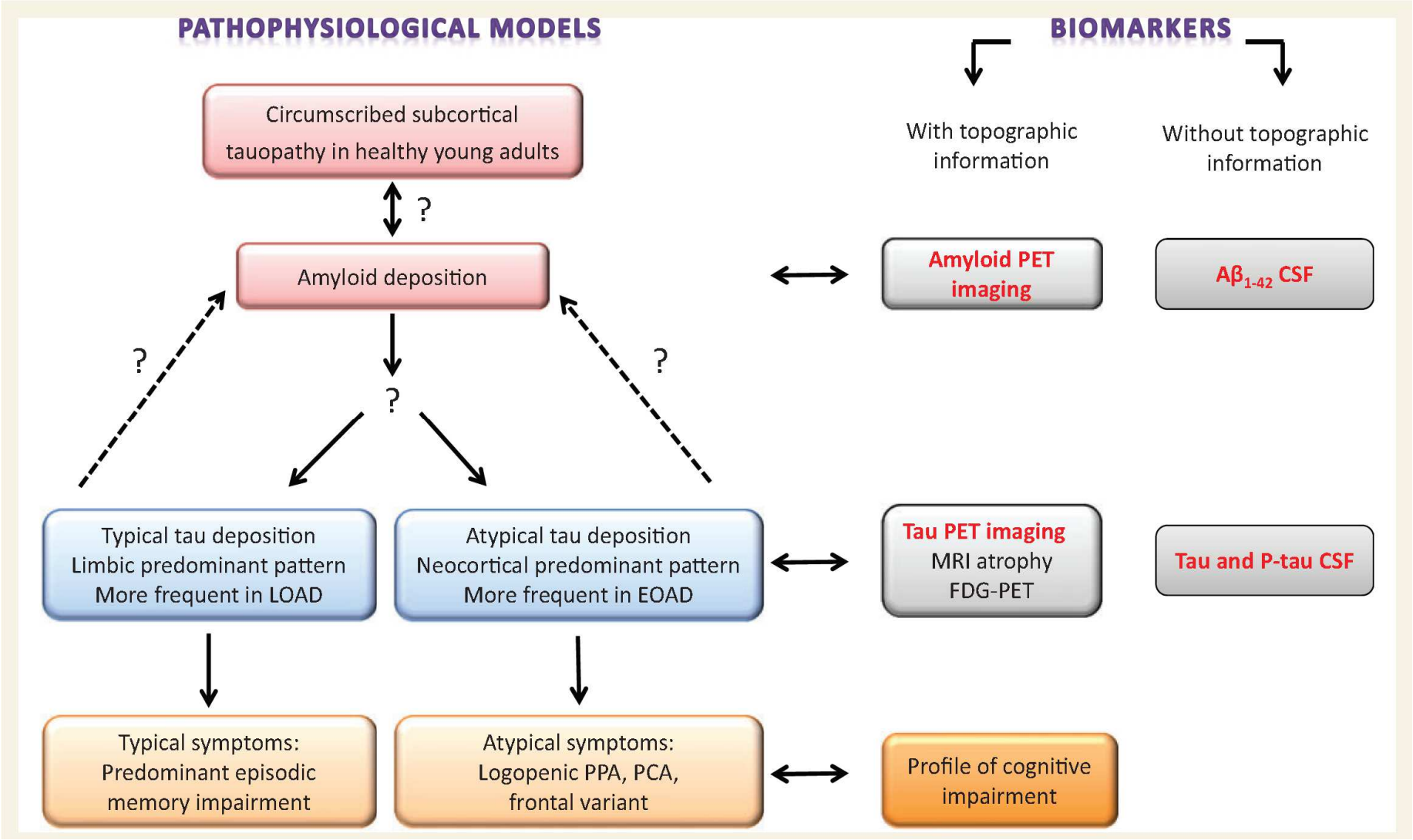


Voxel-wise Intra-subject correlations in an exemplary patient with suspected AD



Perfusion imaging with AV-1451 might be a valid biomarker for assessment of neuronal dysfunction in neurodegenerative diseases.

Routine acquisition of early AV-1451 images might spare additional FDG PET?



Sarazin et al. Brain 2016

IWG-1 → IWG-2

Panel 2: Diagnostic criteria for AD

Probable AD: A plus one or more supportive features B, C, D, or E

Core diagnostic criteria

A. Presence of an early and significant episodic memory impairment that includes the following features:

1. Gradual and progressive change in memory function reported by patients or informants over more than 6 months
2. Objective evidence of significantly impaired episodic memory on testing: this generally consists of recall deficit that does not improve significantly or does not normalise with cueing or recognition testing and after effective encoding of information has been previously controlled
3. The episodic memory impairment can be isolated or associated with other cognitive changes at the onset of AD or as AD advances

Supportive features

B. Presence of medial temporal lobe atrophy

- Volume loss of hippocampi, entorhinal cortex, amygdala evidenced on MRI with qualitative ratings using visual scoring (referenced to well characterised population with age norms) or quantitative volumetry of regions of interest (referenced to well characterised population with age norms)

C. Abnormal cerebrospinal fluid biomarker

- Low amyloid β_{1-42} concentrations, increased total tau concentrations, or increased phospho-tau concentrations, or combinations of the three
- Other well validated markers to be discovered in the future

D. Specific pattern on functional neuroimaging with PET

- Reduced glucose metabolism in bilateral temporal parietal regions
- Other well validated ligands, including those that foreseeably will emerge such as Pittsburg compound B or FDDNP

E. Proven AD autosomal dominant mutation within the immediate family

Lancet Neurol 2007;6:734-46

Panel 5: Definition of AD biomarkers

Diagnostic marker Amyloidosis

- Pathophysiological marker
- Reflects in-vivo pathology
- Is present at all stages of the disease
- Observable even in the asymptomatic state
- Might not be correlated with clinical severity
- Indicated for inclusion in protocols of clinical trials

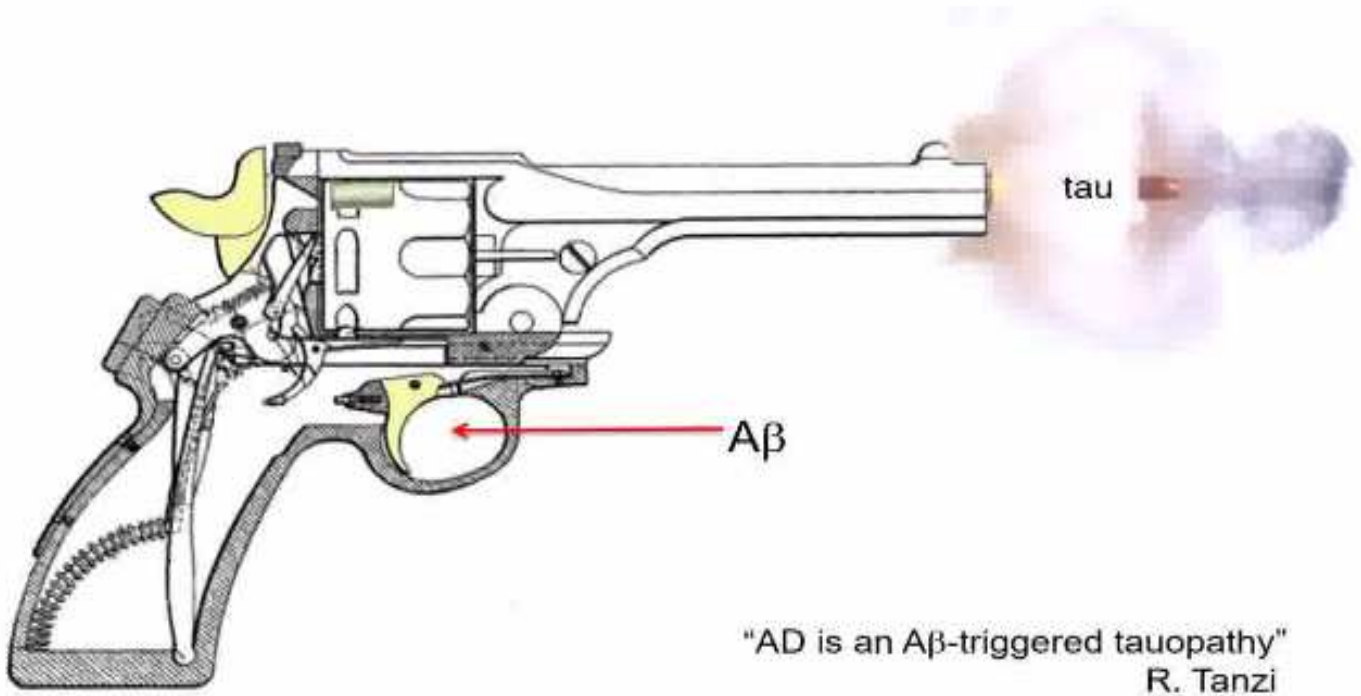
Progression marker Neurodegeneration

- Topographical or downstream marker
- Poor disease specificity
- Indicates clinical severity (staging marker)
- Might not be present in early stages
- Quantifies time to disease milestones
- Indicated for disease progression

FDG-PET
MRI

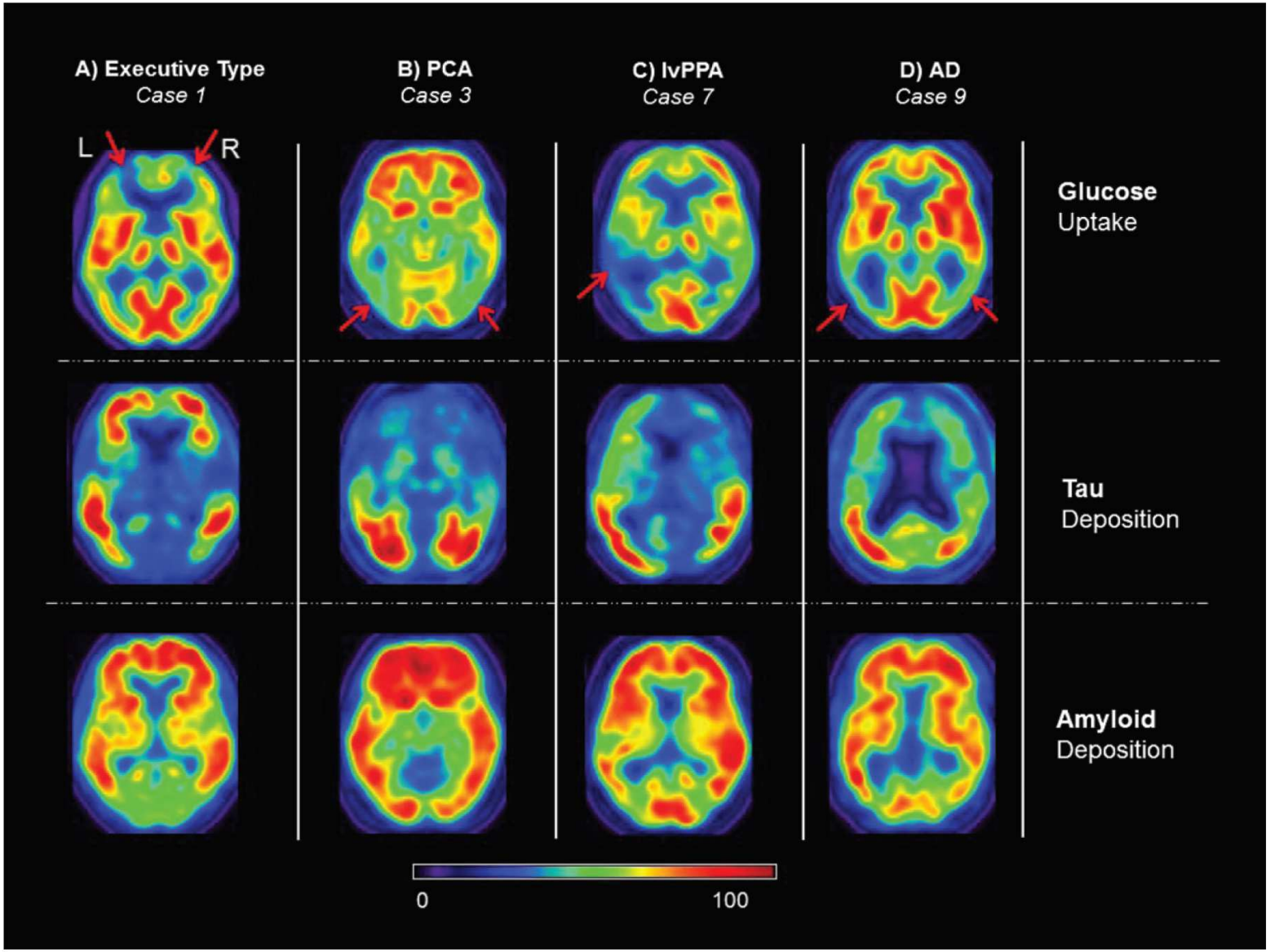
Neurodegeneration Biomarkers may be able to quantify time to disease milestones

Lancet Neurol 2014;13:614-29



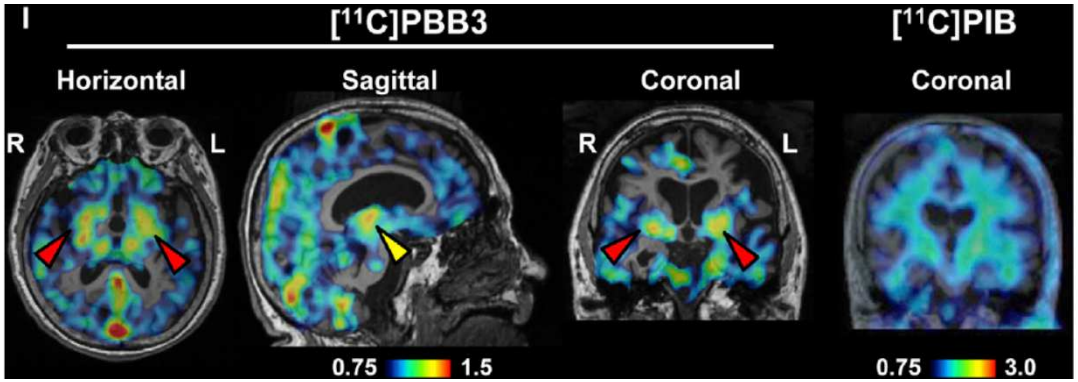
NEURODEGENERATION

Villemagne, Okamura & Rowe. Alzheimers Dement 2016


A) Executive Type
Case 1
B) PCA
Case 3
C) lvPPA
Case 7
D) AD
Case 9
L
R
Glucose
Uptake
Tau
Deposition
Amyloid
Deposition
0
100

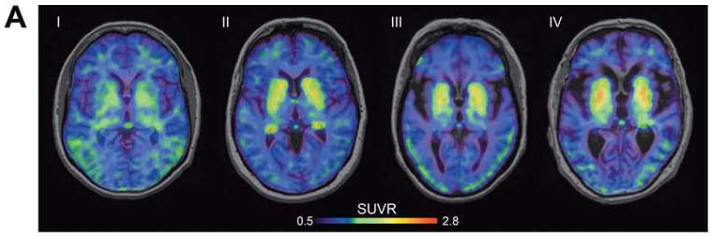
L'imaging con TAU PET al di fuori dell'AD

Cortico Basal Degeneration



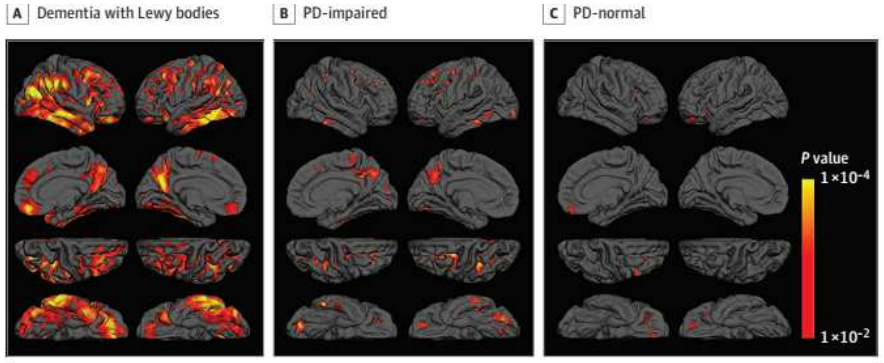
Maruyama et al, Neuron 2014

Progressive Supranuclear Palsy



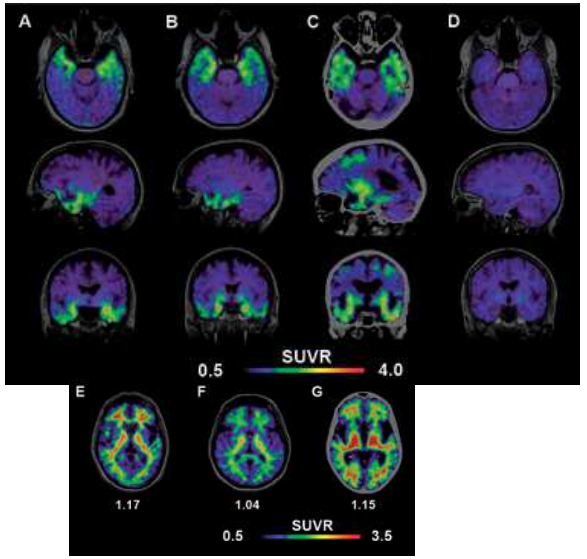
Smith et al, Movement Disorder 2016

Dementia with Lewy Body



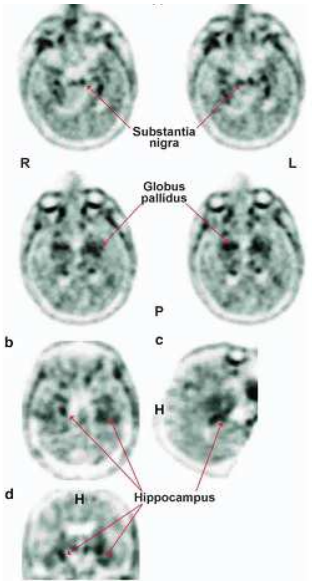
Gomperts et al JAMA Neurology 2016

MAPT mutation carriers



Smith et al, Brain 2016

Traumatic Brain Injury



Mitsis et al
Transl Psychiatry 2014

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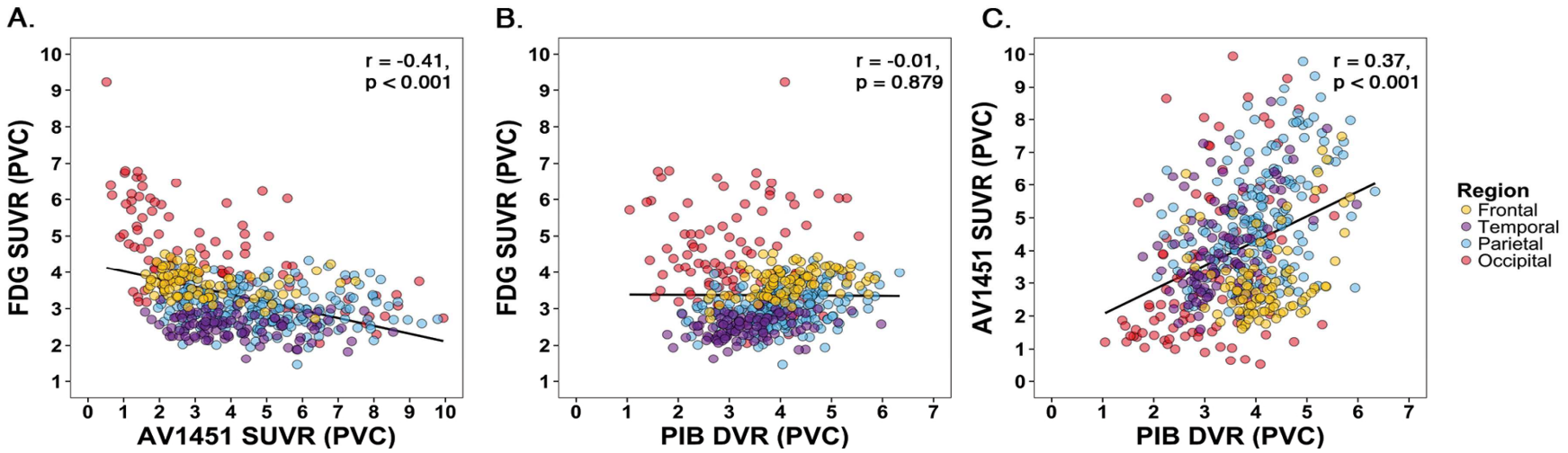
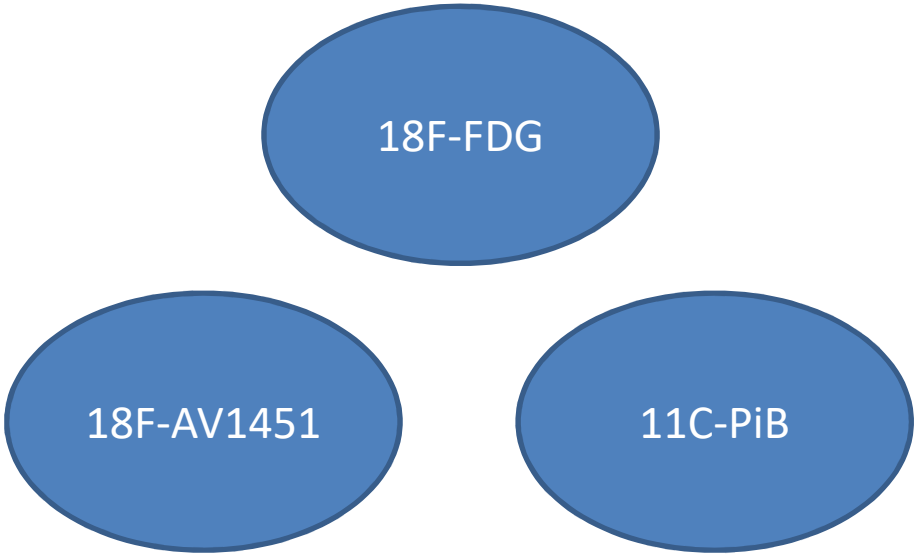


Pearson correlation analyses using *partial volume corrected data* showed a strong association between increased 18F-AV1451 and reduced 18F-FDG uptake and between 18F-AV1451 SUVR and 11C-PiB DVR, while no association was found between 11C-PiB and 18F-FDG SUVR.

The 18F-AV1451 pattern was inversely correlated with regional cortical hypometabolism assessed by FDG-PET, in the cortical brain areas associated with the impaired cognitive functions.



TAU pathology is the major correlate of clinical symptoms and neurodegeneration severity

tau pathology, preferentially occupied brain areas that are critical for cognitive functions uniquely affected in distinct variants of Alzheimer's disease

Amyloid-b pathology, as measured by 11C-PiB PET, affected both clinically affected and unaffected regions and showed weak association with regional glucose metabolism