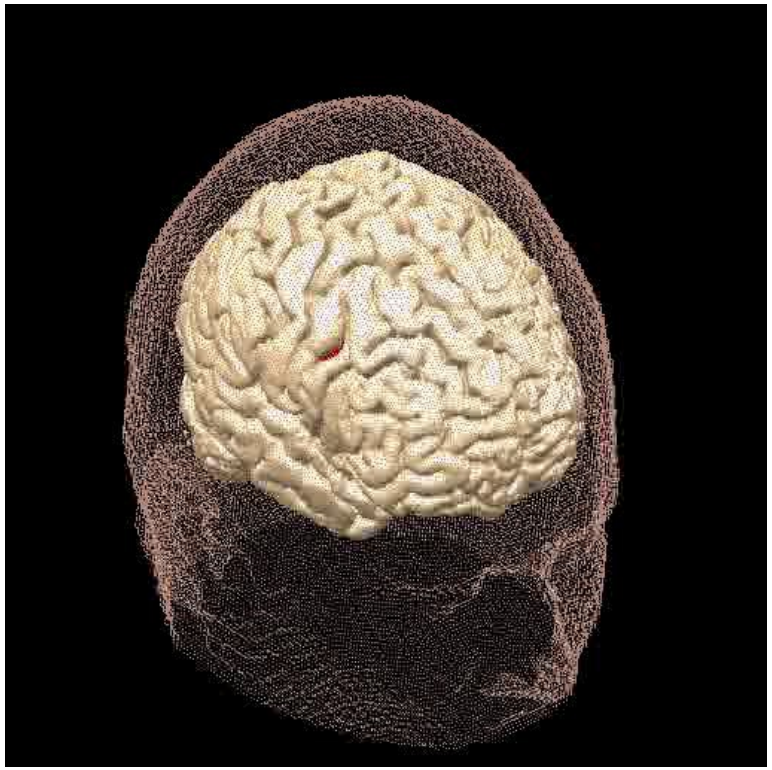
Πρώιμη αναγνώριση και θεραπεία:
Τι νέο υπάρχει; Τι είναι αμφιλεγόμενο; Τι πρακτικά χρήσιμο;



Γιάννης Παπατριανταφύλλου
Κέντρο Ημέρας για τη Τρίτη Ηλικία “IASIS”

ΚΡΙΤΗΡΙΑ

ΔΙΑΓΝΩΣΗ

ΠΡΟΛΗΨΗ

ΘΕΡΑΠΕΙΑ

Διάγνωση της νόσου Alzheimer – *νεότερα δεδομένα: NAI-AA κριτήρια*

ELSEVIER

Alzheimer's & Dementia 7 (2011) 257–262

Alzheimer's & Dementia

Featured Articles

Introduction to the recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease

Clifford R. Jack Jr.[a,*], Marilyn S. Albert[b], David S. Knopman[a], Guy M. McKhann[b], Reisa A. Sperling[c], Maria C. Carrillo[d], Bill Thies[d], Creighton H. Phelps[e]

[a]*Department of Radiology, Mayo Clinic, Rochester, MN, USA*
[b]*Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, USA*
[c]*Center for Alzheimer Research and Treatment, Brigham and Women's Hosptial, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA*
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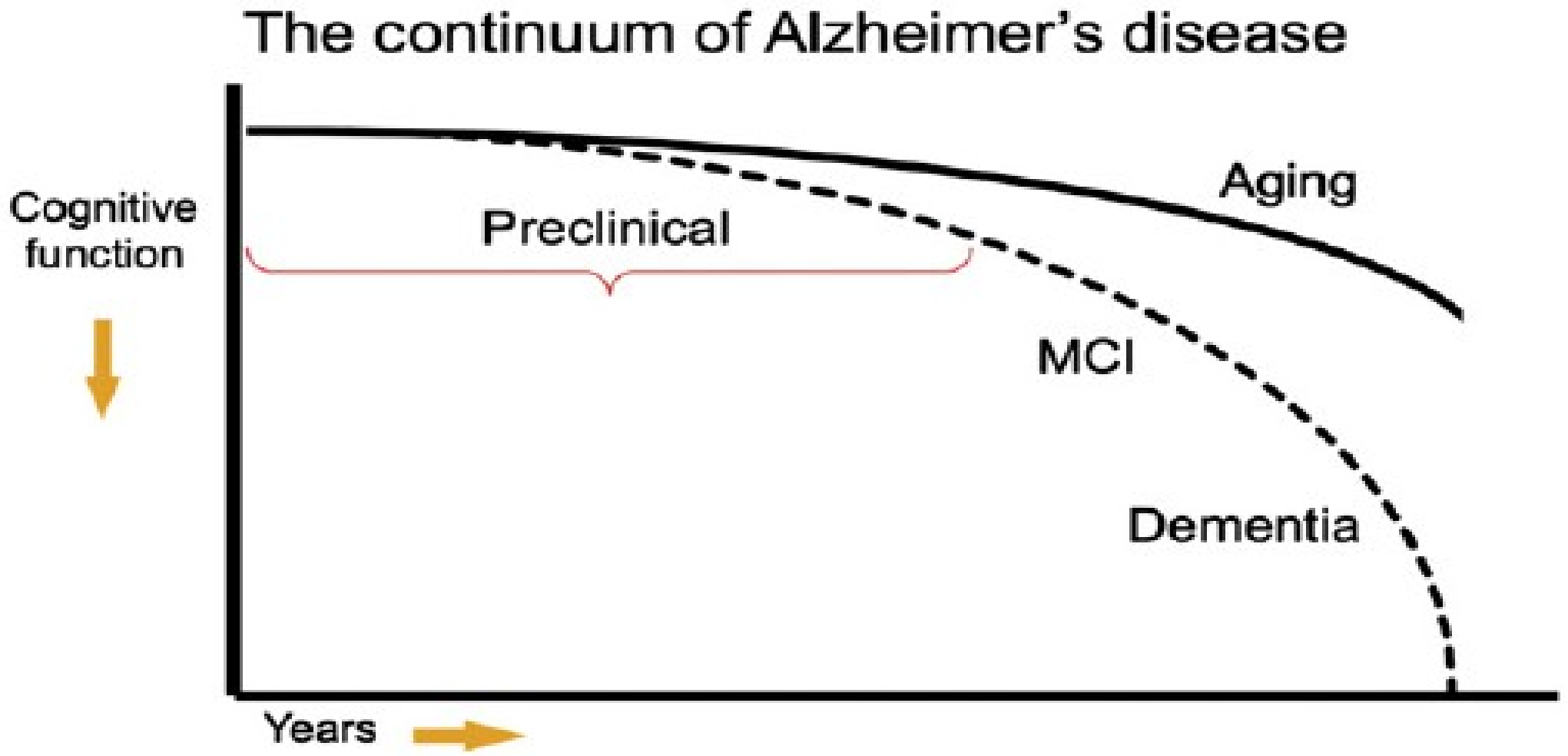
[e]*Division of Neurosciene, National Institute on Aging, Bethesda, MD, USA*


The continuum of Alzheimer's disease
Cognitive function
Aging
Preclinical
MCI
Dementia
Years

Διάγνωση και αντιμετώπιση της νόσου Alzheimer - *νεότερα δεδομένα*

- **Διάγνωση**

Κριτήρια

  - ***Προκλινική ΝΑ***
  - ***ΗΝΔ οφειλόμενη στη ΝΑ***
  - ***Άνοια ΝΑ***

- **Αντιμετώπιση**
  - Υπάρχουσες φαρμ. θεραπείες
  - Μελλοντικές φαρμ. θεραπείες
  - Άλλοι τρόποι

Νέα κριτήρια για τη νόσο Alzheimer

Α. Εικόνα άνοιας σύμφωνα με τον ορισμό αυτής

Β. **Ιστορικό επιδείνωσης των νοητικών λειτουργιών** από αξιόπιστη πηγή πληροφόρησης ή και παρατήρηση του κλινικού

Γ. Τα **πρώτα και προεξάρχοντα** νοητικά συμπτώματα αφορούν

- **Μνήμη- Αμνησιακή εικόνα της νόσου**

  Αφορά στη διαταραχή της πρόσφατης μνήμης με δυσχέρεια στην εκμάθηση κι ανάκληση της πληροφορίας

  Αποτελεί την συχνότερη εικόνα της νόσου

- **Μη αμνησιακή εικόνα της νόσου**
  - Διαταραχές στην **οπτικοχωρική ικανότητα** και προσανατολισμό
  - Διαταραχή **στο λόγο** (εύρεση κατάλληλης λέξης, ονομάτων)
  - Διαταραχή στις **επιτελικές λειτουργίες**

Πιθανή ν. Alzheimer με επιβεβαίωση του παθοφυσιολογικού μηχανισμού

Α. Εξετάσεις που ανιχνεύουν το β-αμυλοειδές

- Pib-PET: καθήλωση του Pib στον εγκέφαλο
- Η ελάττωση στο ΕΝΥ του β-αμυλοειδούς

Β. Εξετάσεις που ανιχνεύουν νευρωνική βλάβη κι ατροφία

- Αύξηση στο ΕΝΥ της τ ή και phosph-t πρωτεΐνης
- Ατροφία του μέσου κροταφικού λοβού (ογκομετρικές μέθοδοι ή και *οπτικές αναλογικές*)
- Υπολειτουργία των κροταφο-βρεγματικών περιοχών στο SPECT ή στο FDG-PET

ΗΝΔ που οφείλεται στη ΝΑ

ELSEVIER

Alzheimer's & Dementia 7 (2011) 270–279

Alzheimer's & Dementia

The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease

Marilyn S. Albert[a,*], Steven T. DeKosky[b,c], Dennis Dickson[d], Bruno Dubois[e], Howard H. Feldman[f], Nick C. Fox[g], Anthony Gamst[h], David M. Holtzman[i,j], William J. Jagust[k], Ronald C. Petersen[l], Peter J. Snyder[m,n], Maria C. Carrillo[o], Bill Thies[o], Creighton H. Phelps[p]

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[b]*Office of the Dean, University of Virginia, Charlottesville, VA, USA*
[c]*Department of Neurology, University of Virginia, Charlottesville, VA, USA*
[d]*Department of Pathology, Mayo Clinic, Jacksonville, FL, USA*
[e]*Institute for Memory and Alzheimer's Disease, INSERM Unit Cognition, Neuro-imagerie et maladies due Cerveau, Groupe Hospitalier Pitie-Salpetriere, Paris, France*
[f]*Bristol-Myers Squibb Neuroscience, Wallingford, CT, USA*
[g]*Institute of Neurology, University College London, London, United Kingdom*
[h]*Department of Neuroscience, University of California, San Diego, CA, USA*
[i]*Department of Neurology, Washington University, St. Louis, MO, USA*
[j]*Knight Alzheimer's Disease Research Center, Washington University, St. Louis, MO, USA*
[k]*Helen Wills Neuroscience Institute, University of California, Berkeley, CA, USA*
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[m]*Rhode Island Hospital, Alpert Medical School of Brown University, Providence, RI, USA.*
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[o]*Alzheimer's Association, Chicago, IL, USA*
[p]*National Institute on Aging, Bethesda, MD, USA*

Κλινική εκτίμηση για την ΗΝΔ που οφείλεται στη ΝΑ

Εκπλήρωση κριτηρίων	Διερεύνηση αιτιολογίας συμβατής με ΝΑ
• Αιτιάσεις Νοητικής έκπτωσης (ασθενούς, φροντιστή) ή και κλινικού	• Αποκλεισμός ΑΕΝ, ΚΕΚ, συστηματικών αιτίων (π.χ. Β12,…)
• Απόδειξη Έκπτωσης σε ≥ 1 τομείς	• *Απόδειξη προοδευτικής έκπτωσης με νευρο-ψυχολογικές δοκιμασίες (≥1sd)*
• Λειτουργικότητα διατηρημένη	• *Πιθανόν να χρειαστεί επανειλημμένες στο χρόνο επανεξετάσεις*

ELSEVIER

CrossMark

Alzheimer's & Dementia 14 (2018) 535-562

Alzheimer's & Dementia

2018 National Institute on Aging—Alzheimer's Association (NIA-AA) Research Framework

NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease

Clifford R. Jack, Jr.,[a,*], David A. Bennett[b], Kaj Blennow[c], Maria C. Carrillo[d], Billy Dunn[e], Samantha Budd Haeberlein[f], David M. Holtzman[g], William Jagust[h], Frank Jessen[i], Jason Karlawish[j], Enchi Liu[k], Jose Luis Molinuevo[l], Thomas Montine[m], Creighton Phelps[n], Katherine P. Rankin[o], Christopher C. Rowe[p], Philip Scheltens[q], Eric Siemers[r], Heather M. Snyder[d], Reisa Sperling[s]

Contributors[†]: Cerise Elliott, Eliezer Masliah, Laurie Ryan, and Nina Silverberg

Table 1

AT(N) biomarker grouping

A: Aggregated Aβ or associated pathologic state
- CSF $A\beta_{42}$, or $A\beta_{42}/A\beta_{40}$ ratio
- Amyloid PET

T: Aggregated tau (neurofibrillary tangles) or associated pathologic state
- CSF phosphorylated tau
- Tau PET

(N): Neurodegeneration or neuronal injury
- Anatomic MRI
- FDG PET
- CSF total tau

- Α-αμυλοειδές στον εγκέφαλο
- Τ- ταυ πρωτείνη στον εγκέφαλο
- Ν- νευροεκφυλιστική διαδικασία

Biomarker profiles and categories

AT(N) profiles	Biomarker category	
A-T-(N)-	Normal AD biomarkers	
A+T-(N)-	Alzheimer's pathologic change	Alzheimer's continuum
A+T+(N)-	Alzheimer's disease	
A+T+(N)+	Alzheimer's disease	
A+T-(N)+	Alzheimer's and concomitant suspected non Alzheimer's pathologic change	
A-T+(N)-	Non-AD pathologic change	
A-T-(N)+	Non-AD pathologic change	
A-T+(N)+	Non-AD pathologic change	

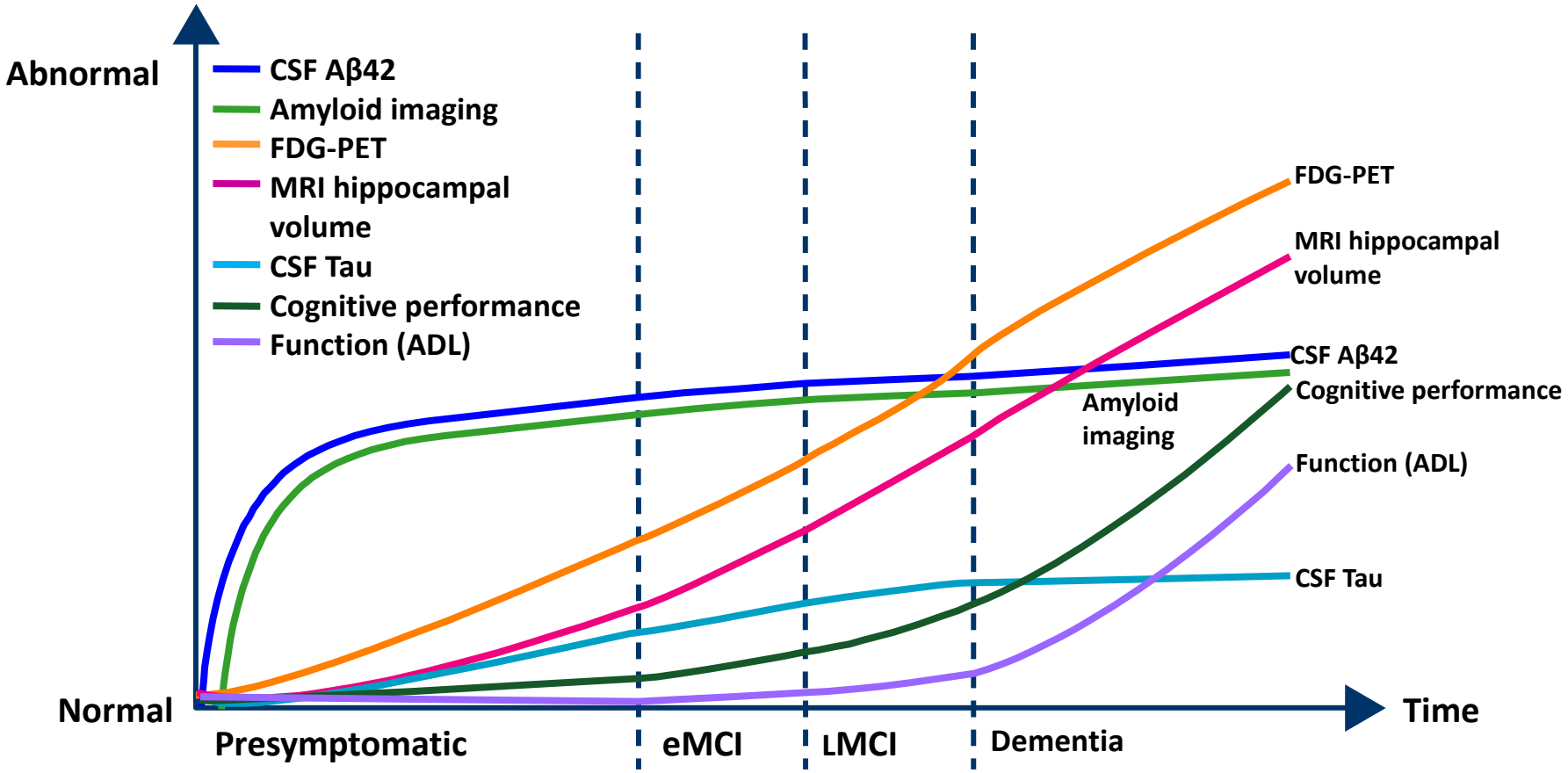
ΚΡΙΤΗΡΙΑ

ΔΙΑΓΝΩΣΗ

ΠΡΟΛΗΨΗ

ΘΕΡΑΠΕΙΑ

AD Progression



Aisen PS, Petersen RC, Donohue MC, et al. *Alzheimers Dement.* 2010;6:239-246.

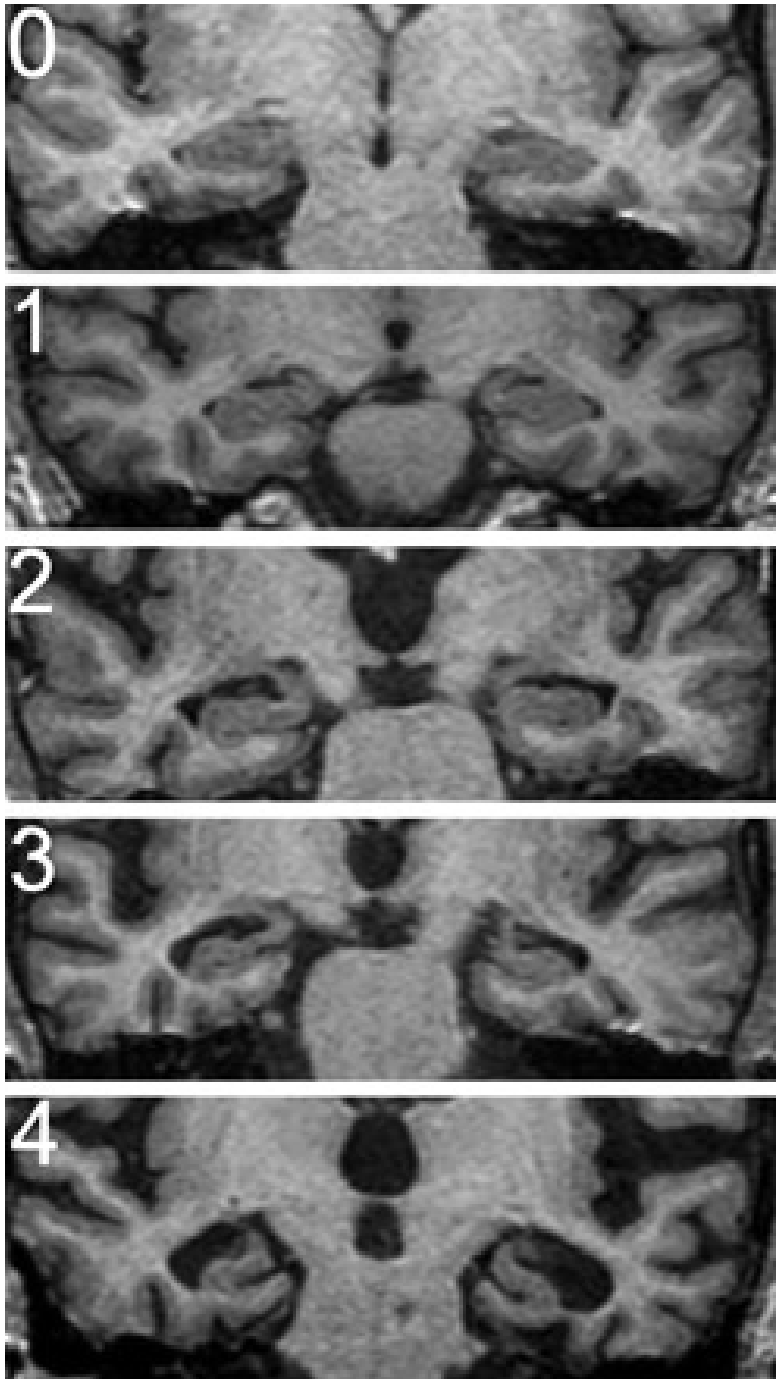
Review

A meta-analysis of hippocampal atrophy rates in Alzheimer's disease

Josephine Barnes [a,*], Jonathan W. Bartlett [b], Laura A. van de Pol [c], Clement T. Loy [d], Rachael I. Scahill [a], Chris Frost [a,b], Paul Thompson [e], Nick C. Fox [a]

Neurobiology of Aging 30 (2009) 1711–1723

- Η μέση ετήσια ατροφία του ιπποκάμπου
  - Σε φυσιολογικούς είναι 1.41% (0.52, 2.30)
  - Σε ασθενείς με AD είναι 4.66% (95% CI 3.92, 5.40)



Οπτική εκτίμηση της Ατροφίας Ιππόκαμπου

Οπτική εκτίμηση (Schelten's scale)

5βαθμη κλίμακα : 0 to 4.

Σε σχέση:

Το εύρος της χοριοειδούς σχισμής

Το εύρος του κροταφικού κέρατος

Το ύψος του ιπποκάμπου

Table 2. Visual assessment of medial-temporal-lobe atrophy

Score	Width of choroid fissure	Width of temporal horn	Height of hippocampus
0	Normal	Normal	Normal
1	↑	Normal	Normal
2	↑↑	↑	↓↓
3	↑↑↑	↑↑	↓↓
4	↑↑↑	↑↑↑	↓↓↓

↑=increased, ↓=decreased. Reproduced with permission of BMJ Publishing Group.[15]

Πλεονεκτήματα:

Κατάλληλο για καθημερινή χρ

Ακριβές και με καλή συσχέτιση με τις ογκομετρικές μετρήσεις

(Scheltens, 2002)

Οπτική εκτίμηση της Ατροφίας Ιππόκαμπου

Ποια είναι η προγνωστική προστιθέμενη αξία στη διάγνωση της AD?

0,91

Όταν η πιθανότητα πριν τη

MRI είναι για AD= 0,60

(ευαισθησία των NINCDS-ADRDA κριτηρίων)

Εάν AI(+) τότε η πιθανότητα = 0,91

Εάν AI (-) τότε η πιθανότητα = 0,20

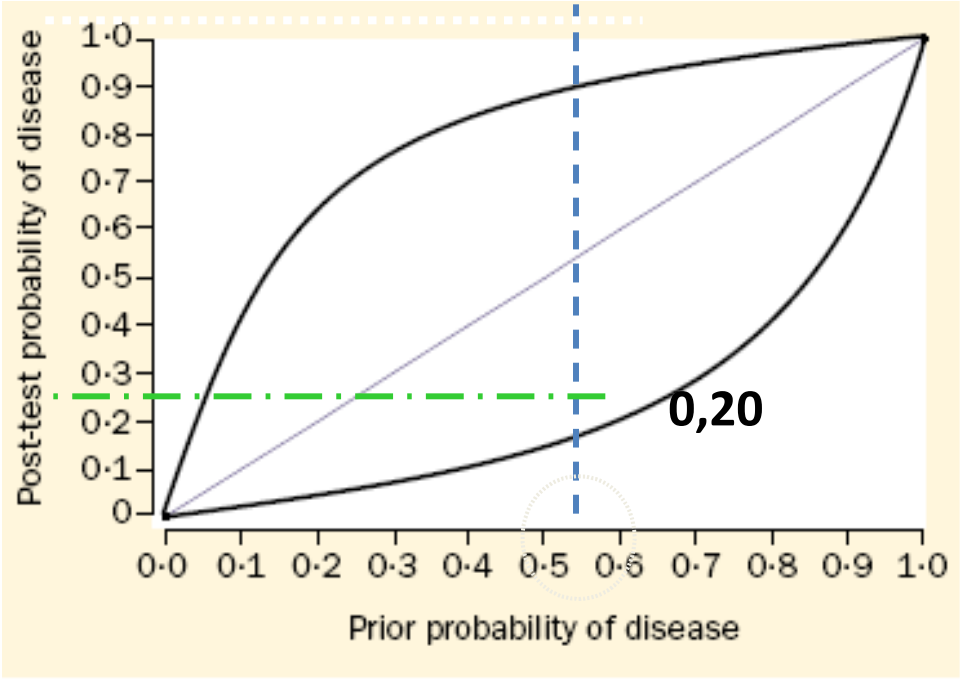


Figure 3. Post-test probability of disease with a test of sensitivity 85% and specificity 88% for any given pretest probability (prevalence of disease). The upper curve shows the incremental diagnostic gain from a positive result of a test (ie, presence of hippocampal atrophy on MRI) and the lower curve shows that from a negative result (ie, presence of hippocampal atrophy on MRI).

Association between CSF biomarkers and incipient Alzheimer's disease in patients with mild cognitive impairment: a follow-up study

Lancet Neurol 2006; 5: 228–34

Oskar Hansson, Henrik Zetterberg, Peder Buchhave, Elisabet Londos, Kaj Blennow, Lennart Minthon

- Σε περίοδο παρακολούθησης 5.2 ετών

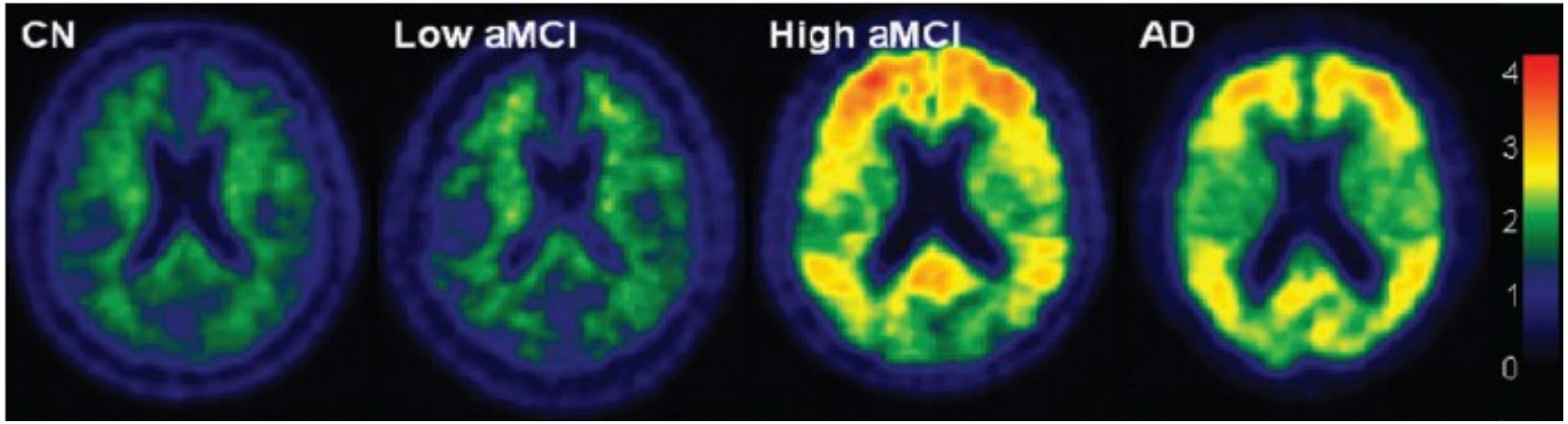
Ο συνδυασμός και Aβ42/p-tau181 έδειξε

- ευαισθησία 95%
- ειδικότητα 87%

doi:10.1093/brain/awm336 *Brain* (2008), **131**, 665–680

^{11}C PiB and structural MRI provide complementary information in imaging of Alzheimer's disease and amnestic mild cognitive impairment

Clifford R. Jack, Jr,[1] Val J. Lowe,[1] Matthew L. Senjem,[2] Stephen D. Weigand,[3] Bradley J. Kemp,[1] Maria M. Shiung,[1] David S. Knopman,[4] Bradley F. Boeve,[4] William E. Klunk,[5] Chester A. Mathis[5] and Ronald C. Petersen[4]



Σχέση αμυλοειδούς (PIB) και ατροφίας (MRI)		
	Αμυλοειδές	Ατροφία
Μετωπιαίοι λοβοί		
Πρόσθια και μέση κροταφική περιοχή		
Κροταφο		

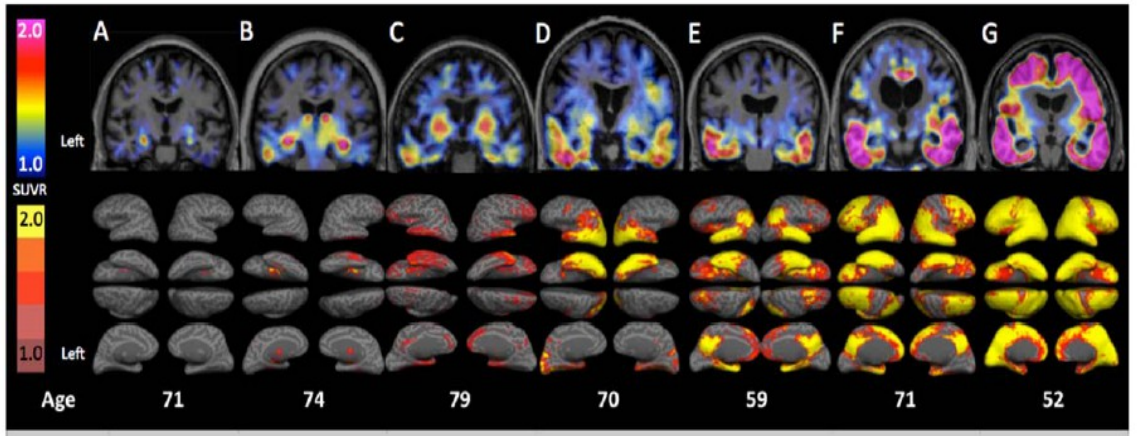
- **Η ύπαρξη αμυλοειδούς προηγείται πολλών χρόνων της κλινικής εμφάνισης συμπτωμάτων**
- **Το PIB είναι εύχρηστο στην αποκάλυψη του αμυλοειδούς**
- **Η MRI είναι εύχρηστη στη**

Tau Positron Emission Tomographic Imaging in Aging and Early Alzheimer Disease

Keith A. Johnson, MD,[1,2,3,4,5] Aaron Schultz, PhD,[1,4,6] Rebecca A. Betensky, PhD,[7,8] J. Alex Becker, PhD,[1,3] Jorge Sepulcre, MD,[1,3,5,6] Dorene Rentz, PsyD,[2,4,5] Elizabeth Mormino, PhD,[2,4] Jasmeer Chhatwal, MD,[2,4,5] Rebecca Amariglio, PhD,[2,4,5] Kate Papp, PhD,[2,4,5] Gad Marshall, MD,[2,4,5] Mark Albers, MD,[2,5] Samantha Mauro, BS,[1,3] Lesley Pepin, BS,[1,3] Jonathan Alverio, BS,[1,3] Kelly Judge, BS,[1,3] Marlie Philiossaint, BS,[1,3] Timothy Shoup, PhD,[1,3] Daniel Yokell, PharmD,[1,3,5] Bradford Dickerson, MD,[1,2,5,6] Teresa Gomez-Isla, MD,[2,5] Bradley Hyman, MD,[2,5] Neil Vasdev, PhD,[1,3,5] and Reisa Sperling, MD[2,4,5,6]

Objective: Detection of focal brain tau deposition during life could greatly facilitate accurate diagnosis of Alzheimer disease (AD), staging and monitoring of disease progression, and development of disease-modifying therapies.
Methods: We acquired tau positron emission tomography (PET) using ^{18}F T807 (AV1451), and amyloid-β PET using ^{11}C Pittsburgh compound B (PiB) in older clinically normal individuals, and symptomatic patients with mild cognitive impairment or mild AD dementia.
Results: We found abnormally high cortical ^{18}F T807 binding in patients with mild cognitive impairment and AD dementia compared to clinically normal controls. Consistent with the neuropathology literature, the presence of elevated neocortical ^{18}F T807 binding particularly in the inferior temporal gyrus was associated with clinical impairment. The association of cognitive impairment was stronger with inferior temporal ^{18}F T807 than with mean cortical ^{11}C PIB. Regional ^{18}F T807 was correlated with mean cortical ^{11}C PiB among both impaired and control subjects.
Interpretation: These findings suggest that ^{18}F T807 PET could have value as a biomarker that reflects both the progression of AD tauopathy and the emergence of clinical impairment.

ANN NEUROL 2016;79:110–119



	A	B	C	D	E	F	G
MMSE	30	30	29	27	26	23	11
PiB (DVR)	Low (1.0)	High (1.2)	High (1.8)	High (1.5)	High (1.7)	High (1.5)	High (1.5)
Dx	CN	CN	CN	MCI	MCI	AD	AD
PET Braak	0, I-II	III-IV	III-IV	III-IV	III-IV	V-VI	V-VI

FIGURE 1: Cortical patterns of 18F T807 binding. Coronal ^{18}F T807 positron emission tomographic (PET) images (top row) and whole-brain surface renderings of standardized uptake value ratio (SUVR; cerebellar reference; second row) from 3 clinically normal (CN) and 4 impaired (2 mild cognitive impairment [MCI] and 2 mild Alzheimer dementia [AD] dementia) participants. Top: (A) A 71-year-old CN subject with low amyloid β (Aβ) by Pittsburgh compound B (PiB) PET (mean cortical distribution volume ratio [DVR] = 1.0) had low, nonspecific ^{18}F T807 binding in cortex, consistent with a Braak stage less than III/IV. (B) A 74-year-old CN subject with high Aβ (DVR = 1.2) with ^{18}F T807 binding in inferior temporal cortex, left > right, consistent with Braak stage III/IV. (C) A 79-year-old CN subject with high Aβ (DVR = 1.8) had binding in inferior temporal neocortex, consistent with Braak stage of III/IV. B and C show focally intense subcortical uptake that is likely due to off-target binding (see Discussion). (D–G) Cognitively impaired participants all with high Aβ and with successively greater levels of cortical ^{18}F T807 binding successively involving temporal, parietal, frontal, and occipital cortices. Bottom: ^{18}F T807 SUVR calculated at vertices (see Subjects and Methods) indicating the extent of cortical binding, with left hemisphere views (lateral, inferior, superior, medial) at left. The 52-year-old AD dementia patient (G) showed confluent ^{18}F T807 binding that is nearly pancortical, sparing only portions of primary cortex and consistent with Braak stage V/VI. Dx = classification; MMSE = Mini-Mental State Examination; PET Braak = estimate of Braak stages based on the anatomic pattern of T807 binding assessed visually and quantitatively in regions and full volume data.

TAU IMAGING: WHAT CAN IT TELL US?

While amyloid pathology is invariably present in AD, it is not consistently associated with severity of symptoms or disease duration.

In contrast, NFT density and distribution increases with cognitive impairment and correlates with neurodegeneration.

While Aβ deposition is a protracted process, **recent reports on tau imaging in Aβ positive MCI or AD subjects show significant** increases over **relatively short time periods**, consistent with the predicted progression of AD

JAMA Neurology | Original Investigation

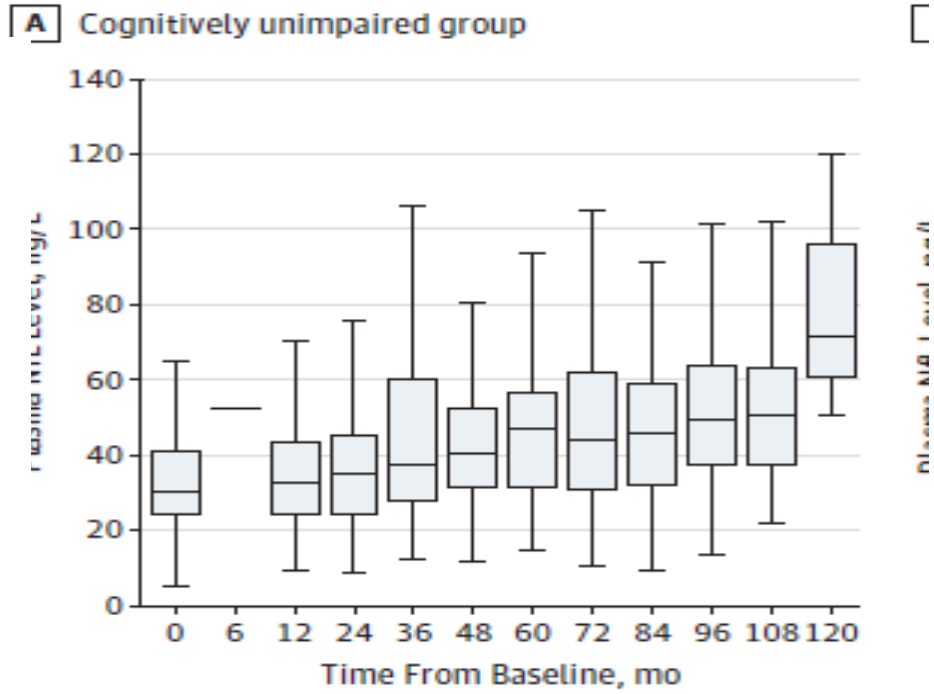
Association Between Longitudinal Plasma Neurofilament Light and Neurodegeneration in Patients With Alzheimer Disease

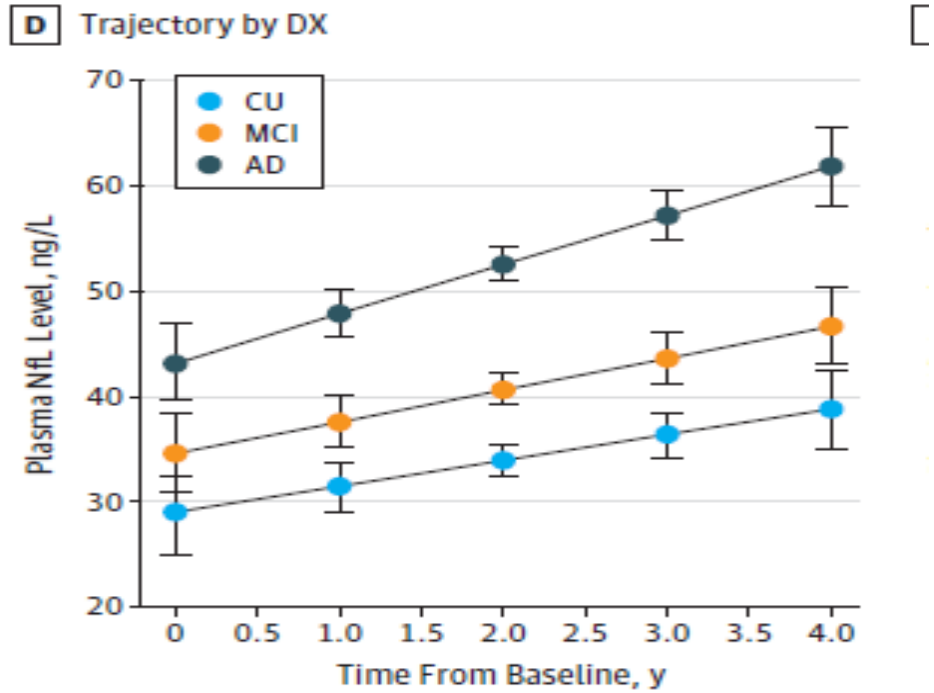
Niklas Mattsson, MD, PhD; Nicholas C. Cullen, BSc; Ulf Andreasson, PhD; Henrik Zetterberg, MD, PhD; Kaj Blennow, MD, PhD

JAMA Neurol.
Published online April 22, 2019.

Meaning

- The findings suggest that plasma neurofilament light **can be used as a noninvasive biomarker to track neurodegeneration** in patients with Alzheimer disease.





Neuropsychological Signs of Alzheimer's Disease 8 Years Prior to Diagnosis

Nicole S. Schmid et al.,

This analysis yielded eleven neuropsychological variables that optimally discriminated the two groups (correct classification rate: 60.4%):

1) Intrusions

2) Response bias in verbal learning and memory tasks

3) delayed figure recall

4–6) three Wechsler Adult Intelligence Scale (WAIS) Block, Design subtest variables

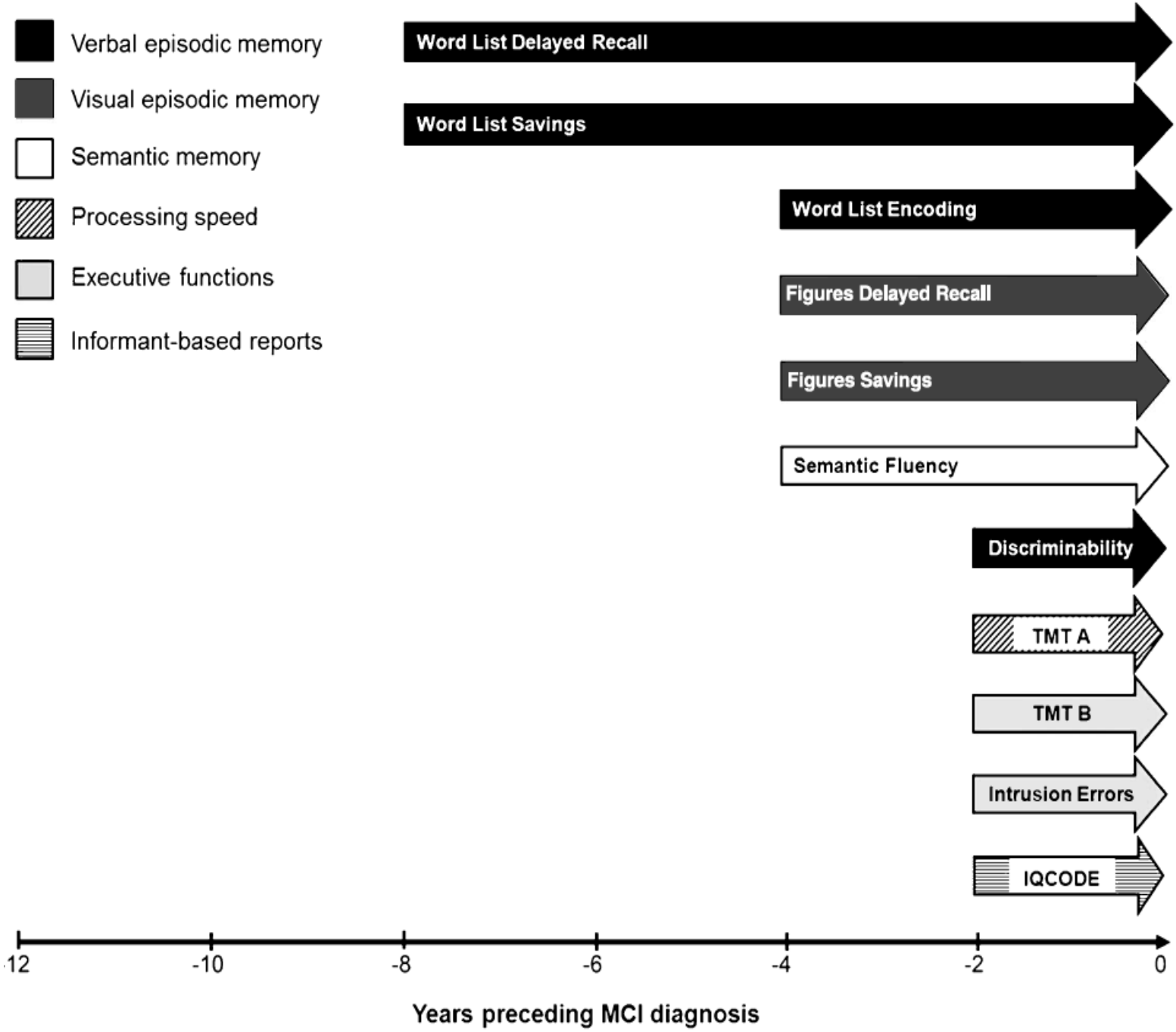
Journal of Alzheimer's Disease 34 (2013) 537–546

7–8) number of errors and repetitions on letter fluency

Journal of Alzheimer's Disease 48 (2015) 1095–1107
DOI 10.3233/JAD-150137
IOS Press

The 12 Years Preceding Mild Cognitive Impairment Due to Alzheimer's Disease: The Temporal Emergence of Cognitive Decline

Panagiota Mistridis[a,b], Sabine Krumm[a,b], Andreas U. Monsch[a,b,*], Manfred Berres[c] and Kirsten I. Taylor[a,b,d,1]



Subjective cognitive complaints and amyloid burden in cognitively normal older individuals

Rebecca E. Amariglio [a,b,*], J. Alex Becker [c], Jeremy Carmasin [c,1], Lauren P. Wadsworth [b], Natacha Lorius [a,b], Caroline Sullivan [b], Jacqueline E. Maye [c], Christopher Gidicsin [c], Lesley C. Pepin [c], Reisa A. Sperling [a,b], Keith A. Johnson [a,b,c], Dorene M. Rentz [a,b]

Neuropsychologia 50 (2012) 2880–2886

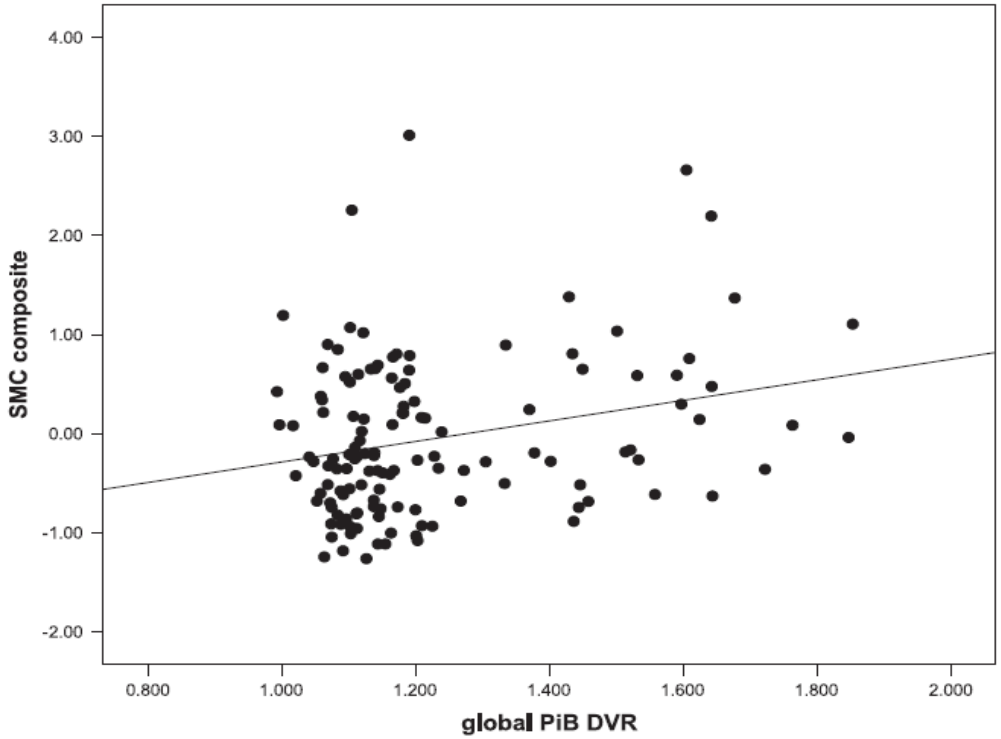


Fig. 1. Scatterplot of PiB retention by subjective memory complaints composite (SMC composite). Higher scores on SMC composite indicate higher SCC.

Our study suggests that SCC may be an early indicator of AD pathology detectable prior to significant objective impairment

Subjective memory complaints in elders: depression, anxiety, or cognitive decline?

Balash Y, Mordechovich M, Shabtai H, Giladi N, Gurevich T, Korczyn AD.

Acta Neurol Scand: 2013: 127: 344–350

Conclusions

Subjective memory complaints are associated with sub-syndromal depression and anxiety in healthy cognitively normal elders

Subjective Cognitive Decline in Older Adults: An Overview of Self-Report Measures Used Across 19 International Research Studies

Laura A. Rabin et al.

Journal of Alzheimer's Disease 48 (2015)

S63–86

- Results document the heterogeneity of approaches across studies to the emerging construct of SCD

- We offer preliminary recommendations for instrument selection and future research directions including identifying items and measure formats associated with important clinical outcomes

Cognitive Complaints in Memory Clinic Patients and in Depressive Patients: An Interpretative Phenomenological Analysis

Lisa Miebach, MSc,[1,2,*] Steffen Wolfsgruber, PhD,[1,2] Ingo Frommann, Dipl. Psych.,[1,2] Klaus Fließbach, PhD,[1,2] Frank Jessen, MD,[2,3] Rachel Buckley, PhD,[4,5] and Michael Wagner, PhD[1,2]

Gerontologist, 2018, in advance

Discussion and Implications:

- We report a comprehensive qualitative description of cognitive complaints in old age which could help to develop questionnaires or structured interviews to better assess AD-related subjective cognitive decline
- This may help to increase specificity in selecting high-risk subjects in research settings and improve clinical judgment of diverse cognitive complaints types mentioned by their patients

Predicting Alzheimer's Disease: Neuropsychological Tests, Self Reports, and Informant Reports of Cognitive Difficulties

Laura A. Rabin et al.
J Am Geriatr Soc. 2012 June ; 60(6): 1128-34

Conclusion

- **Informant ratings improved the prediction of AD conversion above and beyond objective memory impairment in non-demented elders**.

  ……. developed incident AD during a median *of 3.3 years of follow-up*.

- Combining these cognitive measures may provide a useful, empirical method for identifying individuals at high risk for future AD

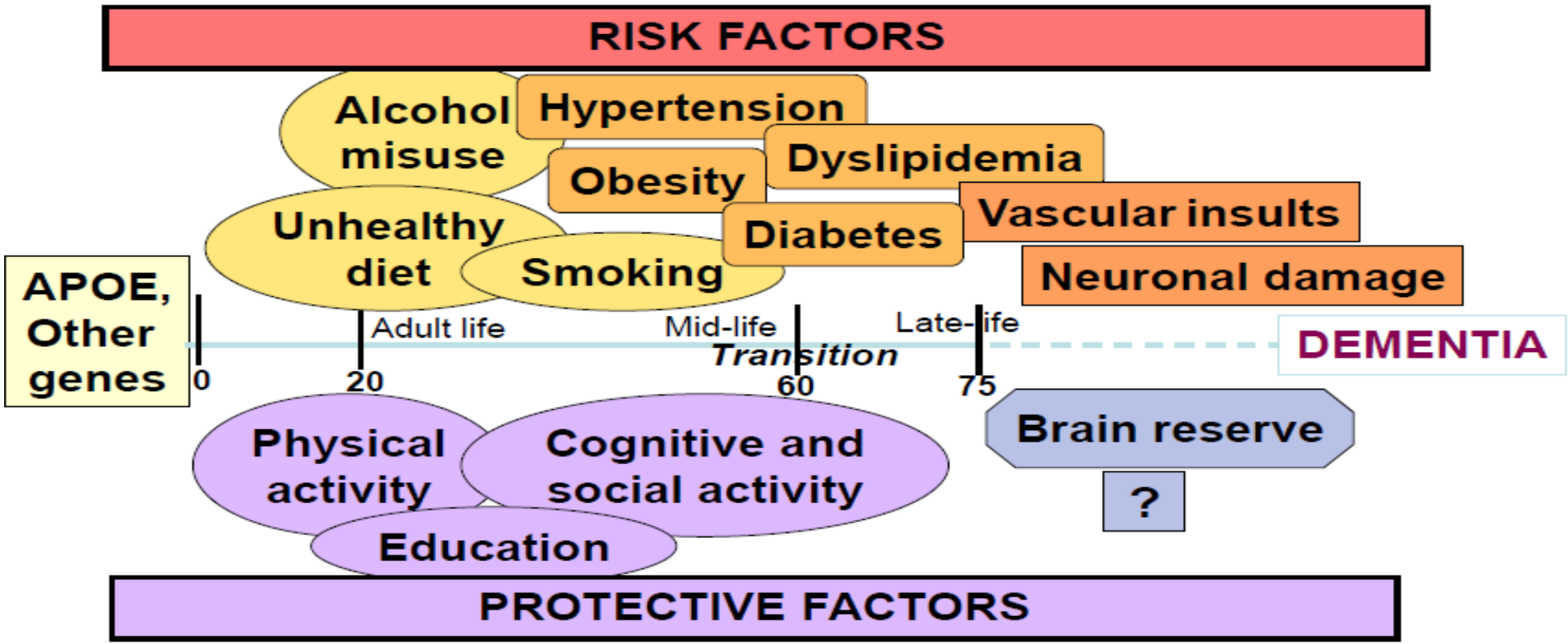
ΚΡΙΤΗΡΙΑ

ΔΙΑΓΝΩΣΗ

ΠΡΟΛΗΨΗ

ΘΕΡΑΠΕΙΑ

WHAT IS ALZHEIMER'S DISEASE?
RISK AND PROTECTIVE FACTORS



Mangialasche, Kivipelto et al., 2012

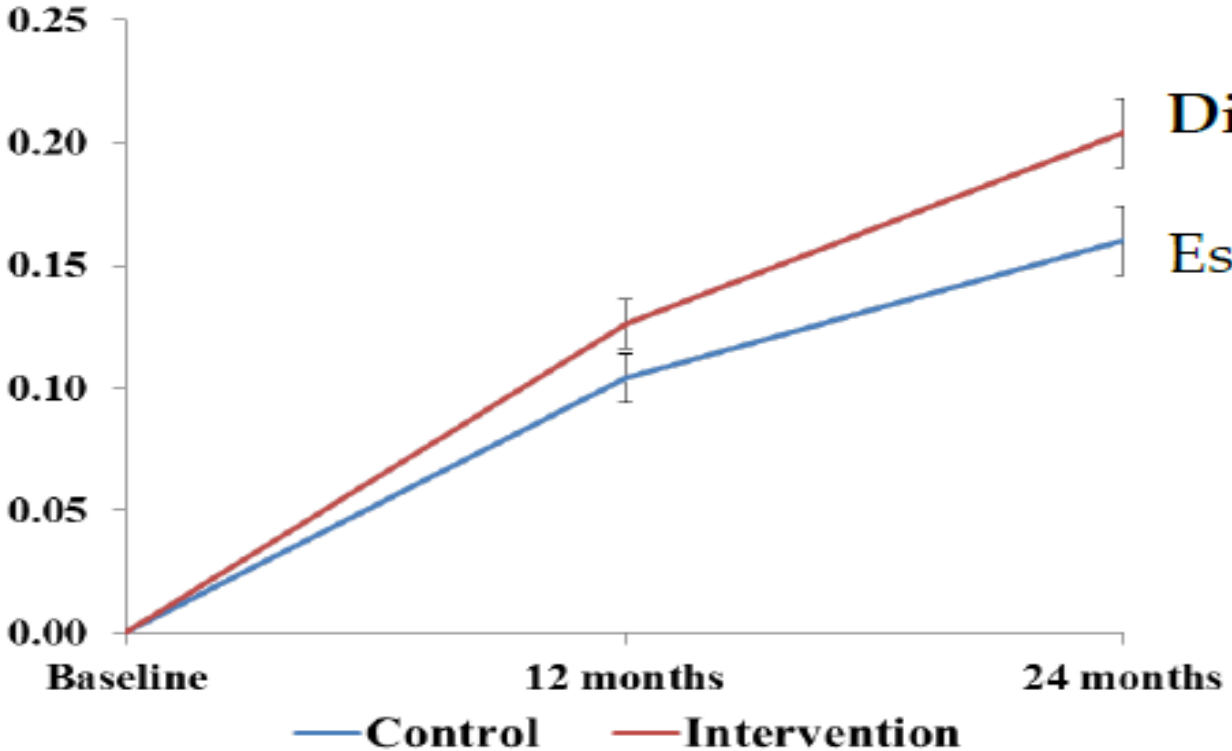
A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial

Tiia Ngandu, Jenni Lehtisalo, Alina Solomon, Esko Levälahti, Satu Ahtiluoto, Riitta Antikainen, Lars Bäckman, Tuomo Hänninen, Antti Jula, Tiina Laatikainen, Jaana Lindström, Francesca Mangialasche, Teemu Paajanen, Satu Pajala, Markku Peltonen, Rainer Rauramaa, Anna Stigsdotter-Neely, Timo Strandberg, Jaakko Tuomilehto, Hilkka Soininen, Miia Kivipelto

The Lancet, 2015

(Published online March 12 2015)

Primary efficacy outcome: overall cognition (NTB composite Z score)



Difference between intervention and control groups per year:

Estimate (95% CI) = 0.022 (0.002-0.042)

p=0.03

Kivipelto et al, Lancet 2015

Lines = estimates for cognitive change from baseline to 12 and 24 months

Higher scores = better performance

Error bars = standard errors.

P-values = difference in trajectories over time between groups

CAIDE Dementia Risk Score		
Age	< 47 years 47-53 years >53 years	**0** **3** **4**
Formal education	≥10 years 7-9 years 0-6 years	**0** **2** **3**
Sex	Women Men	**1** **0**
Systolic BP	≤ 140 mm Hg > 140 mm Hg	**0** **2**
BMI	≤ 30 kg/m2 > 30 kg/m2	**0** **2**
Total cholesterol	≤ 6.5 mmol/l > 6.5 mmol/l	**0** **2**
APOE4	(+)	**2**
Physical activity	Active Inactive	**0** **1**

Kivipelto et al., Lancet Neurol 2006

Η πιθανότητα εμφάνισης άνοιας σε σχέση με τον βαθμό κινδύνου στη μέση ηλικία

The overall occurrence of dementia 4.4%

SCORE	All /Demented, n	% Risk (95% CI)
0-5	401 / 4	1.0 (0.0-2.0)
6-7	270 / 5	1.9 (0.2-3.5)
8-9	312 / 13	4.2 (1.9-6.4)
10-11	245 / 18	7.4 (4.1-10.6)
12-15	122 / 20	16.4 (9.7-23.1)

Kivipelto et al., Lancet Neurology 2006

The Late-Life Dementia Risk Index

Table 2 The late-life dementia risk index

Characteristic	Points
Age 75–79 y*	1
Age 80–100 y*	2
Low 3MS†	2
Low DSST†	2
BMI <18.5	2
≥1 APOE ε4 allele	1
MRI white matter disease (grade ≥3)	1
MRI enlarged ventricles (grade ≥4)	1
Internal carotid artery thickness ≥2.2 mm	1
History of coronary bypass surgery	1
Time to put on and button shirt >45 s	1
Lack of alcohol consumption	1
Possible range	0 to 15
c Statistic (95% CI)	0.81 (0.79–0.83)

Barnes DE, et al.
Neurology 2009;73;173-179;

Midlife predictors of Alzheimer's disease

B.Bendlin et al.

Maturitas. 2010 February ; 65(2): 131–137

Factors that appear non-modifiable may have their influence attenuated by intervention.

- If initiated early, it is possible that aging related hormonal changes may be tempered by hormone therapy;
- hypertension,
- hypercholesterolaemia,
- obesity, and
- diabetes (all of which have genetic contributions)
- **may be modified by diet, exercise, or pharmaceutical intervention**;
- and even the effect of ***APOE most established genetic risk factor for late***

ΚΡΙΤΗΡΙΑ

ΔΙΑΓΝΩΣΗ

ΠΡΟΛΗΨΗ

ΘΕΡΑΠΕΙΑ

Practice guideline update summary: Mild cognitive impairment, ***exercise and cognitive training***

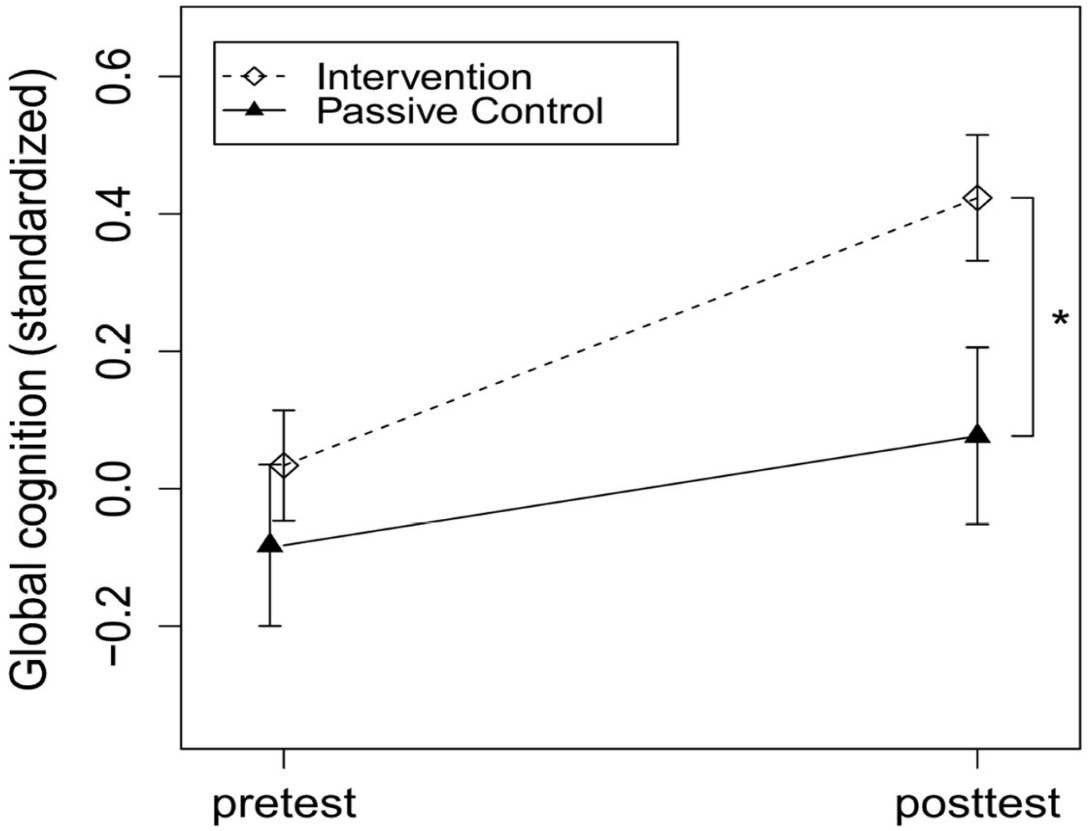
- No high-quality evidence exists to support pharmacologic treatments for MCI
- In patients with MCI, **exercise training (6 months)** is likely to improve cognitive measures and
- **cognitive training** may improve cognitive measures

- **Clinicians should recommend regular exercise** (Level B).
- **Clinicians may recommend cognitive training** (Level C).

Neurology® 2018;90:1-10

Gains in cognition through combined cognitive and physical training: the role of training dosage and severity of neurocognitive disorder

Panagiotis D. Bamidis, Patrick Fissler, Sokratis G. Papageorgiou, Vasiliki Zilidou, Evdokimos I. Konstantinidis, Antonis S. Billis, Evangelia Romanopoulou, Maria Karagianni, Ion Bearatis, Angeliki Tsapanou, Georgia Tsilikopoulou, Eirini Grigoriadou, Aristea Ladas, Athina Kyrillidou, Anthoula Tsolaki, Christos Frantzidis, Efstathios Sidiropoulos, Anastasios Siountas, Stavroula Matsi, John Papatriantafyllou, Eleni Margioti, Aspasia Nika, Winfried Schlee, Thomas Elbert, Magda Tsolaki, Ana B. Vivas and Iris-Tatjana Kolassa



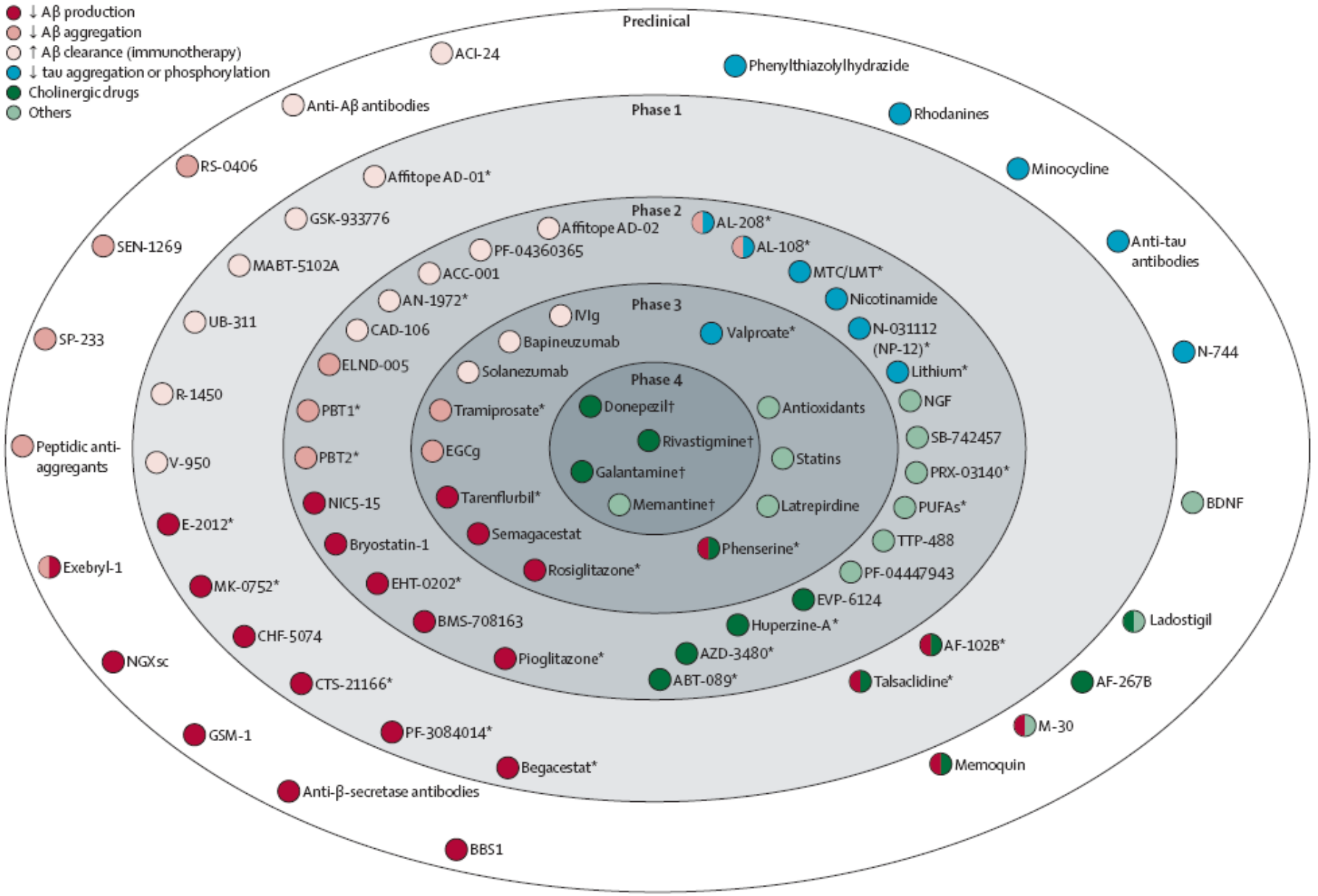
Frontiers of Aging Neuroscience

Alzheimer's disease: clinical trials and drug development

Francesca Mangialasche, Alina Solomon, Bengt Winblad, Patrizia Mecocci, Miia Kivipelto

Lancet Neurol 2010; 9: 702–16

Παραγωγή
Συνάθροιση
Κάθαρση
Φωσφορυλίωση της τ-
Χολινεργικά
Άλλα



Impact of SSRI Therapy on Risk of Conversion From Mild Cognitive Impairment to Alzheimer's Dementia in Individuals With Previous Depression

Claudia Bartels, Ph.D., Michael Wagner, Ph.D., Steffen Wolfsgruber, Ph.D., Hannelore Ehrenreich, M.D., Anja Schneider, M.D., for the Alzheimer's Disease Neuroimaging Initiative

Objective: Depression is associated with an increased risk of Alzheimer's disease. Research has shown that the selective serotonin reuptake inhibitor (SSRI) citalopram decreases amyloid-β generation and plaque load. The authors evaluated the impact of SSRI treatment on CSF biomarkers and progression from mild cognitive impairment (MCI) to Alzheimer's dementia.

Method: Data sets from 755 currently nondepressed participants from the longitudinal Alzheimer's Disease Neuroimaging Initiative were evaluated by Kaplan-Meier analysis and analyses of variance and covariance with ApoE4 status and age as covariates.

Results: In MCI patients with a history of depression, long-term SSRI treatment (>4 years) was significantly associated with a delayed progression to Alzheimer's dementia by approximately 3 years, compared with short-term SSRI treatment, treatment with other antidepressants, or no treatment and compared with MCI patients without a history of depression. No differences in CSF biomarker levels were observed between treatment groups.

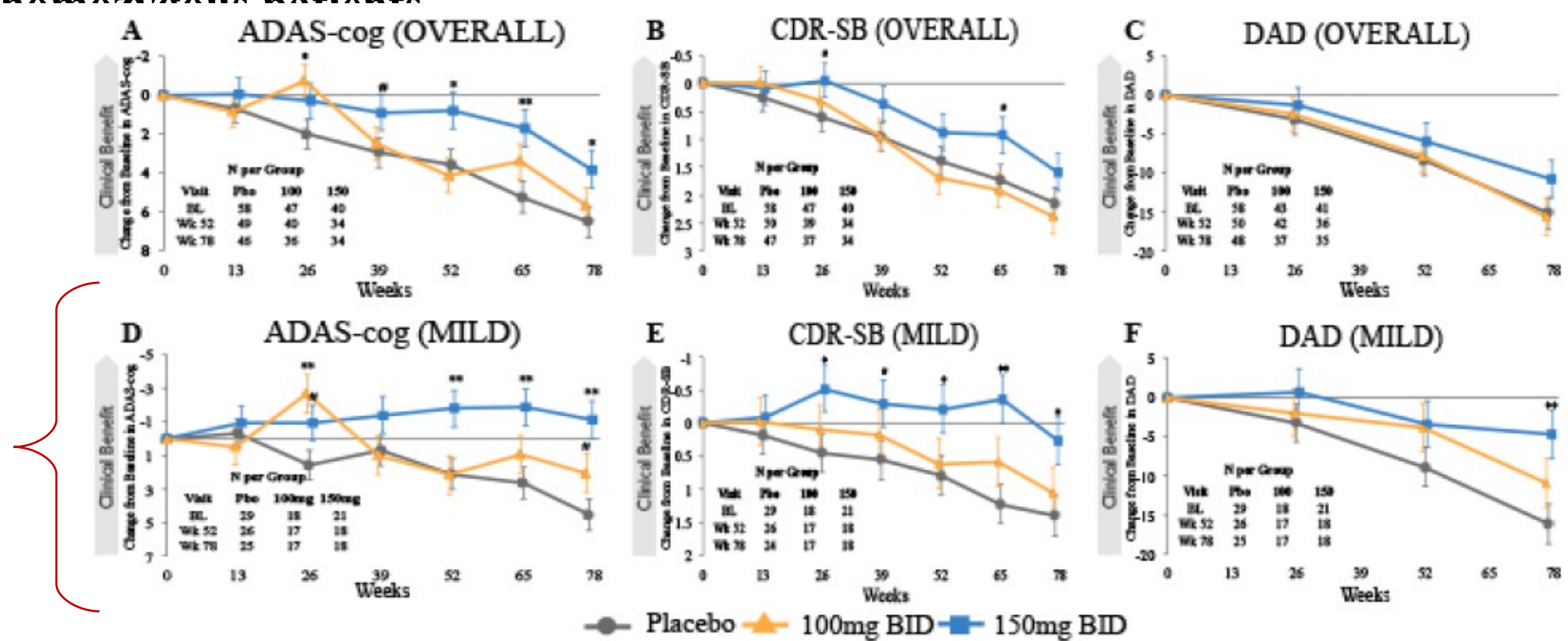
Conclusions: Long-term SSRI treatment may delay progression from MCI to Alzheimer's dementia.

AJP in Advance (doi: 10.1176/appi.ajp.2017.17040404)

New look at old drugs

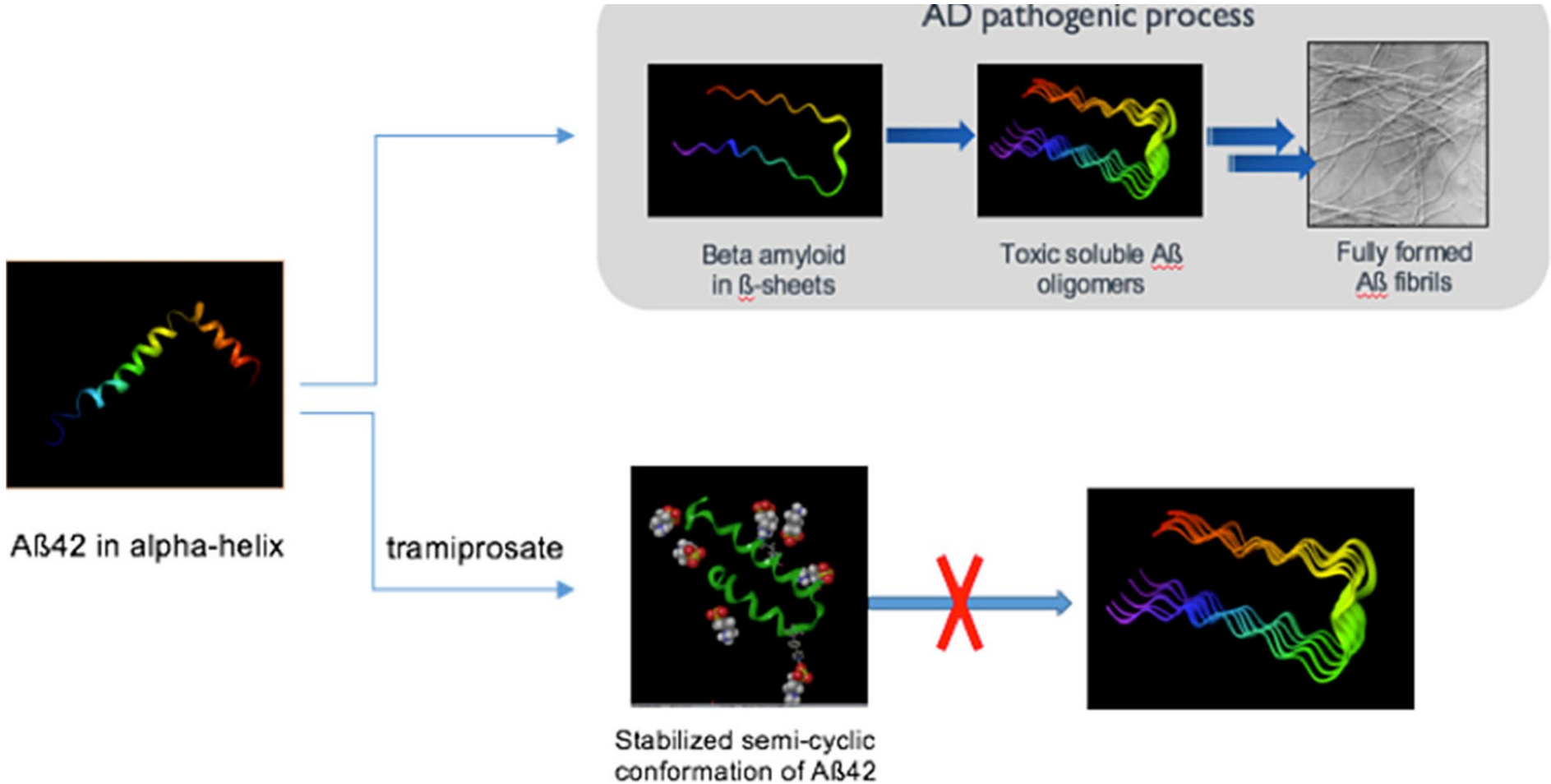
- **Tramiprosate** was tested in mild to moderate AD:

reanalysis showed a potential disease stabilization effect in APOE 4/4 homozygous patients



FDA Grants Fast Track Status to Alzheon's Alzheimer's Therapy Candidate ALZ-801

alzheimersnewstoday.com/2017/10/25/fda-grants-fast-track-status-to-alzheons-alzheimers-therapy-candidate-alz-801/



New look at old drugs

- **Lithium** may have symptomatic and disease stabilization effects

Disease-modifying properties of long-term lithium treatment for amnestic mild cognitive impairment: randomised controlled trial†

Orestes V. Forlenza, Breno S. Diniz, Márcia Radanovic, Franklin S. Santos, Leda L. Talib and Wagner F. Gattaz

Background
Two recent clinical studies support the feasibility of trials to evaluate the disease-modifying properties of lithium in Alzheimer's disease, although no benefits were obtained from short-term treatment.

Aims
To evaluate the effect of long-term lithium treatment on cognitive and biological outcomes in people with **amnestic mild cognitive impairment (aMCI).**

Method
Forty-five participants with aMCI were randomised to receive lithium (0.25–0.5 mmol/l) ($n=24$) or placebo ($n=21$) in a 12-month, double-blind trial. Primary outcome measures were the modification of cognitive and functional test scores, and concentrations of cerebrospinal fluid (CSF) biomarkers (amyloid-beta peptide ($A\beta_{42}$), total tau (T-tau), phosphorylated-tau) (P-tau). Trial registration: NCT01055392.

Results
Lithium treatment was associated with a significant decrease in CSF concentrations of P-tau ($P=0.03$) and better perform-ance on the cognitive subscale of the Alzheimer's Disease Assessment Scale and in attention tasks. Overall tolerability of lithium was good and the adherence rate was 91%.

Conclusions
The present data support the notion that lithium has disease-modifying properties with potential clinical implications in the prevention of Alzheimer's disease.

Declaration of interest
None.

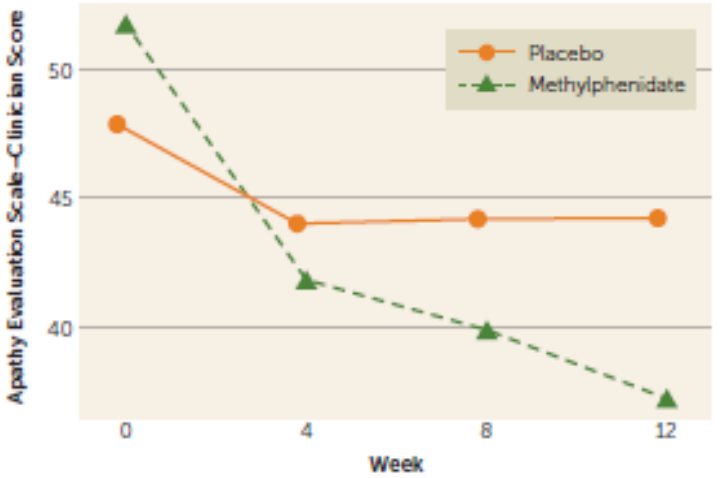
The British Journal of Psychiatry (2011)198, 351–356

Apathy in AD

Methylphenidate for Apathy in Community-Dwelling Older Veterans With Mild Alzheimer's Disease: A Double-Blind, Randomized, Placebo-Controlled Trial

Prasad R. Padala, M.D., M.S., Kalpana P. Padala, M.D., M.S., Shelly Y. Lensing, M.S., Daniel Ramirez, M.S., Varun Monga, M.D., Melinda M. Bopp, B.S., Paula K. Roberson, Ph.D., Richard A. Dennis, Ph.D., Frederick Petty, M.D., Ph.D., Dennis H. Sullivan, M.D., William J. Burke, M.D.

FIGURE 2. Apathy Evaluation Scale–Clinician Scores Over Time in Methylphenidate and Placebo Groups in a Study of Treatment for Apathy in Veterans With Alzheimer's Disease



Conclusions:

- Methylphenidate **improved apathy** in a group of community-dwelling veterans with mild Alzheimer's disease.
- Methylphenidate **also improved cognition, functional status, caregiver burden, CGI scores, and depression**.

American J Psychiatry 2018; 175:159–168

Long-Term Trazodone Use and Cognition: A Potential Therapeutic Role for Slow-Wave Sleep Enhancers

E.Karageorgiou et al.,
Journal of Alzheimer's Disease 67 (2019) 911–21

Conclusions:

These results suggest an **association between trazodone use and delayed cognitive decline,** adding support for a potentially attractive and cost-effective intervention in dementia.

· **Σας Ευχαριστώ**