Degeneración del sistema nervioso central en “oldest old”: descripción de nuevas patologías y repercusión clínica de las mismas

Alberto Rábano

Fundación CIEN, ISCIII, Madrid

Hospital Universitario La Paz,
abril, 2023

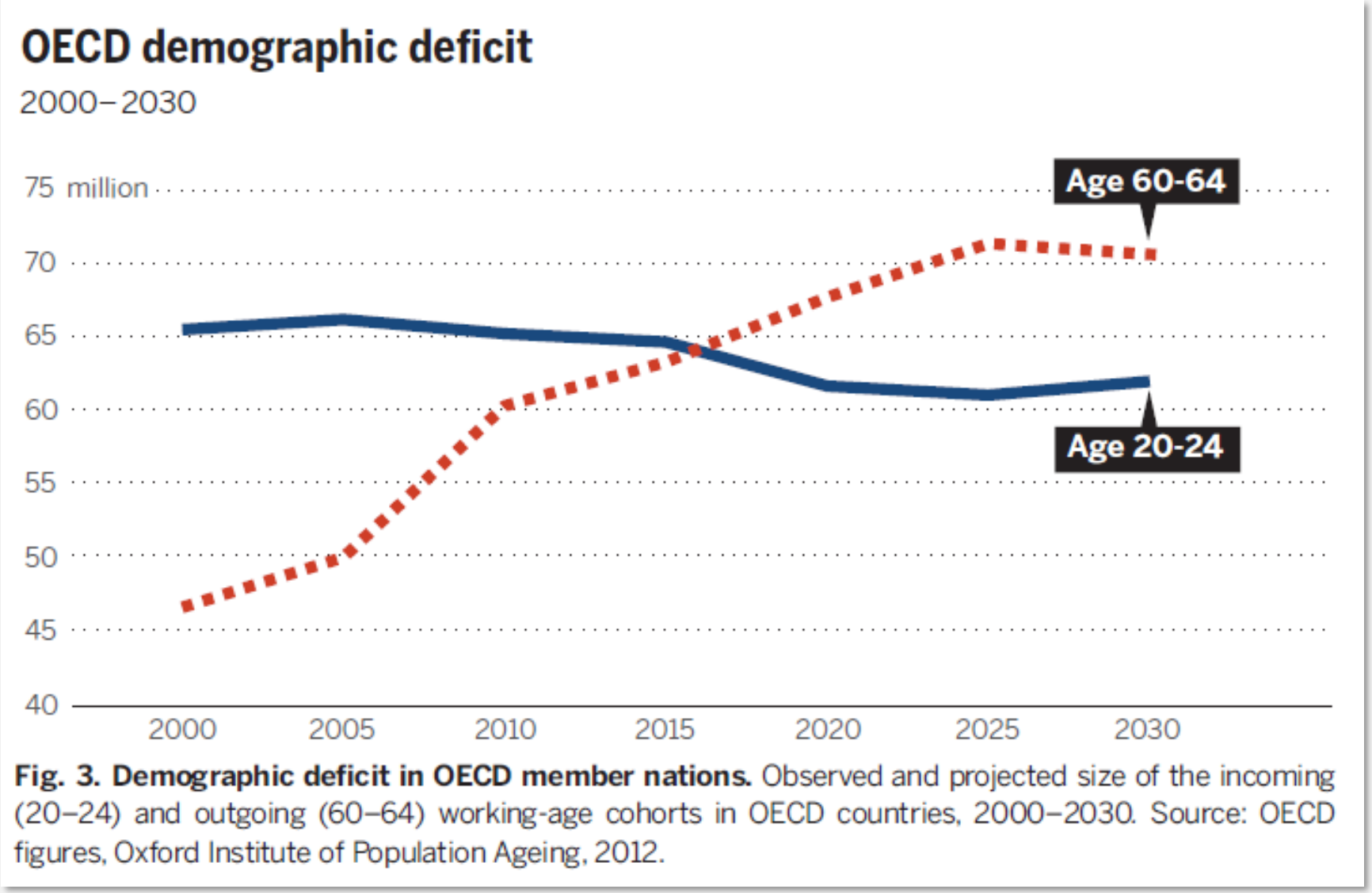
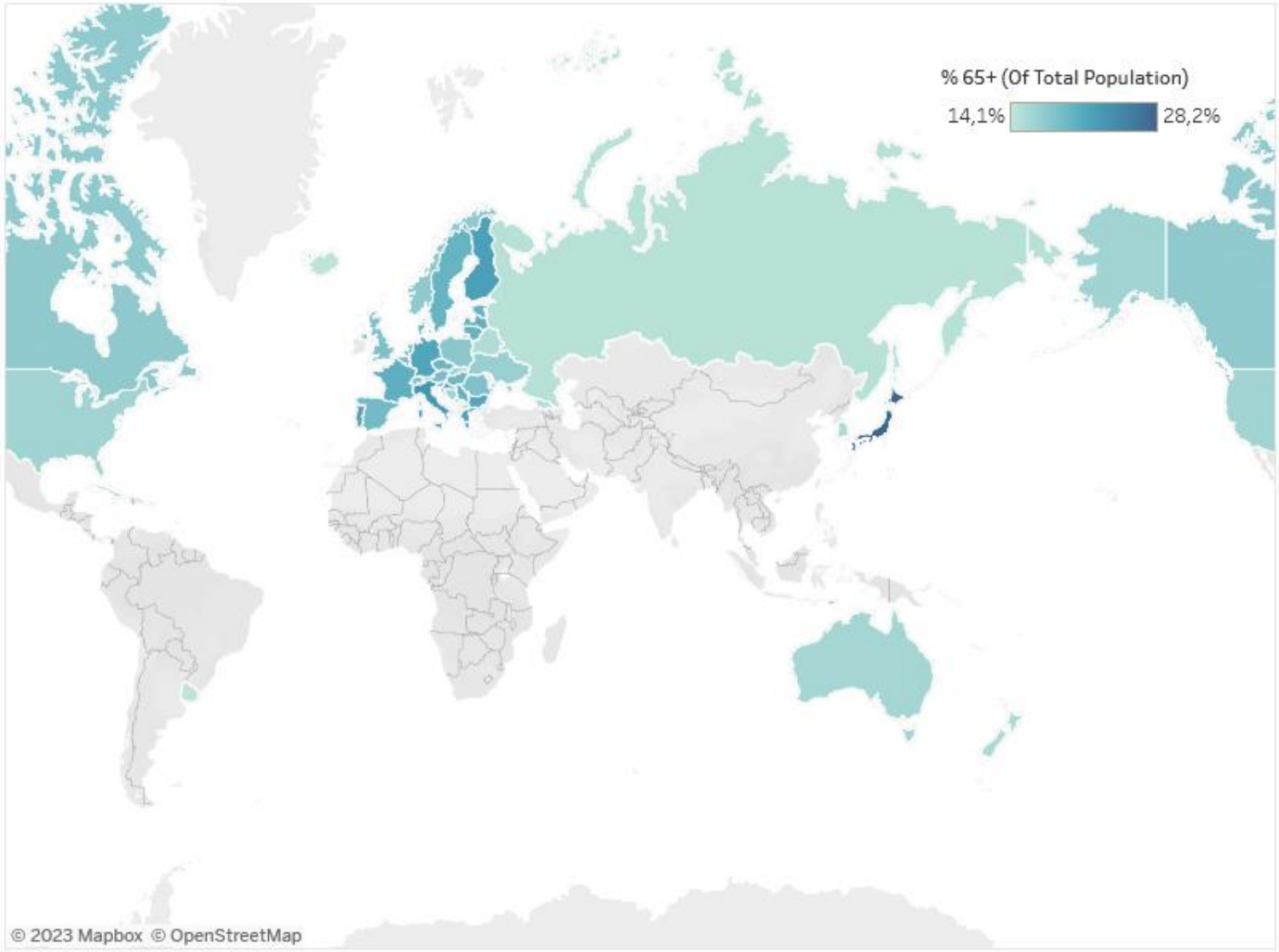


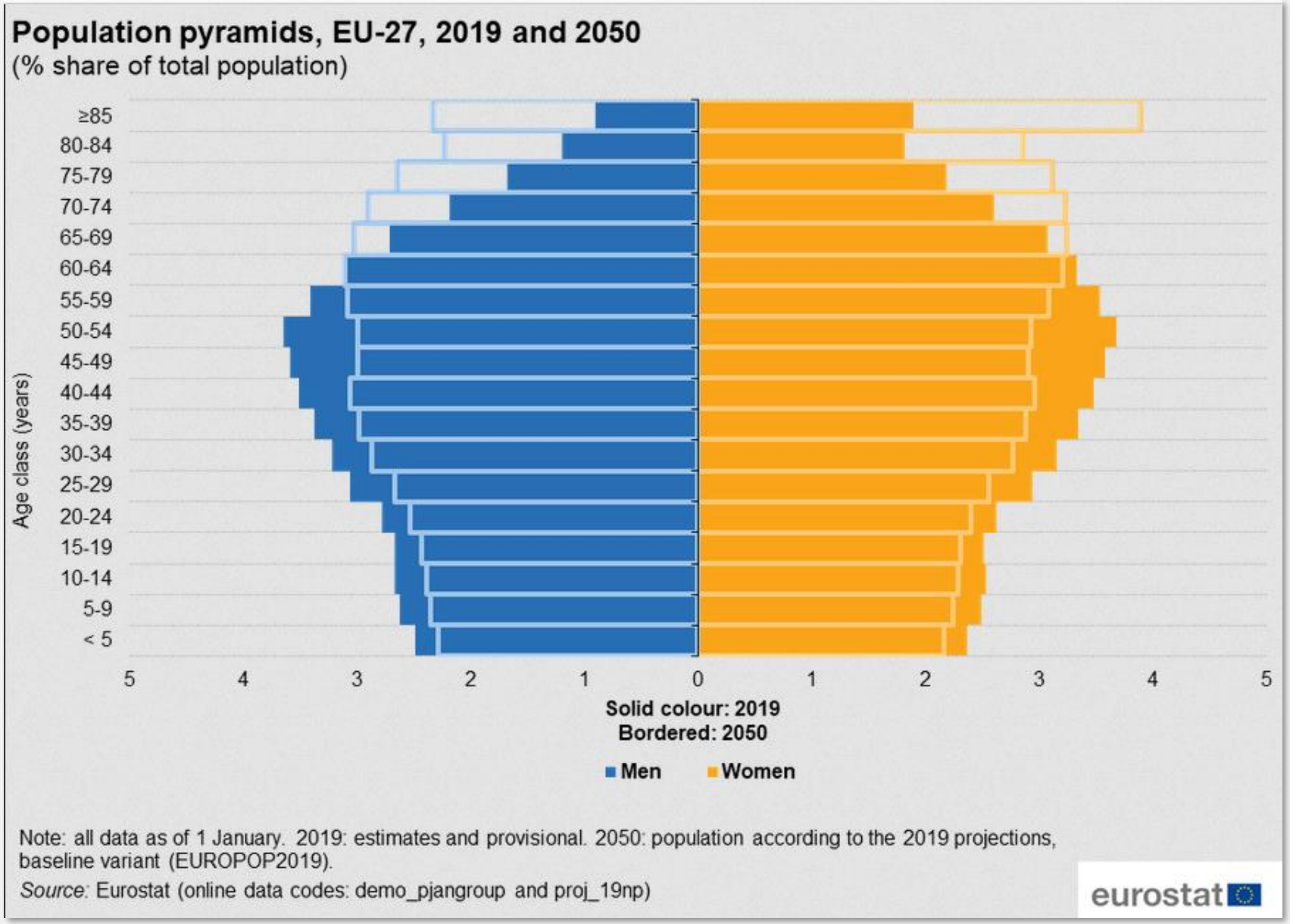
Fig. 3. Demographic deficit in OECD member nations. Observed and projected size of the incoming (20–24) and outgoing (60–64) working-age cohorts in OECD countries, 2000–2030. Source: OECD figures, Oxford Institute of Population Ageing, 2012.

Harper S, Science, 2014

Top 50 Countries With the Largest Percentage of Older Adults



https://www.prb.org/resources/countries-with-the-oldest-populations-in-the-world/


Population pyramids, EU-27, 2019 and 2050
(% share of total population)
≥85
80-84
75-79
70-74
65-69
60-64
55-59
50-54
45-49
40-44
35-39
30-34
25-29
20-24
15-19
10-14
5-9
< 5
Age class (years)
5
4
3
2
1
0
1
2
3
4
5
Solid colour: 2019
Bordered: 2050
Men
Women
Note: all data as of 1 January. 2019: estimates and provisional. 2050: population according to the 2019 projections, baseline variant (EUROPOP2019).
Source: Eurostat (online data codes: demo_pjangroup and proj_19np)
eurostat

ORIGINAL ARTICLE

Age, Neuropathology, and Dementia

George M. Savva, Ph.D., Stephen B. Wharton, F.R.C.Path., Paul G. Ince, M.D., Gillian Forster, B.Sc., Fiona E. Matthews, Ph.D., and Carol Brayne, M.D., for the Medical Research Council Cognitive Function and Ageing Study

N Engl J Med 2009;360:2302-09.

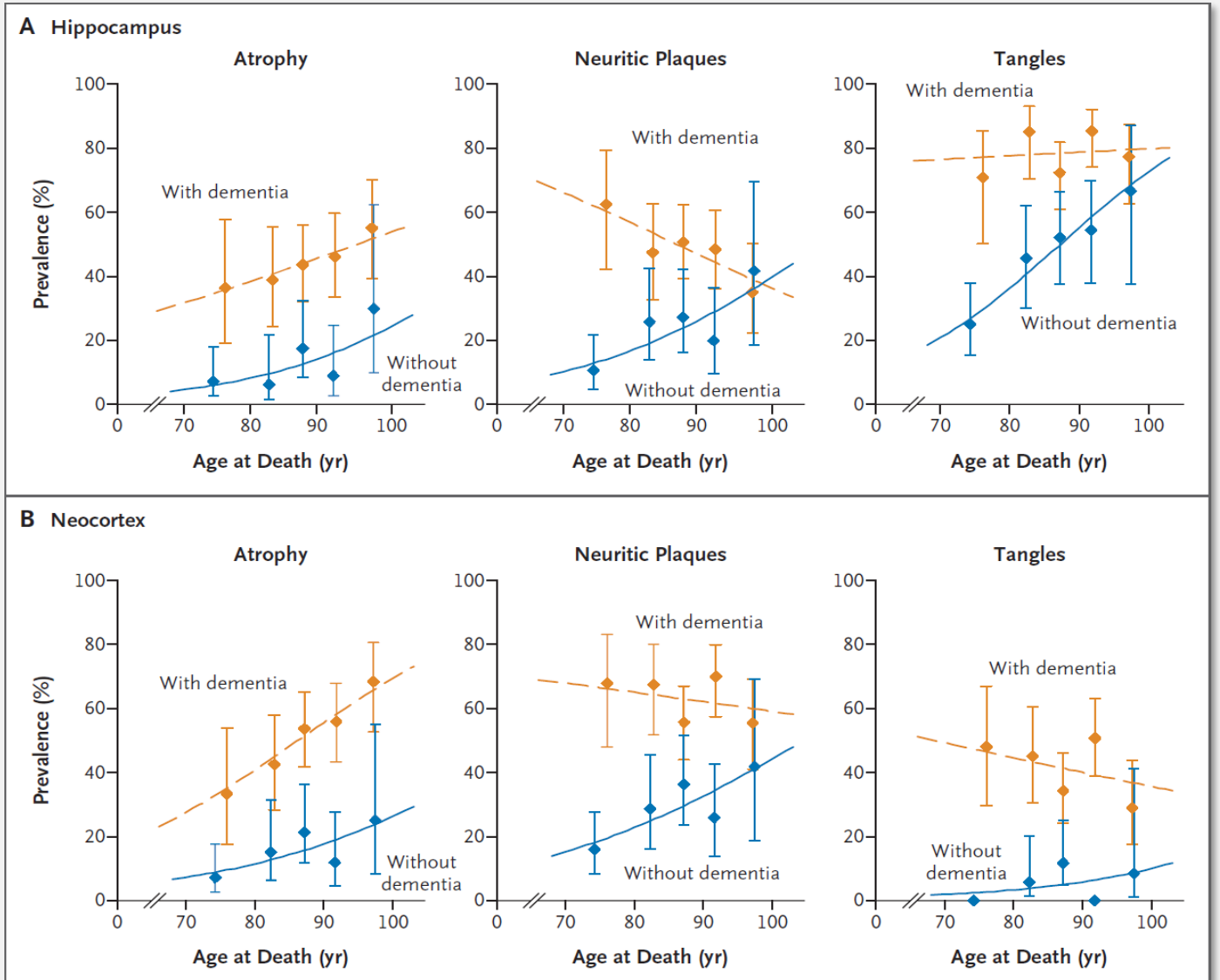


Figure 1. Modeled and Observed Prevalence of Moderate or Severe Pathological Lesions According to Age.

Persons who died with dementia (yellow) are compared with those who died without dementia (blue). Filled symbols represent the observed prevalence of moderate or severe pathological lesions, and I bars show the 95% confidence intervals. The solid and broken lines represent modeled prevalence values.

Neuropathologically defined subtypes of Alzheimer's disease with distinct clinical characteristics: a retrospective study

Melissa E Murray, Neill R Graff-Radford, Owen A Ross, Ronald C Petersen, Ranjan Duara, Dennis W Dickson

Lancet Neurol 2011; 10: 785–96

Varones
↓ edad

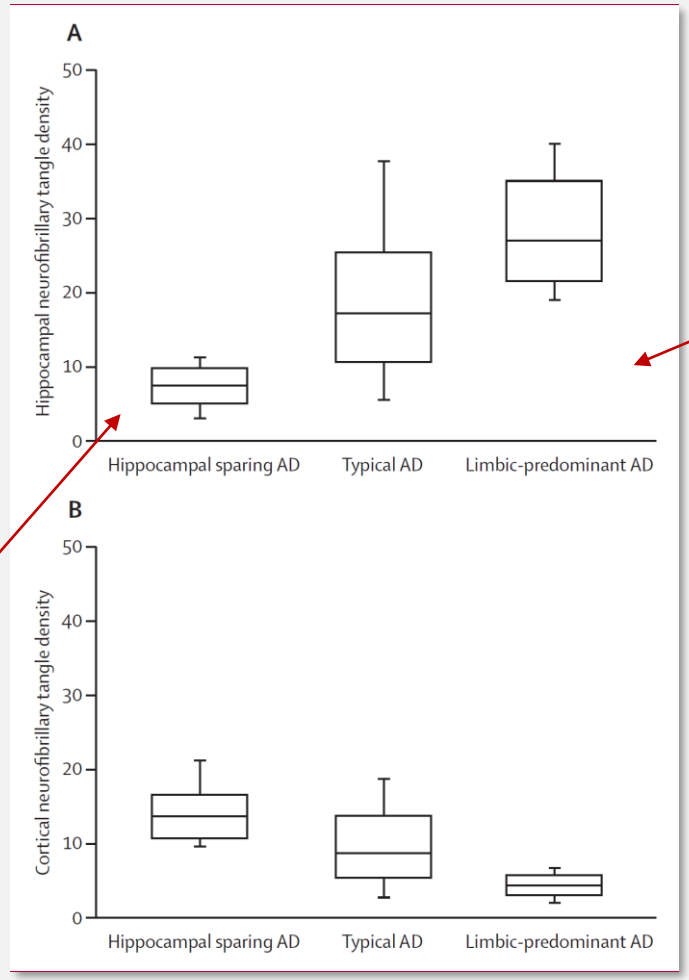
Mujeres
↑ edad

Limbic predominant

Densidad de ONF en hipocampo

Hippocampal sparing

Densidad de ONF en isocórtex temporal



Hippocampal sparing AD

Typical AD

Limbic predominant AD

Primary age-related tauopathy (PART)

Acta Neuropathol (2014) 128:755–766
DOI 10.1007/s00401-014-1349-0

CONSENSUS PAPER

Primary age-related tauopathy (PART): a common pathology associated with human aging

John F. Crary · John Q. Trojanowski · Julie A. Schneider · Jose F.
Steven E. Arnold · Johannes Attems · Thomas G. Beach · Eileen F
Marla Gearing · Lea T. Grinberg · Patrick R. Hof · Bradley T. Hy
Gabor G. Kovacs · David S. Knopman · Julia Kofler · Walter A. K
Ann McKee · Thomas J. Montine · Melissa E. Murray · Janna H.
Alberto Serrano-Pozo · Michael L. Shelanski · Thor Stein · Masal
Juan C. Troncoso · Jean Paul Vonsattel · Charles L. White 3rd · T
Masahito Yamada · Peter T. Nelson

Acta Neuropathol (2015) 129:749–756
DOI 10.1007/s00401-015-1390-7

POSITION PAPER

PART is part of Alzheimer dis

Charles Duyckaerts · Heiko Braak · Jean-Pierr
Michel Goedert · Glenda Halliday · Manuela Neumann · Maria Grazia Spillantini ·
Markus Tolnay · Toshiki Uchihara

Acta Neuropathol
DOI 10.1007/s00401-015-1407-2

CORRESPONDENCE

PART, a distinct tauopathy, different from classical sporadic Alzheimer disease

Kurt A. Jellinger[1] · Irina Alafuzoff[2] · Johannes Attems[3] · Thomas G. Beach[4] · Nigel J. Cairns[5] · John F. Crary[6] · Dennis W. Dickson[7] · Patrick R. Hof[8] · Bradley T. Hyman[9] · Clifford R. Jack Jr.[10] · Gregory A. Jicha[11] · David S. Knopman[12] · Gabor G. Kovacs[13] · Ian R. Mackenzie[14] · Eliezer Masliah[15,16] · Thomas J. Montine[17] · Peter T. Nelson[18] · Frederick Schmitt[11] · Julie A. Schneider[19,20] · Albert Serrano-Pozo[21] · Dietmar R. Thal[22] · Jonathan B. Toledo[23] · John Q. Trojanowski[23] · Juan C. Troncoso[24] · Jean Paul Vonsattel[6] · Thomas Wisniewski[25,26,27]

Acta Neuropathol

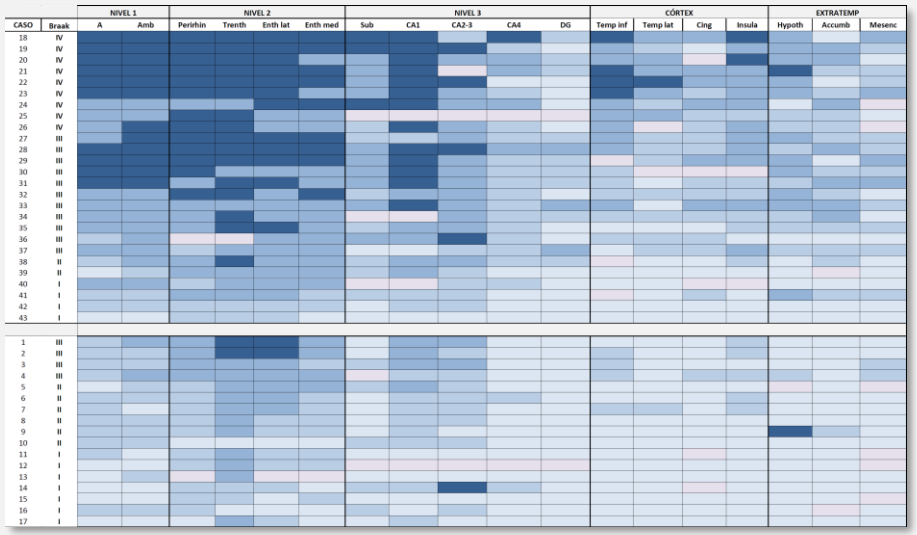
Table 1 Hypothetical correlation between PART and AD

	No AD/no PART	Asymptomatic PART	p-preAD	NFT-predominant Dementia (symptomatic PART)	Symptomatic AD
Aβ phase	0	0–2	1–5	0–2	3–5
Braak-NFT-stage	0	I–IV	0–VI	III, IV	III–VI
Degree of AD pathology	No AD	No or low AD	Low–high AD	No AD or low	Intermediate–high AD
Clinical signs of dementia or cognitive decline	No	No	No	Yes	Yes

PART vs. AD: symptomatic PART and symptomatic AD can be distinguished by Aβ pathology. Asymptomatic PART and p-preAD overlap in those cases with initial Aβ pathology (Aβ phases 1, 2)

PART (-)

PART def



nature medicine

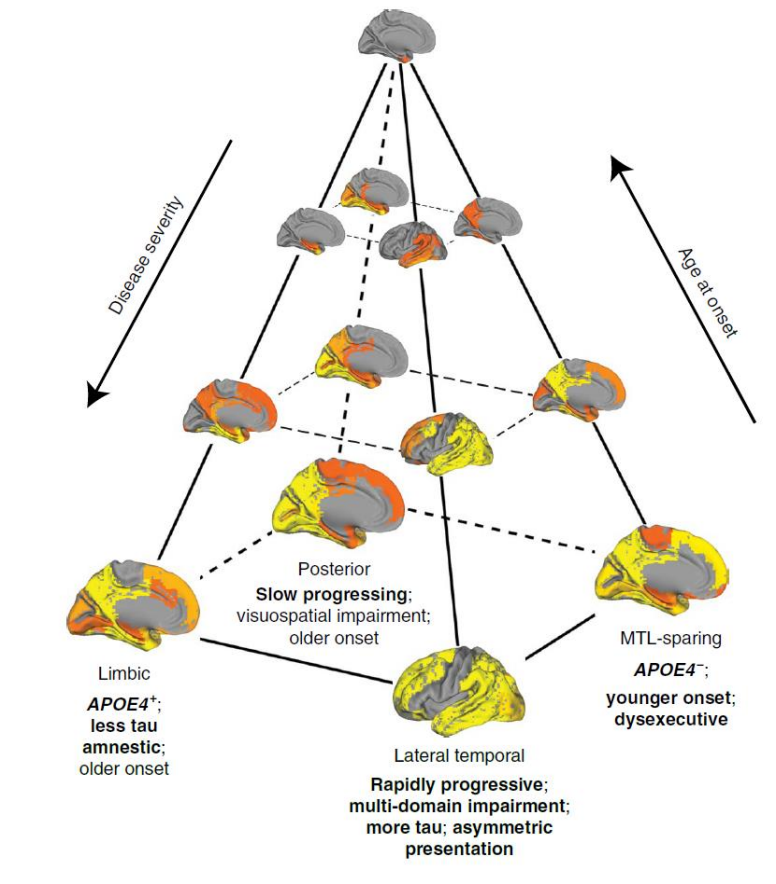
ARTICLES

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

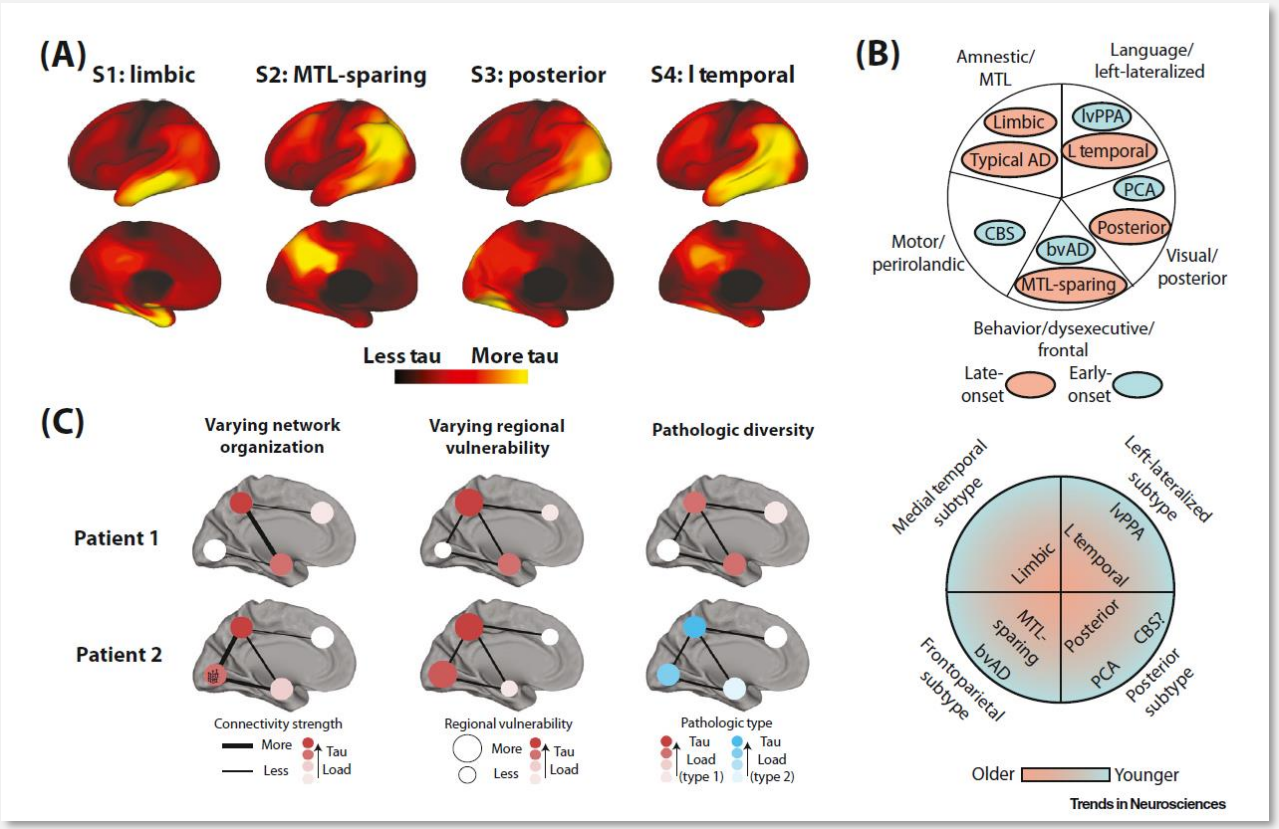
Forum

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

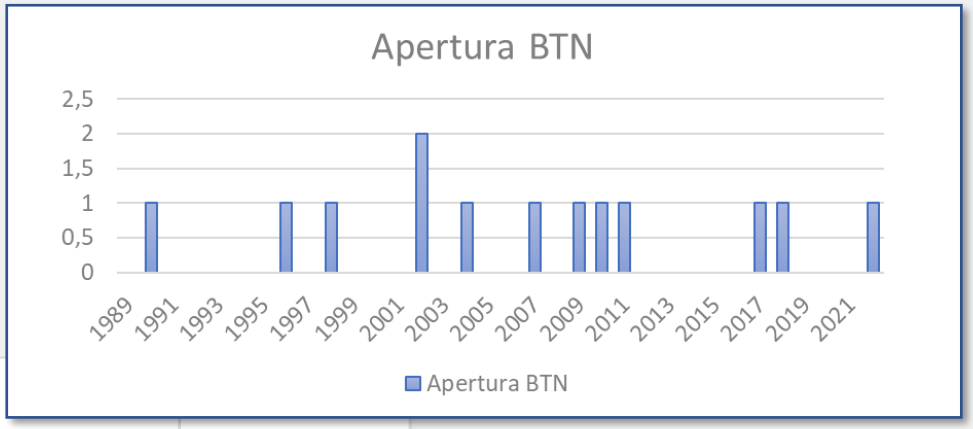
Jacob W. Vogel[1,2,*] and Oskar Hansson[3,4,*]

Trends in Neurosciences

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



A matter of time: chronology of current neuropathological diagnostic guidelines



2000			**2011**			
2001			**2012**	NIA-AA	Vascular score	
2002			**2013**	ALS	GGT	
2003	Braak α-syn		**2014**	PART		
2004	AGD		**2015**			
2005			**2016**	VCING	ARTAG	CTE I	TDP-43
2006			**2017**	DLB IV		
2007	FTLD		**2018**			
2008			**2019**	LATE-NC		
2009			**2020**			
2010			**2021**	LPC	CTE II	

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

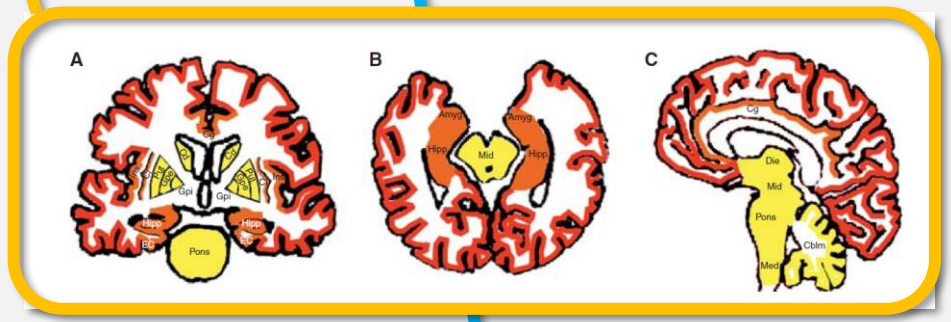
Thomas J. Montine · Creighton H. Phelps · Thomas G. Beach · Eileen H. Bigio · Nigel J. Cairns · Dennis W. Dickson · Charles Duyckaerts · Matthew P. Frosch · Eliezer Masliah · Suzanne S. Mirra · Peter T. Nelson · Julie A. Schneider · Dietmar Rudolf Thal · John Q. Trojanowski · Harry V. Vinters · Bradley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

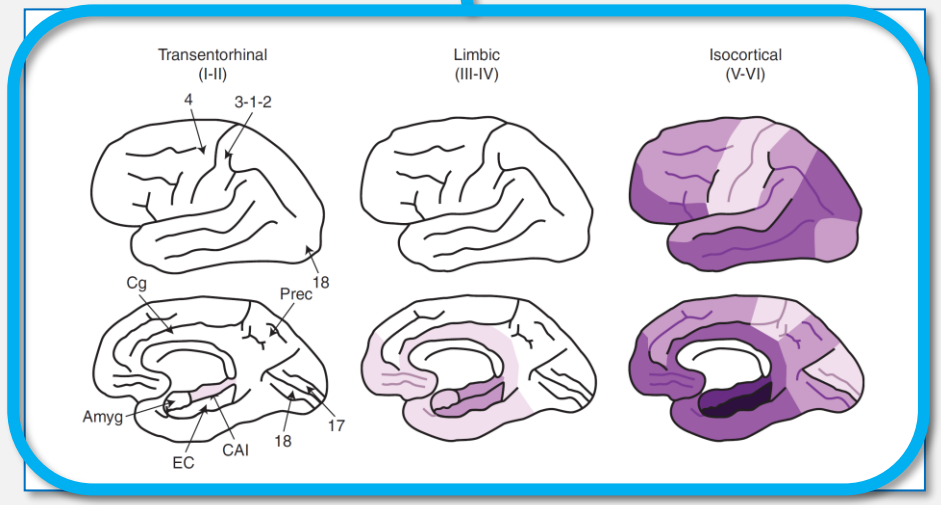
Table 2 "ABC" score for AD neuropathologic change

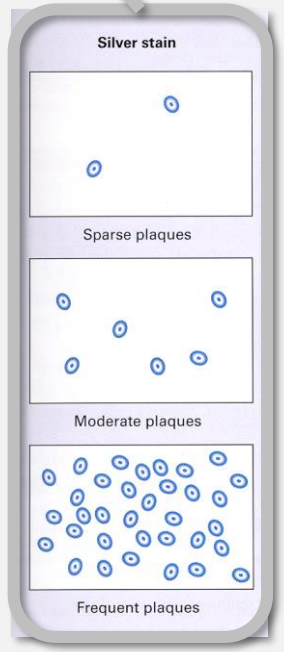
"A"	Thal Phase for Aβ plaques [57]	"B"	Braak and Braak NFT stage [14,15]	"C"	CERAD neuritic plaque score [41]
0	0	0	None	0	None
1	1 or 2	1	I or II	1	Sparse
2	3	2	III or IV	2	Moderate
3	4 or 5	3	V or VI	3	Frequent

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

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)

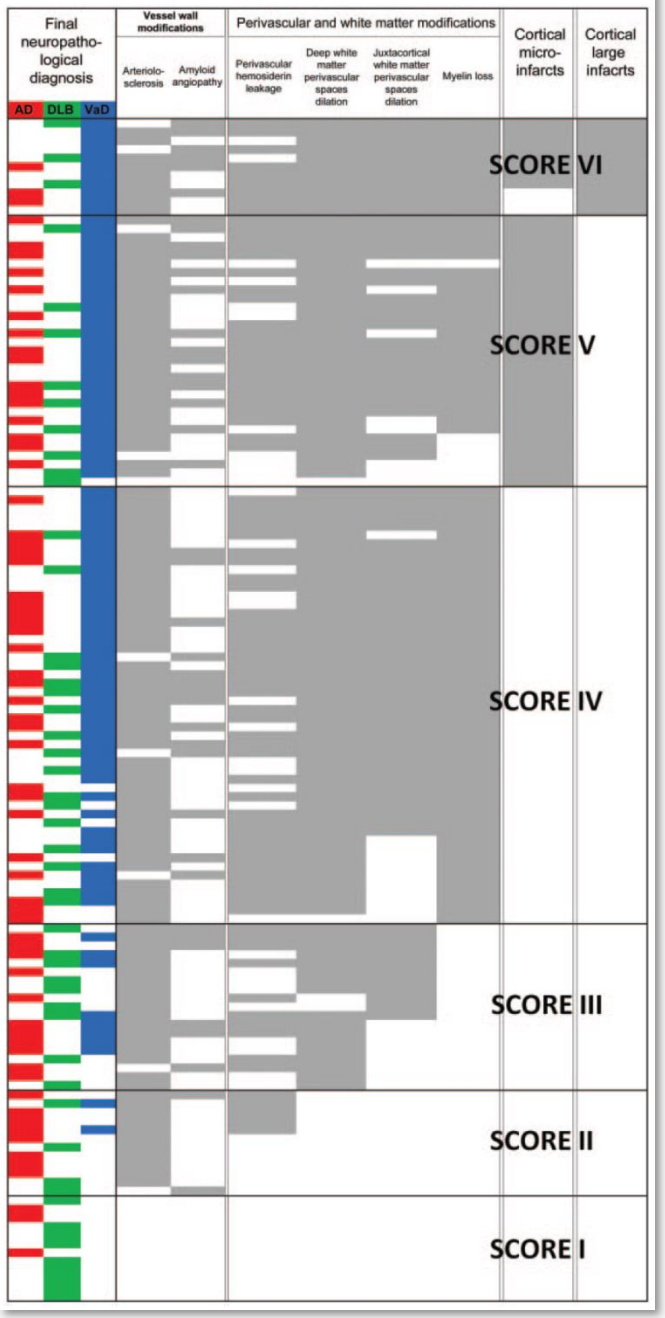
Ganglios basales
(0-4)

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

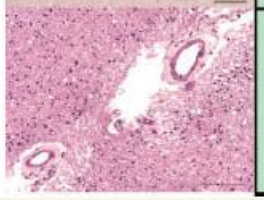
Likelihood that cerebral vascular disease contributed to cognitive impairment		Low (<50%)			Moderate (50-80%)		High (>80%)		
One or more large (> 10 mm) subcortical cerebral infarcts		-	-	-	+	-	+	+	+
Moderate or severe occipital leptomeningeal CAA		-	+	-	-	+	+	-	+
Moderate or severe occipital white matter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

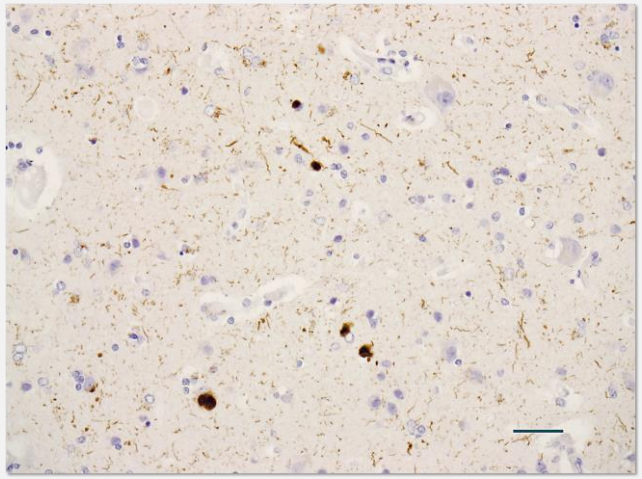
2021

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

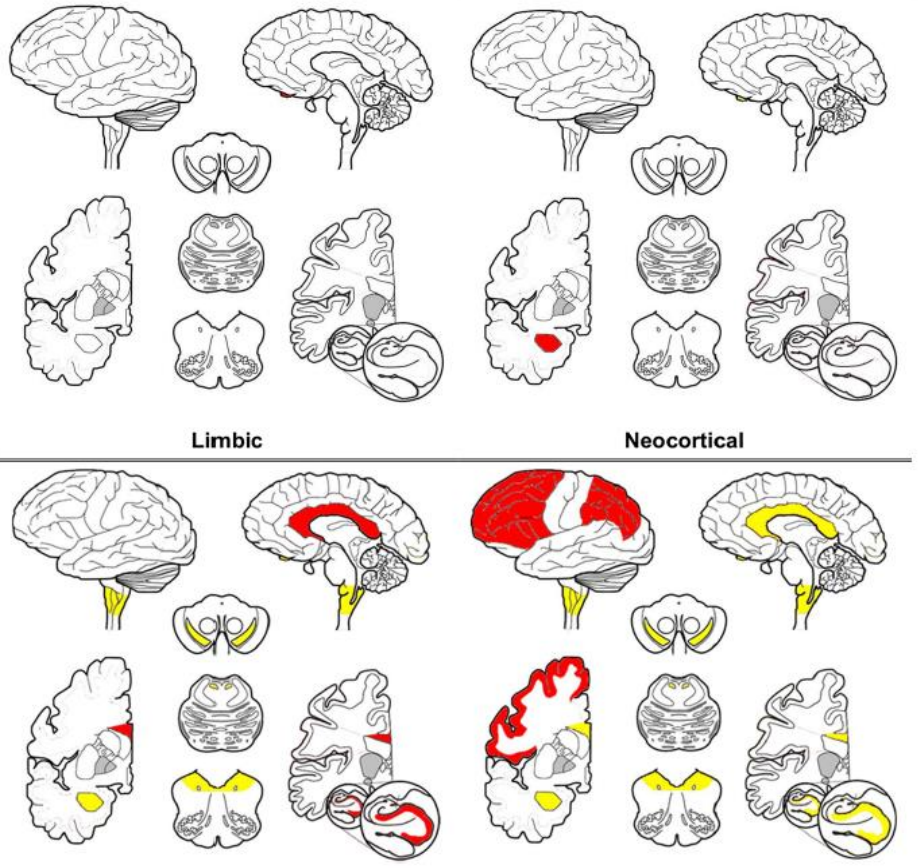
Johannes Attems[1] · Jon B. Toledo[2,3] · Lauren Walker[1] · Ellen Gelpi[4,5] · Steve Gentleman[6] · Glenda Halliday[7] · Tibor Hortobagyi[8,9,10,11] · Kurt Jellinger[12] · Gabor G. Kovacs[13,14] · Edward B. Lee[3] · Seth Love[15] · Kirsty E. McAleese[1] · Peter T. Nelson[16] · Manuela Neumann[17,18] · 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

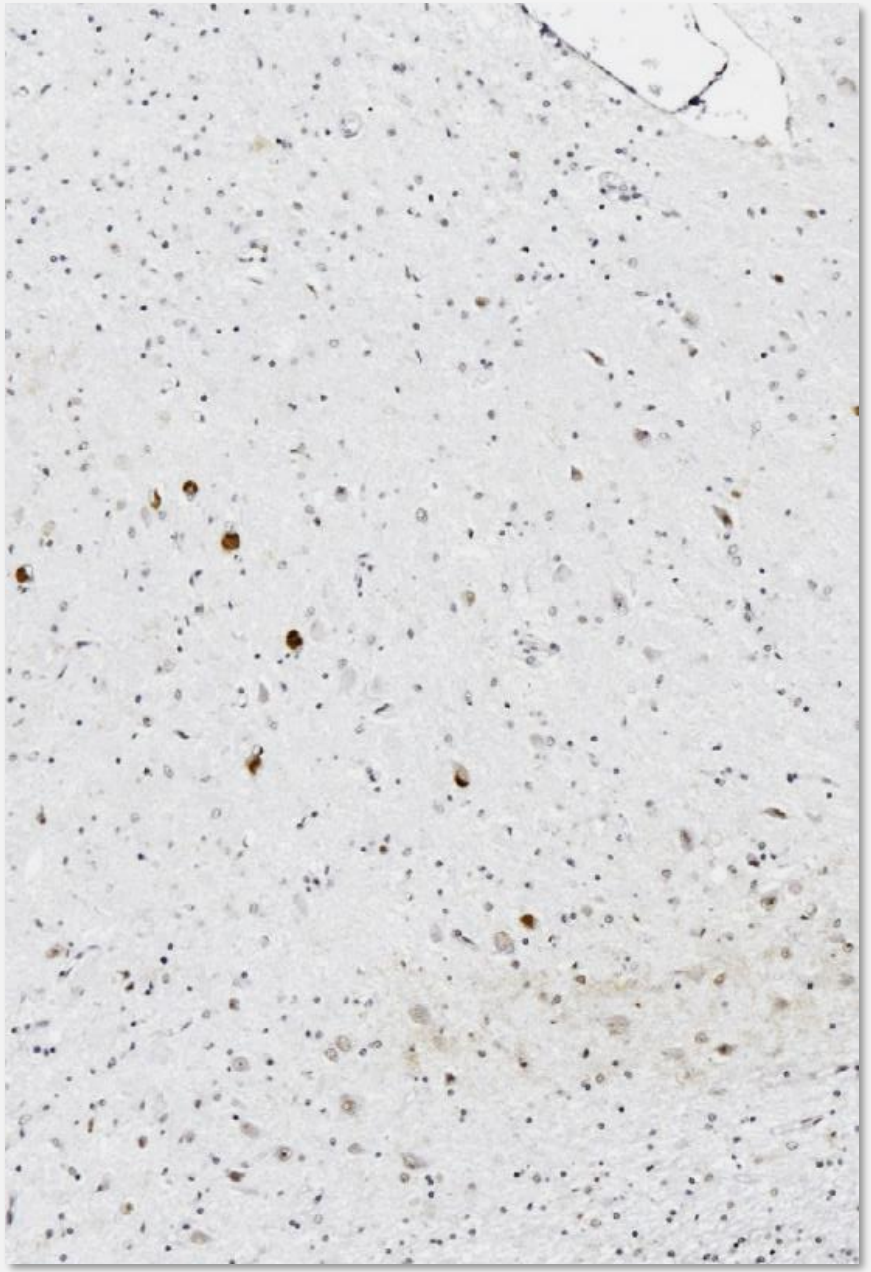
B LATE-NC related stages based on anatomic distribution of TDP-43 pathology

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

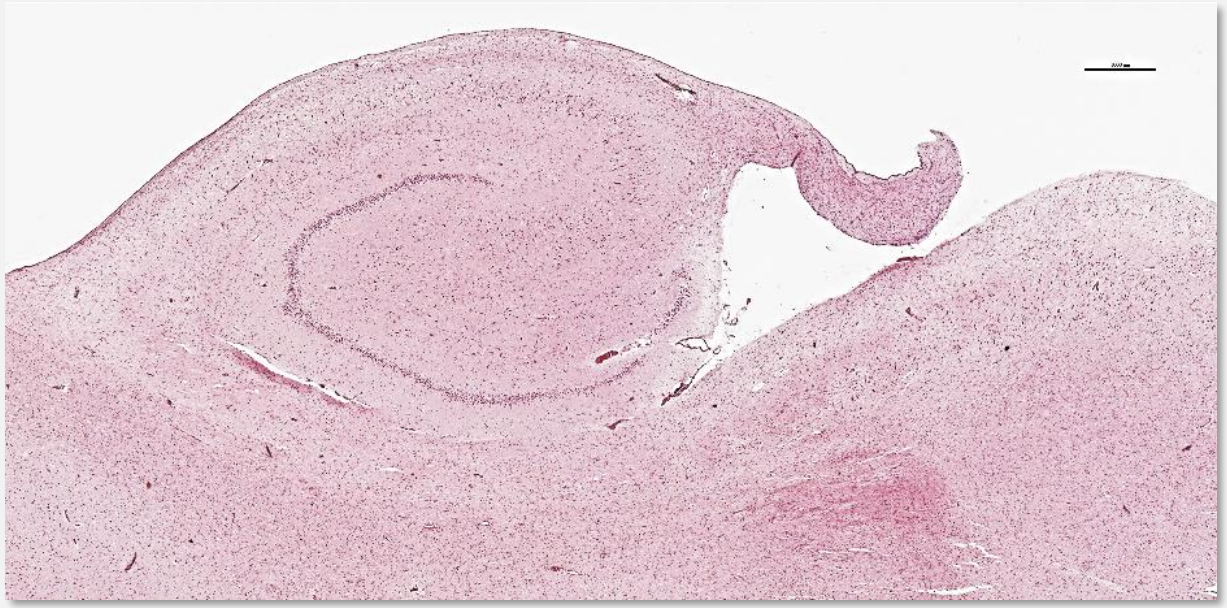
*-*Any* TDP-43 proteinopathy is seen in that anatomic region

Esclerosis del hipocampo

TDP-43



H / E



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

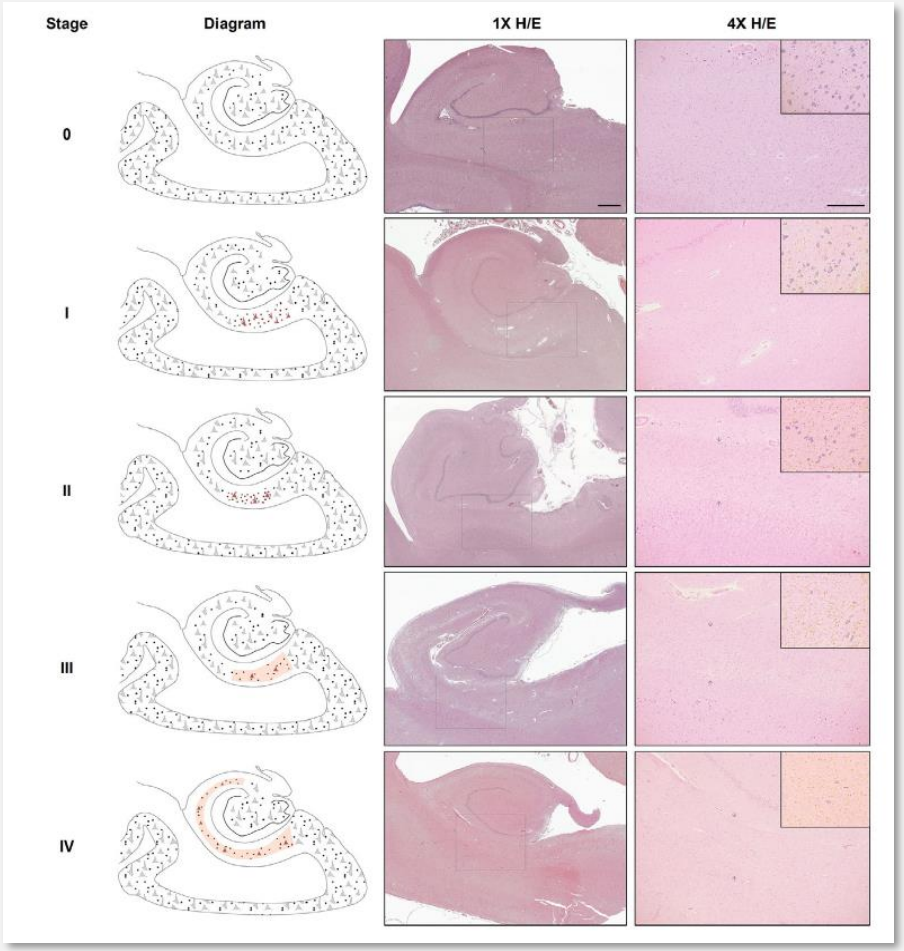
DOI: 10.1002/alz.12942

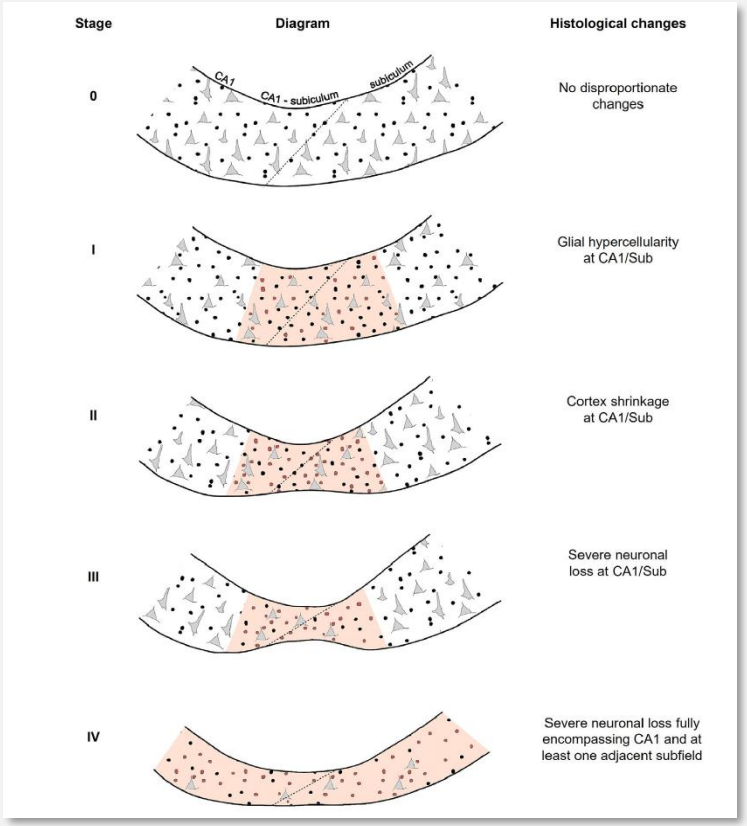
Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

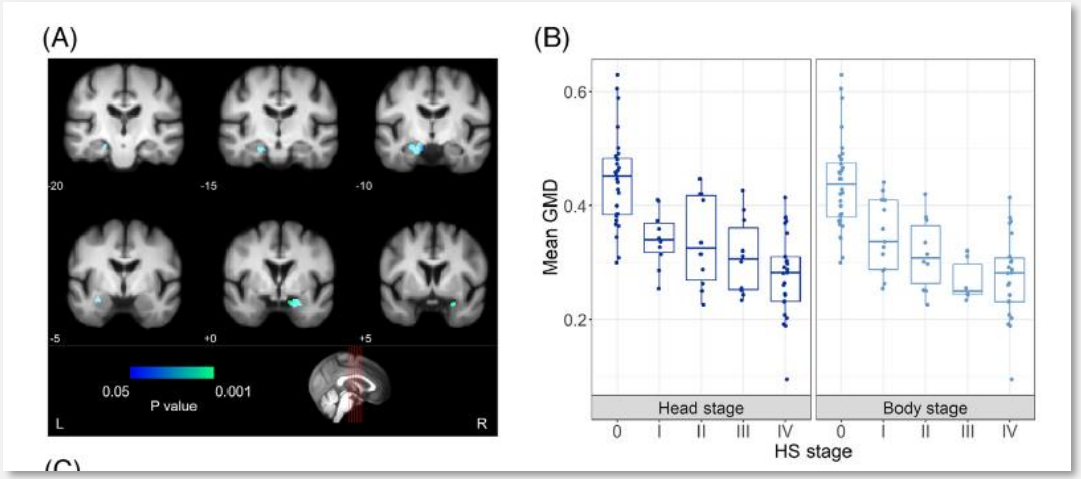
RESEARCH ARTICLE

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]

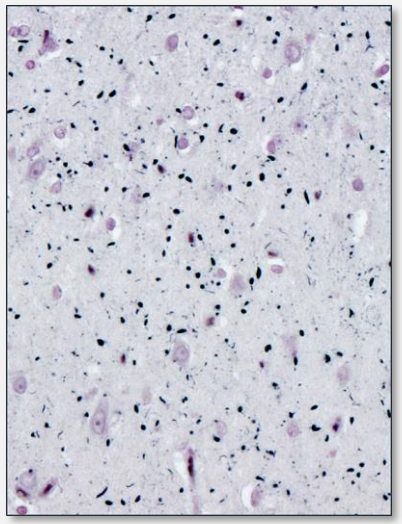




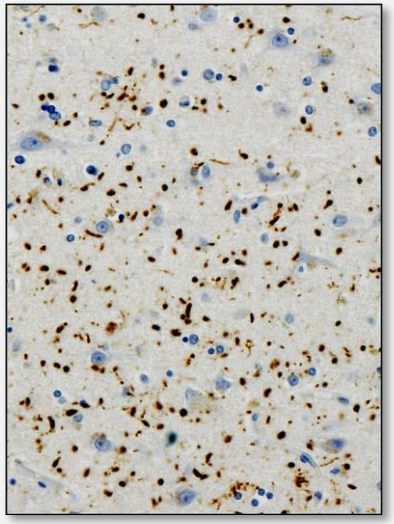


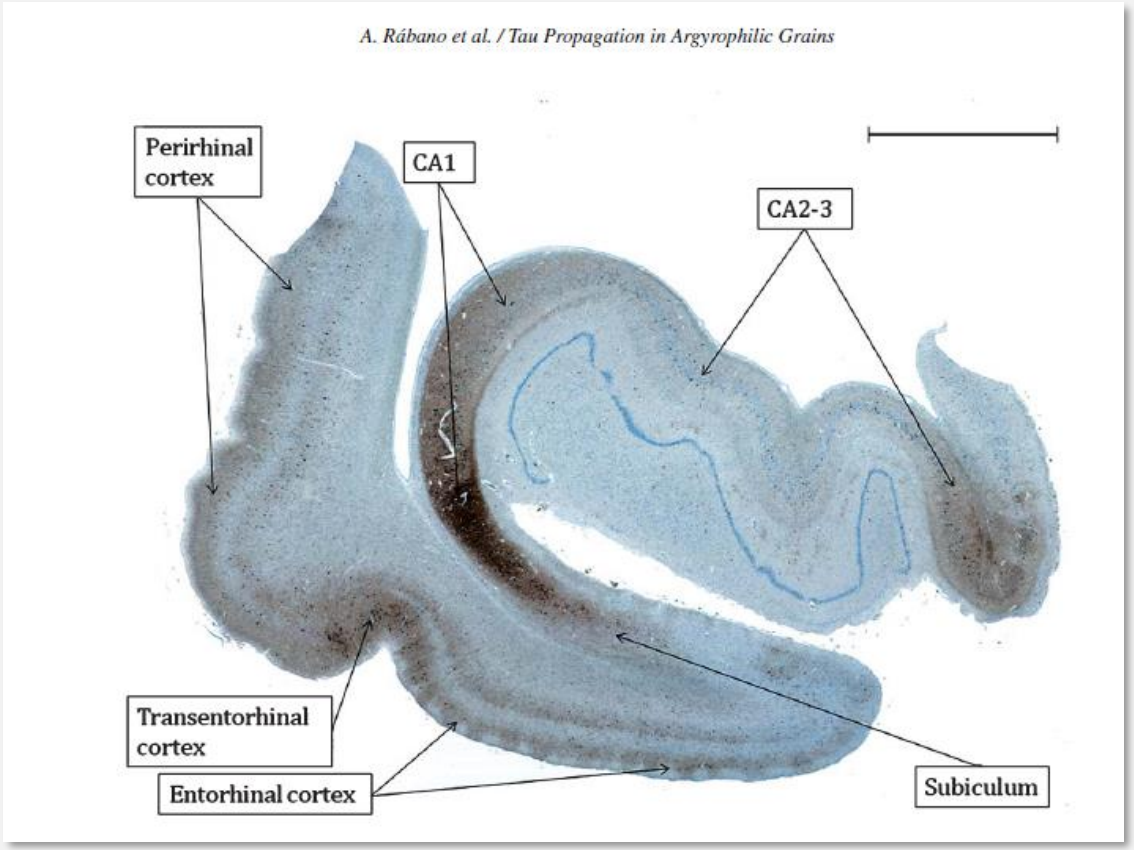
Argyrophilic grain disease

Gallyas

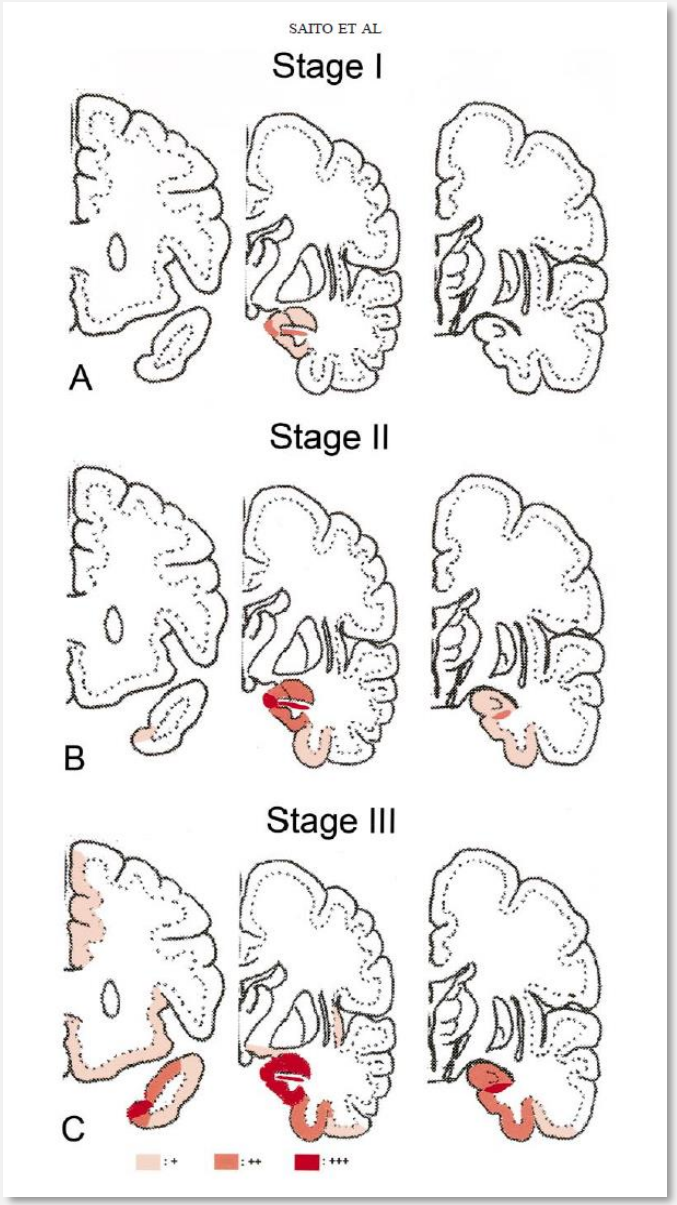


Tau AT8





Rábano *et al*., 2014



Saito *et al*., 2004

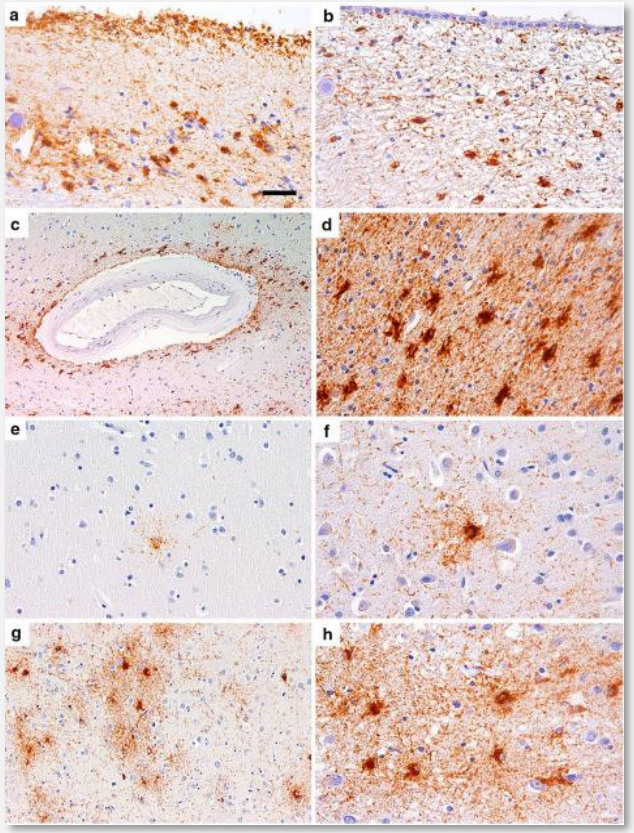
Aging-related tau astrogliopathy (ARTAG)

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*]

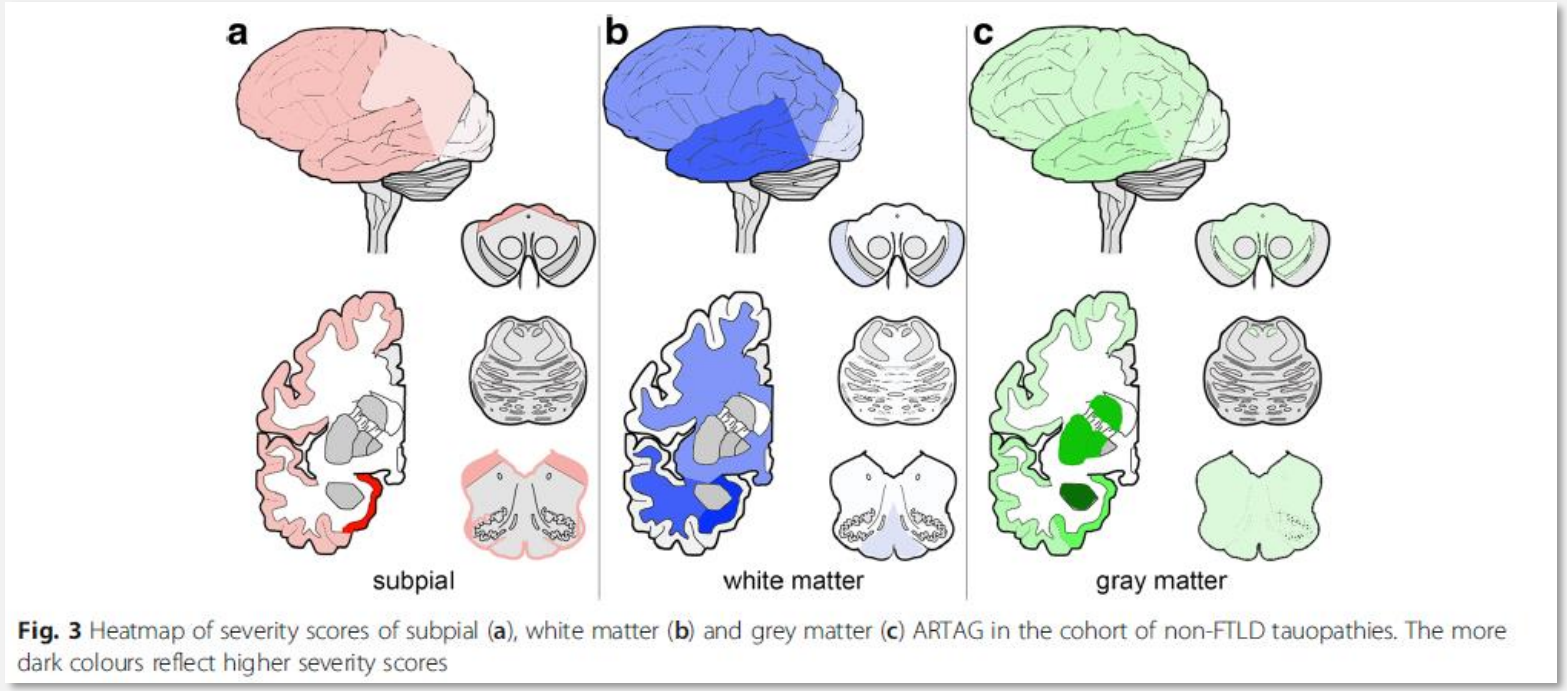


Fig. 3 Heatmap of severity scores of subpial (**a**), white matter (**b**) and grey matter (**c**) ARTAG in the cohort of non-FTLD tauopathies. The more dark colours reflect higher severity scores

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]

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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]

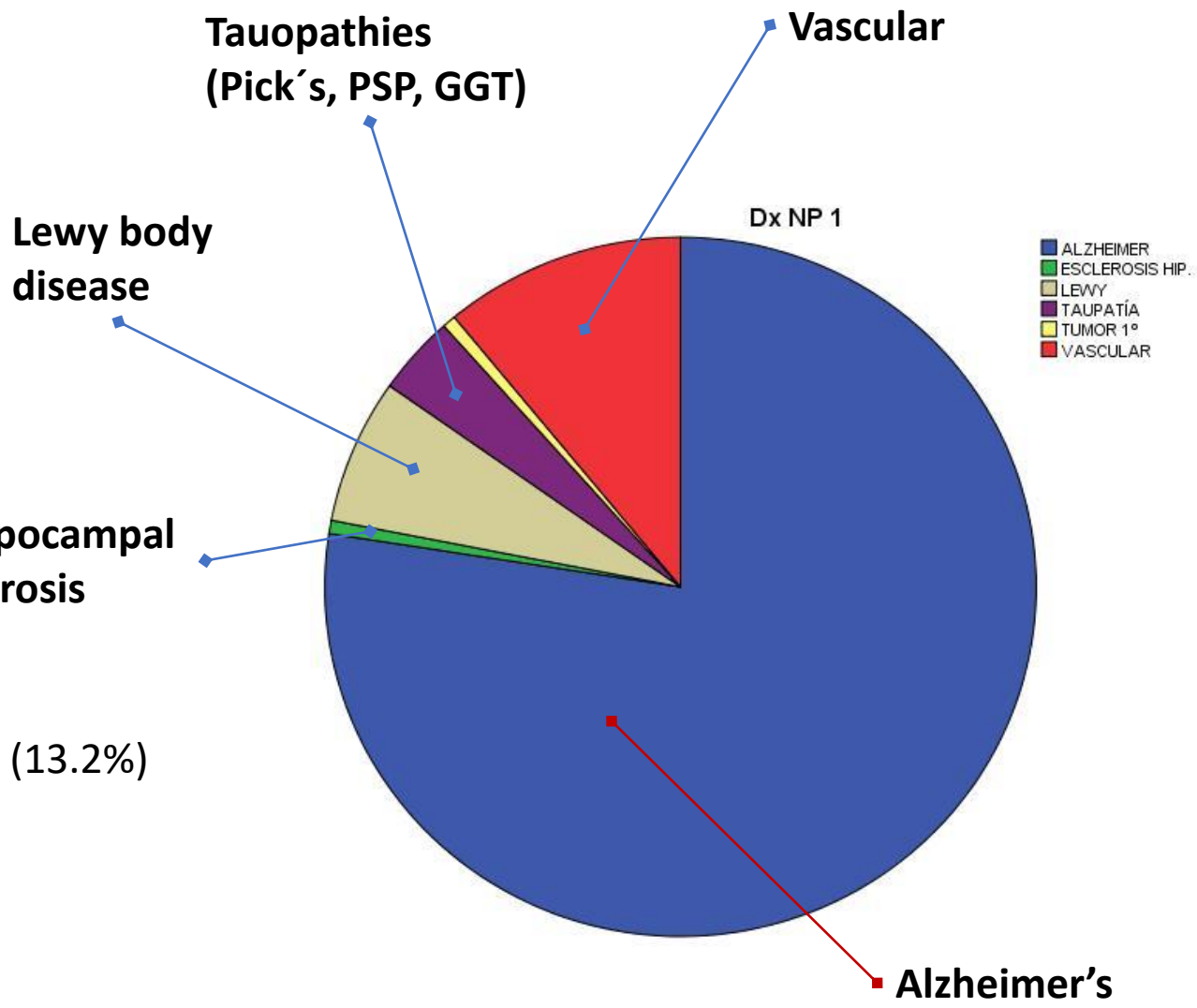
Heterogeneidad patológica y comorbilidad en demencia

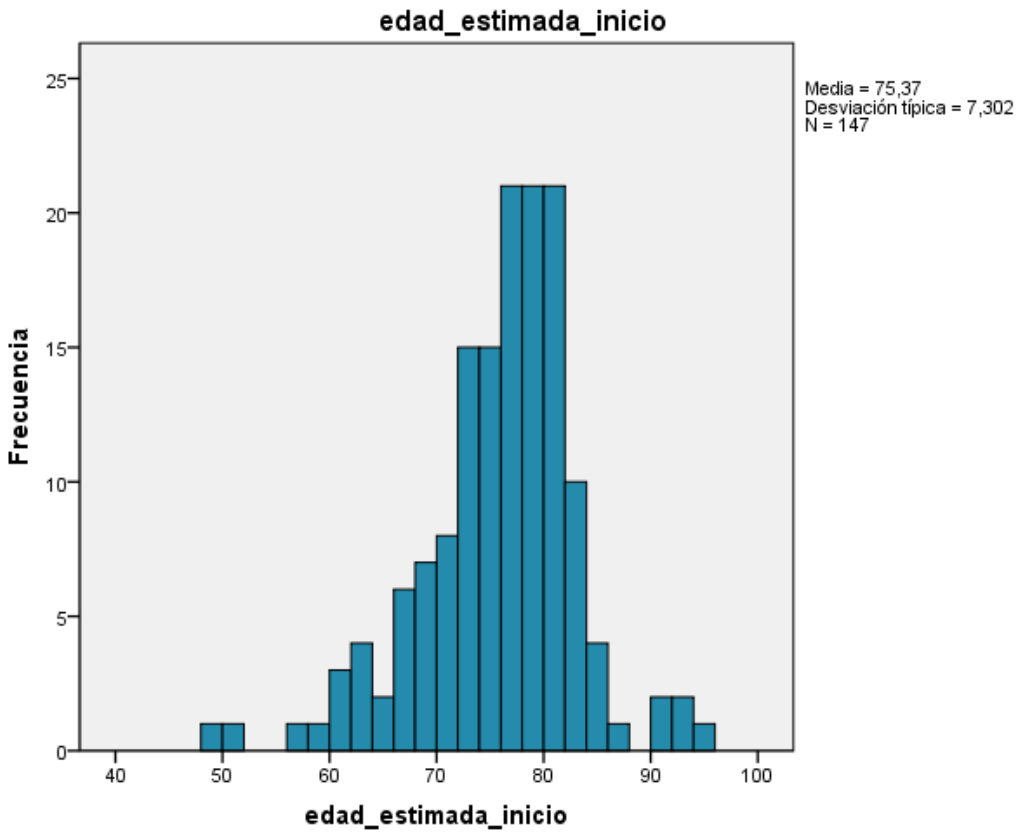
- Patología de tipo Alzheimer
- Patología cerebrovascular
- Patología de tipo Lewy
- Limbic-predominant age-related TDP-43 encephalopathy (LATE)
- Aging-related tau astrogliopathy (ARTAG)
- Enfermedad de granos argirófilos
- Otras patologías

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

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Desviación típica = 7,302
N = 147
Frecuencia
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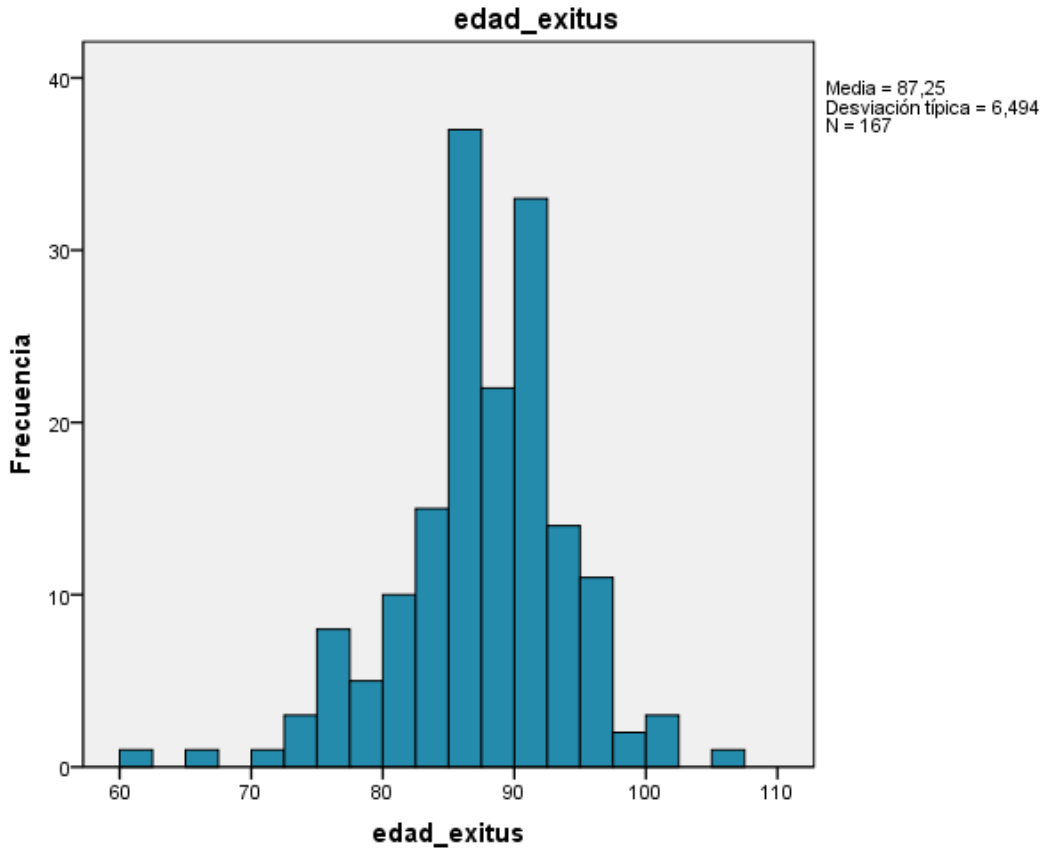
15
20
25
40
50
60
70
80
90
100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Desviación típica = 6,494
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Frecuencia
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40
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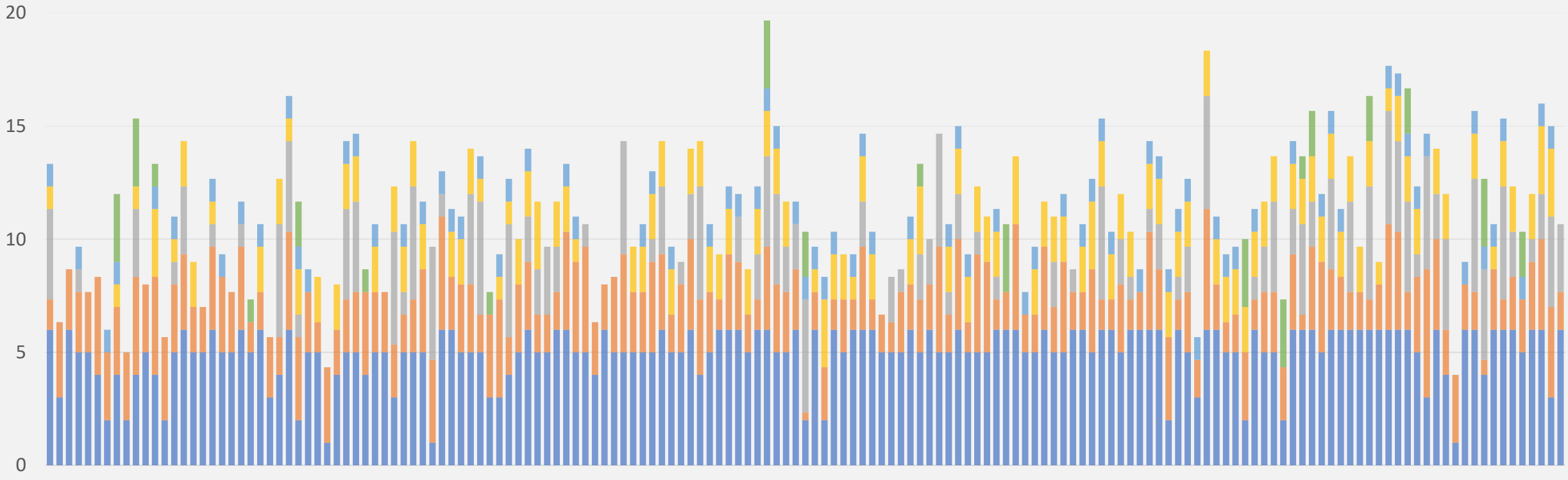
70
80
90
100
110

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]

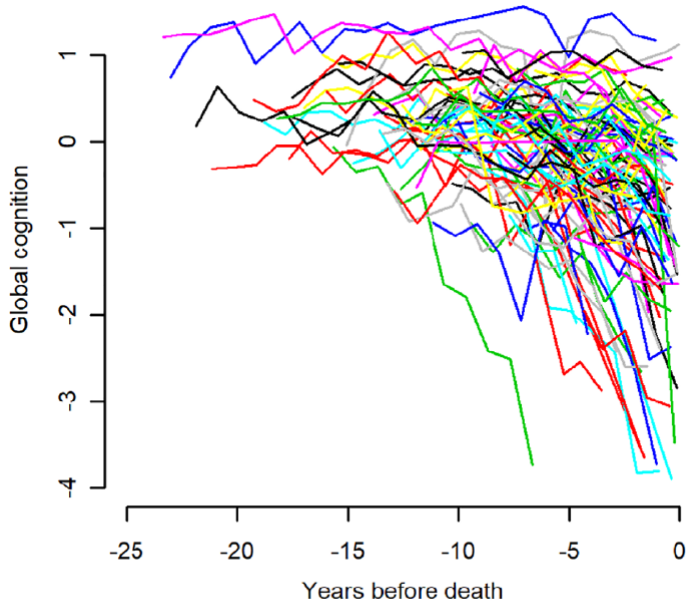
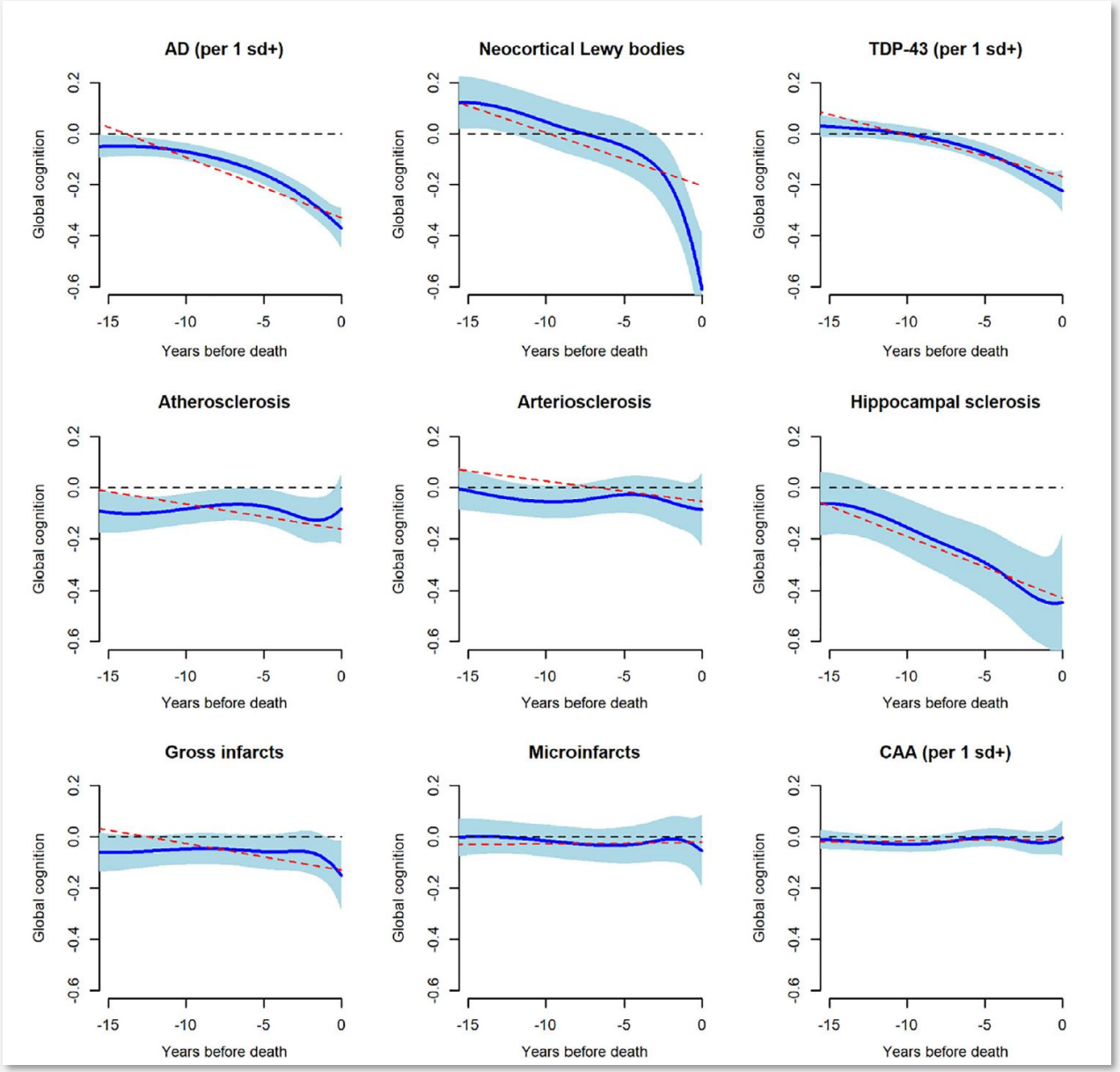


FIGURE 1: Crude trajectories of change in global cognition in 100 randomly selected participants.



SCIENTIFIC REPORTS
nature research

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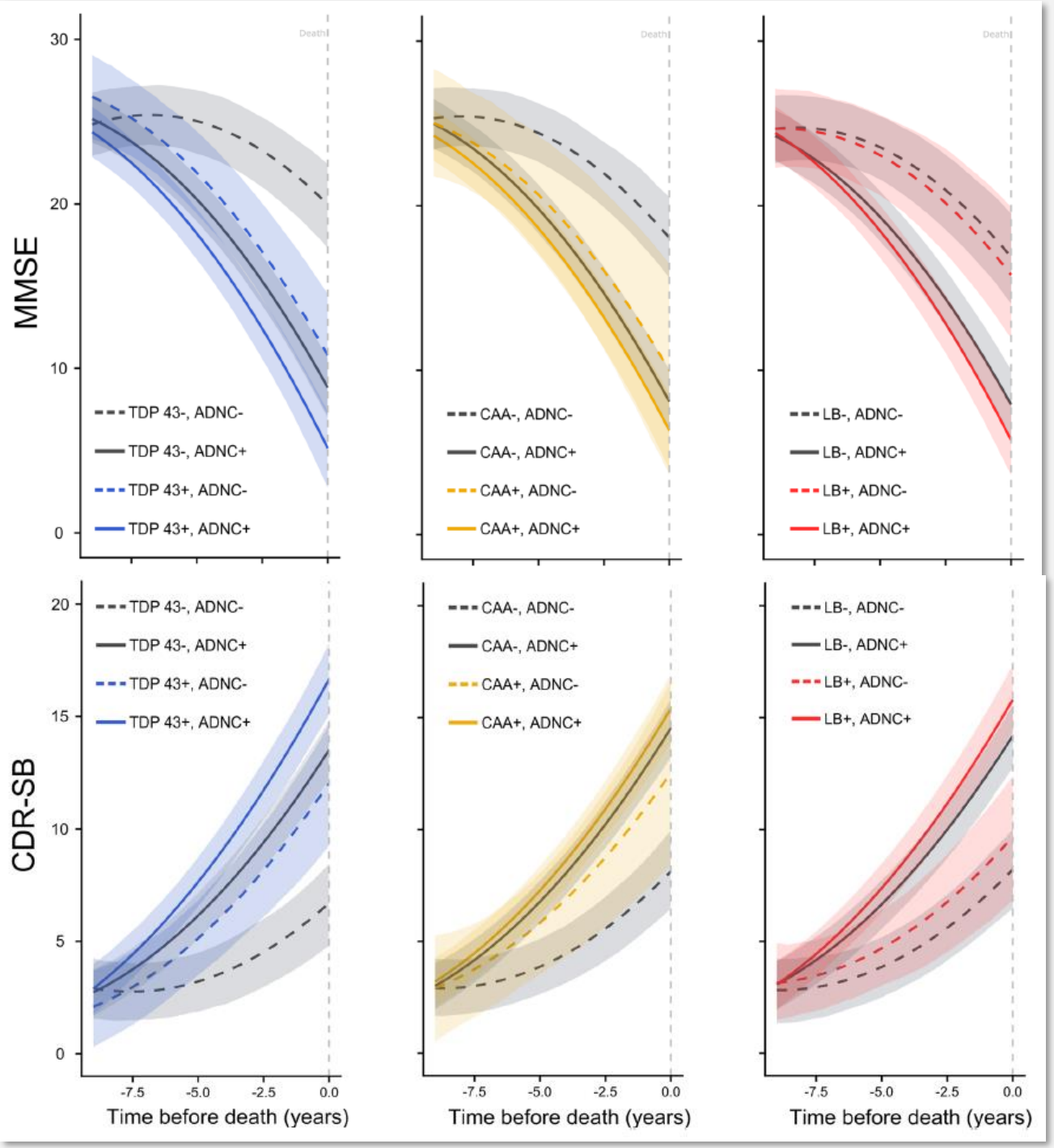
Association of TDP-43 proteinopathy, cerebral amyloid angiopathy, and Lewy bodies with cognitive impairment in individuals with or without Alzheimer's disease neuropathology

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



Takao *et al. Acta Neuropathologica Communications* (2016) 4:97
DOI 10.1186/s40478-016-0368-6

Acta Neuropathologica Communications

RESEARCH Open Access

Neuropathology of supercentenarians - four autopsy case studies

Masaki Takao[1,4*], Nobuyoshi Hirose[2], Yasumichi Arai[2], Ban Mihara[3] and Masaru Mimura[4]

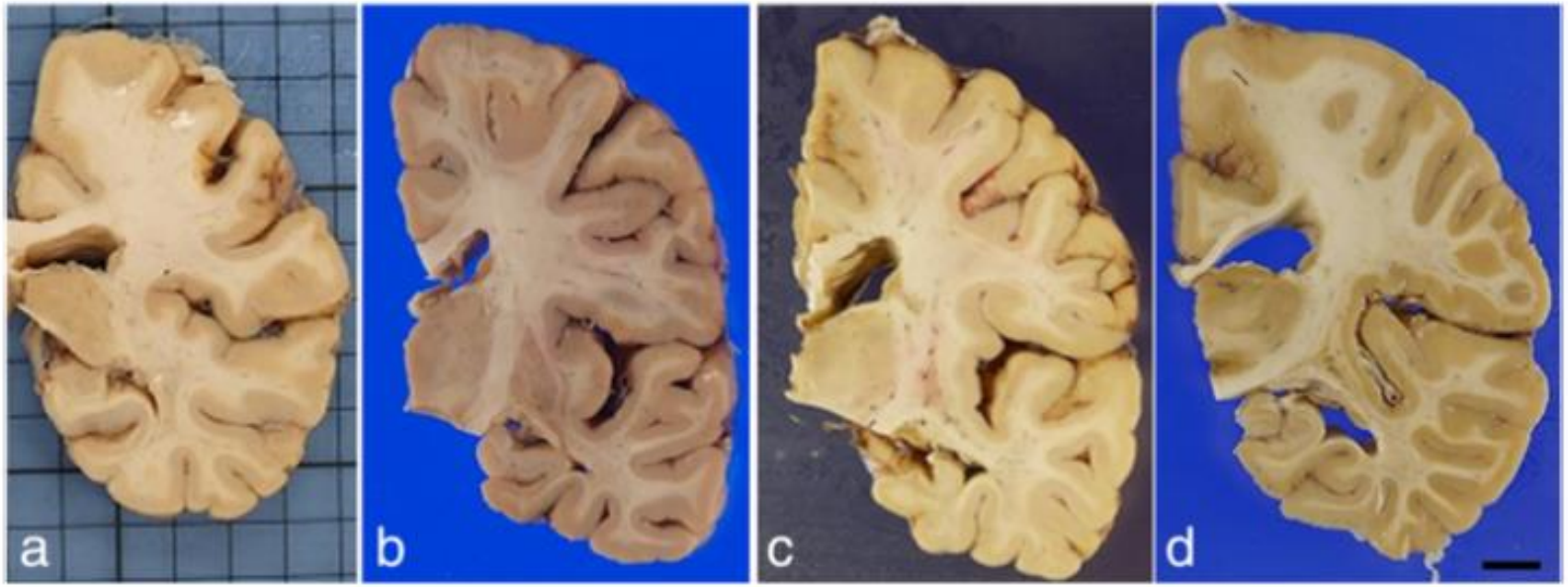


Fig. 2 Coronal sections at the basal ganglia and hippocampus level. Cortical ribbons and cerebral white matter are well-preserved. Small cortical infarct in Case 1 (**a**). **a** Case 1, (**b**) Case 2, (**c**) Case 3, (**d**) Case 4. Bar = 1 cm

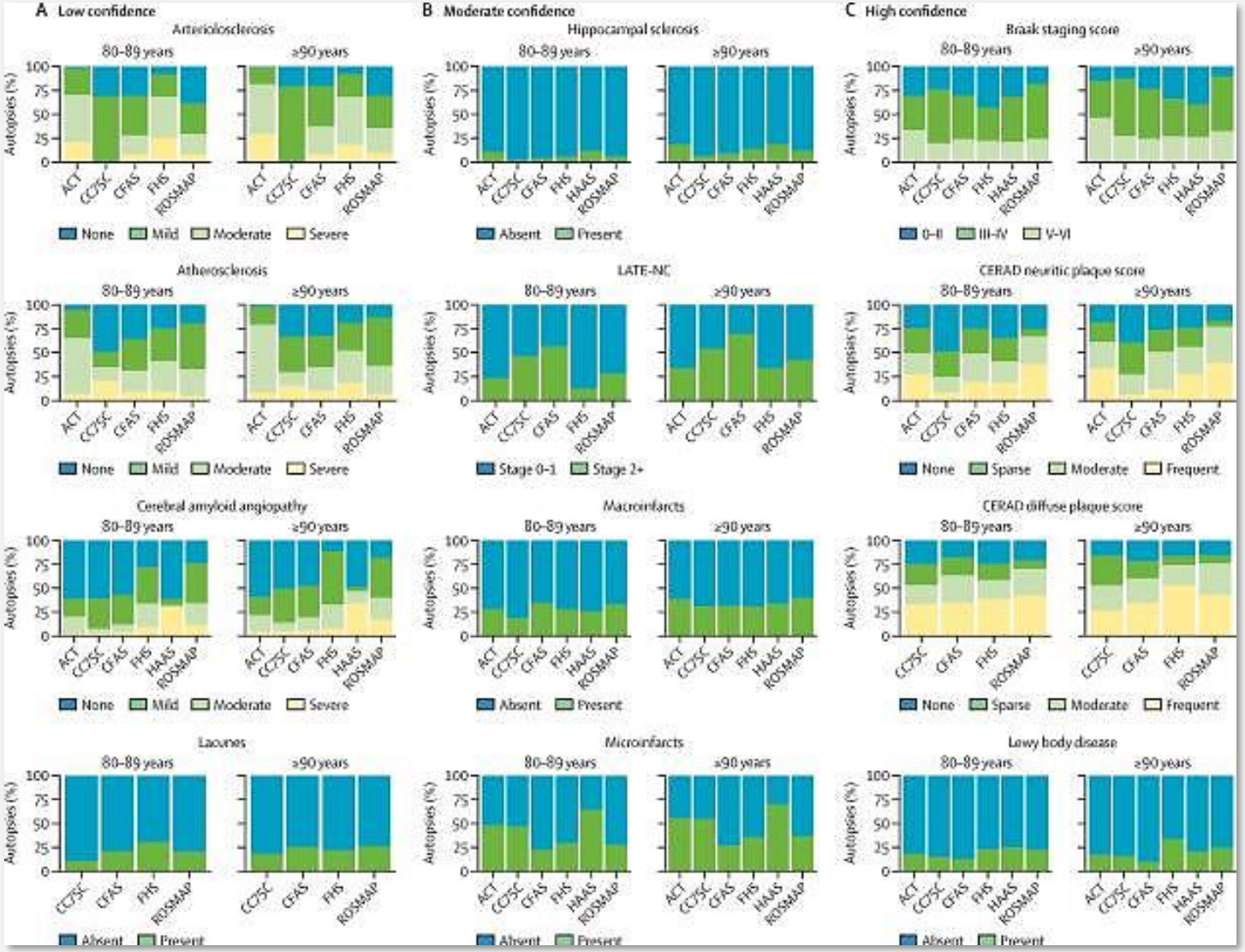
Table 1 Patient demographics and summary of neuropathological analyses

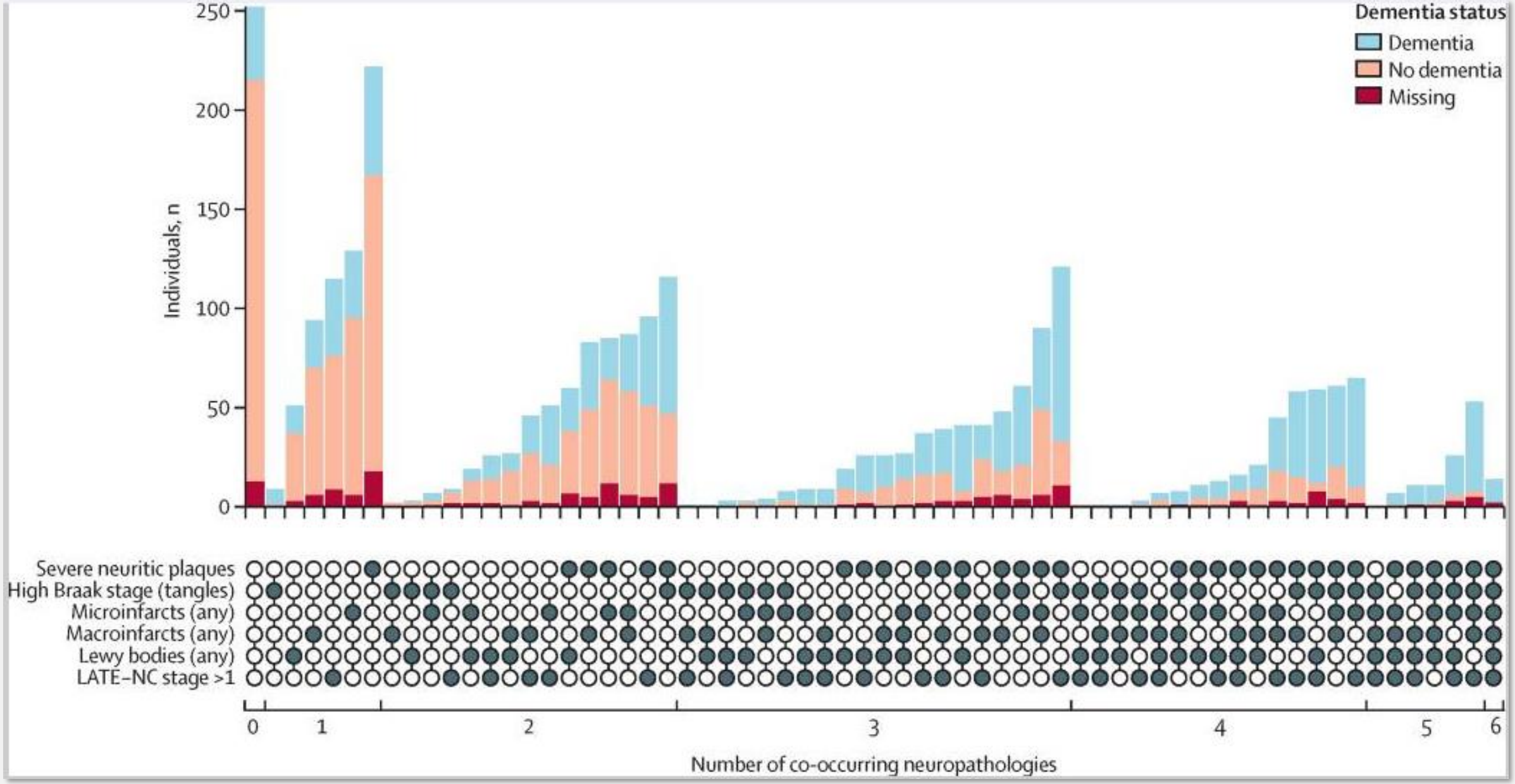
	Case 1 (111 yo)	Case 2 (111 yo)	Case 3 (114 yo)	Case 4 (110 yo)
Sex	Female	Female	Female	Female
Past medical history	HT-, DM-	HT-, DM-	HT-, DM-	HT+, DM-
Clinical condition before death	Clear communication, wheel chair	No dementia	Clear communication, wheel chair	Almost clear communication, wheel chair
Barthel index CDR MMSE	10 0.5 NA due to refusal Age 106	60 NA 15 Age 106	90 0 22 Age 108 MMSE was 18 at age 113 and 114	20 NA NA Age 109
Cause of death	Heart failure	Renal failure	Senility	Sepsis
APOE	2/3	2/3	3/3	3/3
Brain weight (fresh)	460 (left hemisphere)	925	1,015	1,115
Atrophy	F, T	F, T	F, T	T
A-beta, Thal phase	3 (A2)	3 (A2)	1 (A1)	2 (A1)
NFT stage (AT8) (Braak)	III (B2)	IV (B2)	III (B2)	IV (B2)
Neuritic plaques (CERAD)	Moderate (C2)	Moderate (C2)	Sparse (C1)	Moderate (C2)
CAA	None	None	None	Mild
AD pathological changes (NIA-Reagan)	Intermediate	Intermediate	Unclassified	Intermediate
AD pathological changes (NIA-AA)	Intermediate	Intermediate	Low PART possible	Intermediate
ARTAG	Subpial, subependymal, gray matter, white matter, perivascular	Subpial, gray matter, white matter	Subpial, gray matter, white matter	Subpial, subependymal, gray matter, perivascular
Arteriolosclerosis	Mild to moderate	Mild to moderate	Mild to moderate	Mild to moderate
White matter rarefaction	Moderate	Mild	Mild	Moderate
État criblé (basal ganglia and thalamus)	Moderate	Severe	Severe	Moderate
Vascular brain injury	Multiple cortical infarcts	None	None	None
Alpha-synuclein pathology	None	None	None	None
TDP-43 pathology	Present, subiculum, PHG	Present, subiculum, PHG	Uncus, sparse	Uncus, sparse
Hippocampal sclerosis	None	None	None	None
Hirano bodies/GVD (Hippocampus)	Present/present	Present/present	Present/present	Present/present

Lancet Healthy Longev. 2023 Mar; 4(3): e115–e125.
Published online 2023 Mar. doi: 10.1016/S2666-7568(23)00019-3
PMCID: PMC9977689
PMID: 36870337

The prevalence, correlation, and co-occurrence of neuropathology in old age: harmonisation of 12 measures across six community-based autopsy studies of dementia

Emma Nichols, PhD,[a,*] Richard Merrick, MSc,[b] Simon I Hay, Prof, FMedSci,[a] Dibya Himali, MS,[c] Jayandra J Himali, PhD,[c,d,e,f] Sally Hunter, MSc,[b] Hannah A D Keage, Prof, PhD,[g] Caitlin S Latimer, MD,[h] Matthew R Scott, BA,[c,f] Jaimie D Steinmetz, PhD,[a] Jamie M Walker, PhD,[i] Stephen B Wharton, Prof, PhD,[j] Crystal D Wiedner, PhD,[d] Paul K Crane, Prof, MD,[k] C Dirk Keene, Prof, MD,[h] Lenore J Launer, PhD,[l] Fiona E Matthews, Prof, PhD,[m] Julie Schneider, Prof, MD,[n,o] Sudha Seshadri, Prof, MD,[c,d,e] Lon White, MD,[p] Carol Brayne, Prof, MD,[b] and Theo Vos, Prof, PhD[a]




Dementia status
Dementia
No dementia
Missing
Individuals, n
250
200
150
100
50
0
Severe neuritic plaques
High Braak stage (tangles)
Microinfarcts (any)
Macroinfarcts (any)
Lewy bodies (any)
LATE–NC stage >1
0
1
2
3
4
5
6
Number of co-occurring neuropathologies

Gracias!

Web: http://bt.fundacioncien.es/

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