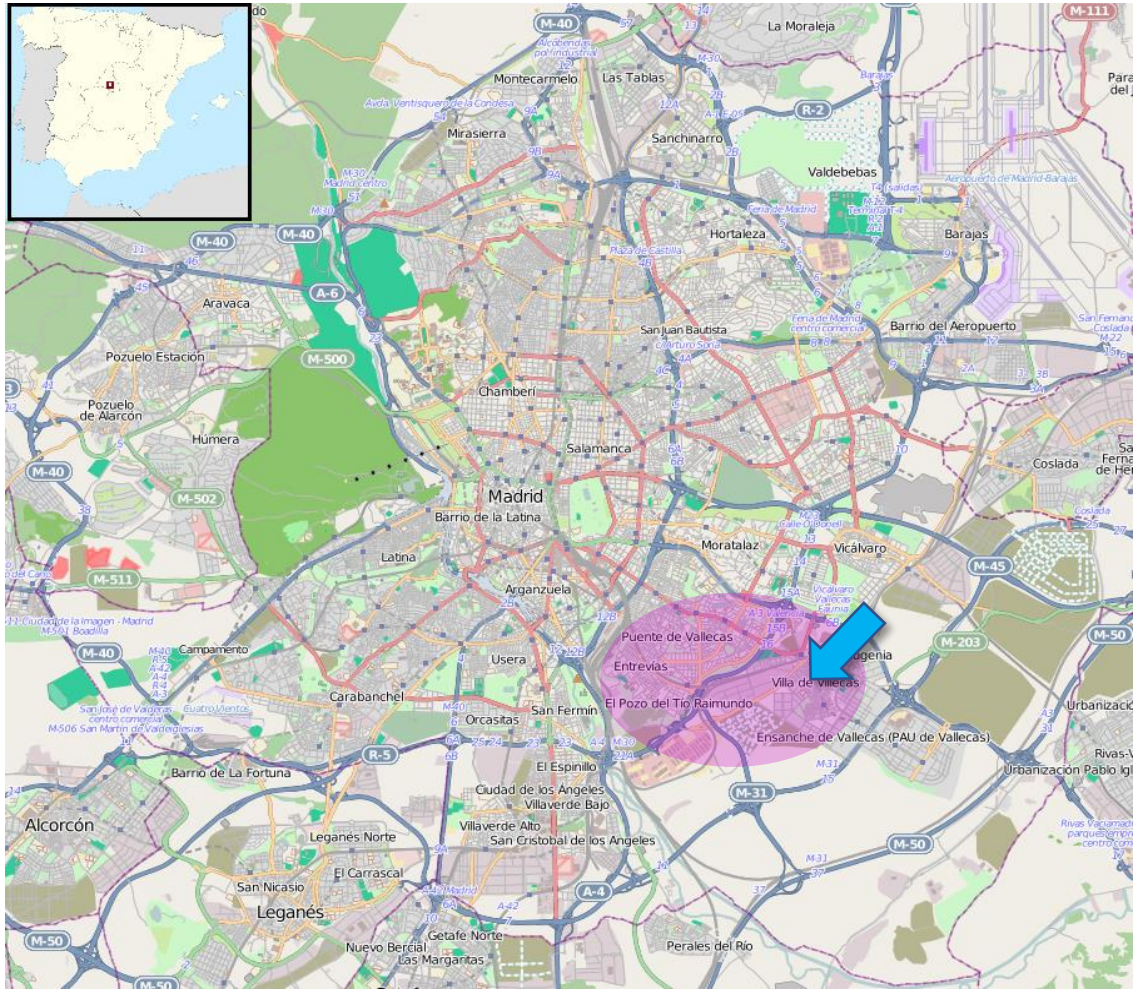
Heterogeneidad clinicopatológica de la enfermedad de Alzheimer

Alberto Rábano

Fundación CIEN, ISCIII, Madrid

Hospital Universitario Infanta Sofía,
abril, 2023

Madrid - Vallecas



Centro Alzheimer Fundación Reina Sofía

Fundación CIEN

La iniciativa de Vallecas: programas de investigación

El Proyecto Alzheimer FRS

- 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.

Cohorte Alzheimer de Vallecas (CAV – CAFRS)

Comunidad de Madrid

CONSEJERÍA DE FAMILIA, JUVENTUD Y POLÍTICA SOCIAL

Instituto de Salud Carlos III

Centro Alzheimer FRS

Fundación CIEN

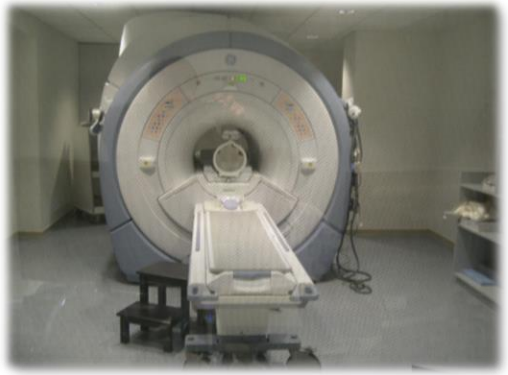
Unidad Multidisciplinar de Apoyo

Seguimiento Cohorte CAV - CAFRS

Datos de seguimiento

Resonancia Magnética 3T

Muestras sangre, cerebro



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

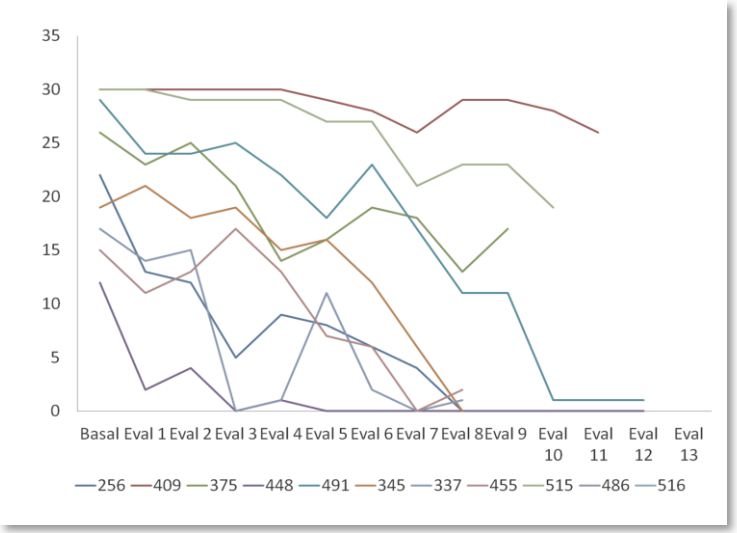
Javier Olazarán[a,*], Luis Agüera-Ortiz[b], Ricardo S. Osorio[a], Beatriz León-Salas[a], José Luis Dobato[a], Isabel Cruz-Orduña[a], Belén González[a], Meritxell Valentí[a], Nuria Gil-Ruiz[a], Belén Frades[c], M.I. Ramos-García[a] and Pablo Martínez-Martín[c]
[a]*Alzheimer Disease Research Unit, CIEN Foundation, Carlos III Institute of Health, Alzheimer Center Reina Sofía Foundation, Madrid, Spain*
[b]*CIBERSAM, Carlos III Institute of Health, Madrid, Spain*
[c]*CIBERNED, Carlos III Institute of Health, Madrid, Spain*

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

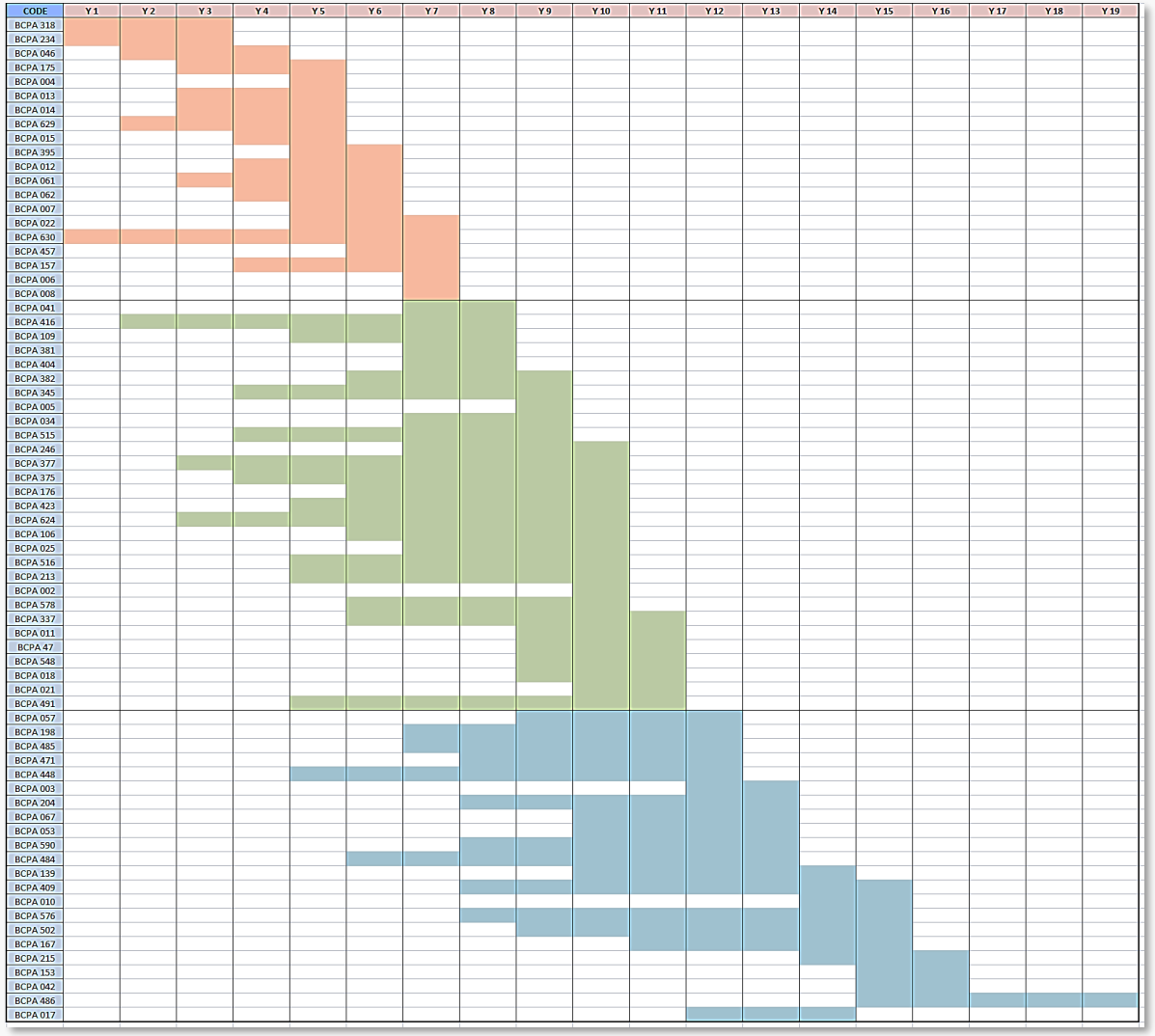
Area	Scale	Objective/Rationale	Observations[1]	References[2]
Cognition	MMSE	General cognition, universal measurement	B, 6	[17, 18]
	sMMSE	General cognition, advanced dementia	B, 6	[19, 20]
	Animals	Verbal fluency, frontotemporal functions	B, 6	[22, 23]
	SIB	General cognition, avoid floor effect	B, 6	[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.

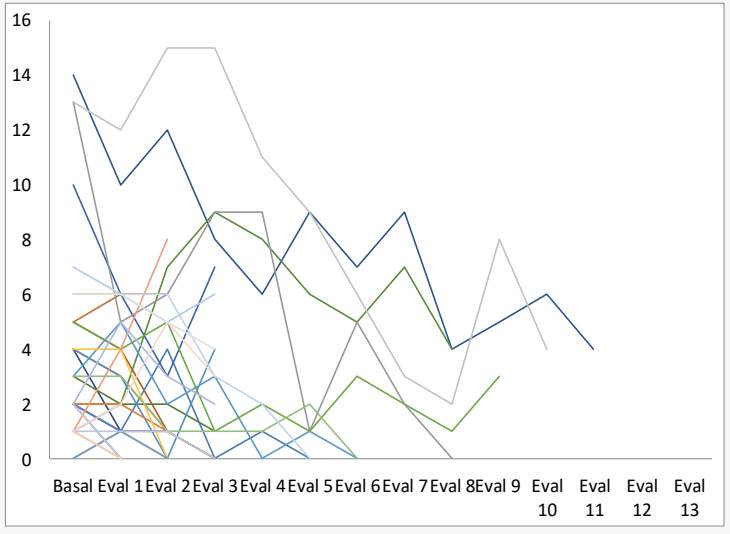
Severe Mini-mental State Examination



Survival time



Semantic fluency: animals



Journal of Alzheimer's Disease 30 (2012) 751–756
DOI 10.3233/JAD-2012-120007
IOS Press

Rapidly Progressive Alzheimer's Disease: A Multicenter Update

Christian Schmidt[a,*], Stephane Haïk[b,c,d,e,g], Katsuya Satoh[l], Alberto Rábano[h], Pablo Martinez-Martin[h], Sigrun Roeber[k], Jean-Philippe Brandel[b,c,d,e], Miguel Calero-Lara[j], Jesús de Pedro-Cuesta[i], Jean-Louis Laplanche[f], Jean-Jaques Hauw[g], Hans Kretzschmar[k] and Inga Zerr[a]

Acta Neuropathologica
https://doi.org/10.1007/s00401-020-02201-2

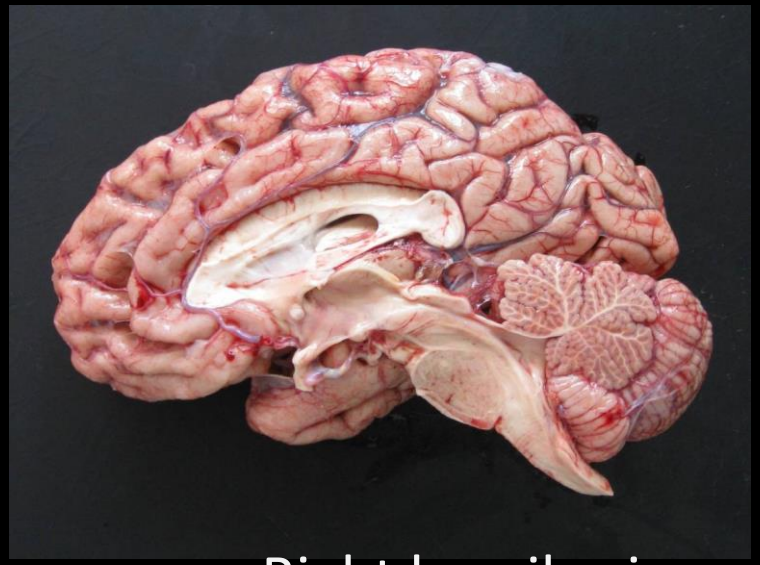
REVIEW

Check for updates

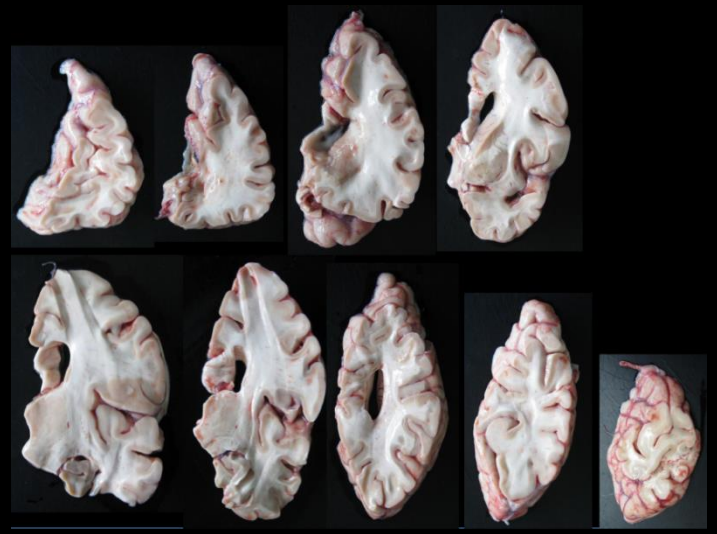
The existence of Aβ strains and their potential for driving phenotypic heterogeneity in Alzheimer's disease

Heather H. C. Lau[1,2] · Martin Ingelsson[1,2,3] · Joel C. Watts[1,2]

Received: 24 June 2020 / Revised: 23 July 2020 / Accepted: 24 July 2020

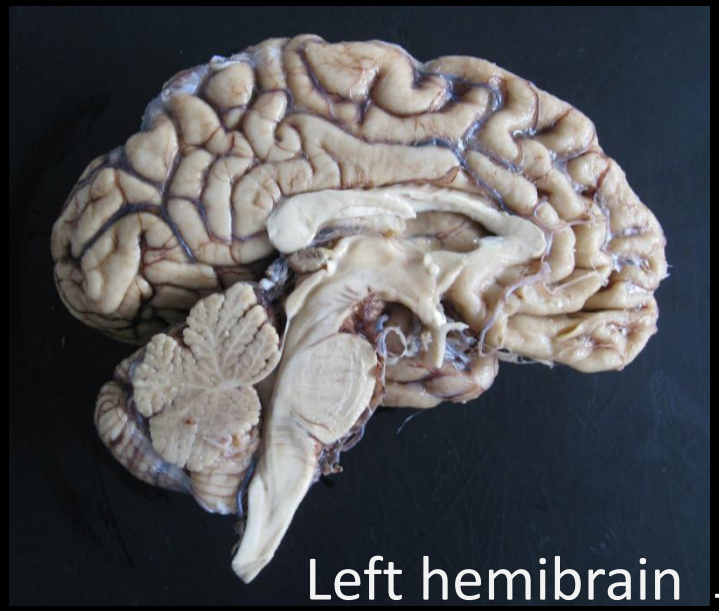


Right hemibrain

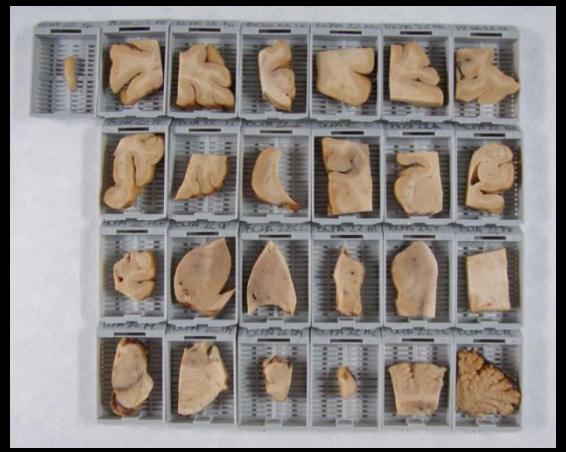


Freezing

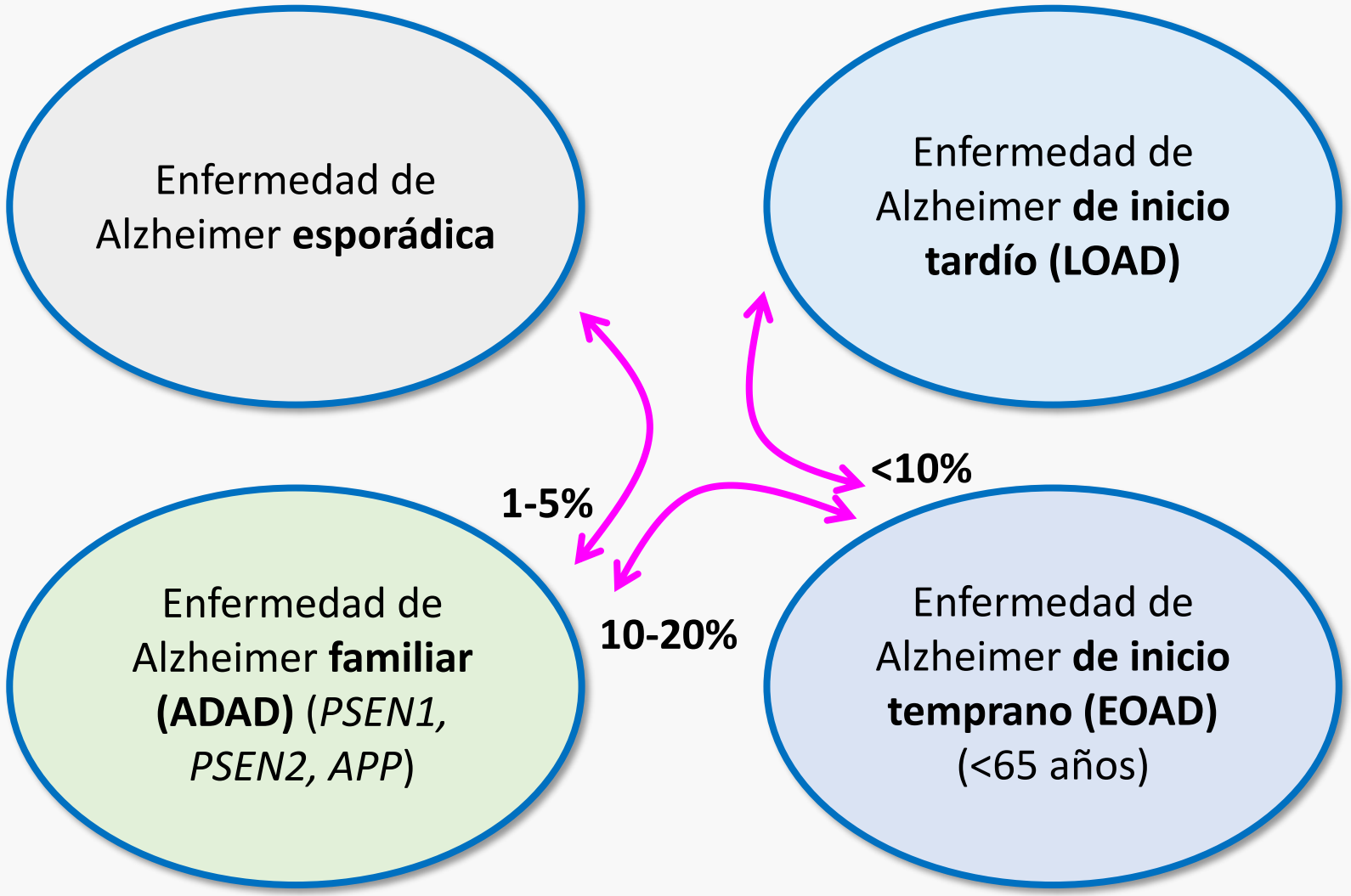
Storage



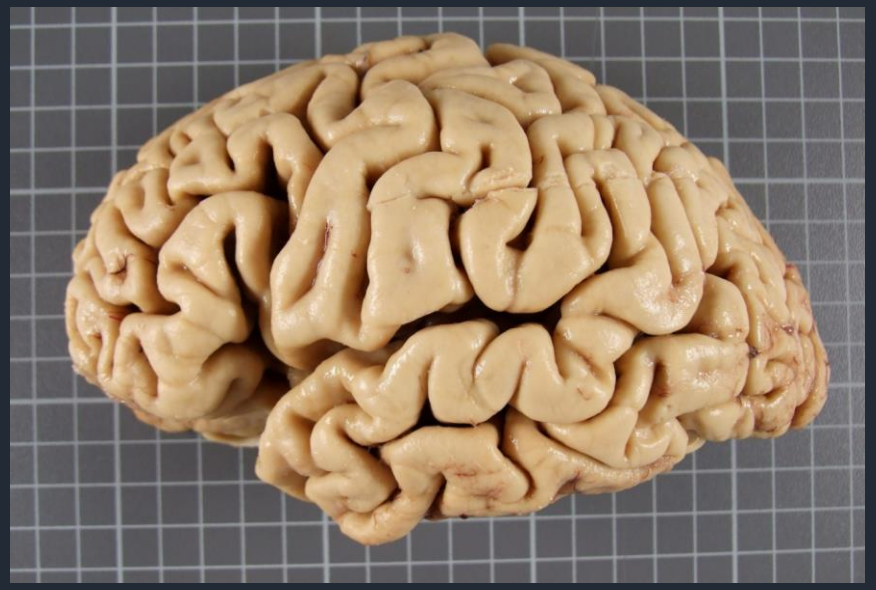
Left hemibrain

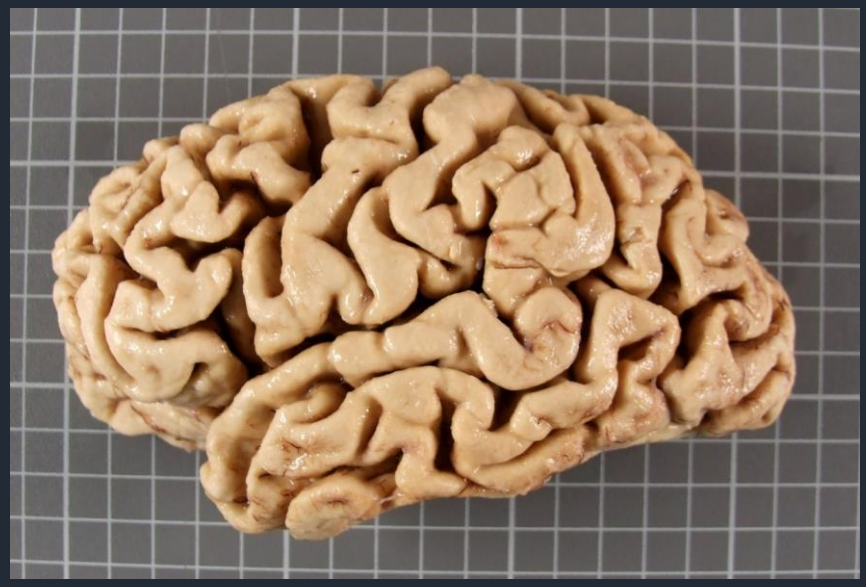


Neuropathology

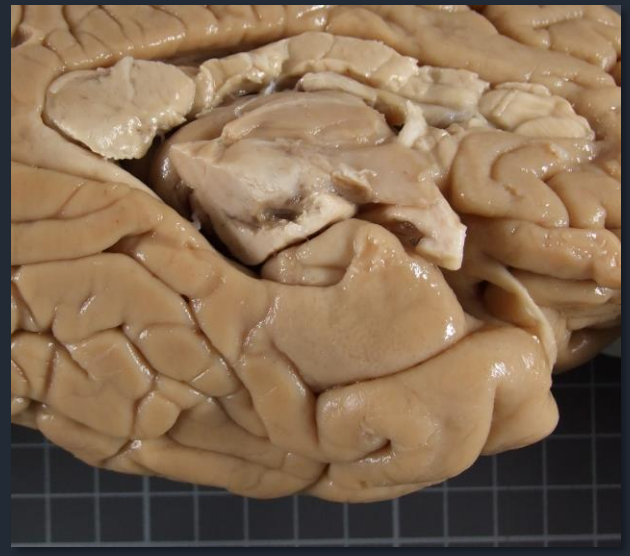

Enfermedad de Alzheimer **esporádica**
Enfermedad de Alzheimer **de inicio tardío (LOAD)**
1-5%
<10%
Enfermedad de Alzheimer **familiar (ADAD)** (*PSEN1, PSEN2, APP*)
10-20%
Enfermedad de Alzheimer **de inicio temprano (EOAD)** (<65 años)

Enfermedad de Alzheimer típica



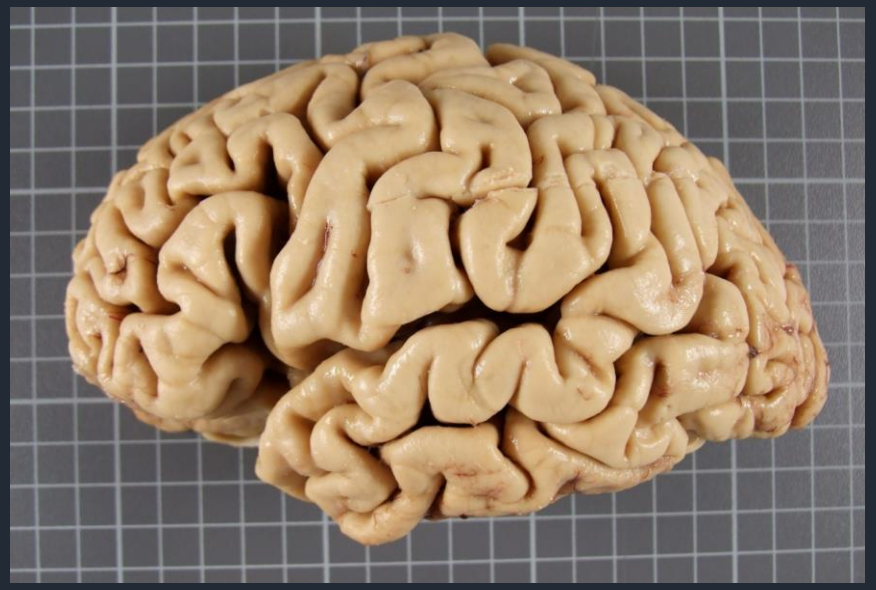


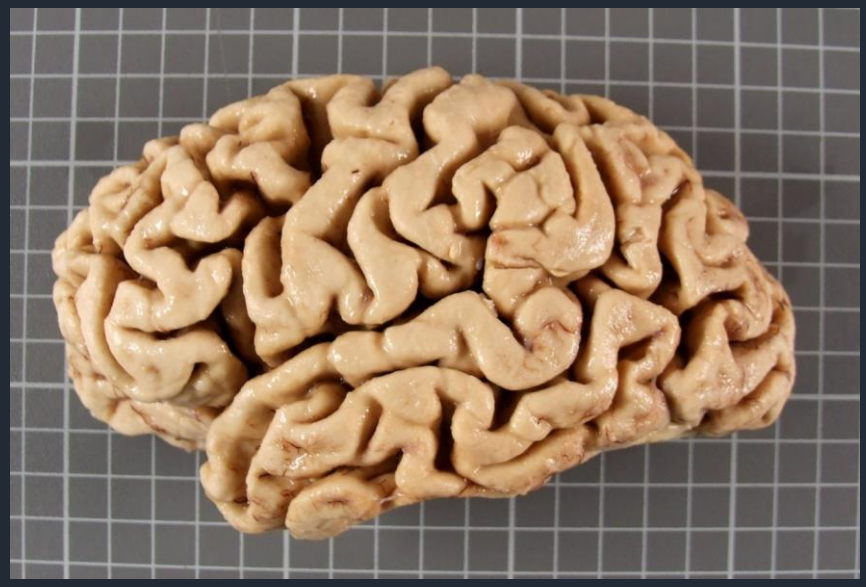
LTM
control



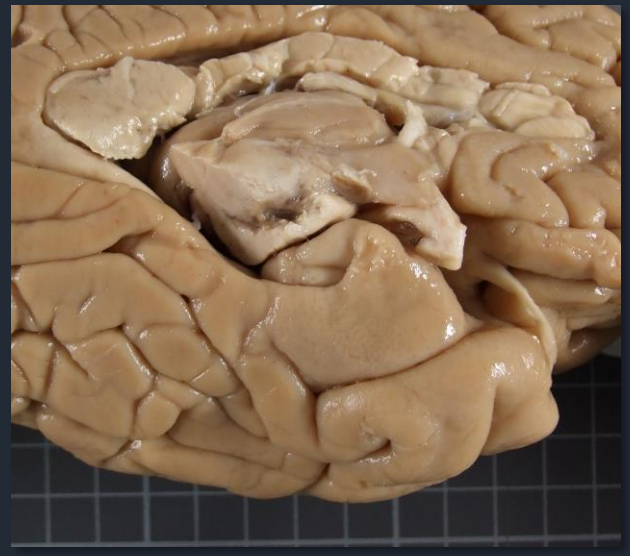
LTM
Alzheimer

Enfermedad de Alzheimer típica

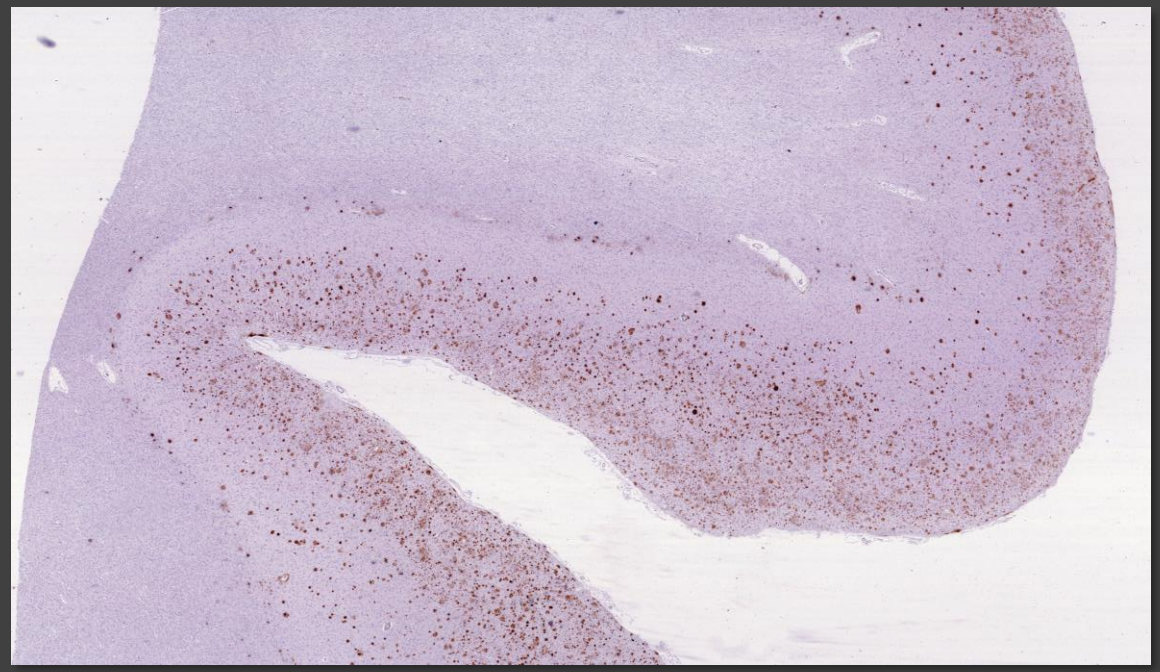


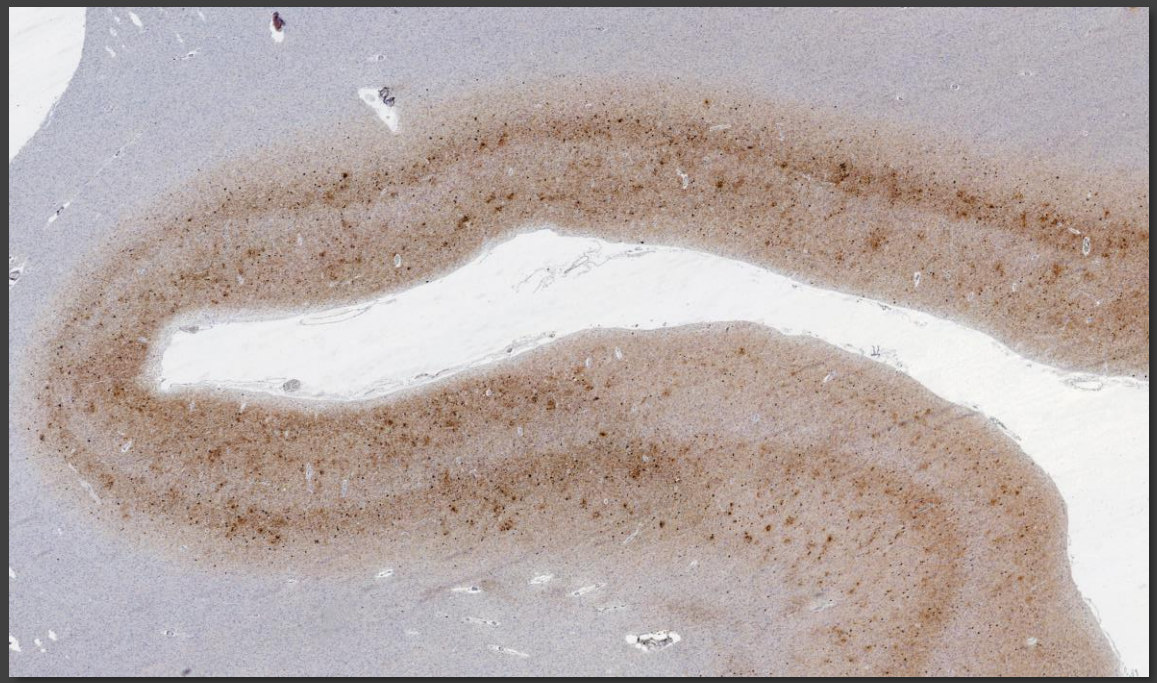


LTM
control

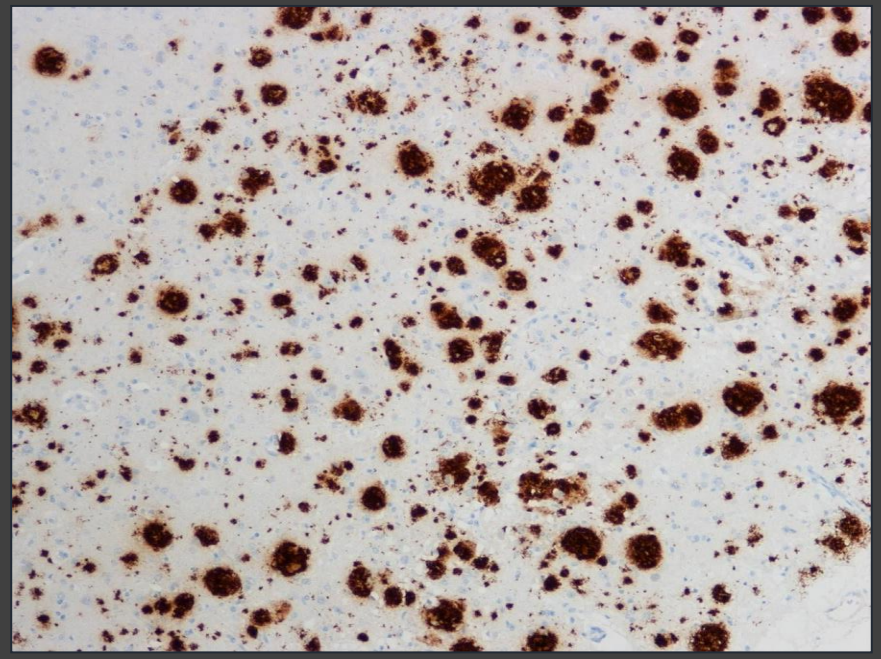


LTM
Alzheimer

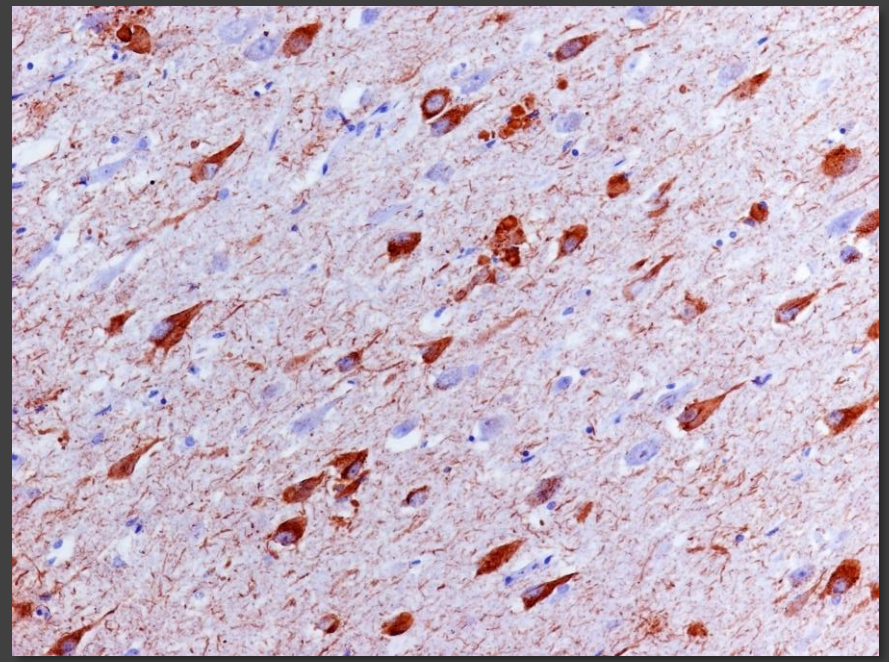




Aβ

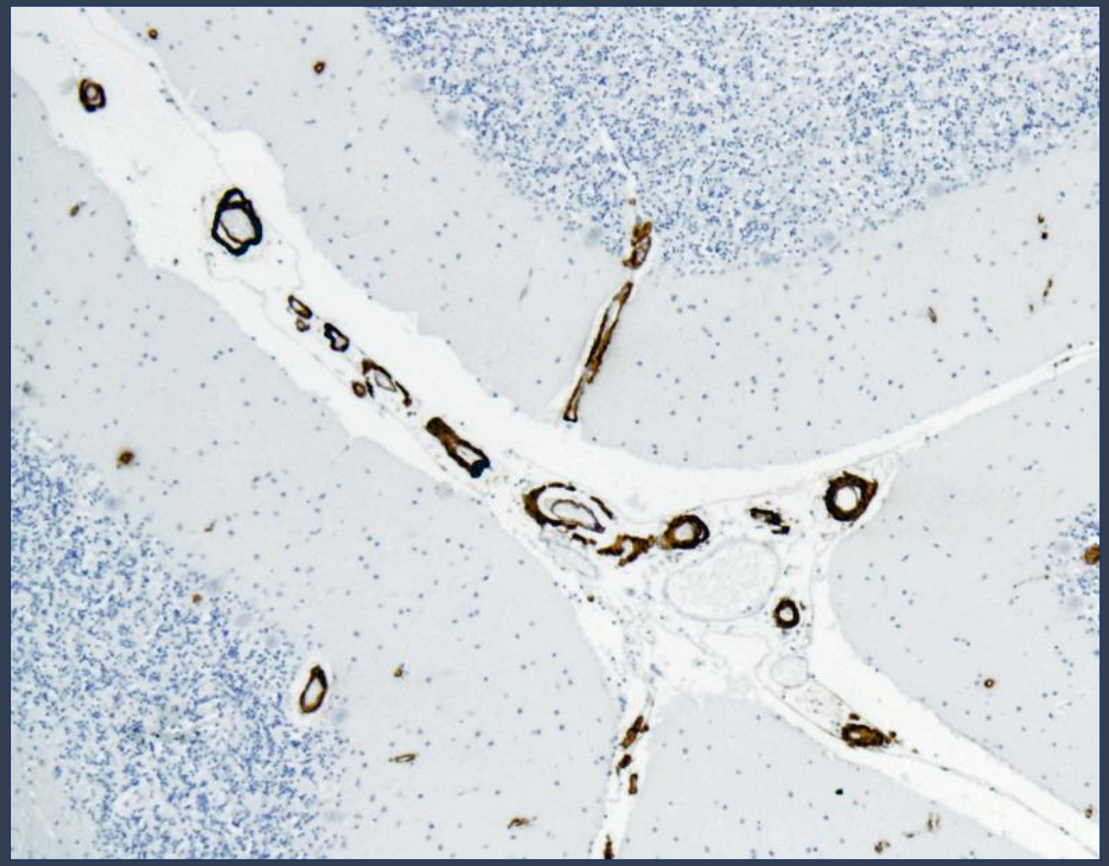


Tau

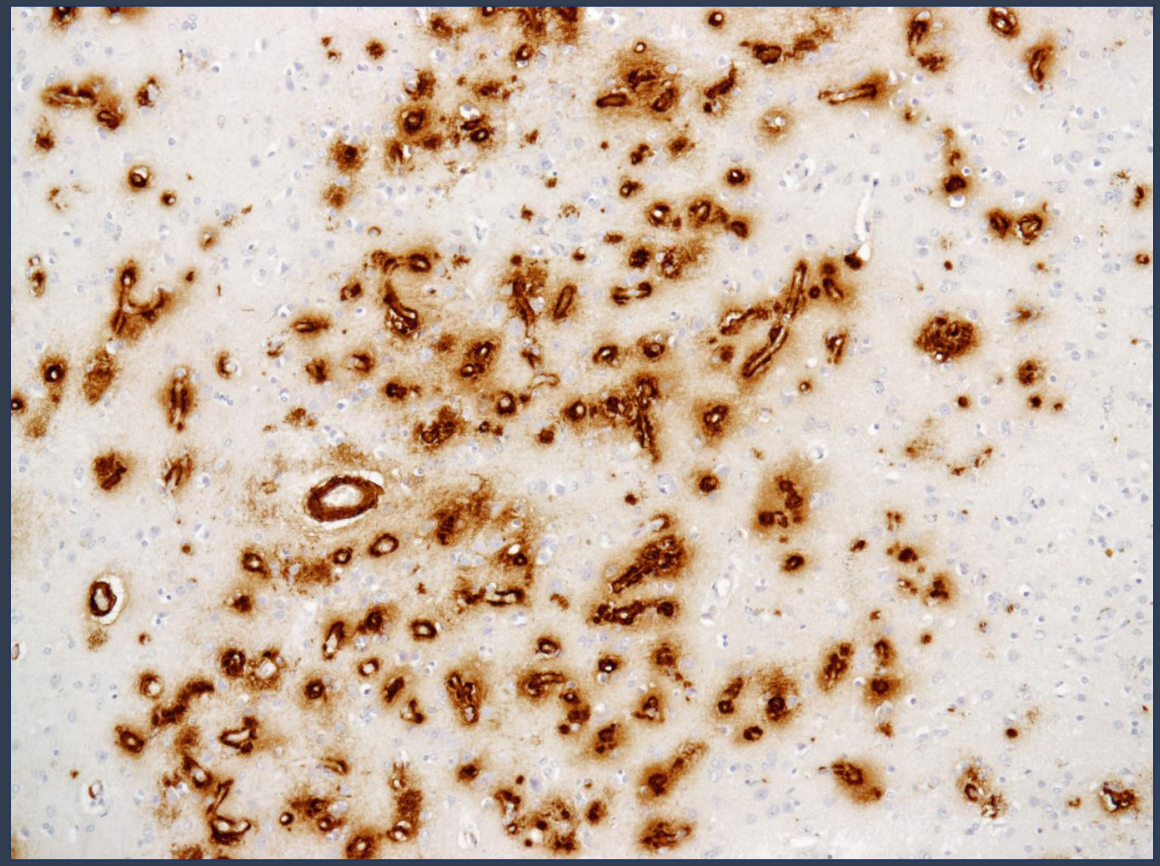


Angiopatía amiloide cerebral (AAC)

AA tipo 2 (Thal)



AA tipo 1, capilar (Thal)



2012

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

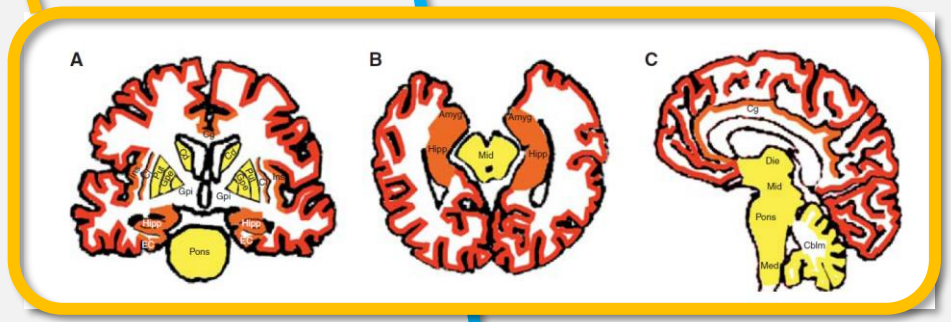
Thomas J. Montine · Creighton H. Phelps · Thomas G. Beach · Eileen H. Bigio · Nigel J. Cairns · Dennis W. Dickson · Charles Duyckaerts · Matthew P. Frosch · Eliezer Masliah · Suzanne S. Mirra · Peter T. Nelson · Julie A. Schneider · Dietmar Rudolf Thal · John Q. Trojanowski · Harry V. Vinters · Bradley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

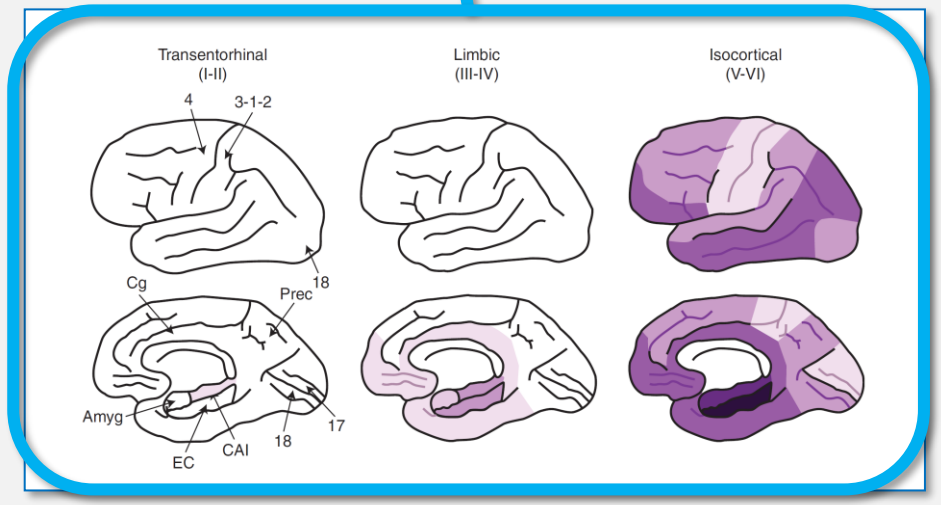
Table 2 "ABC" score for AD neuropathologic change

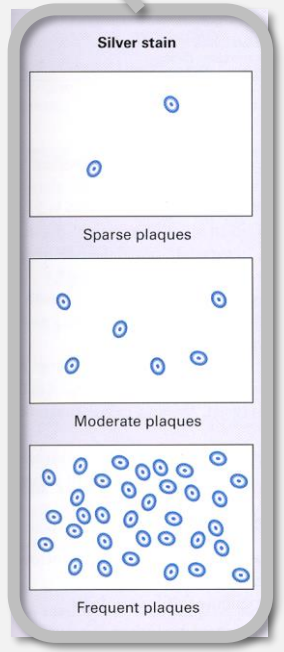
"A"	Thal Phase for Aβ plaques [57]	"B"	Braak and Braak NFT stage [14,15]	"C"	CERAD neuritic plaque score [41]
0	0	0	None	0	None
1	1 or 2	1	I or II	1	Sparse
2	3	2	III or IV	2	Moderate
3	4 or 5	3	V or VI	3	Frequent

Table 3 "ABC" score for level of AD neuropathologic change

AD neuropathologic change		B[a]		
A[b]	C[c]	0 or 1	2	3
0	0	Not[d]	Not[d]	Not[d]
1	0 or 1	Low	Low	Low[e]
	2 or 3[f]	Low	Intermediate	Intermediate[e]
2	Any C	Low[g]	Intermediate	Intermediate[e]
3	0 or 1	Low[g]	Intermediate	Intermediate[e]
	2 or 3	Low[g]	Intermediate	High





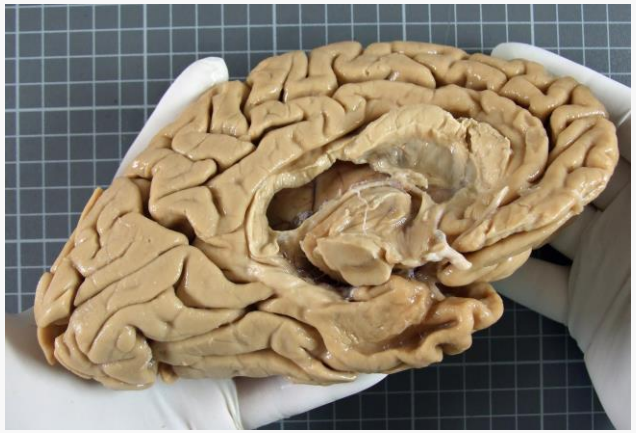


Alzheimer's disease neuropathological change: A1 B2 C3

ENFERMEDAD DE ALZHEIMER ATÍPICA

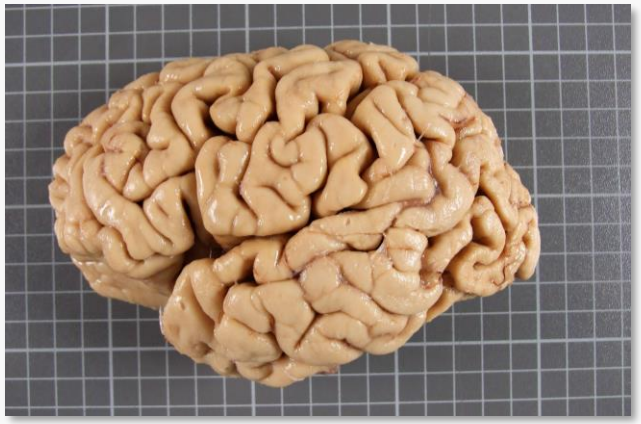
Variante logopénica de afasia progresiva primaria (vlAPP)

Predominio inicial del trastorno del lenguaje, con frecuente anomia, pérdida de fluencia, simplificaciones, sustituciones, circunloquios, dificultades en la repetición y comprensión de frases largas, parafasias fonémicas.



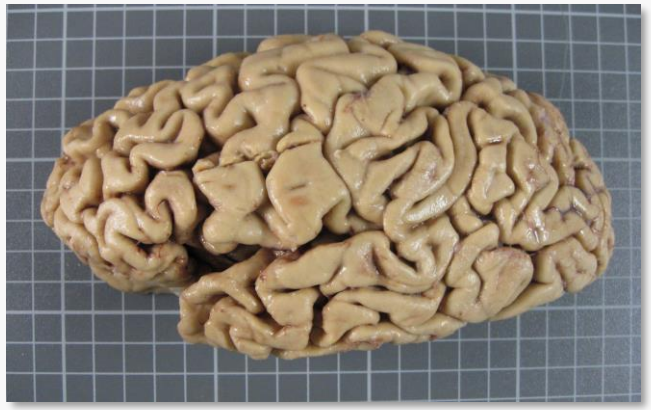
Atrofia cortical posterior (EA visual)

Presentación inicial con agnosia visual, apraxia del vestido, alexia, elementos de los síndromes de Balint y de Gerstmann, apraxia ideomotora y prosopoagnoasia.



Variante frontal (conductual disejecutiva)

Predominio de disfunción conductual y/o disejecutiva. Diagnóstico diferencial con la variante conductual de DFT (aparición más temprana de déficit amnésico).



nature medicine

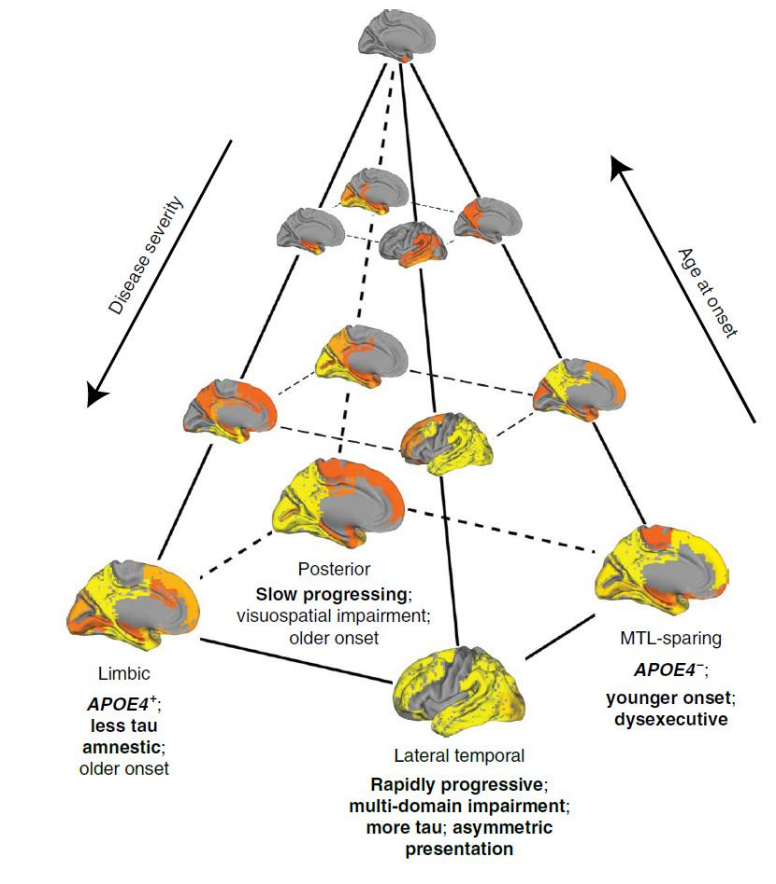
ARTICLES

https://doi.org/10.1038/s41591-021-01309-6

Check for updates

Four distinct trajectories of tau deposition identified in Alzheimer's disease

Jacob W. Vogel[1]✉, Alexandra L. Young[2], Neil P. Oxtoby[3,4], Ruben Smith[5,6], Rik Ossenkoppele[5,7], Olof T. Strandberg[5], Renaud La Joie[8], Leon M. Aksman[3,9], Michel J. Grothe[10,11], Yasser Iturria-Medina[1], the Alzheimer's Disease Neuroimaging Initiative*, Michael J. Pontecorvo[12], Michael D. Devous[12], Gil D. Rabinovici[8,13], Daniel C. Alexander[3,4], Chul Hyoung Lyoo[14], Alan C. Evans[1] and Oskar Hansson[5,15]✉



CellPress
OPEN ACCESS

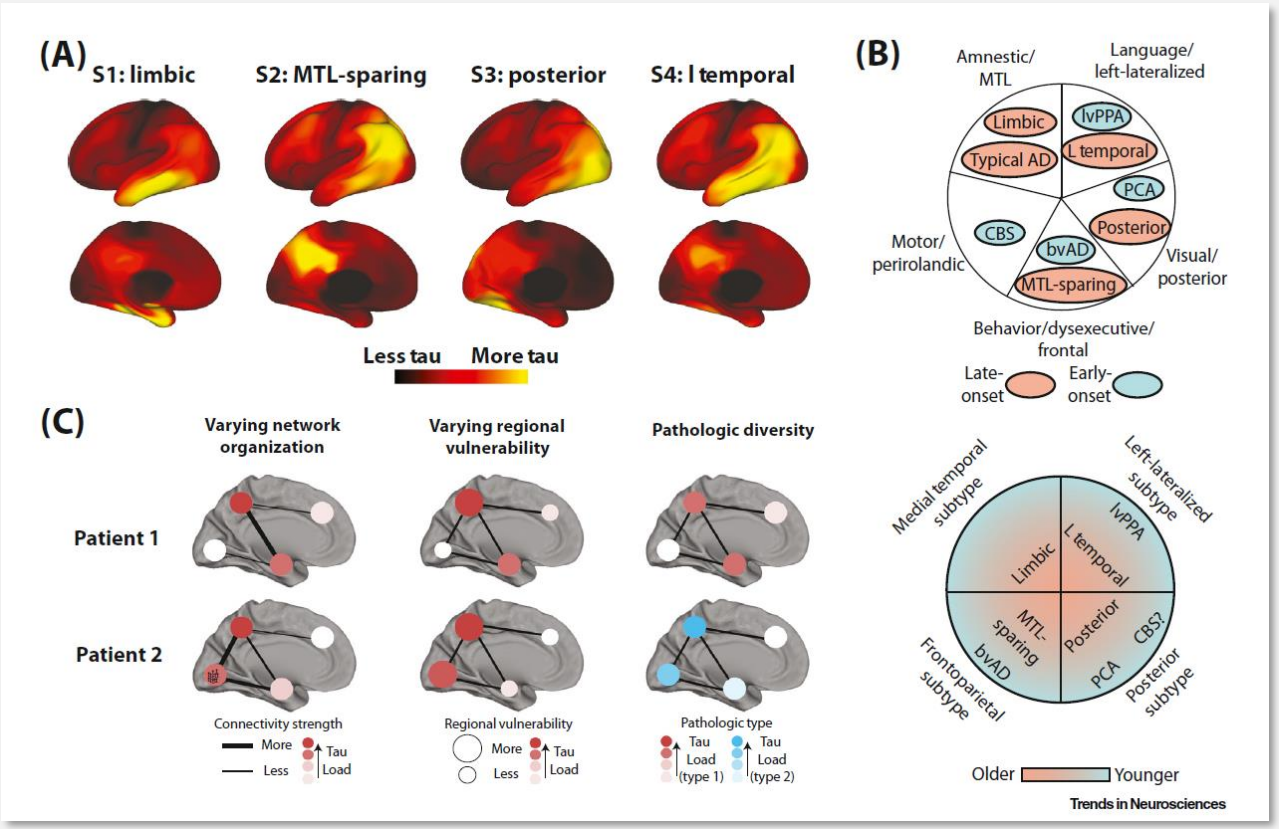
Forum

Subtypes of Alzheimer's disease: questions, controversy, and meaning

Jacob W. Vogel[1,2,*] and Oskar Hansson[3,4,*]

Trends in Neurosciences

Trends in Neurosciences, May 2022, Vol. 45, No. 5



ELSEVIER
CrossMark
Alzheimer's & Dementia: Translational Research & Clinical Interventions 3 (2017) 83-91
Alzheimer's & Dementia

Perspective

Multiple comorbid neuropathologies in the setting of Alzheimer's disease neuropathology and implications for drug development

Gil D. Rabinovici[a], Maria C. Carrillo[b], Mark Forman[c], Susan DeSanti[d], David S. Miller[e], Nicholas Kozauer[f], Ronald C. Petersen[g], Christopher Randolph[h,i], David S. Knopman[g], Eric E. Smith[j], Maria Isaac[k], Niklas Mattsson[l,m], Lisa J. Bain[n], James A. Hendrix[b,*], John R. Sims[o]

Alzheimers Dement. 2017 June ; 13(6): 654–662. doi:10.1016/j.jalz.2016.09.015.

Mixed neuropathologies and estimated rates of clinical progression in a large autopsy sample

Willa D. Brenowitz[1], **Rebecca A. Hubbard**[2], **C. Dirk Keene**[3], **Stephen E. Hawes**[4], **W.T. Longstreth Jr**[1,5], **Randy L. Woltjer**[6], and **Walter A. Kukull**[1]

[1]National Alzheimer's Coordinating Center, Department of Epidemiology, University of Washington, Seattle, Washington, USA

Acta Neuropathol. 2018 September ; 136(3): 377–388. doi:10.1007/s00401-018-1872-5.

Non-Alzheimer's contributions to dementia and cognitive resilience in The 90+ Study

John L. Robinson[1], **Maria M. Corrada**[2], **Gabor G. Kovacs**[1,3], **Myrna Dominique**[1], **Carrie Caswell**[4], **Sharon X. Xie**[4], **Virginia M.-Y. Lee**[1], **Claudia H. Kawas**[5], and **John Q. Trojanowski**[1]

doi:10.1093/brain/awab099 BRAIN 2021: 144; 2186–2198 | 2186
BRAIN
ORIGINAL ARTICLE

Comorbid neuropathological diagnoses in early versus late-onset Alzheimer's disease

Salvatore Spina,[1,†] Renaud La Joie,[1,†] Cathrine Petersen,[1] Amber L. Nolan,[1] Deion Cuevas,[1] Celica Cosme,[1] Mackenzie Hepker,[1] Ji-Hye Hwang,[1] Zachary A. Miller,[1] Eric J. Huang,[2] Anna M. Karydas,[1] Harli Grant,[1] Adam L. Boxer,[1] Maria Luisa Gorno-Tempini,[1] Howard J. Rosen,[1] Joel H. Kramer,[1] Bruce L. Miller,[1] William W. Seeley,[1,2] Gil D. Rabinovici[1,3] and Lea T. Grinberg[1,2]

doi:10.1093/brain/awy146 BRAIN 2018: 141; 2181–2193 | 2181
BRAIN
A JOURNAL OF NEUROLOGY

Neurodegenerative disease concomitant proteinopathies are prevalent, age-related and APOE4-associated

John L. Robinson,[1,2,3,4] Edward B. Lee,[1,2,3,4] Sharon X. Xie,[1,2,3,4,5] Lior Rennert,[1,2,3,4,5] EunRan Suh,[1,2,3,4] Colin Bredenberg,[1,2,3,4] Carrie Caswell,[1,2,3,4,5] Vivianna M. Van Deerlin,[1,2,3,4] Ning Yan,[1,2,3,4,6] Ahmed Yousef,[1,2,3,4] Howard I. Hurtig,[1,2,3,7] Andrew Siderowf,[1,2,3,7] Murray Grossman,[1,2,3,7,8] Corey T. McMillan,[7,8] Bruce Miller,[9] John E. Duda,[3,10] David J. Irwin,[1,2,3,7,8] David Wolk,[1,2,3,7,8,11] Lauren Elman,[3,7] Leo McCluskey,[3,7] Alice Chen-Plotkin,[1,2,3,7] Daniel Weintraub,[2,3,12] Steven E. Arnold,[13] Johannes Brettschneider,[14] Virginia M.-Y. Lee[1,2,3,4,7] and John Q. Trojanowski[1,2,3,4,7]

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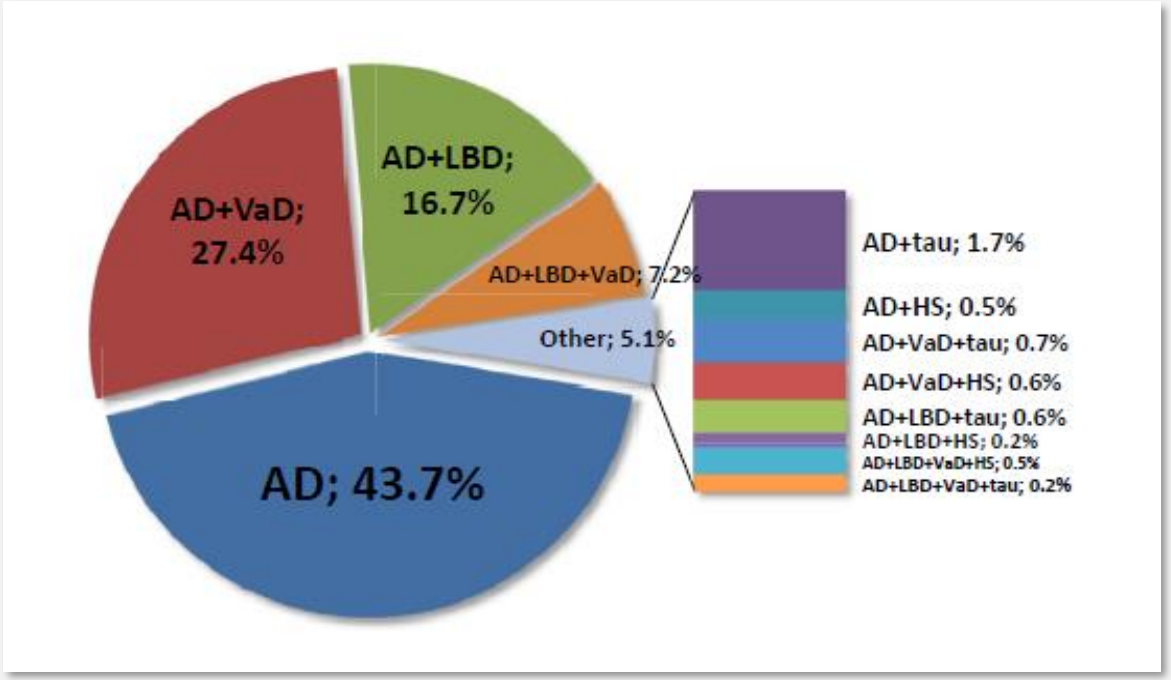
Alzheimer's & Dementia: Translational Research & Clinical Interventions 3 (2017) 83-91
Alzheimer's & Dementia

Perspective

Multiple comorbid neuropathologies in the setting of Alzheimer's disease neuropathology and implications for drug development

Gil D. Rabinovici[a], Maria C. Carrillo[b], Mark Forman[c], Susan DeSanti[d], David S. Miller[e], Nicholas Kozauer[f], Ronald C. Petersen[g], Christopher Randolph[h,i], David S. Knopman[g], Eric E. Smith[j], Maria Isaac[k], Niklas Mattsson[l,m], Lisa J. Bain[n], James A. Hendrix[b,*], John R. Sims[o]



1. Systematic review: This review summarizes the presentations made at the October 2014 Research Roundtable meeting. Each presenter reviewed the literature of recent work of their specific topic area within the overall area of how overlapping pathologies affect the diagnosis and treatment of clinical Alzheimer's disease (AD) and other dementia phenotypes.
2. Interpretation: This article posits that dementia syndrome is most commonly related to multiple pathologies especially in older individuals, rather than a single process.

Heterogeneidad patológica y comorbilidad en demencia

- Patología de tipo Alzheimer
- Patología cerebrovascular
- Patología de tipo Lewy
- Limbic-predominant age-related TDP-43 encephalopathy (LATE)
- Aging-related tau astrogliopathy (ARTAG)
- Enfermedad de granos argirófilos
- Otras patologías

Staging and natural history of cerebrovascular pathology in dementia

2012

Neurology® 2012;78:1-1

V. Deramecourt, MD, PhD
J.Y. Slade, BSc
A.E. Oakley, MBiol
R.H. Perry, FRCPath
P.G. Ince, FRCPath
C.-A. Maurage, MD, PhD
R.N. Kalaria, FRCPath

Lóbulo frontal
Lóbulo temporal
(0-6)

Hipocampo
(0-4)

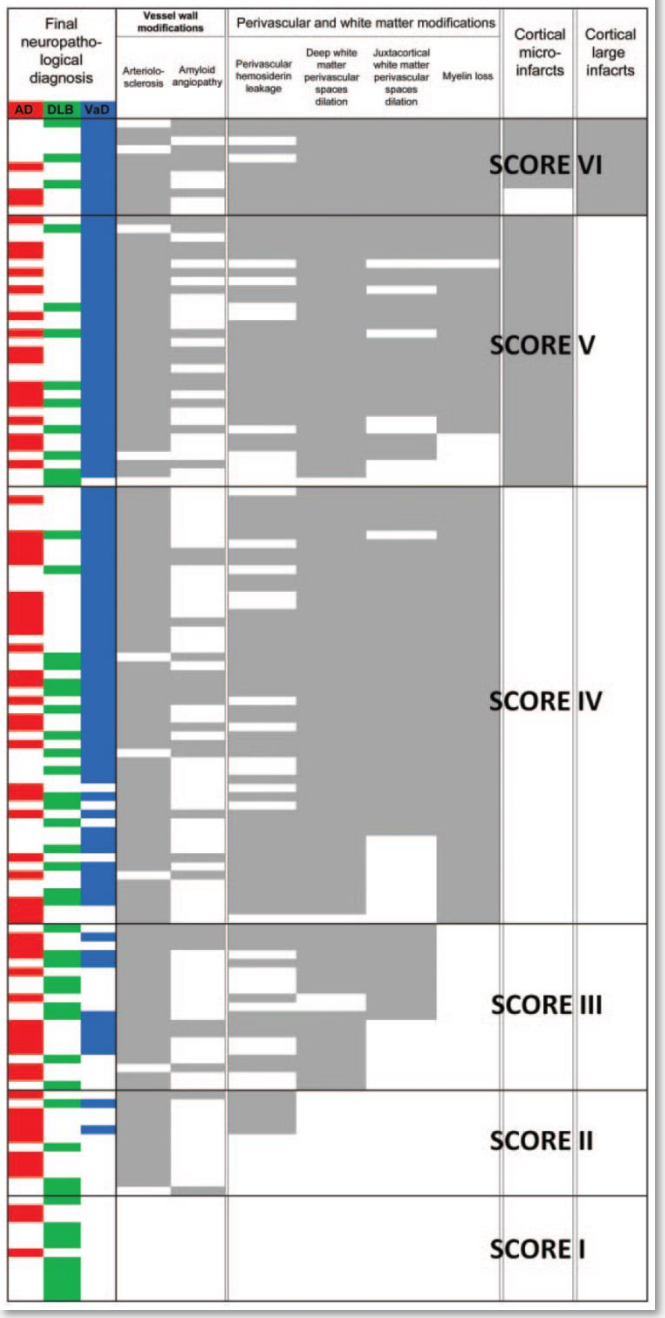
Ganglios basales
(0-4)

Score total (∑)
(0-20)

Table 2 Staging of the cerebrovascular lesions

Score	Staging
Frontal and temporal lobes	
0	Normal appearance of brain, vessels, white matter, and cortex
I	Mild modification of vessel walls, perivascular spaces, or white matter
II	Moderate to severe but isolated modification of the vessel walls (arteriolosclerosis or amyloid angiopathy), usually associated with hemosiderin deposits in the perivascular spaces
III	Moderate to severe perivascular space dilatations either in the deep or the juxtacortical white matter
IV	Moderate to severe myelin loss
V	Presence of cortical microinfarcts
VI	Presence of large infarcts
Hippocampus	
0	Normal appearance
I	Mild modification of vessel walls or perivascular spaces
II	Moderate to severe perivascular space dilatations
III	Presence of microinfarcts (usually in Ammon horn or the subiculum)
IV	Presence of large infarcts
Basal ganglia	
0	Normal appearance
I	Mild modification of vessel walls or perivascular spaces
II	Moderate to severe perivascular space dilatations
III	Presence of microinfarcts
IV	Presence of large infarcts
Total vascular score	
Frontal lobe + Temporal lobe + Hippocampus + Basal ganglia (/20)	

Figure 3 Distribution of the cerebrovascular lesions, example of the frontal lobe



doi:10.1093/brain/aww214 BRAIN 2016: Page 1 of 13 | 1

BRAIN
A JOURNAL OF NEUROLOGY

Vascular cognitive impairment neuropathology guidelines (VCING): the contribution of cerebrovascular pathology to cognitive impairment

Olivia A. Skrobot,[1] Johannes Attems,[2] Margaret Esiri,[3] Tibor Hortobágyi,[4,5] James W. Ironside,[6] Rajesh N. Kalaria,[2] Andrew King,[7] George A. Lammie,[8] David Mann,[9] James Neal,[10] Yoav Ben-Shlomo,[11] Patrick G. Kehoe[1] and Seth Love[1]

2016

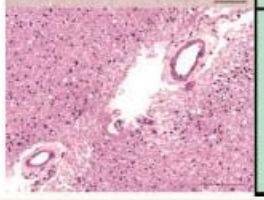
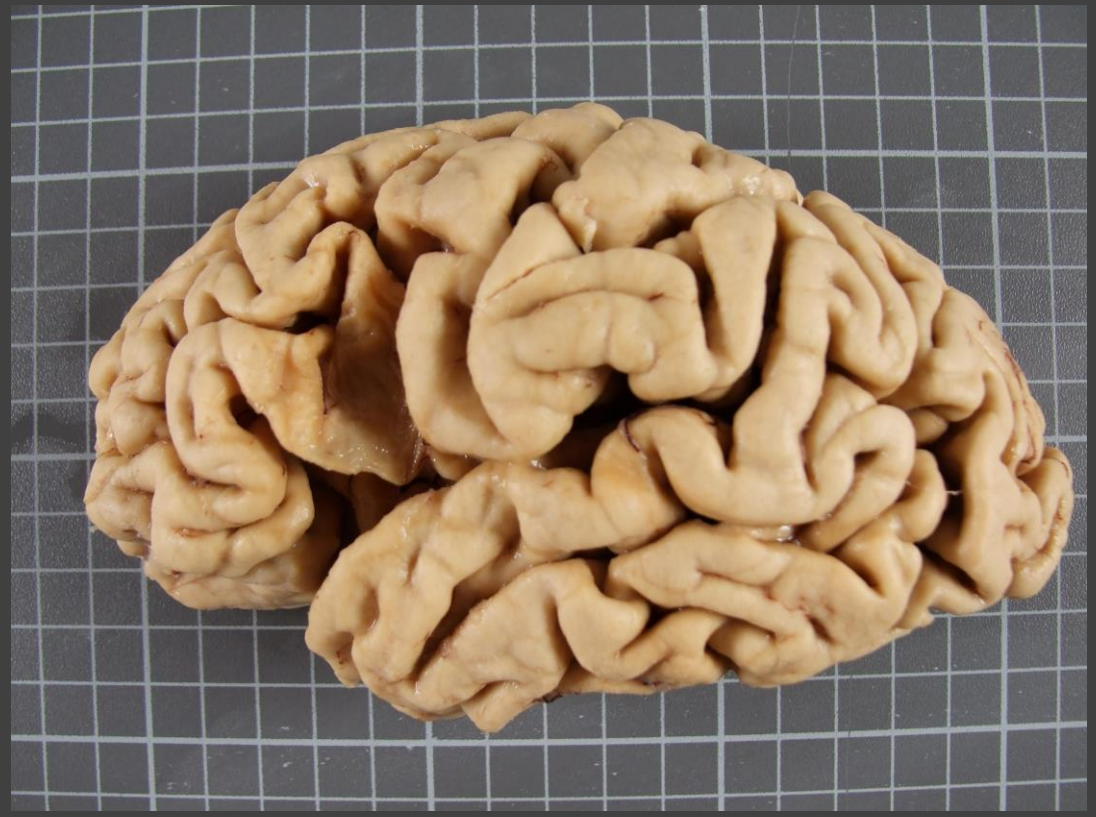
Likelihood that cerebral vascular disease contributed to cognitive impairment		Low (<50%)			Moderate (50-80%)		High (>80%)		
One or more large (> 10 mm) subcortical cerebral infarcts		-	-	-	+	-	+	+	+
Moderate or severe occipital leptomeningeal CAA		-	+	-	-	+	+	-	+
Moderate or severe occipital white matter arteriolosclerosis		-	-	+	-	+	-	+	+

Figure 1 VCING model estimating the likelihood that cerebrovascular disease contributed to cognitive impairment. Combinations of the three main determinants—at least one large (>10 mm diameter) infarct, moderate/severe occipital leptomeningeal CAA, and moderate/severe arteriolosclerosis in the occipital white matter—are used to assign a low, intermediate or high likelihood that cerebrovascular disease contributed to cognitive impairment in an individual case. Scale bars in the *top*, *middle* and *bottom* photomicrographs represent 1 mm, 250 μm and 100 μm, respectively.



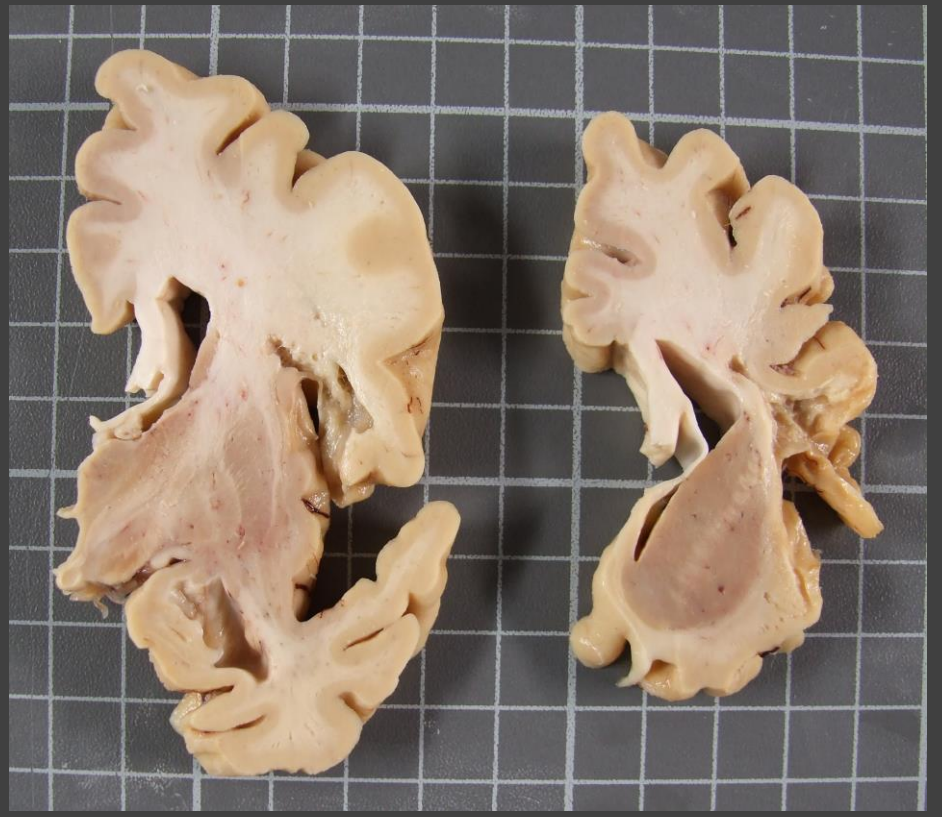


Table 3 "ABC" score for level of AD neuropathologic change

AD neuropathologic change		B[a]		
A[b]	C[c]	0 or 1	2	3
0	0	Not[d]	Not[d]	Not[d]
1	0 or 1	Low	Low	Low[e]
	2 or 3[f]	Low	Intermediate	Intermediate[e]
2	Any C	Low[g]	Intermediate	Intermediate[e]
3	0 or 1	Low[g]	Intermediate	Intermediate[e]
	2 or 3	Low[g]	Intermediate	High

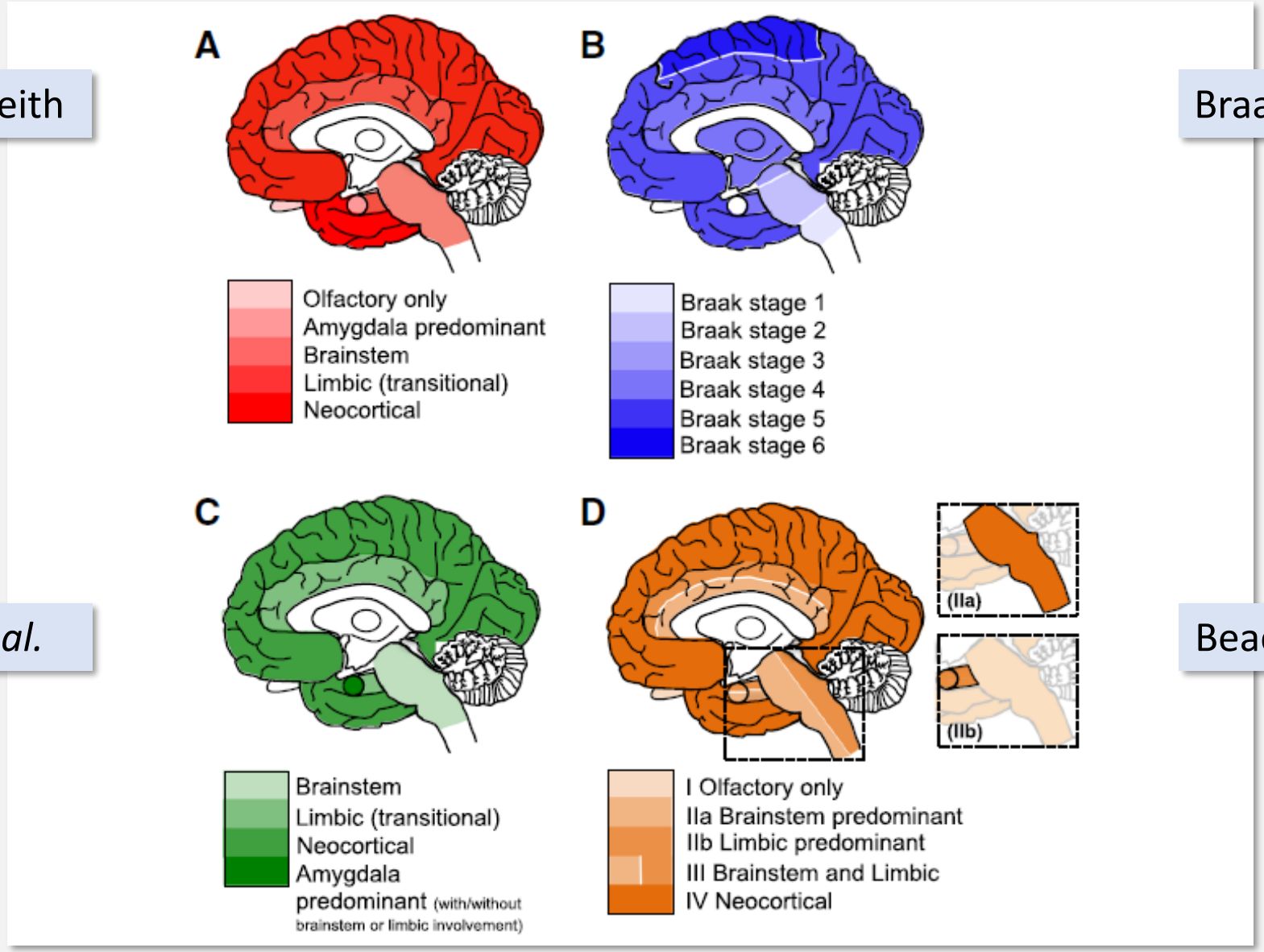
NIA: A3, B3, C3 (alta probabilidad)

Vascular score: 15 (patología intensa)

VCING: 3 (alta probabilidad)

Newcastle-McKeith

Braak



Leverenz *et al.*

Beach *et al.*

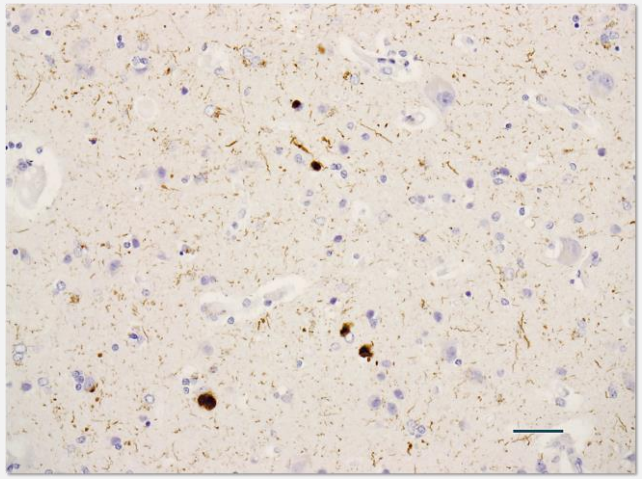
2021

Acta Neuropathologica (2021) 141:159–172
https://doi.org/10.1007/s00401-020-02255-2

ORIGINAL PAPER

Neuropathological consensus criteria for the evaluation of Lewy pathology in post-mortem brains: a multi-centre study

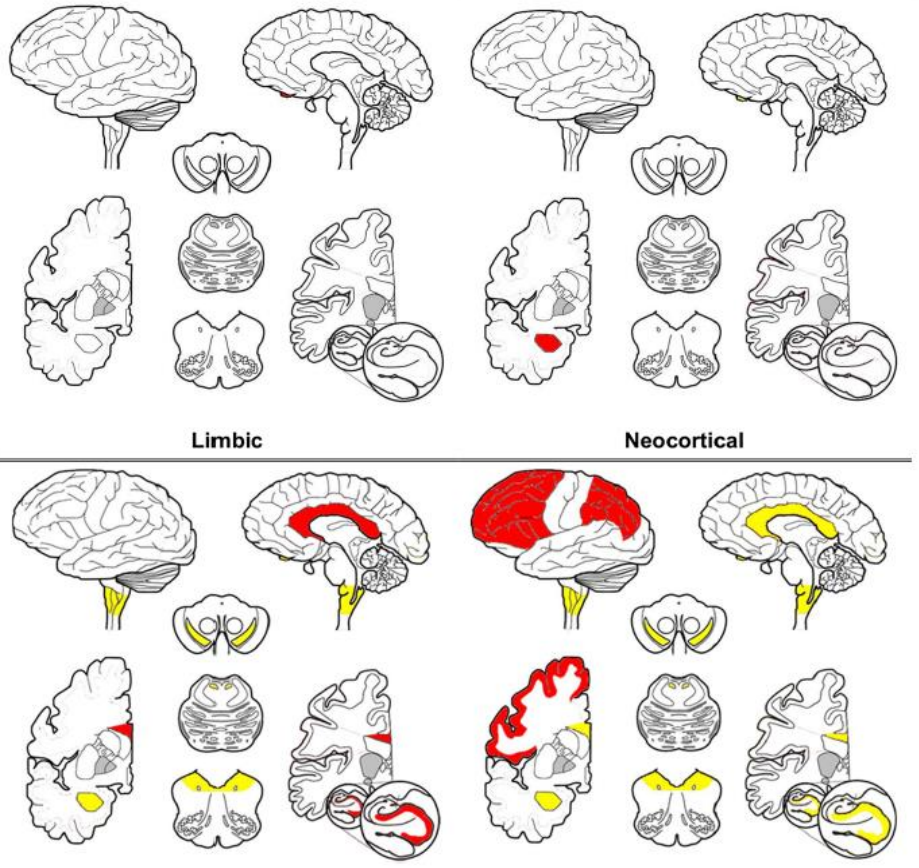
Johannes Attems[1] · Jon B. Toledo[2,3] · Lauren Walker[1] · Ellen Gelpi[4,5] · Steve Gentleman[6] · Glenda Halliday[7] · Tibor Hortobagyi[8,9,10,11] · Kurt Jellinger[12] · Gabor G. Kovacs[13,14] · Edward B. Lee[3] · Seth Love[15] · Kirsty E. McAleese[1] · Peter T. Nelson[16] · Manuela Neumann[17,18] · Laura Parkkinen[19,20] · Tuomo Polvikoski[1] · Beata Sikorska[21] · Colin Smith[22] · Lea Tenenholz Grinberg[23,24] · Dietmar R. Thal[25] · John Q. Trojanowski[3] · Ian G. McKeith[1]



Patología de Lewy cortical (alfa-sinucleína)

Lewy Pathology Consensus Criteria (LPC)

Category of LP	OB	Amy.	dmX or SN (1)	MTL or Cing. (1)	Fr. or Pa. ctx (1)
Olfactory only	+	-	-	-	-
Amygdala predominant	- / +	+	-	-	-
Brainstem predominant	- / +	- / +	+	-	-
Limbic	- / +	- /+	- / +	+	-
Neocortical	- / +	- / +	- / +	- /+	+



2019

doi:10.1093/brain/awz099 BRAIN 2019: Page 1 of 25 | 1

BRAIN
A JOURNAL OF NEUROLOGY

REVIEW

Limbic-predominant age-related TDP-43 encephalopathy (LATE): consensus working group report

Peter T. Nelson,[1] Dennis W. Dickson,[2] John Q. Trojanowski,[3] Clifford R. Jack Jr.,[4] Patricia A. Boyle,[5] Konstantinos Arfanakis,[5,6] Rosa Rademakers,[2] Irina Alafuzoff,[7] Johannes Attems,[8] Carol Brayne,[9] Ian T.S. Coyle-Gilchrist,[9] Helena C. Chui,[10] David W. Fardo,[1] Margaret E. Flanagan,[11] Glenda Halliday,[12] Suvi R.K. Hokkanen,[9] Sally Hunter,[9] Gregory A. Jicha,[1] Yuriko Katsumata,[1] Claudia H. Kawas,[13] C. Dirk Keene,[14] Gabor G. Kovacs,[15] Walter A. Kukull,[14] Allan I. Levey,[16] Nazanin Makkinejad,[6] Thomas J. Montine,[17] Shigeo Murayama,[18] Melissa E. Murray,[2] Sukriti Nag,[5] Robert A. Rissman,[19] William W. Seeley,[20] Reisa A. Sperling,[21] Charles L. White III,[22] Lei Yu[5] and Julie A. Schneider[5]

Limbic-predominant age-related TDP-43 encephalopathy (LATE)

LATE-NC
Stages 0 → 3

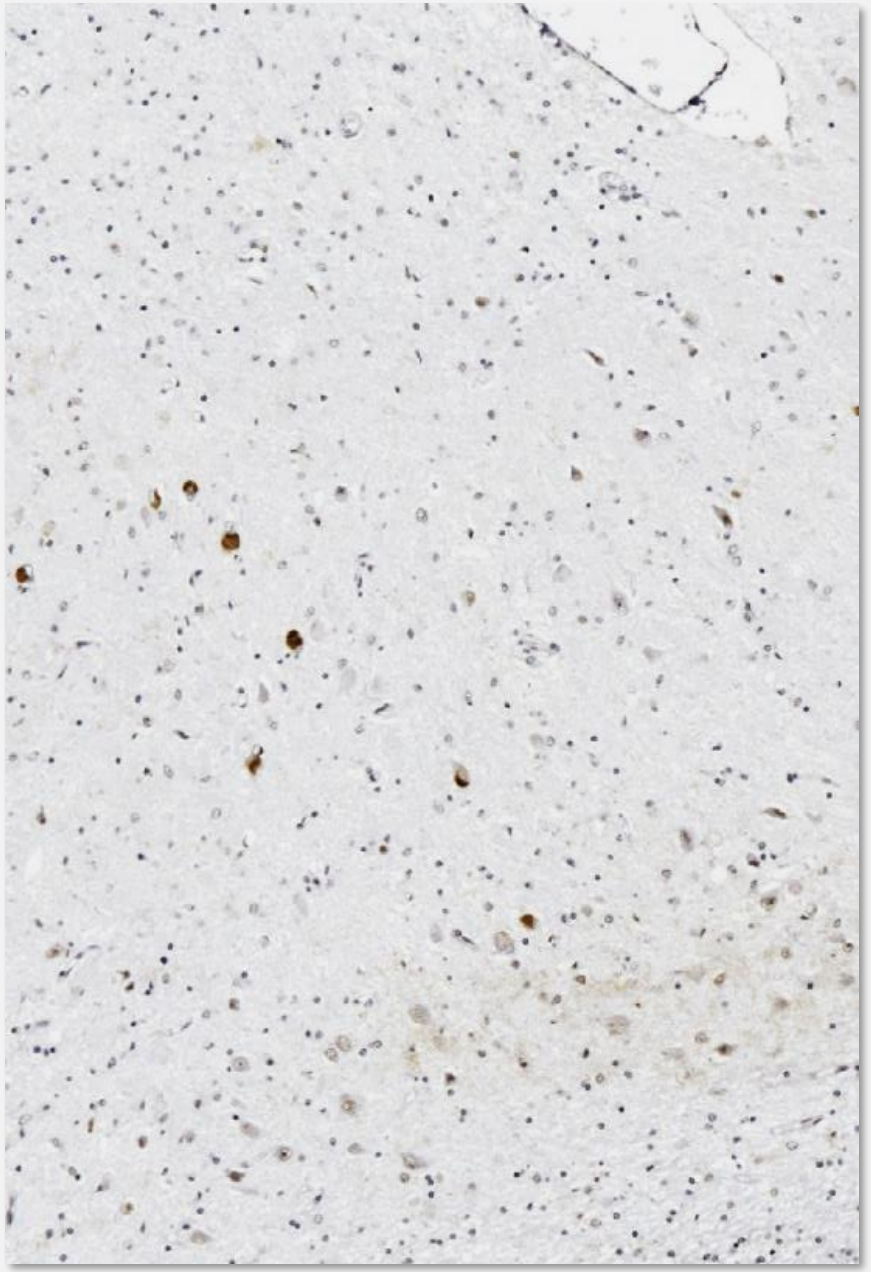
B LATE-NC related stages based on anatomic distribution of TDP-43 pathology

Simplified staging of TDP-43 proteinopathy* for routine LATE-NC diagnosis (consensus recommendation)		Josephs TDP-43 proteinopathy staging (KA Josephs et al, 2013)		Rush University TDP-43 proteinopathy staging (S Nag et al, 2017)	
0	None	0	None	0	None
1	Amygdala	1	Amygdala	1	Amygdala
2	Hippocampus	2	Entorhinal cortex, subiculum	2	Entorhinal cortex, CA1
		3	Dentate, Occipitotemporal cortex	3	Anterior temporal cortex
		4	Insula, Inf temporal cortex	4	Midtemporal and orbitofrontal cortex
		5	Inf olive, midbrain		
3	Middle frontal gyrus (MFG)	6	Basal ganglia, MFG	5	MFG

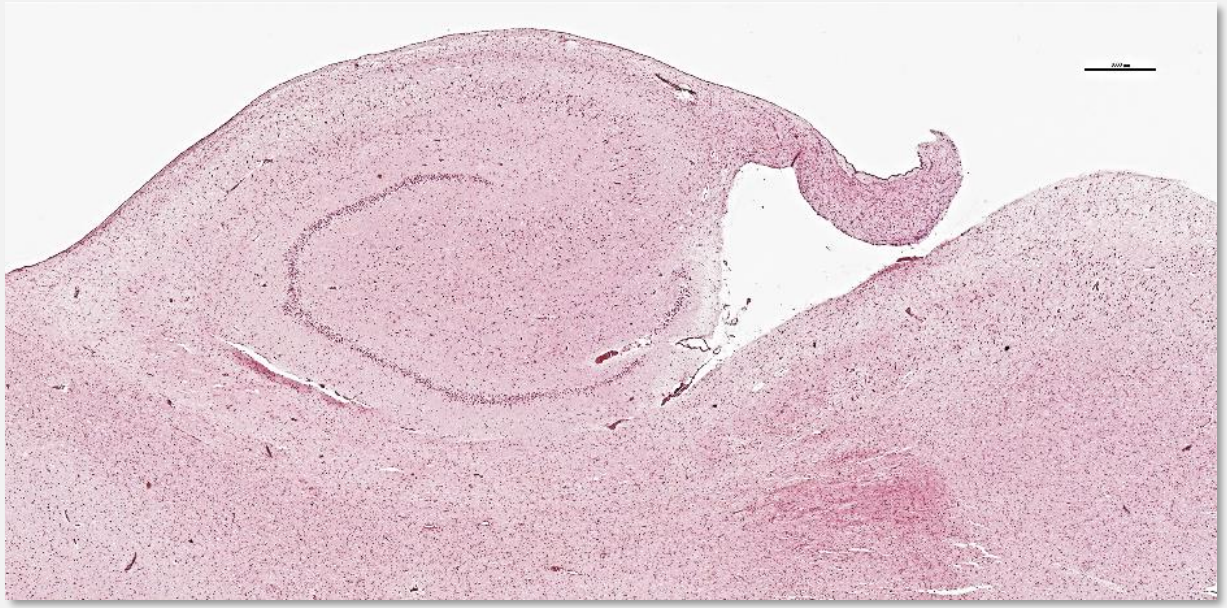
*-*Any* TDP-43 proteinopathy is seen in that anatomic region

Esclerosis del hipocampo

TDP-43



H / E



Received: 6 October 2022 | Revised: 5 December 2022 | Accepted: 21 December 2022

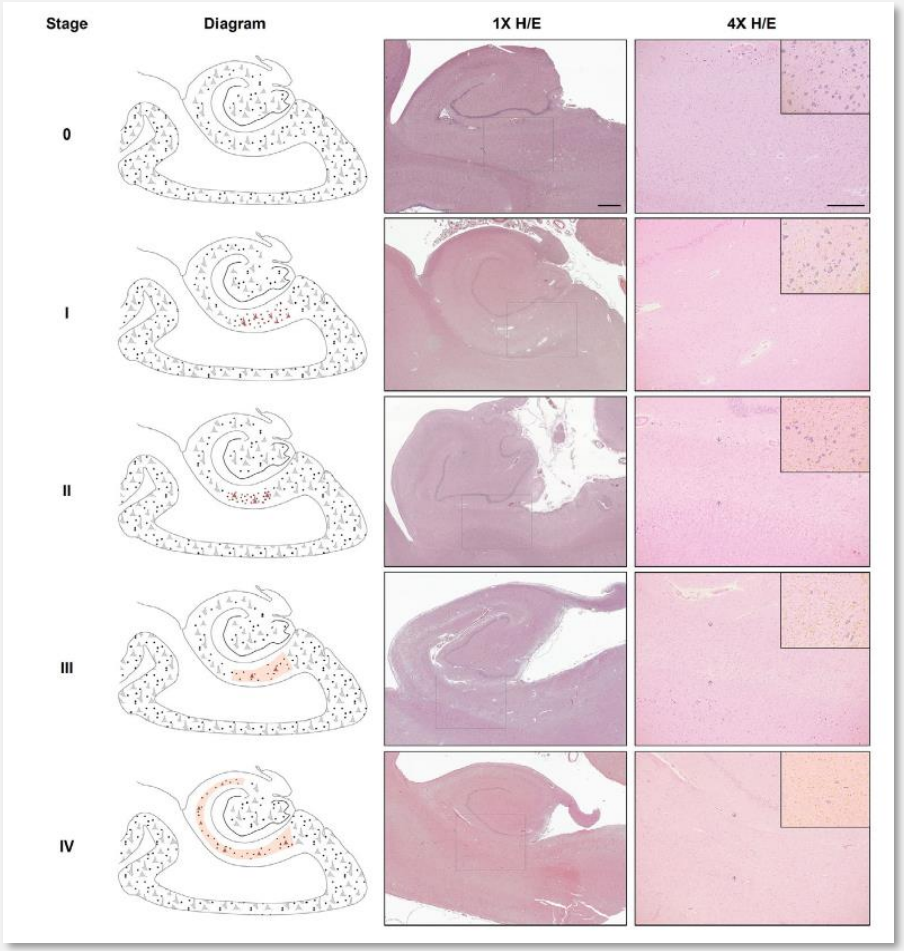
DOI: 10.1002/alz.12942

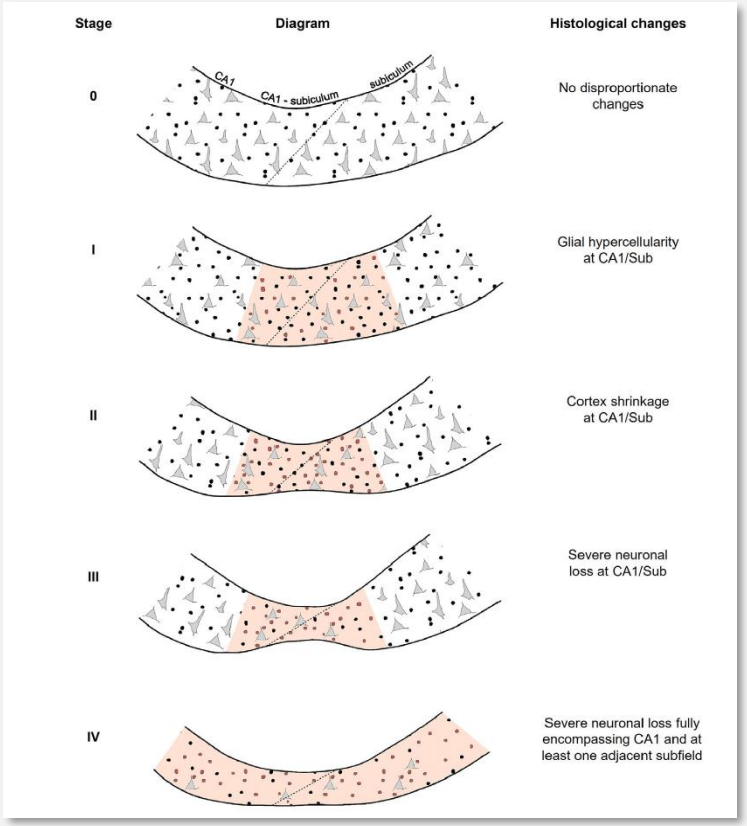
Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

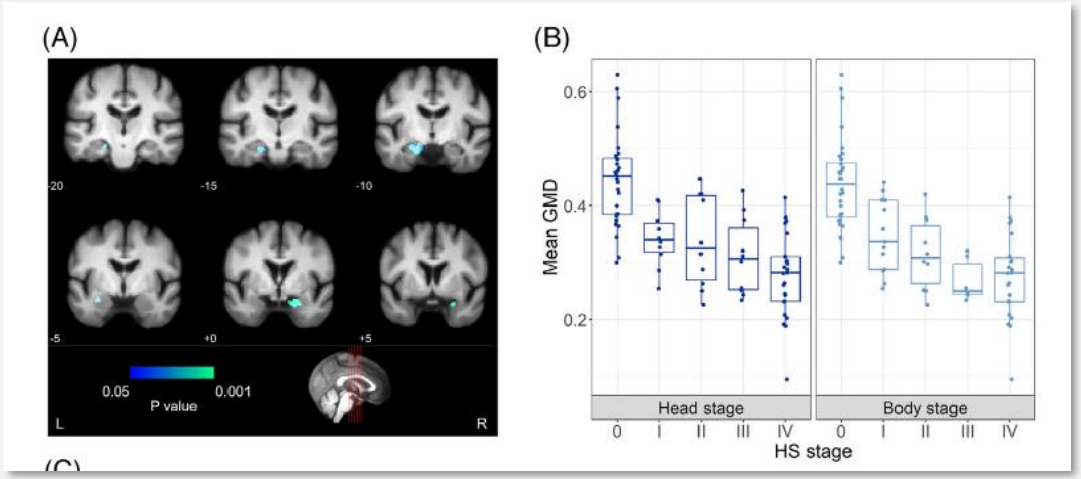
RESEARCH ARTICLE

A novel histological staging of hippocampal sclerosis that is evident in gray matter loss in vivo

Diana Ortega-Cruz[1,2] | Alicia Uceda-Heras[2,3] | Juan Eugenio Iglesias[4,5] | María Ascensión Zea-Sevilla[2] | Bryan Strange[1,2] | Alberto Rabano[2]

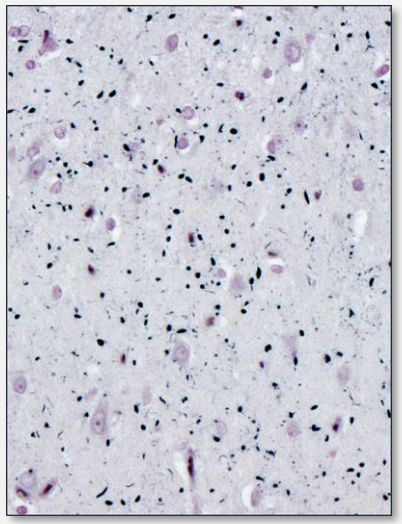




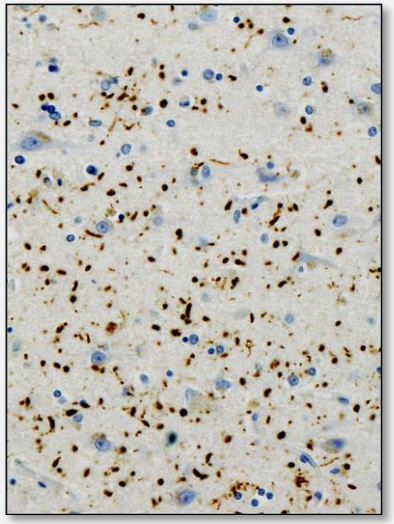


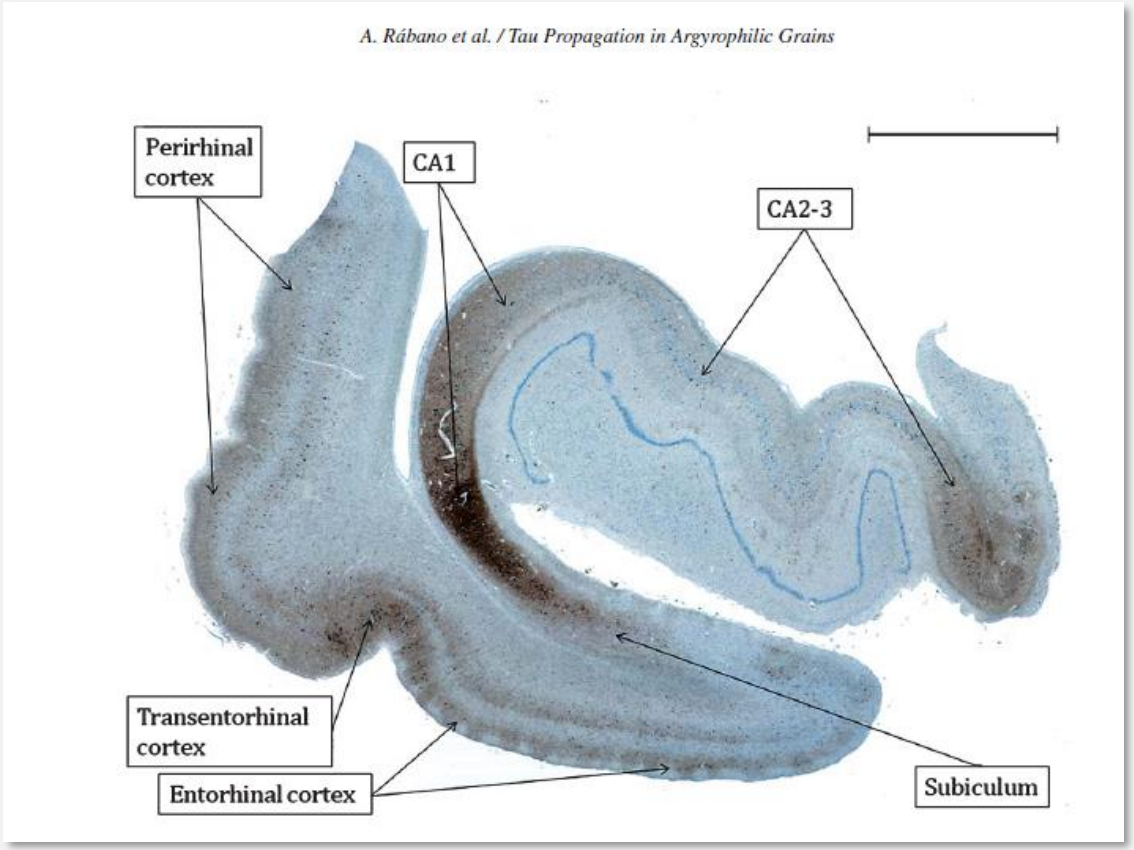
Argyrophilic grain disease

Gallyas

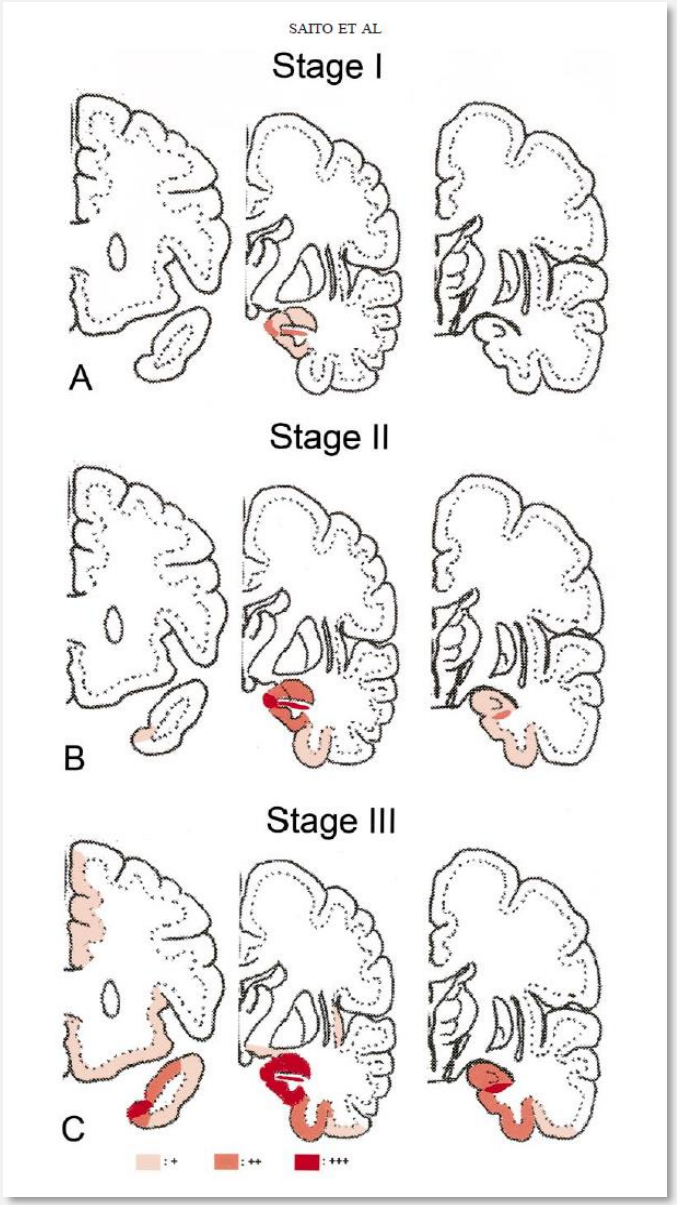


Tau AT8





Rábano *et al*., 2014



Saito *et al*., 2004

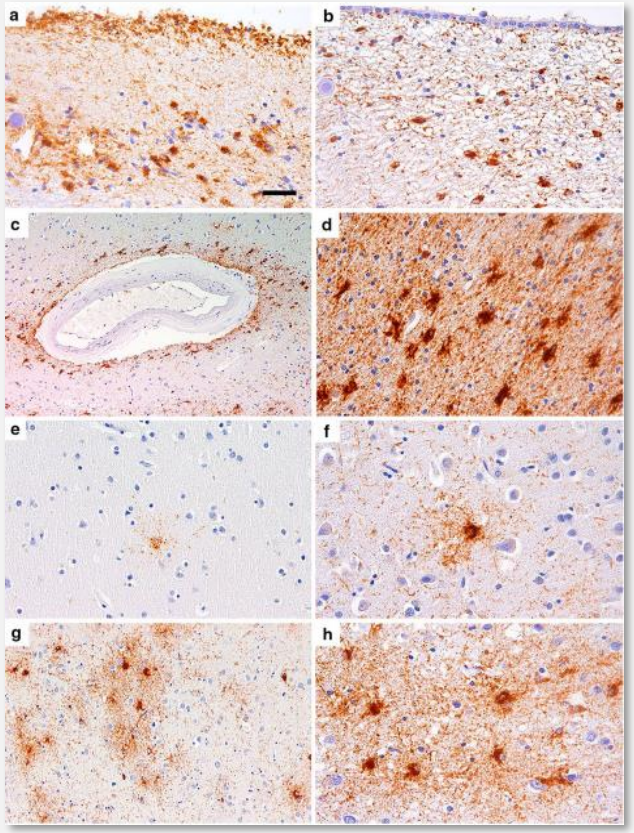
Aging-related tau astrogliopathy (ARTAG)

2016

Acta Neuropathol. 2016 January ; 131(1): 87–102. doi:10.1007/s00401-015-1509-x.

Aging-related tau astrogliopathy (ARTAG): harmonized evaluation strategy

A full list of authors and affiliations appears at the end of the article.



Kovacs *et al. Acta Neuropathologica Communications* (2018) 6:50
https://doi.org/10.1186/s40478-018-0552-y

Acta Neuropathologica Communications

RESEARCH Open Access

Sequential stages and distribution patterns of aging-related tau astrogliopathy (ARTAG) in the human brain

Gabor G. Kovacs[1,2*], Sharon X. Xie[3], John L. Robinson[2], Edward B. Lee[2], Douglas H. Smith[4], Theresa Schuck[2], Virginia M.-Y. Lee[2] and John Q. Trojanowski[2*]

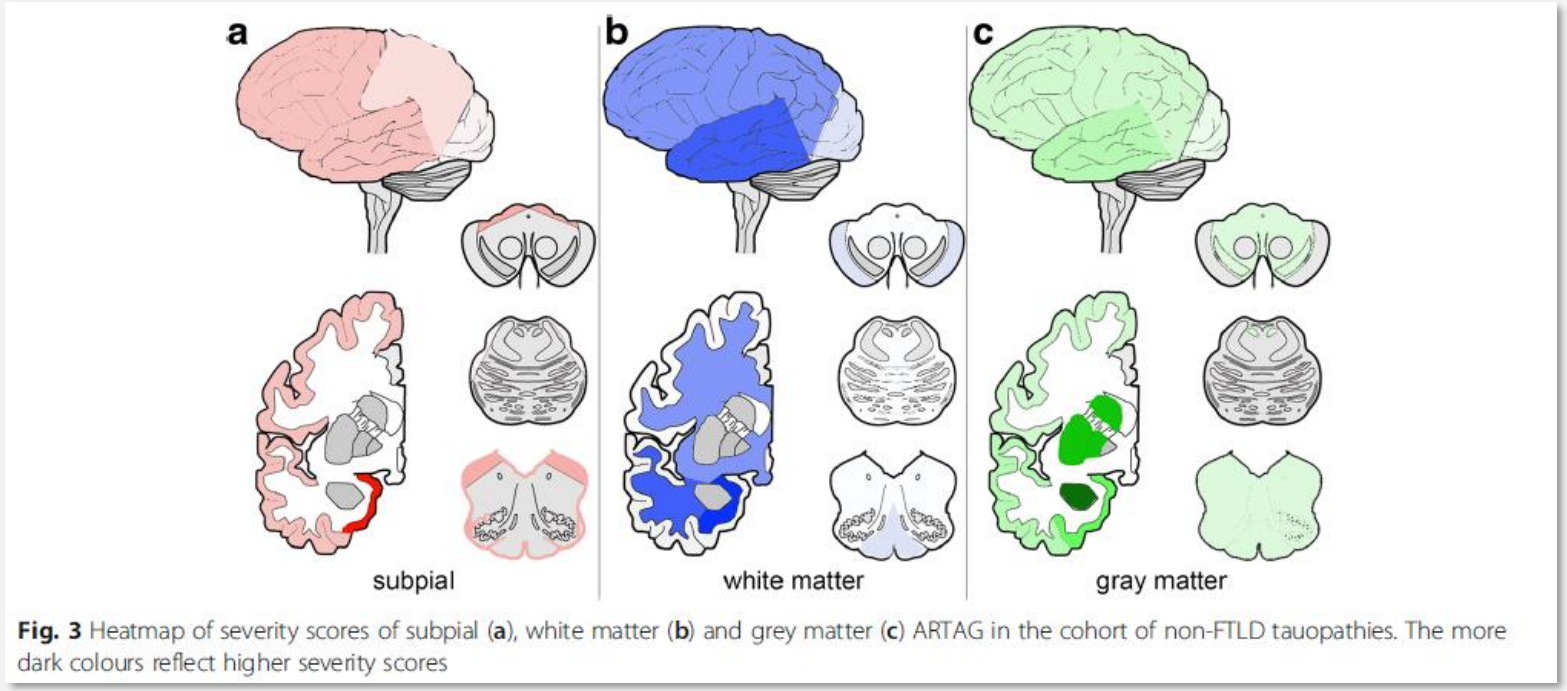
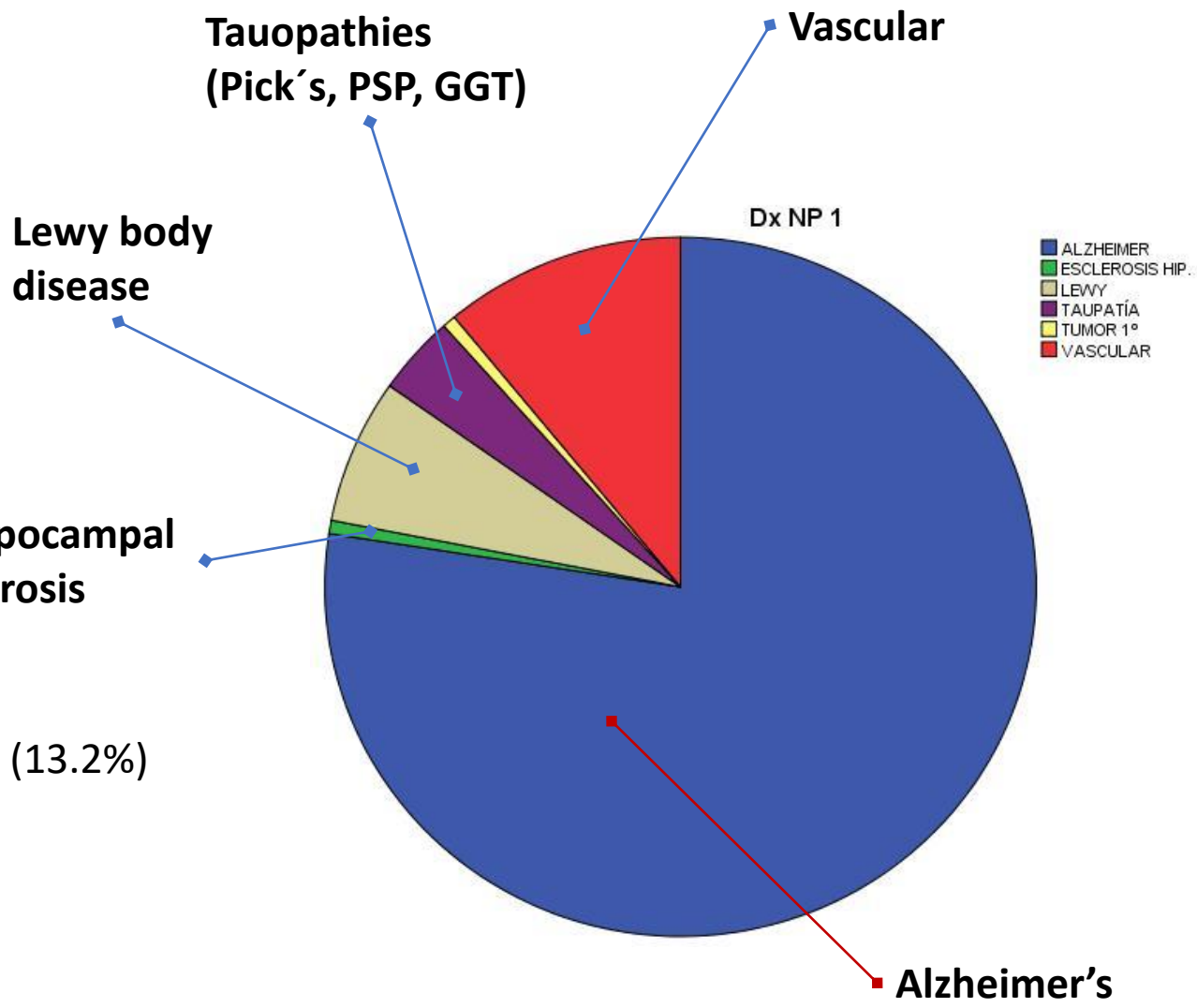


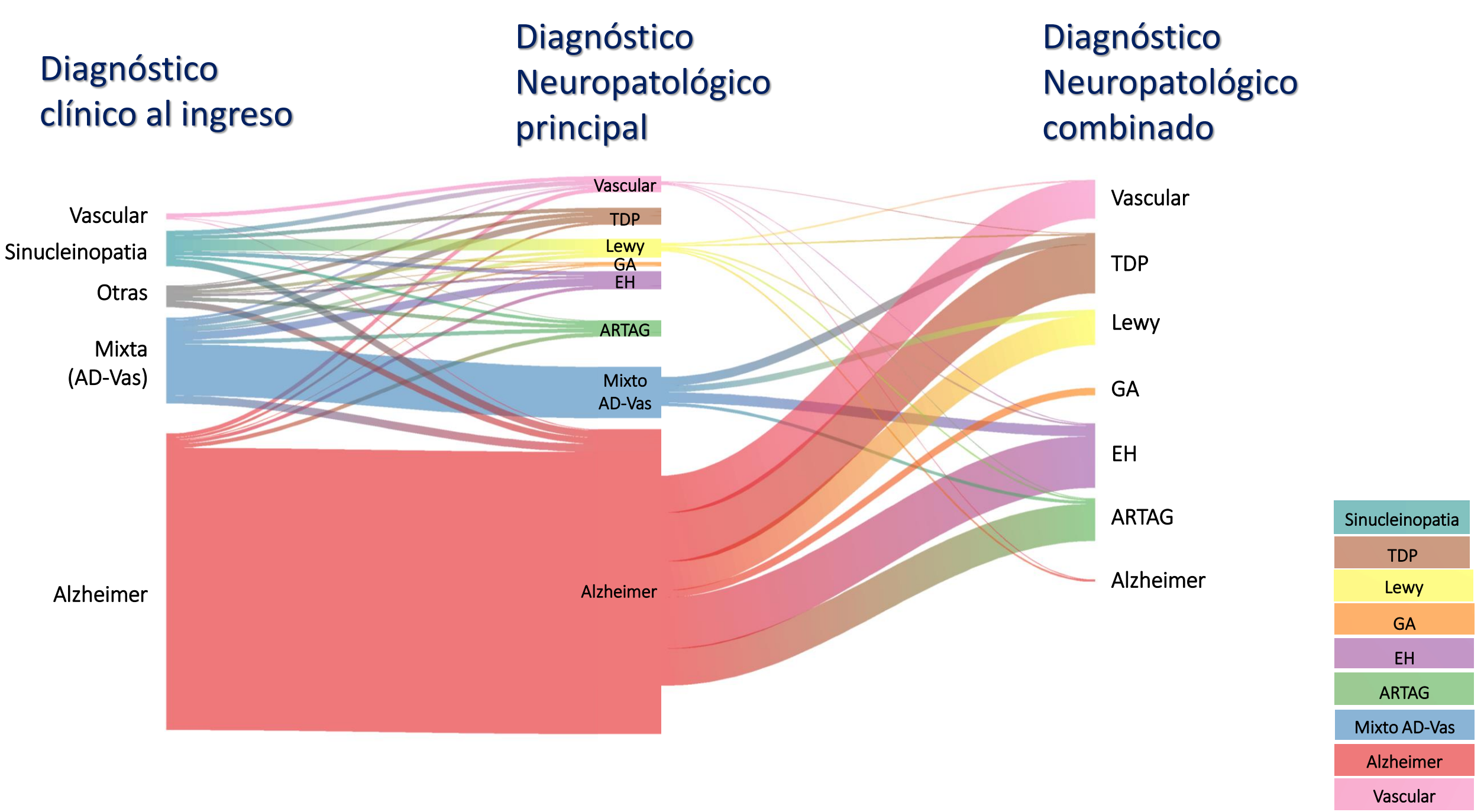
Fig. 3 Heatmap of severity scores of subpial (**a**), white matter (**b**) and grey matter (**c**) ARTAG in the cohort of non-FTLD tauopathies. The more dark colours reflect higher severity scores

N	167
Sex	79% female
T in CAFRS (mths)	52.9 (38.6)
Age at onset	75.4 (7.3)
Age at death	87.2 (6.5)
Survival time	11.9 (4.4)
PMI (hrs.)	4.5 (2.1)
APOE e4	45.2%
High ADNC	75.8%
High vascular path.	54.5%
Lewy path. (LPC>1)*	37.8%
LATE (HS)	71.2% (45.2%)
ARTAG	52.7%
AGD	12%

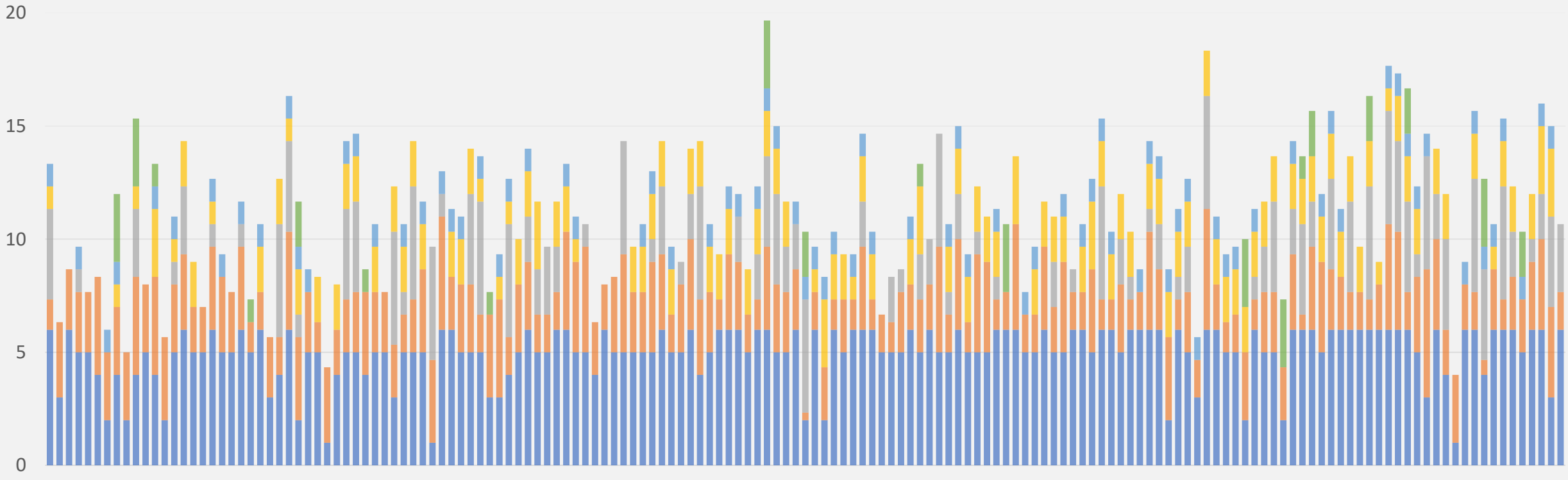
*LPC =1 (13.2%)

Main neuropathological diagnosis




Diagnóstico clínico al ingreso
Diagnóstico Neuropatológico principal
Diagnóstico Neuropatológico combinado
Vascular
Sinucleinopatia
Otras
Mixta (AD-Vas)
Alzheimer
Vascular
TDP
Lewy
GA
EH
ARTAG
Mixto AD-Vas
Alzheimer
Vascular
TDP
Lewy
GA
EH
ARTAG
Alzheimer
Sinucleinopatia
TDP
Lewy
GA
EH
ARTAG
Mixto AD-Vas
Alzheimer
Vascular

Vallecas Alzheimer's Study



- Alzheimer' pathology (Braak stage 0 – 6)
- Cerebrovascular pathology (0 – 5)
- Lewy type pathology (0 – 6)
- TDP-43 pathology (LATE) (0 – 3)
- ARTAG (0 – 1)
- Argyrophilic grain disease (0 – 3)

ANN NEUROL 2020;87:816–829

Normative Cognitive Decline in Old Age

Robert S. Wilson, PhD [1,2,3] Tianhao Wang, PhD,[1,2] Lei Yu, PhD [1,2]
David A. Bennett, MD,[1,2] and Patricia A. Boyle, PhD[1,3]

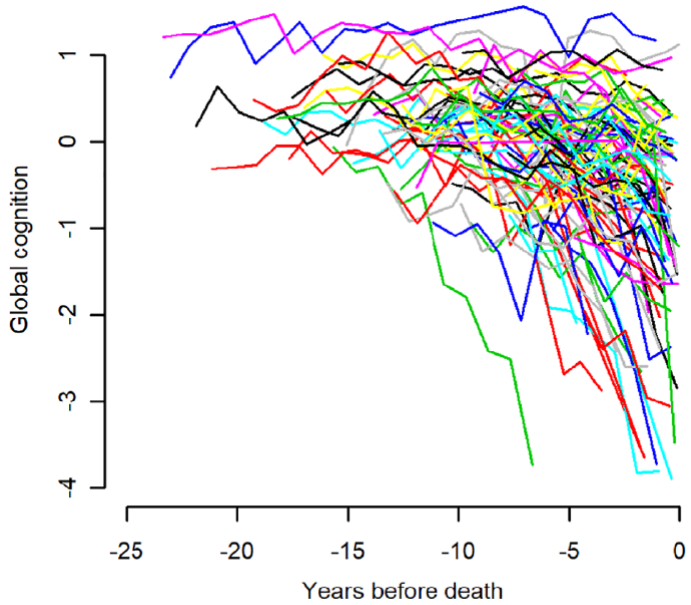
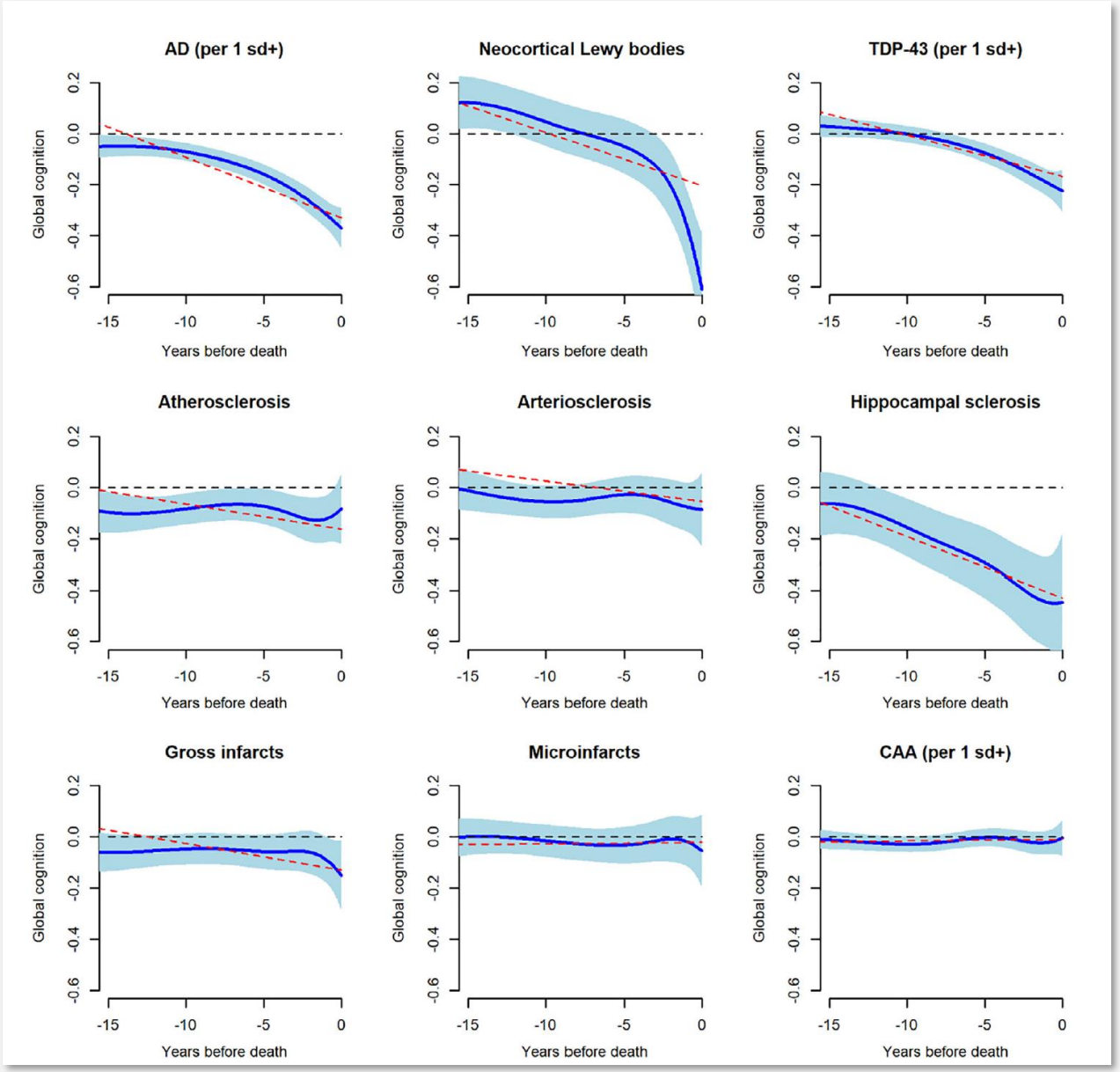


FIGURE 1: Crude trajectories of change in global cognition in 100 randomly selected participants.



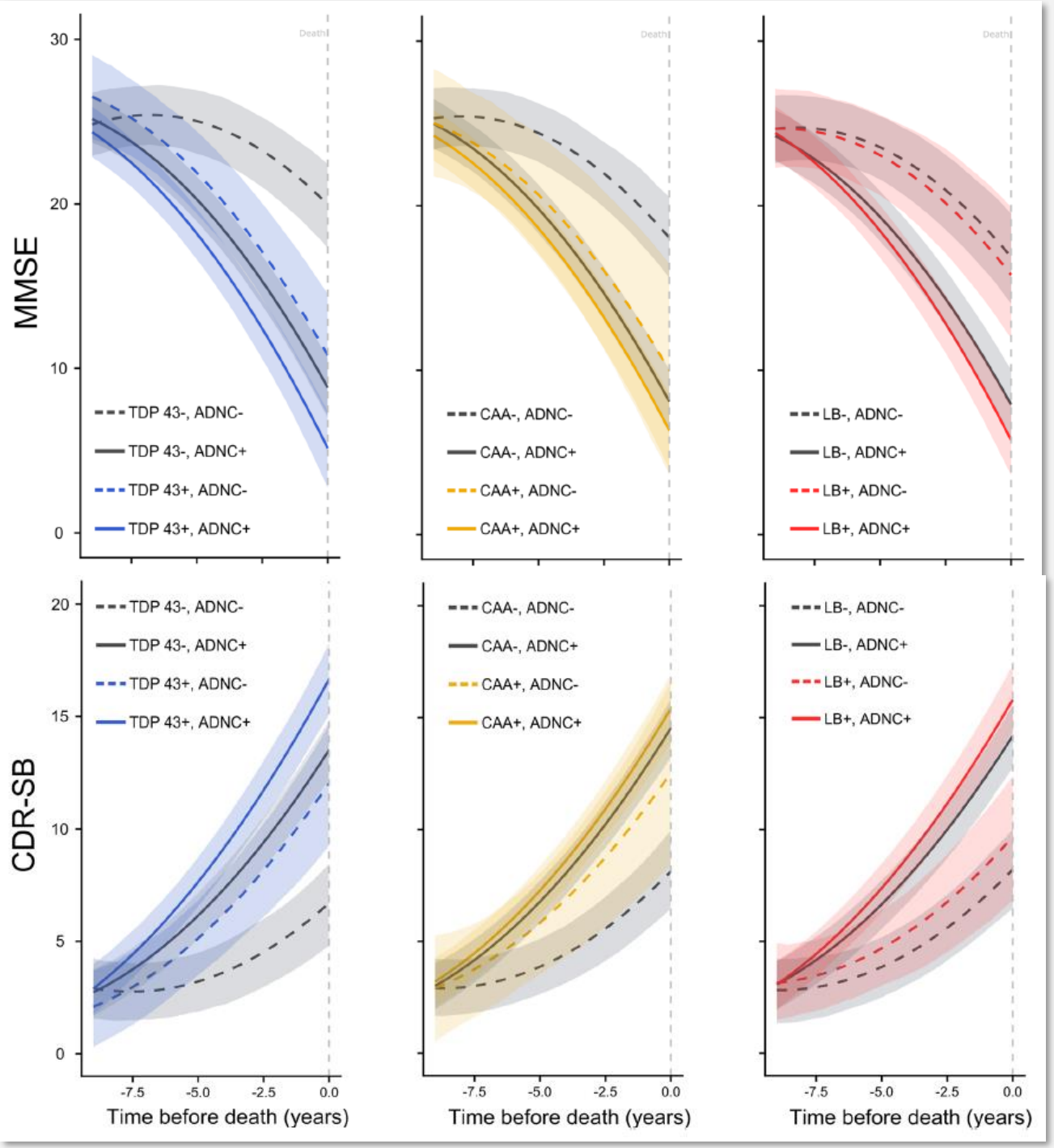
SCIENTIFIC REPORTS
nature research

OPEN

Association of TDP-43 proteinopathy, cerebral amyloid angiopathy, and Lewy bodies with cognitive impairment in individuals with or without Alzheimer's disease neuropathology

David X. Thomas[1,3✉], Sumali Bajaj[2,3], Kevin McRae-McKee[2], Christoforos Hadjichrysanthou[2], Roy M. Anderson[2] & John Collinge[1]

SCIENTIFIC REPORTS | (2020) 10:14579



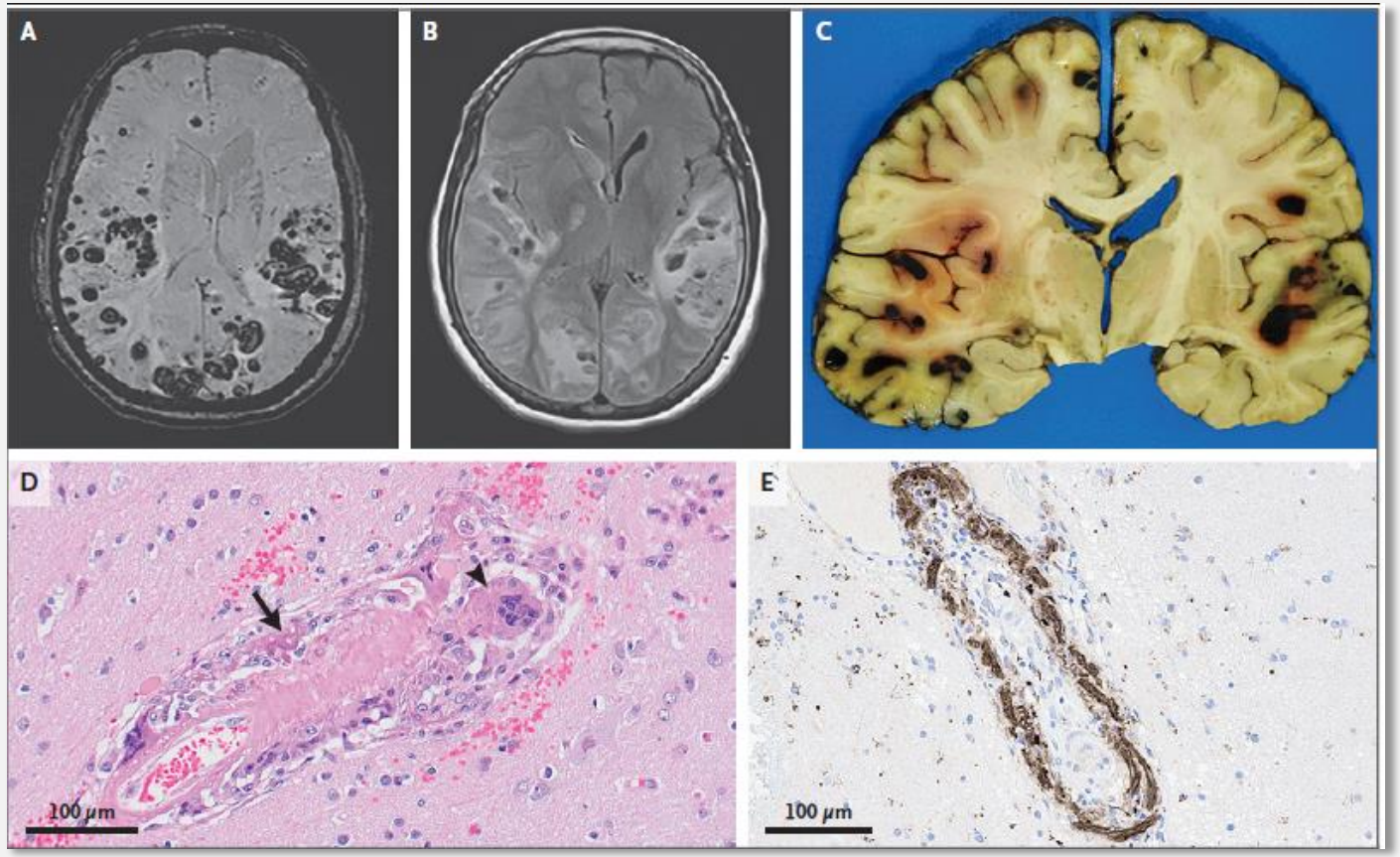
The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Multiple Cerebral Hemorrhages in a Patient Receiving Lecanemab and Treated with t-PA for Stroke

N ENGL J MED 388;5 NEJM.ORG FEBRUARY 2, 2023

¿Heterogeneidad en la angiopatía amiloide cerebral con diferente riesgo de hemorragia cerebral?



Gracias!

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