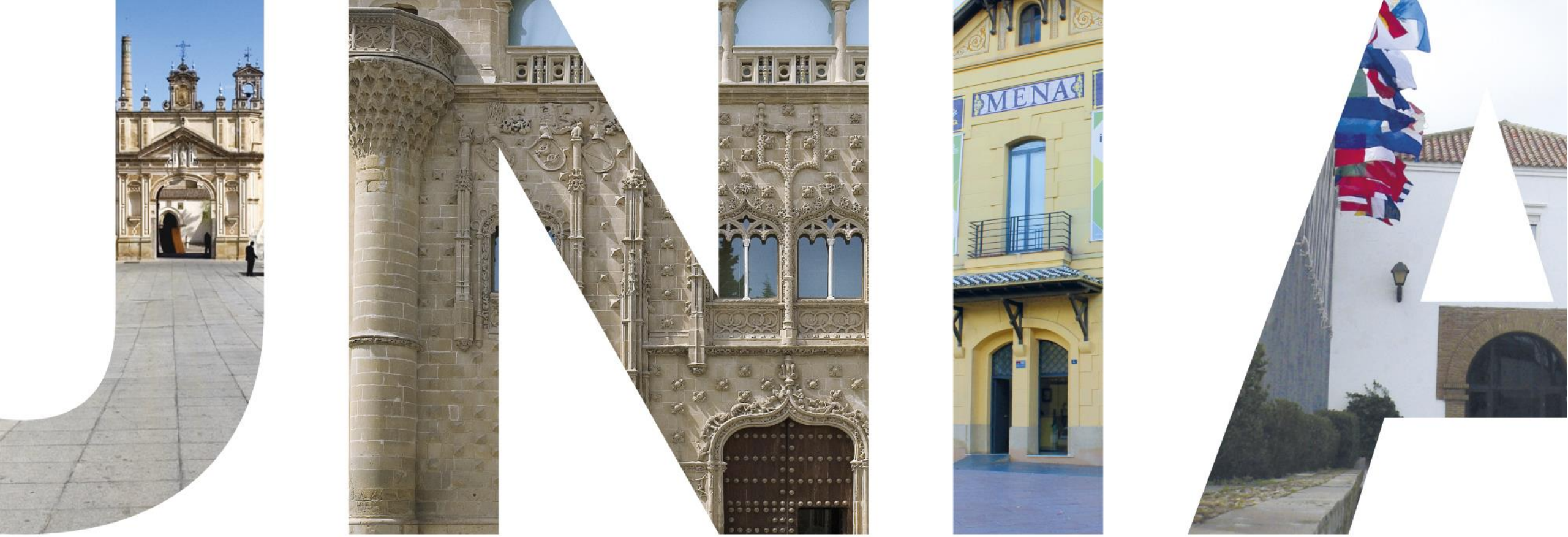

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El futuro de la investigación en la enfermedad de Alzheimer: el papel de los bancos de tejidos neurológicos.

Alberto Rábano
Banco de Tejidos de la Fundación CIEN
Instituto de Salud Carlos III

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“¿Qué puedo saber?”
La enfermedad de Alzheimer desde el punto de vista de la neuropatología.

“¿Qué debo hacer?”
El papel de los bancos de tejidos neurológicos en la investigación de la enfermedad de Alzheimer.

“¿Qué puedo esperar?”
Contribución de los estudios clínico-patológicos al conocimiento y al tratamiento de la enfermedad.

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“¿Qué puedo saber?”

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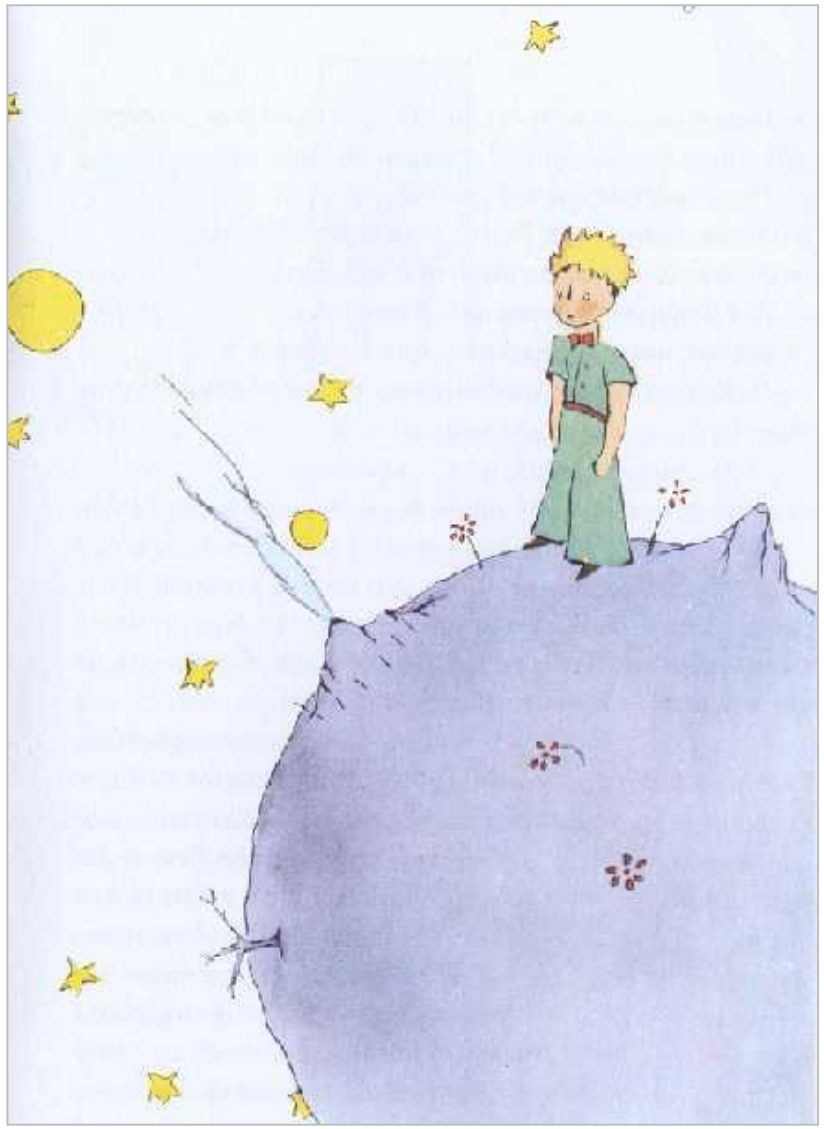

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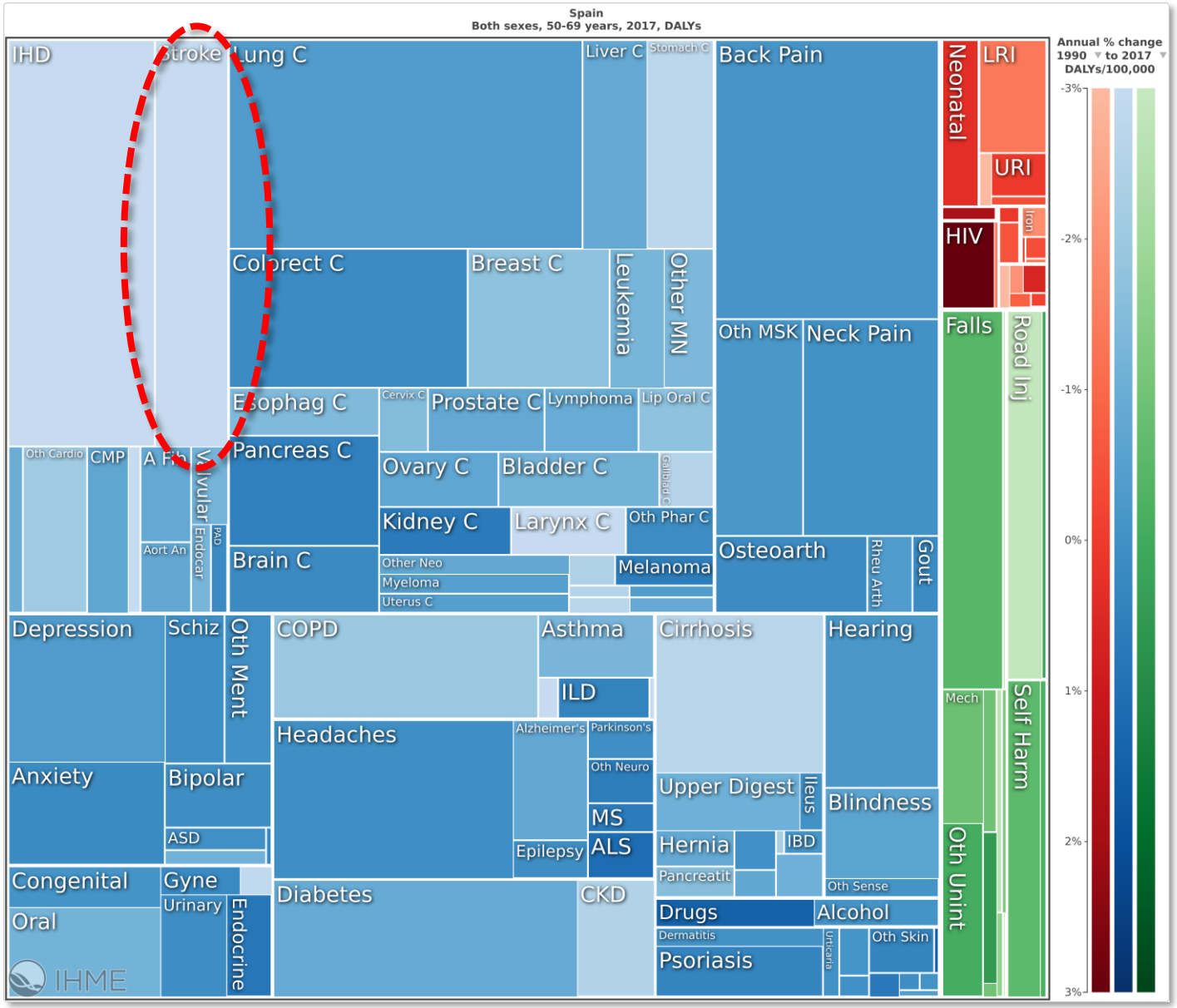
Causas de morbilidad en España, ambos sexos, 50-69 años



https://www.thelancet.com/lancet/visualisations/gbd-compare

Causas de morbilidad en España, ambos sexos, 70+ años

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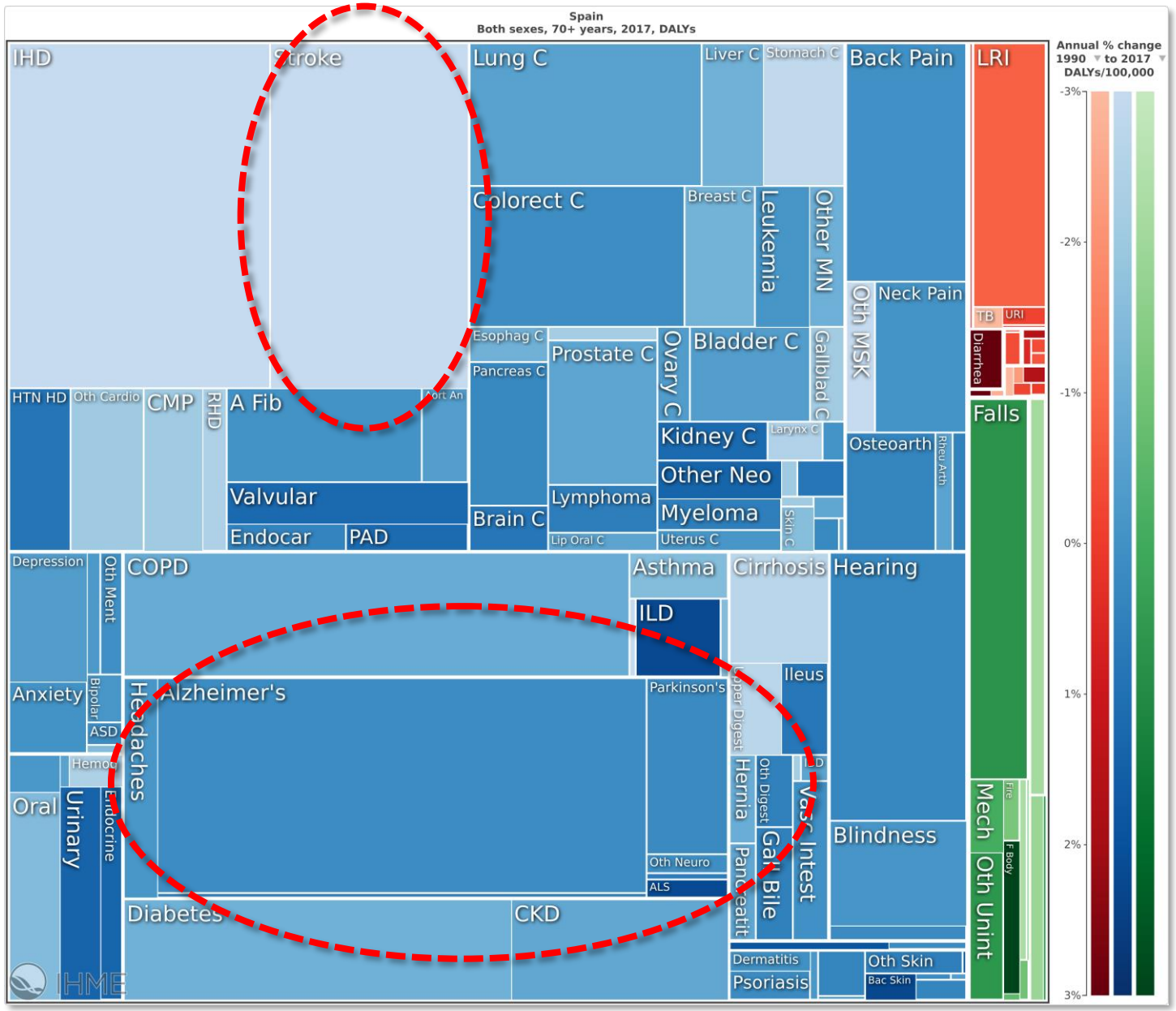

https://www.thelancet.com/lancet/visualisations/gbd-compare

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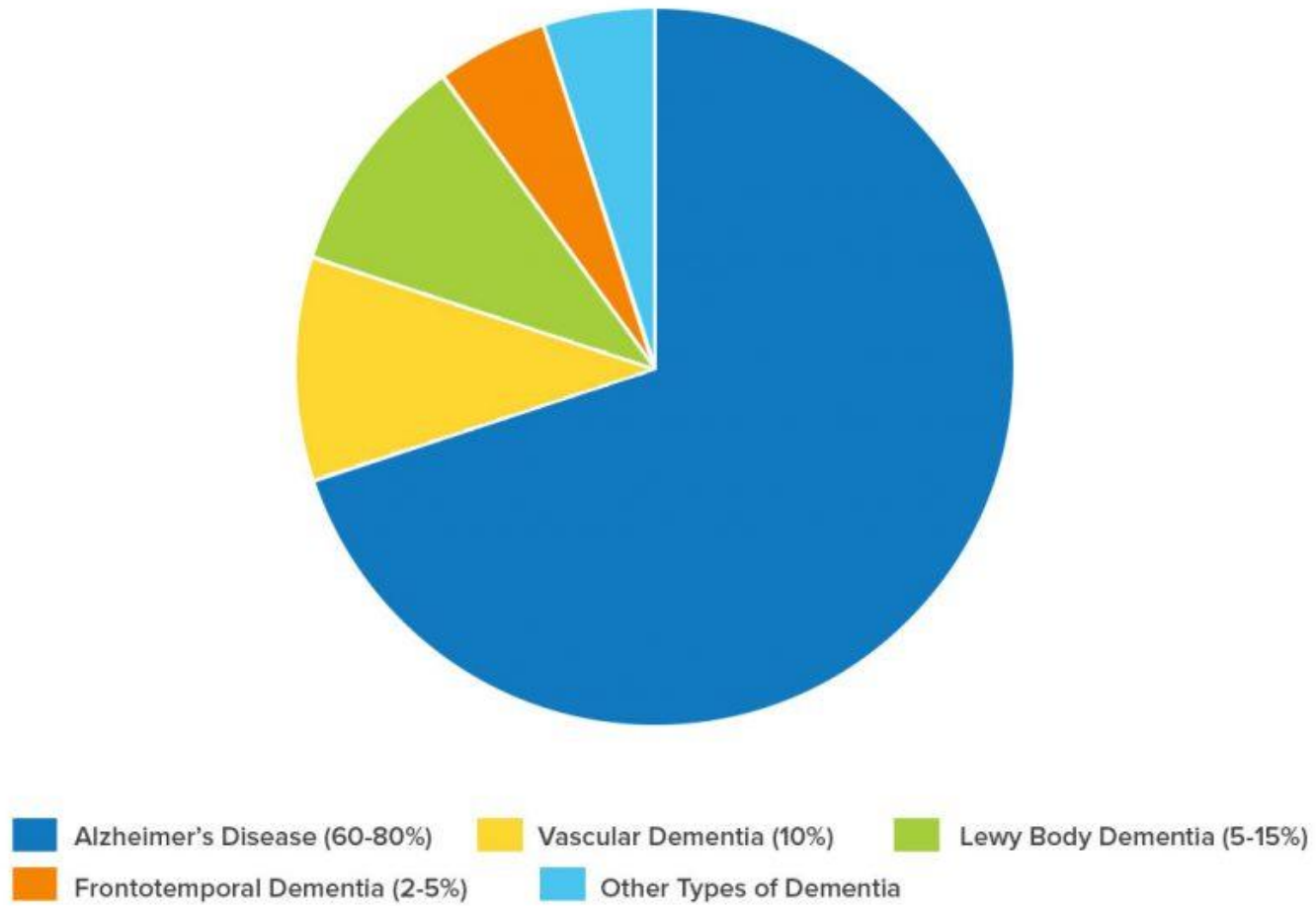
Different Types of Dementia (by %)



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100 años de investigación en la enfermedad de Alzheimer

1906

2006

J Hardy, 2006

Table 1. A Summary of the History of Research into Alzheimer's Disease and Related Disorders

Year	Related Developments	Alzheimer's Disease
1902	Improved silver stains	
1906		Alzheimer's case history of Auguste D.
1910		Alzheimer's Disease named
1922	Lewy body described	
1932		First hereditary case described
1962	L-dopa therapy in Parkinson's	
1963/4		Ultrastructure of plaque and tangle by electron microscopy
1968		Recognition of prevalence of disease in the elderly
1976		Cholinergic deficit described
1983	Huntington's genetic linkage	Sequence of Aβ from Alzheimer's amyloid angiopathy
1984		Sequence of Aβ from Down's syndrome from amyloid angiopathy
1985	Cloning of the prion gene	Sequence of Aβ from plaques
1986		Tau as major component of tangles
1987		Cloning of APP and localization to chromosome 21
1989	Mutations in prion gene in CJD/GSS	
1990	Mutations in APP cause HCHWA-D; prion mutations cause neurodegeneration in mice	Alzheimer's disease genetically heterogeneous
1991		APP mutations in Alzheimer's; a descriptive system of cataloguing the neuropathology determined
1993		ApoE4 associated with Alzheimer's; cholinergic therapy approved for AD
1994		APP mutations increase Aβ42
1995		APP transgenic mice made with plaque pathology; presenilins cloned as loci for early onset Alzheimer's
1996		Presenilin mutations shown to alter APP processing
1997	Synuclein mutations identified in PD; Synuclein identified as major component of Lewy bodies	
1998	Tau mutations identified in FTDP-17	Presenilins identified as γ-secretase
1999		BACE cloned; Aβ immunization in mice reduces amyloid pathology
2000	Mice with tangles made using FTDP-17 mutations	
2001		Mice with plaques and tangles made
2003		Aβ vaccine trials halted because of side effects

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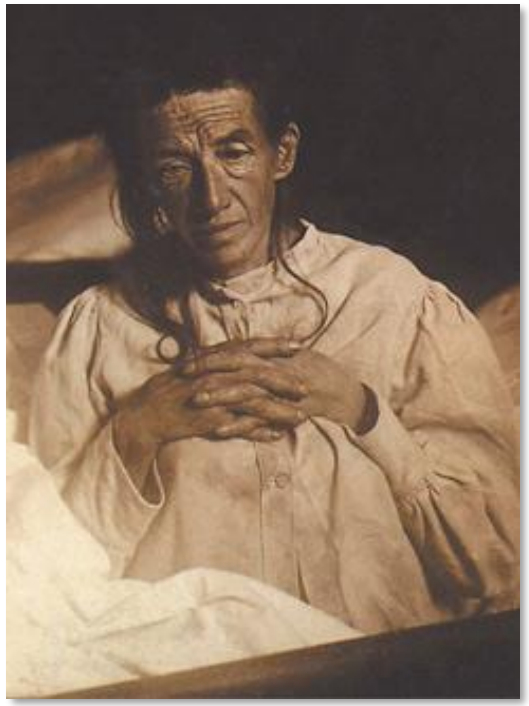
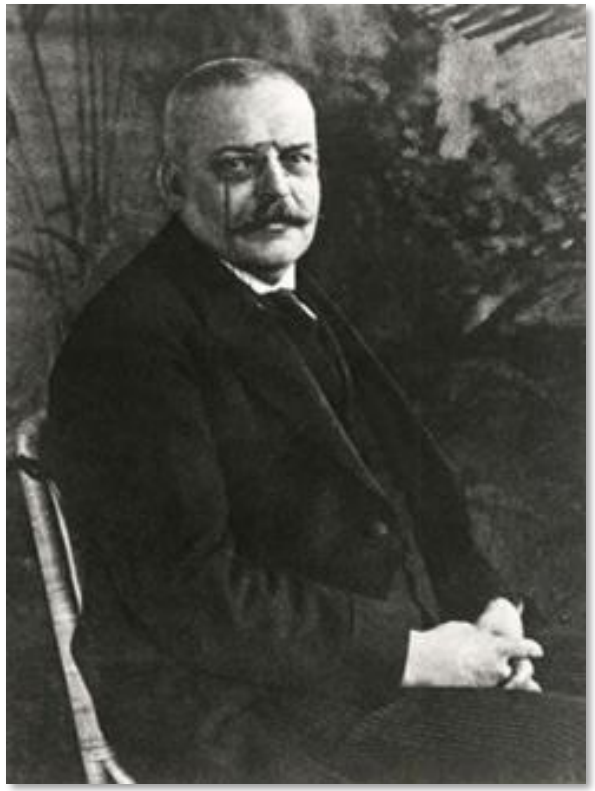
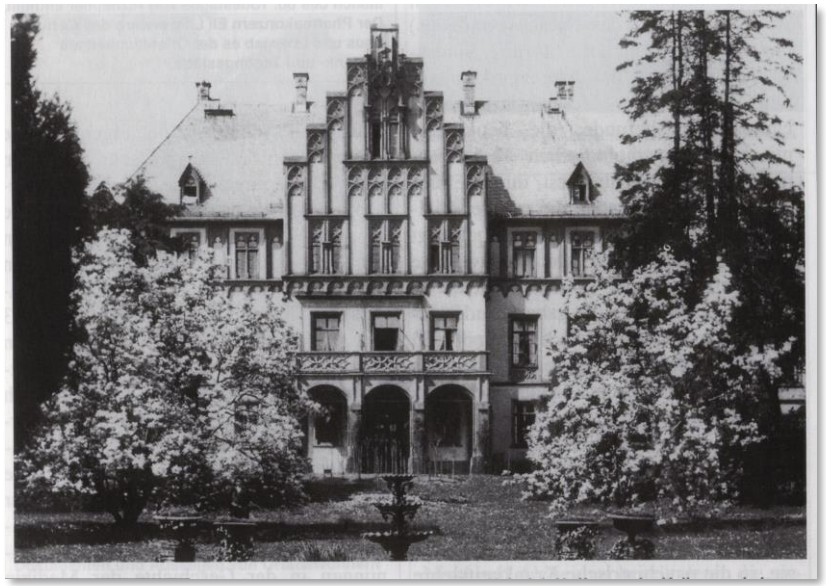


Auguste D.
1906



A. Alzheimer
1864 - 1915



Hospital
Frankfurt

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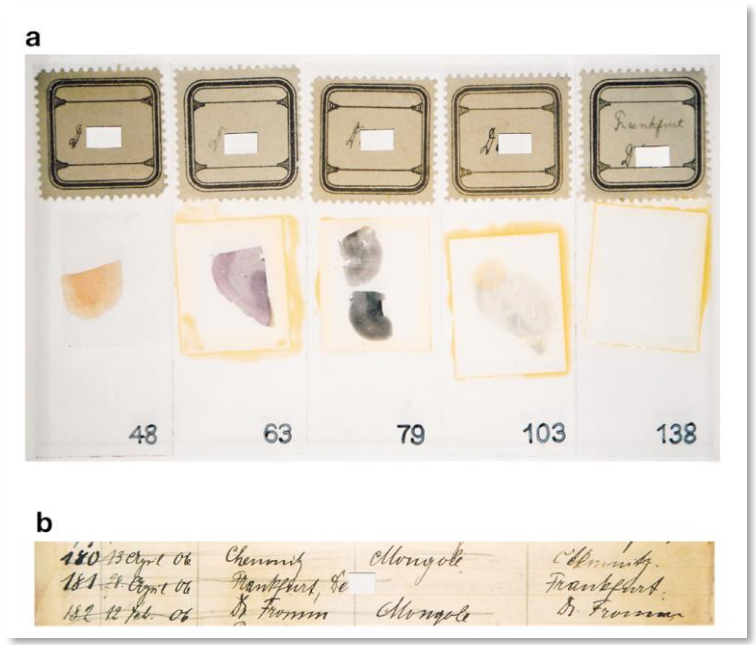

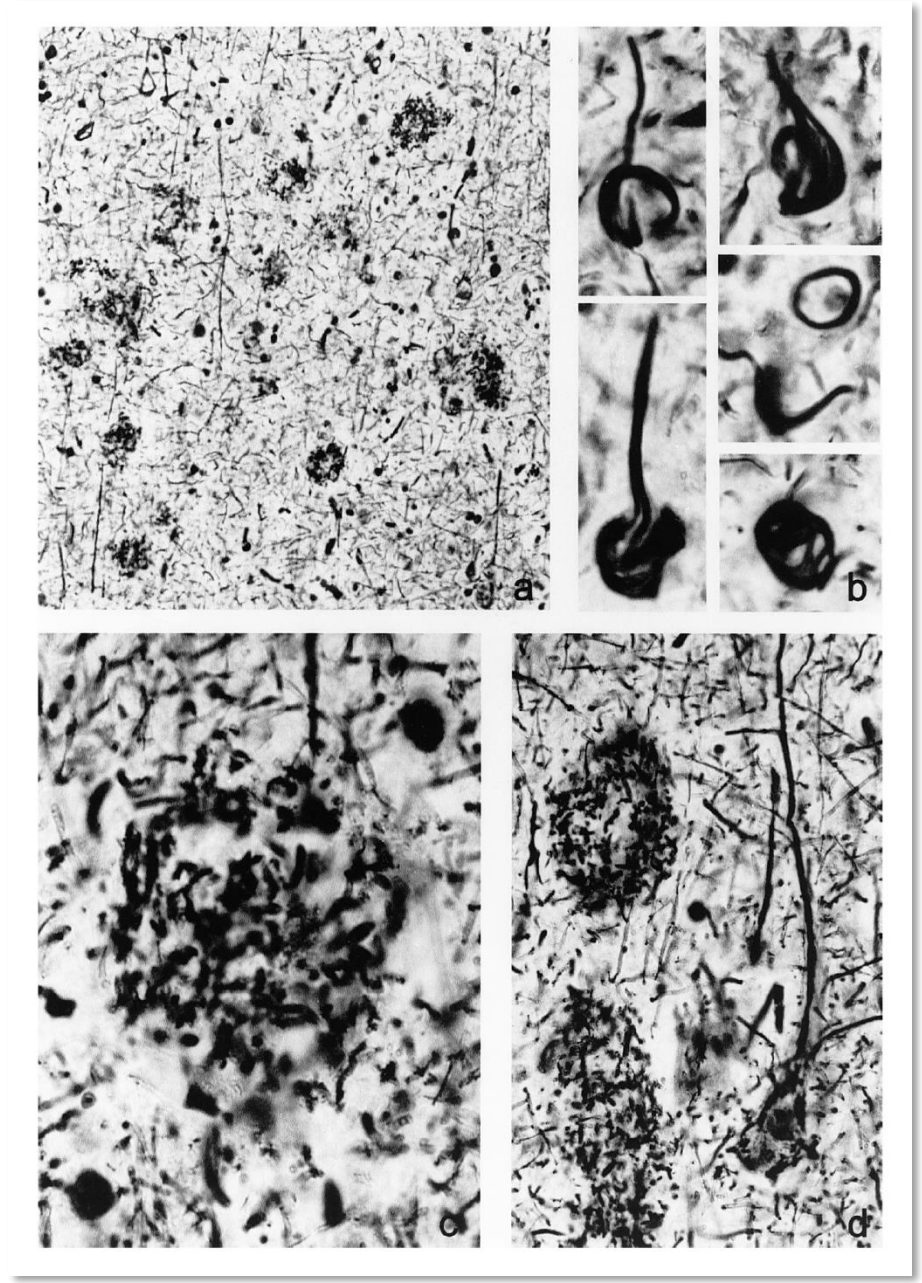

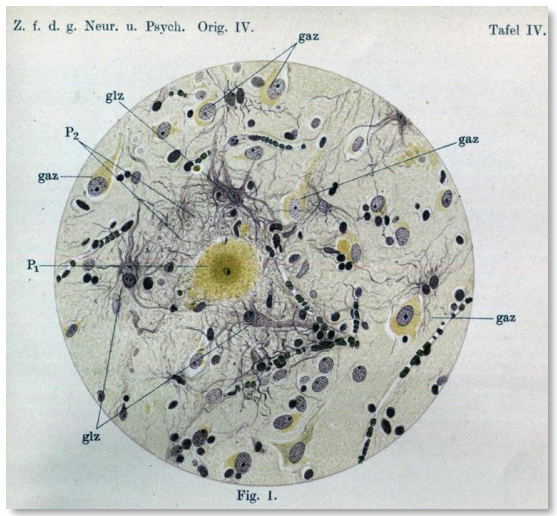

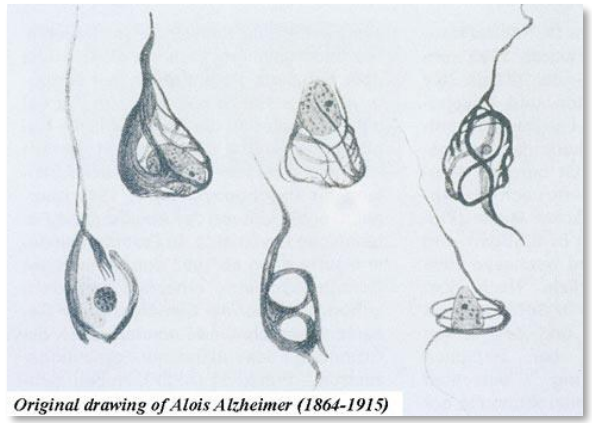
Original drawing of Alois Alzheimer (1864-1915)

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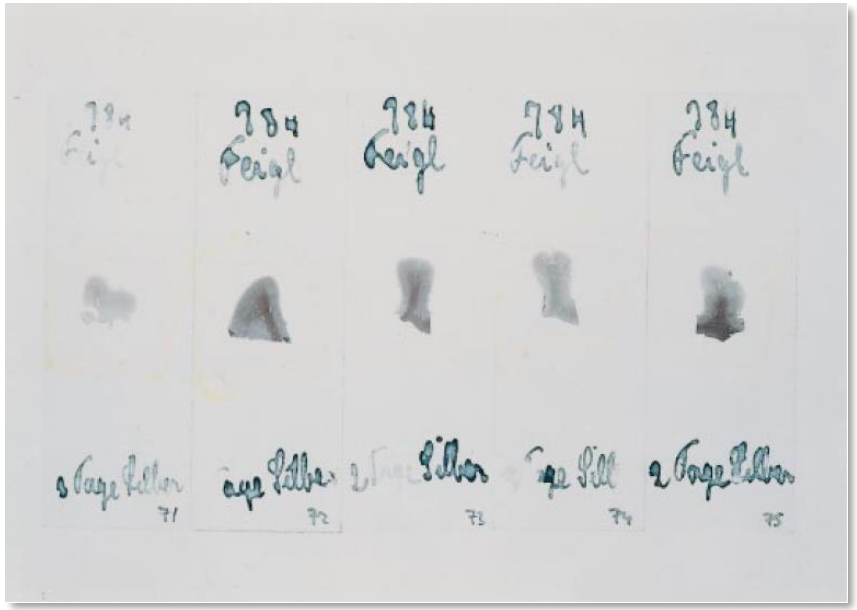
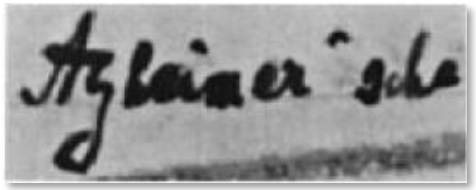
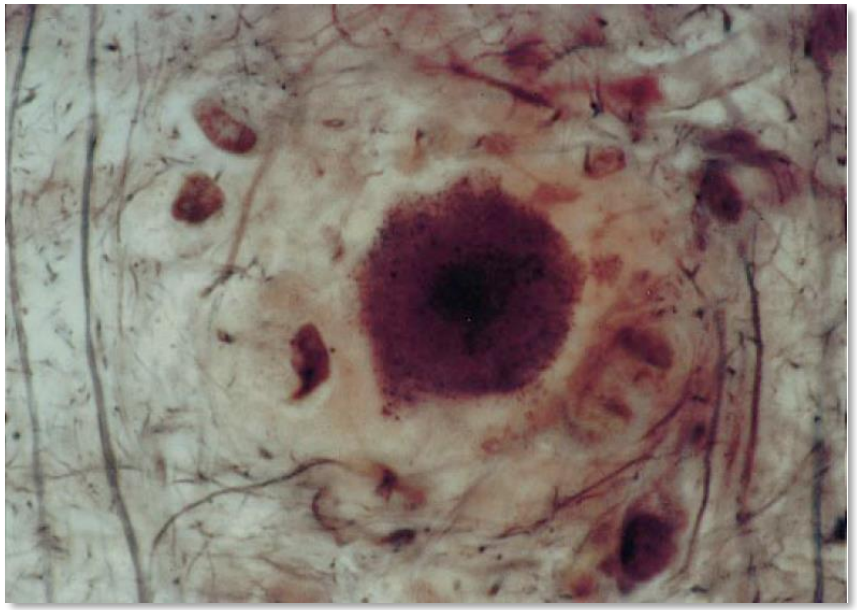
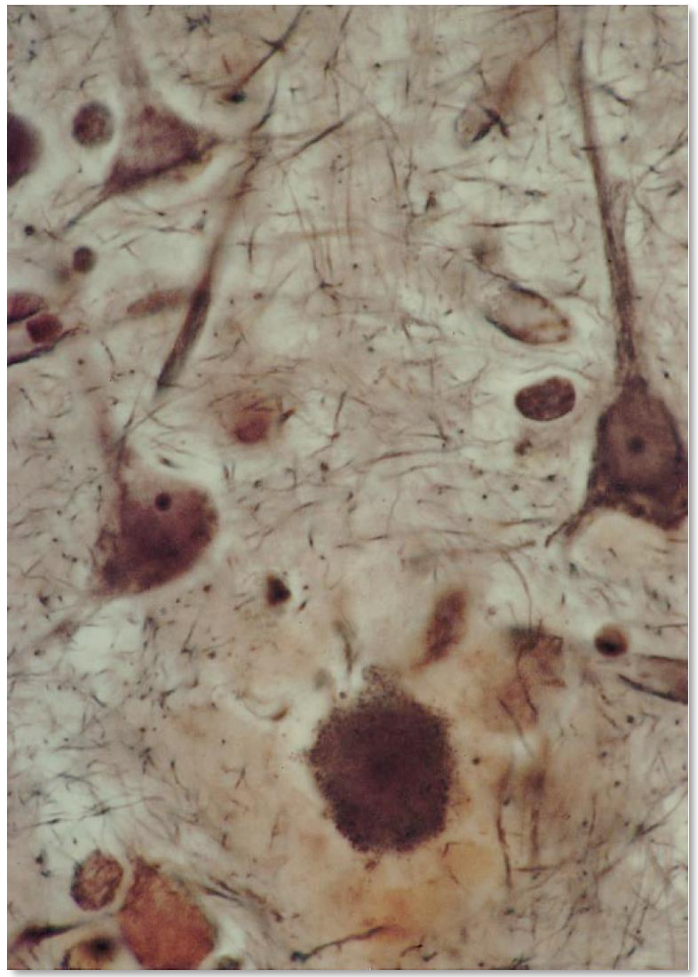
Johann Feigl, 1910









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Santiago Ramón y Cajal

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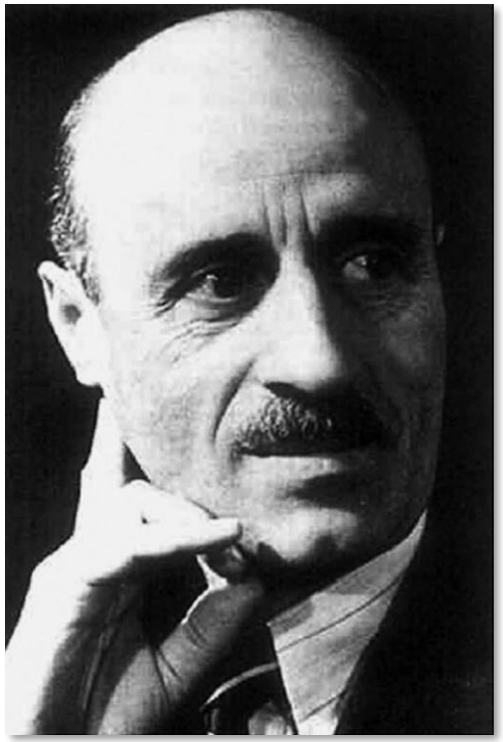
Gonzalo R. Lafora, 1914



Washington

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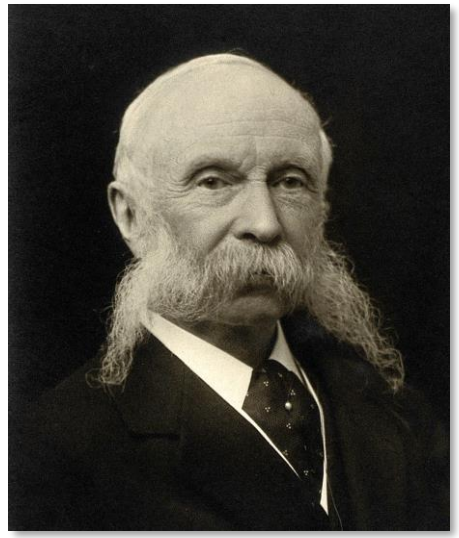
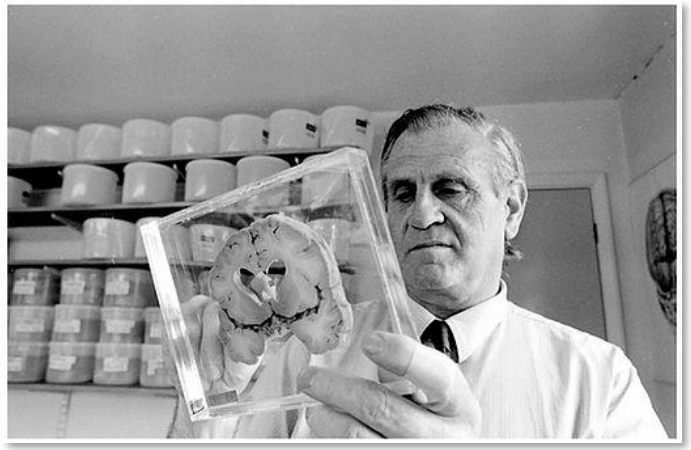
West Riding Lunatic Asylum, Wakefield, Yorkshire



James Crichton-Browne (1840 – 1938)

Runwell Mental Hospital, Essex



John Arthur Nicholas Corsellis (1915 – 1994).

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1968	Recognition of prevalence of disease in the elderly
1976	Cholinergic deficit described

Blessed G, **Tomlinson** BE, **Roth** M.

The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects.

Br J Psychiatry. **1968** Jul;114(512):797-811.

Sir Martin Roth

Sir Bernard Tomlinson

La enfermedad de Alzheimer como demencia más prevalente, diagnóstico y tratamiento.

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Finally, schizophrenic symptoms may make their appearance for the first time late in life in subjects where genetic factors had influenced personality development towards eccentricity and a poor capacity for intimate relationships. Again, and in addition to increasing social isolation, subtle brain changes associated with ageing or with relatively mild degrees of senile or arteriosclerotic dementia may be the final precipitating factors.

Professor M Roth, Dr B E Tomlinson and Dr G Blessed
(*MRC Research Group on the Relation between Functional and Organic Psychiatric Illness, Newcastle upon Tyne*)[1]

The Relationship between Quantitative Measures of Dementia and of Degenerative Changes in the Cerebral Grey Matter of Elde

The
rela

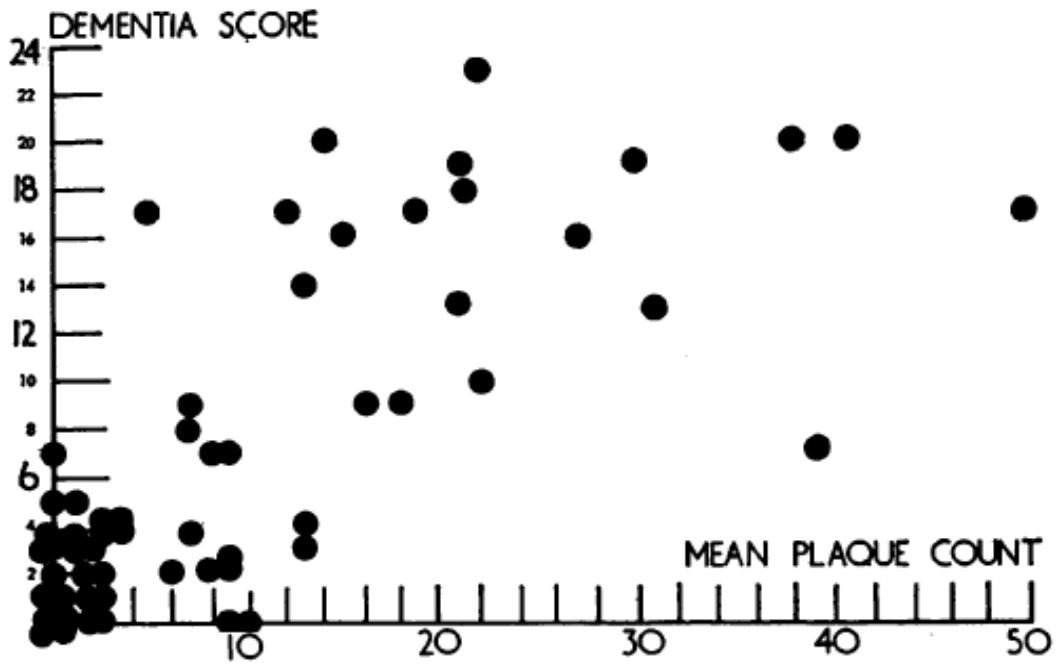

Fig 1 *Relationship of dementia score to mean plaque count in 60 aged subjects*

The recent studies of Corsellis (1962) have shown that neuropathological findings agreed reasonably well with clinical groupings of old age mental disorder first shown to be relatively distinct from one another ten to fifteen years ago (Roth & Morrissey 1952, Norris & Post 1955, Roth 1955, Kay 1959). For example, among the 300 patients who had come to post-mortem in a mental hospital only 25% of those with functional disorders, but 75% of those regarded as suffering from organic psychoses, showed degenerative changes of moderate or severe degree. The overlap was probably due in part to a development of organic changes at an advanced age in some subjects with an initial 'functional' disorder.

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Ludo van Bogaert
1897 - 1988

Mschr Psychiat Neurol 1939;102:275–301

Sur les formes familiales précoces de la maladie d 'Alzheimer, pp. 275–301

van Bogaert L. · Maere M. · de Smedt E.

Département de Neurologie et Pathologie de l'Institut Bunge (Berchem- Anvers)

Nat Genet. 1992 Dec;2(4):335-9.

Mapping of a gene predisposing to early-onset Alzheimer's disease to chromosome 14q24.3.

Van Broeckhoven C, Backhovens H, Cruts M, De Winter G, Bruyland M, Cras P, Martin JJ.

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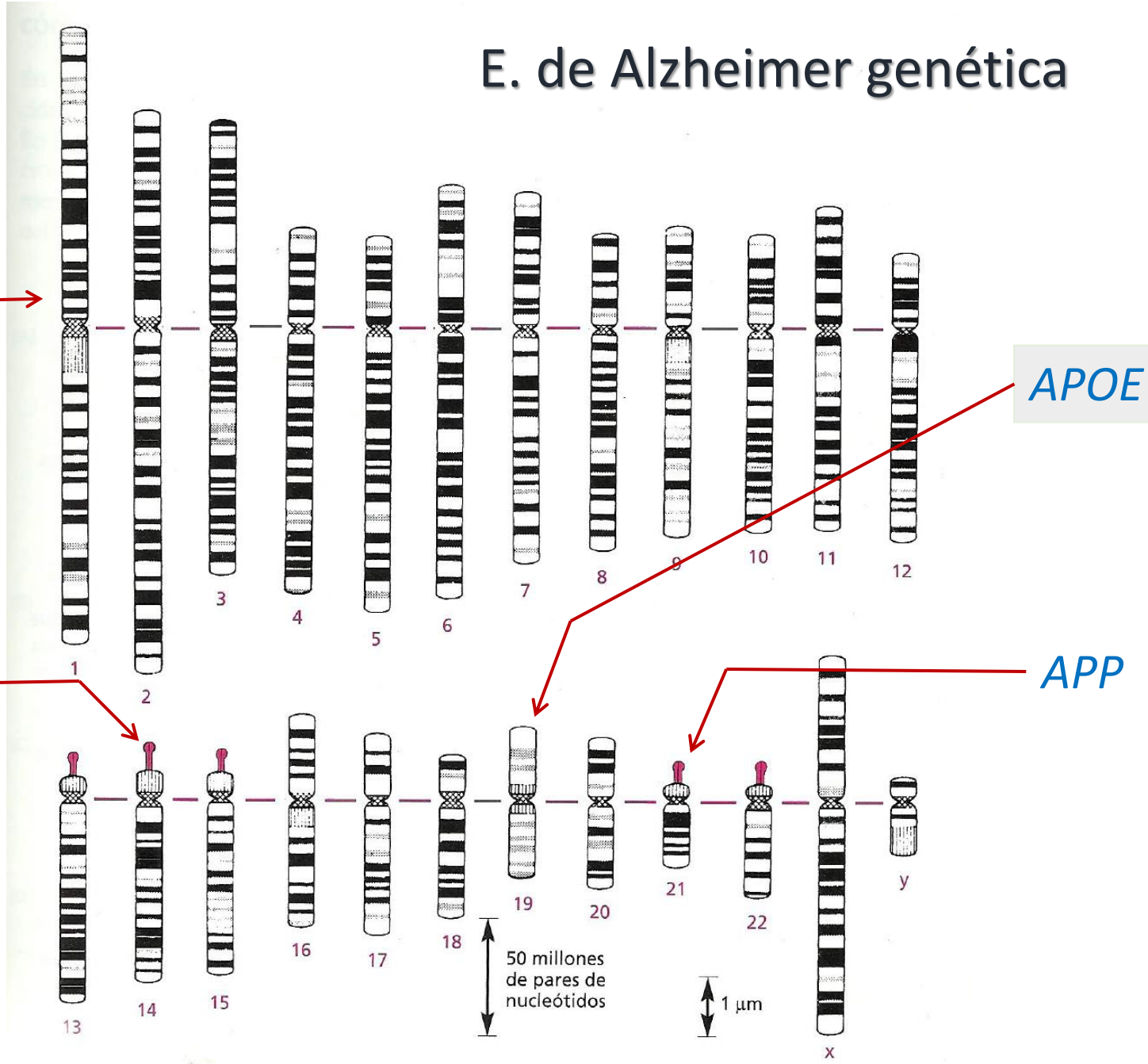
E. de Alzheimer genética



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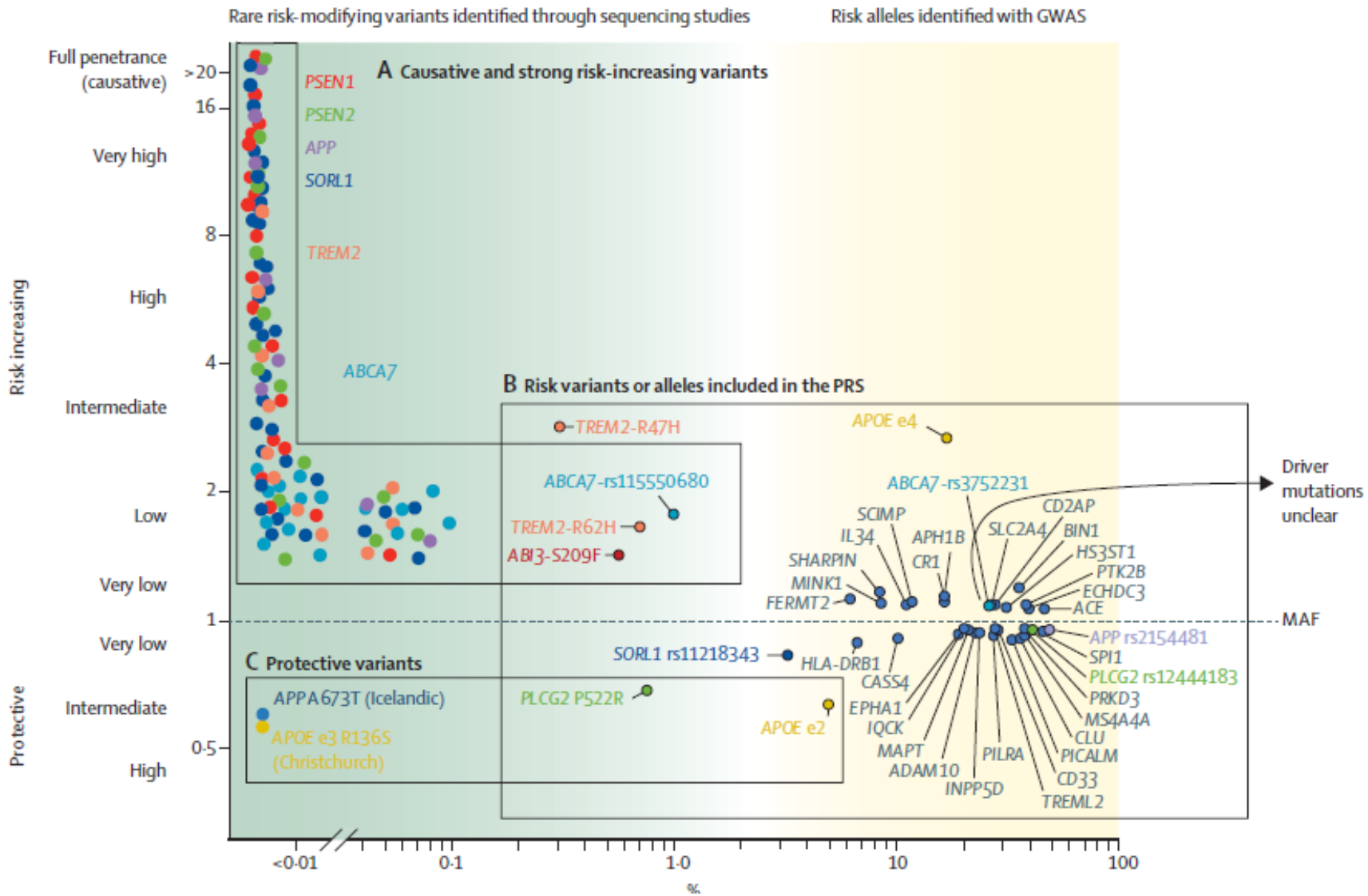

Scheltens *et al.*, 2021

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Enfermedad de Alzheimer de inicio temprano (EOAD)

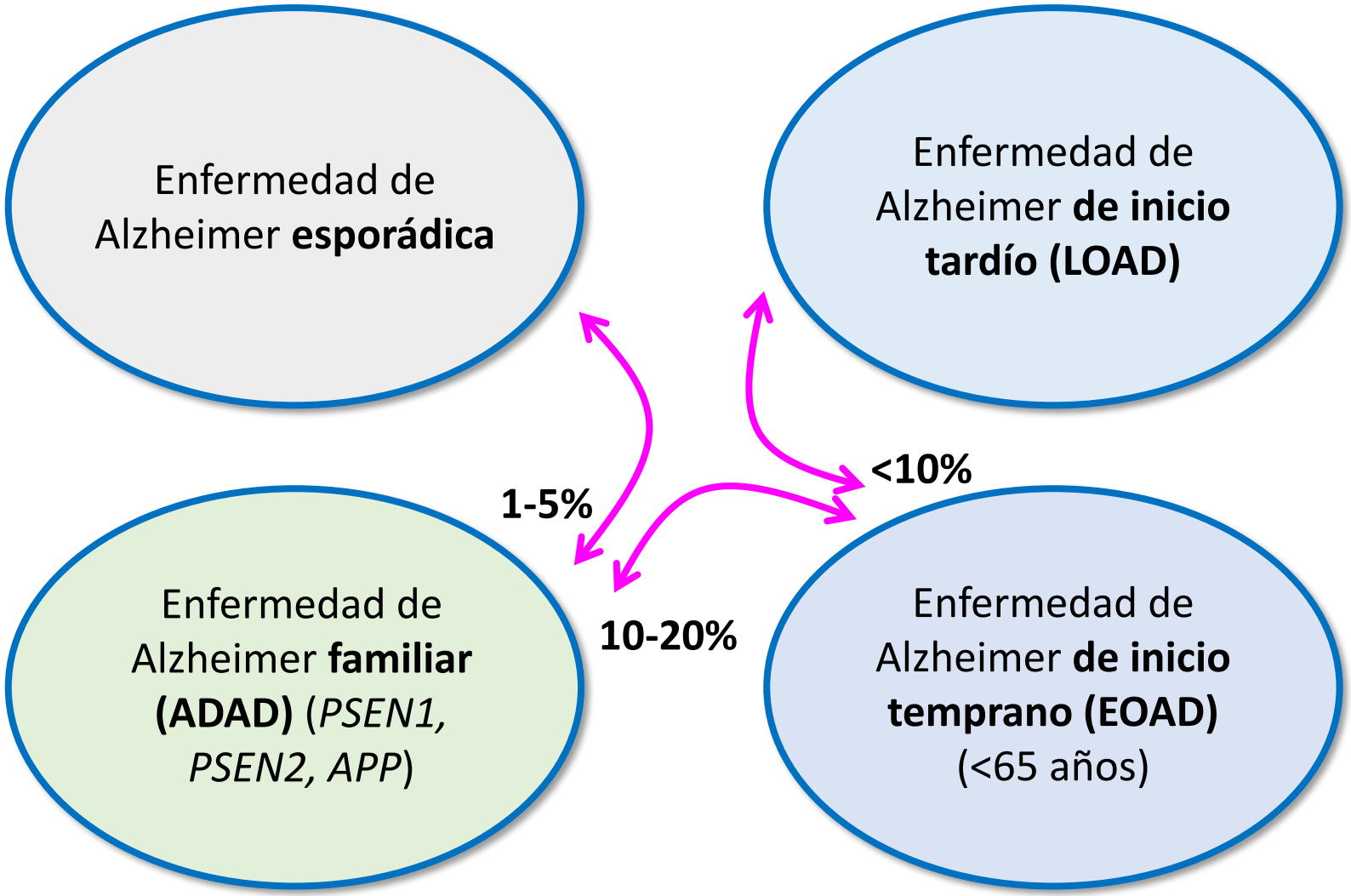

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Table 3
Formal and informal health care costs in community-dwelling patients

	Cognitive impairment[1]				
	Total sample $n=262$ mean (SD)	No indication of $n=45$ mean (SD)	Mild $n=138$ mean (SD)	Moderate $n=74$ mean (SD)	Severe $n=5$ mean (SD)
Formal Care	1,646 € (3,847)	1,100 € (2,730)	1,314 € (3,531)	2,606 € (4,845)	1,464 € (2,032)
Nursing Home Care	510 € (1,959)	394 € (1,658)	273 € (1,417)	1,055 € (2,803)	19 € (42)
Professional Home Care	1,136 € (2,917)	706 € (2,094)	1,042 € (3,025)	1,552 € (3,173)	1,446 € (2,002)
Informal care	16,473 € (17,036)	11,188 € (15,007)	16,735 € (15,693)	18,788 € (19,909)	22,551 € (18,146)
ADL	5,107 € (8,475)	3,909 € (6,149)	4,632 € (7,915)	6,469 € (10,447)	9,109 € (8,034)
IADL	11,386 € (11,324)	7,278 € (10,031)	12,102 € (11,318)	12,406 € (11,598)	13,442 € (13,673)
Productivity losses	1,258 € (5,715)	1,006 € (5,277)	1,397 € (5,953)	1,234 € (5,769)	No Obs.

[1] According to MMSE ADL, activities of daily living; IADL, instrumental activities of daily living; SD, standard deviation; Obs, observations; MMSE, Mini-Mental State Examination.

Michalowsky B *et al.*, 2016

Estimación para 2010, coste de la demencia en España:
> 16.000 millones de euros (15% del gasto sanitario total)

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Factores de riesgo

Edad+

- Sexo
- Nivel educativo (años de educación)
- Factores cardiovasculares (diabetes, hipertensión)
- Actividad mental
- Actividad física
- Consumo de alcohol
- Factores dietéticos
- Depresión
- Actividad social
- Traumatismo craneal

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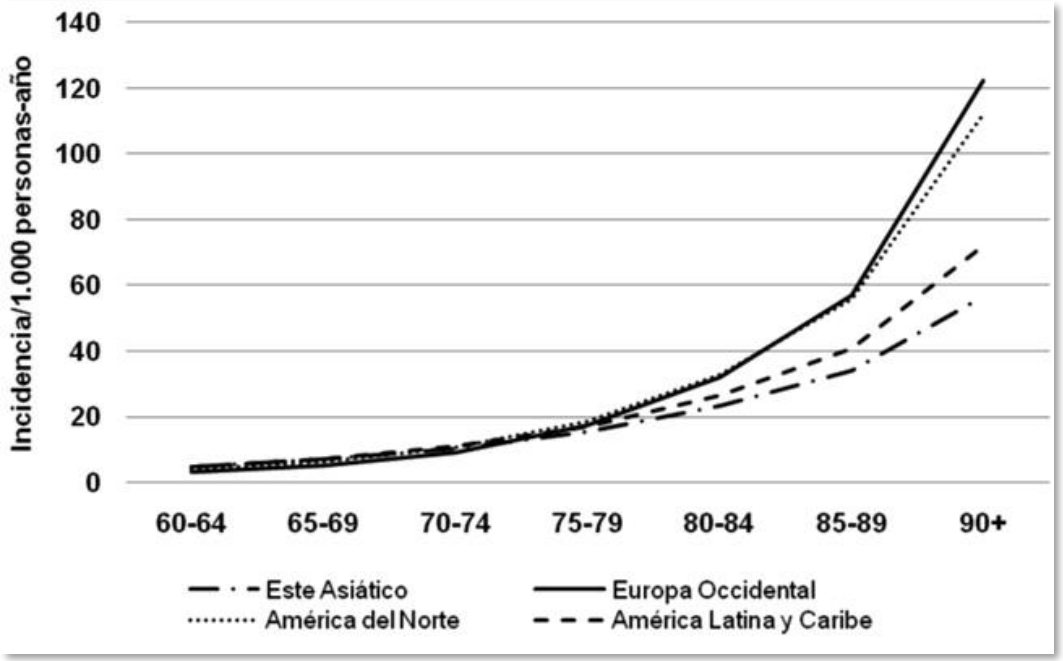

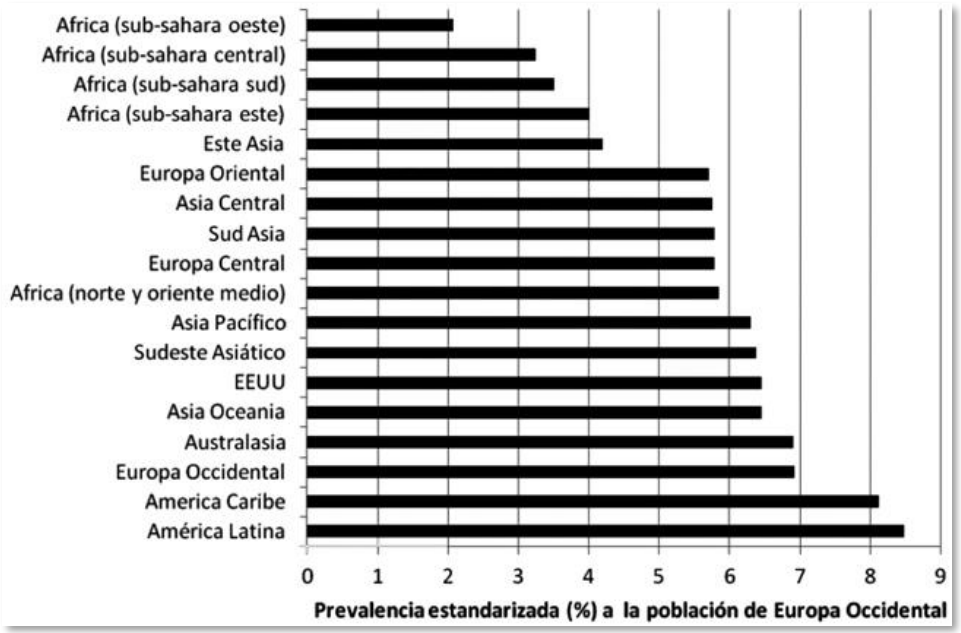

Garre-Olmo J, 2018

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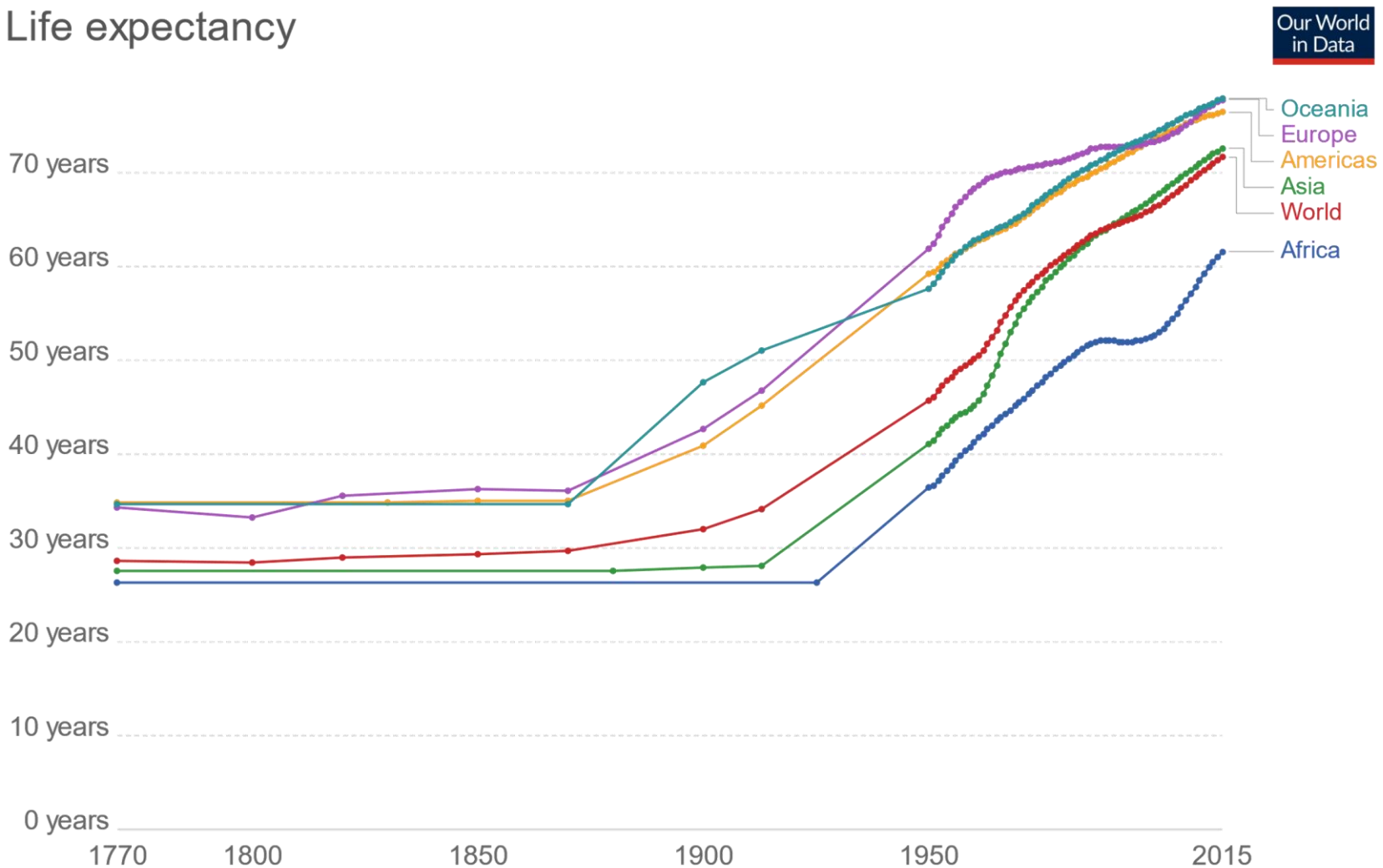
Life expectancy



Source: Riley (2005), Clio Infra (2015), and UN Population Division (2019) OurWorldInData.org/life-expectancy • CC BY
Note: Shown is period life expectancy at birth, the average number of years a newborn would live if the pattern of mortality in the given year were to stay the same throughout its life.

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Tabla 1 Incidencia de demencia en diferentes estudios epidemiológicos, incluyendo los principales realizados en España

	Ámbito de estudio	Incidencia (por 1.000 hab/año)	Incidencia por etiologías (por 1.000 hab/año)
López-Pousa et al.[5]	Población rural ≥ 75 años en Gerona	23,2	10,8 EA 9,5 DV
Bermejo-Pareja et al.[6]	Población ≥ 65 años en 3 regiones centrales de España	10,6	7,4 EA 1,4 DV 0,9 DemEP
Lobo et al.[7]	Población urbana ≥ 55 años en Zaragoza	8,6	5,4 EA
Estudio de Rotterdam[8]	Población ≥ 55 años en Rotterdam	9,8	7,2 EA 1,5 DV
Matsui et al.[9]	Población ≥ 65 años en Japón	32,3	14,6 EA 9,5 DV 1,4 DC Lewy 3,8 mixta 3,1 otras

DC Lewy: demencia por cuerpos de Lewy; DemEP: demencia en la enfermedad de Parkinson; DV: demencia vascular; EA: enfermedad de Alzheimer.

Villarejo A et al., 2017

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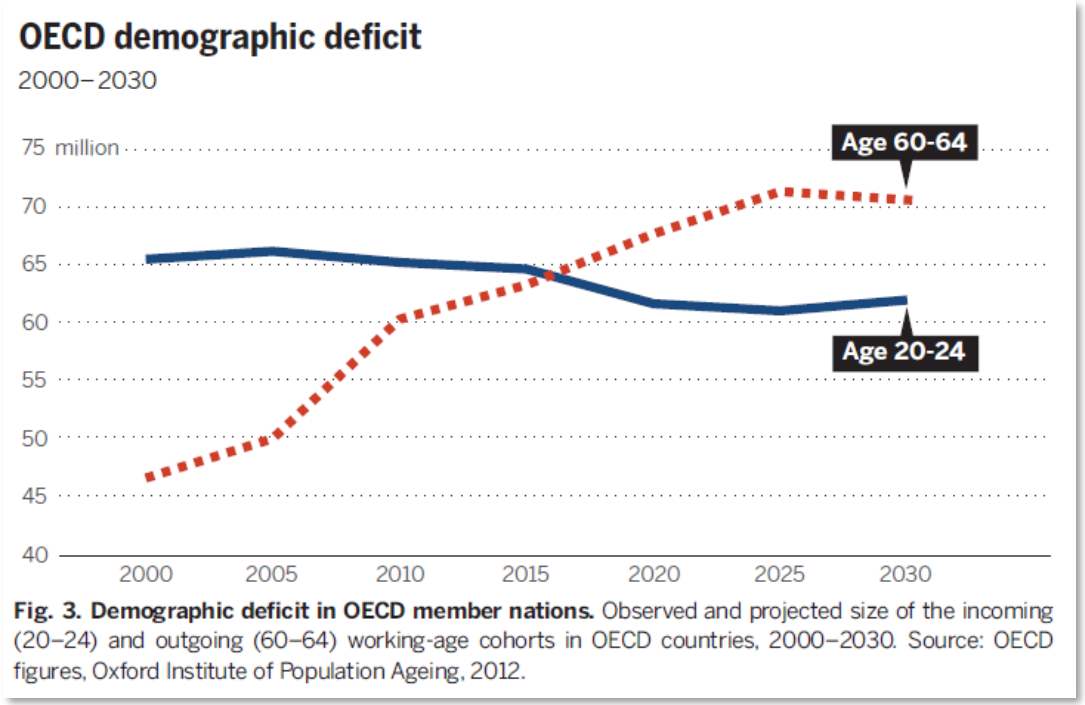
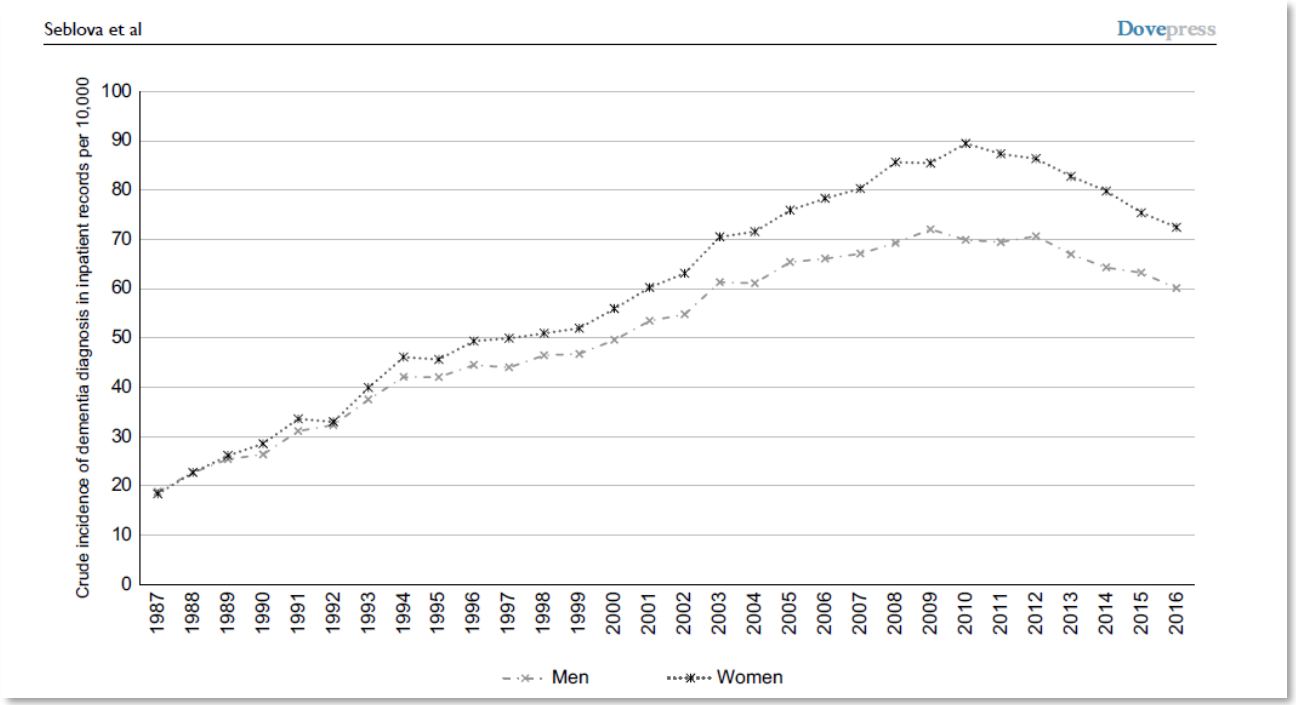


Fig. 3. Demographic deficit in OECD member nations. Observed and projected size of the incoming (20–24) and outgoing (60–64) working-age cohorts in OECD countries, 2000–2030. Source: OECD figures, Oxford Institute of Population Ageing, 2012.

Harper S, Science, 2014



Evolución de la incidencia de demencia en Suecia

Seblova D et al., 2018

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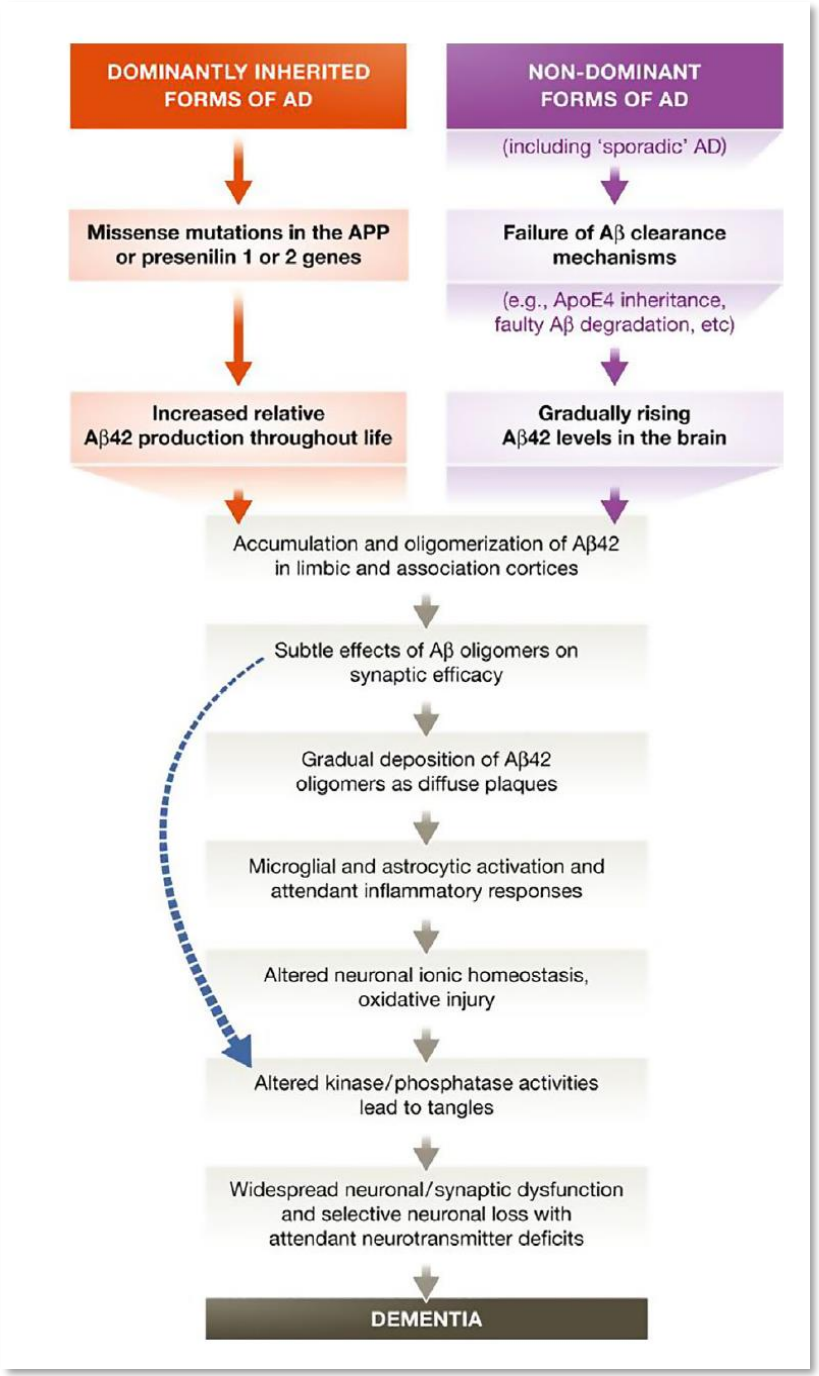
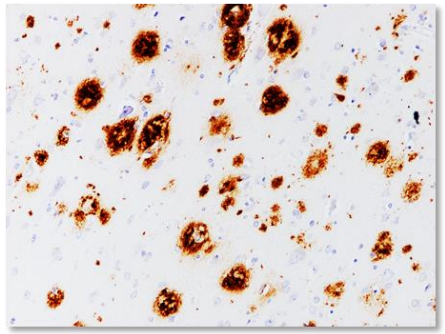
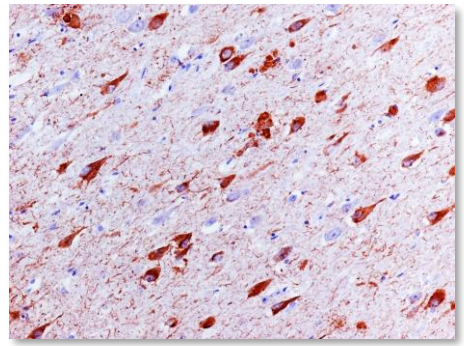


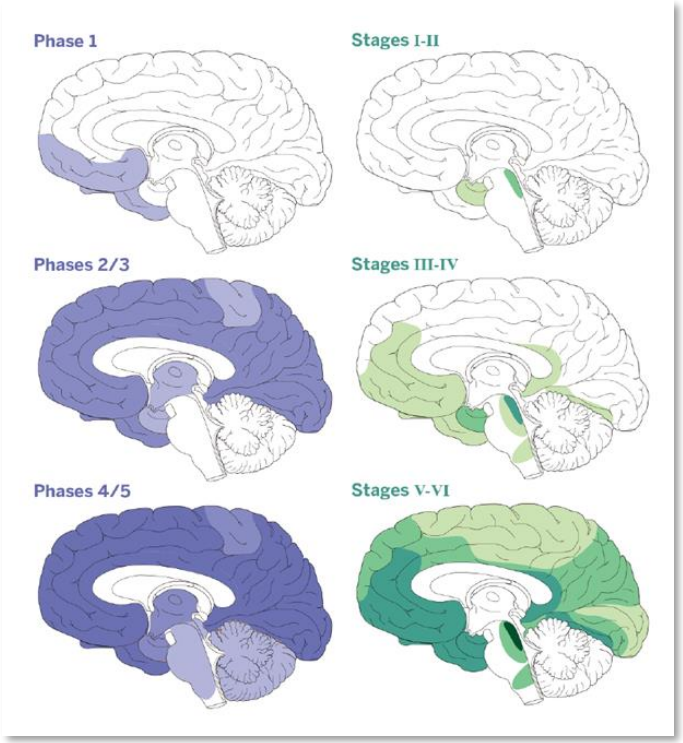
Lane CA *et al*., 2018

Patología β-amiloide: placas



Patología tau: ovillos





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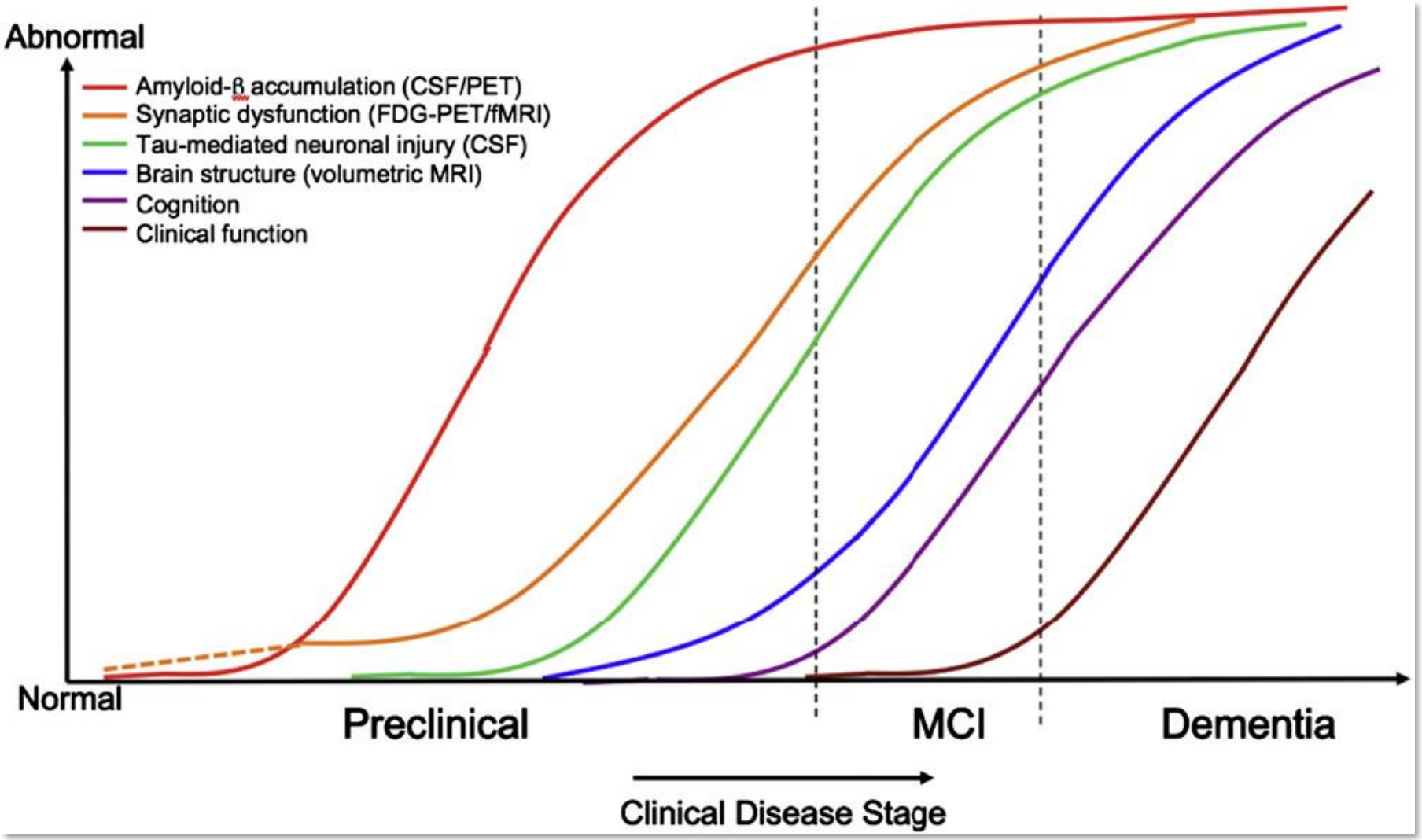
Concepto biológico de la enfermedad de Alzheimer



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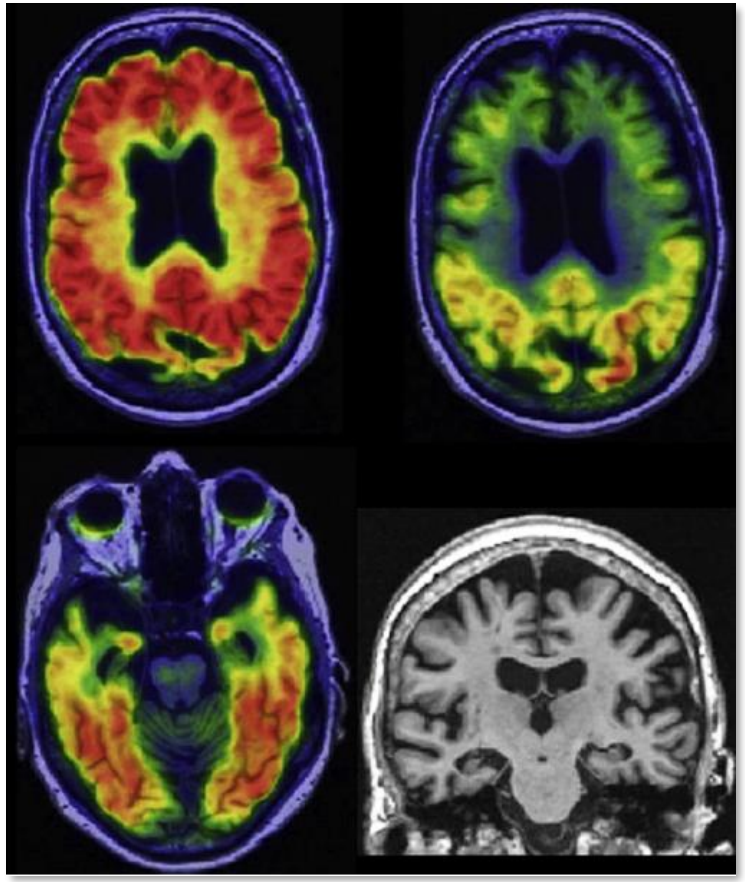
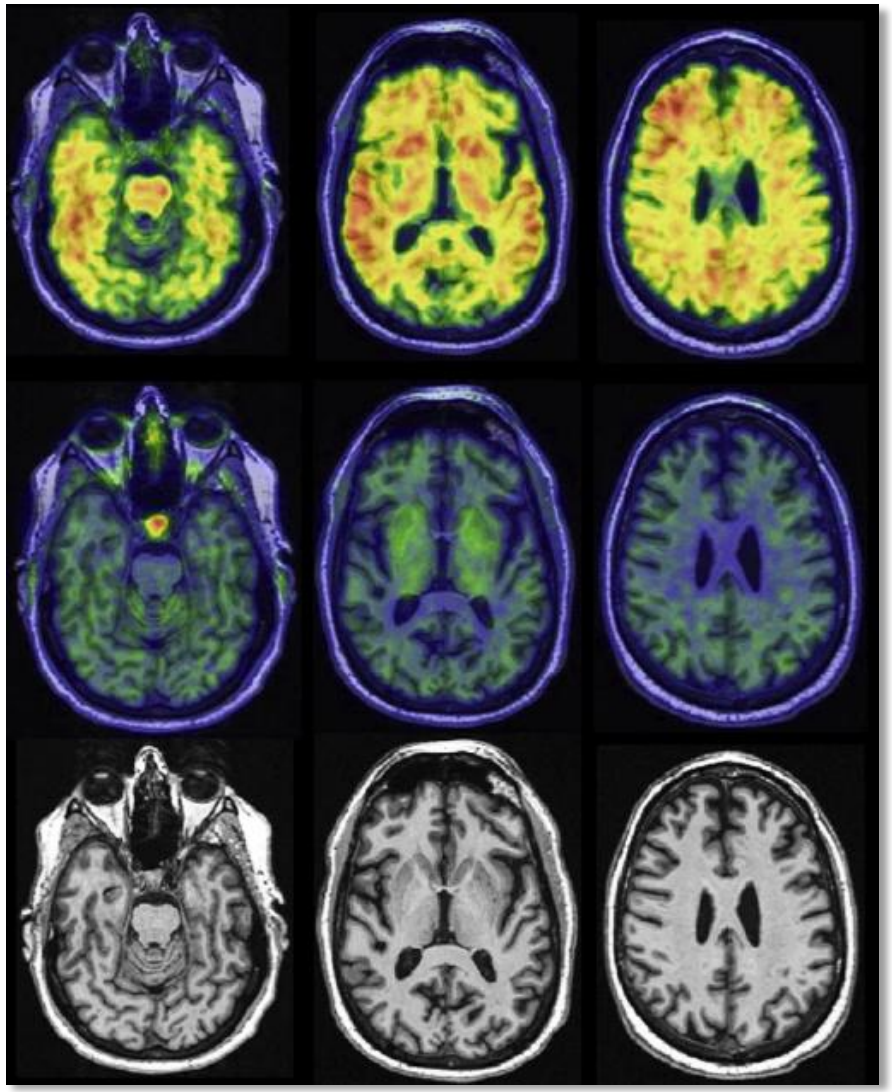
Neuroimagen:
PET de amiloide + RM



Enfermedad de Alzheimer (EA)
+ demencia



Cambio patológico de EA,
sin demencia

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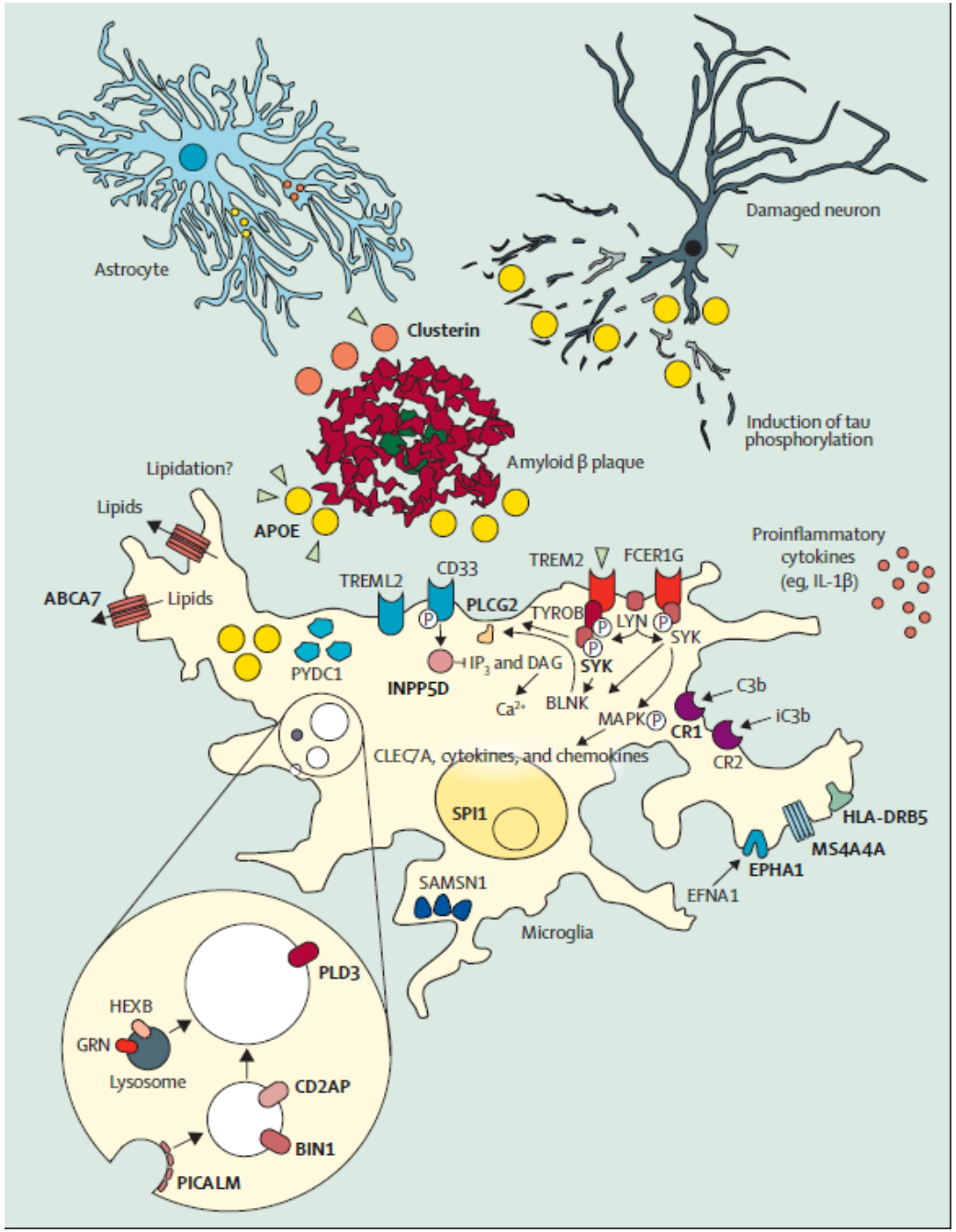
Fase celular de la enfermedad de Alzheimer



Scheltens *et al*., 2021

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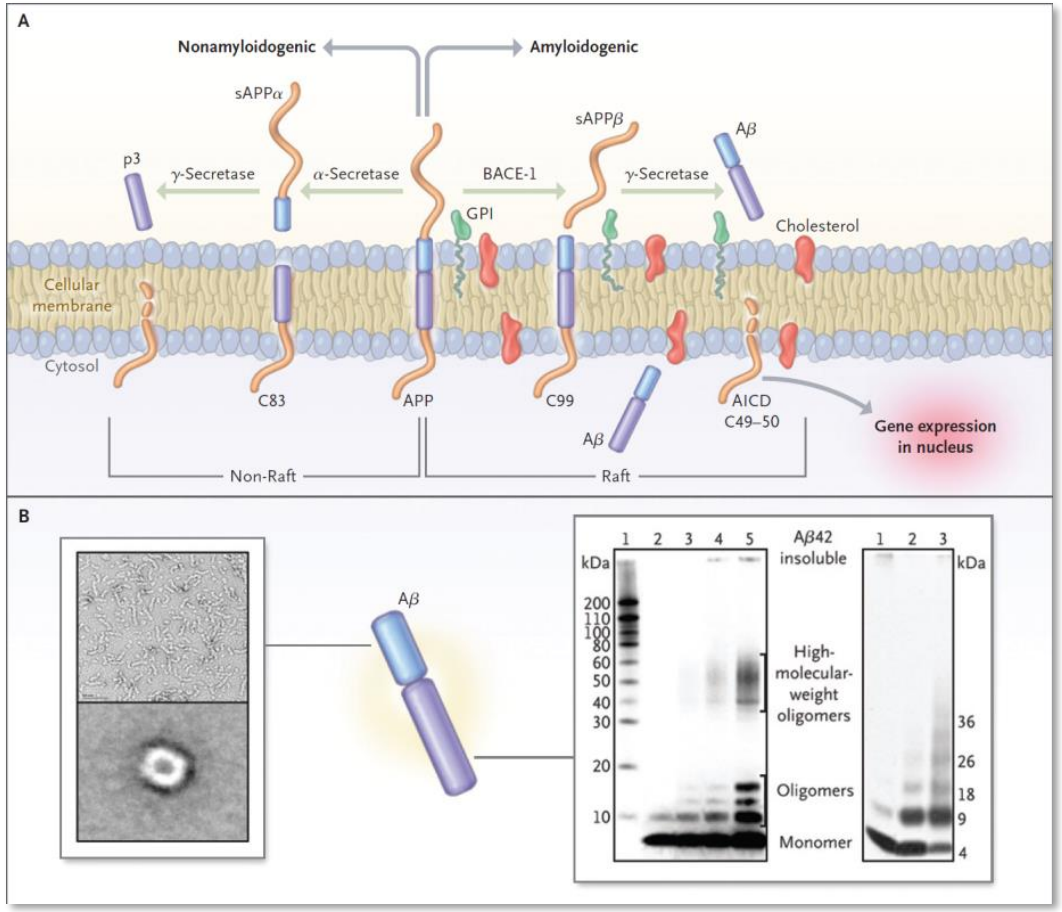
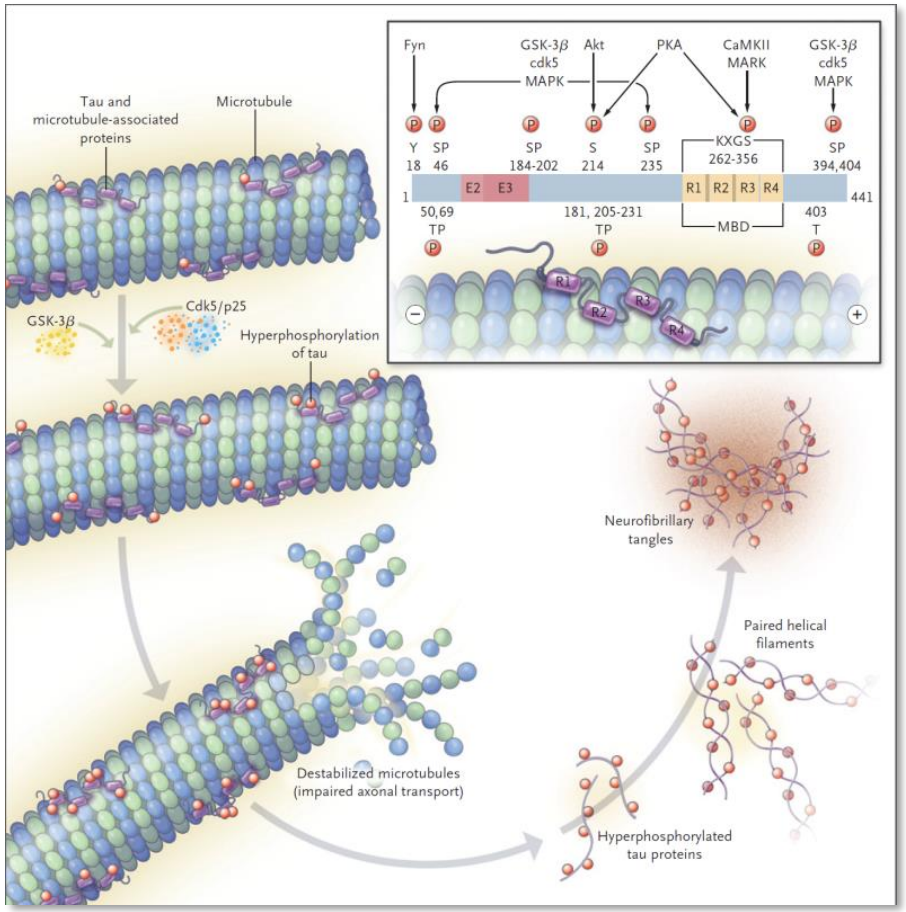
Patología de tipo Alzheimer

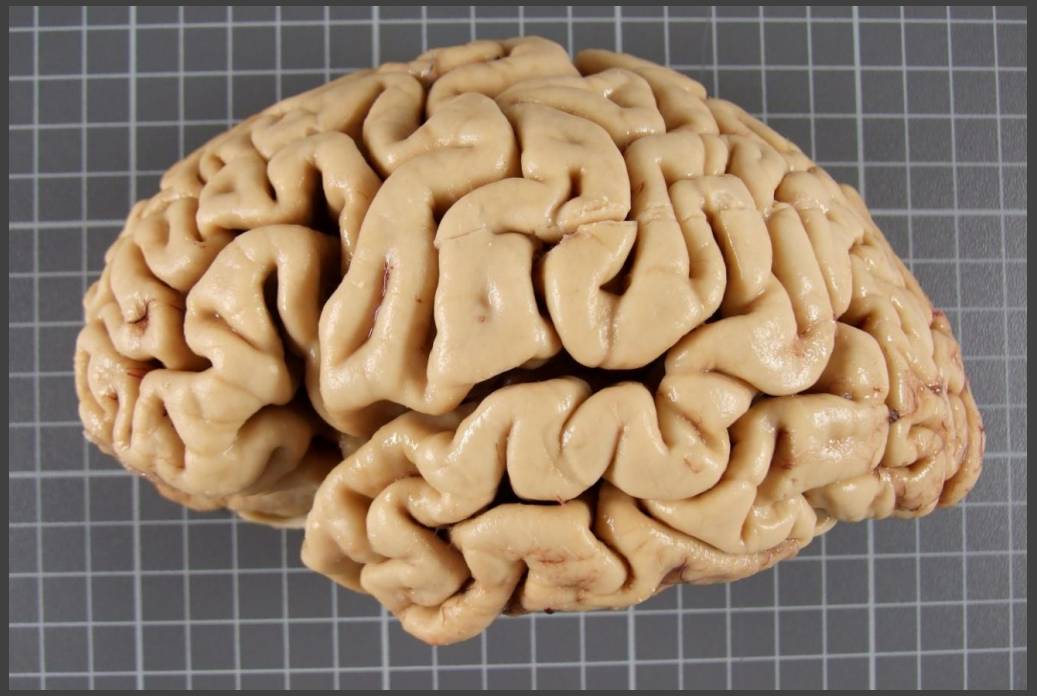
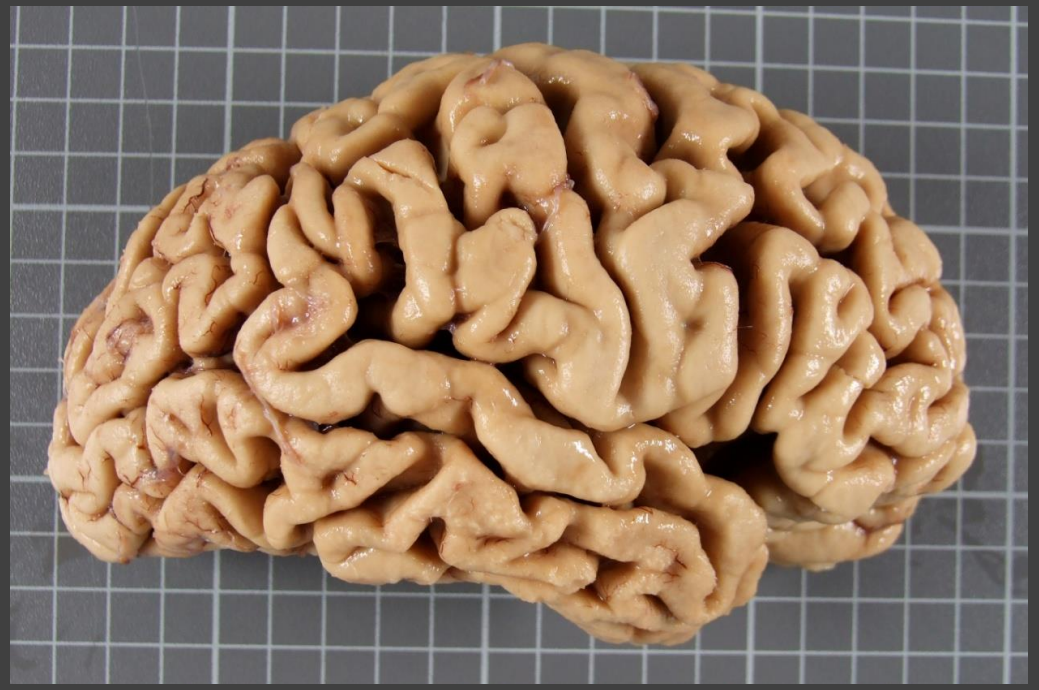
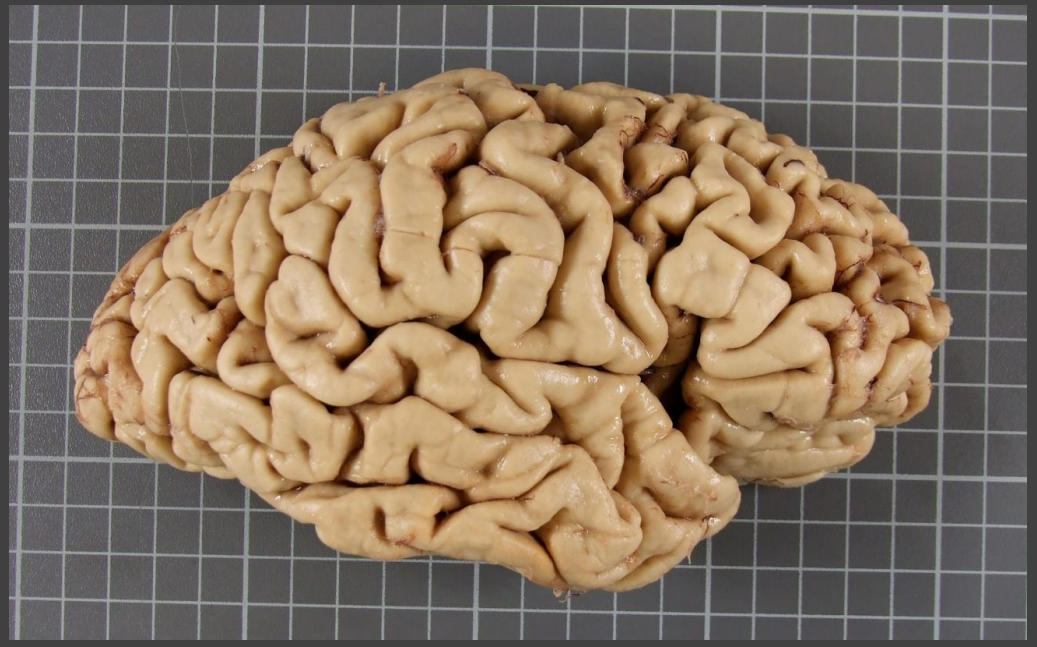
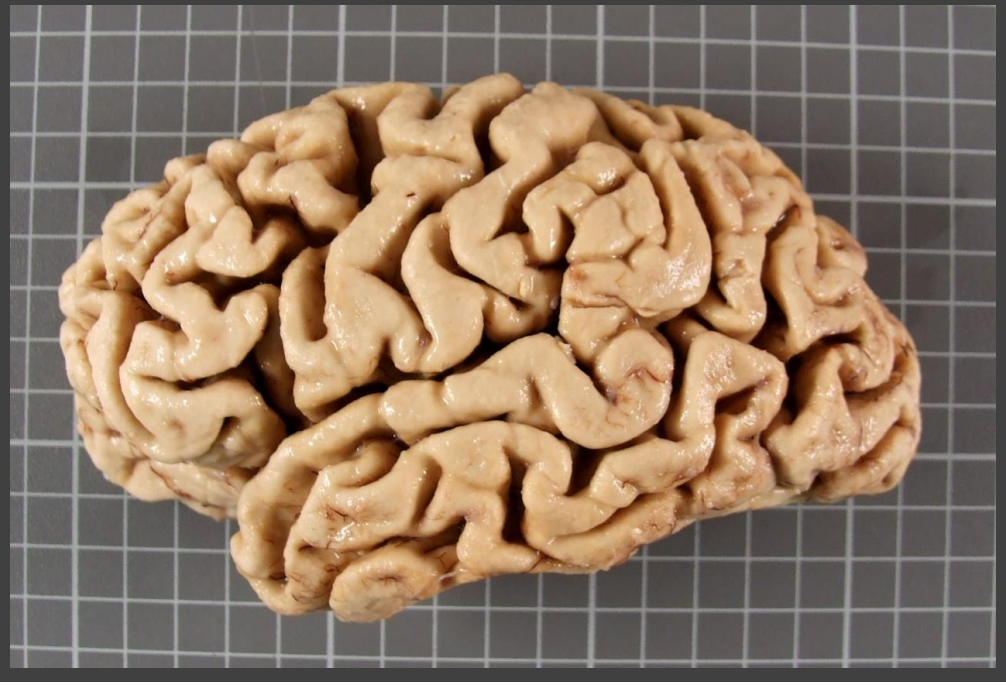
β-amiloide



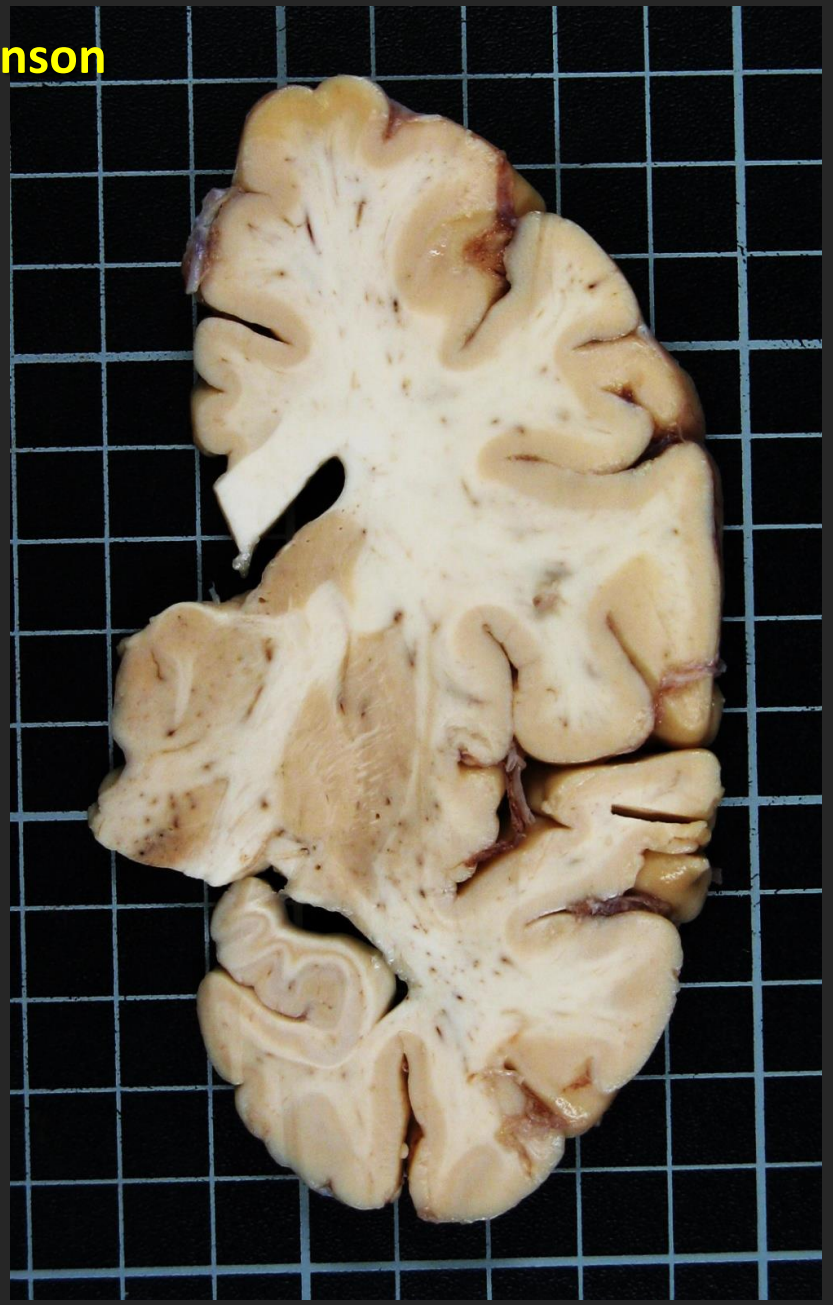
Tau



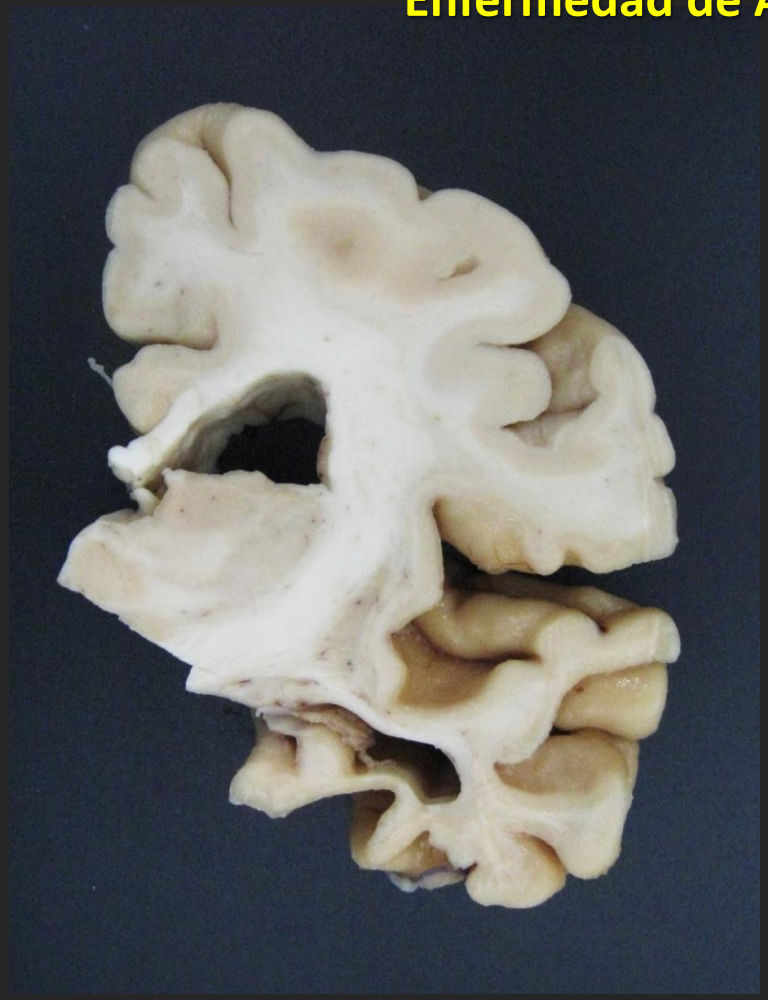
Querfurth & LaFerla, 2010

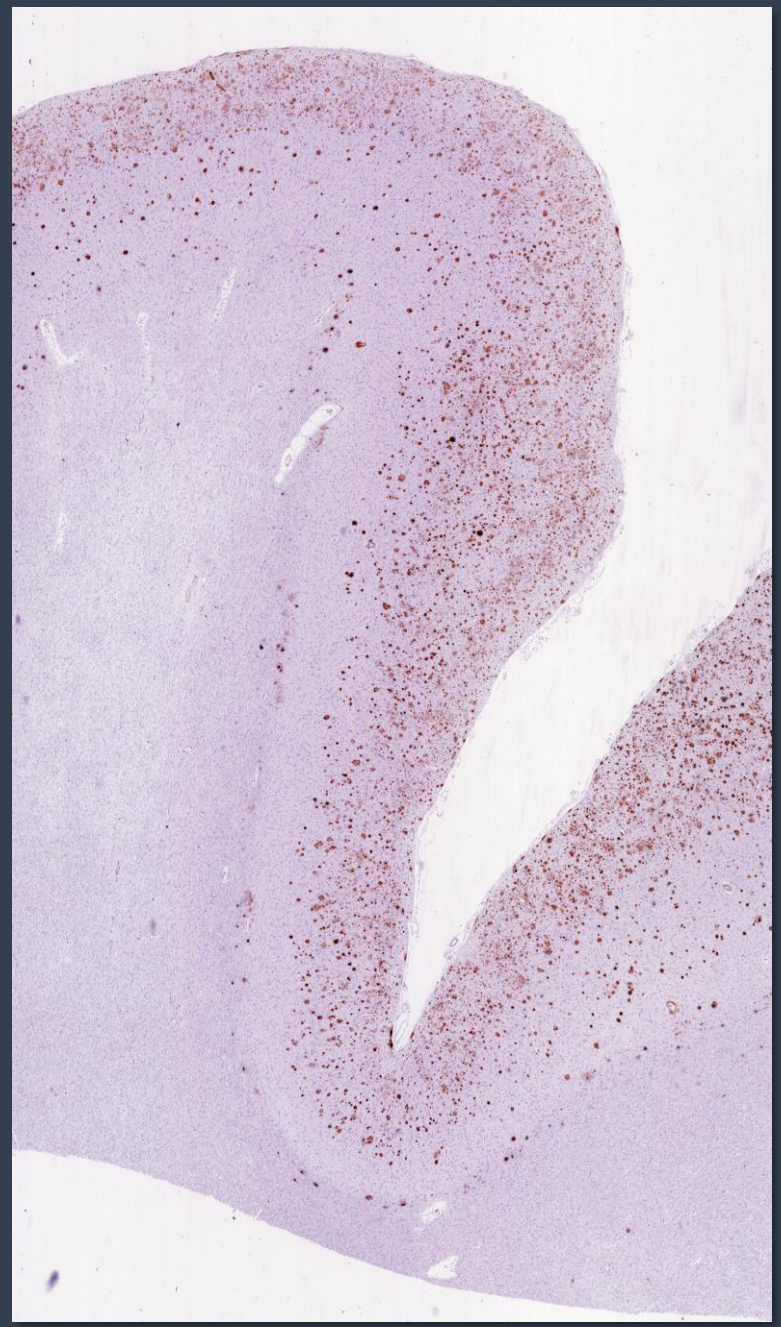
Enfermedad de Parkinson

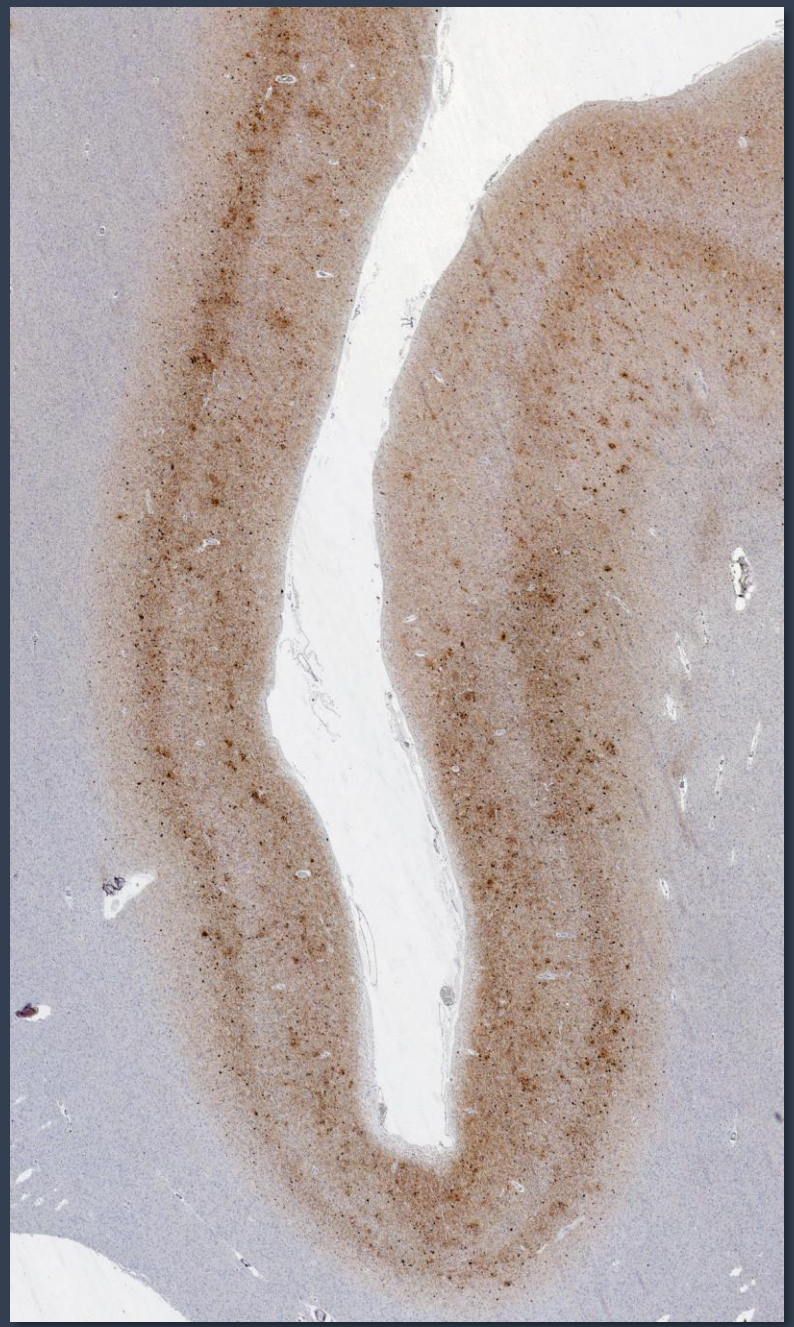


Enfermedad de Alzheimer



Córtex parietal
CERAD,
β-amiloide





Córtex
temporal
CERAD,
Tau AT100

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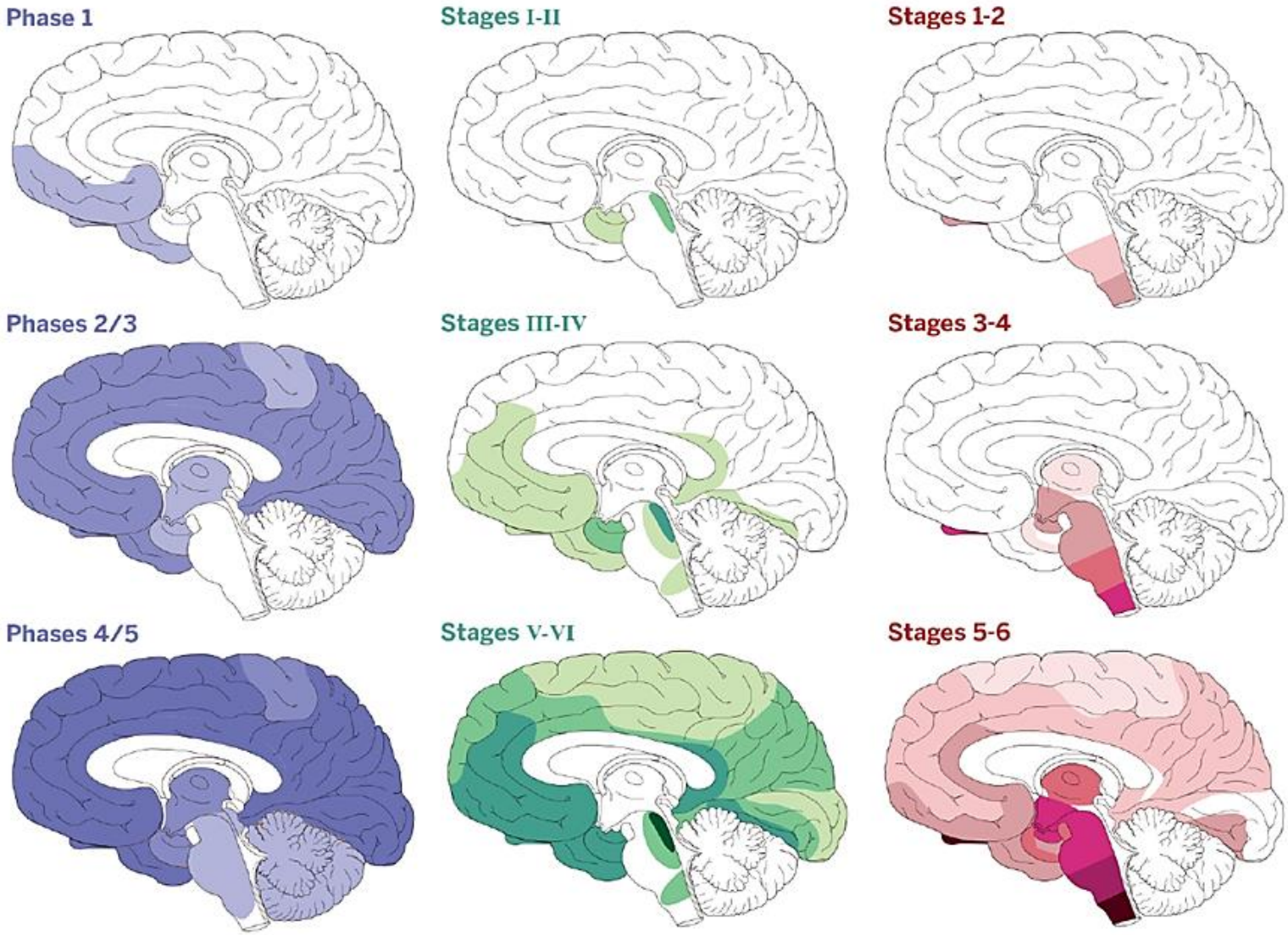
Heiko Braak,
1937 -



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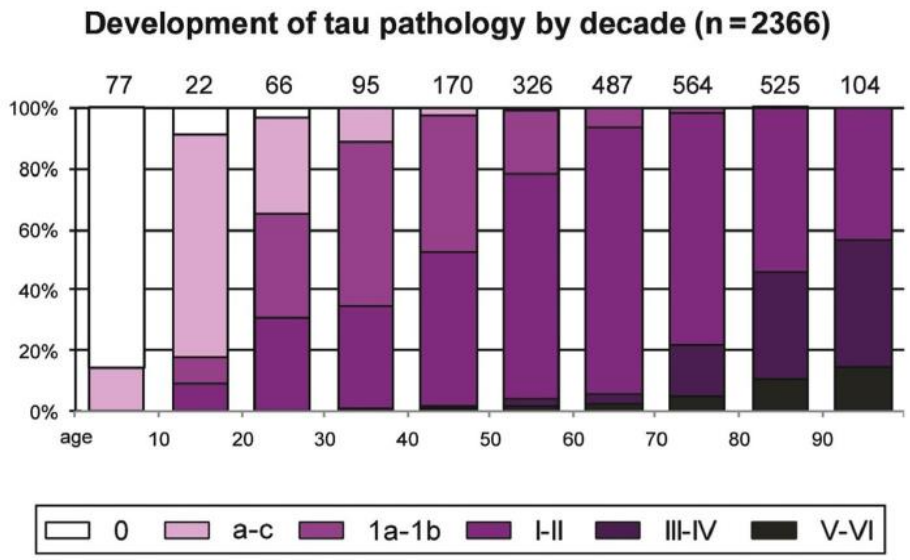
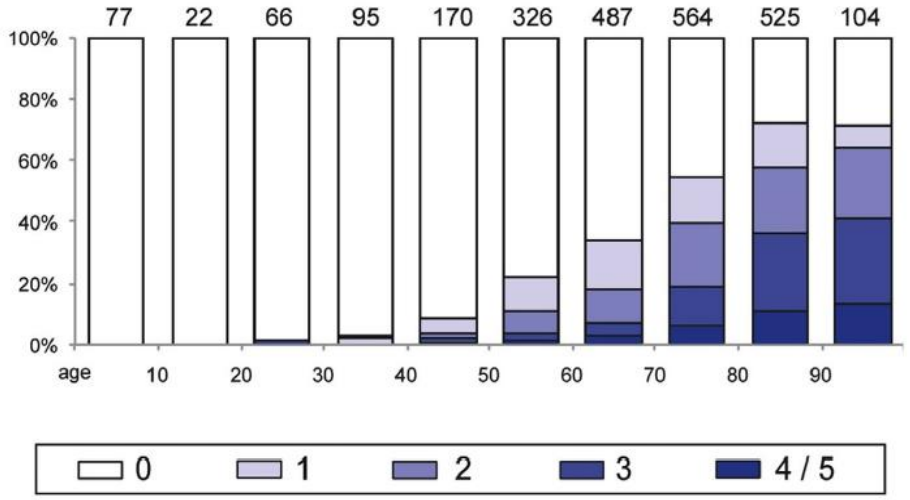
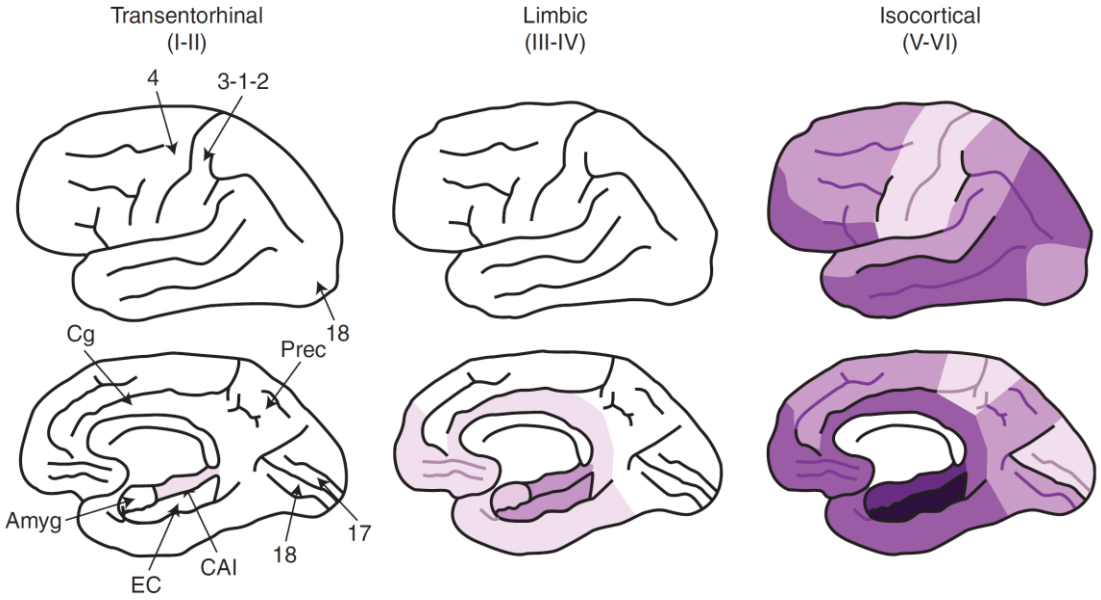
A

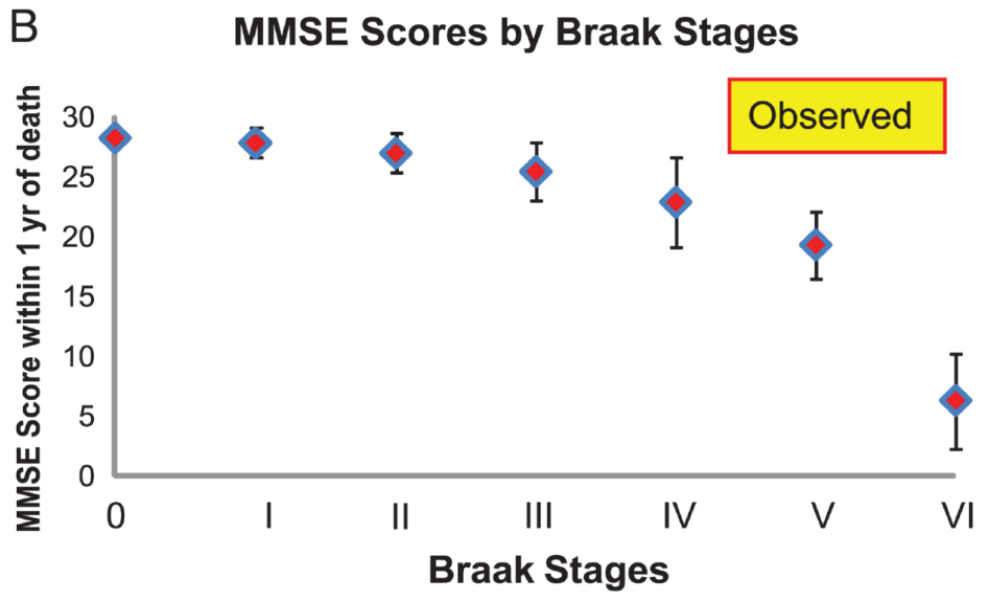


B



Arnsten AFT *et al.*,2020





Nelson *et al*., J Neuropathol Exp neurol. 2009; 68(1): 1-14.

El paradigma prionoide

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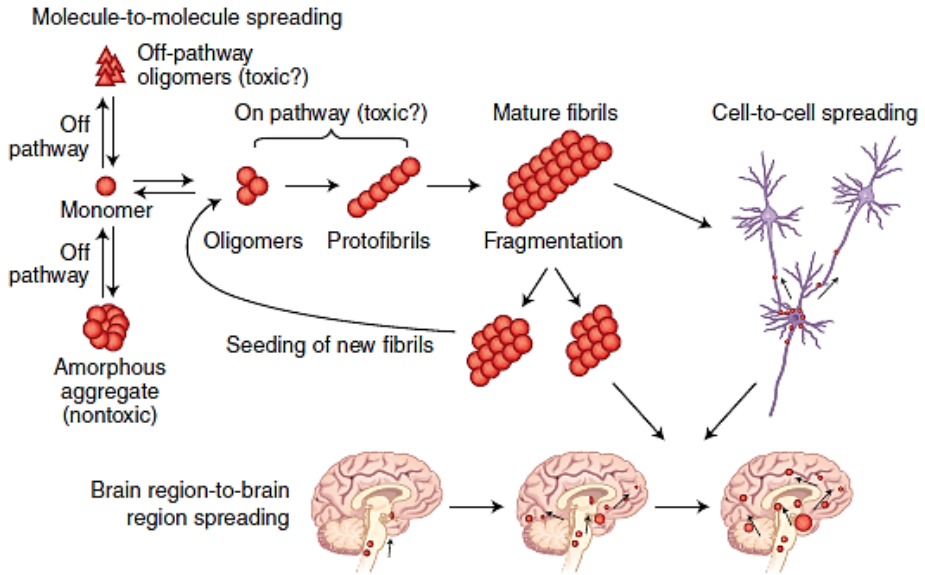
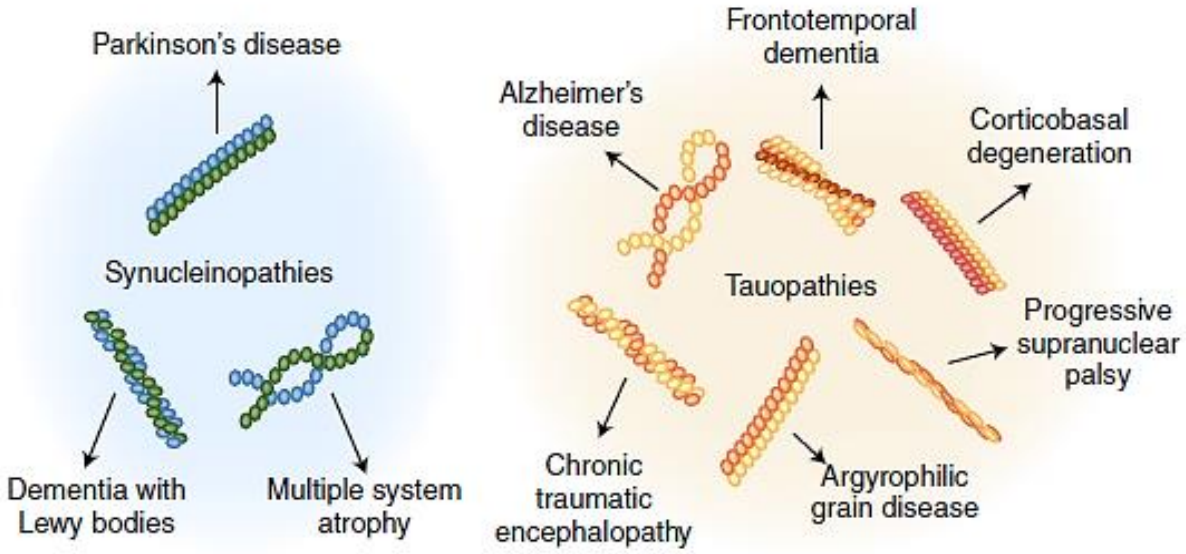
REVIEW ARTICLE | FOCUS
https://doi.org/10.1038/s41593-018-0235-9
nature neuroscience

Protein misfolding, aggregation, and conformational strains in neurodegenerative diseases

Claudio Soto* and Sandra Pritzkow

NATURE NEUROSCIENCE | VOL 21 | OCTOBER 2018 | 1332–1340 |






FAIR

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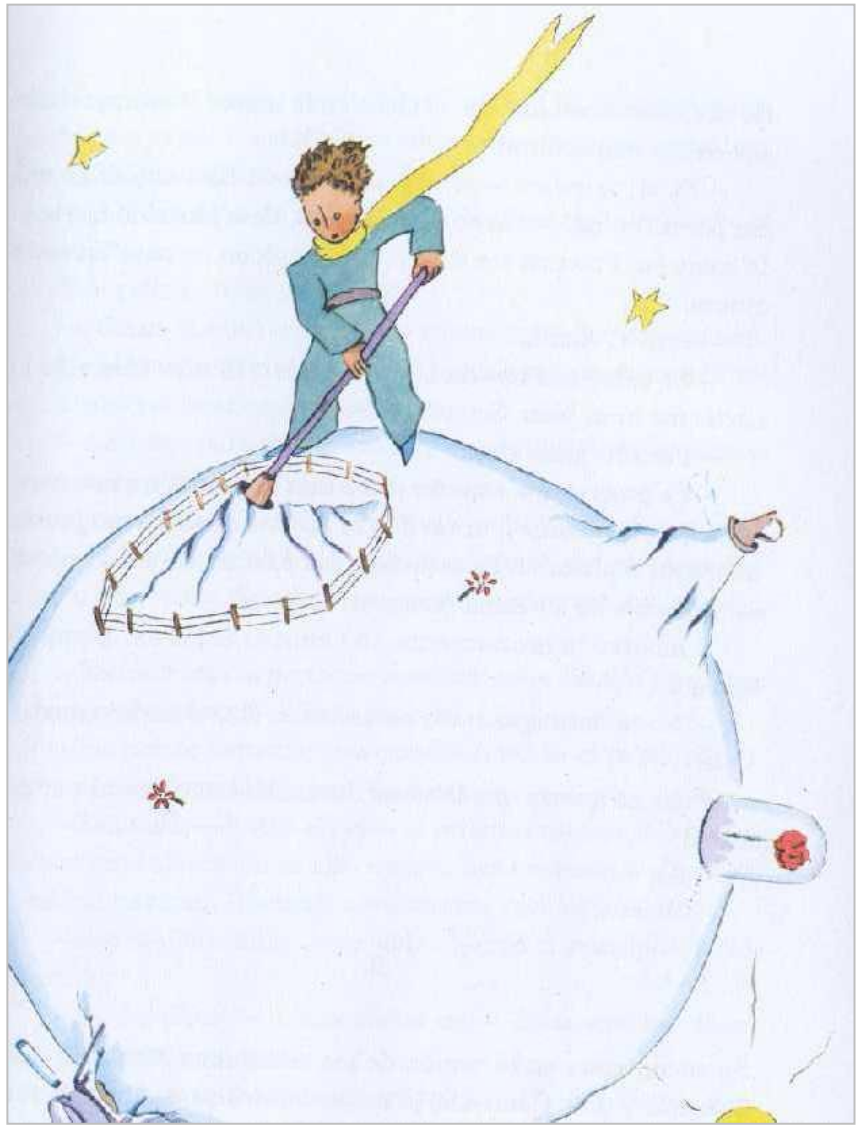
DE ANDALUCÍA

“¿Qué debo hacer?”

El papel de los bancos de tejidos neurológicos en la investigación de la enfermedad de Alzheimer.



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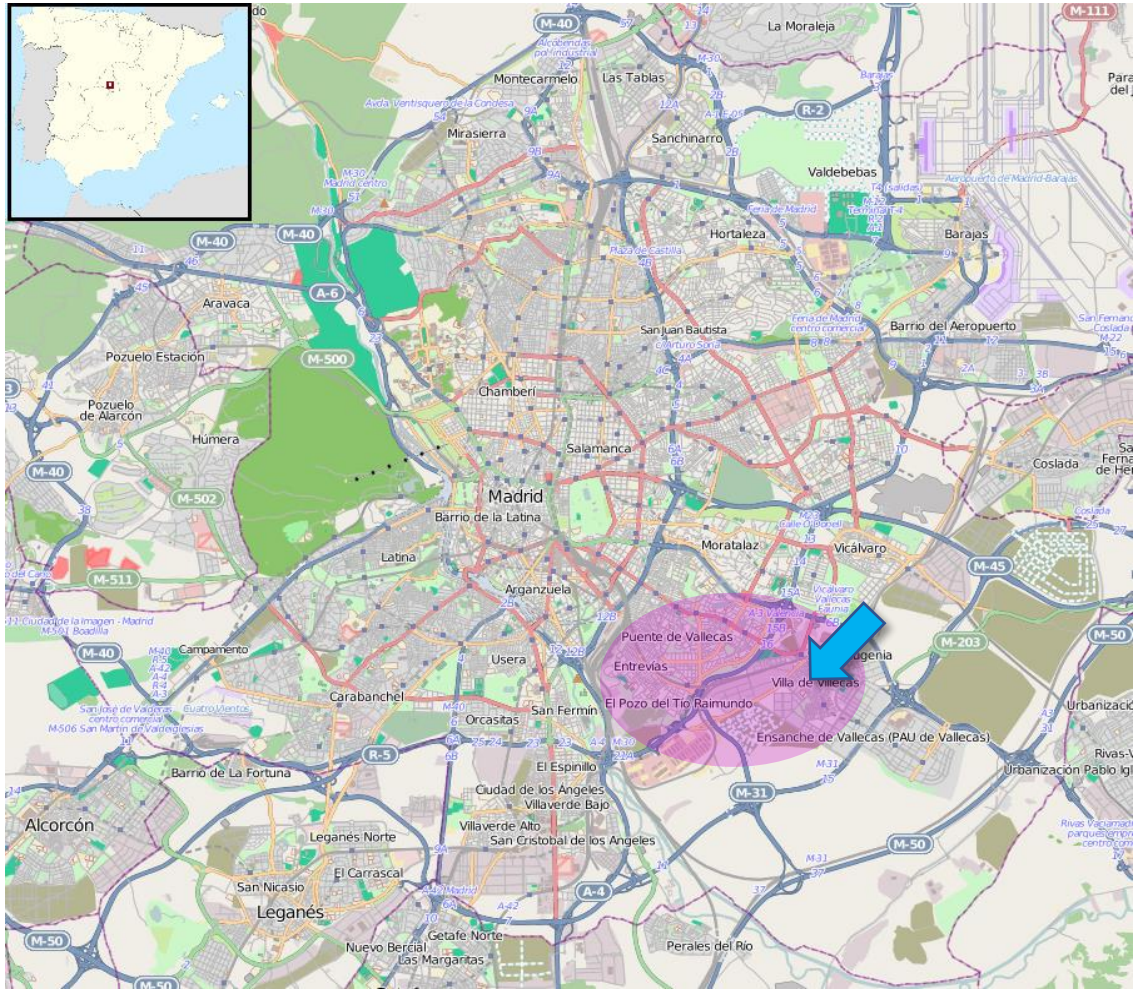
Madrid - Vallecas



Centro Alzheimer Fundación Reina Sofía

Fundación CIEN

UNIVERSIDAD INTERNACIONAL DE ANDALUCÍA

La iniciativa de Vallecas: programas de investigación

El Proyecto Alzheimer Fundación Reina Sofía

- Una residencia para pacientes con demencia.
- Una cohorte de pacientes institucionalizados para la investigación en demencia.

El Banco de Tejidos CIEN

- Un banco de cerebros de enfermedades neurodegenerativas.
- Muestras neurológicas de pacientes incluidas en cohortes de investigación.

El Proyecto Vallecas

- Un estudio longitudinal de envejecimiento cognitivo.
- Voluntarios para la investigación en demencia.

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DE ANDALUCÍA

El Proyecto Alzheimer Fundación Reina Sofía

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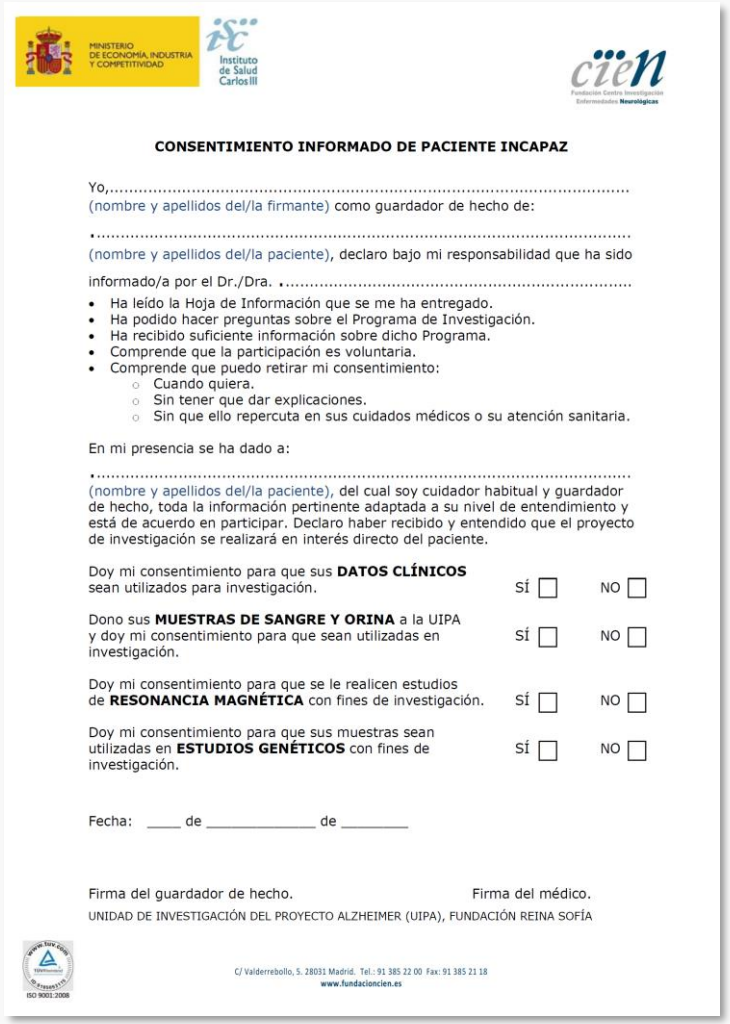
Cohorte del Centro Alzheimer de Vallecas: Consentimiento informado

- Para pacientes incapaces de dar su consentimiento



MINISTERIO DE ECONOMÍA, INDUSTRIA Y COMPETITIVIDAD — Instituto de Salud Carlos III — cien Fundación Centro Investigación Enfermedades Neurológicas

CONSENTIMIENTO INFORMADO DE PACIENTE INCAPAZ

Yo,.....
(nombre y apellidos del/la firmante) como guardador de hecho de:

.....
(nombre y apellidos del/la paciente), declaro bajo mi responsabilidad que ha sido informado/a por el Dr./Dra. .....

- Ha leído la Hoja de Información que se me ha entregado.
- Ha podido hacer preguntas sobre el Programa de Investigación.
- Ha recibido suficiente información sobre dicho Programa.
- Comprende que la participación es voluntaria.
- Comprende que puedo retirar mi consentimiento:
  - Cuando quiera.
  - Sin tener que dar explicaciones.
  - Sin que ello repercuta en sus cuidados médicos o su atención sanitaria.

En mi presencia se ha dado a:

.....
(nombre y apellidos del/la paciente), del cual soy cuidador habitual y guardador de hecho, toda la información pertinente adaptada a su nivel de entendimiento y está de acuerdo en participar. Declaro haber recibido y entendido que el proyecto de investigación se realizará en interés directo del paciente.

Doy mi consentimiento para que sus **DATOS CLÍNICOS** sean utilizados para investigación. SÍ ☐ NO ☐

Dono sus **MUESTRAS DE SANGRE Y ORINA** a la UIPA y doy mi consentimiento para que sean utilizadas en investigación. SÍ ☐ NO ☐

Doy mi consentimiento para que se le realicen estudios de **RESONANCIA MAGNÉTICA** con fines de investigación. SÍ ☐ NO ☐

Doy mi consentimiento para que sus muestras sean utilizadas en **ESTUDIOS GENÉTICOS** con fines de investigación. SÍ ☐ NO ☐

Fecha: ____ de _____ de _____

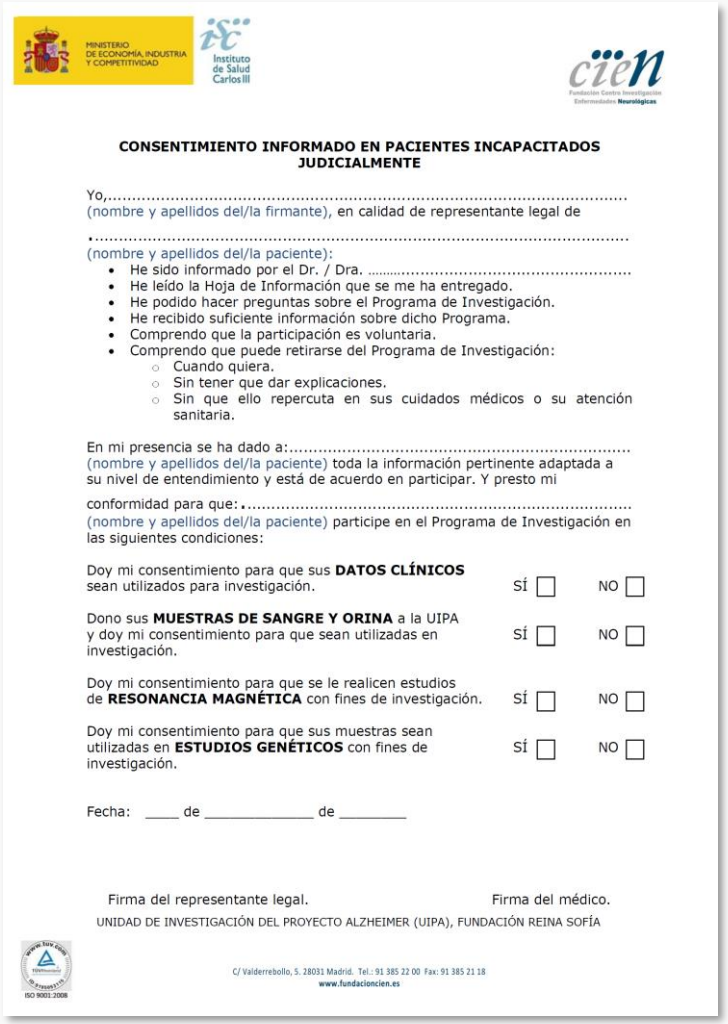
Firma del guardador de hecho. Firma del médico.

UNIDAD DE INVESTIGACIÓN DEL PROYECTO ALZHEIMER (UIPA), FUNDACIÓN REINA SOFÍA

ISO 9001:2008

C/ Valderrebollo, 5. 28031 Madrid. Tel.: 91 385 22 00 Fax: 91 385 21 18
www.fundacioncien.es

- Para pacientes con un tutor legal



MINISTERIO DE ECONOMÍA, INDUSTRIA Y COMPETITIVIDAD — Instituto de Salud Carlos III — cien Fundación Centro Investigación Enfermedades Neurológicas

CONSENTIMIENTO INFORMADO EN PACIENTES INCAPACITADOS JUDICIALMENTE

Yo,.....
(nombre y apellidos del/la firmante), en calidad de representante legal de

.....
(nombre y apellidos del/la paciente):

- He sido informado por el Dr. / Dra. .....
- He leído la Hoja de Información que se me ha entregado.
- He podido hacer preguntas sobre el Programa de Investigación.
- He recibido suficiente información sobre dicho Programa.
- Comprendo que la participación es voluntaria.
- Comprendo que puede retirarse del Programa de Investigación:
  - Cuando quiera.
  - Sin tener que dar explicaciones.
  - Sin que ello repercuta en sus cuidados médicos o su atención sanitaria.

En mi presencia se ha dado a:.....
(nombre y apellidos del/la paciente) toda la información pertinente adaptada a su nivel de entendimiento y está de acuerdo en participar. Y presto mi conformidad para que:.....
(nombre y apellidos del/la paciente) participe en el Programa de Investigación en las siguientes condiciones:

Doy mi consentimiento para que sus **DATOS CLÍNICOS** sean utilizados para investigación. SÍ ☐ NO ☐

Dono sus **MUESTRAS DE SANGRE Y ORINA** a la UIPA y doy mi consentimiento para que sean utilizadas en investigación. SÍ ☐ NO ☐

Doy mi consentimiento para que se le realicen estudios de **RESONANCIA MAGNÉTICA** con fines de investigación. SÍ ☐ NO ☐

Doy mi consentimiento para que sus muestras sean utilizadas en **ESTUDIOS GENÉTICOS** con fines de investigación. SÍ ☐ NO ☐

Fecha: ____ de _____ de _____

Firma del representante legal. Firma del médico.

UNIDAD DE INVESTIGACIÓN DEL PROYECTO ALZHEIMER (UIPA), FUNDACIÓN REINA SOFÍA

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Journal of Alzheimer's Disease 28 (2012) 211–222
DOI 10.3233/JAD-2011-110875
IOS Press

Promoting Research in Advanced Dementia: Early Clinical Results of the Alzheimer Center Reina Sofía Foundation

Javier Olazarán[a,*], Luis Agüera-Ortiz[b], Ricardo S. Osorio[a], Beatriz León-Salas[a], José Luis Dobato[a], Isabel Cruz-Orduña[a], Belén González[a], Meritxell Valentí[a], Nuria Gil-Ruiz[a], Belén Frades[c], M.I. Ramos-Garc
[a]*Alzheimer Disease*
Foundation, Madri
[b]*CIBERSAM, Carl*
[c]*CIBERNED, Carl*

Table 3
Scale measures in the final clinical protocol of the ACRSF

Area	Scale	Objective/Rationale	Observations[1]	References[2]
Cognition	MMSE	General cognition, universal measurement	B, 6	[17, 18]
	sMMSE	General cognition, advanced dementia	B, 6	[19, 20]
	Animals	Verbal fluency, frontotemporal functions	B, 6	[22, 23]
	SIB	General cognition, avoid floor effect	B, 6	[46, 47]
Behavior and mood	NPI	Overall picture of behavior problems	B, 6	[14–16]
	APADEM	Apathy in advanced dementia	B, 6	[48]
	CMAI	Agitation, detailed assessment	B, 12	[49, 50]
	CSDD	Depression, using both informant and patient observation	B, 12	[51, 52]
Personality	NEO-FFI	Premorbid personality traits, understand behavior problems	B	[56, 57]
ADL	FAST	AD specific, detailed for severe dementia	B, 6	[26, 27]
	BI	Basic ADL, sensitive to change	B, 6	[58, 59]
	IADL	Instrumental AVD	B, 6, DC	[60, 61]
Motor area	SCOPA-motor	Parkinsonism, predictor of gait dysfunction and functional dependence	B, 6	[31, 32]
	Up & Go test	Mobility, predictor of falls	B, 6	[33, 34]
	ADGS	Gait, predictor of functional dependence and QoL	B, 6	[35, 36]
	POMA	Balance, predictor of falls	B, 6	[63, 64]
QoL	QUALID	QoL in advanced dementia	B, 6, NH	[66, 67]
	QoL- AD	QoL as perceived by patient and caregiver	B, 6, DC	[41, 42]

[1]B: administered at baseline; 6: administered every six months; 12: administered every 12 months; NH: administered only to the nursing home patients; DC: administered only to the day-care patients.
[2]The original reference appears first, followed by reference of the most relevant validation studies in Spanish samples.
ACRSF: Alzheimer Center Reina Sofía Foundation; AD: Alzheimer's disease; ADL: activities of daily living; ADGS: Alzheimer's Disease Gait Scale; APADEM: Apathy in Dementia Scale; BI: Barthel Index; CMAI: Cohen-Mansfield Agitation Inventory; FAST: Functional Assessment Staging; GDS: Global Deterioration Scale; IADL: Instrumental Activities of Daily Living Scale; MMSE: Mini-mental State Examination; NEO-FFI: NEO Five-Factor Inventory; NPI: Neuropsychiatric Inventory; POMA: Tinetti Performance Oriented Mobility Assessment; QoL-AD: Quality of Life in Alzheimer's Disease Scale; QUALID: Quality of Life in Late-stage Dementia Scale; SCOPA-Motor: motor evaluation scale of the Scales for Outcomes in Parkinson's Disease; SIB: Severe Impairment Battery; sMMSE: Severe Mini-mental State Examination.

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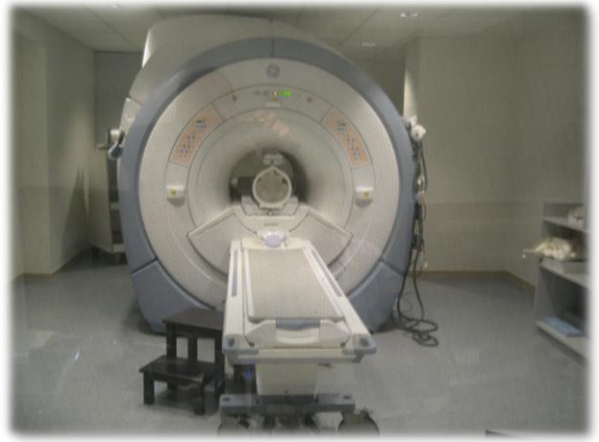
Cohorte Alzheimer de Vallecas - CAFRS

Centro Alzheimer FRS

Fundación CIEN

Unidad Multidisciplinar de Apoyo

Seguimiento Cohorte CAV



Datos de seguimiento

Resonancia Magnética 3T

Muestras sangre, cerebro

una Universidad Internacional de Andalucía

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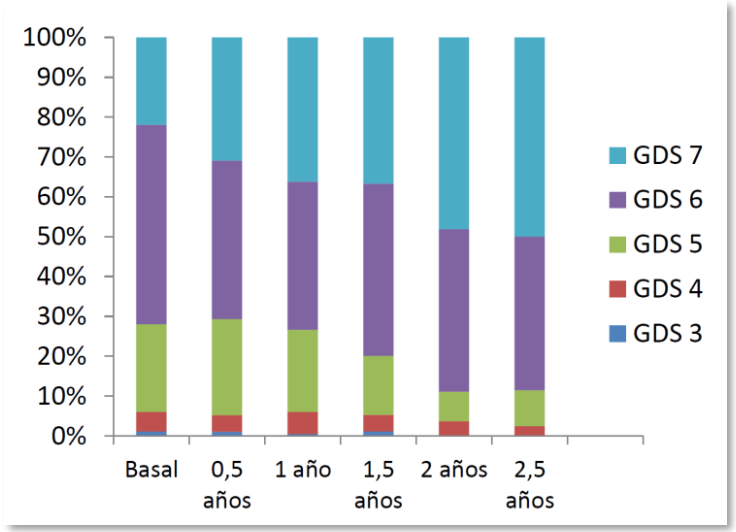
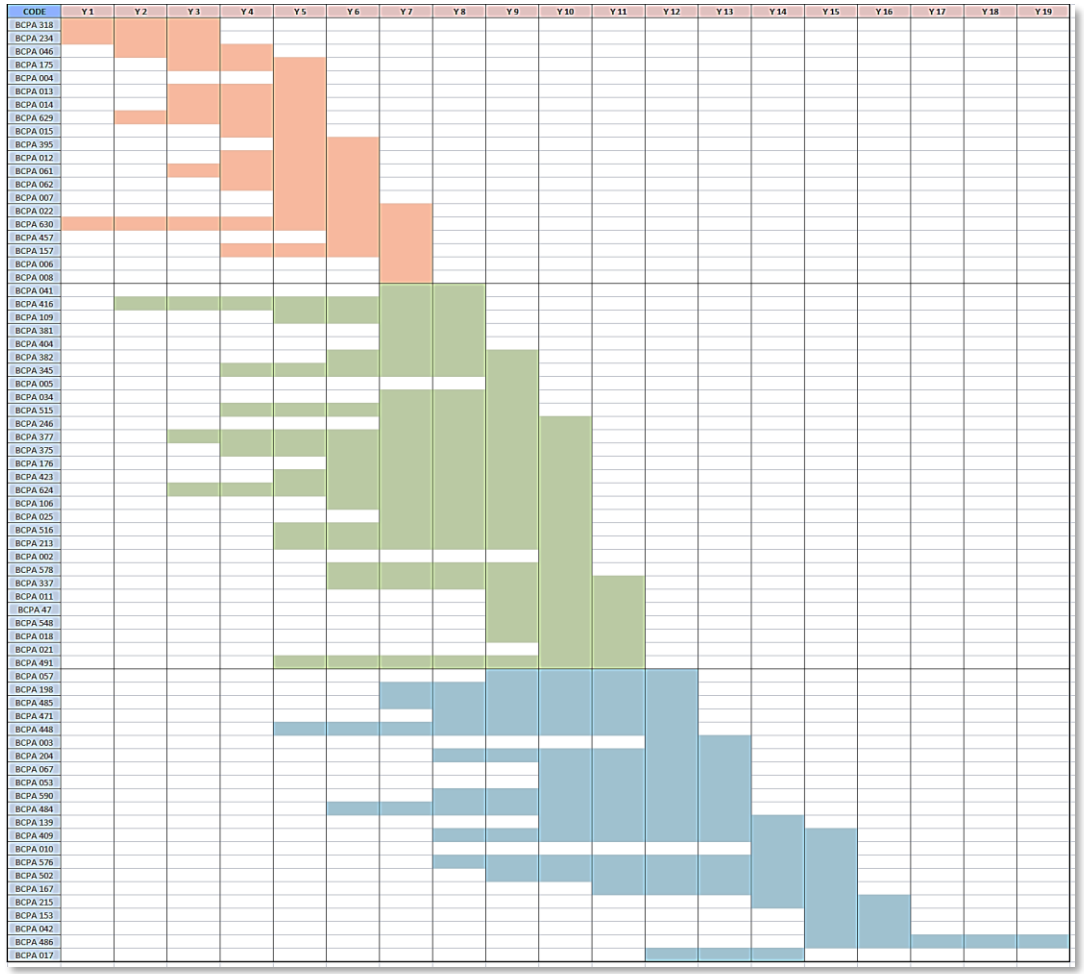
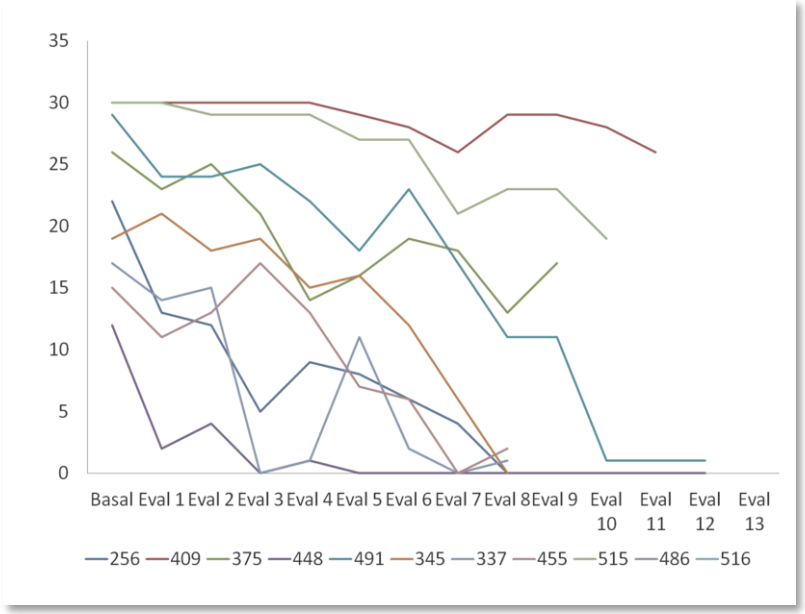


Tiempo de supervivencia





Severe Mini-Mental State Examination

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Archives of Gerontology and Geriatrics 57 (2013) 257–262

Contents lists available at SciVerse ScienceDirect

Archives of Gerontology and Geriatrics

Quality
Alzheim

Beatriz Le
José Luis D
Pablo Mar

Am J Geriatr Psychiatry. 2015 Feb;23(2):149-59.

A Novel Rating Scale for the Measurement of
A

J Neurol
DOI 10.1007/s00415-015-7692-9

ORIGINAL COMMUNICATION

Lui
Isa

Validation
dementia:
dementia

Sloane Heller · C
Laura Carrasco
Pablo Martínez-

REV NEUROL 2015;60:1-9

ORIGINAL

Fiabilidad y validez de la batería de evaluación del deterioro grave, versión abreviada (SIB-s), en pacientes con demencia en España

Isabel Cruz-Orduña, Luis F. Agüera-Ortiz, Ignacio Montorio-Cerrato, Beatriz León-Salas, M. Cristina Valle de Juan, Pablo Martínez-Martín

ELSEVIER

Alzheimer's & Dementia

Alzheimer's & Dementia ■ (2015) 1-9

Combined Alzheimer
ac

María Ascensión Zea-Sev
Ped

[a]Alzheimer Disease Research Unit, CIEN
[b]Unidad Funcional de Investigaci
[c]Hospit

Journal of Alzheimer's Disease xx (2020) x–xx
DOI 10.3233/JAD-200600
IOS Press

Pathological Correlations of Neuropsychiatric Symptoms in Institutionalized People with Dementia

Ester Esteban de Antonio[a], Jorge López-Álvarez[b], Alberto Rábano[c], Luis Agüera-Ortiz[b,d], Antonio Sánchez-Soblechero[a], Laura Amaya[a], Sofía Portela[a], Carlos Cátedra[a] and Javier Olazarán[a,e,*]

[a]*Neurology Service, University Hospital Gregorio Marañón, Madrid, Spain*
[b]*Psychiatry Department, University Hospital 12 de Octubre, Madrid, Spain*
[c]*Alzheimer's Center Reina Sofía Foundation - CIEN Foundation and CIBERNED, Carlos III Institute of Health, Madrid, Spain*
[d]*CIBERSAM, Madrid, Spain*
[e]*Memory Disorders Unit, HM Hospitals, Madrid, Spain*

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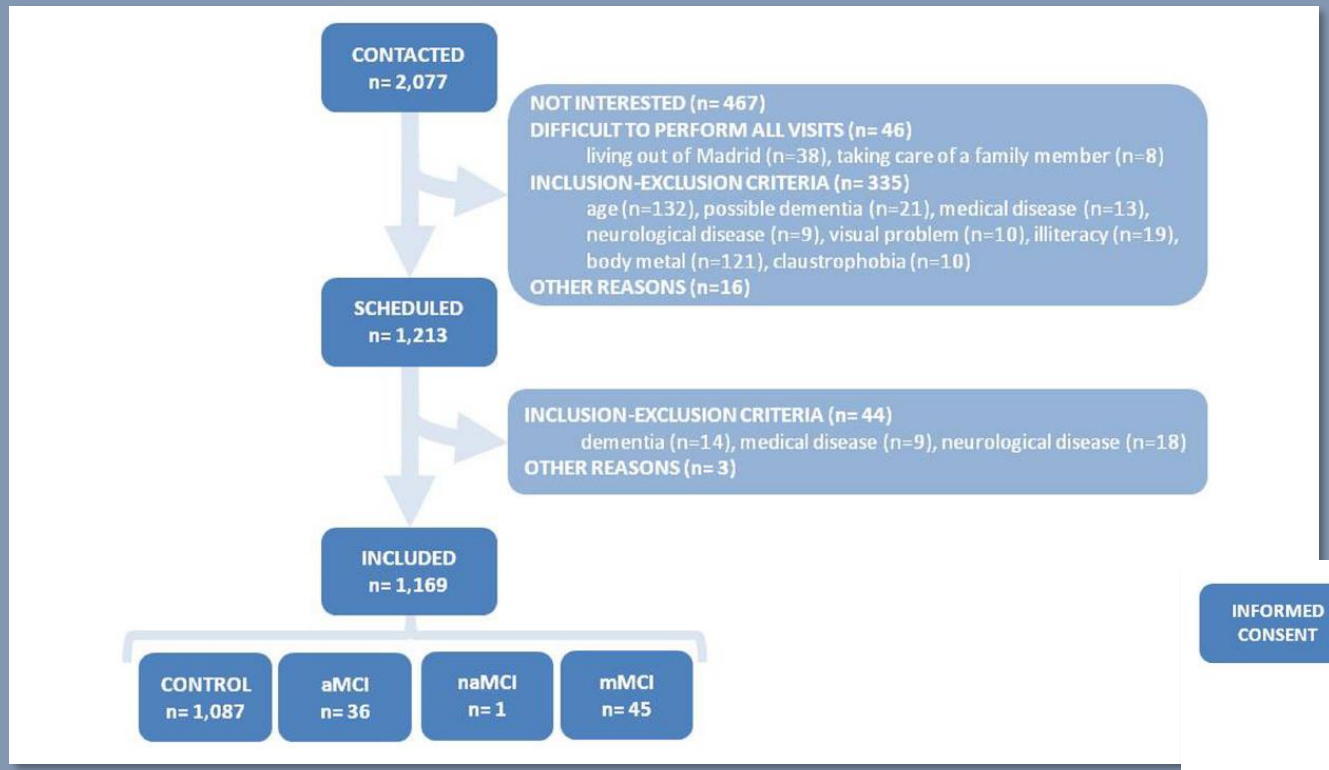
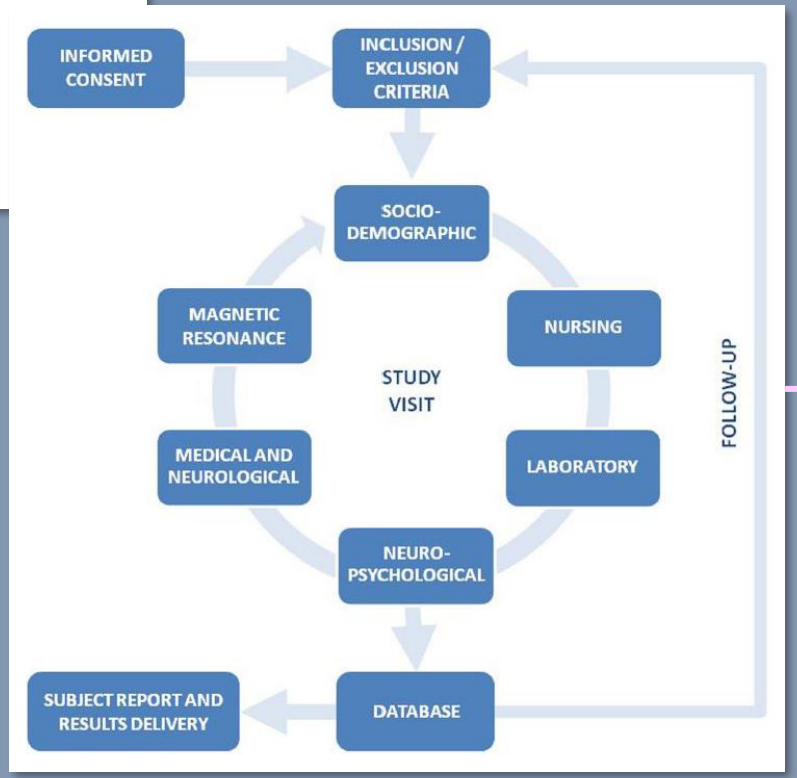
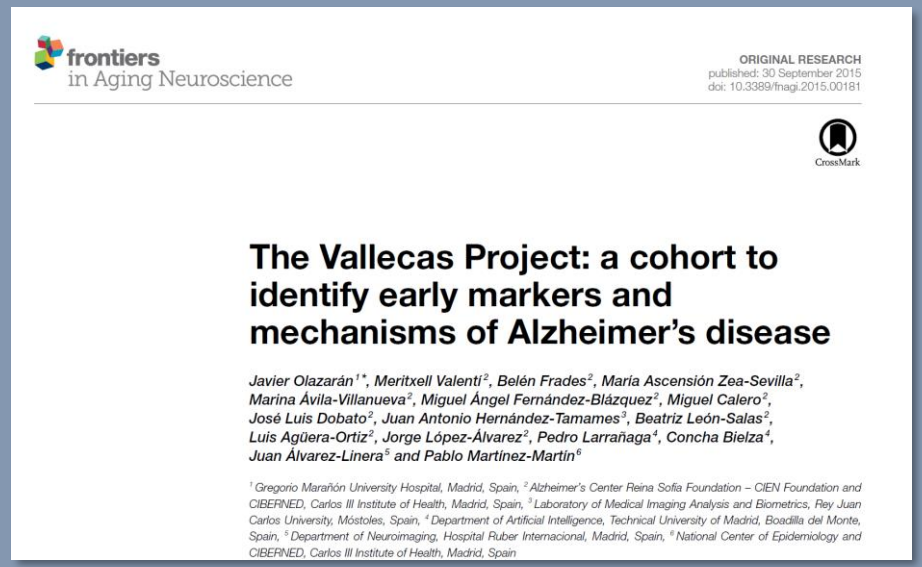
El Proyecto Vallecas





btcien
Banco de Tejidos de la Fundación Cien



frontiers in Aging Neuroscience

ORIGINAL RESEARCH
published: 30 September 2015
doi: 10.3389/fnagi.2015.00181

CrossMark

The Vallecas Project: a cohort to identify early markers and mechanisms of Alzheimer's disease

Javier Olazarán[1], Meritxell Valentí[2], Belén Frades[2], María Ascensión Zea-Sevilla[2], Marina Ávila-Villanueva[2], Miguel Ángel Fernández-Blázquez[2], Miguel Calero[2], José Luis Dobato[2], Juan Antonio Hernández-Tamames[3], Beatriz León-Salas[2], Luis Agüera-Ortiz[2], Jorge López-Álvarez[2], Pedro Larrañaga[4], Concha Bielza[4], Juan Álvarez-Linera[5] and Pablo Martínez-Martín[6]*

[1] Gregorio Marañón University Hospital, Madrid, Spain, [2] Alzheimer's Center Reina Sofía Foundation – CIEN Foundation and CIBERNED, Carlos III Institute of Health, Madrid, Spain, [3] Laboratory of Medical Imaging Analysis and Biometrics, Rey Juan Carlos University, Móstoles, Spain, [4] Department of Artificial Intelligence, Technical University of Madrid, Boadilla del Monte, Spain, [5] Department of Neuroimaging, Hospital Ruber Internacional, Madrid, Spain, [6] National Center of Epidemiology and CIBERNED, Carlos III Institute of Health, Madrid, Spain

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Gerontology

Clinical Section: Research Article

Gerontology
DOI: 10.1159/000513182

Received: July 14, 2020
Accepted: November 14, 2020
Published online: January 11, 2021

Residence, Clinical Features, and Genetic Risk Factors Associated with Symptoms of COVID-19 in a Cohort of Older People in Madrid

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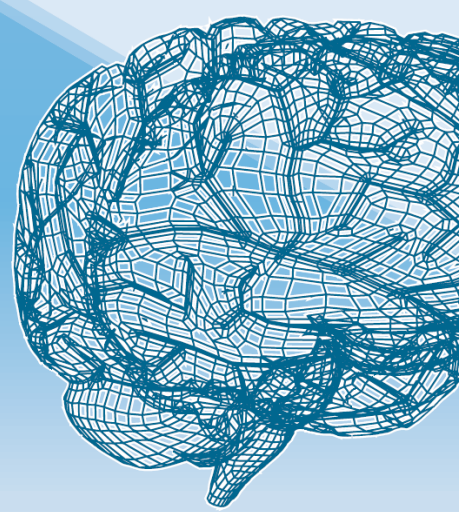

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JEFATURA DEL ESTADO

12945 *LEY 14/2007, de 3 de julio, de Investigación biomédica.*

JUAN CARLOS I

REY DE ESPAÑA

A todos los que la presente vieren y entendieren.
Sabed: Que las Cortes Generales han aprobado y Yo vengo en sancionar la siguiente ley.

PREÁMBULO

I

humanos y las infraestructuras necesarias para impulsarla. Tanto la Administración General del Estado, en ejercicio de la competencia de fomento y coordinación general de la investigación científica y técnica que prevé el artículo 149.1.15.ª de la Constitución, como las administraciones de las comunidades autónomas, que en sus Estatutos han recogido de manera unánime la competencia de fomento de la investigación, están configurando estructuras de investigación biomédica en red abiertas a la participación y colaboración de las entidades privadas, de los distintos organismos de investigación y las universidades y de los propios centros del Sistema Nacional de Salud, con el objetivo de aprovechar de manera eficiente los recursos disponibles y obtener, a partir de la aportación de los distintos grupos de investigación, unos resultados trasladables a la mejora de la salud de los ciudadanos. De esta forma se cumple en el ámbito de la investigación biomédica con el mandato recogido en el artículo 44.2 de la Constitución Española, que encomienda

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Datos del Donante

Nombre	Primer Apellido	Segundo Apellido	D.N.I.	Edad

Persona del Biobanco ***BT-CIEN*** que informa

Nombre	Apellidos	DNI	Nº Col.
Dr.			

El abajo firmante declara haber sido informado por escrito y verbalmente sobre el programa de donación de tejido cerebral y su destino exclusivo para la investigación biomédica en enfermedades neurológicas, habiendo comprendido su significado y estar conforme con ello:

Autoriza la donación post mórtem del tejido cerebral, al Biobanco de Tejidos de la Fundación del Centro de Investigación de Enfermedades Neurológicas, ***BT-CIEN***, para que en el futuro, sus muestras y los datos asociados, puedan ser cedidos gratuitamente para su uso en proyectos de investigación en enfermedades neurológicas, siguiendo el procedimiento establecido por la Ley de Investigación Biomédica (L.I.B. 14/2007), y según el protocolo de este Biobanco.

Entiende además que esta decisión que ahora formaliza con su firma, en virtud de la Ley de Investigación Biomédica y la Ley de Protección de Datos Personales (L.O.P.D. 15/1999) y sus normas de desarrollo, podrá revocarla en cualquier momento, sin necesidad de justificación alguna.

El DONANTE	PERSONA QUE INFORMA
Firma	Dr. Banco de Tejidos de la Fundación CIEN

En Madrid, a , de , de 201

C/. Valderrebollo, nº 5. 28031 Madrid. Tel.: 91 385 22 00 Fax: 91 385 21 18 e-mail: biobanco@fundacioncien.es
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ISO 9001:2008

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DOCUMENTO ACREDITATIVO PARA LA DONACIÓN POSTMÓRTEM DE TEJIDO CEREBRAL ANTE TESTIGOS

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Datos del Testigo/ Familiar/ Cuidador

Nombre	Apellidos	D.N.I.	Relación

Persona del Biobanco ***BT-CIEN*** que informa

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Dr.			

El abajo firmante como testigo / familiar/ cuidador, declara haber sido informado por escrito y verbalmente sobre el programa de donación de tejido cerebral del ***BT-CIEN*** y su destino exclusivo para la investigación biomédica en enfermedades neurológicas y habiendo comprendido su significado, está conforme con ello.

Acredita así mismo, que no le consta que el Donante a lo largo de su vida manifestase oposición a la donación ni dejó constancia expresa de ello y con su firma actúa como testigo de la Donación e incorporación al Banco de Tejidos de la Fundación CIEN del material biológico extraído **post mórtem** al Donante, el día mediante autopsia neuropatológica, realizada en las instalaciones de este Biobanco para que en el futuro puedan ser cedidos gratuitamente para su uso en proyectos de investigación en enfermedades neurológicas, siguiendo el procedimiento establecido por la Ley de Investigación Biomédica (L.I.B. 14/2007) y el protocolo del ***BT-CIEN***.

EL TESTIGO/ FAMILIAR/ CUIDADOR	PERSONA DEL BIOBANCO QUE INFORMA
Firma	Banco de Tejidos de la Fundación CIEN

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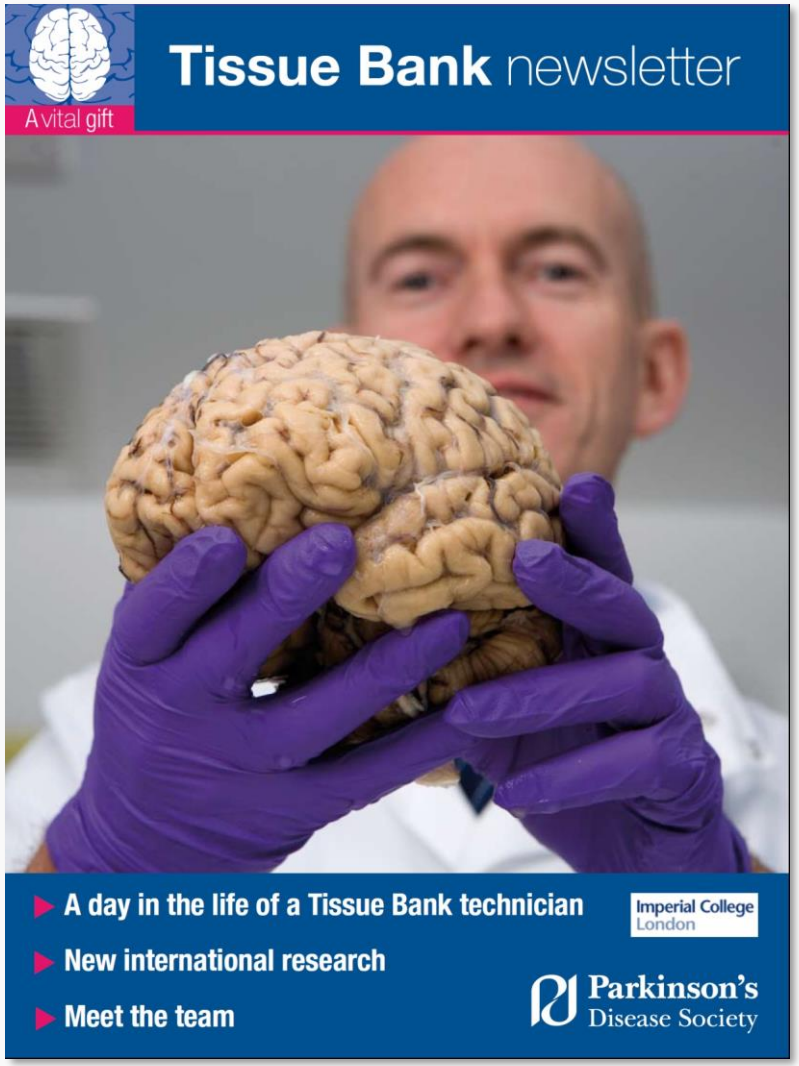
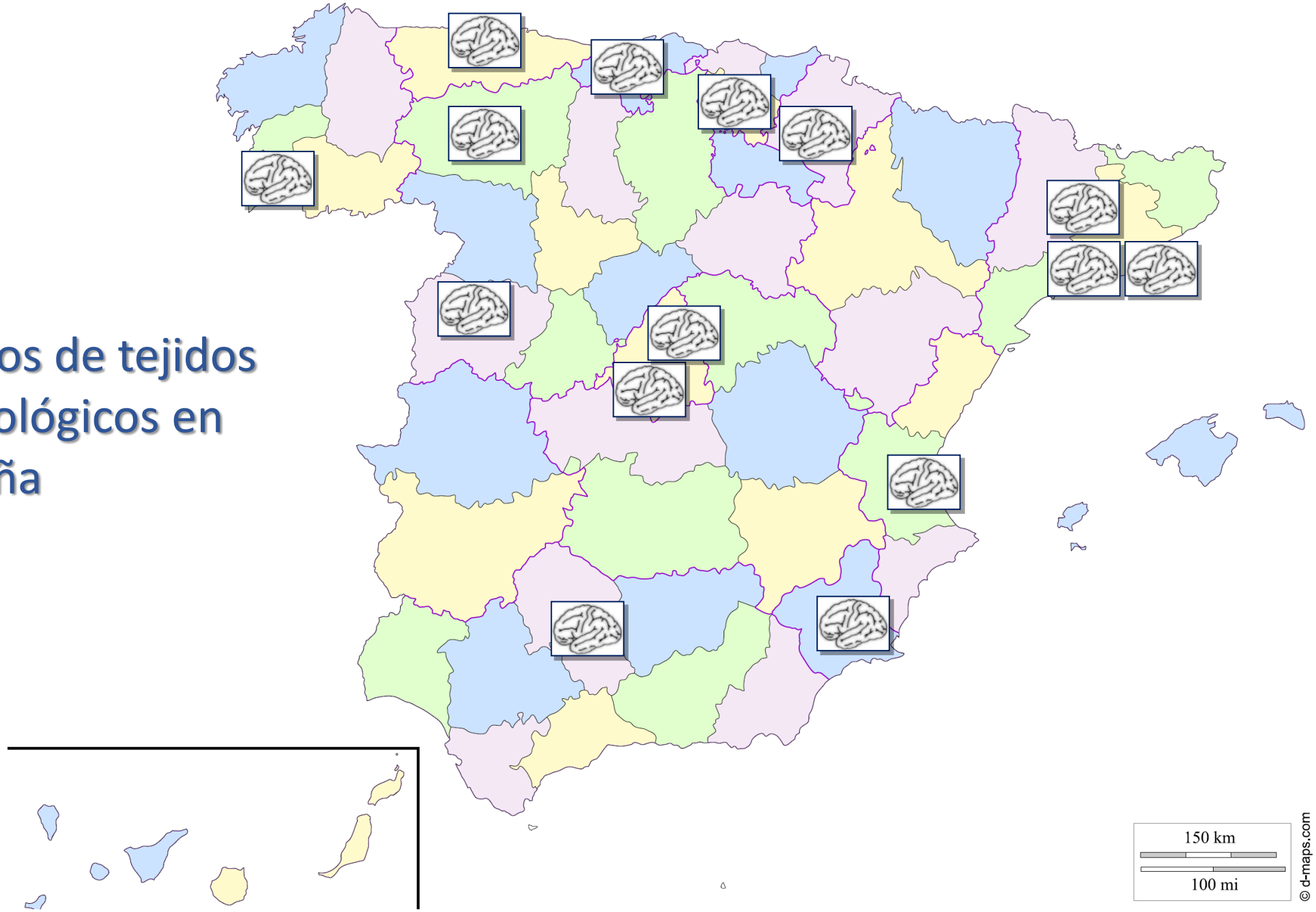
Bancos de cerebros – Bancos de tejidos neurológicos

- Donación de tejido post mortem.
- Obtención de tejido fijado y tejido fresco congelado.
- Diagnóstico neuropatológico en el tejido fijado.



Bancos de tejidos neurológicos en España



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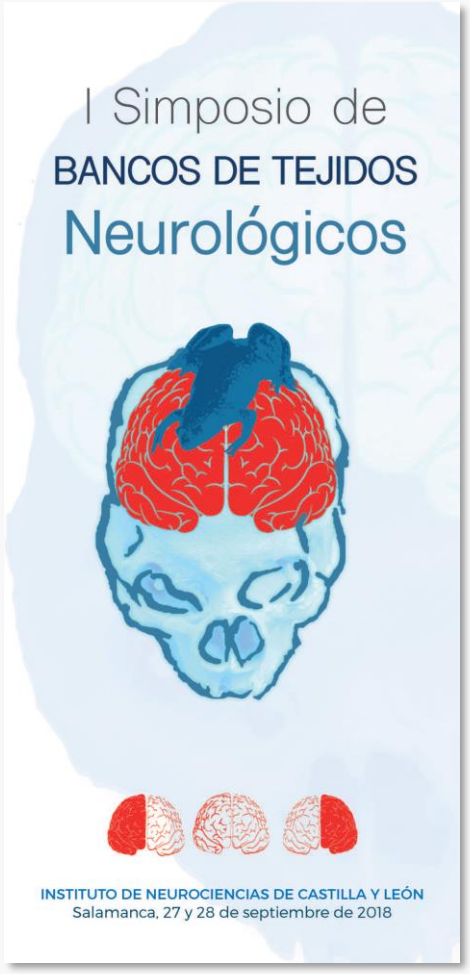
2018



I Symposium of Neurological Tissue Banks– Castilla y León Neuroscience Institute, Salamanca, September 27-28, 2018.

2019

First Joint Meeting of the Portuguese Society of Neuropathology and the Spanish Club of Neuropathology – Colegio Arzobispo Fonseca, Salamanca, October 7, 2019.

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Programas de donación de tejido cerebral

Programa de donación interno

- Centro Alzheimer Fundación Reina Sofía
- Seguimiento semestral, RM, muestras de sangre

165

Programa de donación externo

- Población general, residencias, hospitales
- No hay seguimiento de los donantes

552

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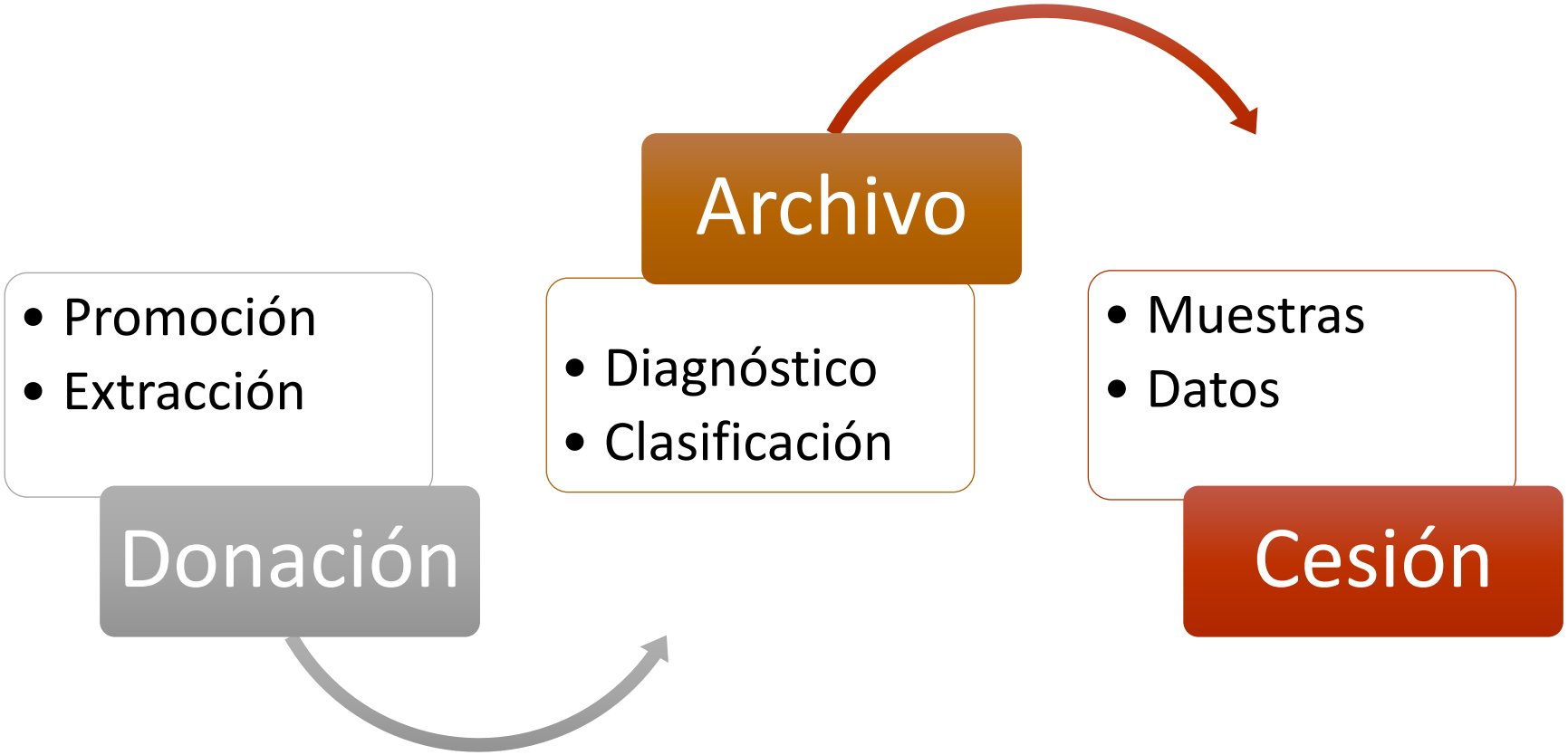
Procedimientos básicos del BT-CIEN



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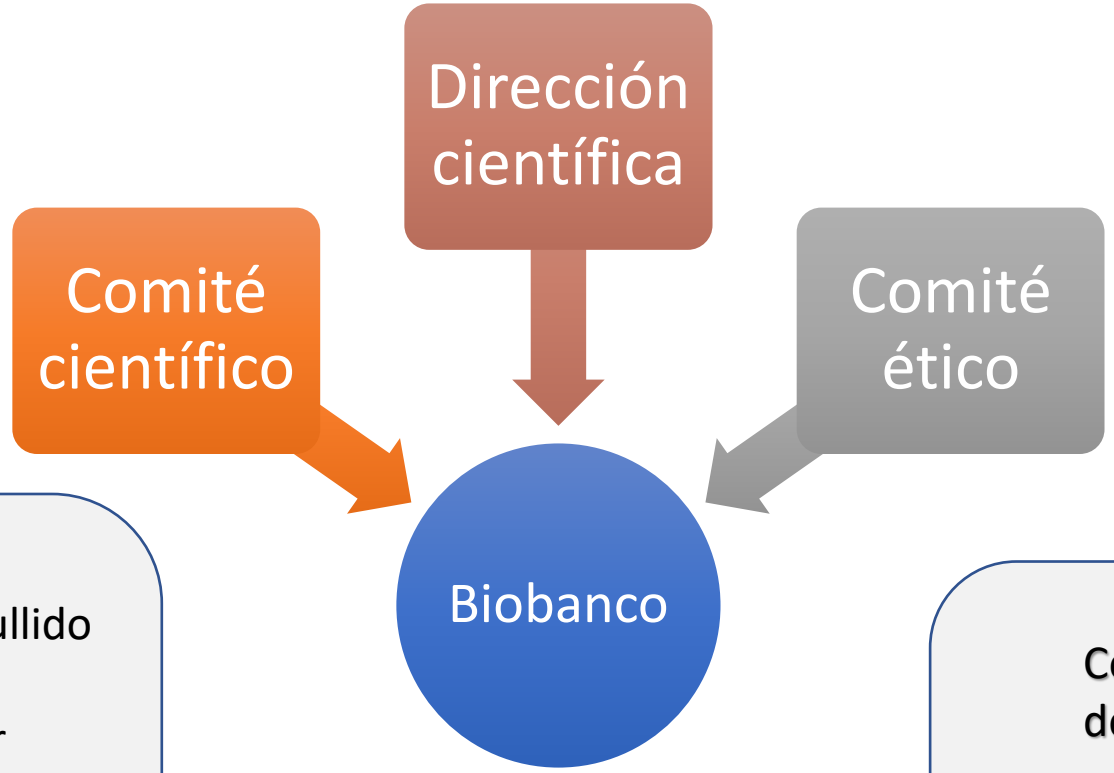
BT-CIEN: Dirección y comités externos



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- Familiares
  - Informe Neuropatológico
  - Diagnóstico definitivo
  - ¿Enfermedad genética?
- Clínicos
  - Informe Neuropatológico
  - Correlación clinicopatológica
  - Formación
  - Investigación clínica
- Investigado-res
  - Muestras biológicas
  - Clasificación de los casos
  - Datos clínicos asociados
  - Control de calidad (muestras y datos)

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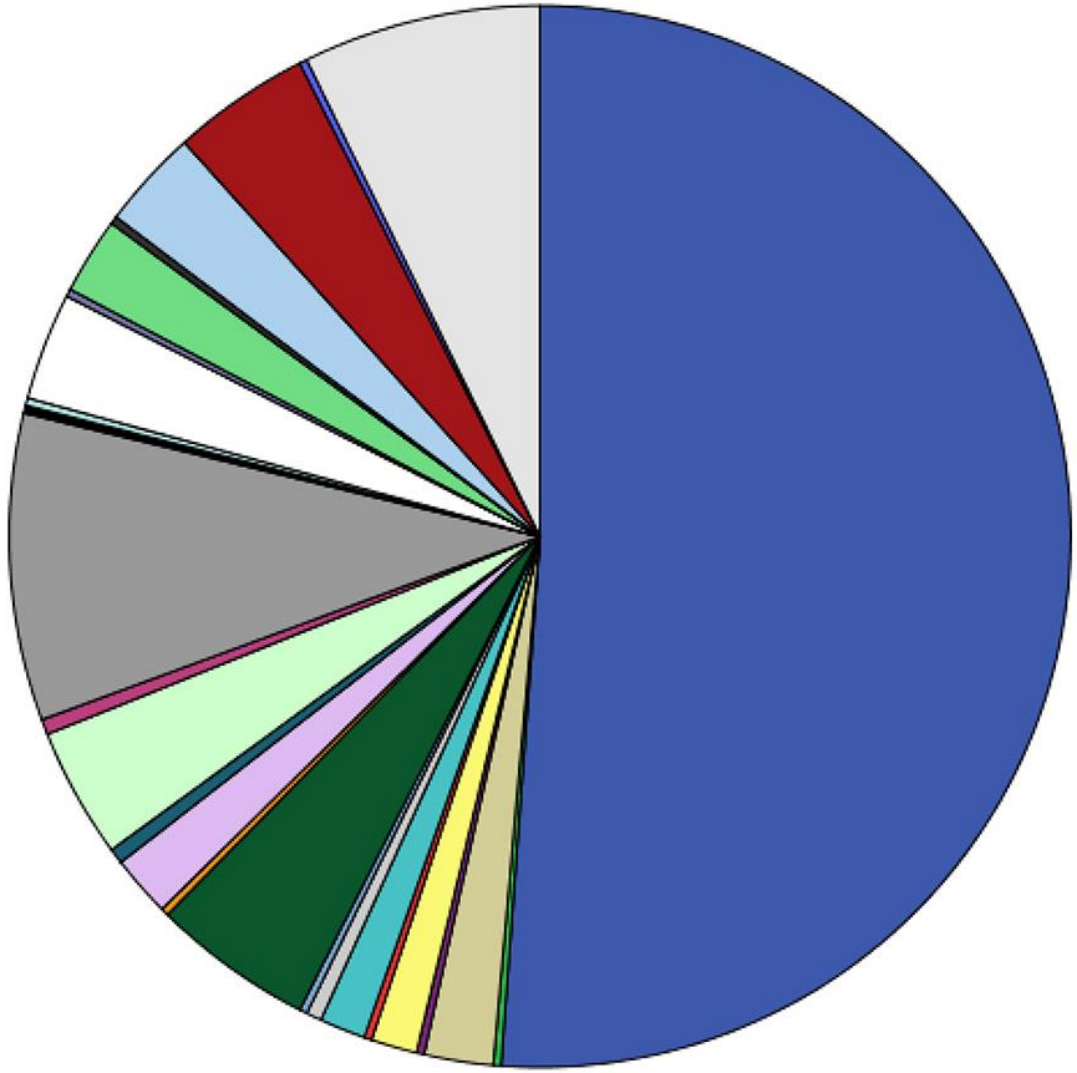
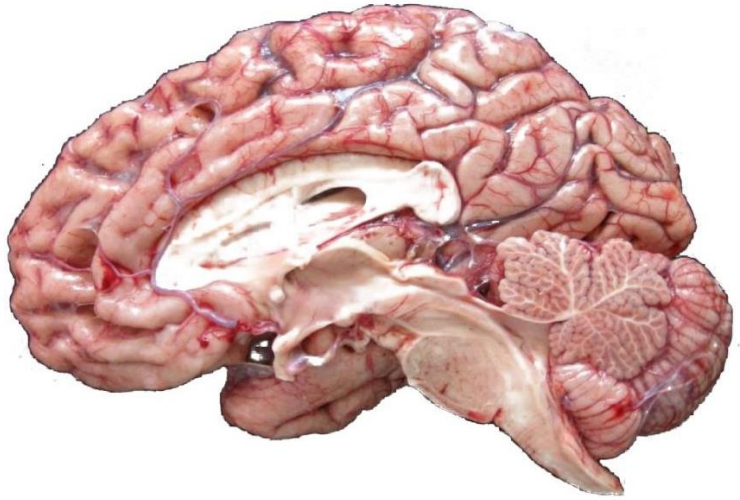
Diagnósticos neuropatológicos principales

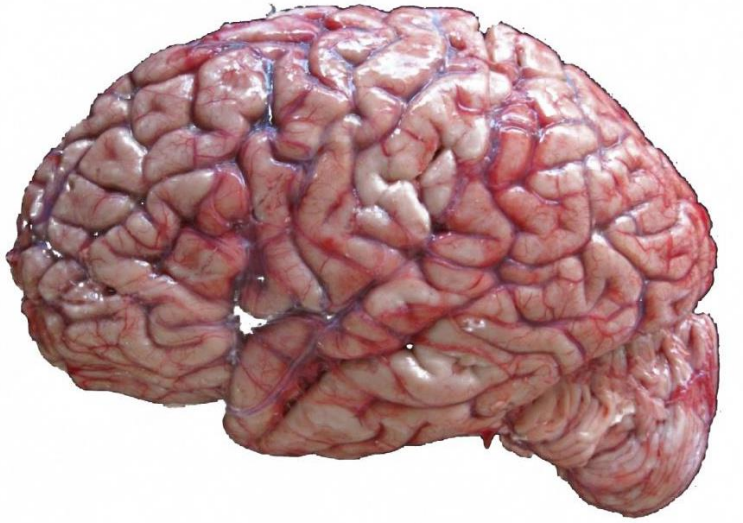


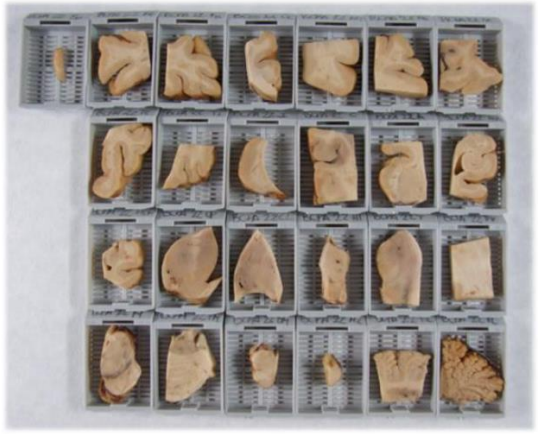
ALZH	Enfermedad de Alzheimer esporádica
ALZHf	Enfermedad de Alzheimer familiar
AMS	Atrofia multisistémica
ARTAG	ARTAG
ATAXIA	Ataxias degenerativas
CADASIL	CADASIL
CONT	Cerebros de control
DCB	Degeneración córticobasal
DCB-PSP	Degeneración córtico-basal - PSP
DCL	Demencia con cuerpos de Lewy
DLFT-FUS	Degeneración lobar frontotemporal - FUS
DLFT-PICK	Degeneración lobar frontotemporal - Pick
DLFT-TAU	Degeneración lobar frontotemporal - tau
DLFT-TDP	Degeneración lobar frontotemporal - TDP
EGA	Enfermedad de granos argirófilos
ELA	Esclerosis lateral amiotrófica
ELP	Esclerosis lateral primaria
HPN	Hidrocefalia a presión normal
HUNT	Enfermedad de Huntington
INESP	Hallazgos inespecíficos
LEWY	Enfermedad de cuerpos de Lewy
OPCA	Atrofia olivopontocerebelosa
PARK	Enfermedad de Parkinson
PSP	Parálisis supranuclear progresiva
TAUP	Taupatías (otras)
VASC	Enfermedad cerebrovascular



Derecho ⟶ Congelación

- Diagnóstico molecular
- Investigación molecular



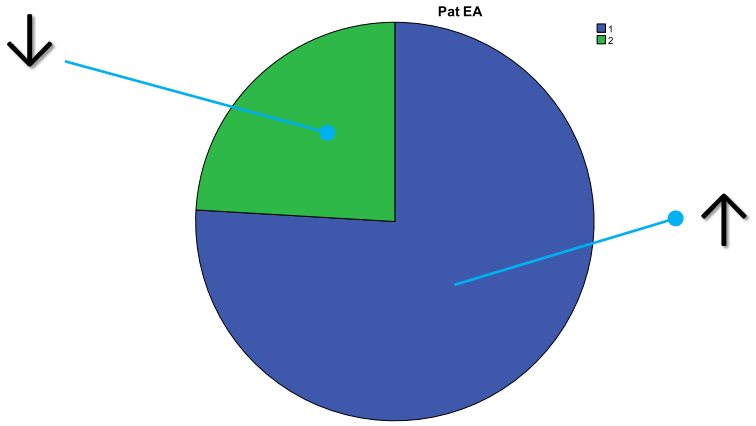


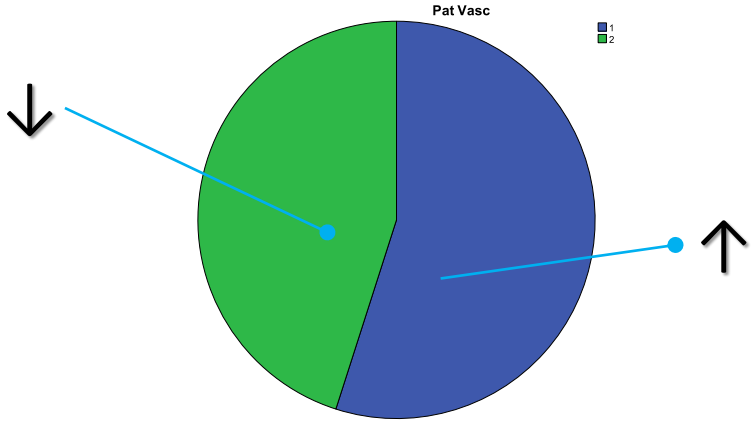
Izquierdo ⟶ Neuropatología

- Diagnóstico neuropatológico
- Investigación neuropatológica y clinicopatológica

Alzheimer's Project cohort (n = 165): main pathological groups

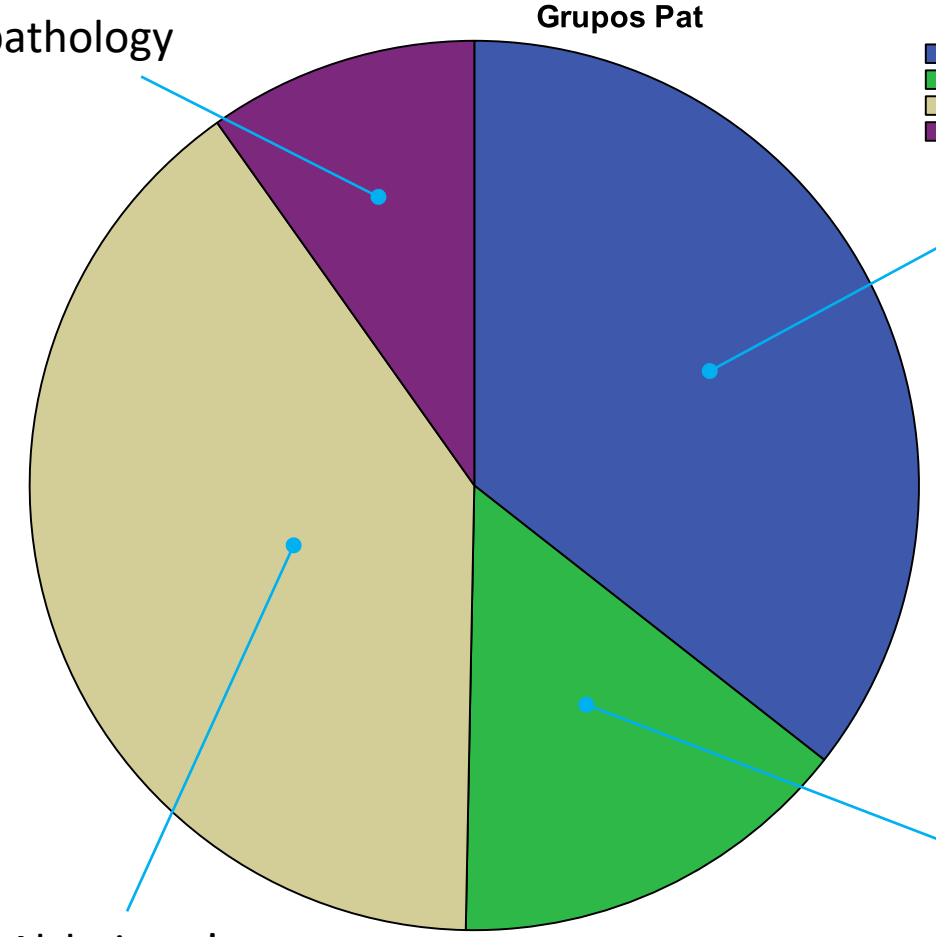
Alzheimer's pathology





Vascular pathology

No Alzheimer's
No Vascular
pathology

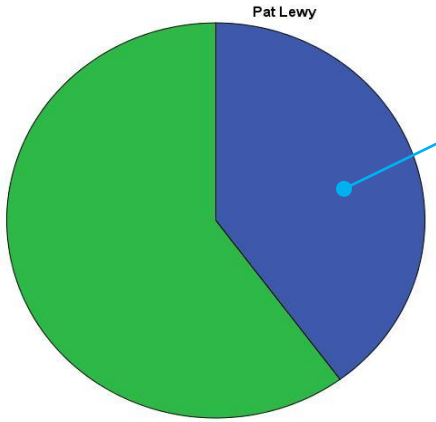


Alzheimer's
pathology

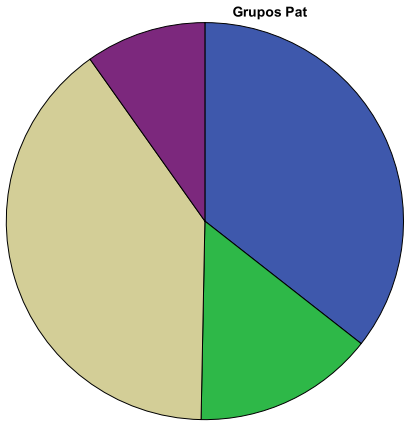
Alzheimer's
+ Vascular
pathology

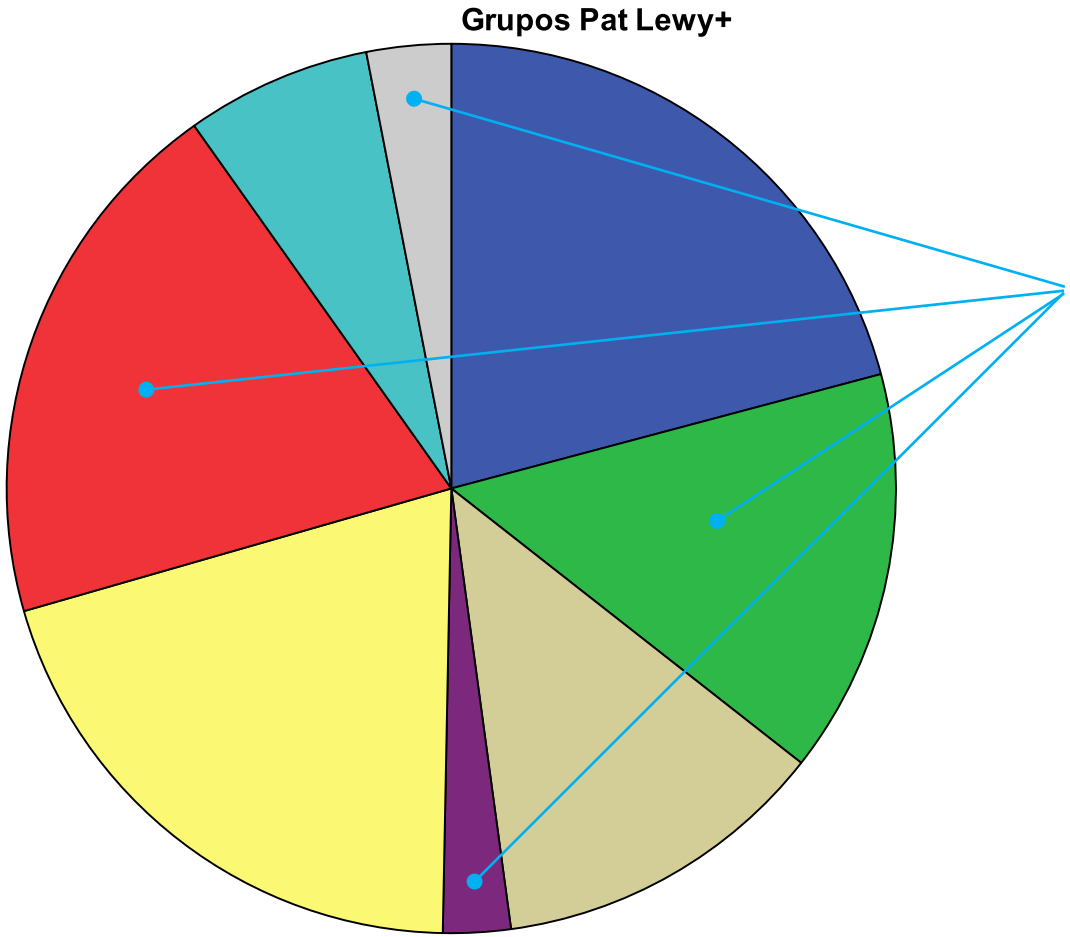
Vascular
pathology

Alzheimer's Project cohort (n = 165): main pathological groups



+ Lewy body pathology





+ Lewy body pathology


Toma de muestras Transferencia
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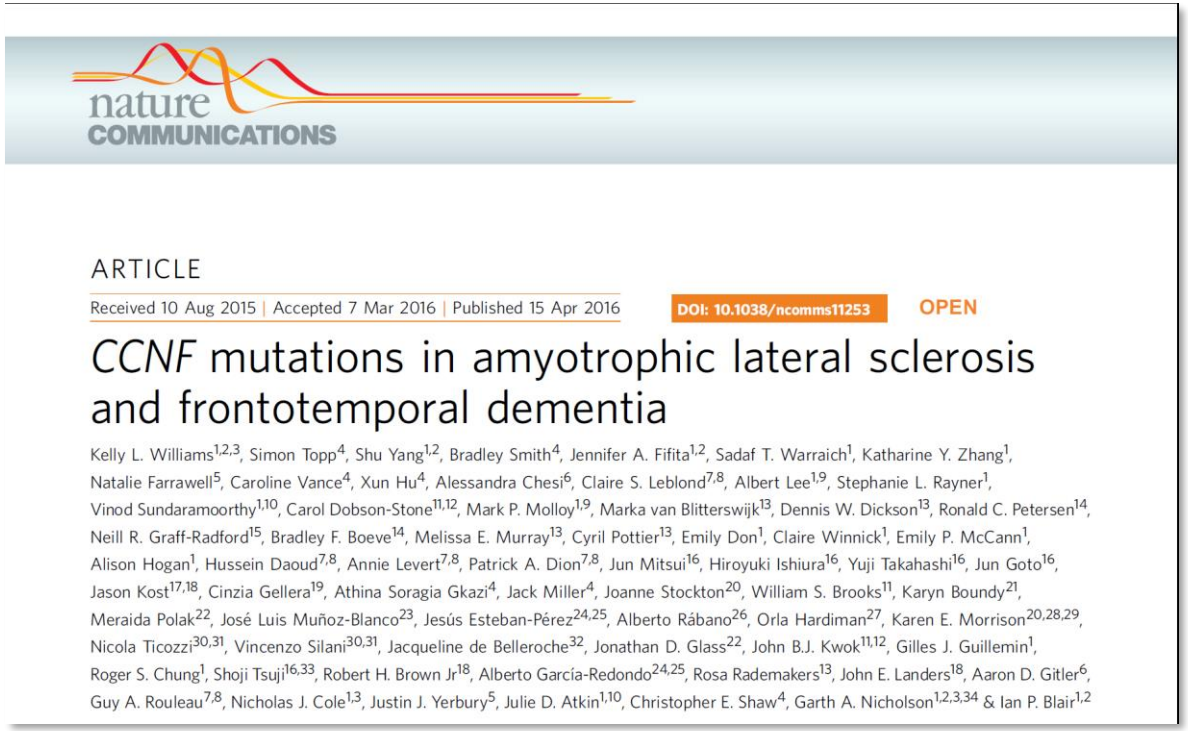

nature COMMUNICATIONS

ARTICLE

Received 10 Aug 2015 | Accepted 7 Mar 2016 | Published 15 Apr 2016

DOI: 10.1038/ncomms11253 OPEN

CCNF mutations in amyotrophic lateral sclerosis and frontotemporal dementia

Kelly L. Williams[1,2,3], Simon Topp[4], Shu Yang[1,2], Bradley Smith[4], Jennifer A. Fifita[1,2], Sadaf T. Warraich[1], Katharine Y. Zhang[1], Natalie Farrawell[5], Caroline Vance[4], Xun Hu[4], Alessandra Chesi[6], Claire S. Leblond[7,8], Albert Lee[1,9], Stephanie L. Rayner[1], Vinod Sundaramoorthy[1,10], Carol Dobson-Stone[11,12], Mark P. Molloy[1,9], Marka van Blitterswijk[13], Dennis W. Dickson[13], Ronald C. Petersen[14], Neill R. Graff-Radford[15], Bradley F. Boeve[14], Melissa E. Murray[13], Cyril Pottier[13], Emily Don[1], Claire Winnick[1], Emily P. McCann[1], Alison Hogan[1], Hussein Daoud[7,8], Annie Levert[7,8], Patrick A. Dion[7,8], Jun Mitsui[16], Hiroyuki Ishiura[16], Yuji Takahashi[16], Jun Goto[16], Jason Kost[17,18], Cinzia Gellera[19], Athina Soragia Gkazi[4], Jack Miller[4], Joanne Stockton[20], William S. Brooks[11], Karyn Boundy[21], Meraida Polak[22], José Luis Muñoz-Blanco[23], Jesús Esteban-Pérez[24,25], Alberto Rábano[26], Orla Hardiman[27], Karen E. Morrison[20,28,29], Nicola Ticozzi[30,31], Vincenzo Silani[30,31], Jacqueline de Belleroche[32], Jonathan D. Glass[22], John B.J. Kwok[11,12], Gilles J. Guillemin[1], Roger S. Chung[1], Shoji Tsuji[16,33], Robert H. Brown Jr[18], Alberto García-Redondo[24,25], Rosa Rademakers[13], John E. Landers[18], Aaron D. Gitler[6], Guy A. Rouleau[7,8], Nicholas J. Cole[1,3], Justin J. Yerbury[5], Julie D. Atkin[1,10], Christopher E. Shaw[4], Garth A. Nicholson[1,2,3,34] & Ian P. Blair[1,2]

Here we use genome-wide linkage analysis in a large ALS/FTD kindred to identify a novel disease locus on chromosome 16p13.3. Whole-exome sequencing identified a *CCNF* missense mutation at this locus. Interrogation of international cohorts identified additional novel *CCNF* variants in familial and sporadic ALS and FTD.

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doi:10.1093/brain/awy137 BRAIN 2018: 0; 1–17 | 1

BRAIN
A JOURNAL OF NEUROLOGY

Clinical, genetic and neuropathological characterization of spinocerebellar ataxia type 37

Marc Corral-Juan,[1] Carmen Serrano-Munuera,[2] Alberto Rábano,[3] Daniel Cota-González,[1] Anna Segarra-Roca,[1] Lourdes Ispierto,[4] Antonio Tomás Cano-Orgaz,[5] Astrid D. Adarmes,[6] Carlota Méndez-del-Barrio,[6] Silvia Jesús,[6] Pablo Mir,[6,7] Victor Volpini,[8] Ramiro Alvarez-Ramo,[4] Ivelisse Sánchez[1] and Antoni Matilla-Dueñas[1]

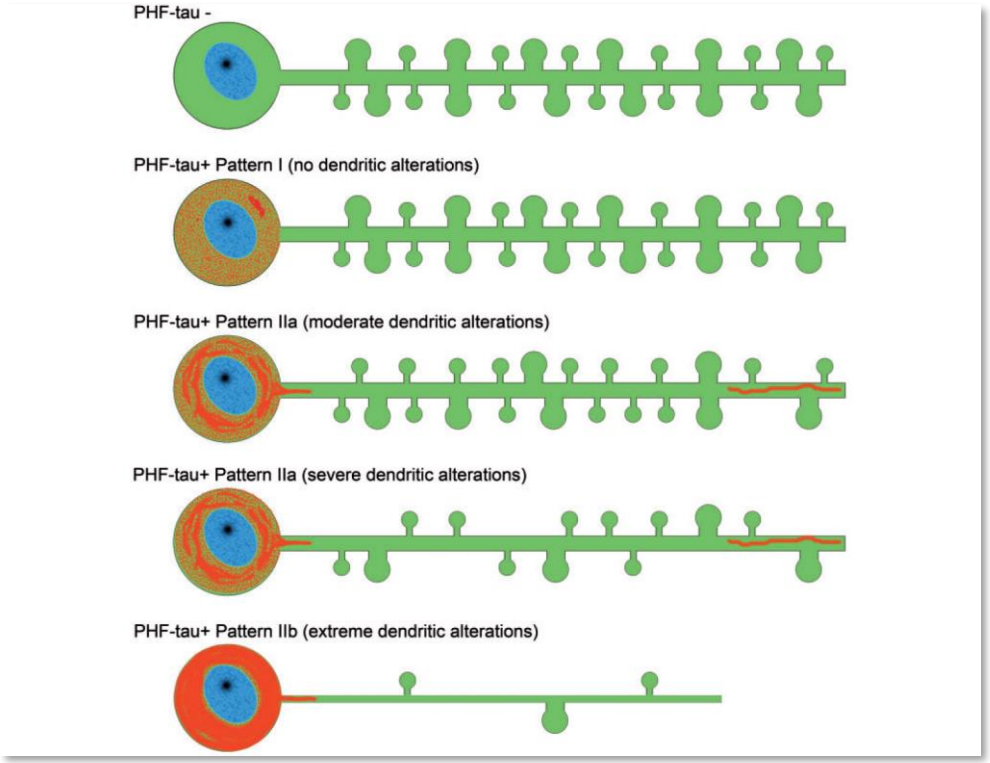
We describe the clinical-genetic correlation and the first SCA37 neuropathological findings caused by dysregulation of cerebellar DAB1 expression.

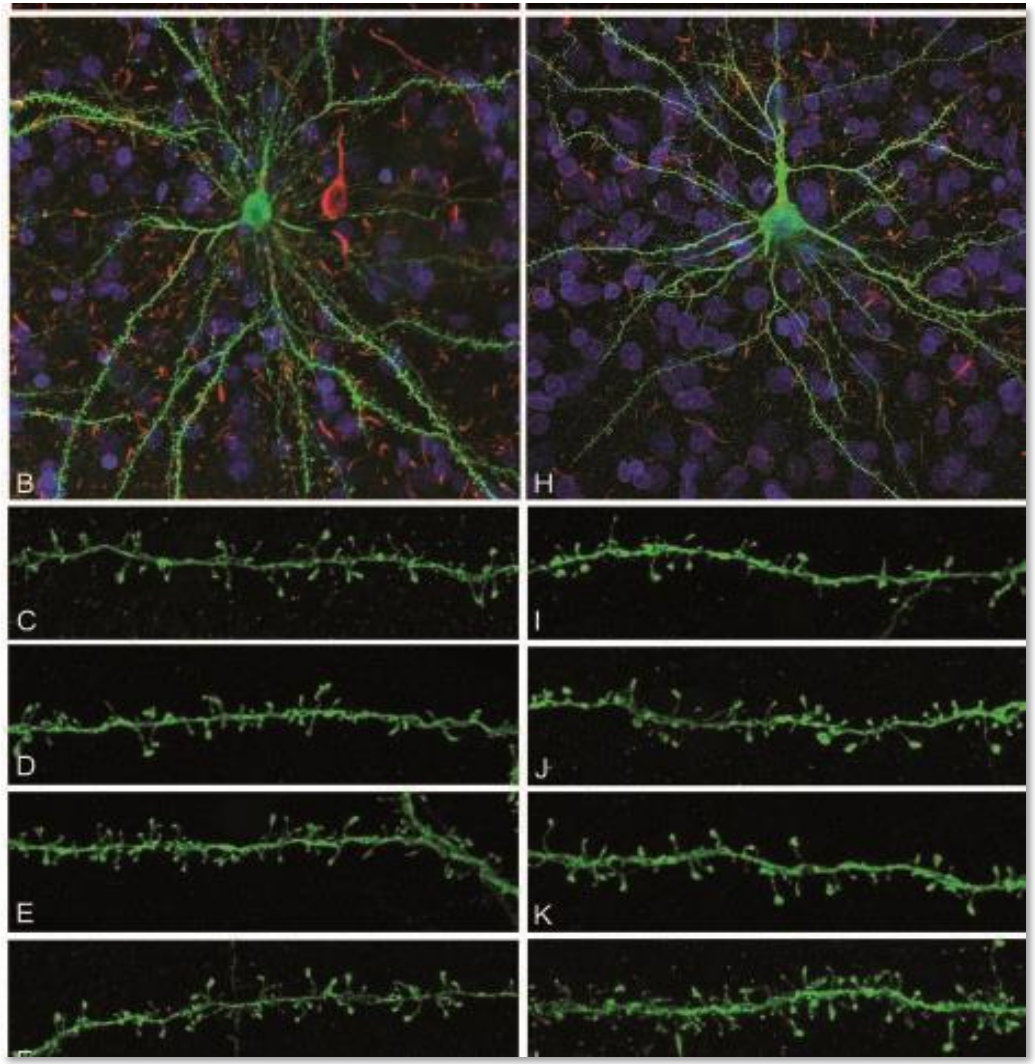
doi:10.1093/brain/awt088 Brain 2013: Page 1 of 16 | 1

BRAIN
A JOURNAL OF NEUROLOGY

The influence of phospho-tau on dendritic spines of cortical pyramidal neurons in patients with Alzheimer's disease

Paula Merino-Serrais,[1,2,3] Ruth Benavides-Piccione,[1,2,3] Lidia Blazquez-Llorca,[1,2,3] Asta Kastanauskaite,[1,2,3] Alberto Rábano,[4] Jesús Avila[3,5] and Javier DeFelipe[1,2,3]





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SCIENTIFIC REPORTS

OPEN

Different Brain Regions are Infected with Fungi in Alzheimer's Disease

Received: 19 May 2015
Accepted: 15 September 2015
Published: 15 October 2015

Diana Pisa[1], Ruth Alonso[1], Alberto Rábano[2], Izaskun Rodal[2] & Luis Carrasco[1]

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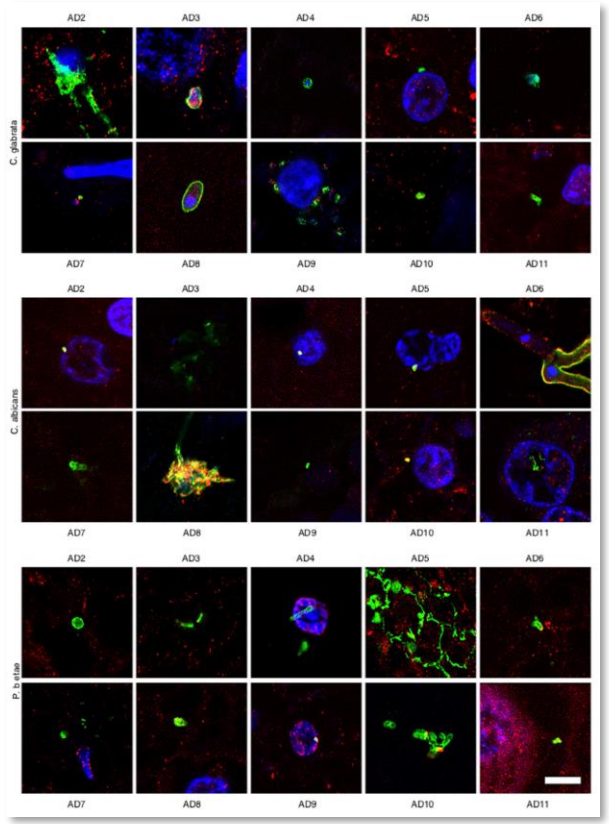

frontiers in Neuroscience

ORIGINAL RESEARCH
published: 08 March 2016
doi: 10.3389/fnins.2016.00086

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Corpora Amylacea of Brain Tissue from Neurodegenerative Diseases Are Stained with Specific Antifungal Antibodies

*Diana Pisa[1], Ruth Alonso[1], Alberto Rábano[2] and Luis Carrasco[1]**

[1] Centro de Biología Molecular "Severo Ochoa," Universidad Autónoma de Madrid, Madrid, Spain, [2] Department of Neuropathology and Tissue Bank, Unidad de Investigación Proyecto Alzheimer, Fundación Centro de Investigación de Enfermedades Neurologicas, Instituto de Salud Carlos III, Madrid, Spain

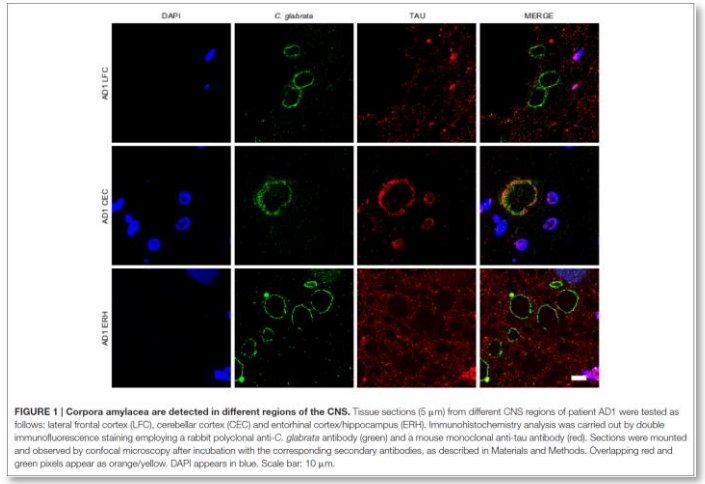

FIGURE 1 | Corpora amylacea are detected in different regions of the CNS. Tissue sections (5 μm) from different CNS regions of patient AD1 were tested as follows: lateral frontal cortex (LFC), cerebellar cortex (CEC) and entorhinal cortex/hippocampus (ERH). Immunohistochemistry analysis was carried out by double immunofluorescence staining employing a rabbit polyclonal anti-*C. glabrata* antibody (green) and a mouse monoclonal anti-tau antibody (red). Sections were mounted and observed by confocal microscopy after incubation with the corresponding secondary antibodies, as described in Materials and Methods. Overlapping red and green pixels appear as orange/yellow. DAPI appears in blue. Scale bar: 10 μm.

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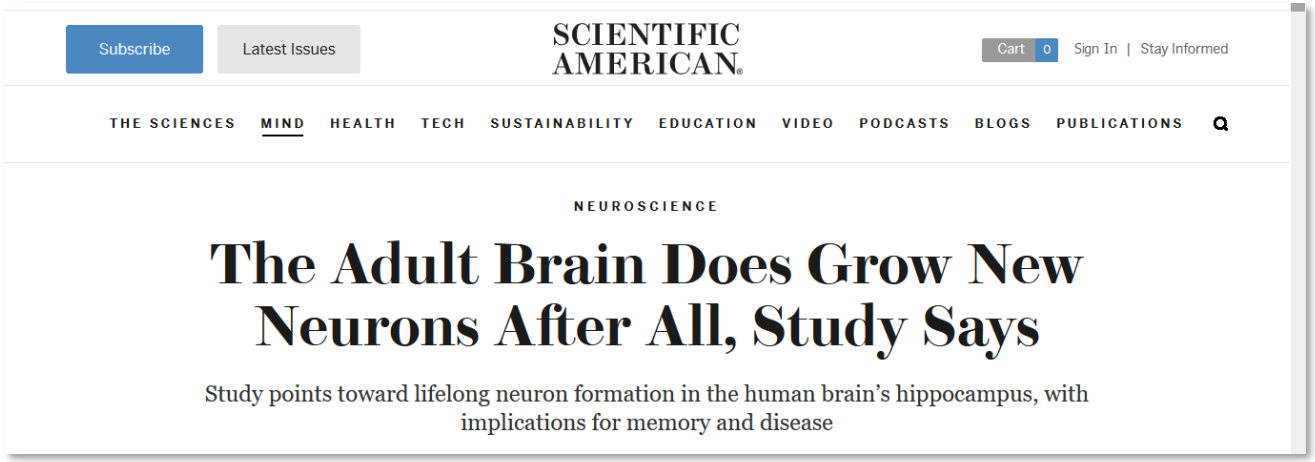

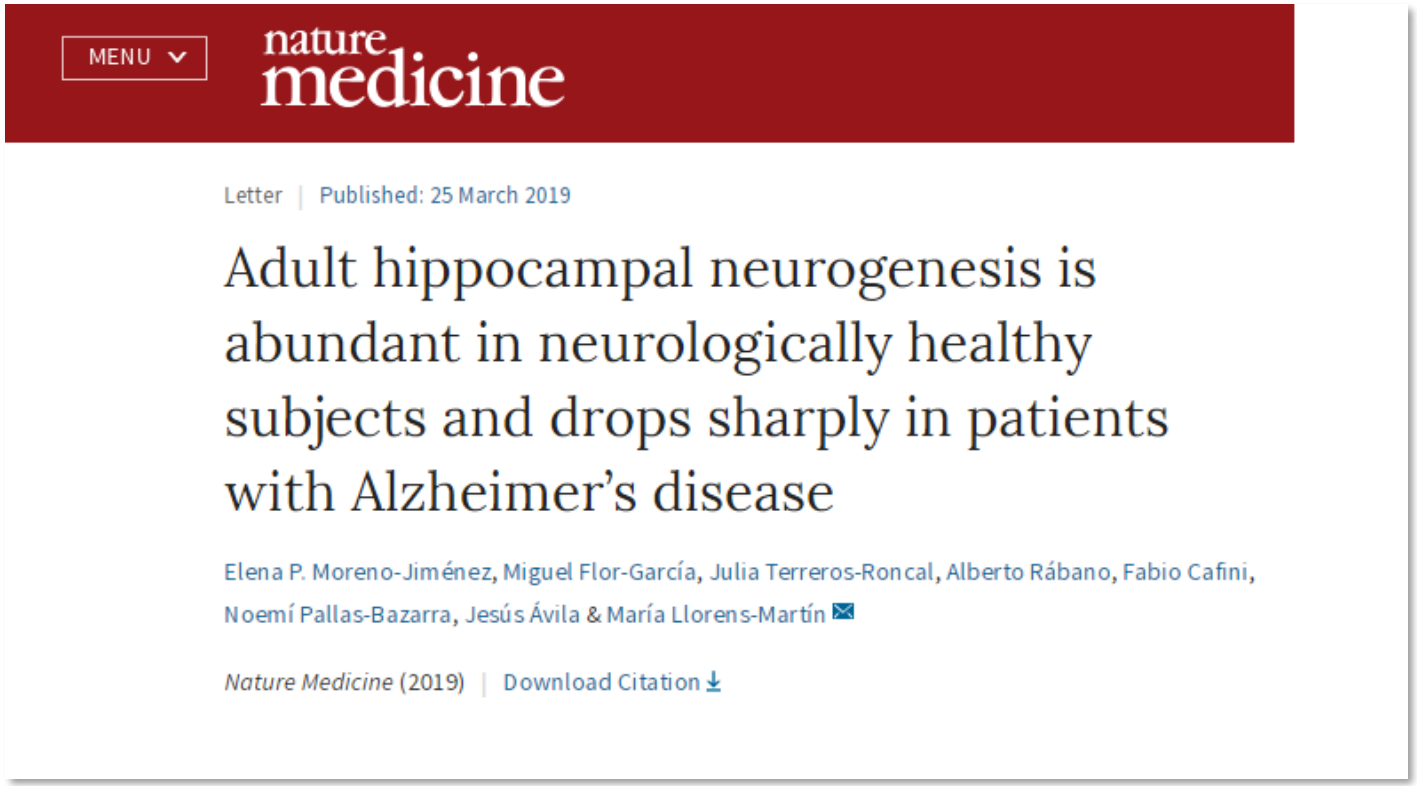

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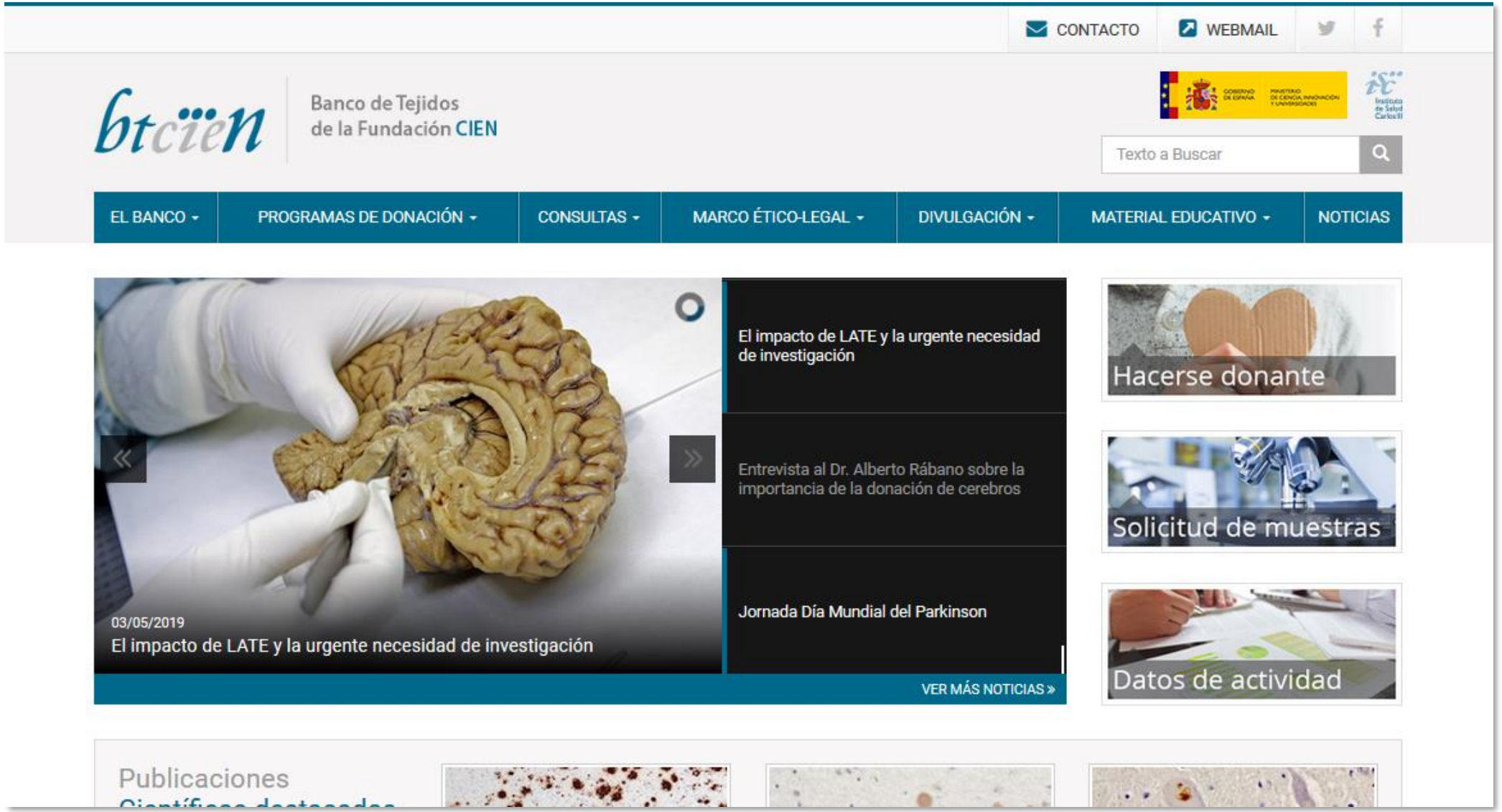
https://www.google.com/search?client=firefox-b-e&q=banco+de+tejidos+cien



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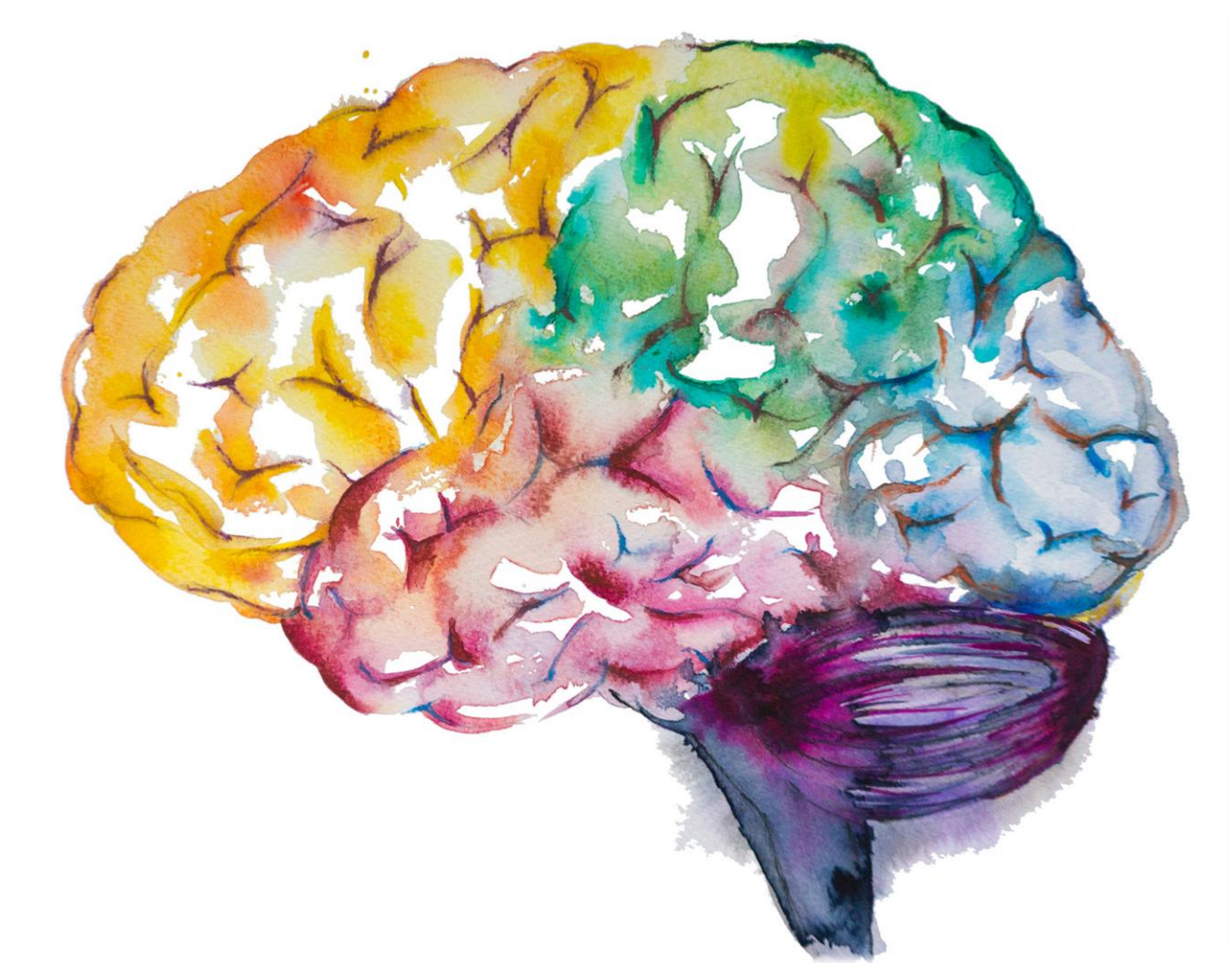

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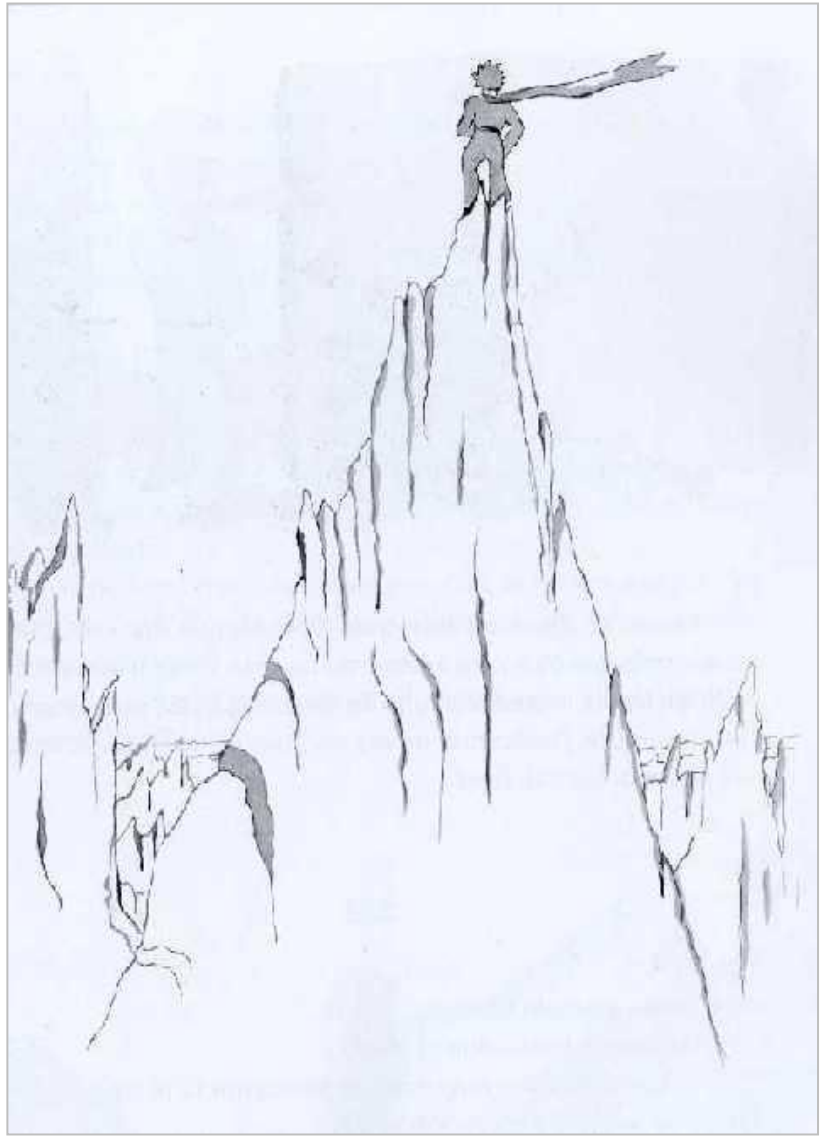
“¿Qué puedo esperar?”

Contribución de los estudios clínico-patológicos al conocimiento y al tratamiento de la enfermedad.



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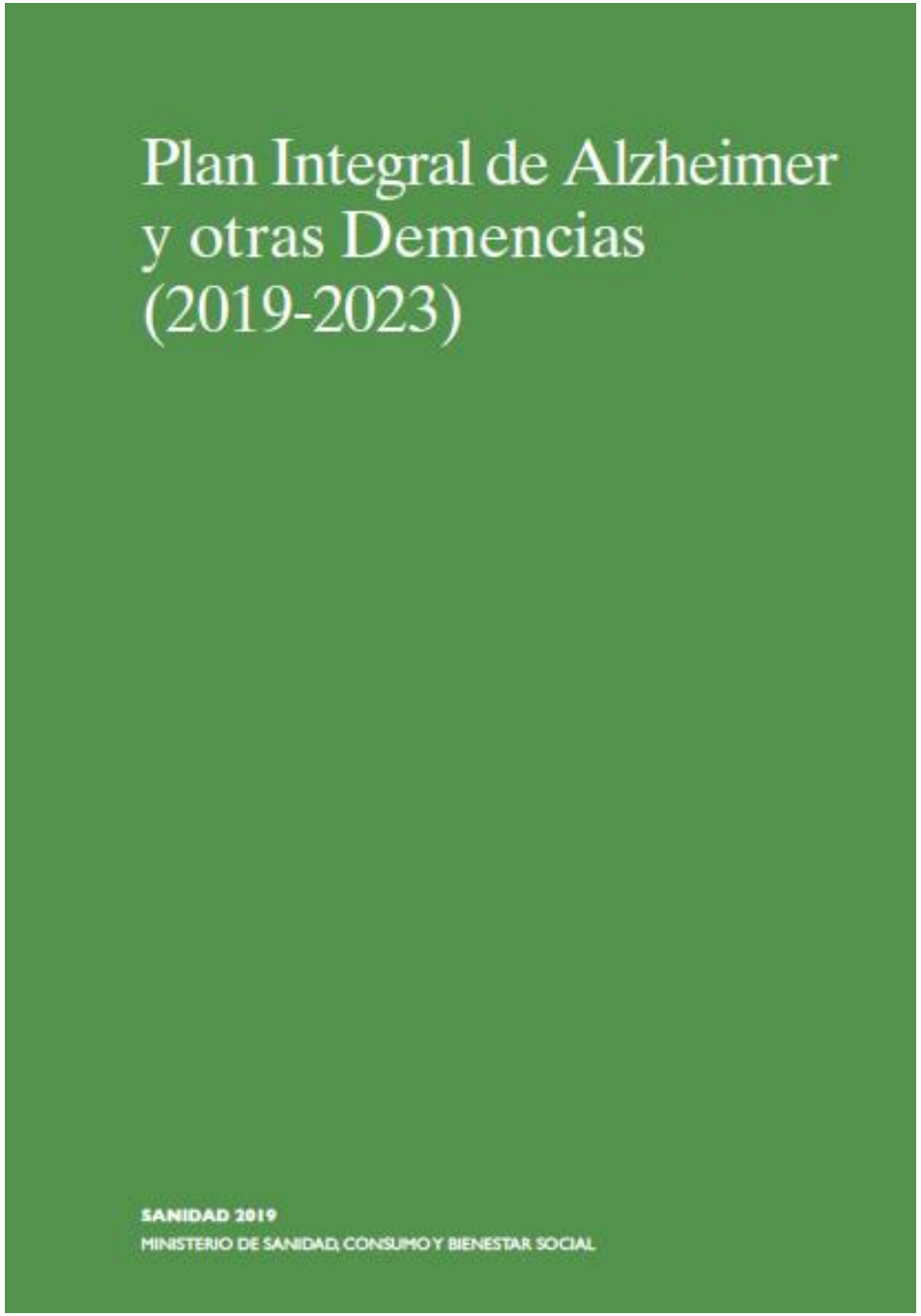

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Índice

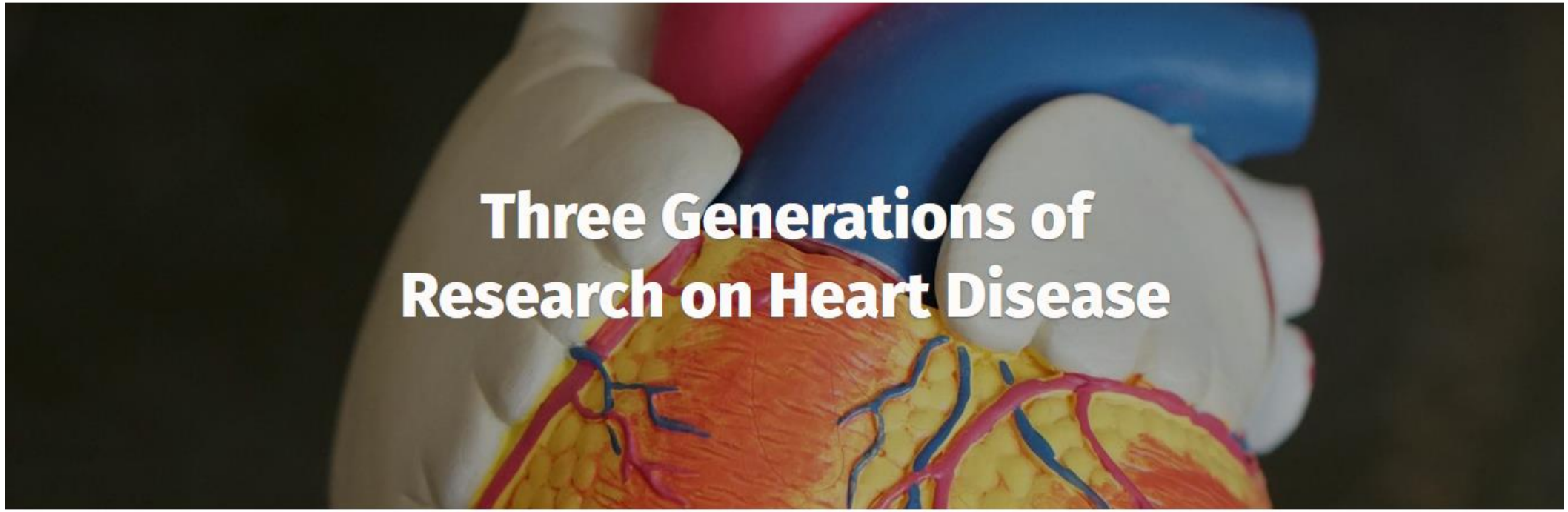
- España ha forjado una buena red de bancos de cerebros y tejidos neurológicos. Dentro de la Plataforma de Biobancos ISCIII se acaba de poner en marcha el grupo de trabajo del Banco de Tejidos Neurológicos GT-BTN, para crear un protocolo de extracción y procesamiento de tejido cerebral para todos los hospitales de la red, un protocolo de donación de tejido cerebral en extracción de órganos para trasplante, un protocolo para la obtención de tejido cerebral en autopsias médico-legales, la incorporaciones de las colecciones al Eurobiobank, un programa de formación específico de BTN, un programa de control, de calidad específico para BTN, la codificación SNOMED-CT de las donaciones del Grupo, y la promoción de diversos estudios colaborativos nacionales (DEGESCO, COPPADIS) e internacionales (ENROLL), entre otras.
- Sin embargo, el 86% de los cuidadores/as de personas con alzhéimer desconoce la posibilidad de donación de cerebro o la existencia de estos bancos en su área.
- Numerosos centros públicos y privados participan activamente en la realización de ensayos clínicos promovidos por la industria farmacéutica o los propios investigadores sobre nuevos fármacos y estudios observacionales. La mayoría de usuarios y muchos profesionales desconocen la existencia de tales estudios y cómo acceder a los mismos.
- Existen pocos proyectos de investigación sobre programas de prevención primaria y secundaria de alzhéimer y las iniciativas actuales no están coordinadas con el sistema sanitario, lo que impide capturar el continuo de la enfermedad de Alzheimer. La mayoría de los estudios de prevención secundaria son realizados por iniciativas con financiación no competitiva.
- Las estrategias de prevención primaria de la enfermedad de Alzheimer actualmente más aceptadas se basan en el control de factores de riesgo vascular y promoción de estilos de vida saludable en dieta y actividad física, intelectual y social. La validez etiológica de las asociaciones es todavía discutida y los datos experimentales son insuficientes.
- Es necesario avanzar en hacer participar a los pacientes, cuidadores familiares y sociedad en la investigación, establecer jornadas formativas utilizando el movimiento asociativo, la sociedad debe conocer la investigación que se está desarrollando con fondos públicos y los investigadores deben difundir sus resultados, fomentando una participación activa de pacientes, cuidadores y familiares facilitaríamos su incorporación a ensayos clínicos, donaciones etc.

Tabla 3: Objetivos, líneas de actuación y metas (horizonte 2023). Eje 3: Derechos, ética y dignidad de la persona

	4.2.3. Creación de una plataforma informativa de ensayos clínicos farmacológicos u otros estudios clínicos (incluyendo programas de donación de tejidos neurológicos) nacional accesible a los pacientes y sus familias. Utilizar el potencial del tejido asociativo en este ámbito y considerar dispositivos disponibles como la web de la Agencia Española de Medicamentos y Productos sanitarios (AEMPS).	Existencia de plataforma informativa.
	4.2.4. Potenciación de la plataforma de biobancos y, específicamente, de los biobancos de tejido neurológico, fomentando la donación de sujetos con estudios previos de biomarcadores en fases sintomáticas o asintomáticas. Los centros que realicen estudios de cohortes en sujetos sintomáticos o en riesgo establecerán vínculos con los biobancos para las muestras resultantes de los citados estudios. Las nuevas líneas estratégicas al respecto deben orientarse a una donación controlada, a partir de muestras perfectamente caracterizadas y fenotipadas. Los programas deberán incluir donaciones de participantes de cohortes longitudinales que parten de personas cognitiva y neurológicamente sanas cuando son incluidos en la cohorte. También se debe prever que la red de comunicación, recogida, etc. garantice condiciones para su adecuado desarrollo.	Transformaciones hacia una nueva generación de bancos de cerebros, mediante la vinculación con programas de investigación sobre cohortes de sujetos sintomáticos o a riesgo.
	4.2.5. Fomentar la investigación dirigida a la propuesta y validación de nuevas pruebas e instrumentos neuropsicológicos sensibles a las fases muy incipientes de la enfermedad de Alzheimer y su diferenciación con el envejecimiento no patológico. (Vinculado al objetivo 2.2.)	Vinculado a 2.2.
	4.2.6. Incorporar a pacientes familiares, asociaciones a actividades de investigación realizadas en CIBERNED, facilitando así el conocimiento de estas e incluso su participación en la toma de decisiones lo que contribuiría a incrementar el compromiso entre investigadores y sociedad.	Evaluación de la propuesta.

Framingham Heart Study
Three Generations of Dedication

About Participants For Researchers Internal Full Menu



Postmortem Brain Tissue Donation Program

The Framingham Heart Study has been conducting research on neurological disorders for decades. In 1997, we began a postmortem brain tissue donation program, which has contributed significant information on the aging process.

Analyzing postmortem brain tissue may confirm a previous diagnosis of stroke, Alzheimer's disease, Parkinson's disease or other neurological illness. It may also provide a diagnosis that was unclear earlier, document the extent of a disease or discover an unsuspected problem. Having a definite diagnosis may benefit the donor's family, by giving them a better idea of their genetic risks.

Participants →

Cohorts

Consent Forms

Medical History Update

Brain Tissue Donation Program

C4R COVID-19 Research Study

July 2020 Participant Town Hall

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

N Engl J Med 2016;374:523-32.

Incidence of Dementia over Three Decades in the Framingham Heart Study

Claudia L. Satizabal, Ph.D., Alexa S. Beiser, Ph.D., Vincent Chouraki, M.D., Ph.D., Geneviève Chêne, M.D., Ph.D., Carole Dufouil, Ph.D., and Sudha Seshadri, M.D.

Table 2. Temporal Trends in the Incidence of Dementia.*

Subtype	No. of Cases	Total No. of Observation Periods	5-Yr Cumulative Hazard Rate (95% CI)†				5-Yr Hazard Ratio (95% CI)‡				P Value for Trend
			Epoch 1	Epoch 2	Epoch 3	Epoch 4	Epoch 2	Epoch 3	Epoch 4	Trend§	
Overall dementia	371	9015	3.6 (2.9–4.4)	2.8 (2.2–3.5)	2.2 (1.8–2.8)	2.0 (1.5–2.6)	0.78 (0.59–1.04)	0.62 (0.47–0.83)	0.56 (0.41–0.77)	0.80 (0.72–0.90)	<0.001
Alzheimer's disease	264	9015	2.0 (1.5–2.6)	2.0 (1.5–2.6)	1.7 (1.3–2.3)	1.4 (1.0–1.9)	1.00 (0.70–1.43)	0.88 (0.62–1.25)	0.70 (0.48–1.03)	0.88 (0.77–1.00)	0.052
Vascular dementia	84	9014	0.8 (0.6–1.3)	0.8 (0.5–1.2)	0.4 (0.2–0.7)	0.4 (0.2–0.7)	0.89 (0.51–1.56)	0.46 (0.25–0.86)	0.45 (0.23–0.87)	0.71 (0.56–0.90)	0.004

* The baseline examination period was between 1977 and 1983 for the first epoch, between 1986 and 1991 for the second epoch, between 1992 and 1998 for the third epoch, and between 2004 and 2008 for the fourth epoch.
† The 5-year cumulative hazard rates (the cumulative incidence of dementia per 100 persons over a period of 5 years) are adjusted for age and sex.
‡ The 5-year hazard ratios (the incidence of dementia during each epoch relative to the incidence during the first epoch) are adjusted for age and sex.
§ We estimated linear trends (the decline per decade in the 5-year incidence of dementia) using the elapsed mean time (in decades) between the first epoch and each consecutive epoch.

and fourth epochs, respectively. This risk reduction was observed only among persons who had at least a high school diploma (hazard ratio, 0.77; 95% confidence interval, 0.67 to 0.88). The prevalence of most vascular risk factors (except obesity and diabetes) and the risk of dementia associated with stroke, atrial fibrillation, or heart failure have decreased over time, but none of these trends completely explain the decrease in the incidence of dementia.

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CFAS Cognitive Function & Ageing Study

Home | MRC CFAS | CFAS II | CFAS Wales | Key Findings | Publications | Research Team | Participant Info | Internal

Welcome to CFAS

What are the Cognitive Function and Ageing Studies?

The Cognitive Function and Ageing Studies (CFAS) are population based studies of individuals aged 65 and over living in the community, including institutions. CFAS is the only large multi-centred, population-based study in the UK that has reached sufficient maturity. There are three main studies within the CFAS group; MRC CFAS, the original study which began in 1989, the comparison study CFAS II (2008 onward) and CFAS Wales (2011).

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Latest News

CFAS DTC – 1st Annual Scientific Meeting

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Pathological correlates of late-onset dementia in a multicentre, community-based population in England and Wales

*Neuropathology Group of the Medical Research Council Cognitive Function and Ageing Study (MRC CFAS)**

Lancet 2001; **357:** 169–75

Findings We report on the first 209 individuals who have come to necropsy. The median age at death was 85 years for men, and 86 years for women. Cerebrovascular (78%) and Alzheimer-type (70%) pathology were common. Dementia was present in 100 (48%), of whom 64% had features indicating probable or definite Alzheimer's disease. However, 33% of the 109 non-demented people had equivalent densities of neocortical neuritic plaques. Some degree of neocortical neurofibrillary pathology was found in 61% of demented and 34% of non-demented individuals. Vascular lesions were equally common in both groups, although the proportion with multiple vascular pathology was higher in the demented group (46% *vs* 33%).

Interpretation Alzheimer-type and vascular pathology were the major pathological correlates of cognitive decline in this elderly sample, as expected, but most patients had mixed disease. There were no clear thresholds of these features that predicted dementia status. The findings therefore challenge conventional dementia diagnostic criteria in this setting. Additional factors must determine whether moderate burdens of cerebral Alzheimer-type pathology and vascular lesions are associated with cognitive failure.

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www.thelancet.com Published online July 16, 2013

A two-decade comparison of prevalence of dementia in individuals aged 65 years and older from three geographical areas of England: results of the Cognitive Function and Ageing Study I and II

Fiona E Matthews, Antony Arthur, Linda E Barnes, John Bond, Carol Jagger, Louise Robinson, Carol Brayne, on behalf of the Medical Research Council Cognitive Function and Ageing Collaboration

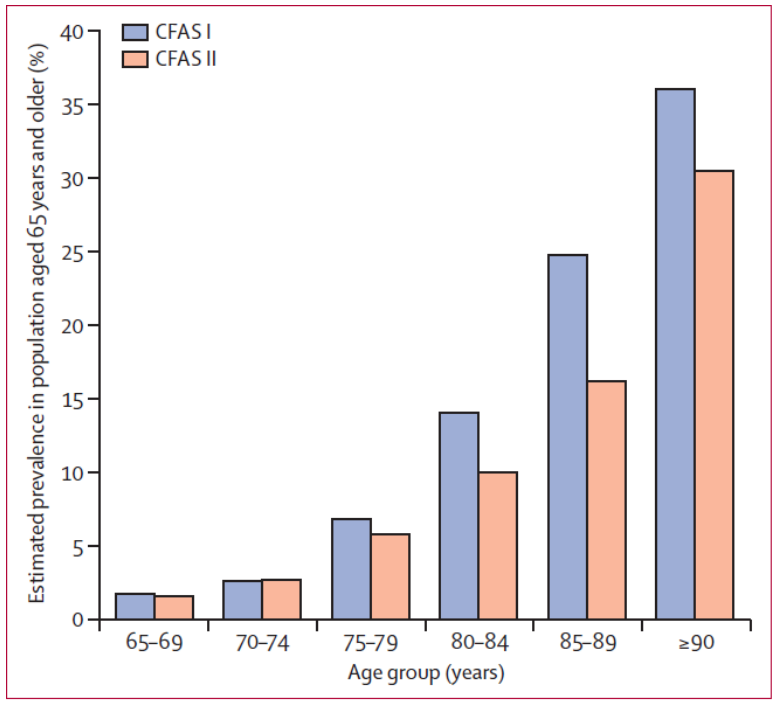
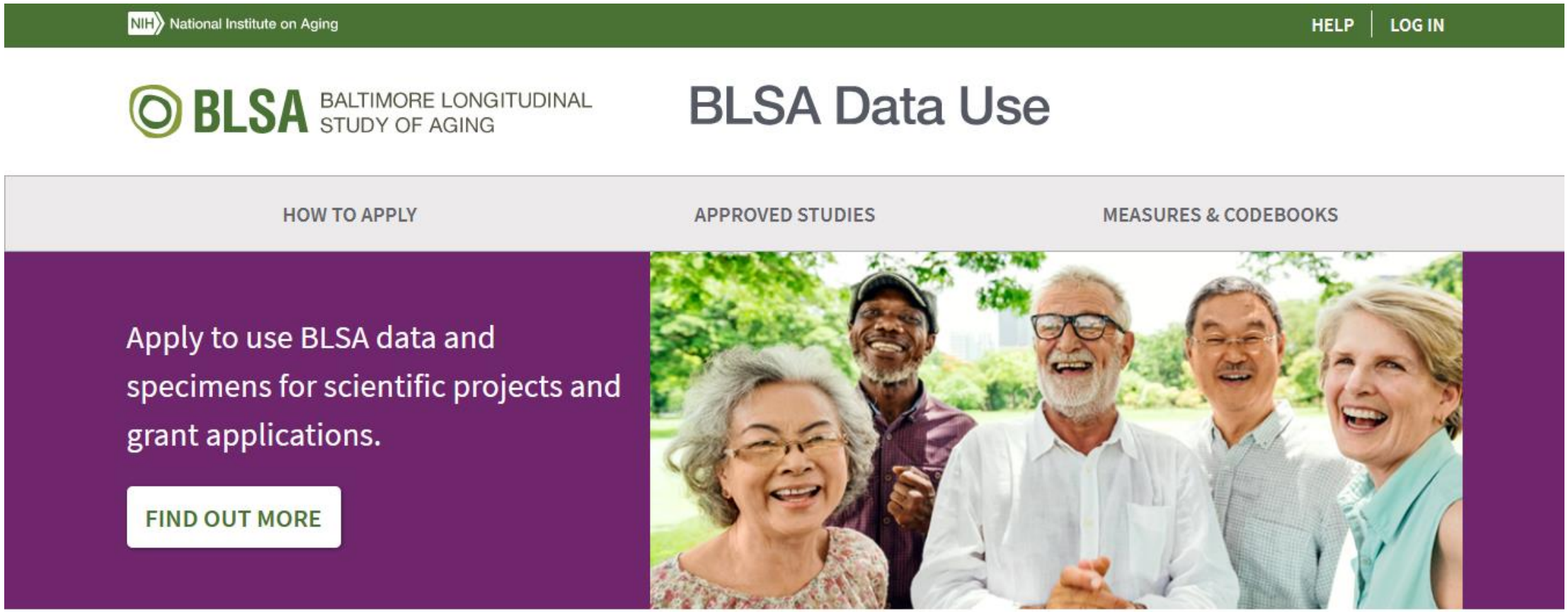


Figure 1: **CFAS I and CFAS II age-specific dementia prevalence**
CFAS=Cognitive Function and Ageing Study.

"Our findings suggest that brain health is improving significantly in the UK across generations, particularly among men, but that deprivation is still putting people at a disadvantage. The UK in earlier eras has seen major societal investments into improving population health and this appears to be helping protect older people from dementia." – Professor Carol Brayne.


NIH National Institute on Aging
HELP
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BLSA BALTIMORE LONGITUDINAL STUDY OF AGING
BLSA Data Use
HOW TO APPLY
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FIND OUT MORE
HOW TO APPLY
In general you will begin the process with a pre-analysis plan in which you should
News and Updates

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The Baltimore Longitudinal Study of Aging

America's Longest-Running Study of Human Aging

The National Institute on Aging's Baltimore Longitudinal Study of Aging (BLSA) answers critical questions about what happens as people get older.

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Impact of Alzheimer's Pathology on Cognitive Trajectories in Nondemented Elderly

Ira Driscoll, PhD,[1] Susan M. Resnick, PhD,[1] Juan C. Troncoso, MD,[2,3] Yang An, MS,[1] Richard O'Brien, MD, PhD,[2,3] and Alan B. Zonderman, PhD[1]

Ann Neurol 2006;60:688–695

Table 2. Distribution of Consortium to Establish a Registry for Alzheimer's Disease and Braak Raw Scores per Group

Group	N	Cognitive Decline (+/−)	Neuropathology (+/−)	CERAD[a]	*M* (SD)	Braak[b]	*M* (SD)
Normal	27	−	−	0 or 1	0.26 (0.45)	≤2	1.63 (0.56)
Asymptomatic-AD	21	−	+	2 or 3	2.14 (0.36)	≥2	3.48 (1.17)
MCI/AD	33	+	+	2 or 3	2.64 (0.49)	≥2	4.48 (1.03)
MCI	7				2.43 (0.53)		4.00 (1.00)
AD	26				2.69 (0.47)		4.62 (1.02)

[a]Consortium to Establish a Registry for Alzheimer's Disease (CERAD) scores: 0 = none; 1 = rare (A); 2 = moderate (B); 3 = frequent (C).
[b]Braak scores: 0 to 6.

SD = standard deviation; AD = Alzheimer's disease; MCI = mild cognitive impairment; M = mean.

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Preclinical Alzheimer's Disease
Schmitt FA et al., *Neurology* 2000.

High pathology controls
Lue LF et al., *JNEN* 1996.

High plaque non-demented subjects
Benzing WC et al., Brain Res 1993.

Asymptomatic Alzheimer's Disease (ASYMAD)
Riudavets MA et al., *Neurobiol Aging* 2007.

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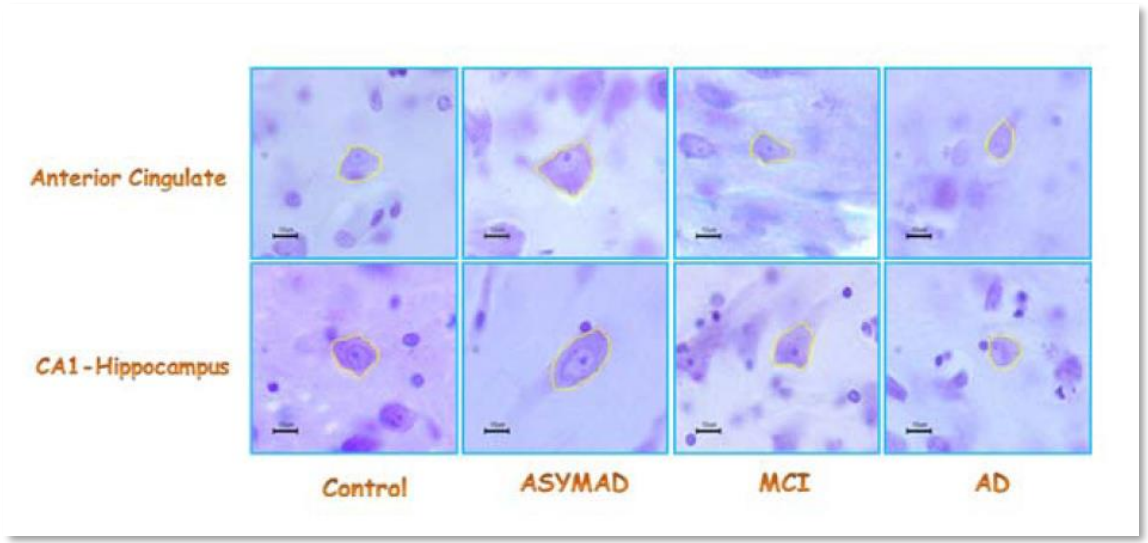
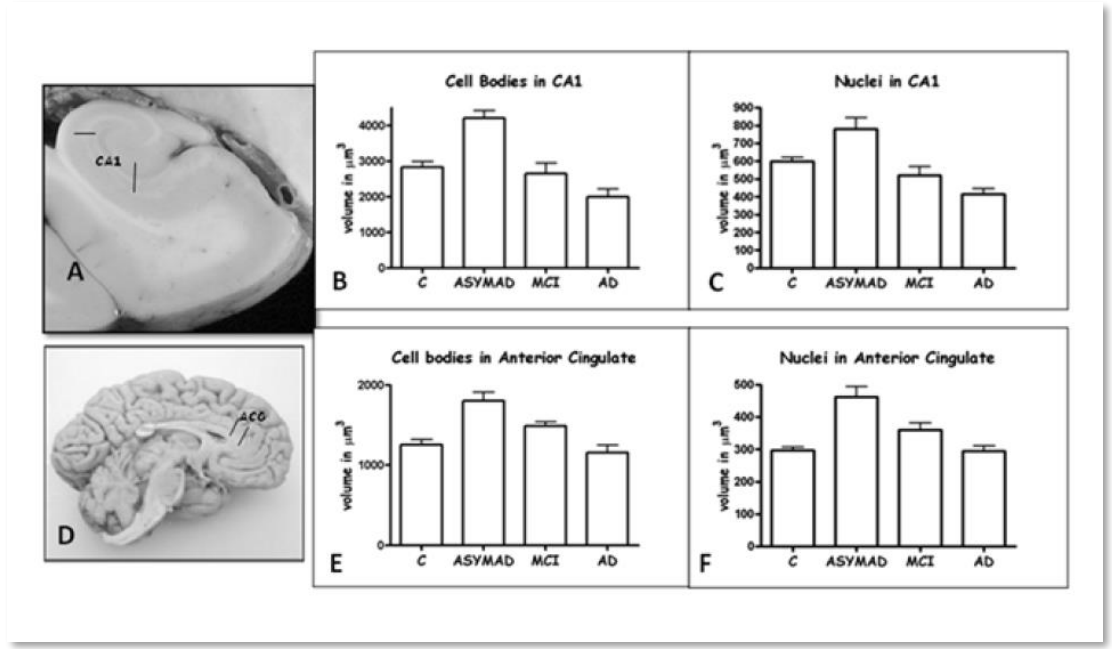
J Alzheimers Dis. 2009 ; 18(3): 665–675. doi:10.3233/JAD-2009-1179.

Neuropathologic Studies of the Baltimore Longitudinal Study of Aging (BLSA)

Richard J. O'Brien[a], Susan M. Resnick[b], Alan B. Zonderman[b], Luigi Ferrucci[c], Barbara J. Crain[d], Olga Pletnikova[d], Gay Rudow[d], Diego Iacono[d], Miguel A. Riudavets[e], Ira Driscoll[b], Donald L. Price[d], Lee J. Martin[d], and Juan C. Troncoso[a,d,*]





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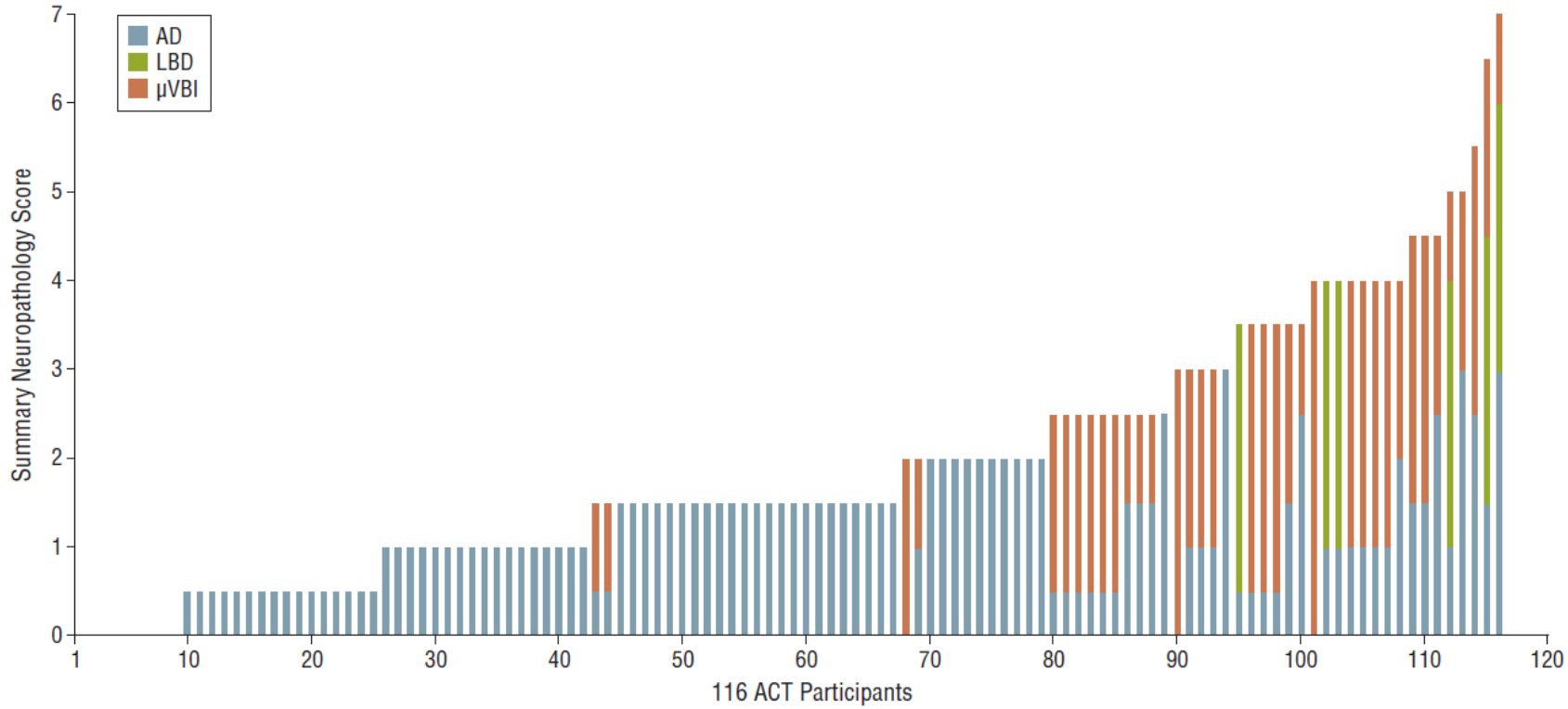
ORIGINAL CONTRIBUTION

Ecology of the Aging Human Brain

Joshua A. Sonnen, MD; Karen Santa Cruz, MD; Laura S. Hemmy, PhD; Randall Woltjer, MD, PhD; James B. Leverenz, MD; Kathleen S. Montine, PhD; Clifford R. Jack, MD; Jeffrey Kaye, MD; Kelvin Lim, MD; Eric B. Larson, MD, MPH; Lon White, MD, MPH; Thomas J. Montine, MD, PhD

Arch Neurol. 2011;68(8):1049-1056



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Epidemologic Research
CEDHA
Latino CORE Study
Memory and Aging Project
Minority Aging Research Study
Religious Orders Study

Religious Orders Study

The Religious Orders Study is a collaborative study with Rush and other U.S. medical centers. It involves more than 1,100 older religious clergy (nuns, priests and brothers) who have agreed to medical and psychological evaluation each year and brain donation after death. Researchers are using information from the study to discover what changes in the brain are responsible for memory and movement problems. The study also looks closely at the transition from normal functioning of the aging brain to the mild cognitive impairment that can be an early sign of Alzheimer's disease.

Funding for the Religious Orders Study by the National Institute on Aging began in 1993, and current funding will continue through June 2016. By that time, the Religious Orders Study will have up to 22 years of clinical data on more than 1,100 people and brain tissue from over 350 people. This rich and diverse resource will allow the Study to continue

erous investigators. It will also offer the Alzheimer's disease research

J Alzheimers Dis. 2009 November ; 18(3): 691–701. doi:10.3233/JAD-2009-1227.

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The Neuropathology of Older Persons with and Without Dementia from Community versus Clinic Cohorts

Julie A. Schneider[a,b,c,*], **Neelum T. Aggarwal**[a,b], **Lisa Barnes**[a,b,d], **Patricia Boyle**[a,d], and **David A. Bennett**[a,b]

Sin deterioro cognitivo

Table 2: Demographics [mean (SD)] and distribution [number (%)] of pathology in persons with no cognitive impairment in community compared to clinic cohorts.

	Community Cohorts	Clinical Cohort
Number	188	14
Age at death	83.8 (SD=6.4)	81.6 (SD=10.7)
Education	17.0 (SD=3.9)	14.7 (SD=3.0)
MMSE	28.3 (SD=1.6)	27.8 (SD=1.6)
Pathologic diagnosis of AD (NIA-Reagan)	73 (38.8%)	8 (57.1%)
High	2 (1.1%)	1 (7.1%)
Intermediate	71 (37.8%)	7 (50.0%)
Infarct (any)	73 (38.8%)	5 (35.7%)
Macroscopic	41 (21.8%)	1 (7.1%)
Microscopic	41 (21.8%)	5 (35.7%)
Lewy bodies (any)	23 (12.2%)	1 (7.1%)
Neocortical	5 (2.7%)	1 (7.1%)
One pathology (AD, infarcts, or Lewy bodies)	87 (46.3%)	6 (42.9%)
Mixed pathology	16 (8.5%)	2 (14.3%)
FTLD or other atypical pathology	0	0

Enfermedad de Alzheimer probable

Table 4: Demographics [mean (SD)] and distribution [number (%)] with clinically probable AD in community compared to clinic cohorts.

	Community Cohorts	Clinical Cohort
Number	194	280
Age at death	89.8 (SD=5.5)	79.2 (SD=10.1)
Education	16.8 (SD=3.6)	12.8 (SD=3.2)
MMSE	14.1 (SD=8.5)	6.0 (SD=8.0)
Pathologic diagnosis of AD (NIA-Reagan)	170 (87.6%)	252 (90%)
High	78 (40.2%)	193 (68.9%)
Intermediate	92 (47.4%)	59 (21.1%)
Infarcts (any)	105 (54.1%)	77 (27.5%)
Macroscopic	76 (39.2%)	50 (17.9%)
Microscopic	60 (30.9%)	49 (17.5%)
Lewy bodies (any)	48 (24.7%)	60 (21.4%)
Neocortical	30 (15.5%)	40 (14.3%)
One pathology (AD, infarcts, or Lewy bodies)	96 (49.5%)	185 (66.1%)
Mixed pathology	86 (44.3%)	77 (27.5%)
FTLD or other atypical pathology	3 (1.5%)	17 (6.1%)

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The Neuropathology of Probable Alzheimer Disease and Mild Cognitive Impairment

Julie A. Schneider, MD,[1,2,3] Zoe Arvanitakis, MD,[1,2] Sue E. Leurgans, PhD,[1,2] and David A. Bennett, MD[1,2]

Ann Neurol 2009;66:200–208

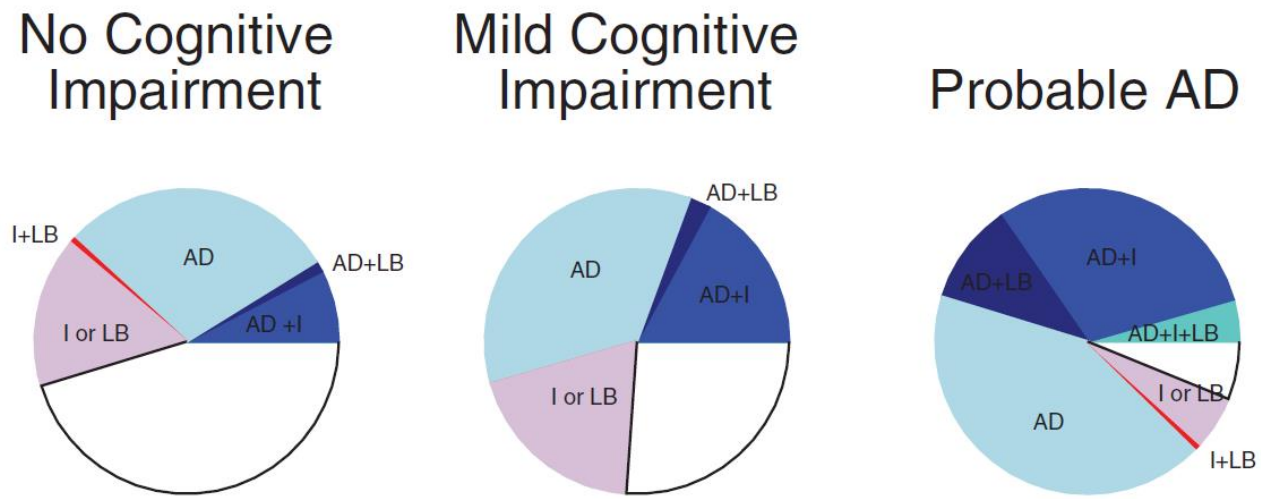

*Fig. Pathology by clinical status proximate to death. (*Blue shades*) Pathologic diagnosis of Alzheimer disease (AD). Clockwise: light blue = pathologic diagnosis of AD only; dark blue = pathologic diagnosis of AD and neocortical Lewy bodies (LB); medium blue = pathologic diagnosis of AD and cerebral infarcts (I); aqua = pathologic diagnosis of AD, I, and LB. (*Red shades*) I and/or LB (with no pathologic diagnosis of AD). Clockwise: pink = I or LB; red = I and LB. (*White*) No pathologic diagnosis of AD, no I, no LB.*

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Lancet Neurol 2007; 6: 734–46

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*

Panel 1: Glossary of terms

Mild cognitive impairment
Variably defined but includes subjective memory or cognitive symptoms or both, objective memory or cognitive impairment or both, and generally unaffected activities of daily living; affected people do not meet currently accepted dementia or AD diagnostic criteria

Amnestic mild cognitive impairment
A more specified term describing a subtype of mild cognitive impairment, in which there are subjective memory symptoms and objective memory impairment; other cognitive domains and activities of daily living are generally unaffected; affected people do not meet currently accepted dementia or AD diagnostic criteria

Preclinical AD
The long asymptomatic period between the first brain lesions and the first appearance of symptoms and which concerns normal individuals that later fulfil AD diagnostic criteria

Prodromal AD
The symptomatic predementia phase of AD, generally included in the mild cognitive impairment category; this phase is characterised by symptoms not severe enough to meet currently accepted diagnostic criteria for AD

AD dementia
The phase of AD where symptoms are sufficiently severe to meet currently accepted dementia and AD diagnostic criteria

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Alzheimer's & Dementia 8 (2012) 1–13

Alzheimer's & Dementia

Featured Articles

National Institute on Aging–Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease

Bradley T. Hyman[a], Creighton H. Phelps[b], Thomas G. Beach[c], Eileen H. Bigio[d], Nigel J. Cairns[e,f], Maria C. Carrillo[g], Dennis W. Dickson[h], Charles Duyckaerts[i], Matthew P. Frosch[j], Eliezer Masliah[k,l], Suzanne S. Mirra[m], Peter T. Nelson[n], Julie A. Schneider[o,p,q], Dietmar Rudolf Thal[r], Bill Thies[g], John Q. Trojanowski[s], Harry V. Vinters[t,u], Thomas J. Montine[v,*]

Acta Neuropathol (2012) 123:1–11
DOI 10.1007/s00401-011-0910-3

CONSENSUS PAPER

National Institute on Aging–Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease: a practical approach

Thomas J. Montine · Creighton H. Phelps · Thomas G. Beach · Eileen H. Bigio · Nigel J. Cairns · Dennis W. Dickson · Charles Duyckaerts · Matthew P. Frosch · Eliezer Masliah · Suzanne S. Mirra · Peter T. Nelson · Julie A. Schneider · Dietmar Rudolf Thal · John Q. Trojanowski · Harry V. Vinters · Bradley T. Hyman

Ageing Research Reviews 58 (2020) 101002

Contents lists available at ScienceDirect

Ageing Research Reviews

journal homepage: www.elsevier.com/locate/arr

A third of community-dwelling elderly with intermediate and high level of Alzheimer's neuropathologic changes are not demented: A meta-analysis

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Neuropsychologia 47 (2009) 2015–2028

Contents lists available at ScienceDirect

Neuropsychologia

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Reviews and perspectives

Cognitive reserve☆

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Carga patológica	Cerebro 1 = Cerebro 2
Nivel cognitivo	Paciente 1 ≠ Paciente 2
Reserva cognitiva	Paciente 1 ≠ Paciente 2

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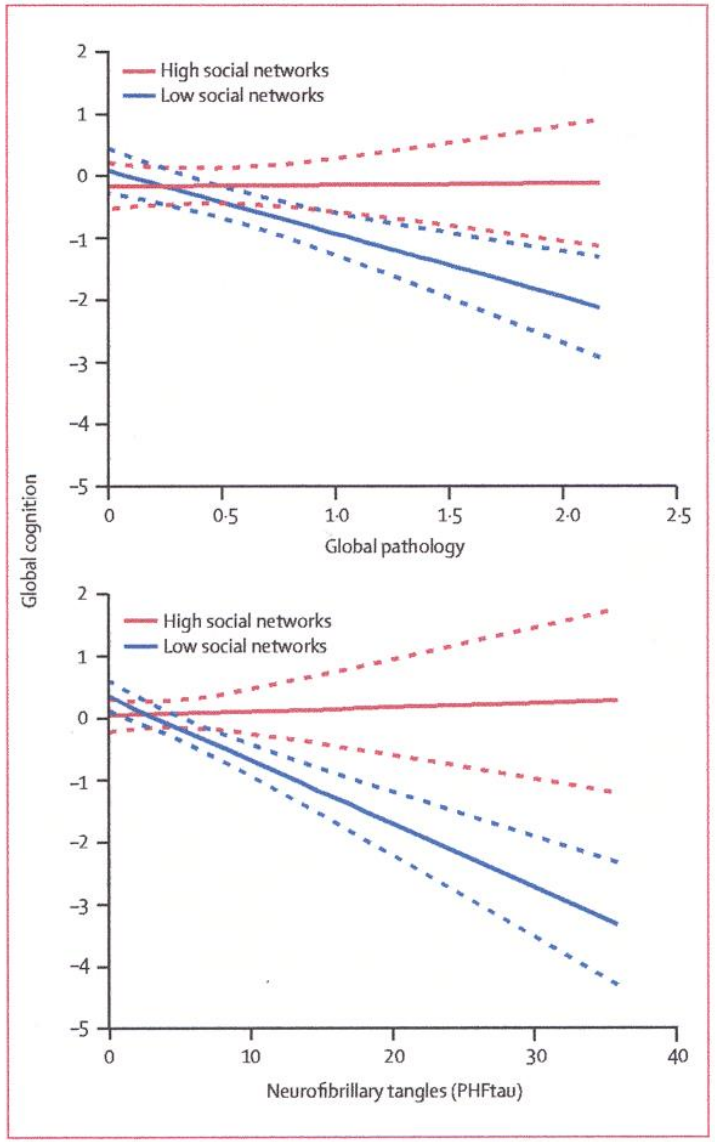

***Figure 1*: Predicted association between pathology and global cognitive function score proximate to death**
Upper=global Alzheimer's disease pathology. Lower=PHFtau tangles. Red line=90th percentile of social network size (13 participants). Blue line=10th percentile of social network size (two participants). Dotted lines indicate 95% CIs. Both models controlled for age, sex, education, and main effects for social networks and each pathological index.

Lancet Neurol 2006; 5: 406–12

The effect of social networks on the relation between Alzheimer's disease pathology and level of cognitive function in old people: a longitudinal cohort study

David A Bennett, Julie A Schneider, Yuxiao Tang, Steven E Arnold, Robert S Wilson

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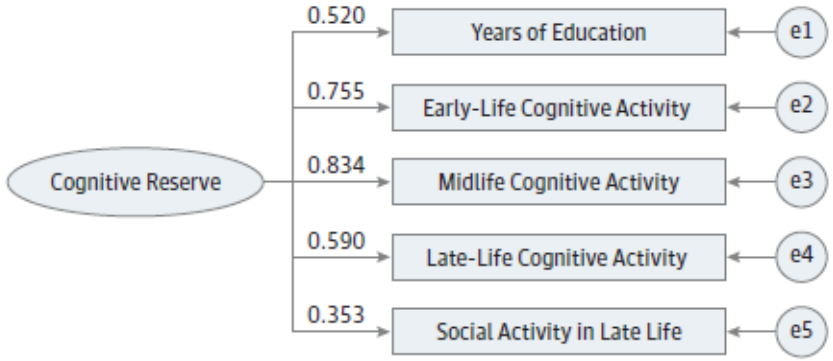
JAMA Neurology | Original Investigation

Association of Lifespan Cognitive Reserve Indicator With Dementia Risk in the Presence of Brain Pathologies

Hui Xu, MSc; Rongrong Yang, MSc; Xiuying Qi, PhD; Christina Dintica, MSc; Ruixue Song, MSc; David A. Bennett, MD; Weili Xu, MD, PhD

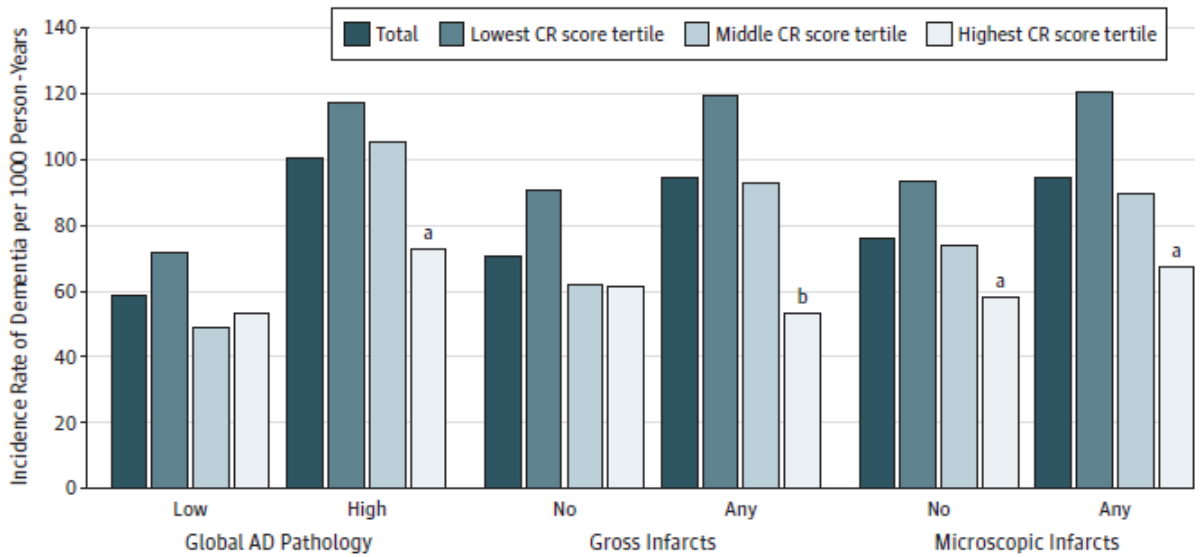
JAMA Neurol. doi:10.1001/jamaneurol.2019.2455
Published online July 14, 2019.

Figure 1. Standardized Estimates From the Structural Equation Model With 5 Observable Factors of a Latent Reserve Construct



The values indicate the loadings of the 5 factors to cognitive reserve. e1, e2, e3, e4, and e5 indicate the measurement error for each cognitive reserve factor. Structural equation modeling fit statistics: $\chi^2_5 = 41.919$; $P < .001$; comparative fit index = 0.981; standardized root mean squared residual = 0.026; root mean squared error of approximation = 0.068.

Figure 2. Incidence Rates of Dementia per 1000 Person-Years by Cognitive Reserve (CR) Tertile and Brain Pathology



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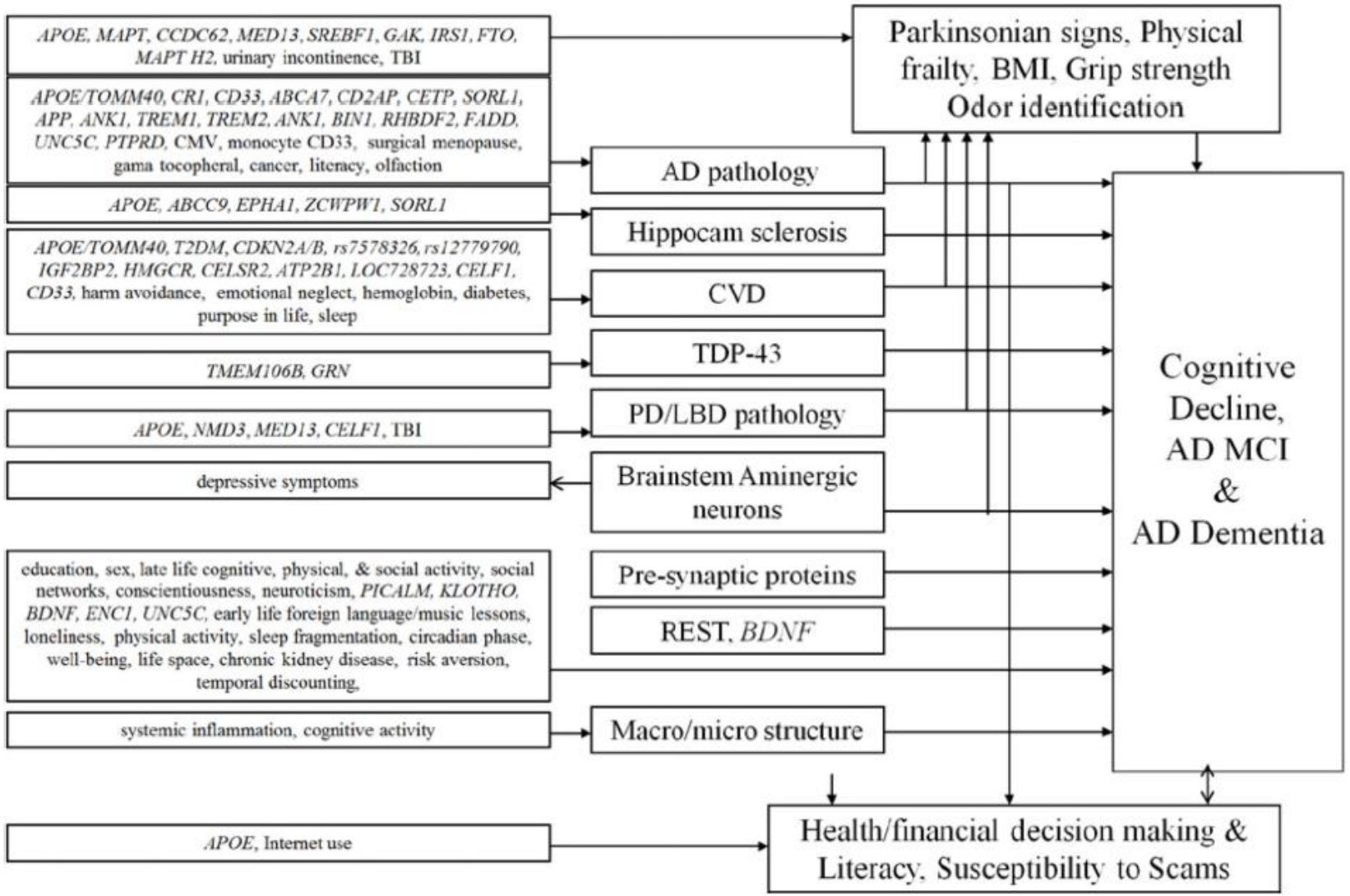

Fig 2.
Neurobiologic pathways linking risk factors to AD clinical phenotypes.

Bennett DA *et. al*, 2018

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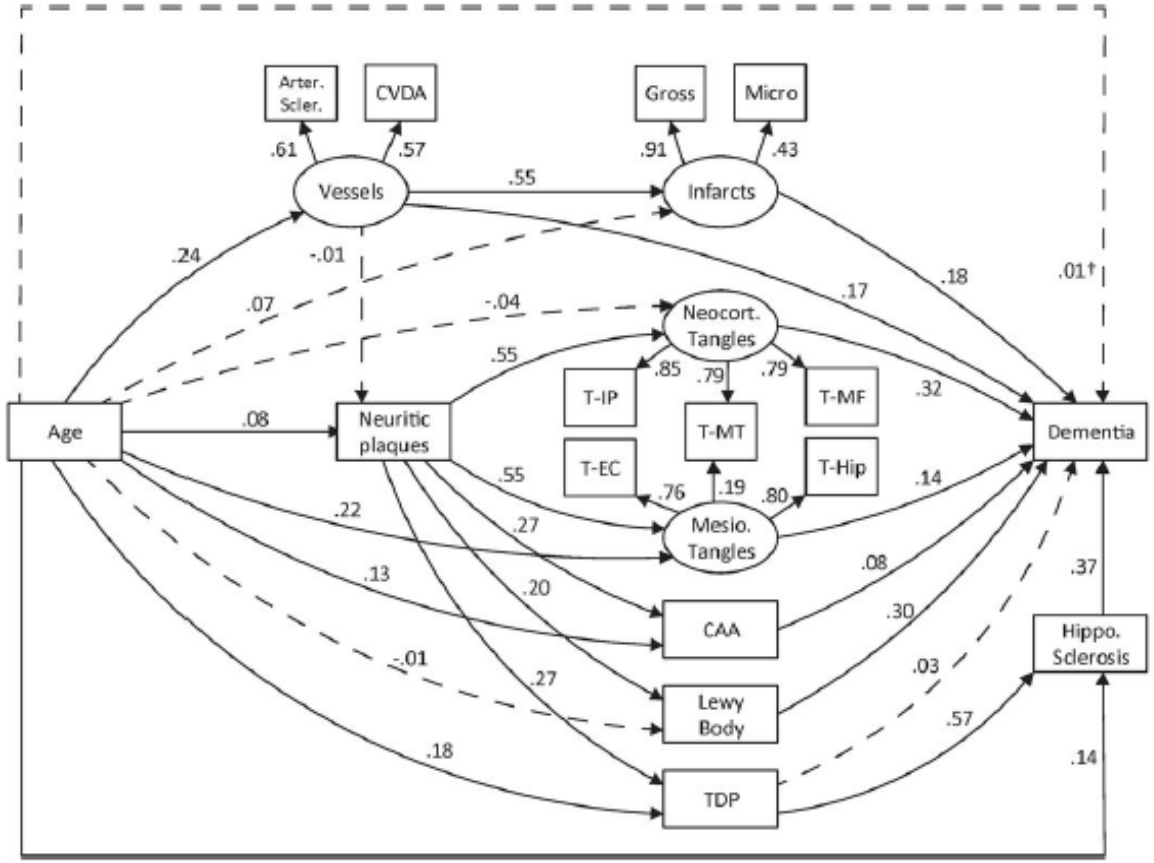
Ann Neurol. 2018 July ; 84(1): 10–22. doi:10.1002/ana.25246.

Combined neuropathological pathways account for age-related risk of dementia

Melinda C. Power, ScD[1], Elizabeth Mormino, PhD[2], Anja Soldan, PhD[3], Bryan D. James, PhD[4,5], Lei Yu, PhD[6], Nicole M. Armstrong, PhD[7], Katherine J. Bangen, PhD[8,9], Lisa Delano-Wood, PhD[8,9], Melissa Lamar, PhD[4,10], Yen Ying Lim, PhD[11], Kelly Nudelman, PhD[12], Laura Zahodne, PhD[13], Alden L. Gross, MHS,PhD[7,14,15], Dan Mungas, PhD[16], Keith F. Widaman, PhD[17], and Julie Schneider, MD[4,6,18]



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Amyloid deposition is decreasing in aging brains

An autopsy study of 1,599 older people

Enikö Kövari, MD
François R. Herrmann, MD, MPH
Constantin Bouras, MD
Gabriel Gold, MD

Neurology® 2014;82:326-331

Figure 1 Period effect on amyloid deposition in cases without dementia

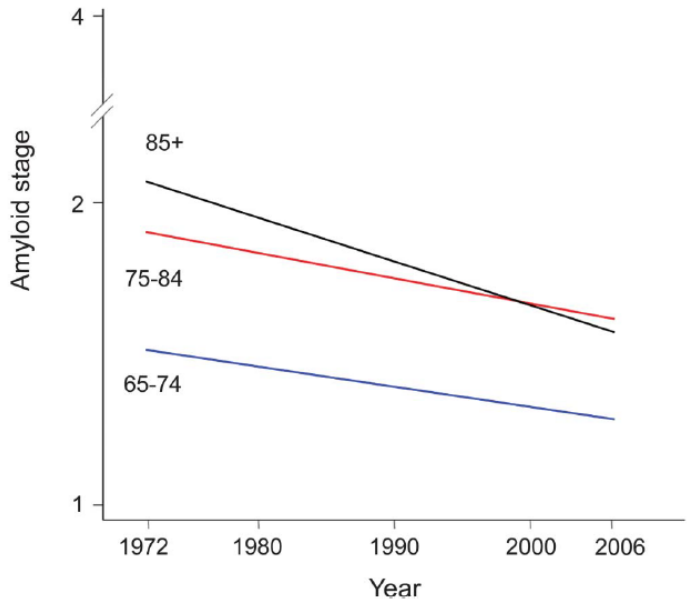
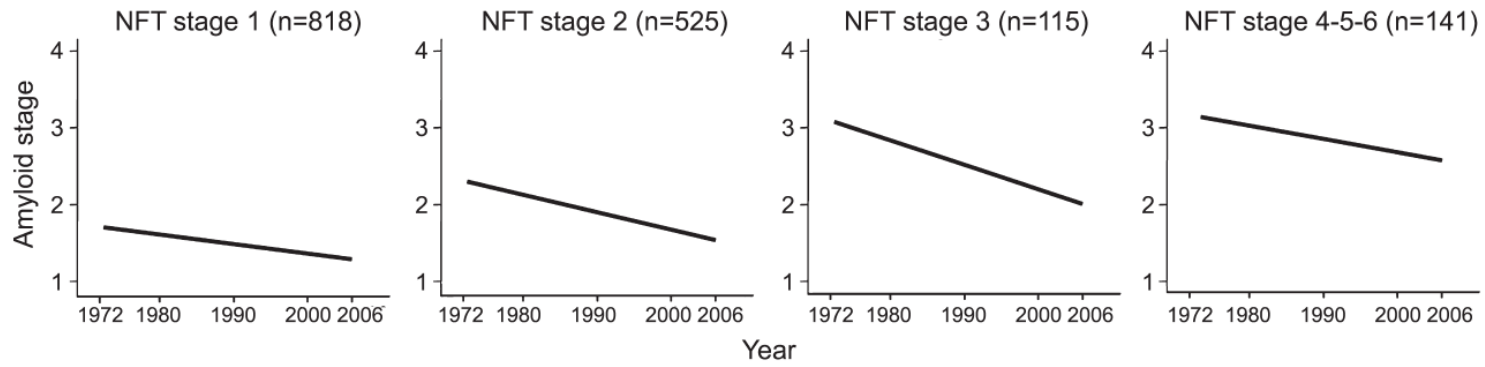


Figure 2 Mean amyloid deposition according to NFT stage



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JAMA Network Open

JAMA Network Open. 2020;3(6):e207559. doi:10.1001/jamanetworkopen.2020.7559

Original Investigation | Public Health

Association of Neighborhood-Level Disadvantage With Alzheimer Disease Neuropathology

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Table 2. Neuropathologic Features of Decedent Sample

Neuropathologic feature	Overall sample (N = 447)
AD neuropathology, No. (%)	
No	53 (12)
Yes	394 (88)
Diffuse plaque, No. (%)	
Not present	73 (16)
Present	374 (84)
Neuritic plaque, No. (%)	
Not present	69 (15)
Present	378 (85)

Abbreviation: AD, Alzheimer disease.

eTable 2. Unadjusted and Adjusted Results with Neighborhood Disadvantage Placed into Tertile Groupings Based on Study Sample

	Main AD Neuropathology Analysis[b]			
Characteristic	Unadjusted OR	95% CI	Adjusted OR[a]	95% CI
Neighborhood disadvantage tertile groups				
Least disadvantaged (ADI deciles 1 & 2)	1.000	(reference)	1.000	(reference)
Middle disadvantaged (ADI deciles 3 & 4)	1.170	1.152 - 1.189	1.130	1.068 - 1.196
Most disadvantaged (ADI deciles 5 to 10)	1.274	1.038 - 1.564	1.262	1.103 - 1.445
Age			1.022	1.016 - 1.028
Sex				
Female			1.000	(reference)
Male			0.835	0.772 - 0.903
Year of Death			0.984	0.914 - 1.058

AD, Alzheimer's disease; ADI, Area Deprivation Index; CI, confidence interval; OR, odds ratio
[a] Adjusted for age, sex, and year of death
[b] AD neuropathology defined as presence of either diffuse plaques or neuritic plaques (n=447)

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Gracias!

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