PET con traccianti per Amiloide

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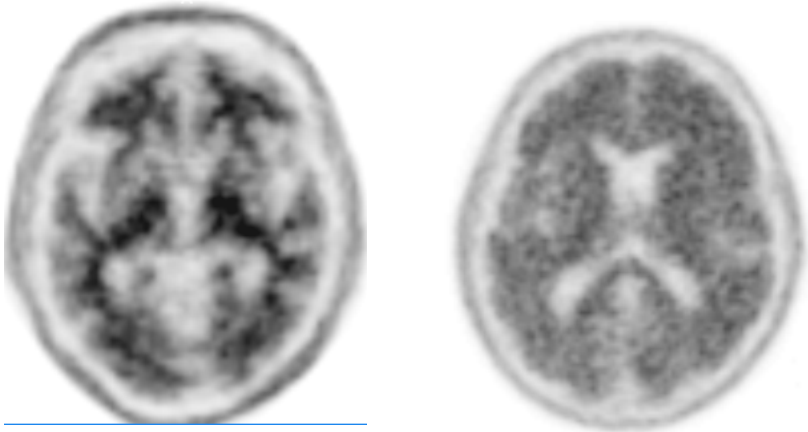
Universita' di Genova

Articolo su Amyloid PET: come lo avrei voluto…

Ruolo Diagnostico

Potenziale ruolo nello sviluppo di nuove strategie terapeutiche

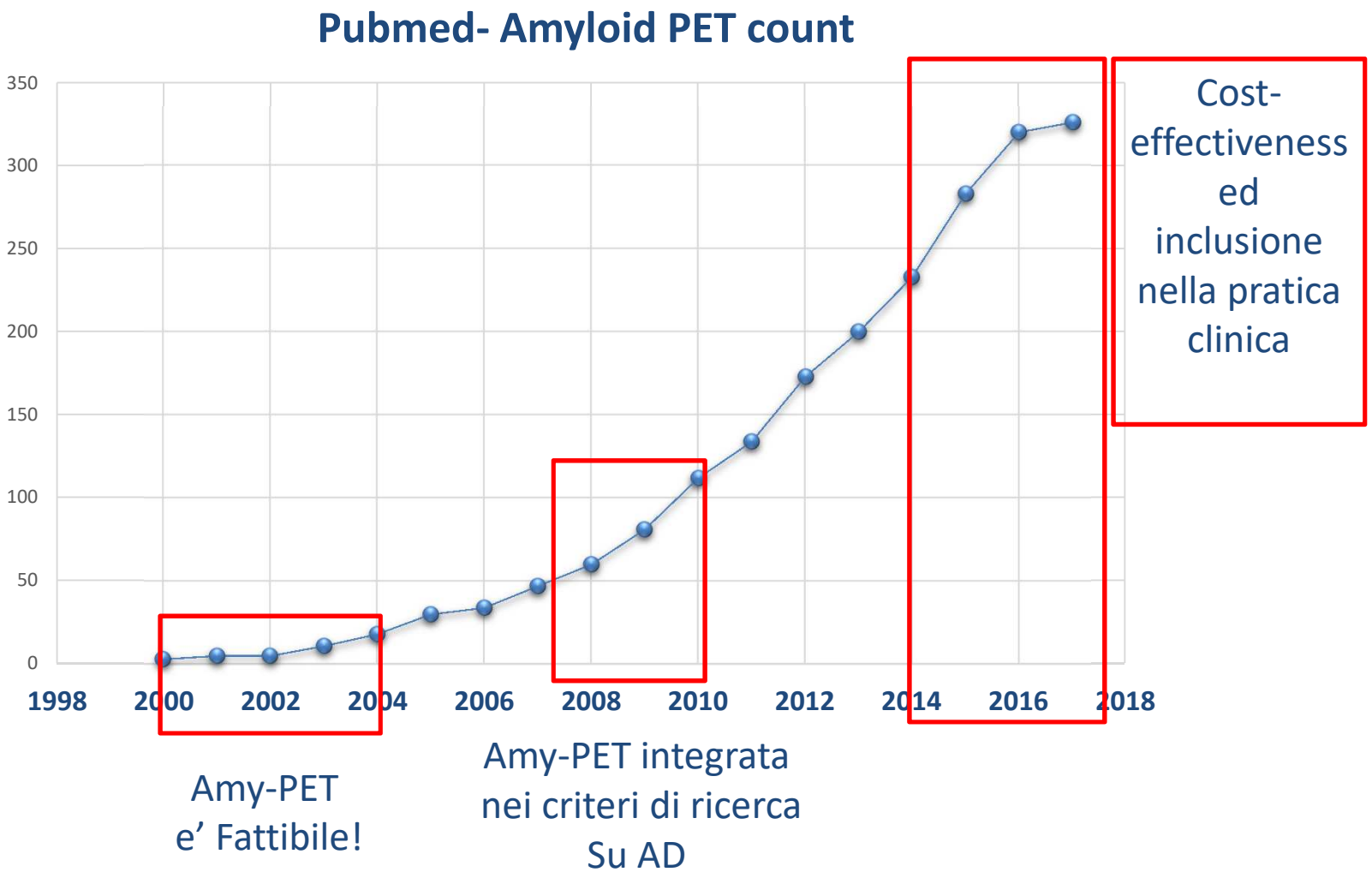


Prevalenza/Rilevanza nell'invecchiamento fisiologico

Impatto sulla gestione clinica dei pazienti con AD

Rilevanza Fisiopatologica nell'AD

Un articolo letto nell'ultimo anno su Amyloid PET



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Ann Neurol 1988;23:138–144

Clinical, Pathological, and Neurochemical Changes in Dementia: A Subgroup with Preserved Mental Status and Numerous Neocortical Plaques

Robert Katzman, MD,* Robert Terry, MD,* Richard DeTeresa, BS,* Theodore Brown, PhD,† Peter Davies, PhD,‡§ Paula Fuld, PhD,‖ Xiong Renbing, MA,† and Arthur Peck, MD¶

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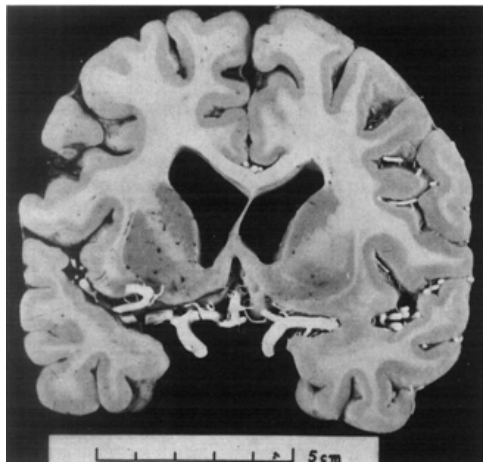
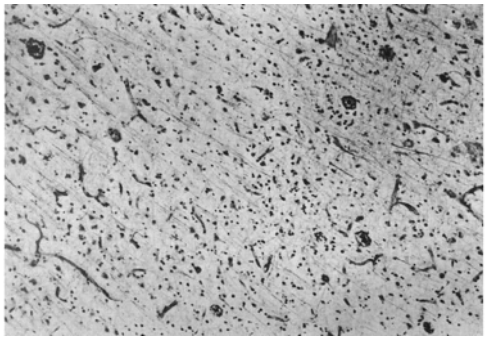
Observations on the Brains of Non-Demented Old People

B. E. TOMLINSON, G. BLESSED AND M. ROTH

Medical Research Council Group on the Relationship between Functional and Organic Psychiatric Illnesses, Department of Psychological Medicine, University of Newcastle upon Tyne, and Department of Pathology, Newcastle General Hospital, Newcastle upon Tyne (Great Britain)

(Received 16 February, 1968)





Brit. J. Psychiat. (1968), **114**, 797–811

The Association Between Quantitative Measures of Dementia and of Senile Change in the Cerebral Grey Matter of Elderly Subjects

By G. BLESSED, B. E. TOMLINSON and MARTIN ROTH

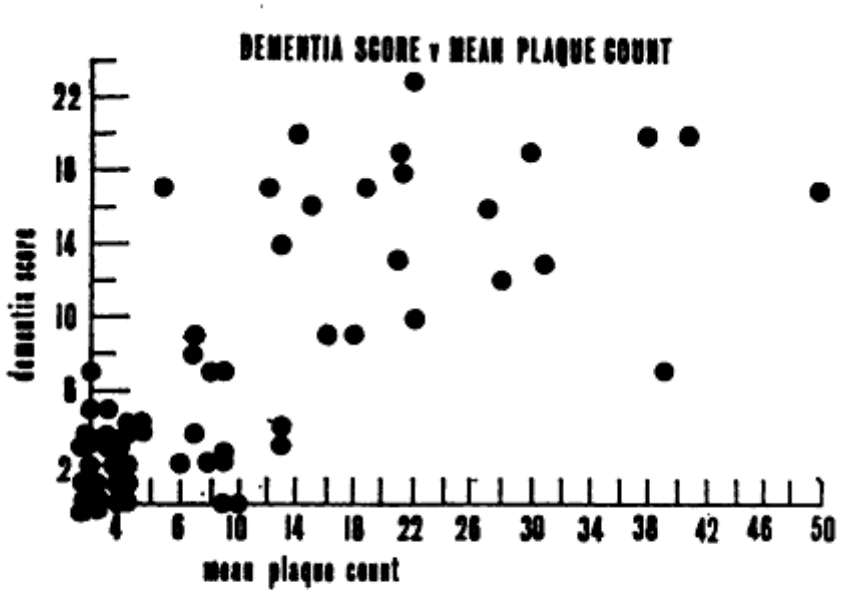
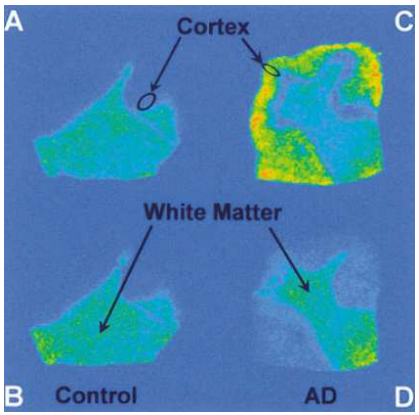


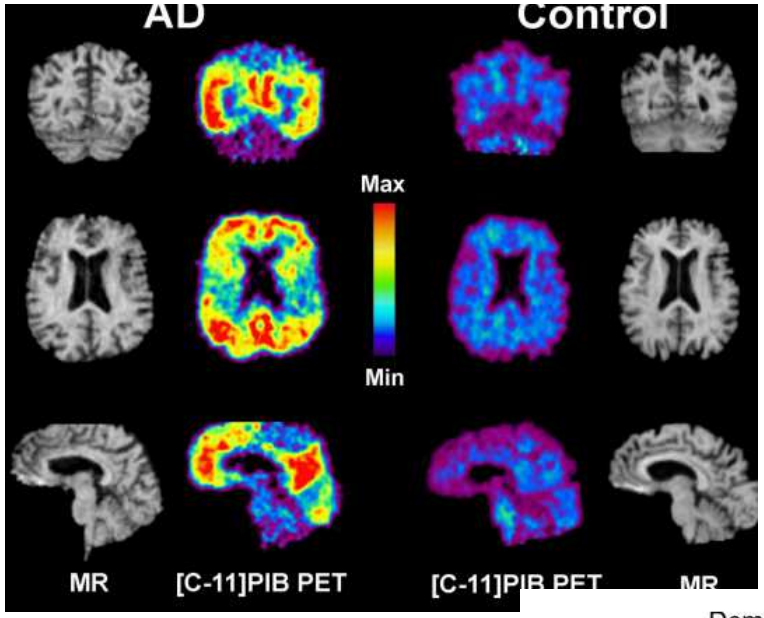
FIG. 3.—Relationship of dementia score to mean plaque count in 60 aged subjects.

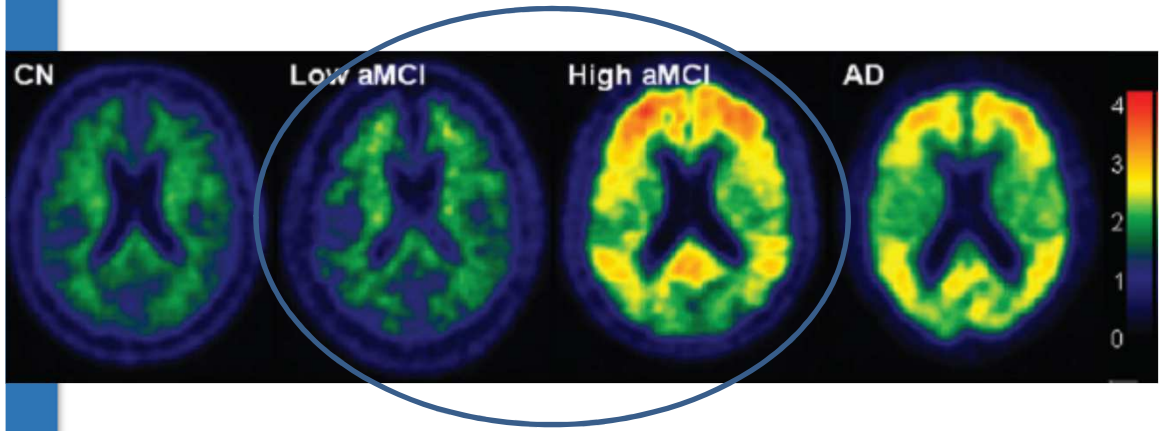
Background Diagnostico



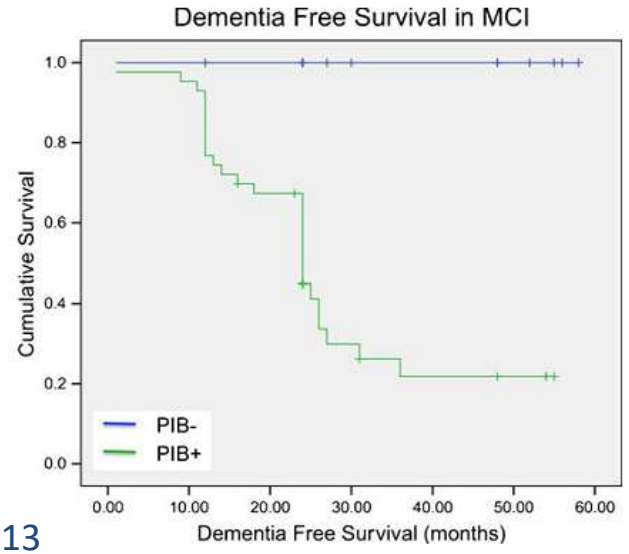
post-mortem

Ann Neurol 2004;55:306–319





Jack et al Brain 2008



Nordberg et al 2013

Scopi e Metodi

Clinical, Pathological, and Neurochemical Changes in Dementia: A Subgroup with Preserved Mental Status and Numerous Neocortical Plaques

Ann Neurol 1988;23:138–144

137 resident in a nursing facility subjects who underwent postmortem examination

To assess the correlation between mental status scores and plaque and tangle counts

To correlate pathology with Memory (Recall) and Fluency scores

To compare results with computer-assisted counts of cells in neocortex, and measures of the neurotransmitter markers choline acetyltransferase (ChAT) activity

Risultati:

Clinical, Pathological, and Neurochemical Changes in Dementia: A Subgroup with Preserved Mental Status and Numerous Neocortical Plaques

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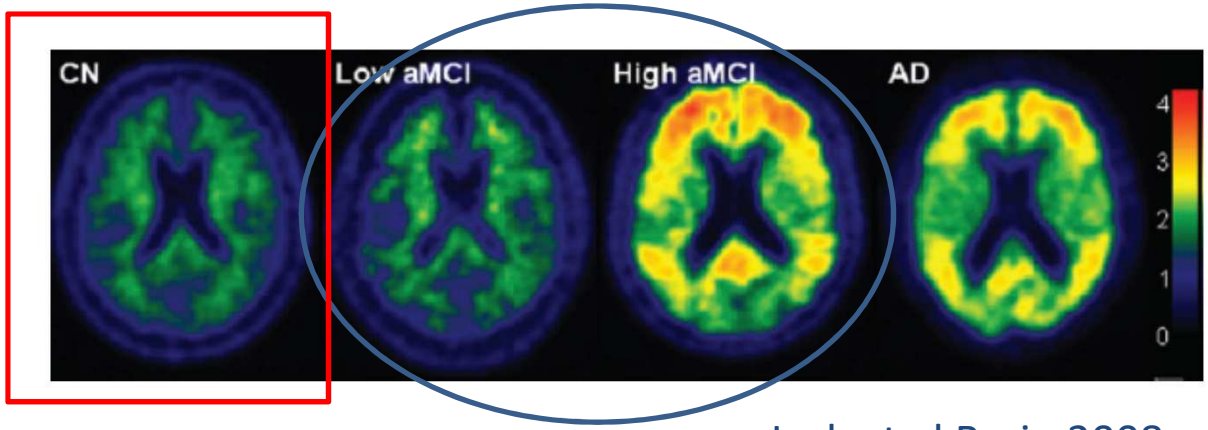
Clin. Dx	Normal	Demented	Demented	Normal
Path Dx	No AD	AD	No AD	AD
N	10 (9)	51 (25)	12 (20)	5 (5)
Age	84 (n=19)	86 (n=76)	86 (n=32)	87 (n=10)
Sex	17F	62F	25F	7F
BIMC	4	23	19	4
Retrieval	5	2	3	5
Fluency	30	13	14	25

???

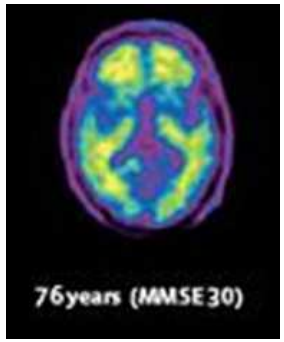
"10/137 cases of cognitively normal elders who were discovered to have advanced AD pathology in their brains at death"

Ruolo Diagnostico



Jack et al Brain 2008

Control (??)



Rowe
Lancet Neurology 2008

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Path Dx	No AD	AD	No AD	AD
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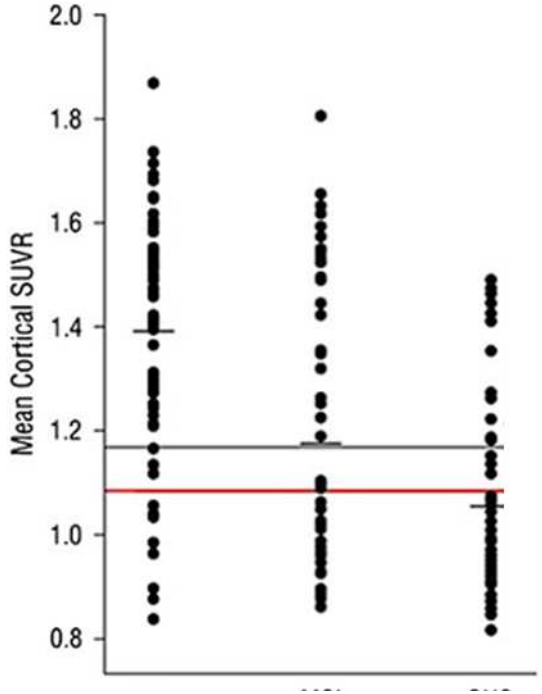
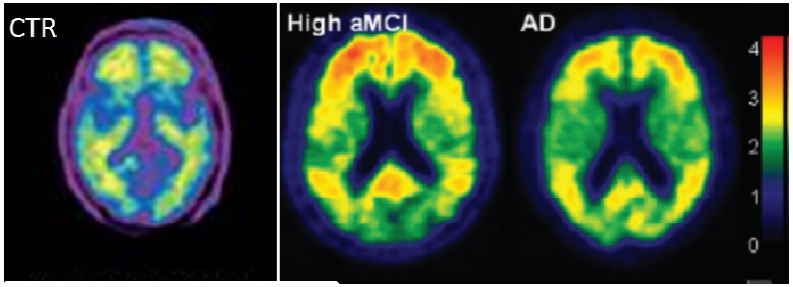
Amyloid-β imaging with PET in AD: is it feasible with current radiotracers and technologies?

Moghbel MC. Eur J Nucl Med Mol Imaging 2012





"Huge overlap among AD, MCI, and NC subjects which limits huge overlap among AD, MCI, and NC subjects, which limits PET imaging utility for diagnostic purposes"

Amiloidosi Cerebrale: prevalenza ‘secondo’ la PET

Table 2. Clinical Measures[a]

	Nondemented				Demented			
	A		B		C		D	
Measure	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD
Age (yr)	10	86.7 ± 3.9	19	83.8 ± 8.4	76	85.5 ± 7.1	32	85.7 ± 6.6
Function								
F1[b]	8	1.2 ± 2.0	17	3.5 ± 4.1	63	8.5 ± 4.5	26	7.6 ± 5.2
F2[b]	8	2.0 ± 2.6	16	3.5 ± 4.1	59	6.2 ± 4.0	25	4.1 ± 3.7
Blessed IMC[b]	10	3.8 ± 3.3	17	4.3 ± 2.8	60	22.7 ± 6.9	26	18.6 ± 5.8
Retrieval								
Five trials[b]	10	29.9 ± 12.8	17	26.8 ± 14.2	46	8.4 ± 10.3	18	17.2 ± 10.5
First trial[b]	10	5.3 ± 2.5	17	5.1 ± 2.1	46	1.8 ± 2.0	18	3.4 ± 1.8
Fluency (three categories)[b]	10	24.9 ± 8.0	16	29.4 ± 11.3	41	13.1 ± 7.4	17	14.4 ± 6.4

[a]Patients in Groups A, C = Alzheimer's pathology; B = no brain lesions; D = no Alzheimer's pathology.
[b]$p < 0.001$, comparison of groups using rank order (Kruskal-Wallis).
IMC = information–memory–concentration test.

Katzmann et al 1988

Normal
AD
5 (5)
87 (n=10) 7F
4
5
25

Panel 1: **Criteria for the appropriateness of routine clinical use of amyloid PET (according to Johnson and colleagues[40])**

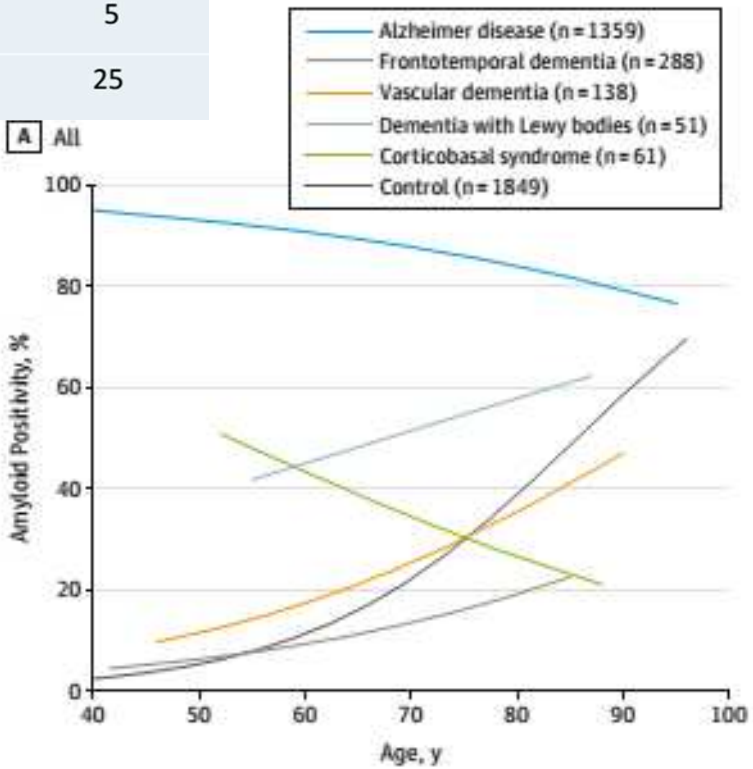
2013

Appropriate use of amyloid PET

- Persistent or progressive unexplained memory loss
- Unusual clinical presentation
- Atypically early age of onset (before age 65 years)

Inappropriate use of amyloid-PET

- In patients who are 65 years or older and meet standard definitions and tests for Alzheimer's disease
- In patients without clinical confirmation of cognitive impairment
- To determine dementia severity
- If requested solely on the basis of a family history of dementia or the presence of *APOE* ε4
- As a substitute for genotyping
- For non-medical reasons



Ossenkopelle et al JAMA 2015

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Path Dx	AD	No AD	AD	No AD
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Sex	7F	17F	62F	25F
BIMC	4	4	23	19
Retrieval	5	5	2	3
Fluency	25	30	13	14

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They had greater number of neurons > 90 μm^2 as compared to age-matched nursing home control subjects.

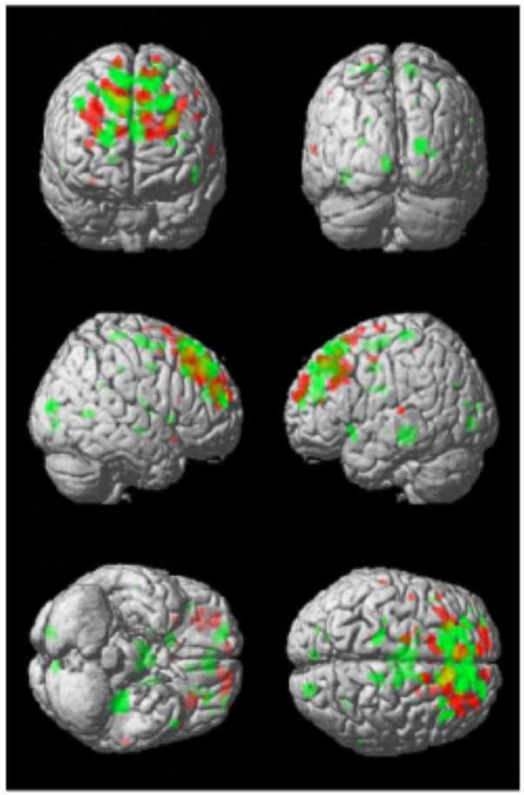
Clin. Dx	Normal	Normal	Demented	Demented
Path Dx	AD	No AD	AD	No AD
MF small neurons	857	847	840	804
MF large neurons	137	111	99	120
IP small neurons	1103	879	863	844
IP large neurons	145	100	74	88
ST small neurons	814	788	796	785
ST large neurons	133	100	73	92

"…these people did not express the clinical features of AD as it might be said they had a greater reserve."

These people might have started with a larger brain and more large neurons (Katzmann et al 1988)

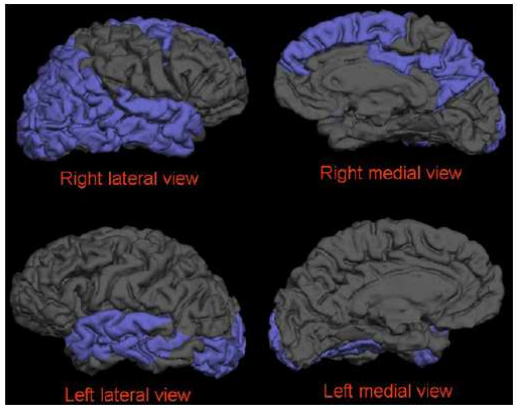
Resting state fMRI

CR-related brain activation



Stern, Cereb Cortex 2008

Structural MRI

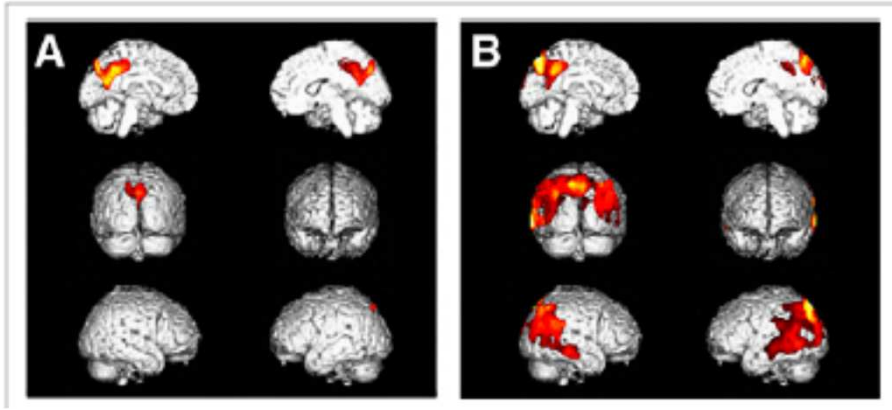


Liu et al 2012 Neuroradiology

18F-FDG PET

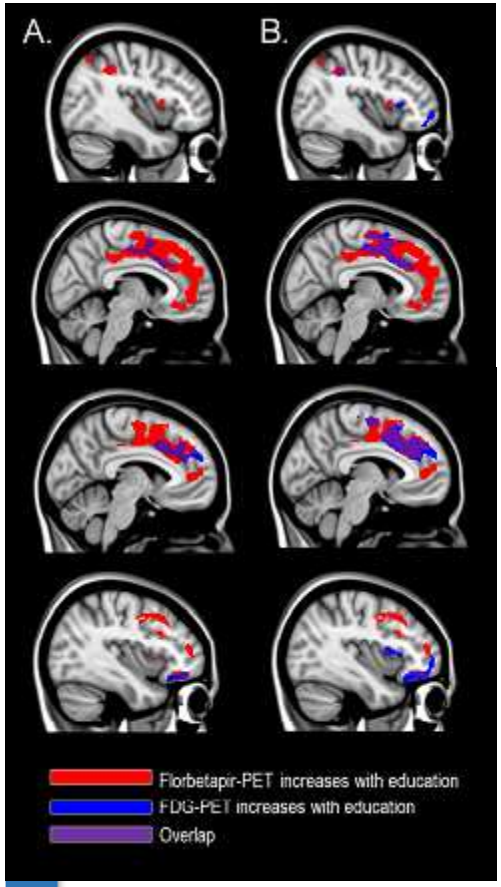
Poorly Educated

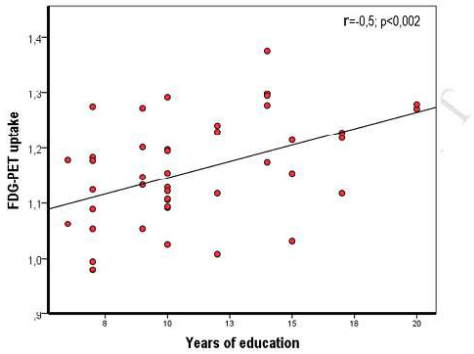
Highly Educated



Morbelli et al JNM 2013

Riserva versus Resilienza

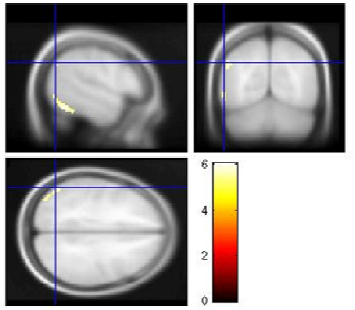




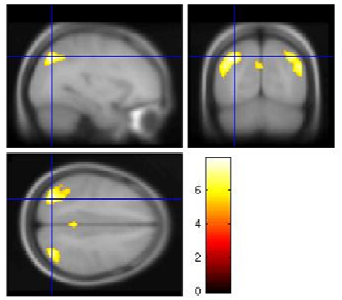
Arenaza-Urquijo et al
Neurobiol Aging 2017 in press

AMY+ MCI

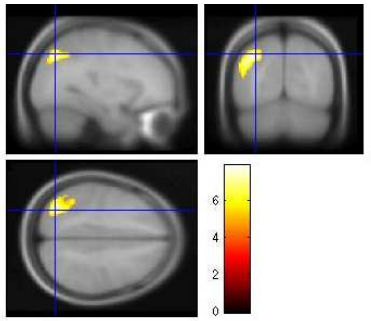
CTR > LOW-EDUC MCI



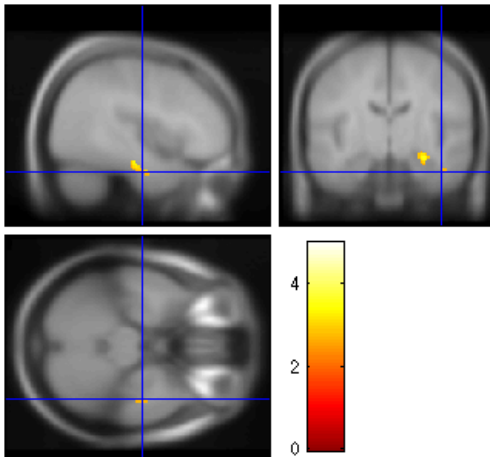
CTR > HIGH-EDUC MCI



CTR > EXCEPTIONALLY EDUC AMY+ MCI



Preserved Metabolism in
Exceptionally
educated AMY+ MCI



Bauckneht et
al submitted

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Rilevanza Fiosiopatologica

ALZFORUM
NETWORKING FOR A CURE

New Dementia Trials to Test Lifestyle Interventions

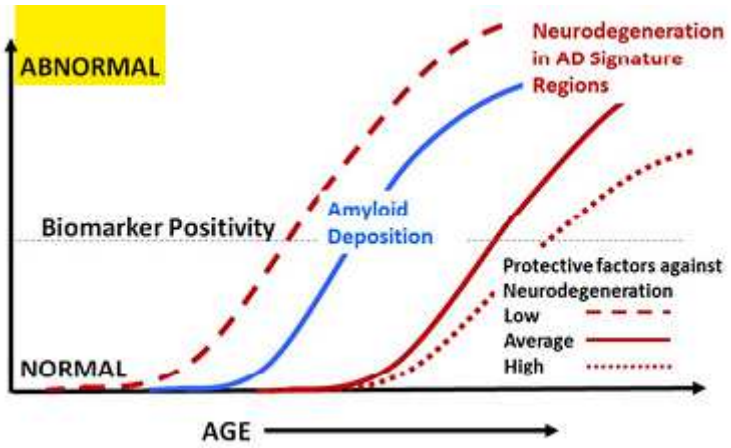
11 Aug 2017

Alzheimer's & Dementia ■ (2017) 1-8

Multidomain lifestyle intervention benefits a large elderly population at risk for cognitive decline and dementia regardless of baseline characteristics: The FINGER trial

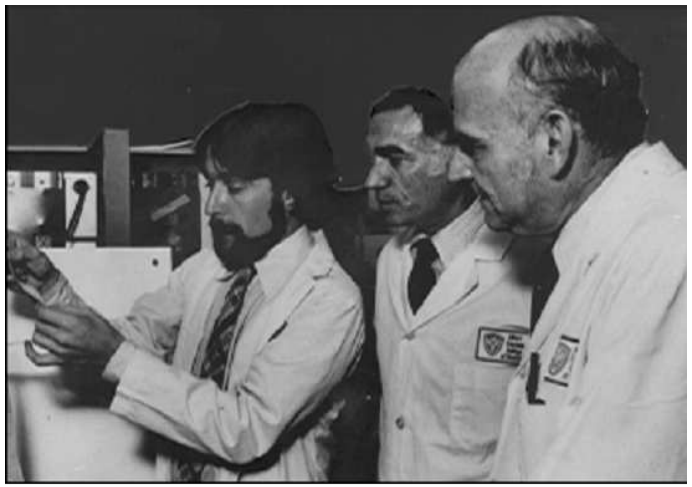
Introduction: The 2-year Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) multidomain lifestyle intervention trial (NCT01041989) demonstrated beneficial effects on cognition. We investigated whether sociodemographics, socioeconomic status, baseline cognition, or cardiovascular factors influenced intervention effects on cognition.

Conclusions: The FINGER intervention was beneficial regardless of participants' characteristics and can thus be implemented in a large elderly population at increased risk for dementia.



Vemuri et al
Jama Neurol 2017

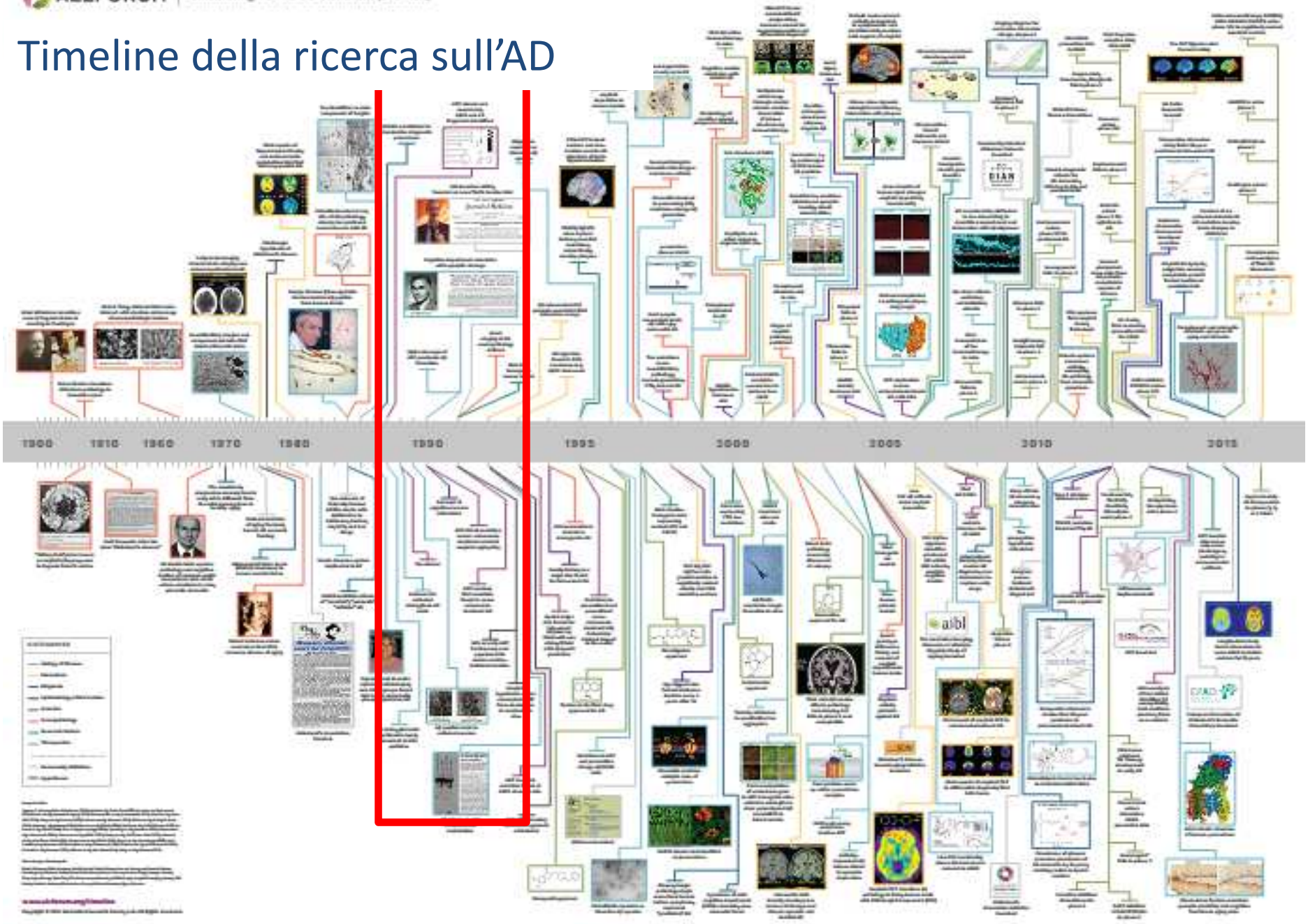
Grazie per l’attenzione ma soprattutto grazie a…



Peter Davies, Robert D. Terry, and Robert Katzman.

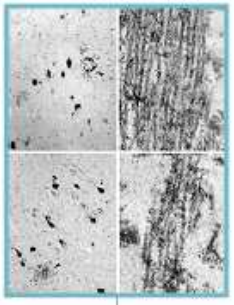
ALZFORUM | Celebrating 20 Years of Alzforum (1996 - 2016)

Timeline della ricerca sull'AD



CERAD established to standardize diagnostic procedures

Tau identified as main component of tangles



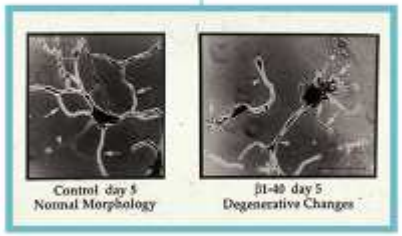
Braak staging of AD neuropathology defined

1980

1990

Alzheimer's Association founded

NINCDS-ADRDA criteria of "possible", "probable", "definite" AD



Aβ peptide toxic to cultured neurons