Debolezze e certezze dell'ipotesi amiloidea.

Luca Rozzini

Research criteria for the diagnosis of Alzheimer's disease: revising the NINCDS–ADRDA criteria

Bruno Dubois, Howard H Feldman*, Claudia Jacova, Steven T DeKosky, Pascale Barberger-Gateau, Jeffrey Cummings, André Delacourte, Douglas Galasko, Serge Gauthier, Gregory Jicha, Kenichi Meguro, John O'Brien, Florence Pasquier, Philippe Robert, Martin Rossor, Steven Salloway, Yaakov Stern, Pieter J Visser, Philip Scheltens*

The NINCDS–ADRDA and the DSM-IV-TR criteria for Alzheimer's disease (AD) are the prevailing diagnostic standards in research; however, they have now fallen behind the unprecedented growth of scientific knowledge. Distinctive and reliable biomarkers of AD are now available through structural MRI, molecular neuroimaging with PET, and cerebrospinal fluid analyses. This progress provides the impetus for our proposal of revised diagnostic criteria for AD. Our framework was developed to capture both the earliest stages, before full-blown dementia, as well

"Viene previsto che ci debbano essere almeno uno o più biomarkers anormali tra neuroimaging strutturale con MRI, neuroimaging molecolare con PET e l'analisi del liquido cerebrospinale di β amiloide o di proteine tau."

Lancet Neurol 2007; 6: 734–46

alzheimer's association

DIAGNOSTIC CRITERIA FOR PROBABLE AD IN 2011 (NIA-AA)

Dementia established clinically, eg deficit in two or more areas or cognition, interfering with daily life, progressing gradually.

No disturbance of consciousness.

Any age.

Absence of other brain or systemic disease that could account for the dementia.

Optional evidence of AD pathophysiology using biomarkers.

I marker biologici

per Malattia di Alzheimer possono essere suddivisi in patofisiologici e topografici.

I marker biologici possono essere suddivisi in patofisiologici e topografici.

Riduzione della concentrazione di beta amiloide, aumento della proteina tau totale e della fosfo-tau nel liquido cerebrospinale si associano a percentuali molto alte di progressione da Mild Cognitive Impairment amnesico a malattia di Alzheimer e hanno mostrato ripetutamente elevata sensibilità e specificità nei modelli predittivi.

La PET con Pittsburgh compound B (PiB) o altri radioligandi (Amivid et all.).

L'utilizzo di PiB-PET sono predittive di declino cognitivo e di sviluppo di segni clinici di malattia di Alzheimer in soggetti anziani cognitivamente normali.

I marker biologici possono essere suddivisi in patofisiologici e topografici.

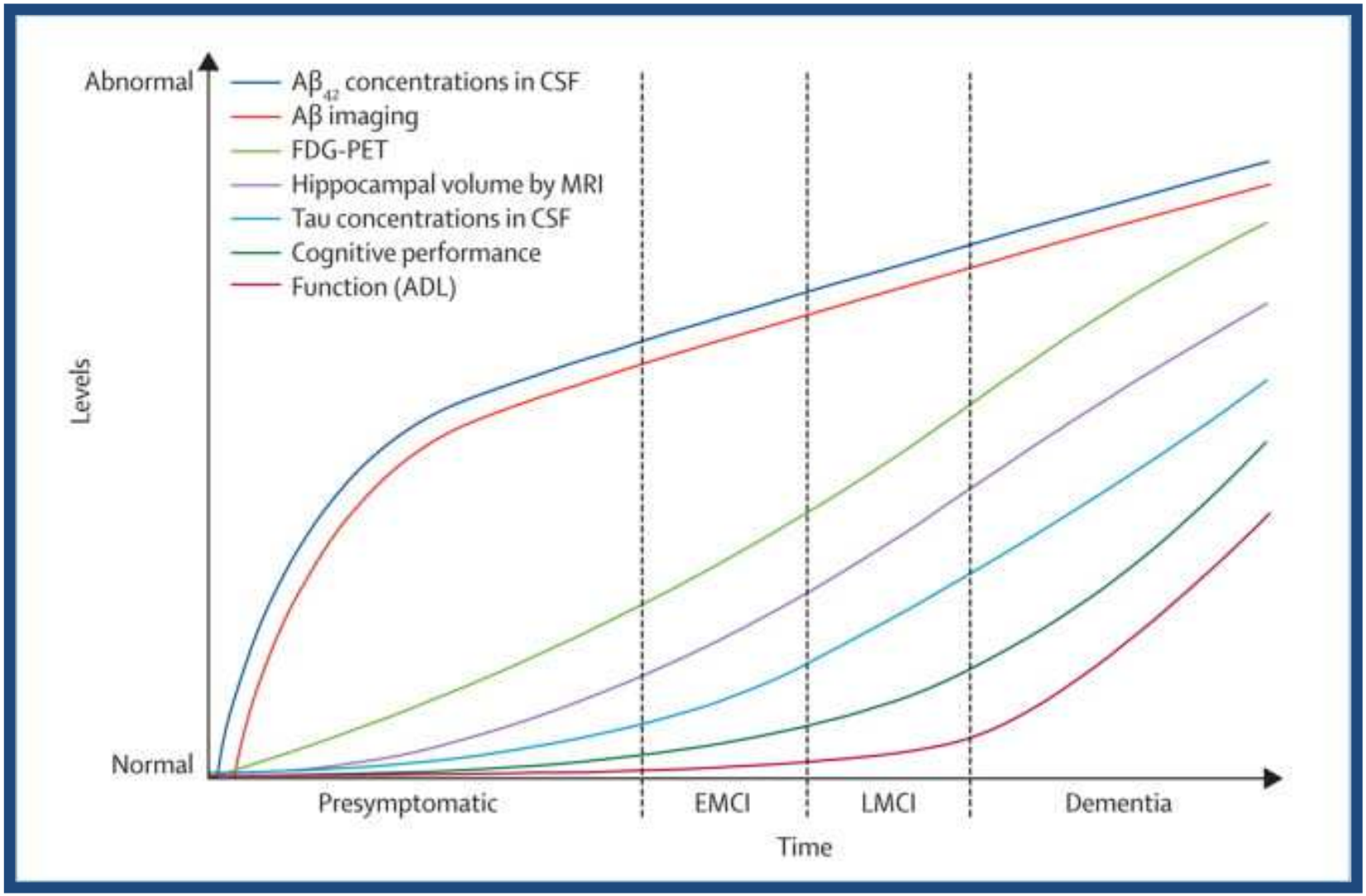
I marker topografici sono usati per valutare modificazioni cerebrali meno specifiche che correlano con la distribuzione regionale della malattia di Alzheimer e includono l'atrofia del lobo temporale mesiale e la riduzione del metabolismo del glucosio nelle regioni temporo-parietali alla PET con fluorodesossiglucosio.

Questi marker sono indicatori validi perché i cambiamenti strutturali cerebrali permettono di identificare lo stadio della deposizione di grovigli neurofibrillari.

	Pathophysiological markers	Topographical markers
Cerebrospinal fluid		
Amyloid β_{42}	Yes	No
Total tau, phospho-tau	Yes	No
PET		
Amyloid tracer uptake	Yes	No
Fluorodeoxyglucose	No	Yes
Structural MRI		
Medial temporal atrophy	No	Yes

AD=Alzheimer's disease.

Table 1: **Categorisation of the current, most-validated AD biomarkers**



The Lancet Neurology 2010; 9:4-5)

The NEW ENGLAND JOURNAL of MEDICINE

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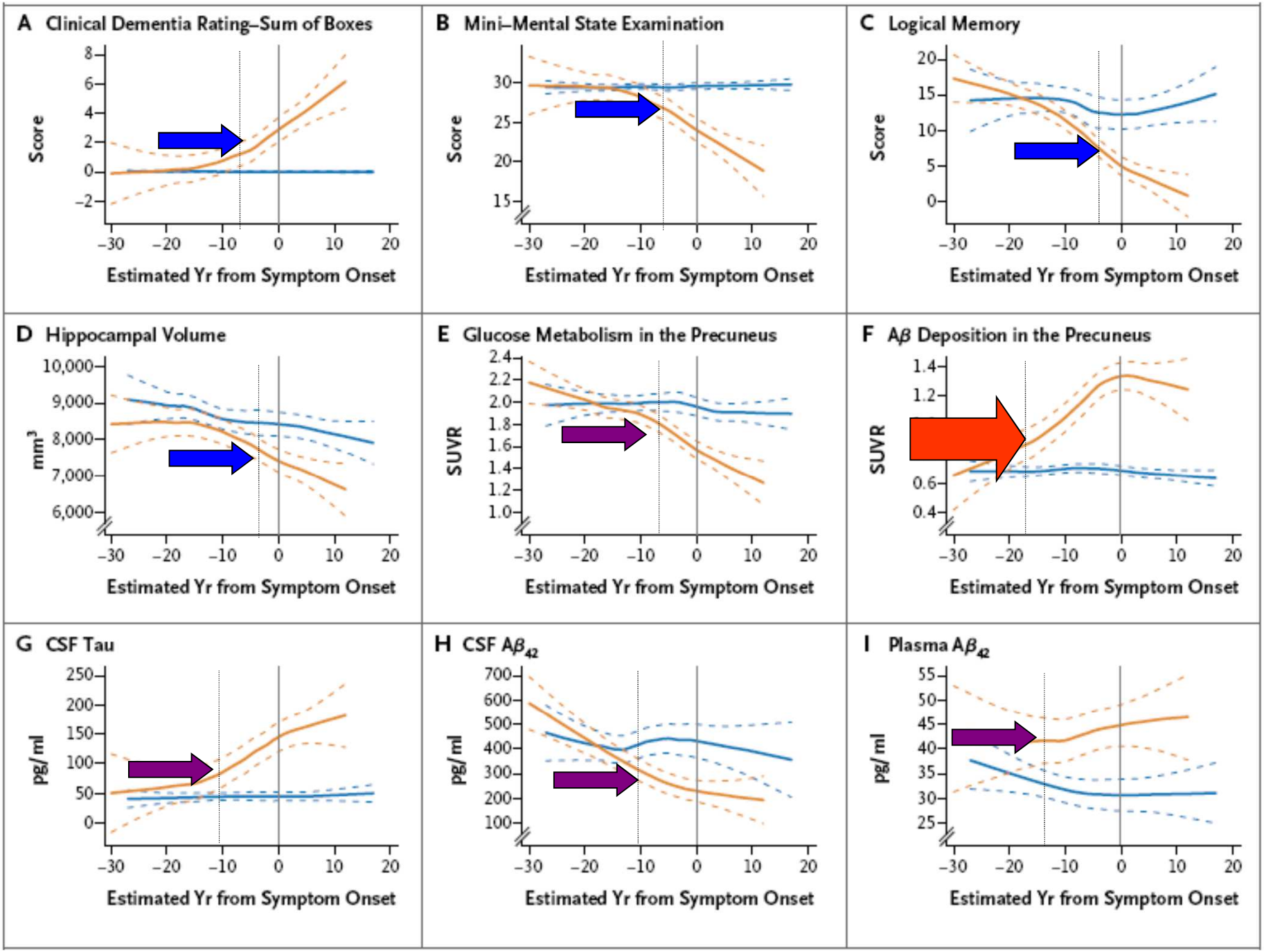
Clinical and Biomarker Changes in Dominantly Inherited Alzheimer's Disease

Randall J. Bateman, M.D., Chengjie Xiong, Ph.D., Tammie L.S. Benzinger, M.D., Ph.D., Anne M. Fagan, Ph.D., Alison Goate, Ph.D., Nick C. Fox, M.D., Daniel S. Marcus, Ph.D., Nigel J. Cairns, Ph.D., Xianyun Xie, M.S., Tyler M. Blazey, B.S., David M. Holtzman, M.D., Anna Santacruz, B.S., Virginia Buckles, Ph.D., Angela Oliver, R.N.,, Krista Moulder, Ph.D., Paul S. Aisen, M.D., Bernardino Ghetti, M.D., William E. Klunk, M.D., Eric McDade, M.D., Ralph N. Martins, Ph.D., Colin L. Masters, M.D., Richard Mayeux, M.D., John M. Ringman, M.D., Martin N. Rossor, M.D., Peter R. Schofield, Ph.D., D.Sc., Reisa A. Sperling, M.D., Stephen Salloway, M.D., and John C. Morris, M.D., for the Dominantly Inherited Alzheimer Network

Characteristic	Carriers (N=88)	Noncarriers (N=40)	P Value
Age — yr	39.1±10.3	39.5±8.9	0.92
Male sex — no. (%)	36 (41)	17 (42)	0.85
Education level — yr	13.9±2.5	15.0±2.5	0.04
Cognitive status — no. (%)†			
Symptomatic	43 (49)	1 (2)	0.29
Asymptomatic	45 (51)	39 (98)	
Positive for apolipoprotein E ε4 allele — no. (%)	22 (25)	9 (22)	0.69


A Clinical Dementia Rating–Sum of Boxes
Score
Estimated Yr from Symptom Onset
B Mini–Mental State Examination
Score
Estimated Yr from Symptom Onset
C Logical Memory
Score
Estimated Yr from Symptom Onset
D Hippocampal Volume
mm3
Estimated Yr from Symptom Onset
E Glucose Metabolism in the Precuneus
SUVR
Estimated Yr from Symptom Onset
F Aβ Deposition in the Precuneus
SUVR
Estimated Yr from Symptom Onset
G CSF Tau
pg/ml
Estimated Yr from Symptom Onset
H CSF Aβ42
pg/ml
Estimated Yr from Symptom Onset
I Plasma Aβ42
pg/ml
Estimated Yr from Symptom Onset

REVIEW ARTICLE

International Journal of Geriatric Psychiatry

PET imaging of brain amyloid in dementia: a review

Harriet Quigley, Sean J. Colloby and John T. O'Brien

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PET utilizes biologically active molecules in micromolar or nanomolar concentrations that have been labelled with short-lived positron-emitting isotopes such as 15^{O} (half-life 2 min), 11^{C} (20 min) and 18^{F} (110 min).

…However, the use of 15^{O} and 11^{C} limit their use to fully equipped PET centres with cyclotron and radiopharmacy.

Amyvid (Florbetapir F 18 Injection) for intravenous use (Initial U.S. Approval: 2012)

Amyvid is a radioactive diagnostic agent for Positron Emission Tomography (PET)

imaging of the brain to estimate β-amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for Alzheimer's Disease (AD) and other causes of cognitive decline.

INDICATIONS AND USAGE

Amyvid is indicated for Positron Emission Tomography (PET) imaging of the brain to estimate β-amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for Alzheimer's Disease (AD) and other causes of cognitive decline.

A negative Amyvid scan indicates sparse to no neuritic plaques, and is inconsistent with a neuropathological diagnosis of AD at the time of image acquisition; a negative scan result reduces the likelihood thata patient's cognitive impairment is due to AD.

A positive Amyvid scan indicates moderate to frequent amyloid neuritic plaques; neuropathological examination has shown this amount of amyloid neuritic plaque is present in patients with AD, but may also be present in patients with other types of neurologic conditions as well as older people with normal cognition. Amyvid is an adjunct to other diagnostic evaluations.

Limitations of Use

A positive Amyvid scan does not establish a diagnosis of AD or other cognitive disorder.

Safety and effectiveness of Amyvid have not been established for:

predicting development of dementia or other neurologic condition;

monitoring responses to therapies.

Il 14 Gennaio 2013 la Commissione europea ha rilasciato un'autorizzazione all'immissione in commercio per Amyvid, valida in tutta l'Unione europea.

Determina Aifa 14.10.13

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Medicinale solo per uso diagnostico.
Amyvid è un radiofarmaco indicato per rilevare con la tomografia ad emissione di positroni (PET) le immagini della densità delle placche neuritiche di ß-amiloide nel cervello di pazienti adulti con decadimento cognitivo che vengono valutati per la malattia di Alzheimer (AD) e altre cause di decadimento cognitivo.
Amyvid deve essere usato congiuntamente alla valutazione clinica.
Una scansione negativa indica la presenza di poche placche o l'assenza di placche, il che non è coerente con una diagnosi di AD.
Una scansione PET con florbetapir deve essere richiesta da medici con esperienza nella gestione clinica delle patologie neurodegenerative.
Le immagini ottenute con Amyvid devono essere interpretate solo da valutatori che hanno effettuato un training su come interpretare le immagini della PET con florbetapir (18 F).

Nei casi in cui con la scansione PET è difficile localizzare la sostanza grigia e il margine della sostanza bianca/grigia, si raccomanda un esame recente con tomografia computerizzata (TC) o con risonanza magnetica (RM), co-registrato con l'esame PET, per ottenere un'immagine combinata PET-TC o PET-RM.
Una scansione negativa indica una densità scarsa o assente di placche neuritiche corticali di ß-amiloide. Una scansione positiva indica una densità da moderata a frequente. Sono stati osservati errori di interpretazione dell'immagine nella valutazione della densità delle placche neuritiche cerebrali di ß-amiloide, inclusi dei falsi negativi.

Dati farmaco in scheda

La sensibilità della scansione con Amyvid nel rilevare la percentuale di passaggio da MCI ad AD nei 9 pazienti è stata del 66,7% (95% IC: 35–88%), la specificità nei 38 pazienti che non hanno avuto questa evoluzione è stata del 71,0% (95% IC: 55–83%) e il quoziente di probabilità positivo è stato di 2.31 (95% IC:1.2–4.5%).

Il disegno di questo studio non permette di stimare il rischio di evoluzione da MCI ad AD clinicamente manifesta.

JAMA Neurology | Original Investigation

Assessment of the Incremental Diagnostic Value of Florbetapir F 18 Imaging in Patients With Cognitive Impairment

The Incremental Diagnostic Value of Amyloid PET With [^{18}F]-Florbetapir (INDIA-FBP) Study

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OBJECTIVE To evaluate the incremental diagnostic value of amyloid PET with florbetapir F 18 in addition to the routine clinical diagnostic assessment of patients evaluated for cognitive impairment.

CONCLUSIONS AND RELEVANCE Amyloid PET in addition to routine assessment in patients with cognitive impairment has a significant effect on diagnosis, diagnostic confidence, and drug treatment. The effect on health outcomes, such as morbidity and mortality, remains to be assessed.

Original Research Article

Effectiveness of Florbetapir PET Imaging in Changing Patient Management

Michael J. Pontecorvo[a] Andrew Siderowf[a] Bruno Dubois[b]
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Flavio Nobili[h] Carl H. Sadowsky[i] Stephen Salloway[j] Anupa K. Arora[a]
Antoine Chevrette[a] Walter Deberdt[k] Grazia Dell'Agnello[l]
Matthew Flitter[a] Nick Galante[a] Mark J. Lowrey[a] Ming Lu[a]
Anne McGeehan[a] Michael D. Devous Sr.[a] Mark A. Mintun[a]

Dement Geriatr Cogn Disord 2017;44:129–143
DOI: 10.1159/000478007

Conclusion: Knowledge of the amyloid status affects the diagnosis and alters patient management.

Strategic roadmap for an early diagnosis of Alzheimer's disease based on biomarkers

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Lancet Neurol. 2017 Aug;16(8):661-676

The diagnosis of Alzheimer's disease can be improved by the use of biological measures. Biomarkers of functional impairment, neuronal loss, and protein deposition that can be assessed by neuroimaging (ie, MRI and PET) or CSF analysis are increasingly being used to diagnose Alzheimer's disease in research studies and specialist clinical settings. However, the validation of the clinical usefulness of these biomarkers is incomplete, and that is hampering reimbursement for these tests by health insurance providers, their widespread clinical implementation, and improvements in quality of health care. We have developed a strategic five-phase roadmap to foster the clinical validation of biomarkers in Alzheimer's disease, adapted from the approach for cancer biomarkers. Sufficient evidence of analytical validity (phase 1 of a structured framework adapted from oncology) is available for all biomarkers, but their clinical validity (phases 2 and 3) and clinical utility (phases 4 and 5) are incomplete. To complete these phases, research priorities include the standardisation of the readout of these assays and thresholds for normality, the evaluation of their performance in detecting early disease, the development of diagnostic algorithms comprising combinations of biomarkers, and the development of clinical guidelines for the use of biomarkers in qualified memory clinics.

JAMA Psychiatry | Original Investigation

Association of Cerebral Amyloid-β Aggregation With Cognitive Functioning in Persons Without Dementia

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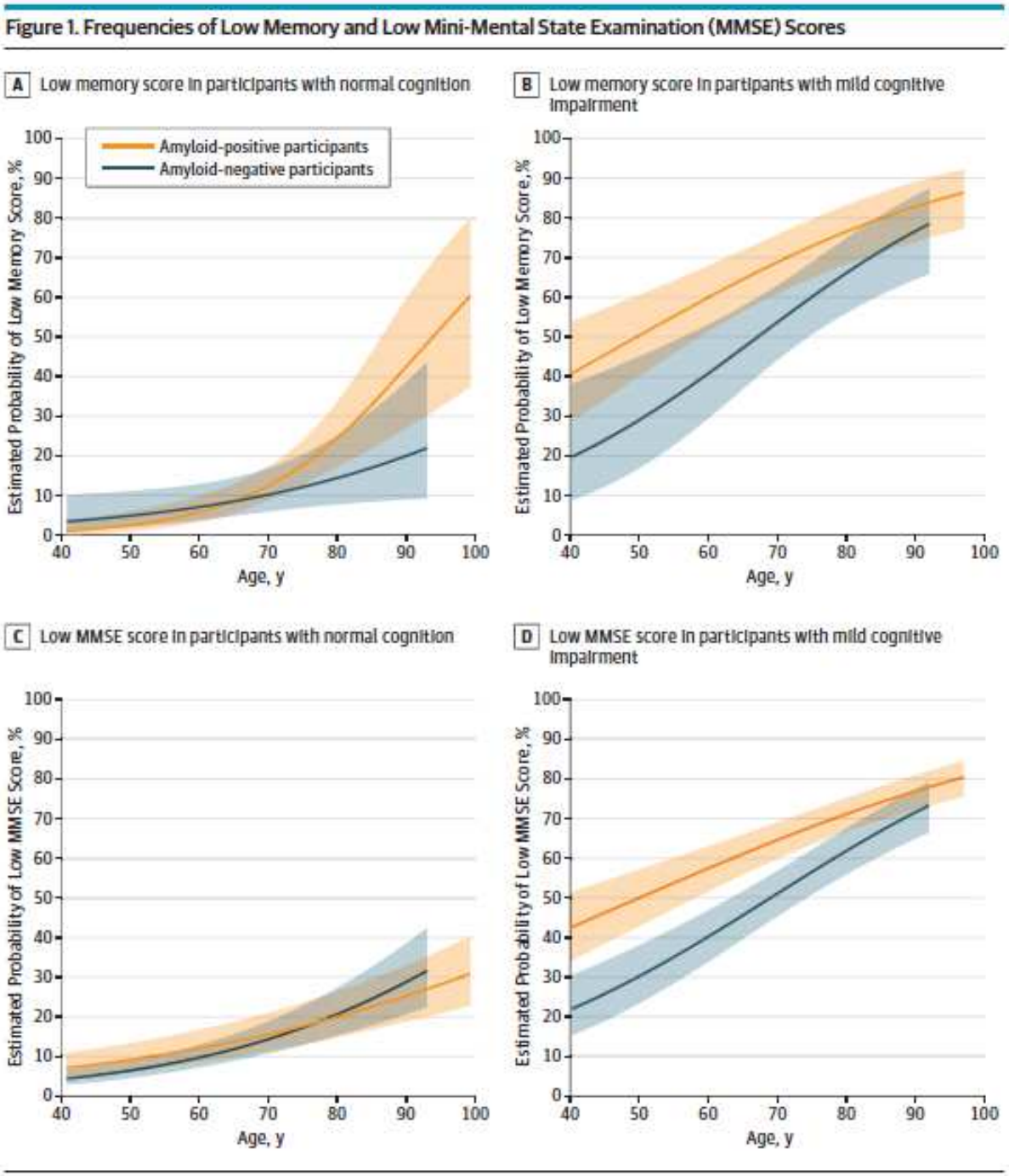
JAMA Psychiatry Published online November 29, 2017

JAMA Psychiatry | Original Investigation

Association of Cerebral Amyloid-β Aggregation With Cognitive Functioning in Persons Without Dementia

OBJECTIVE To investigate whether amyloid-β aggregation is associated with cognitive functioning in persons without dementia.

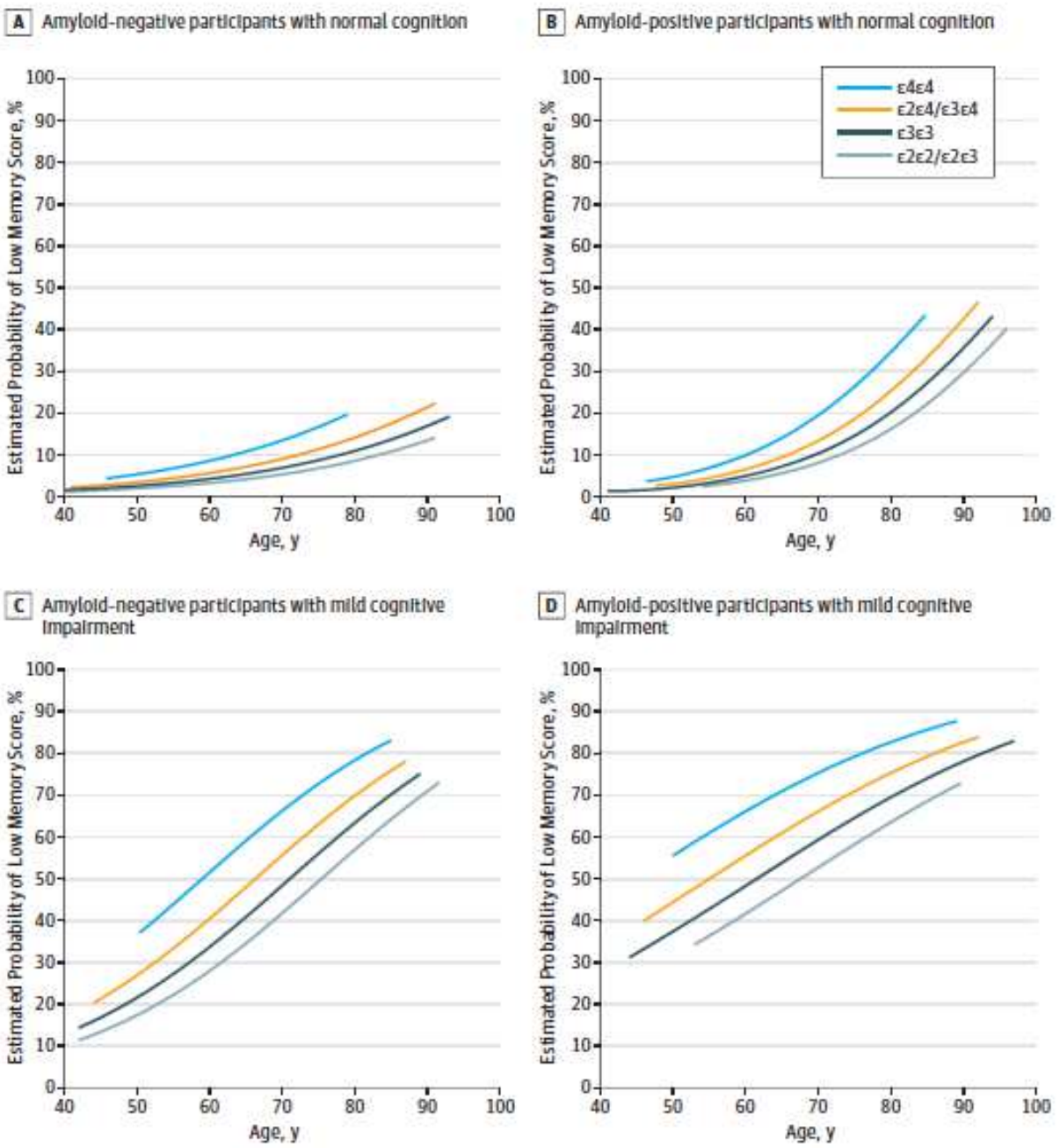
DESIGN, SETTING, AND PARTICIPANTS This cross-sectional study included 2908 participants with normal cognition and 4133 with mild cognitive impairment (MCI) from 53 studies in the multicenter Amyloid Biomarker Study. Normal cognition was defined as having no cognitive concerns for which medical help was sought and scores within the normal range on cognitive tests. Mild cognitive impairment was diagnosed according to published criteria. Study inclusion began in 2013 and is ongoing. Data analysis was performed in January 2017.



Nei soggetti sani ultra 70 anni è emersa un'associazione tra beta amiloide e il deficit mnesico (memory score) così come negli MCI ma in ogni età.

Negli MCI c'è un'associazione tra beta amiloide e MMSE ma non nei soggetti normali per qualsiasi fascia d'età.

Figure 2. Frequency of Low Memory Score According to Apolipoprotein E (*APOE*) Genotype



Conclusions

Although low memory scores are an early marker of amyloid positivity, their value as a screening measure for early AD among persons without dementia is limited.

JAMA Neurology | Original Investigation

Association of β-Amyloid and Apolipoprotein E ε4 With Memory Decline in Preclinical Alzheimer Disease

Key Points

Question What is the association of β-amyloid and the presence of the apolipoprotein E (*APOE*) ε4 with memory decline with increasing age?

Findings In this longitudinal study of 447 cognitively healthy older adults, memory decline in β-amyloid–positive ε4 carriers began earlier (64.5 years of age) than in β-amyloid–positive ε4 noncarriers (76.5 years of age). The rate of decline was also faster, such that by 85 years of age, β-amyloid–positive ε4 carriers performed worse than β-amyloid–positive ε4 noncarriers.

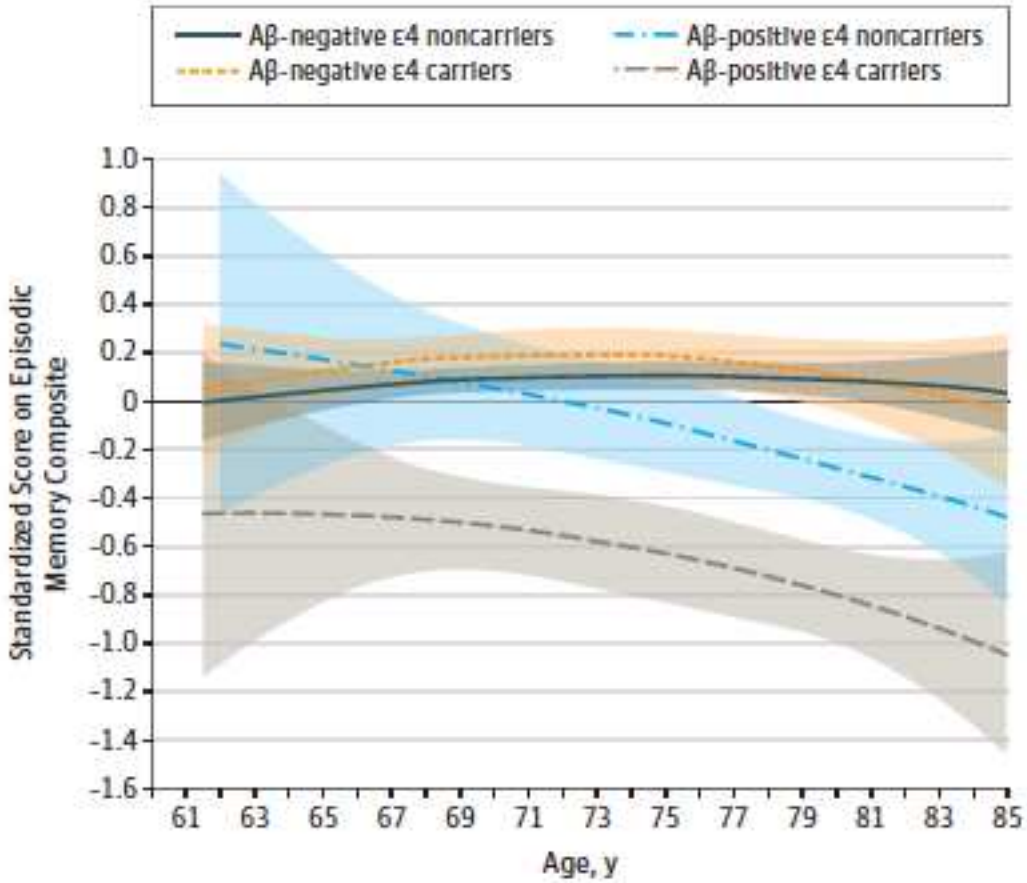
Meaning These results suggest that memory decline in β-amyloid–positive adults may accelerate with older age and that this increase in acceleration may be associated with the *APOE* ε4 allele.

JAMA Neurology January 22, 2018 (Reprinted

Table 1. Demographic and Clinical Characteristics of the Sample

Characteristic	Aβ-Negative ε4 Noncarriers (n = 260)	Aβ-Negative ε4 Carriers (n = 64)	Aβ-Positive ε4 Noncarriers (n = 51)	Aβ-Positive ε4 Carriers (n = 72)	Planned Comparison, *P* Value		
					Aβ-Negative ε4 Carriers vs Noncarriers	Aβ-Positive ε4 Carriers vs Noncarriers	Aβ-Negative ε4 Noncarriers vs Aβ-Positive ε4 Carriers
Female, No. (%)	145 (55.8)	35 (54.7)	24 (47.1)	40 (55.6)	.88	.35	.97
Age, mean (SD), y	70.2 (5.7)	69.4 (6.0)	75.7 (5.9)	73.1 (6.4)	.32	.02	<.001
Premorbid IQ, mean (SD)	108.6 (6.8)	107.9 (7.6)	110.3 (7.9)	108.2 (8.1)	.50	.17	.70
GDS score, mean (SD)[a]	0.91 (1.33)	1.02 (1.49)	0.85 (1.22)	1.11 (1.26)	.56	.26	.25
BECKET	1.28 (0.24)	1.33 (0.32)	2.11 (0.37)	1.88 (0.46)	.17	.004	<.001
Time between PET scans, mean (SD), y[b]	3.20 (1.55)	2.69 (1.51)	2.66 (1.73)	1.99 (1.40)	.02	.02	<.001
CDR score, mean (SD)[c]	0.04 (0.14)	0.06 (0.17)	0.17 (0.26)	0.19 (0.24)	.33	.66	<.001
CDR sum of boxes score, mean (SD)[c]	0.07 (0.25)	0.10 (0.30)	0.22 (0.41)	0.43 (0.77)	.41	.08	<.001
MMSE score, mean (SD)[d]	28.91 (1.25)	28.90 (1.16)	28.67 (1.45)	28.10 (1.79)	.95	.06	<.001

Figure. Standardized Score on the Episodic Memory Composite by Age



In vivo staging of regional amyloid deposition

Michel J. Grothe, PhD
Henryk Barthel, MD
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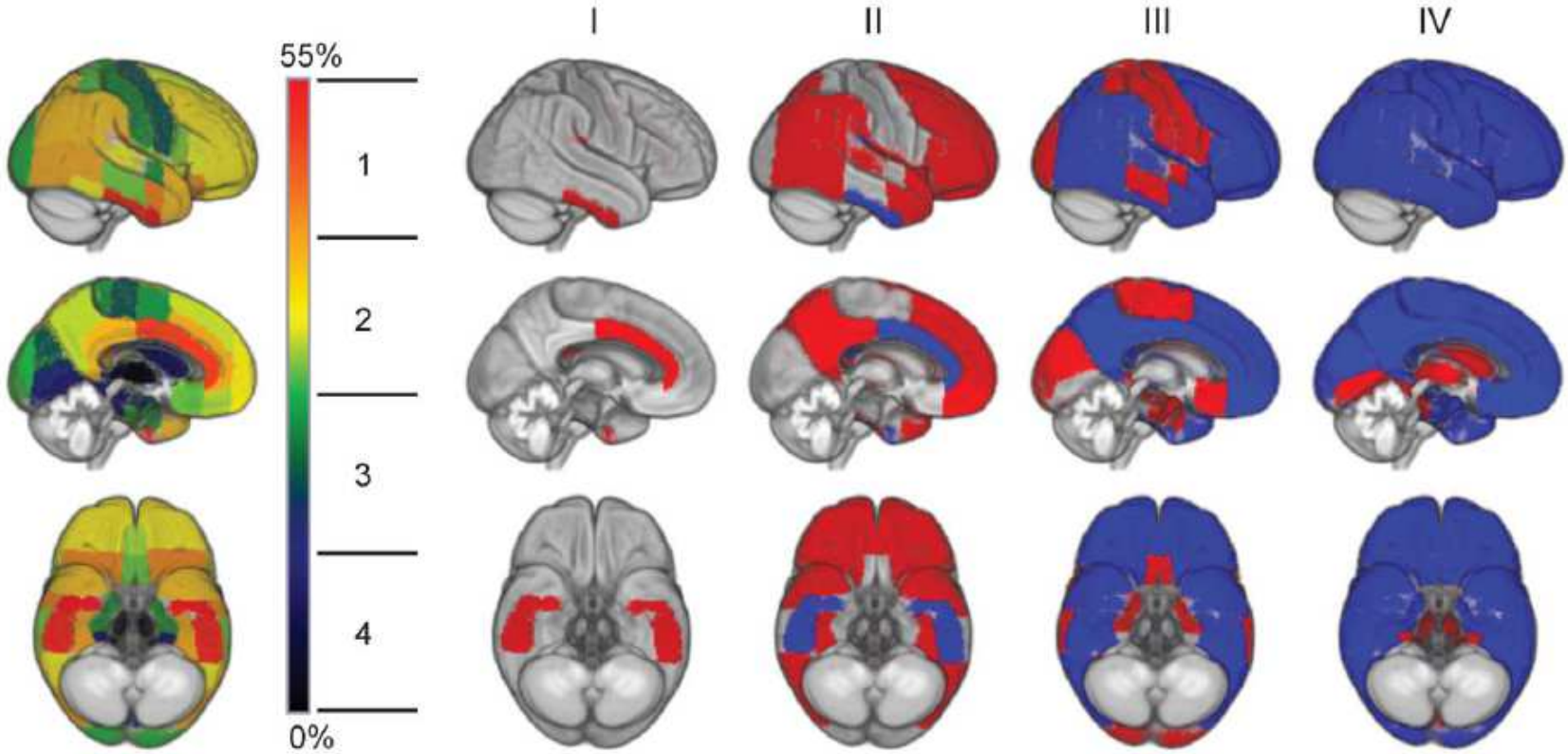
For the Alzheimer's Disease Neuroimaging Initiative

In this issue of Neurology®, Grothe et al.2 used multiregional analysis of cross-sectional Ab PET data to propose a 4-stage model of progressing amyloid accumulation, based on the frequency of regional Ab positivity in cognitively normal older individuals.
The consistency of the hierarchical staging model was then tested in an independent cohort of older individuals ranging from cognitively normal to AD dementia.

Neurology 89 November 14, 2017

Figure 1 Model of regional amyloid progression and staging scheme



Brain renderings on the left illustrate the frequency of regional amyloid positivity across individuals on a color scale from black/blue (lowest) to yellow/red (highest). The 52 brain regions are merged into 4 larger anatomic divisions based on equal partitions of the frequency range (1–4). In the resulting 4-stage model of regional amyloid progression (I–IV), incremental stages are defined by involvement of higher numbered anatomic divisions (in red), in addition to the affected areas of the previous stage (blue).

Amyloid PET scan

Staging beyond reading?

Gaël Chételat, MD, PhD
Melissa E. Murray, MD, PhD

Voxelwise or regional analyses should thus be preferred to detect the earliest stages of amyloidosis, both for diagnostic purposes and for enrollment in clinical trials. The added value would be considerable because 81% of people in stage 1 would have been considered as amyloid-negative based on global cortical SUVR.

Yet one could wonder how many of those are falsely positive.

Neurology® 2017;89:1–2

The earliest in vivo amyloid stages identify participants with regionally restricted amyloid deposits probably entirely missed in clinical routine n specific neocortical association areas that are binary visual assessment, and mostly missed by semiquantitative classification approaches based on suprathreshold global cortical signal, even at a relatively lenient cutoff.

These first stages were associated with decreased CSF Ab compared to stage 0, suggesting that they really reflect changes in physiologic Ab; yet this was observed at the group level, so it is possible that, at the individual level, some were false-positives.

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IOS Press

Clinic-Based Validation of Cerebrospinal Fluid Biomarkers with Florbetapir PET

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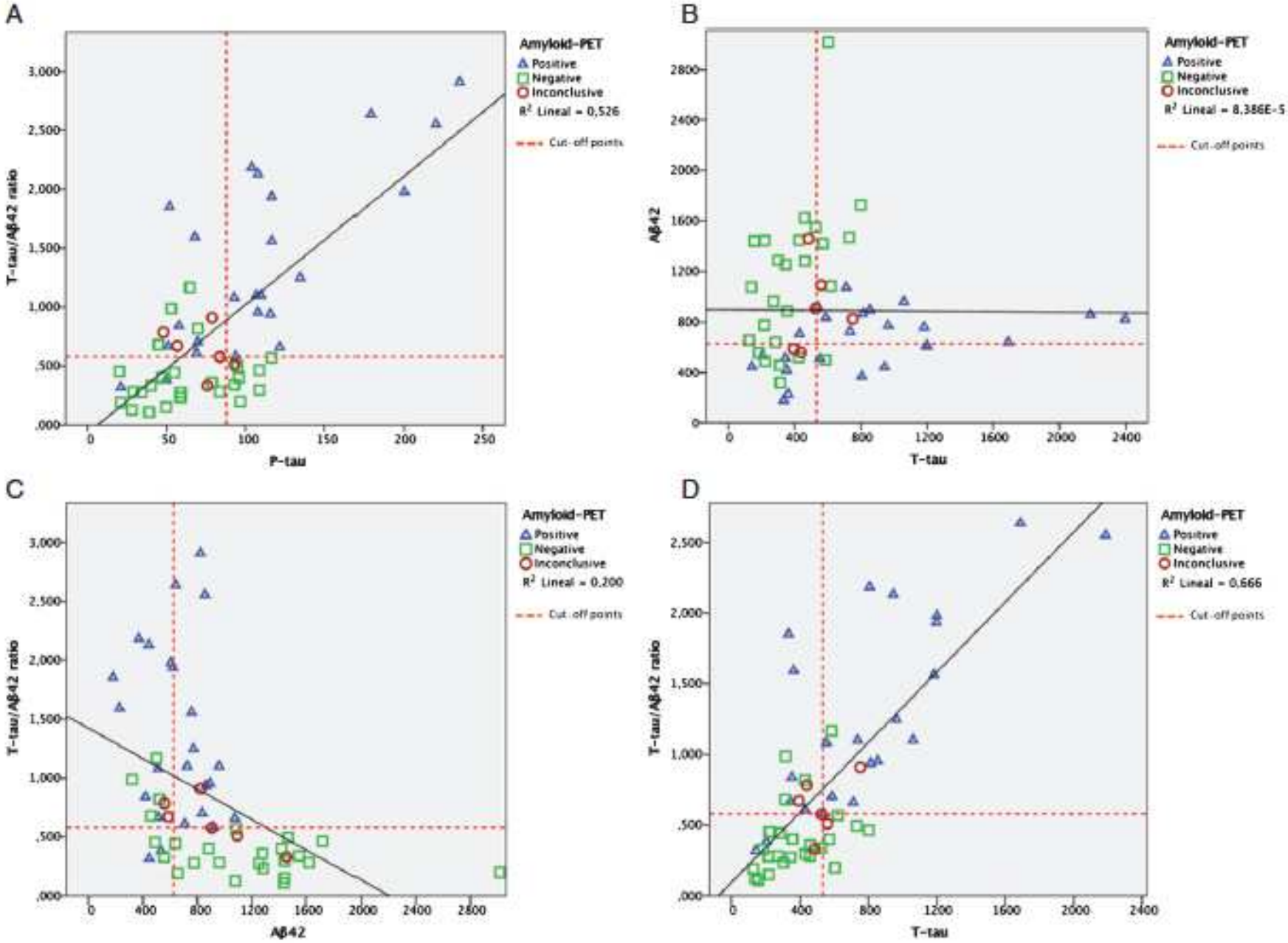

Fig. 1. Scatter plots of CSF markers according to Amyloid-PET results.

Conclusion: This study confirms strong concordance between CSF biomarkers and PET A-amyloid status is independent of immunoassay platform, supporting their utility as biomarkers in clinical practice for the diagnosis of AD and for participant enrichment in clinical trials.

JAMA Neurology | Original Investigation

Comprehension of an Elevated Amyloid Positron Emission Tomography Biomarker Result by Cognitively Normal Older Adults

Jessica Mozersky, PhD; Pamela Sankar, PhD; Kristin Harkins, MPH; Sara Hachey, BSc; Jason Karlawish, MD

OBJECTIVE To determine the comprehension of an elevated amyloid positron emission tomographic (PET) biomarker result by cognitively unimpaired adults.

JAMA Neurology Published online October 23, 2017

MAIN OUTCOMES AND MEASURES

Participant (NORMAL) comprehension of an elevated amyloid result was assessed by analyzing their responses to the following questions:

“What was the result of your amyloid PET scan?” (followed by “Can you tell me in your own words what that means?” or “How would you explain it to a friend?”),

“Was it the result you expected?” and “Did the result teach you anything or clarify anything for you?”

In this sample of 50 cognitively normal older adults enrolled in a clinical trial who learned they had elevated amyloid, more than half had expected the result of elevated amyloid.

Most explained that this expectation was based on their family history of AD. This explanation makes sense because 80% of the sample reported a family history of AD, and family history is among the motivators for learning biomarker results.

Participants also reported subjective memory concerns as a reason for expecting their elevated amyloid result.
This suggests that some people who are cognitively normal but symptomatic will use an AD biomarker test to explain their memory concerns, potentially pathologizing normal and non disease related cognitive aging. This result also suggests the need to determine whether persons with subjective memory problems who learn their AD biomarker status will experience an exacerbation of their preexisting memory concerns, which could then affect cognitive performance.

Conclusions

To slow the onset of cognitive decline caused by Alzheimer disease, researchers and clinicians will have to adopt a novel practice: telling a cognitively unimpaired older adult an Alzheimer biomarker result. This study of cognitively unimpaired adults who learned of an amyloid PET result shows that clinicians should be prepared to explain how and why a dimensional biomarker, in this case amyloid-β as measured using PET, is converted to a categorical state, in this case "elevated" and "not elevated," and what the result means in terms of a person's risk for developing Alzheimer disease dementia.

JAMA Neurology | Original Investigation

Rates of Amyloid Imaging Positivity in Patients With Primary Progressive Aphasia

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JAMA Neurology Published online January 8, 2018

OBJECTIVE To determine the rates of positron emission tomography (PET) amyloid positivity in the main clinical variants of primary progressive aphasia (PPA).

La classificazione della Afasia Primaria Progressiva (PPA) e delle sue varianti

Gorno Tempini ML, Neurology 2010

PNFA variante non fluente agrammatica

PPA variante semantica

PPA Primaria Progressiva variante logopenica

Meaning Primary progressive aphasia variant diagnosis according to the current classification scheme is highly predictive of Alzheimer disease biomarker status; biomarker positivity for Alzheimer disease may be more predictive of mixed pathology rather than primary Alzheimer disease.

The NEW ENGLAND JOURNAL of MEDICINE

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Trial of Solanezumab for Mild Dementia Due to Alzheimer's Disease

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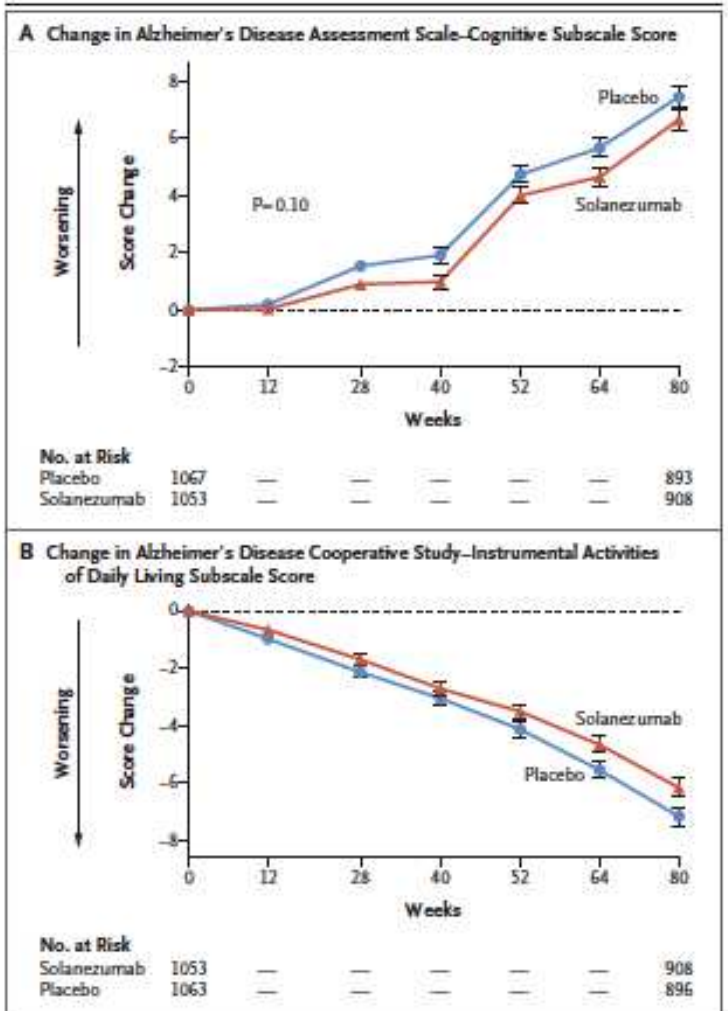

Figure 2. Primary Outcome and Secondary Functional Outcome.

Panel A shows the results for the primary outcome, the least-squares mean change from baseline (dashed line) in the score on the 14-item cognitive subscale of the Alzheimer's Disease Assessment Scale (on a scale from 0 to 90, with higher scores indicating greater cognitive impairment). Panel B shows the results regarding the secondary functional outcome of the least-squares mean change from baseline (dashed line) in the instrumental subscale of the Alzheimer's Disease Cooperative Study Activities of Daily Living Inventory; this subscale assesses complex activities such as using public transportation, managing finances, or shopping (on a scale from 0 to 56, with lower scores indicating greater functional loss). In both graphs, I bars indicate the standard error.

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIALS

Amyloid-Beta Solubility in the Treatment of Alzheimer's Disease

M. Paul Murphy, Ph.D.

Although it is possible that the magnitude of reduction in soluble Aβ was simply insufficient to create a measurable clinical benefit, recent results from an early trial of aducanumab could indicate that the ability of an antiamyloid therapy to clear insoluble Aβ is an important factor in the success of treatment.

If clearing previously deposited amyloid from the brain is more important than preventing its production, this could also at least partially explain the lack of success with other strategies such as beta-secretase inhibitors that have, after initial promise, proved disappointing.

It is also possible that some other characteristic of aducanumab, such as its relatively higher penetration in the brain, as compared with solanezumab, explains the difference.

There is some hope that a combination of therapeutic approaches might help, since there is evidence that the different pathologic aspects of Alzheimer's disease are interactive.

We may very well be nearing the end of the amyloid-hypothesis rope, at which point one or two more failures will cause us to loosen our grip and let go.

Alzheimer's research questioned as another drug fails

Alzheimer’s research questioned as another drug fails

Wrong target?

If 30 percent of the people in your anti-amyloid clinical trial don't have amyloid in their brain, right off the bat your trial is probably going to fail because 30 percent of the people aren't going to respond to your therapeutic.

Although the genetic evidence has been convincing that amyloid drives the disease, that doesn't mean that removing the protein from people already in the throes of Alzheimer's is going to help them, Murphy said.
"I think really it might be fairer to think that what happens is amyloid pathology is more like a trigger in the disease," he said.

Other factors at play

Seniors' brains also are vulnerable to other problems of aging known to contribute to Alzheimer's and dementia, such as high cholesterol and elevated blood pressure, Murphy said. So researchers have started thinking that any successful treatment for Alzheimer's will resemble the "cure" that HIV patients are given — a multi-pronged drug and lifestyle regimen that keeps their illness at bay.

An interesting thing we're learning from Tau PET imaging is that Tau shows up very close to when symptoms occur. That makes it a tantalizing drug candidate as well," .

Come biomarcatore isolato forse non serve.
È indispensabile per casi complessi.
E’ anche il biomarcatore indispensabile per attuali trial.
E’ necessario si misuri la quantità di beta amiloide.
Indispensabile fornire corretta spiegazione del perché del test ed interpretazione del risultato ottenuto.
E non è un problema di costi.