Enfermedades neurodegenerativas en el adulto joven

IV JORNADES DE L' ESTRATÈGIA DE MALALTIES NEURODEGENERATIVES DE LES ILLES BALEARS

15 de desembre de 2023

Guillermo Amer Ferrer. Servicio de Neurología. HUSE

Designed by macrovector / Freepik

https://www.dreamstime.com/

Enfermedad neurodegenerativa de inicio presenil/temprano/adulto joven

< 65 años de edad

Algunos ejemplos

- Parálisis supranuclear progresiva
- Enfermedad de Parkinson
- Atrofia multisistémica
- Ataxias
  - Genéticas (AD, AR, ligada al X, mitocondrial)
  - Esporádicas
- Enfermedad de Huntington
- Enfermedad de motoneurona
- Demencia en el adulto joven
  - Enfermedad de Alzheimer
  - Degeneración fronto-temporal
  - Demencia con cuerpos de Lewy

Presentación clínica

- Similar al anciano
- Diferentes a las del anciano.

Journal of Neurology (2023) 270:6103–6112
https://doi.org/10.1007/s00415-023-11976-9

ORIGINAL COMMUNICATION

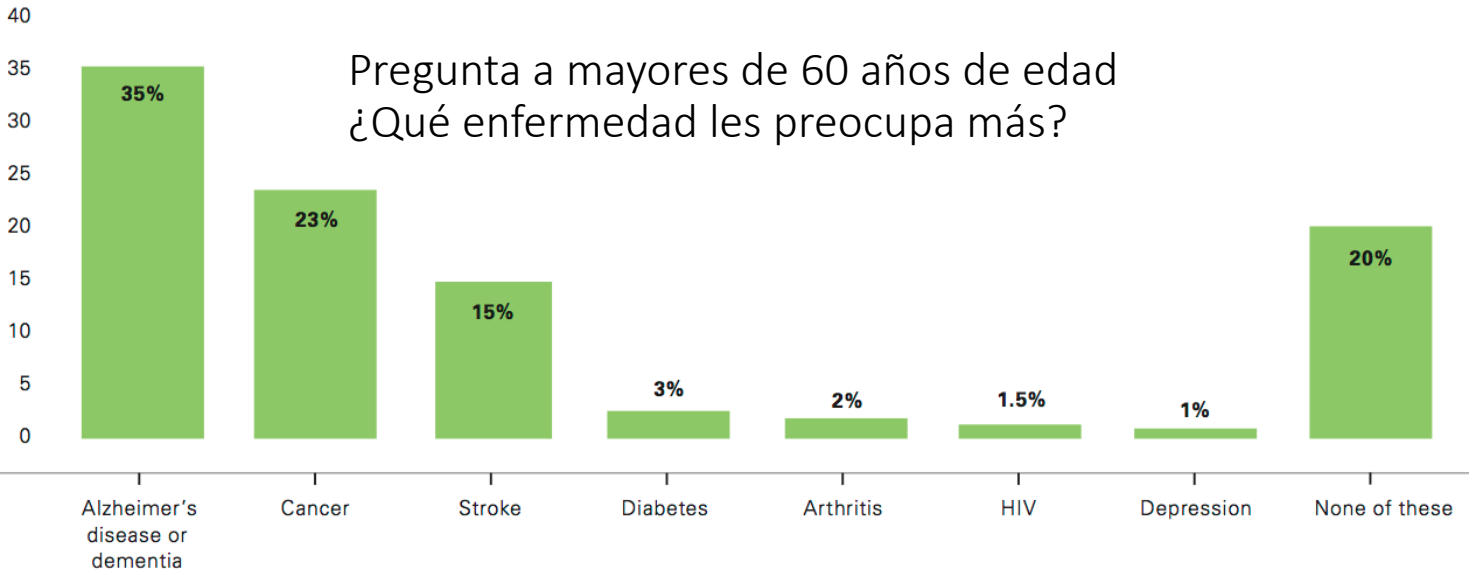
Check for updates

Investigating differences in young- and late-onset progressive supranuclear palsy

Batoul A. AlWazan[1,12] · Indira Garcia-Cordero[2] · Blas Couto[3] · Marta Lamartine Monteiro[1,13] · Michelle Y. Tsang[4] · Jeffrey Antwi[5] · Jonathan Sasitharan[5] · Puja Bhakta[5] · Gabor G. Kovacs[2,4,5,6,7,8] · Susan Fox[4,5] · David F. Tang-Wai[4,7,9,10,11] · Anthony E. Lang[5] · Maria Carmela Tartaglia[4,5,13]

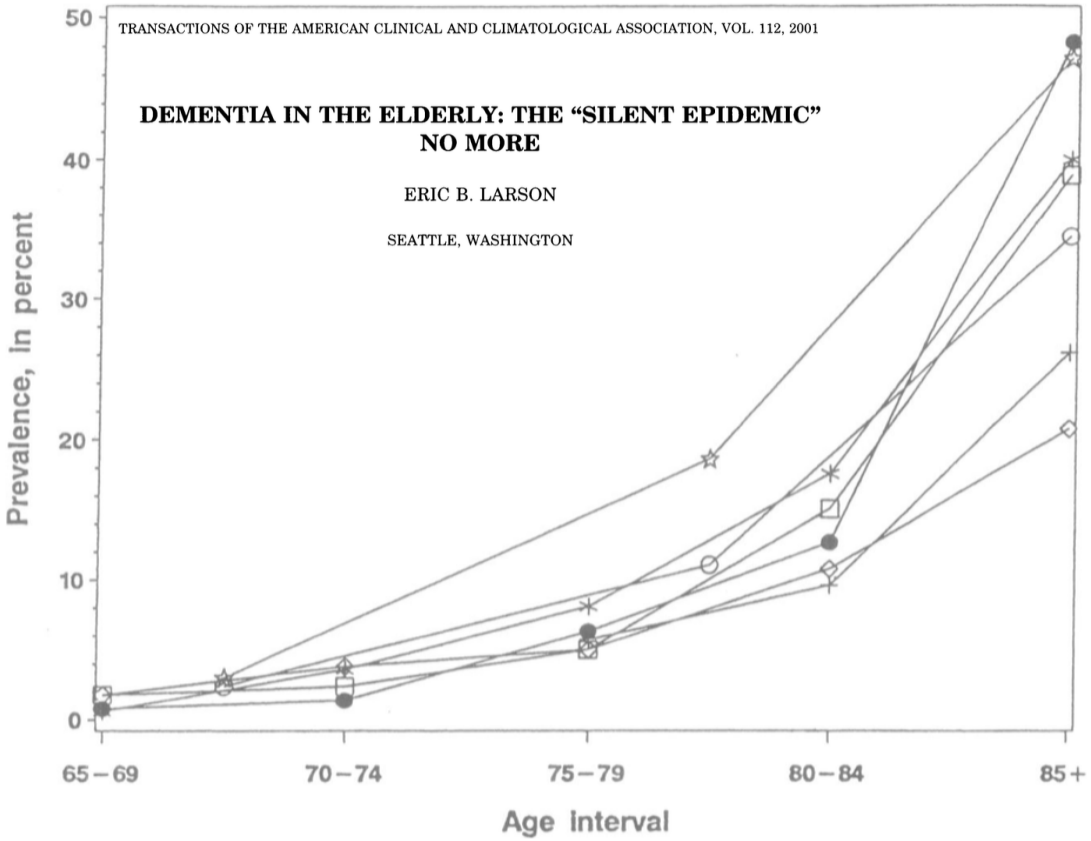
Demencia

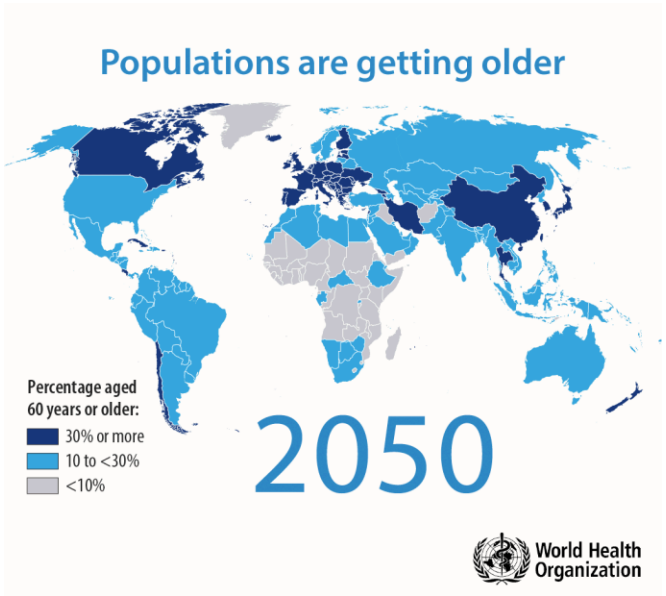
- Proceso patológico
  - Heterogéneo: Demencias
  - Distinto del envejecimiento
    - La demencia no es inherente al envejecimiento
    - La edad aumenta el riesgo de demencia
- Carácter epidémico de las demencias
  - Envejecimiento progresivo de la población



Pregunta a mayores de 60 años de edad
¿Qué enfermedad les preocupa más?

Created from data from the YouGov survey.[A25]





http://www.who.int/ageing/events/world-report-2015-launch/populations-are-getting-older-full.gif

Acceso 22/5/2018

Alzheimer's, A. (2014). "2014 Alzheimer's disease facts and figures." Alzheimers Dement **10**(2): e47-92

Deterioro cognitivo en el adulto joven

- Impacto en el enfermo y su entorno aún mayor que en el anciano
  - Mayor repercusión económica (fracaso en actividad laboral)
  - Mayor repercusión psicológica en el paciente
  - Mayor repercusión familiar
    - Posibilidad de hijos todavía dependientes de los padres
    - Cambio en la relación de pareja
    - Cambio de rol de cada uno de los componentes de la familia, más marcado que en el paciente anciano
  - Mayor repercusión en el entorno social
    - Deterioro de las relaciones sociales del paciente y su núcleo familiar
      - riesgo de aislamiento social
    - Implicación de otros familiares, amigos, vecinos en el cuidado y apoyo al enfermo y su familia
    - Mayor necesidad de apoyo económico
      - Directo para el cuidado del paciente
      - Indirecto por la pérdida en la capacidad económica de su núcleo familiar
    - Necesidad de recursos específicos para tratamiento no farmacológico
      - Psicología clínica (apoyo psicológico similar al ofrecido por psico-oncología p.e.)
      - Entrenamiento cognitivo
      - Terapia ocupacional
      - Fisioterapia
  - Mayor repercusión legal
    - Mayor dificultad para encontrar el equilibrio entre el principio de autonomía y el principio de beneficencia

Deterioro cognitivo en el adulto joven

- Epidemiología
  - Prevalencia de 40 – 119/100.000 habitantes
  - Causa neurodegenerativa ≈ 50 %
    - Enfermedad de Alzheimer: representa ≈ 5 % de todos los pacientes con EA
    - Demencia frontotemporal
    - Demencia con cuerpos de Lewy
- Abordaje clínico diferente al del anciano
  - El diagnóstico diferencial es más amplio
  - A menudo precisa de más pruebas complementarias
  - Hay que considerar enfermedades frecuentes y raras

Deterioro cognitivo en el adulto joven Diagnóstico Diferencial (algunos ejemplos)

- Enfermedad cerebral vascular
  - Asociada a factores de riesgo cerebrovascular
  - Angiopatía amiloide, asociada o no a E. de Alzheimer
  - Vasculitis (cerebral primaria o sistémica)
  - Genética (CADASIL, CARASIL, …)
- Infecciones
  - Enfermedades por priones
  - Enfermedades por virus
    - Trastorno neurocognitivo asociado VIH
    - Encefalitis herpética
    - Leucoencefalopatía multifocal progresiva
  - Enfermedades por bacterias
    - Tuberculosis
    - Neurosífilis
    - Enfermedad de Whipple
- Enfermedades inflamatorias autoinmunes
  - Esclerosis Múltiple
  - Encefalitis autoinmune
- Enfermedades metabólicas
  - Enfermedades mitocondriales
  - Leucodistrofias
  - Lipofuscinosis ceroide neuronal del adulto
  - Enfermedad de Wilson
- Enfermedades psiquiátricas
  - Depresión primaria
  - Trastorno bipolar
  - Trastorno obsesivo compulsivo
  - Trastorno del espectro autista
  - Trastorno de personalidad
- Otros
  - Encefalopatía crónica asociada a TCE
  - Abuso de alcohol
  - Hidrocefalia crónica del adulto
  - Síndrome frontotemporal asociado a hundimiento cerebral
  - Síndrome de apnea-hipoapnea del sueño
  - Trastorno por déficit de atención
  - Trastorno de aprendizaje

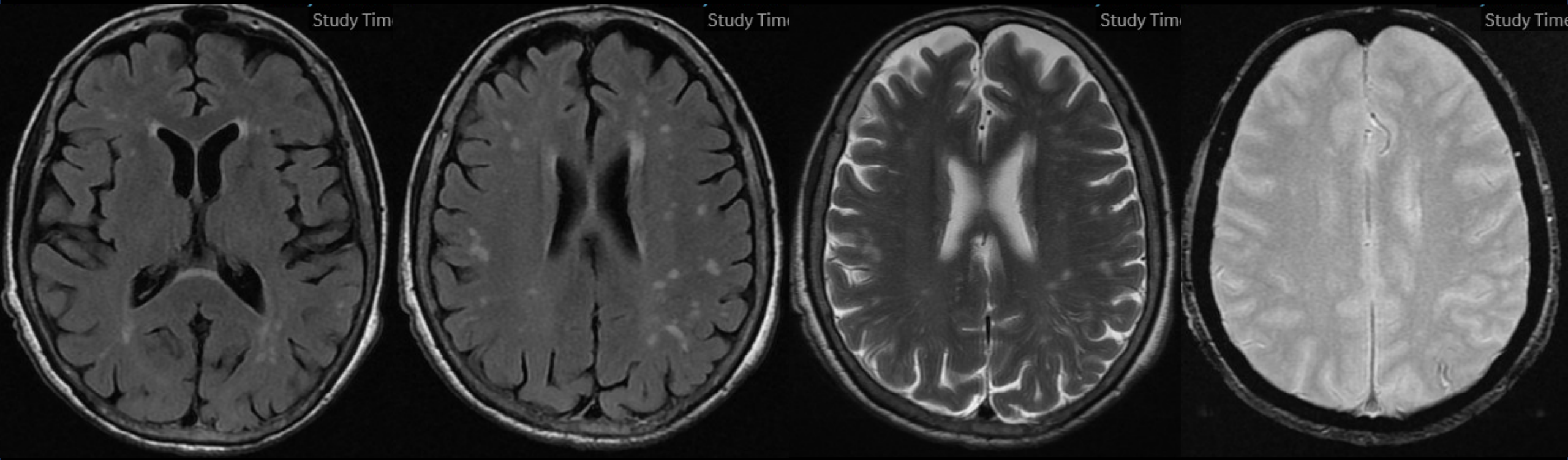
Angiopatía Amiloide

Ausencia de lesiones basales

Patrón salpicado (“multispot”)

Espacios perivasculares dilatados

Hemosiderosis cortical



Deterioro cognitivo en el adulto joven Diagnóstico Diferencial (algunos ejemplos)

- Enfermedad cerebral vascular
  - Asociada a factores de riesgo cerebrovascular
  - Angiopatía amiloide, asociada o no a E. de Alzheimer
  - Vasculitis (cerebral primaria o sistémica)
  - Genética (CADASIL, CARASIL, …)
- Infecciones
  - Enfermedades por priones
  - Enfermedades por virus
    - Trastorno neurocognitivo asociado VIH
    - Encefalitis herpética
    - Leucoencefalopatía multifocal progresiva
  - Enfermedades por bacterias
    - Tuberculosis
    - Neurosífilis
    - Enfermedad de Whipple
- Enfermedades inflamatorias autoinmunes
  - Esclerosis Múltiple
  - Encefalitis autoinmune
- Enfermedades metabólicas
  - Enfermedades mitocondriales
  - Leucodistrofias
  - Lipofuscinosis ceroide neuronal del adulto
  - Enfermedad de Wilson
- Enfermedades psiquiátricas
  - Depresión primaria
  - Trastorno bipolar
  - Trastorno obsesivo compulsivo
  - Trastorno del espectro autista
  - Trastorno de personalidad
- Otros
  - Encefalopatía crónica asociada a TCE
  - Abuso de alcohol
  - Hidrocefalia crónica del adulto
  - Síndrome frontotemporal asociado a hundimiento cerebral
  - Síndrome de apnea-hipoapnea del sueño
  - Trastorno por déficit de atención
  - Trastorno de aprendizaje

Psychiatric Screening Measures in Behavioral Variant Frontotemporal Dementia

Peter S. Pressman, M.D., Joie Molden, Ph.D., Hal S. Wortzel, M.D., Evan Plys, Ph.D., Jonathan H. Woodcock, M.D., Christopher M. Filley, M.D., David B. Arciniegas, M.D.

Objective: Behavioral variant frontotemporal dementia (bvFTD) is sometimes misdiagnosed as a primary psychiatric disorder, such as major depressive disorder, bipolar disorder, an anxiety disorder, autism spectrum disorder (ASD), or attention-deficit hyperactivity disorder (ADHD). Nonspecialists often use screening measures for primary psychiatric disorders in early assessments of persons with bvFTD. The investigators aimed to evaluate the manifestations of bvFTD in surveys intended to screen for primary psychiatric disorders.

Methods: Patients with bvFTD (N=27) presenting to an academic neurobehavior specialty clinic and their caregivers were provided questionnaire packets including the Mood Disorder Questionnaire (MDQ), the Patient Health Questionnaire–9 (PHQ-9), the Generalized Anxiety Disorder–7 scale (GAD-7), the Adult ADHD Self-Report Scale, version 1.1, the Ritvo Autism and Asperger Diagnostic Scale, and the Neuropsychiatric Inventory Questionnaire. Established cutoff scores suggesting the presence of a primary psychiatric disorder were used to define a "positive" response. Individual questions from each screening questionnaire were examined for a more granular characterization of bvFTD.

Results: Overall, 15% of bvFTD patients screened positive for bipolar disorder, 54% screened positive for ADHD, and 89% screened positive for ASD. Hyperactivity or hypersensitivity symptoms were infrequently endorsed. In addition, 57% of respondents screened positive for depressive symptoms on the PHQ-9, and 43% screened positive for anxiety symptoms on the GAD-7.

Conclusions: The use of cutoff scores on screening measures for primary psychiatric disorders resulted in potentially problematic positive screens of primary psychiatric disorders among persons with bvFTD. Identifying specific questions that distinguish between bvFTD and primary psychiatric disorders requires further study.

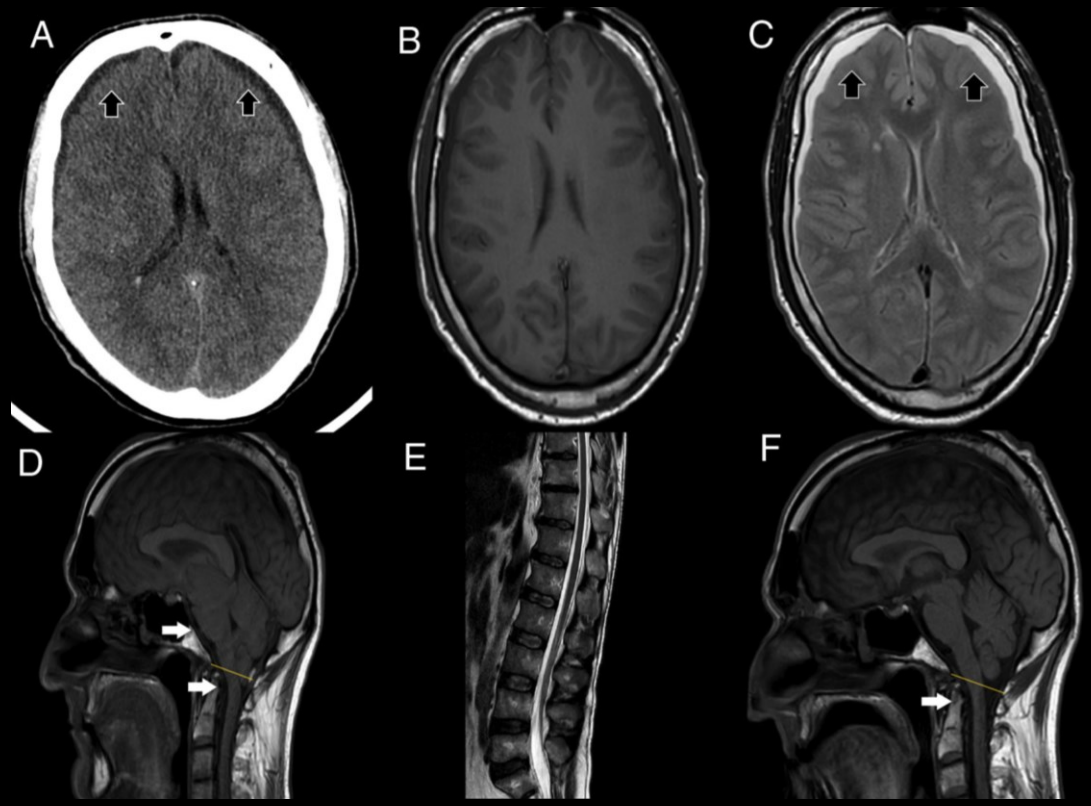
JNCN in Advance (doi: 10.1176/appi.neuropsych.20230041)

T Bipolar	15%
TDAH	54%
TEA	89%
Dep	57%
Ansiedad	43%

Deterioro cognitivo en el adulto joven Diagnóstico Diferencial (algunos ejemplos)

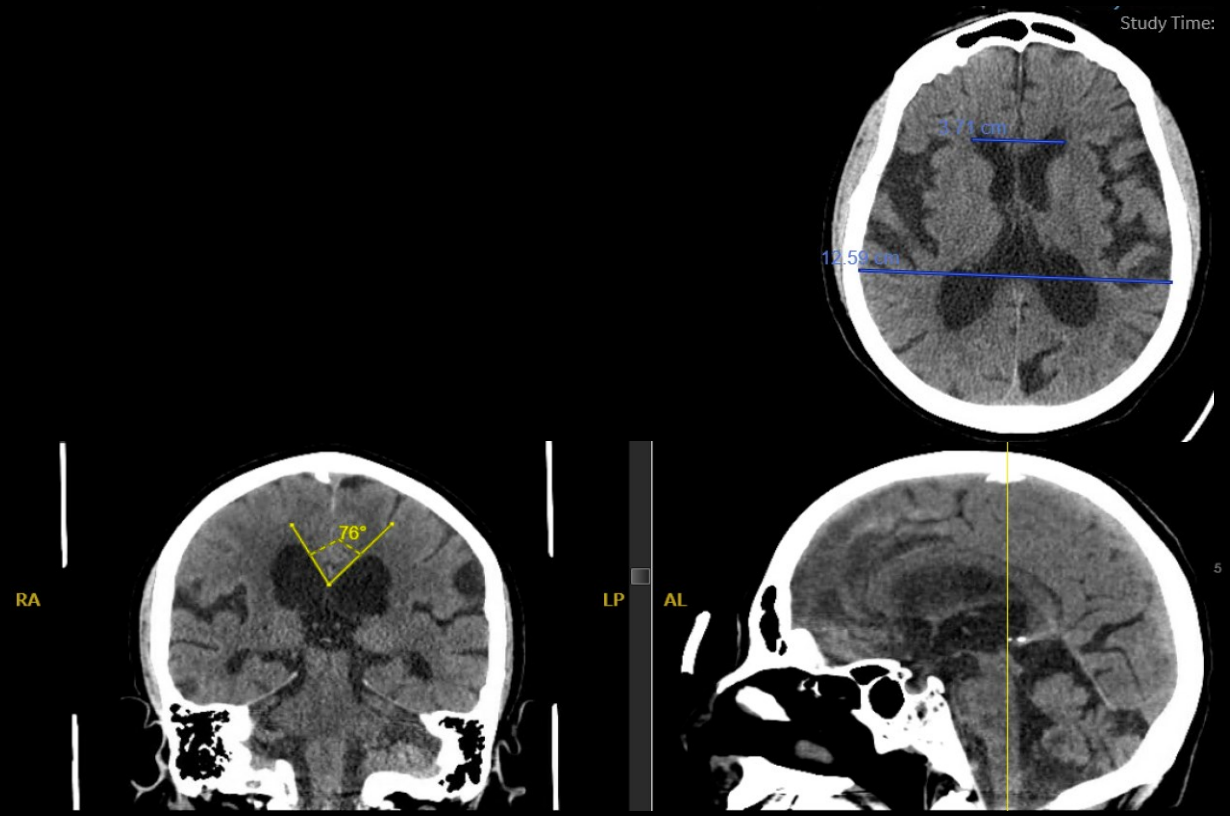
- Enfermedad cerebral vascular
  - Asociada a factores de riesgo cerebrovascular
  - Angiopatía amiloide, asociada o no a E. de Alzheimer
  - Vasculitis (cerebral primaria o sistémica)
  - Genética (CADASIL, CARASIL, …)
- Infecciones
  - Enfermedades por priones
  - Enfermedades por virus
    - Trastorno neurocognitivo asociado VIH
    - Encefalitis herpética
    - Leucoencefalopatía multifocal progresiva
  - Enfermedades por bacterias
    - Tuberculosis
    - Neurosífilis
    - Enfermedad de Whipple
- Enfermedades inflamatorias autoinmunes
  - Esclerosis Múltiple
  - Encefalitis autoinmune
- Enfermedades metabólicas
  - Enfermedades mitocondriales
  - Leucodistrofias
  - Lipofuscinosis ceroide neuronal del adulto
  - Enfermedad de Wilson
- Enfermedades psiquiátricas
  - Depresión primaria
  - Trastorno bipolar
  - Trastorno obsesivo compulsivo
  - Trastorno del espectro autista
  - Trastorno de personalidad
- Otros
  - Encefalopatía crónica asociada a TCE
  - Abuso de alcohol
  - Hidrocefalia crónica del adulto
  - Síndrome frontotemporal asociado a hundimiento cerebral
  - Síndrome de apnea-hipoapnea del sueño
  - Trastorno por déficit de atención
  - Trastorno de aprendizaje

Síndrome de hundimiento cerebral



Dominguez, D. L., et al. (2023). Neurologia (Engl Ed) **38**(3): 221-223

Hidrocefalia crónica del adulto



Deterioro cognitivo en el adulto joven Diagnóstico Diferencial (algunos ejemplos)

- Enfermedad cerebral vascular
  - Asociada a factores de riesgo cerebrovascular
  - Angiopatía amiloide, asociada o no a E. de Alzheimer
  - Vasculitis (cerebral primaria o sistémica)
  - Genética (CADASIL, CARASIL, …)
- Infecciones
  - Enfermedades por priones
  - Enfermedades por virus
    - Trastorno neurocognitivo asociado VIH
    - Encefalitis herpética
    - Leucoencefalopatía multifocal progresiva
  - Enfermedades por bacterias
    - Tuberculosis
    - Neurosífilis
    - Enfermedad de Whipple
- Enfermedades inflamatorias autoinmunes
  - Esclerosis Múltiple
  - Encefalitis autoinmune
- Enfermedades metabólicas
  - Enfermedades mitocondriales
  - Leucodistrofias
  - Lipofuscinosis ceroide neuronal del adulto
  - Enfermedad de Wilson
- Enfermedades psiquiátricas
  - Depresión primaria
  - Trastorno bipolar
  - Trastorno obsesivo compulsivo
  - Trastorno del espectro autista
  - Trastorno de personalidad
- Otros
  - Encefalopatía crónica asociada a TCE
  - Abuso de alcohol
  - Hidrocefalia crónica del adulto
  - Síndrome frontotemporal asociado a hundimiento cerebral
  - Síndrome de apnea-hipoapnea del sueño
  - Trastorno por déficit de atención
  - Trastorno de aprendizaje

Avances en el conocimiento de la historia natural de las demencias (ejemplo E. Alzheimer)

- Demencia (síntomas y signos con repercusión funcional)
  - Forma típica (inicio amnésico seguido s. afaso-apraxo-agnósico)
  - Formas atípicas
    - Variante de predominio amnésico (límbico)
    - Variante frontal
    - Variente APP logopénica
    - Variante posterior (visuoperceptiva)
    - Variante cortico-basal
  - Curso clínico con evolución más rápida en el adulto joven
- Deterioro cognitivo Leve (síntomas y signos sin repercusión funcional)
  - Amnésico
  - No amnésico
- Declinar cognitivo subjetivo (Síntomas sin signos ni repercusión funcional)

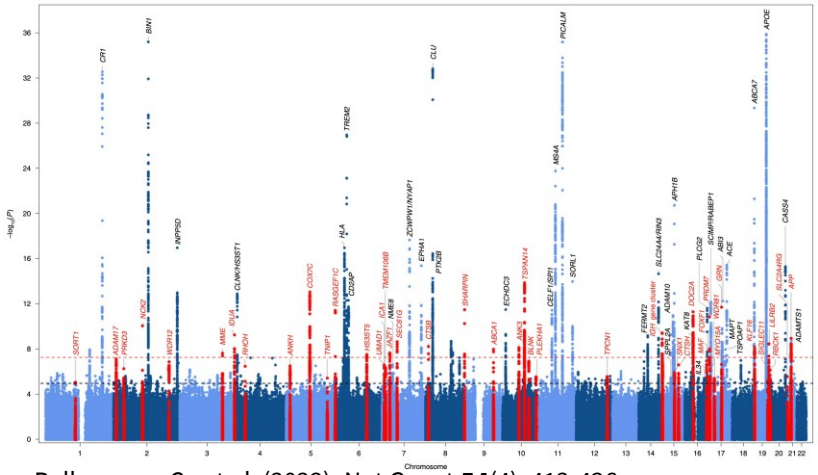
Etiología EA adulto joven

- Esporádica: > 90 %
  - Poligénica (riesgo)
- HAD monogénica: 1 - 6 %
  - Mutaciones gen Presenilina 1: ≈ 50 %
  - Mutaciones gen Presenilina 2: < 2%
  - Mutaciones gen APP: ≈ 15 %
  - Mutaciones en otros genes: ≈ 33%
- Trisomía 21 (Síndrome de Down)

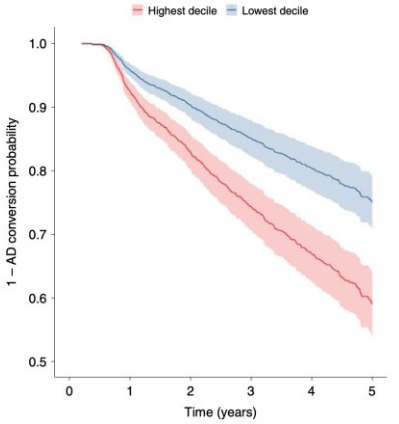
ARTICLES
https://doi.org/10.1038/s41588-022-01024-z
nature genetics
Check for updates

OPEN

New insights into the genetic etiology of Alzheimer's disease and related dementias



Puntuación de riesgo genético
(83 variantes significativas, excluida *APOE)*



Bellenguez, C., et al. (2022). Nat Genet **54**(4): 412-436.

Longitudinal clinical, cognitive, and biomarker profiles in dominantly inherited versus sporadic early-onset Alzheimer's disease.

STUDY POPULATION

Early Onset Alzheimer's Disease (EOAD):

Sporadic AD (sEOAD), n=118

Dominantly Inherited (DIAD), n=117

ASSESSMENTS/OUTCOMES

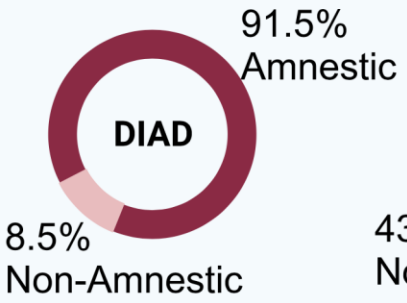
Clinical-Cognitive & neuro exam

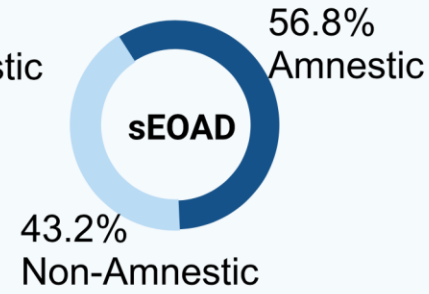
Fluid Biomarkers

- Clinical presentation
- Rate of change
- Biomarker levels

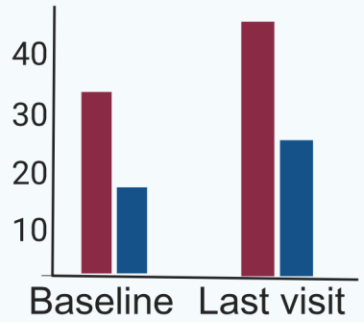
FINDINGS

A Baseline Clinical presentation

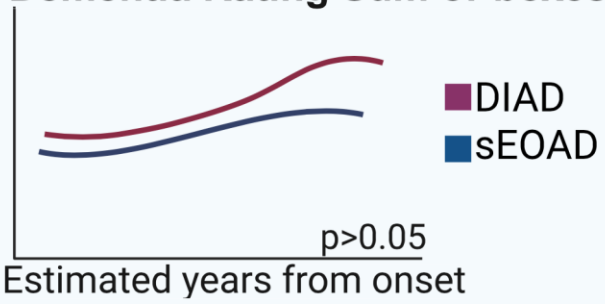




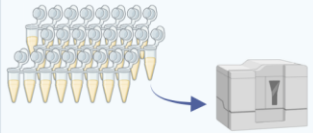
B Motor symptoms (%)



C Rate of change Clinical Dementia Rating Sum of boxes



D CSF biomarker levels DIAD vs sEOAD.



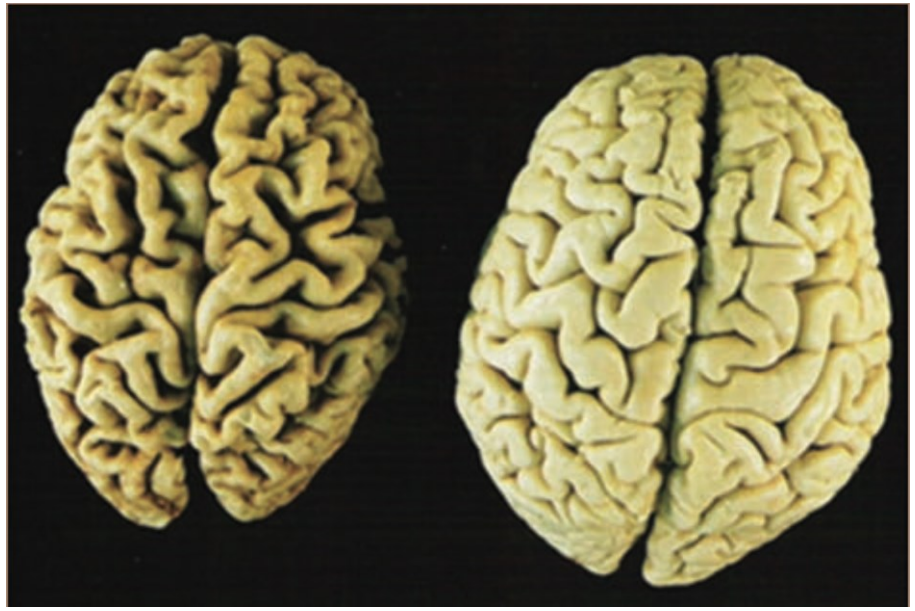
1. No significant differences in CSF amyloid βeta 42 levels (p=0.06).
2. CSF phosphorylated at threonine 181 levels were higher in the DIAD cohort (p=0.01)
3. No significant differences in CSF total tau levels (p=0.35).

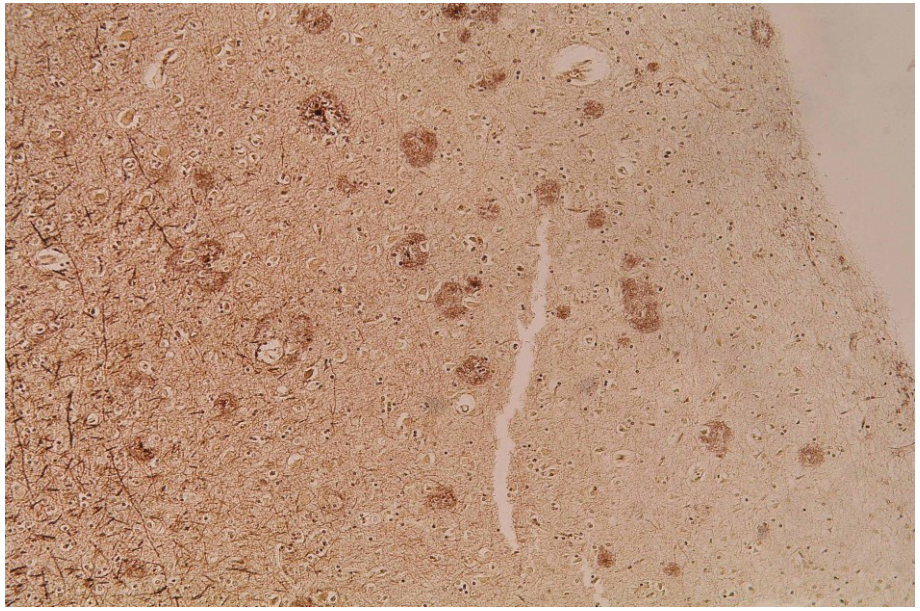
CONCLUSIONS

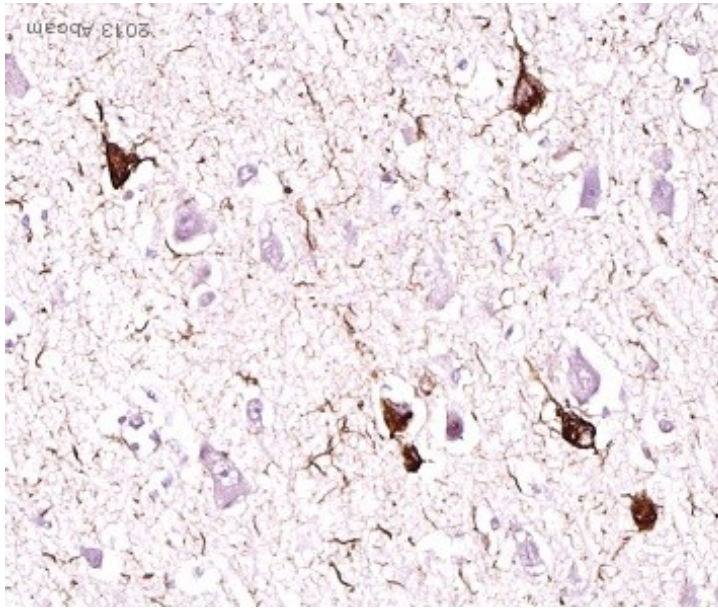
Sporadic and inherited EOAD differed in baseline profiles, sEOAD is best distinguished from DIAD by the later age at onset, the high frequency of atypical clinical presentations and worse executive performance at baseline. Longitudinal clinical decline in early stages is similar across both groups.

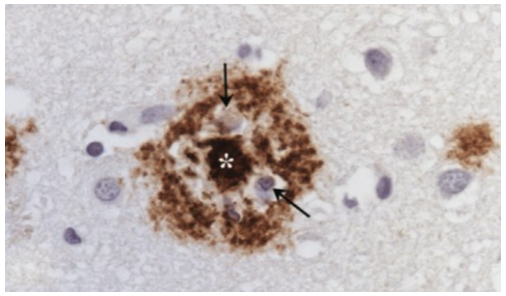
Llibre-Guerra, J. J., et al. (2023). Brain Commun **5**(6): fcad280.

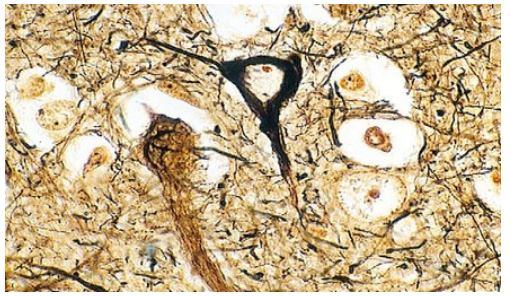
Neuropatología de la EA

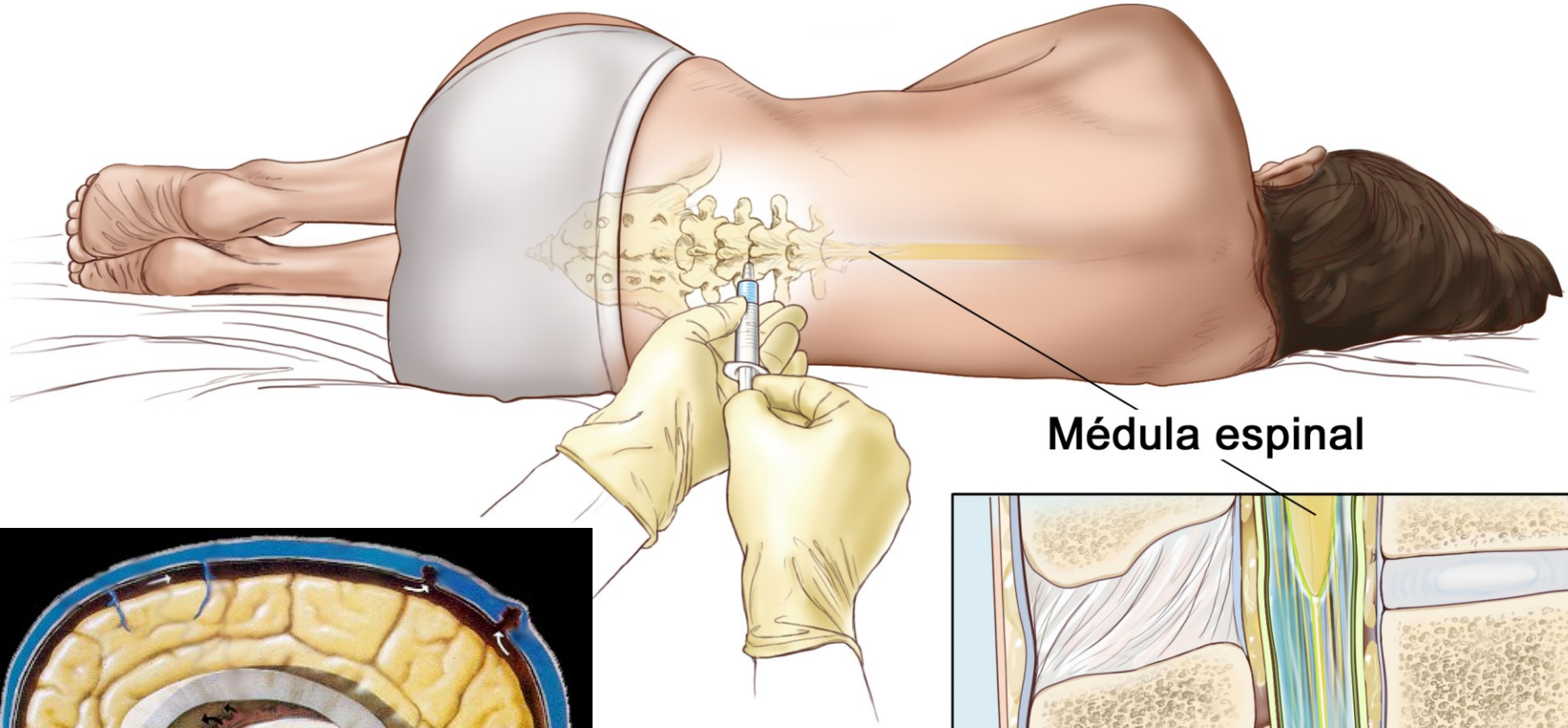




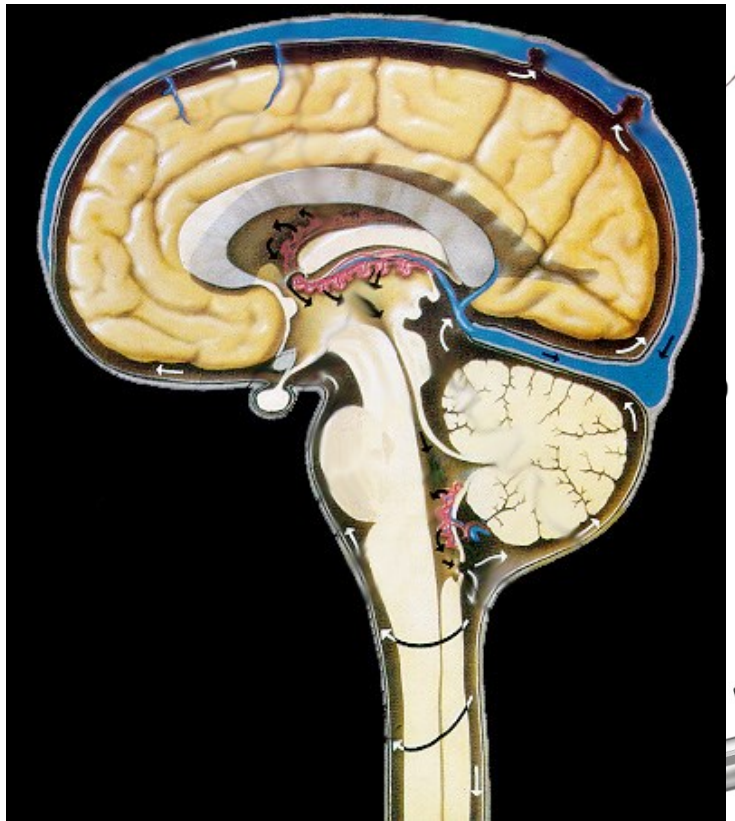






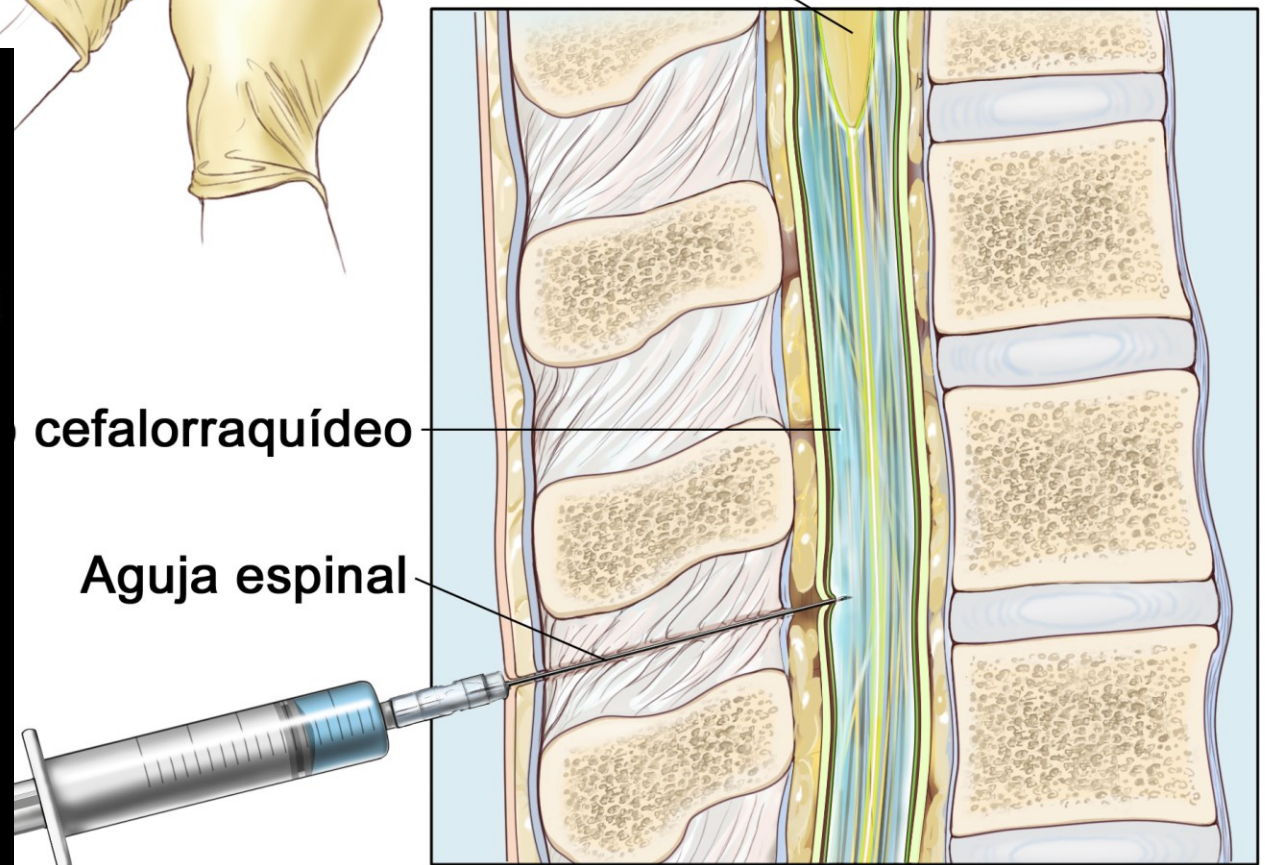


Médula espinal

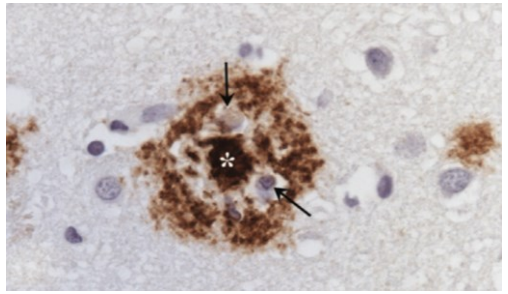


cefalorraquídeo

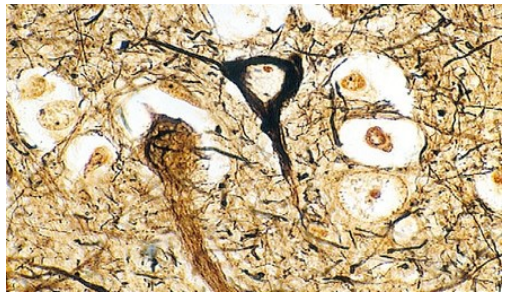
Aguja espinal



Biomarcadores EA en LCR



- Beta-amiloide (patología amiloide)
  - $A\beta_{1-42}$
  - Cociente $A\beta_{1-42}/A\beta_{1-40}$ (compensa variabilidad interindividual)



- Tau
  - Tau-p (degeneración neurofibrilar)
  - Tau-total (neurodegeneración)

Cerebrospinal Fluid Tau and β-Amyloid 42 Proteins Identify Alzheimer Disease in Subjects With Mild Cognitive Impairment

M. Riemenschneider, MD; N. Lautenschlager, MD; S. Wagenpfeil, PhD; J. Diehl, MD; A. Drzezga, MD; A. Kurz, MD

Arch Neurol. 2002;59:1729-1734

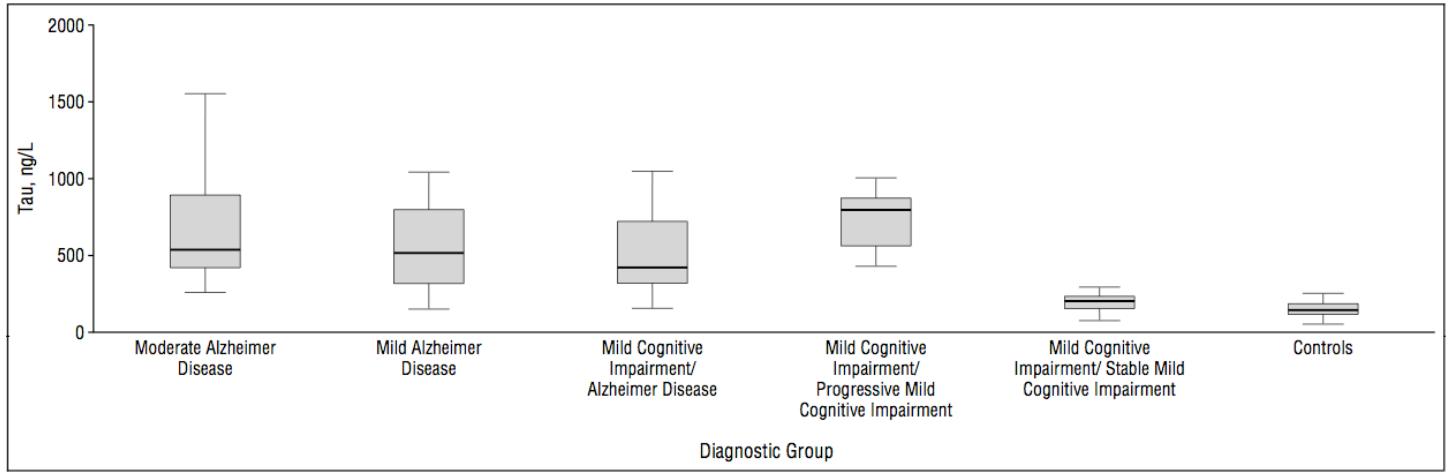


Figure 1. Cerebrospinal fluid tau level by diagnostic group.

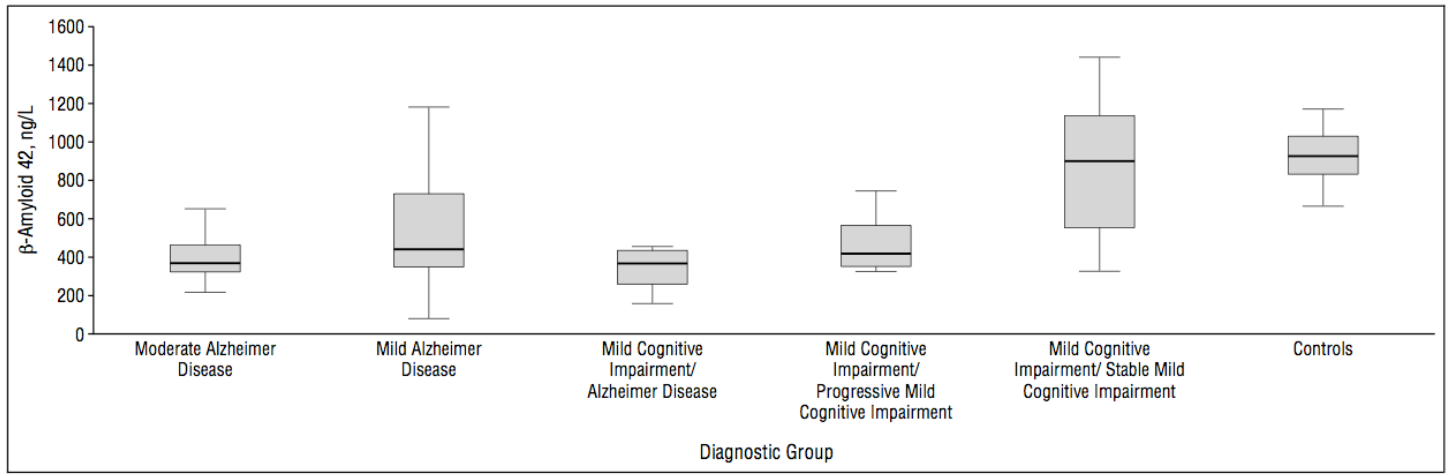


Figure 2. Cerebrospinal fluid β-amyloid 42 level by diagnostic group.

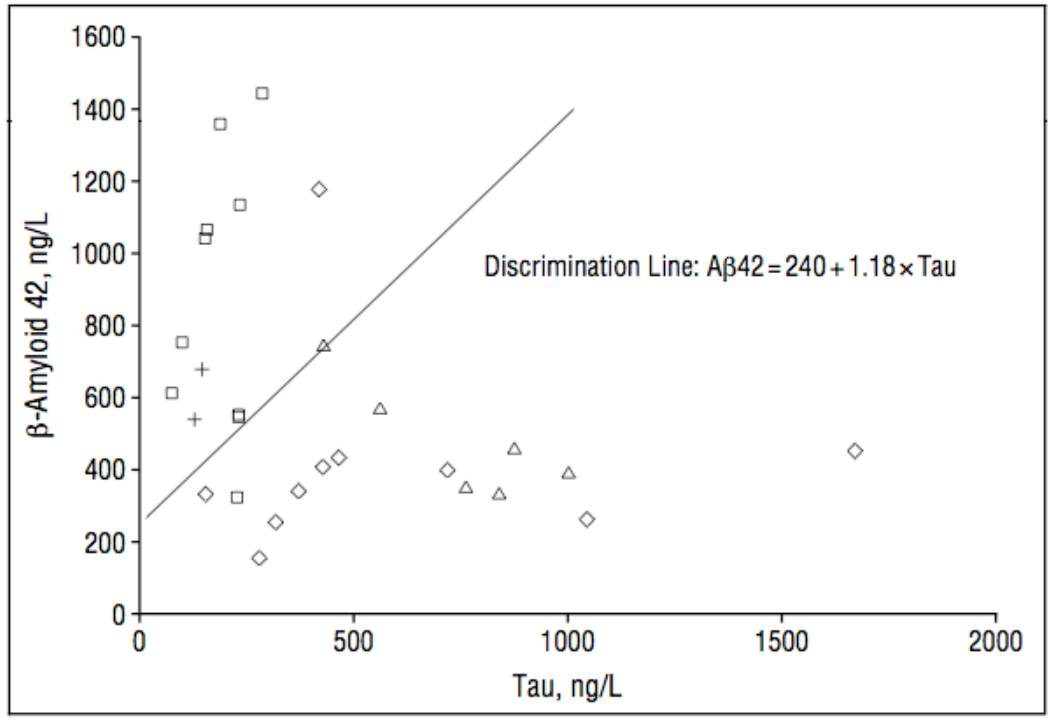
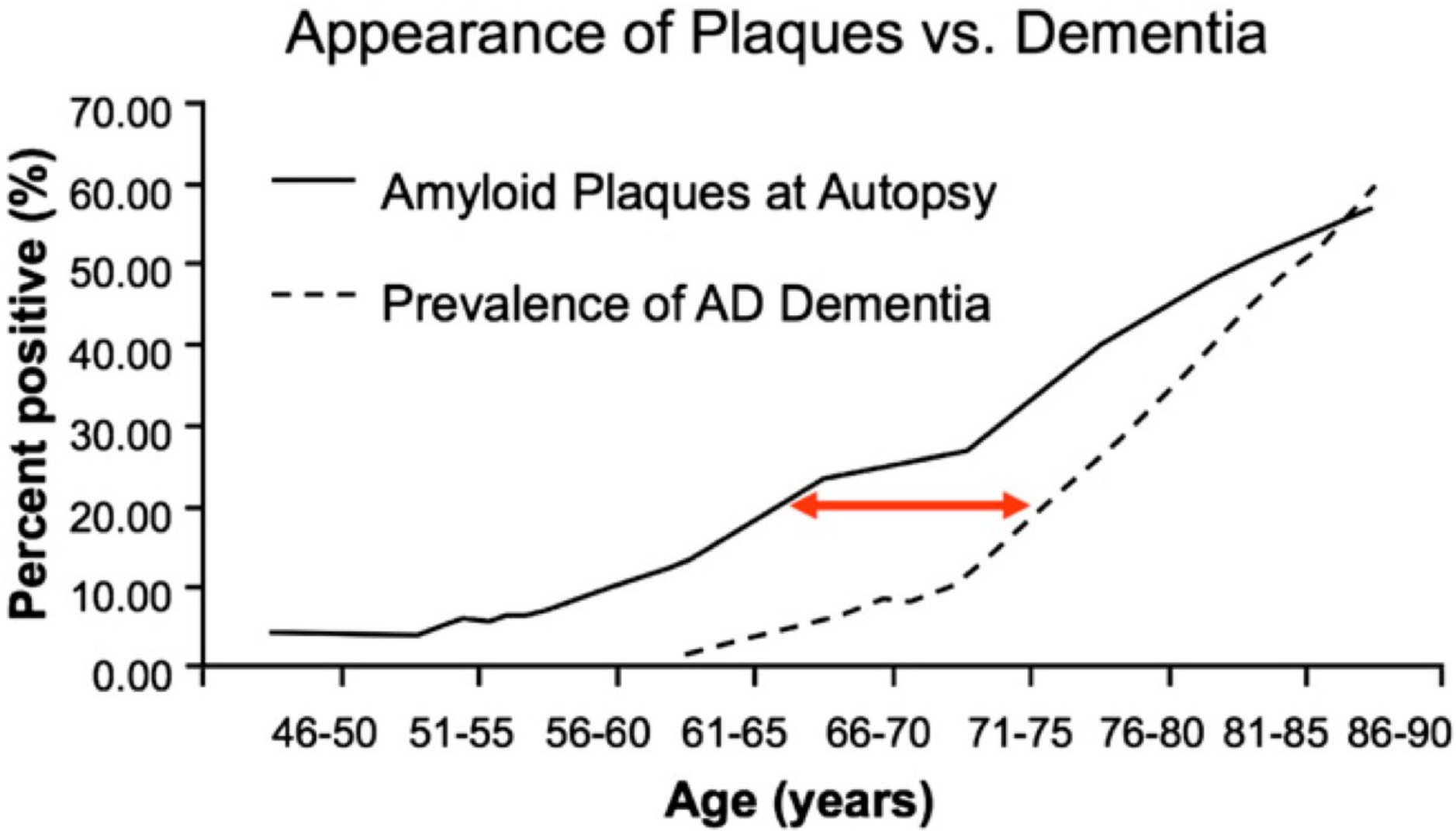
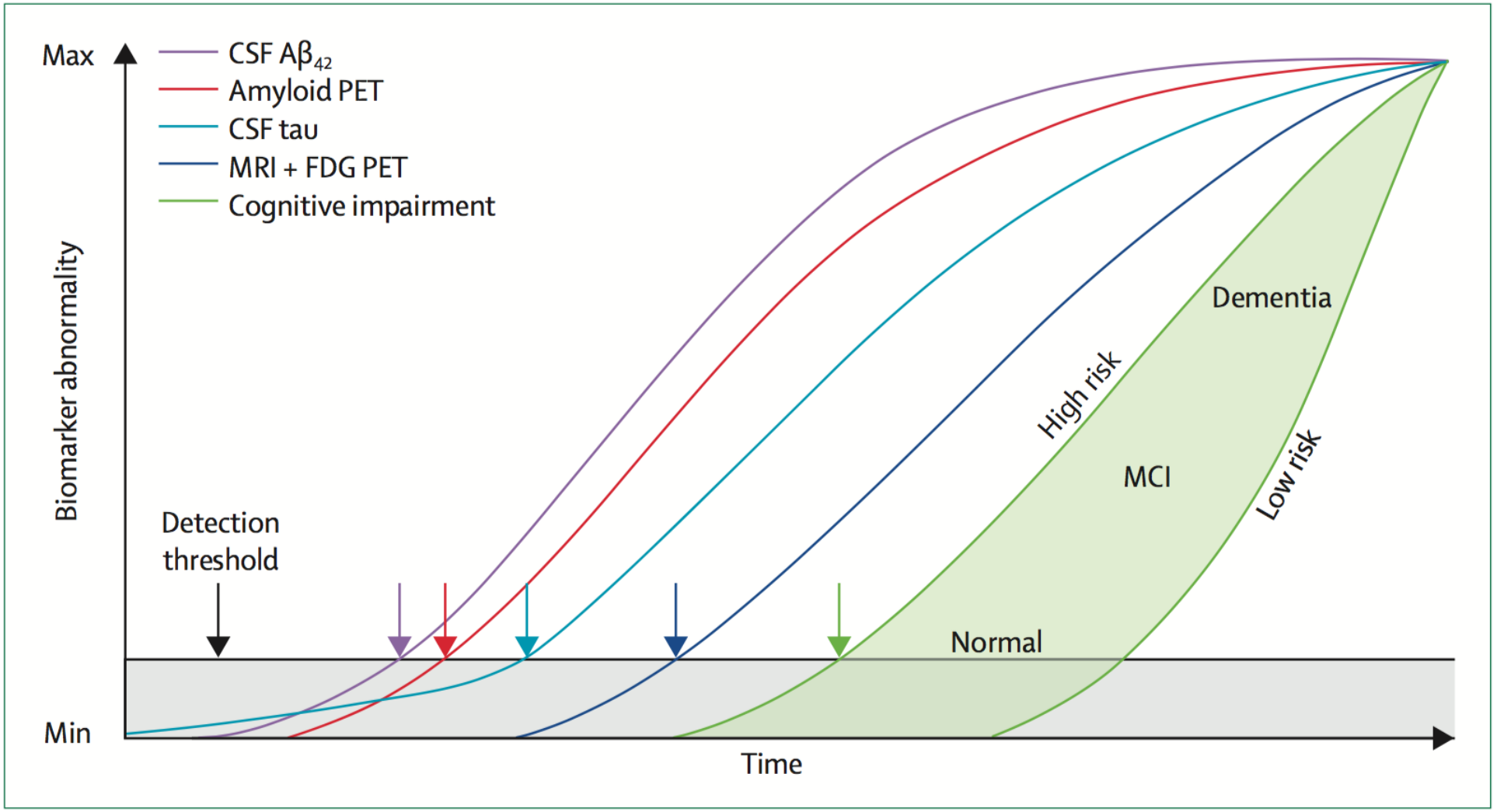


Figure 3. Scatter plot of cerebrospinal fluid tau and β-amyloid 42 (Aβ42) concentrations in subjects with mild cognitive impairment (MCI) at baseline by diagnosis at 18-month follow-up. The line within the figure indicates the best discrimination line. Squares indicate stable MCI; plus signs, frontotemporal dementia; triangles, progressive MCI; and diamonds, Alzheimer disease.


Appearance of Plaques vs. Dementia
Percent positive (%)
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
Amyloid Plaques at Autopsy
Prevalence of AD Dementia
46-50
51-55
56-60
61-65
66-70
71-75
76-80
81-85
86-90
Age (years)



Jack, C. R., et al. (2013). Lancet Neurol **12**(2): 207-216.

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]

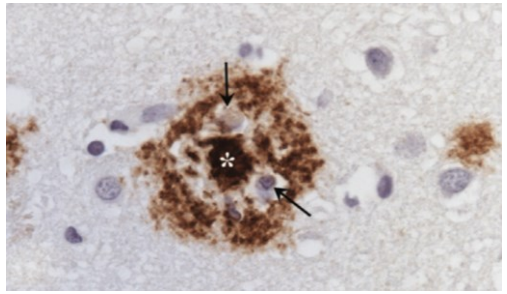
Contributors[†]**:** Cerise Elliott, Eliezer Masliah, Laurie Ryan, and Nina Silverberg

AT(N) biomarker grouping

A: Aggregated Aβ or associated pathologic state

CSF $A\beta_{42}$, or $A\beta_{42}/A\beta_{40}$ ratio

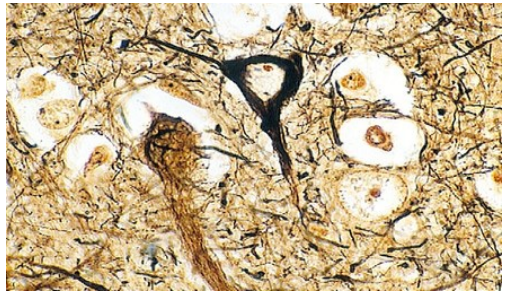
Amyloid PET



T: Aggregated tau (neurofibrillary tangles) or associated pathologic state

CSF phosphorylated tau

Tau PET

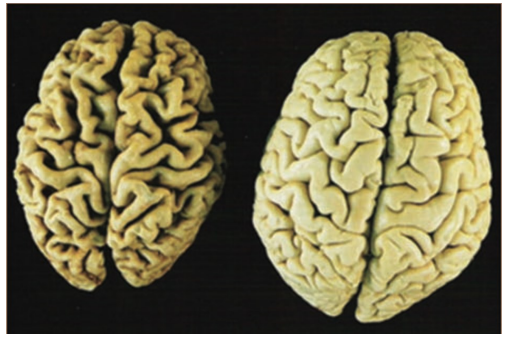


(N): Neurodegeneration or neuronal injury

Anatomic MRI

FDG PET

CSF total tau



Biomarker profiles and categories

AT(N) profiles	Biomarker category
A-T-(N)-	Normal AD biomarkers
A+T-(N)-	Alzheimer's pathologic change
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

Text Box 1
Glossary

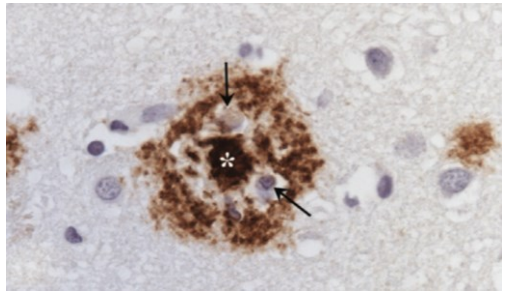
- **Alzheimer disease (AD)**—refers to Aβ plaques and pathologic tau deposits, defined *in vivo* by abnormal biomarkers of Aβ and pathologic tau (both are required)
- **Alzheimer's pathologic change**—early stage of Alzheimer's continuum, defined *in vivo* by an abnormal Aβ biomarker with normal pathologic tau biomarker
- **Alzheimer's continuum**—refers to individuals with biomarker designation of either AD or Alzheimer's pathologic change
- **Alzheimer's clinical syndrome**—recommended terminology for clinically ascertained multi- (or single-) domain amnestic syndrome or a classic syndromal variant (i.e., what has historically been labeled "possible or probable AD"). It applies to both mildly impaired and demented individuals. The term "Alzheimer's disease" is reserved for situations where neuropathologic or biomarker evidence of the disease (i.e., Aβ plaques and pathologic tau deposits) is present
- **Biomarker group**—refers to three different pathologic processes of AD that a biomarker can measure: Aβ (A), pathologic tau (T), and neurodegeneration/neuronal injury (N)
- **Biomarker profile**—binarizing each of the three biomarker groups into normal/abnormal (+/−) results in eight possible biomarker profiles: A+T−(N)−, A+T+(N)−, etc.
- **Biomarker category**—biomarker profiles are grouped into three possible biomarker categories: normal AD biomarkers, A−T−(N)−; Alzheimer's continuum, any A+ combination; and non-Alzheimer's pathologic change (i.e., suspected non-Alzheimer's pathophysiology or SNAP), A−T+(N)−, A−T−(N)+, or A−T+(N)+
- **Cognitively unimpaired**—cognitive performance in the nonimpaired range for that individual, defined as not mild cognitive impairment or demented
- **Neurobehavioral symptoms**—symptoms attributable to mood or behavioral disorders, for example, anxiety, depression, and apathy
- **Transitional cognitive decline**—cognitive performance in the nonimpaired range but with a subjective complaint of cognitive decline, or a subtle decline measured on longitudinal cognitive testing, or neurobehavioral symptoms, or combinations of these.

AT(N) biomarker grouping

A: Aggregated Aβ or associated pathologic state

CSF $A\beta_{42}$, or $A\beta_{42}/A\beta_{40}$ ratio

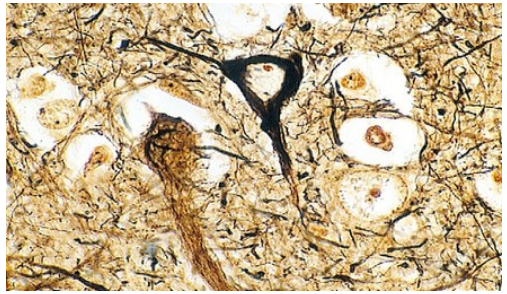
Amyloid PET



T: Aggregated tau (neurofibrillary tangles) or associated pathologic state

CSF phosphorylated tau

Tau PET

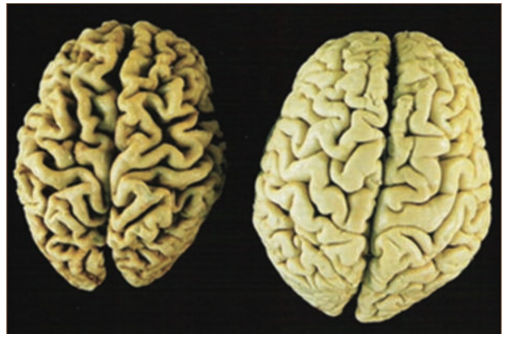


(N): Neurodegeneration or neuronal injury

Anatomic MRI

FDG PET

CSF total tau



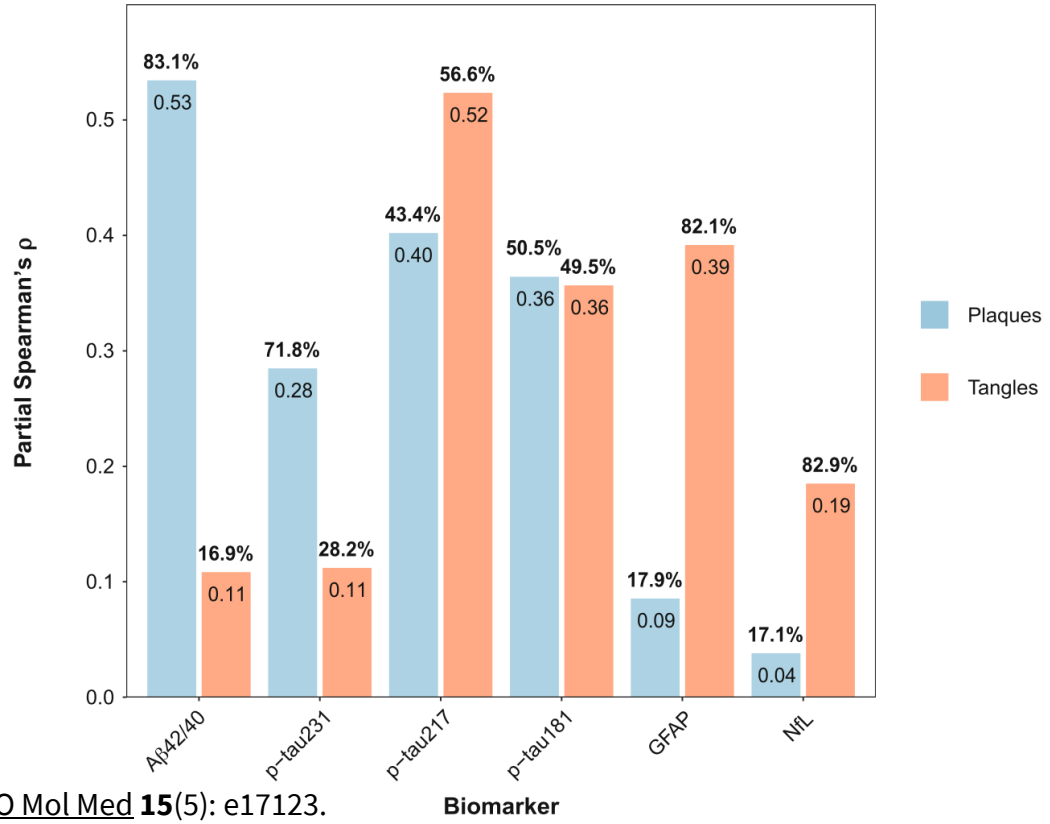
Article

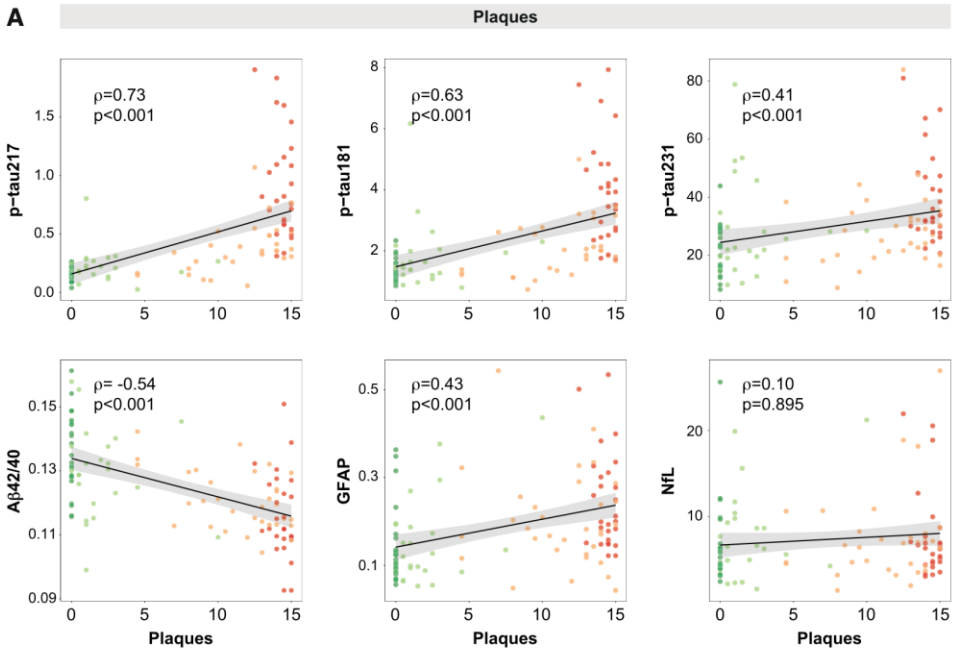
TRANSPARENT PROCESS OPEN ACCESS

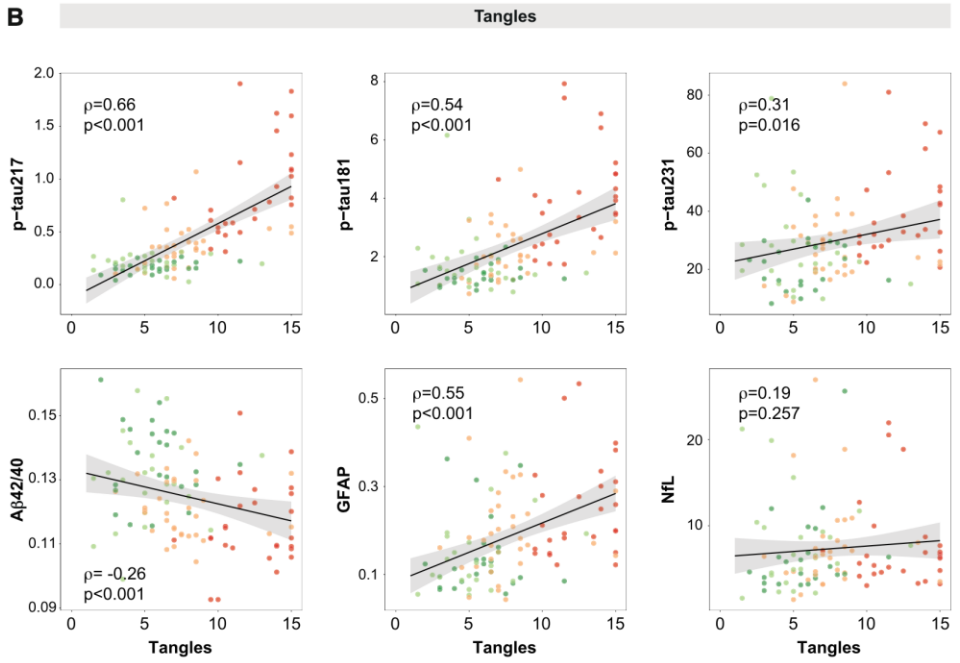
EMBO Molecular Medicine

Specific associations between plasma biomarkers and postmortem amyloid plaque and tau tangle loads

Gemma Salvadó[1,*], Rik Ossenkoppele[1,2,3], Nicholas J Ashton[4,5,6], Thomas G Beach[7], Geidy E Serrano[7], Eric M Reiman[8], Henrik Zetterberg[4,9,10,11,12], Niklas Mattsson-Carlgren[1,13,14], Shorena Janelidze[1], Kaj Blennow[4,9] & Oskar Hansson[1,15,**]







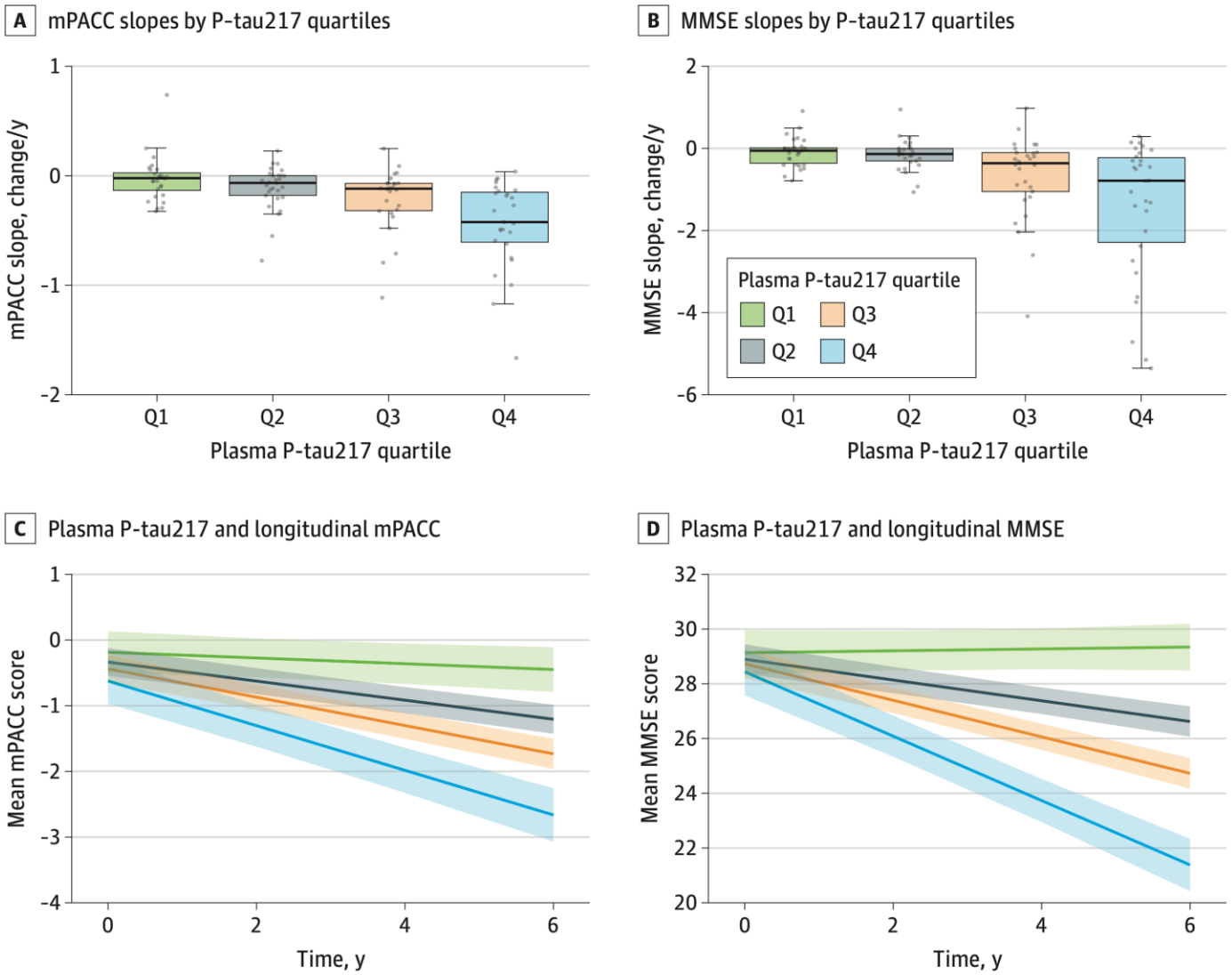
Salvado, G., et al. (2023). EMBO Mol Med **15**(5): e17123.

JAMA Neurology | Original Investigation

Prediction of Longitudinal Cognitive Decline in Preclinical Alzheimer Disease Using Plasma Biomarkers

Mattsson-Carlgren, N., et al. (2023). JAMA Neurol **80**(4): 360-369.

Figure 1. Plasma P-tau217 and Longitudinal Cognition in β-Amyloid (Aβ)–Positive Cognitively Unimpaired Individuals



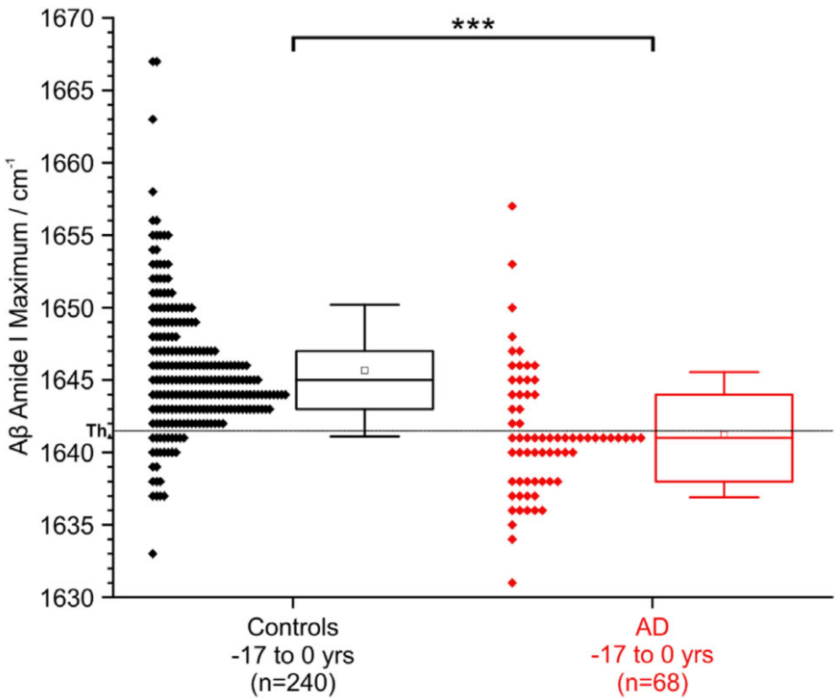
Received: 25 February 2022 | Revised: 29 May 2022 | Accepted: 10 June 2022
DOI: 10.1002/alz.12745

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

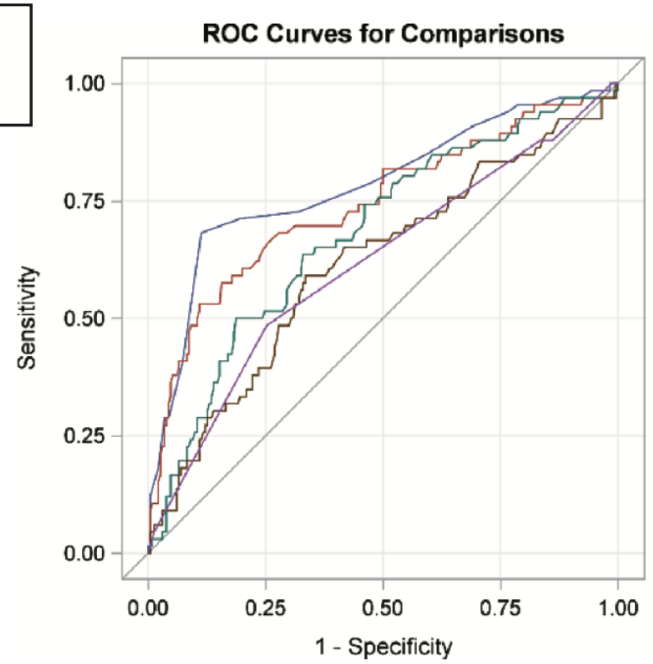
FEATURED ARTICLE

Amyloid-beta misfolding and GFAP predict risk of clinical Alzheimer's disease diagnosis within 17 years

Léon Beyer[1,2] | Hannah Stocker[3,4] | Dan Rujescu[5] | Bernd Holleczek[6] | Julia Stockmann[1,2] | Andreas Nabers[1,2] | Hermann Brenner[3,4] | Klaus Gerwert[1,2]

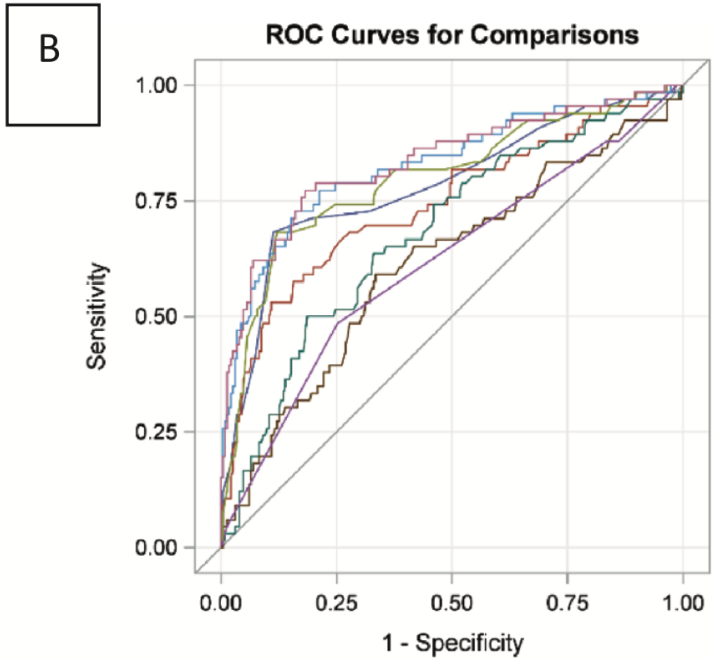


A



Predictor	AUC (95% CI)
Aβ misfolding	0.784 (0.713-0.854)
GFAP	0.741 (0.666-0.816)
NfL	0.680 (0.606-0.755)
P-tau181	0.615 (0.534-0.696)
APOE	0.615 (0.541-0.690)

B

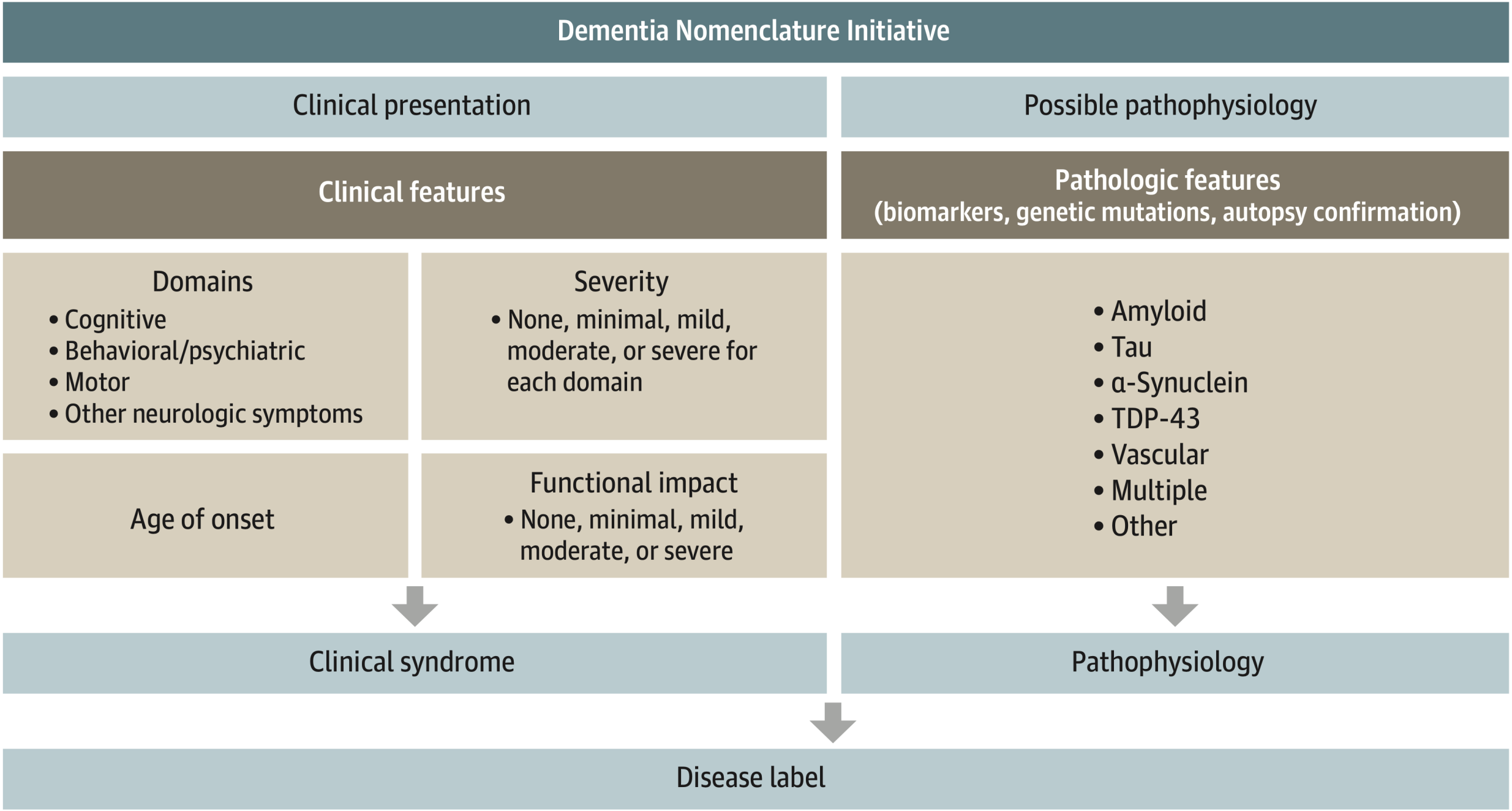


Predictor	AUC (95% CI)
Aβ misfolding	0.784 (0.713-0.854)
GFAP	0.741 (0.666-0.816)
NfL	0.680 (0.606-0.755)
P-tau181	0.615 (0.534-0.696)
APOE	0.615 (0.541-0.690)
Aβ misfolding + *APOE*	0.798 (0.730-0.865)
Aβ misfolding + GFAP	0.828 (0.764-0.891)
Aβ misfolding + GFAP + *APOE*	0.835 (0.772-0.897)

JAMA Neurology | Special Communication

A New Framework for Dementia Nomenclature

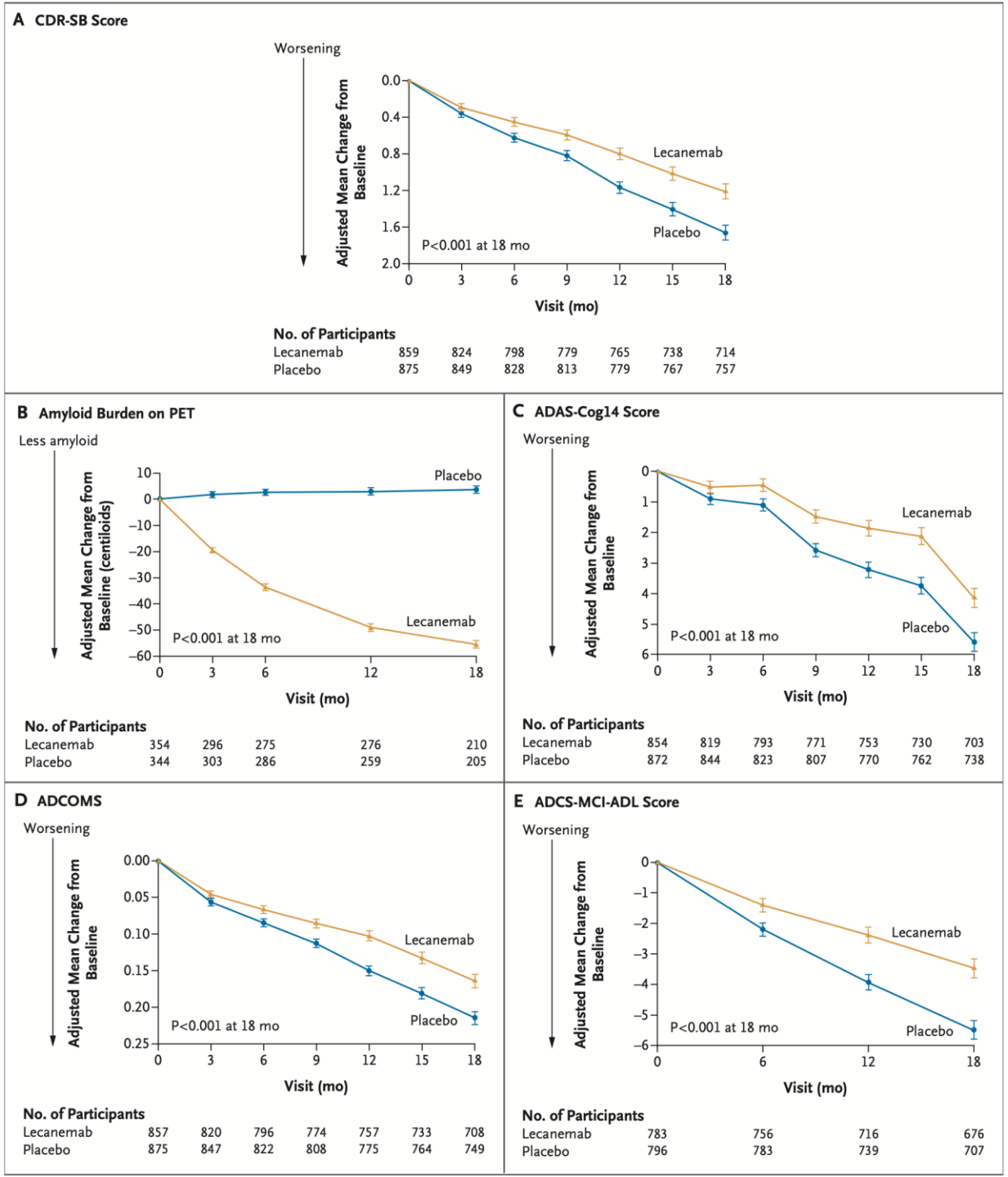
Ronald C. Petersen, MD, PhD; Sandra Weintraub, PhD; Marwan Sabbagh, MD; Jason Karlawish, MD; Charles H. Adler, MD, PhD; Peggye Dilworth-Anderson, PhD; Lori Frank, PhD; Cynthia Huling Hummel, DMin; Angela Taylor, BMus; for the Dementia Nomenclature Initiative



Petersen, R. C., et al. (2023). "A New Framework for Dementia Nomenclature." JAMA Neurol **80**(12): 1364-1370.

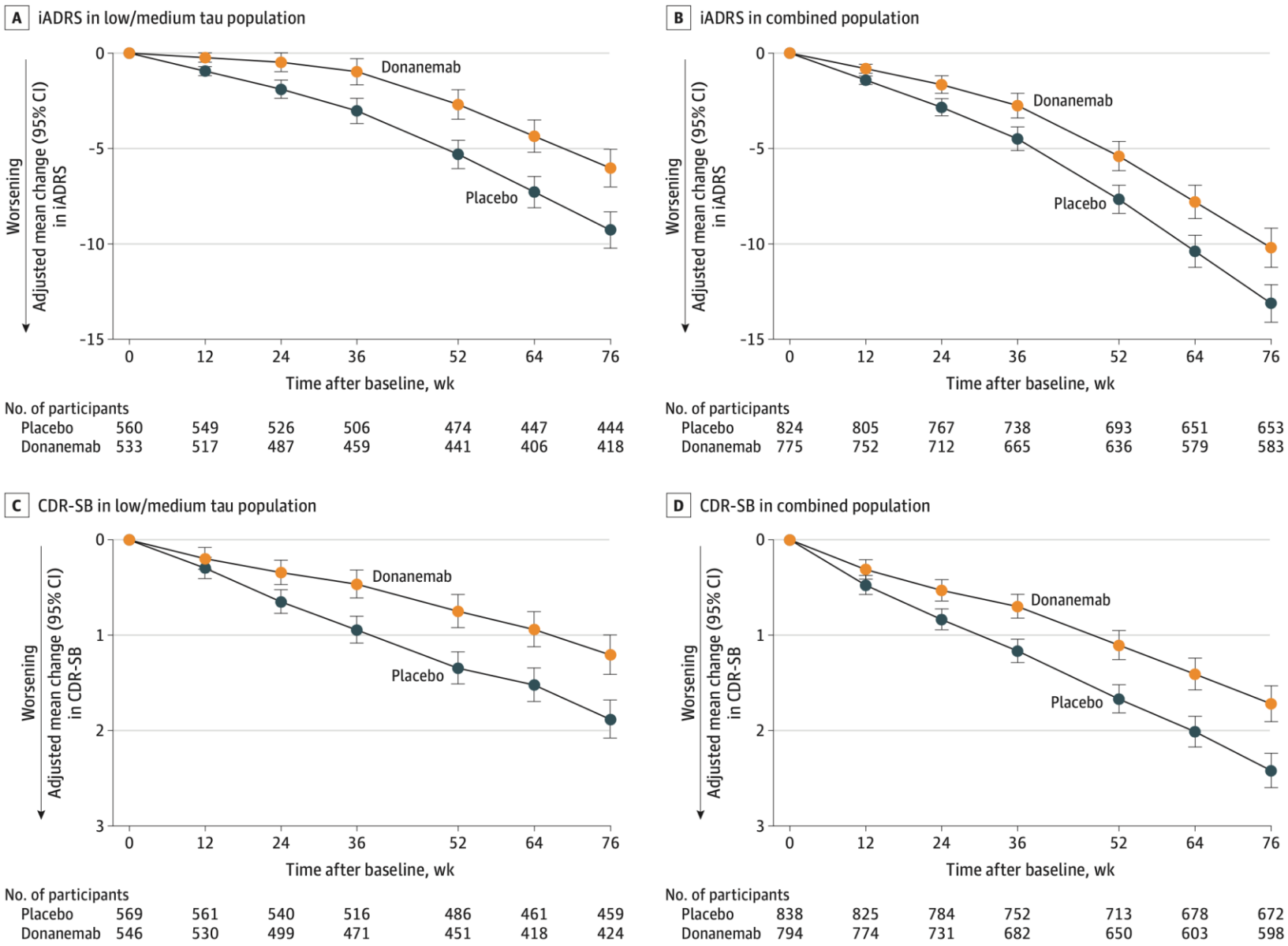
Tratamiento

- Tratamiento farmacológico
  - Sintomático
    - Específicos para EA
      - Inhibidores de la colinesterasa
      - Antagonista no competitivo de receptor glutamatérgico NMDA
    - Otros sin un mecanismo de acción específico para EA
      - Ansiolíticos
      - Antidepresivos
      - Antipsicóticos
      - Hipnóticos
      - Antiepilépticos
  - Tratamientos modificadores de la enfermedad
- Tratamiento no farmacológico



van Dyck, C. H., et al. (2023). N Engl J Med **388**(1): 9-21.

Figure 2. Integrated Alzheimer Disease Rating Scale (iADRS) and Sum of Boxes of the Clinical Dementia Rating Scale (CDR-SB) From Baseline to 76 Weeks



Sims, J. R., et al. (2023). Jama **330**(6): 512-527.

J Prev Alz Dis 2023;3(10):362-377
Published online March 27, 2023, http://dx.doi.org/10.14283/jpad.2023.30

Review

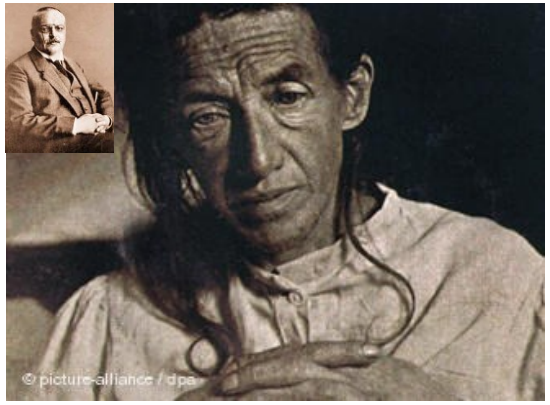
Lecanemab: Appropriate Use Recommendations

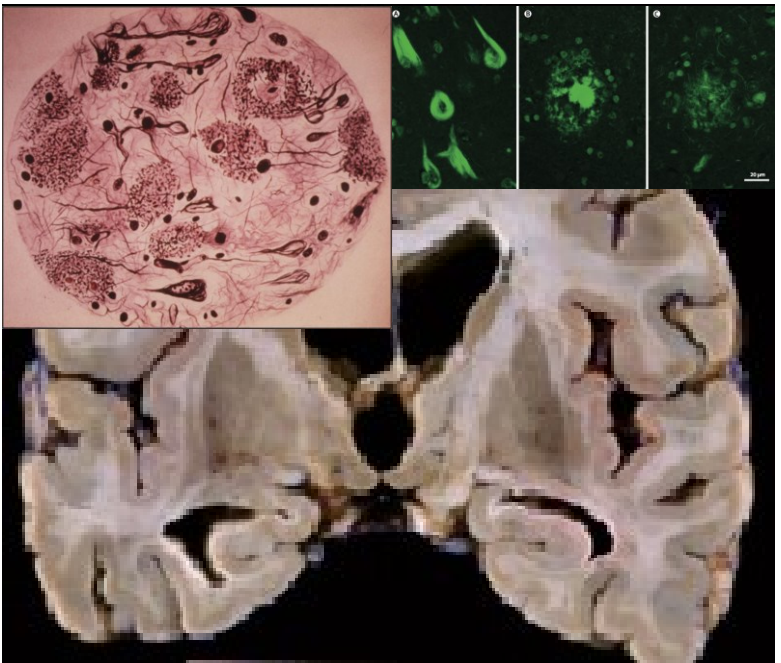
J. Cummings[1], L. Apostolova[2], G.D. Rabinovici[3], A. Atri[4], P. Aisen[5], S. Greenberg[6], S. Hendrix[7], D. Selkoe[8], M. Weiner[9], R.C. Petersen[10], S. Salloway[11], For the Alzheimer's Disease and Related Disorders Therapeutics Work Group

Cambio de concepto

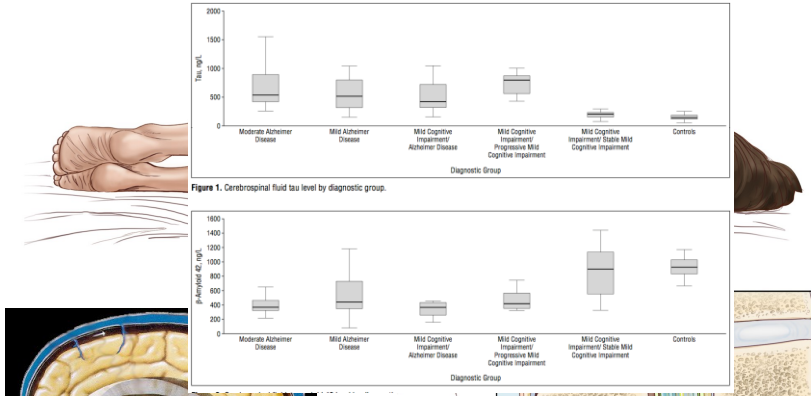
Siglo XX → Siglo XXI

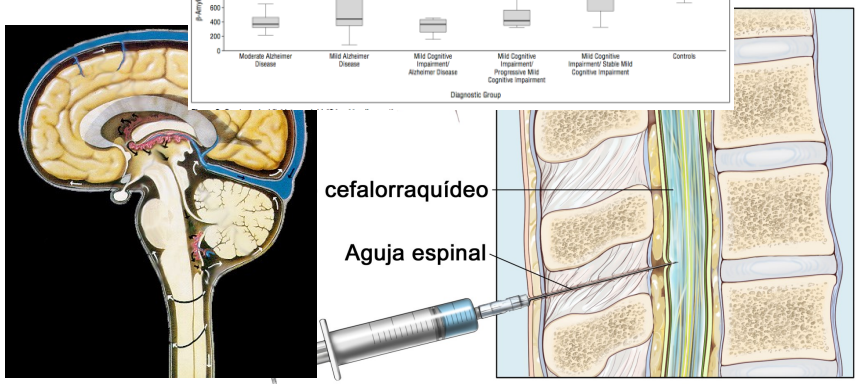
Clínico-patológico



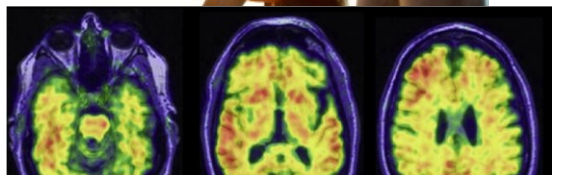


Clínico-biológico





Biológico

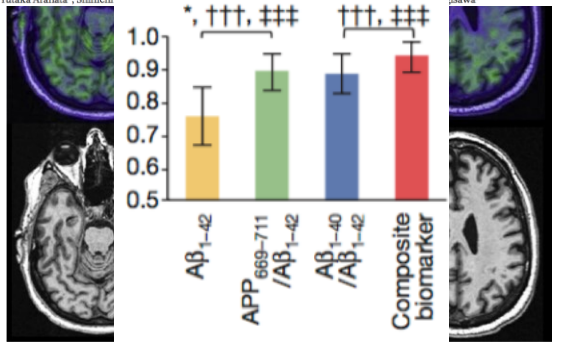


LETTER

doi:10.1038/nature25456

High performance plasma amyloid-β biomarkers for Alzheimer's disease

Akinori Nakamura[1], Naoki Kaneko[2], Victor L. Villemagne[3,4], Takashi Kato[1,5], James Doecke[6], Vincent Doré[3,6], Chris Fowler[4], Qiao-Xin Li[4], Ralph Martins[7], Christopher Rowe[3,4], Taisuke Tomita[8], Katsumi Matsuzaki[9], Kenji Ishii[10], Kazunari Ishii[11], Yutaka Arahata[5], Shinichi [illegible]sawa[1]



Cambio de tratamiento

Siglo XX

Siglo XXI

Enfermedad crónica/Dx tardío

Diagnóstico temprano

Terminal

Socio-sanitario/Tx Sintomático

Reducción de riesgo

Tx modificador