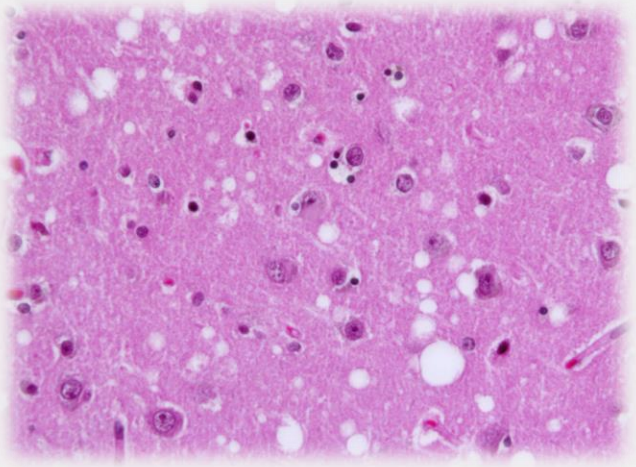
REUNIÓN ANUAL DEL GE NEUROLOGÍA DE LA CONDUCTA Y DEMENCIAS

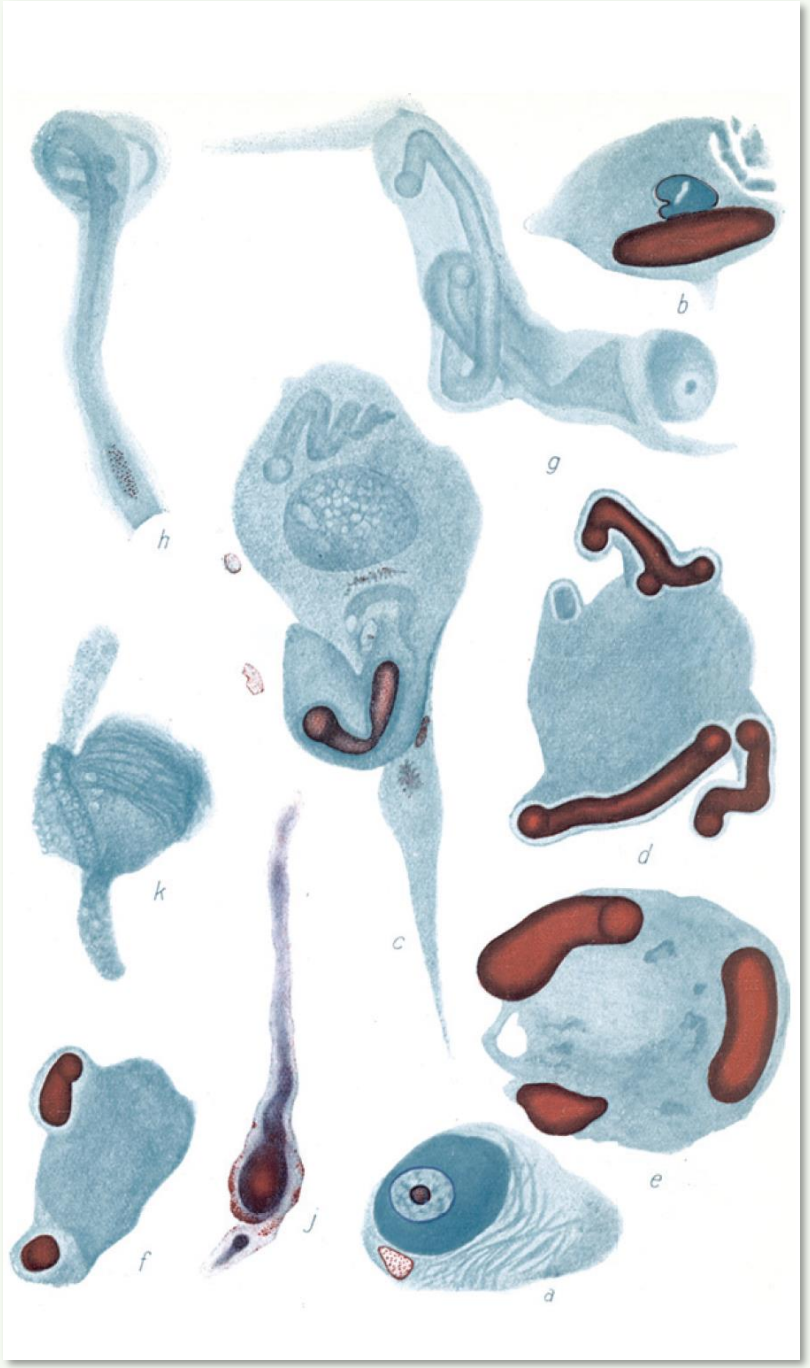
Neuropatología de la demencia por cuerpos de Lewy.



Alberto Rábano

Fundación CIEN, ISCIII, Madrid

Reunión Anual de la SEN
Sevilla, noviembre 2022



Lewy FH. Paralysis agitans. 1. Pathologische Anatomie. In: Lewandowsky M, editor. Handbuch der Neurologie, Dritter Band, Spezielle Neurologie I. Berlin: Julius Springer; 1912. p. 920-33

Lafora GR. Contribución a la histopatologia de la parálisis agitante. Trab Lab Invest Biol Univers Madrid. 1913;11:43-54

E. de Parkinson, n. motor dorsal del n. vago. F.H. Lewy, 1923

Contribución á la histopatología de la parálisis agitante

POR

GONZALO R. LAFORA

A las primeras hipótesis de Parkinson y otros, según los cuales las lesiones causales de la parálisis agitante yacerían probablemente en el

Lafora GR. Contribución a la histopatologia de la parálisis agitante.
Trab Lab Invest Biol Univers Madrid. 1913;11:43-54

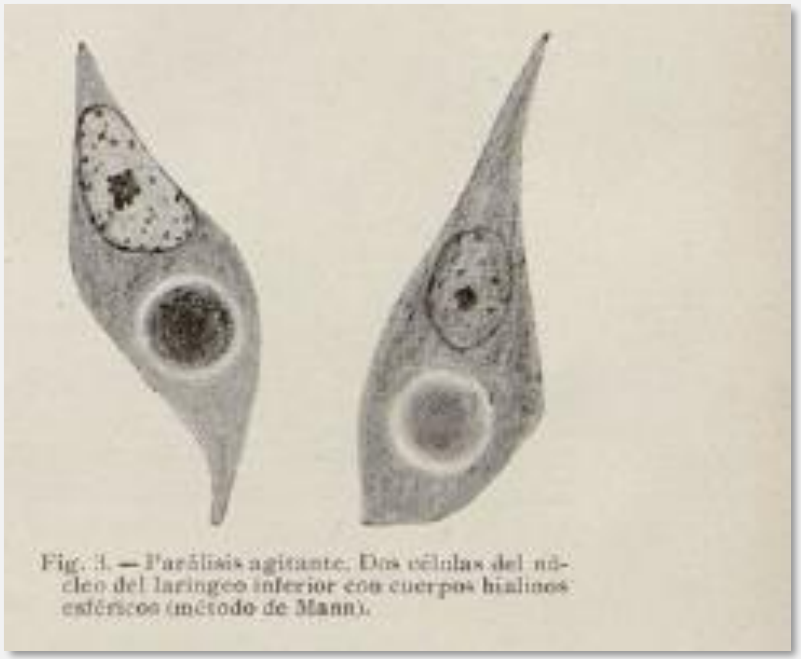


Fig. 3. — Parálisis agitante. Dos células del núcleo del laríngeo inferior con cuerpos hialinos esféricos (método de Mann).

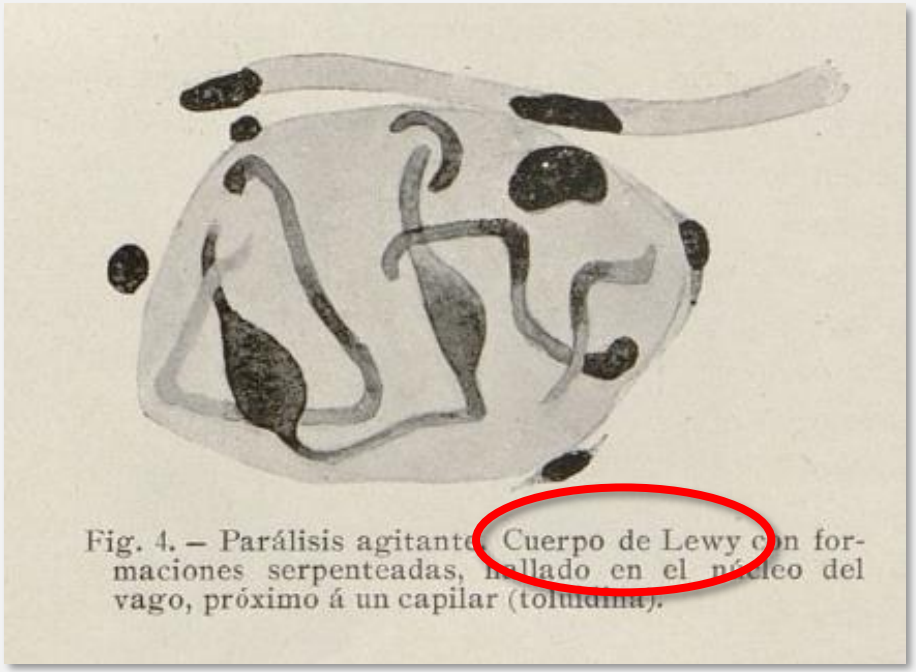
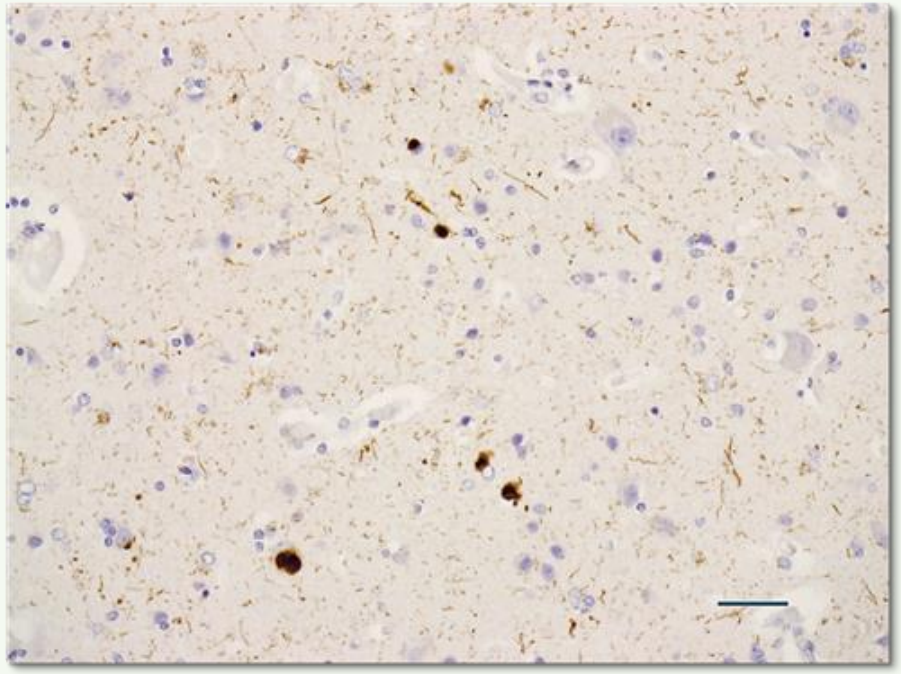
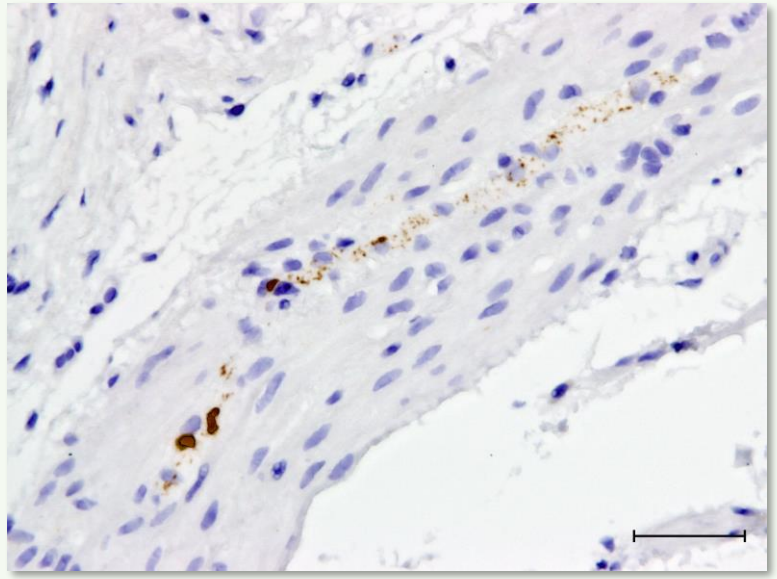


Fig. 4. — Parálisis agitante. Cuerpo de Lewy con formaciones serpenteadas, hallado en el núcleo del vago, próximo á un capilar (toluidina).

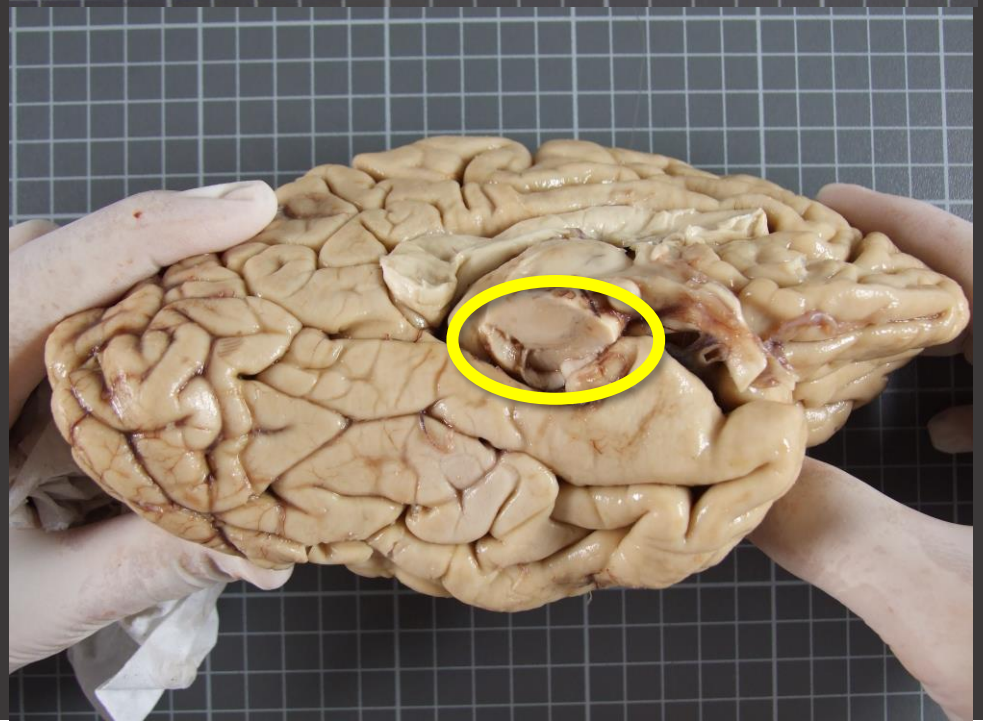


Patología de Lewy cortical, α-sinucleína total



Fibras + en la mucosa gástrica, α-sinucleína fosforilada

Sánchez-Ferro Á, Rábano A *et al*., Mov Disord, 2015



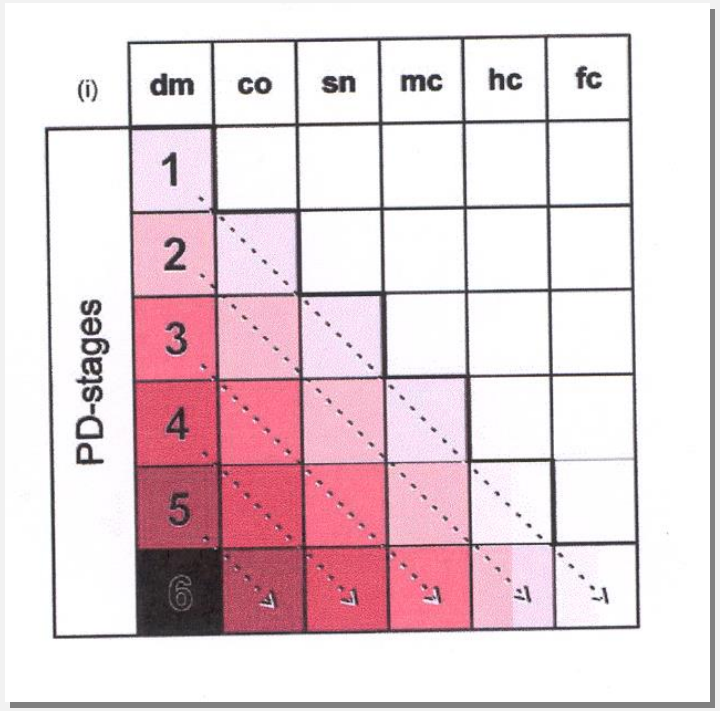
Staging of brain pathology related to sporadic Parkinson's disease

Heiko Braak [a,*], Kelly Del Tredici [a], Udo Rüb [a], Rob A.I. de Vos [b], Ernst N.H. Jansen Steur [b], Eva Braak [a,†]

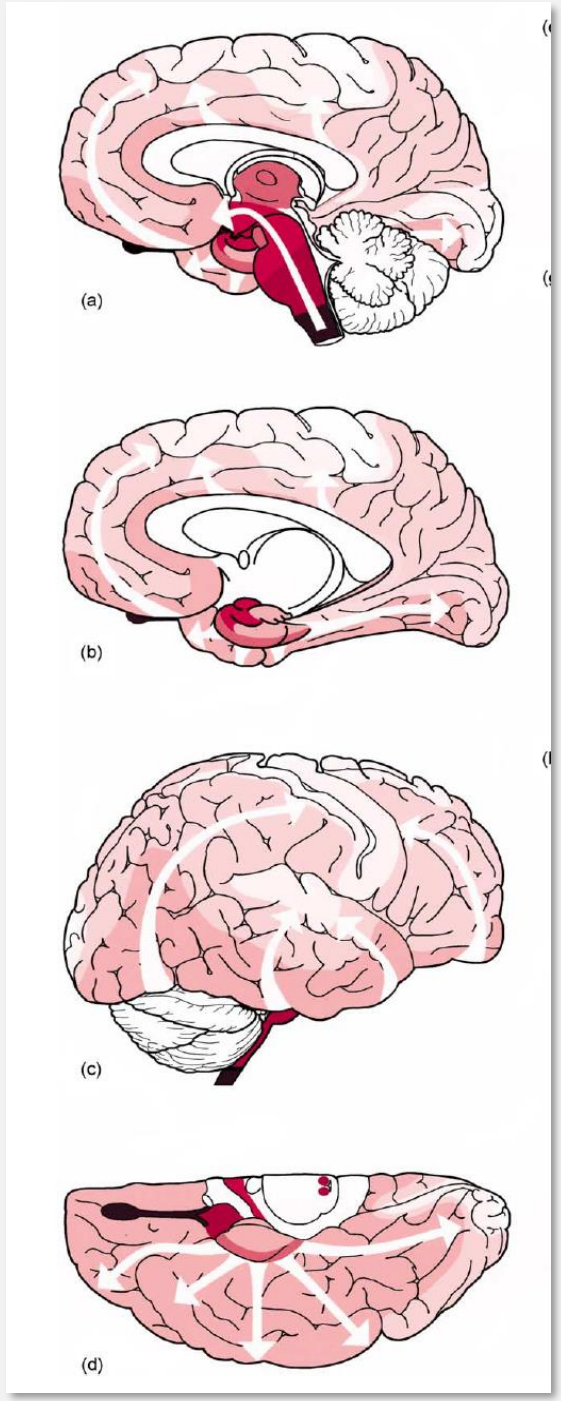
[a] Department of Clinical Neuroanatomy, J.W. Goethe University, Theodor Stern Kai 7, D-60590 Frankfurt/Main, Germany
[b] Department of Neurology MST Hospital Group and Laboratorium Pathologie Oost Nederland, Burg. Edo Bergsmalaan, 7512 AD Enschede, The Netherlands

Neurobiol Aging, 2003 : 197-211.

Heiko Braak, 1937 -



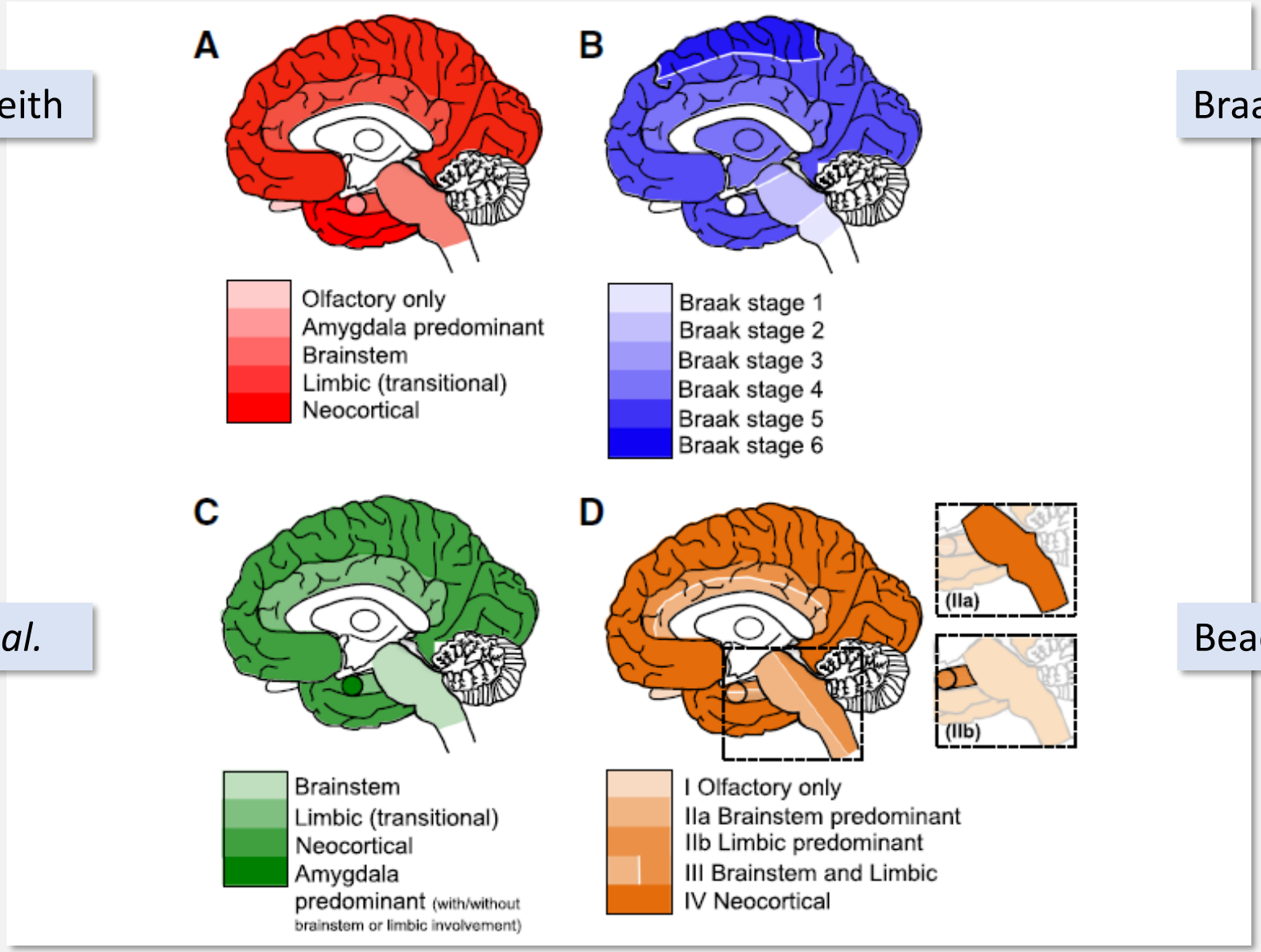
Del Tredici K, Braak H. Neuropathology and neuroanatomy of TDP-43 amyotrophic lateral sclerosis. Curr Opin Neurol. 2022 Oct 1;35(5):660-671.



Sistemas de clasificación de la patología de Lewy

Newcastle-McKeith

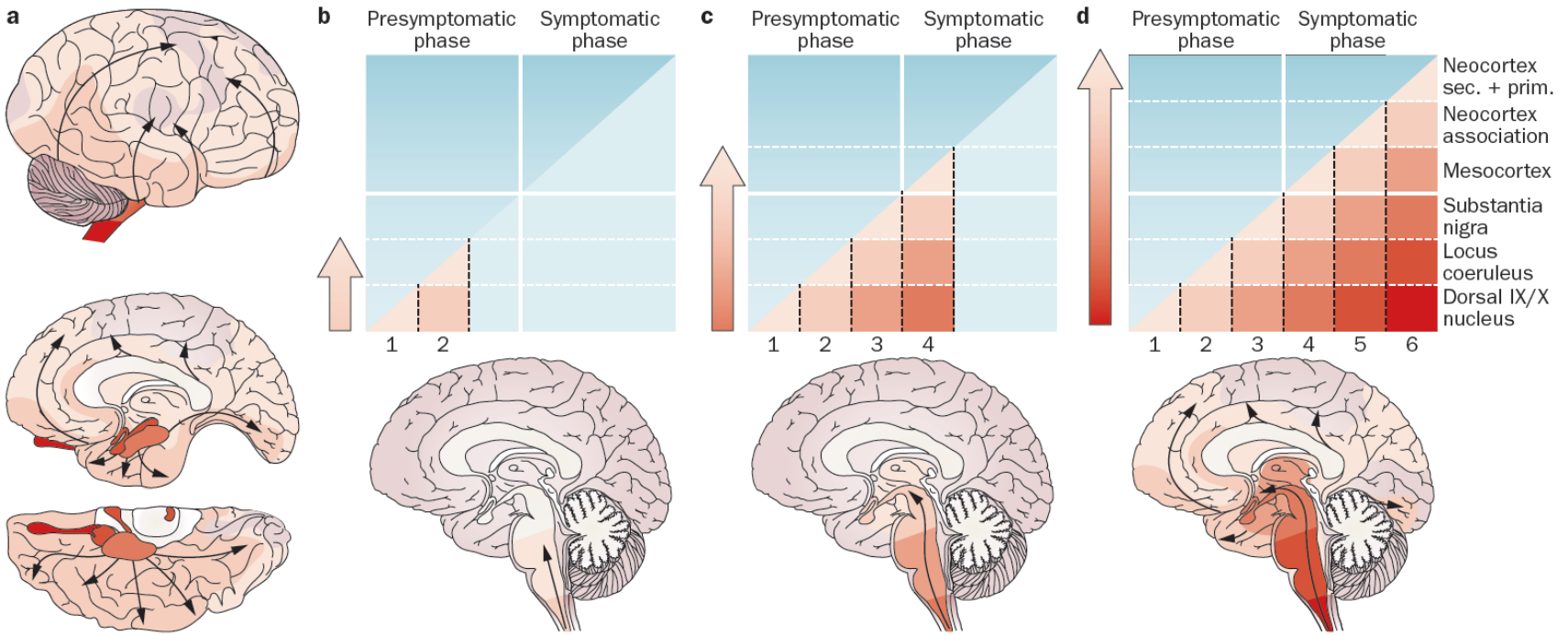
Braak



Leverenz *et al.*

Beach *et al.*

Outeiro TF *et al.*, 2019



Goedert M *et al.*, 2013

Alafuzoff I *et al.*, 2009 (Brainnet consortium)

Sampled brain areas	Medulla		Pons		Midbrain	Basal Forebrain		Hippocampus		Gyrus cinguli	Temporal cortex	Frontal cortex	Parietal cortex
Anatomical region	dmV	irx	LC	R	SN	nbM	AC	CA2	TOcx	grey matter	grey matter	grey matter	grey matter
Braak stage	1	1	2	2	3	3	4	3	4	5	5	6	6
McKeith type	BRAINSTEM					LIMBIC						NEOCORTICAL	
Amygdala predominant							AC predominant						
Lesion type requested	LBs and / or LNs						LBs	LNs		LBs			

Necesidad de un sistema de clasificación de la patología de Lewy que permita:

1. Un alto grado de concordancia entre evaluadores.

2. La clasificación inequívoca de todos los casos posibles.

3. Fácilmente aplicable en la rutina de diagnóstico neuropatológico.

2021

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

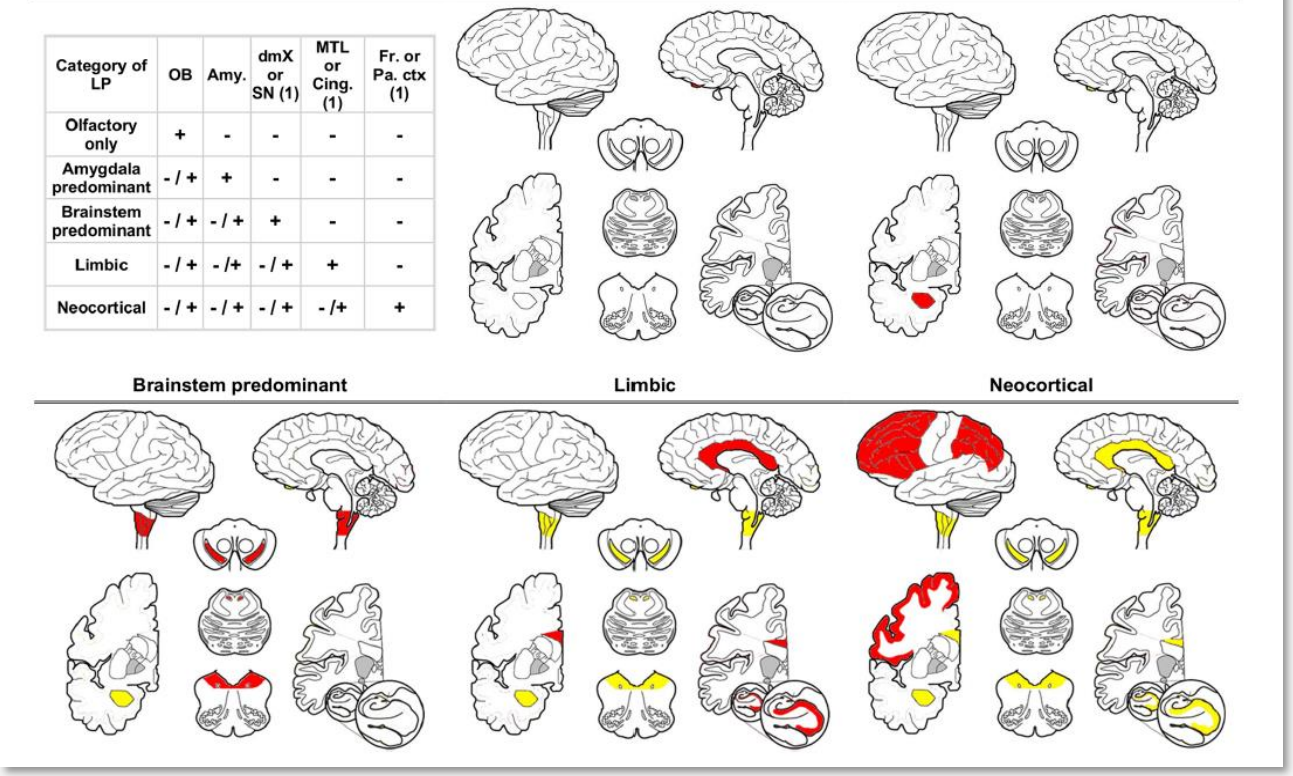
ORIGINAL PAPER

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

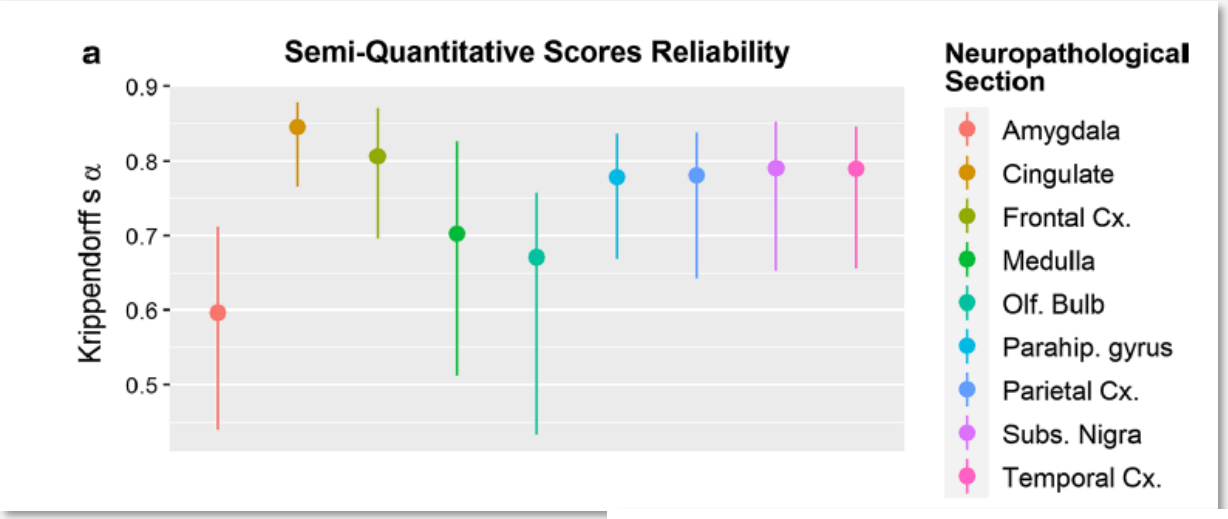
Johannes Attems[1] · Jon B. Toledo[2,3] · Lauren Walker[1] · Ellen Gelpi[4,5] · Steve Gentleman[6] · Glenda Halliday[7] · Tibor Hortobagyi[8,9,10,11] · Kurt Jellinger[12] · Gabor G. Kovacs[13,14] · Edward B. Lee[3] · Seth Love[15] · Kirsty E. McAleese[1] · Peter T. Nelson[16] · Manuela Neumann[17,18]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

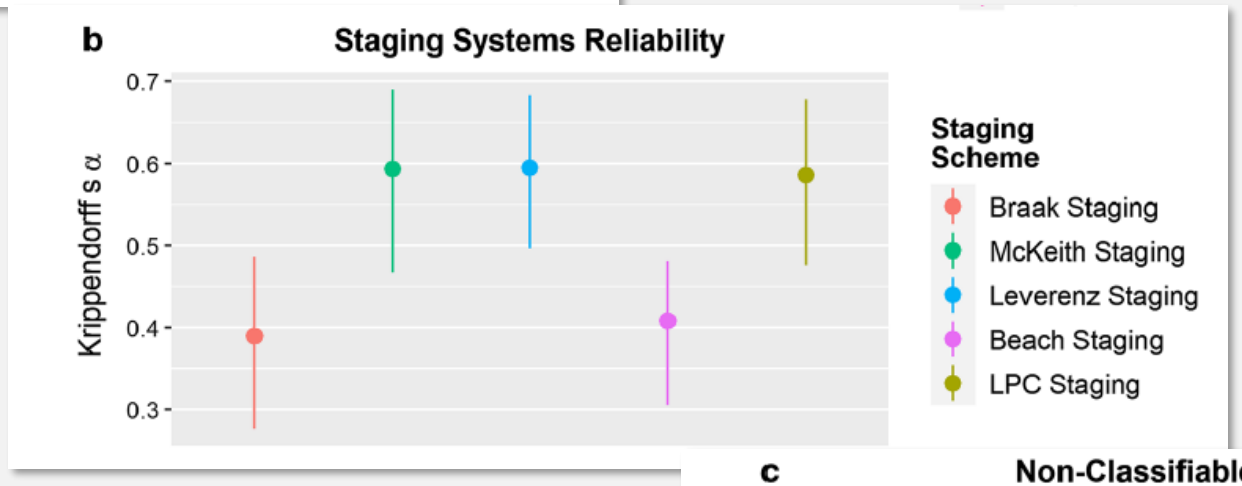
Category of LP	OB	Amy.	dmX or SN (1)	MTL or Cing. (1)	Fr. or Pa. ctx (1)
Olfactory only	+	-	-	-	-
Amygdala predominant	- / +	+	-	-	-
Brainstem predominant	- / +	- / +	+	-	-
Limbic	- / +	- /+	- / +	+	-
Neocortical	- / +	- / +	- / +	- /+	+

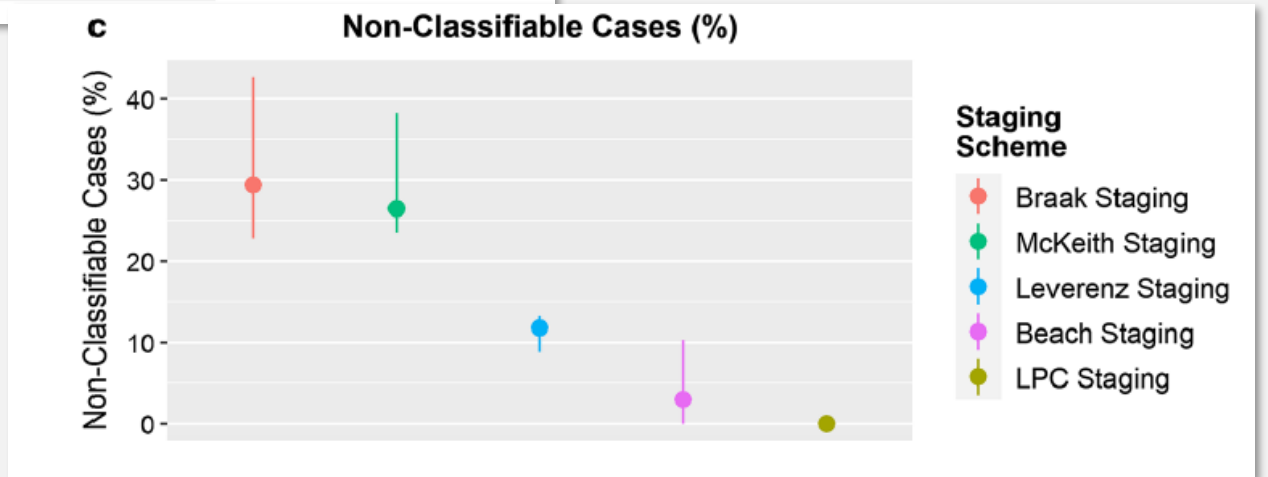
Lewy Pathology Consensus Criteria (LPC)



- Evaluación dicotómica (presencia/ausencia) de CL o NL
- Región (+) si al menos score 1 en el sistema de McKeith.





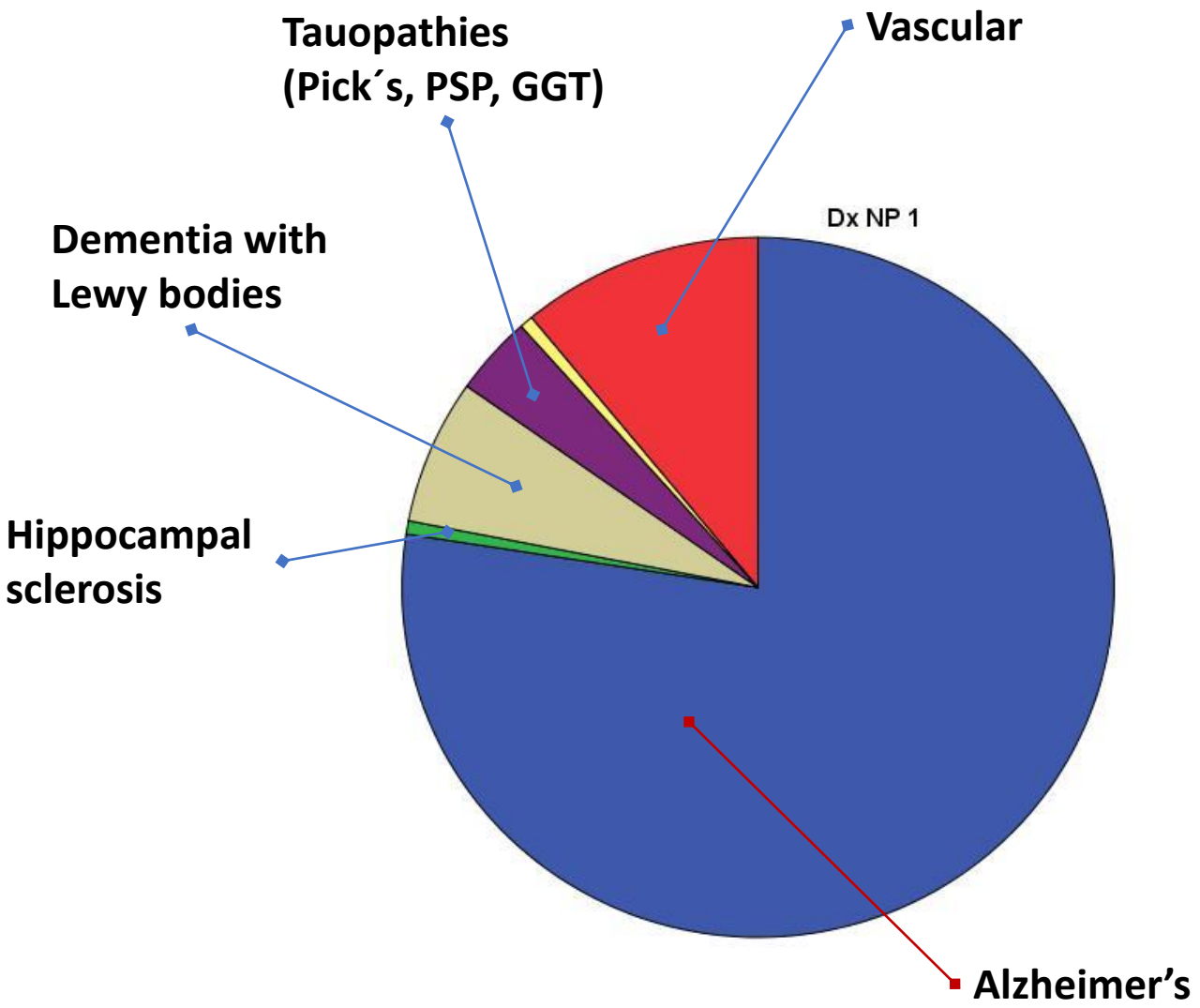


Attems J *et al.*, 2021

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.	55.6%
LATE (HS)	71.2% (45.2%)
ARTAG	52.7%
AGD	12%

Vallecas Alzheimer's Study

Main neuropathological diagnosis

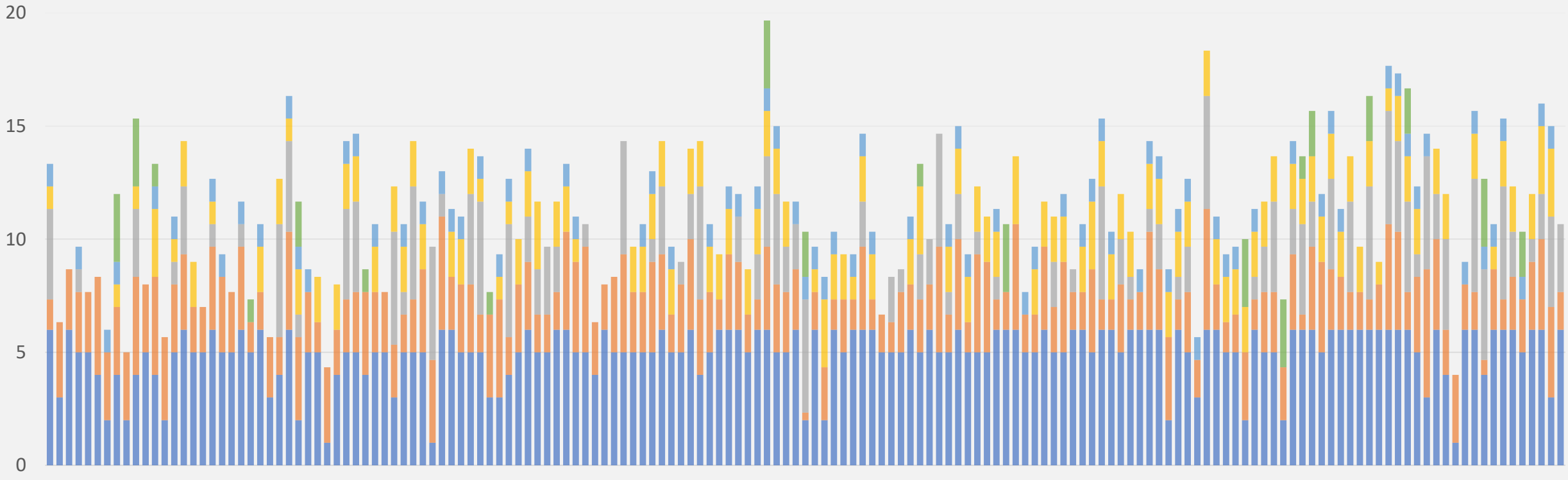


Inmunohistoquímica para alfa-sinucleína

- Braak / McKeith
  - Fase 1
  - Fase 2

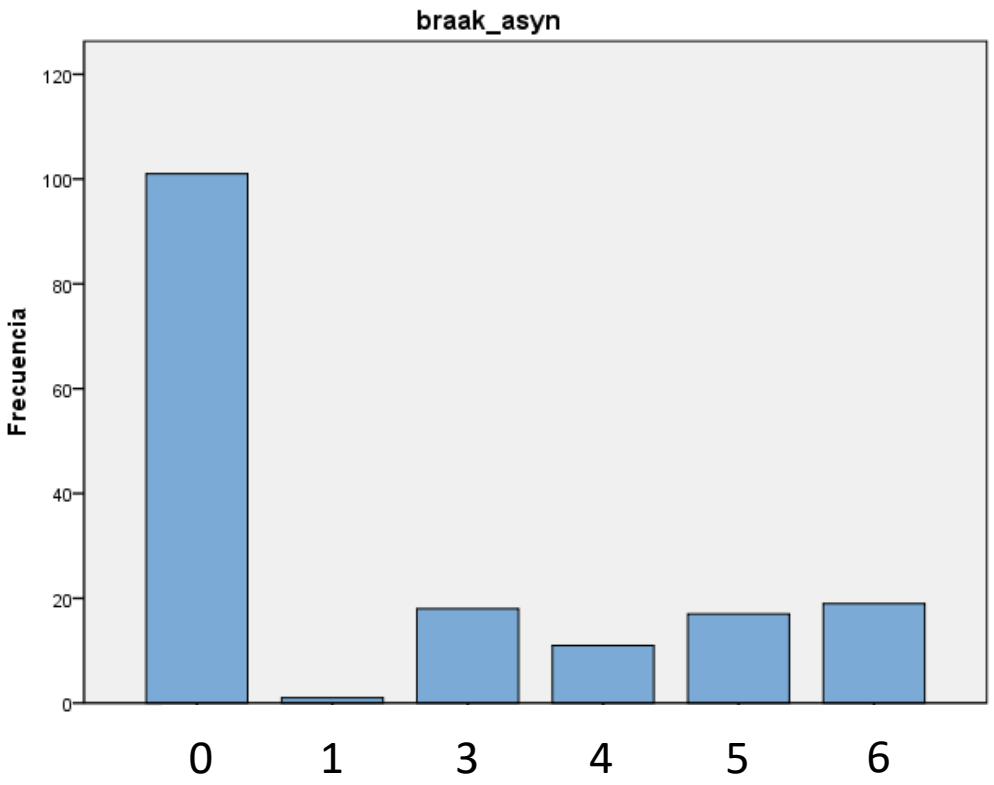
- LPC

Vallecas Alzheimer's Study

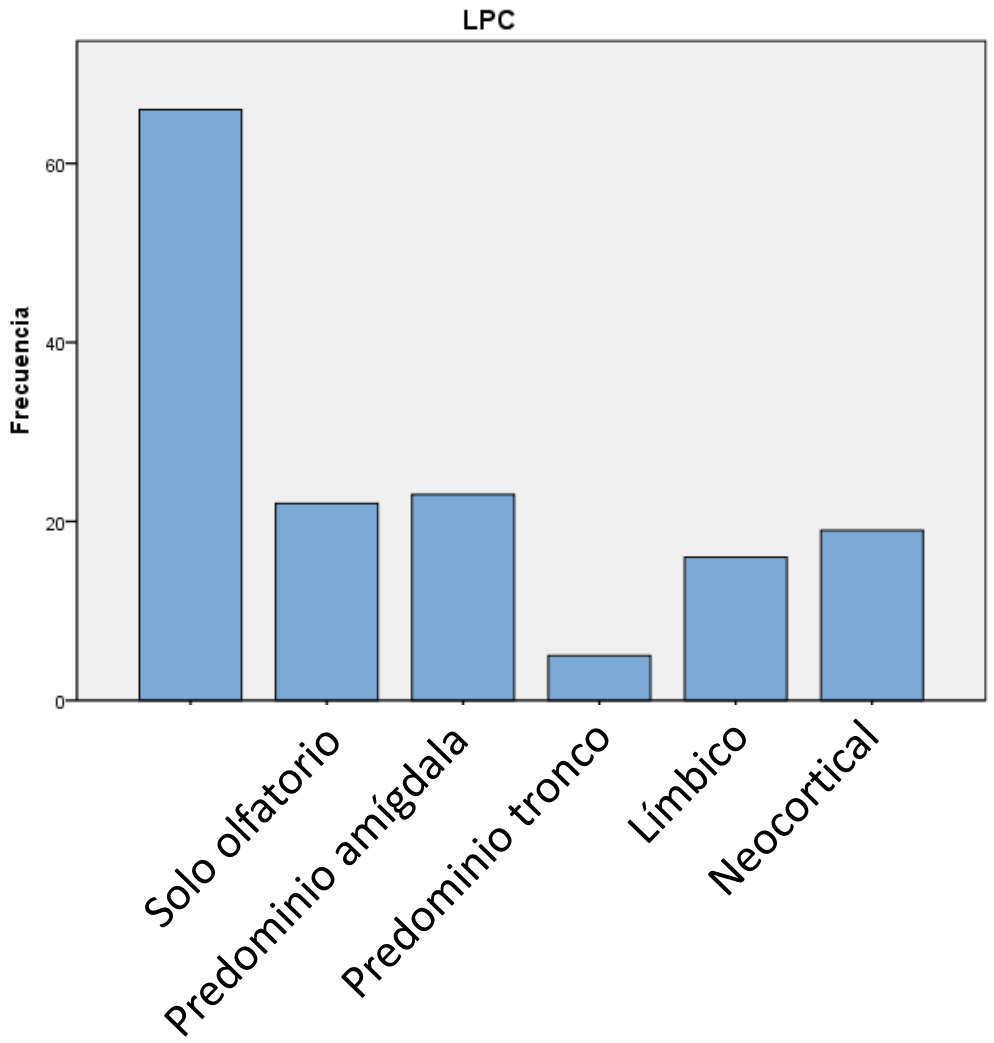


- Alzheimer' pathology (Braak stage 0 – 6)
- Cerebrovascular pathology (0 – 5)
- Lewy type pathology (0 – 6)
- TDP-43 pathology (LATE) (0 – 3)
- ARTAG (0 – 1)
- Argyrophilic grain disease (0 – 3)

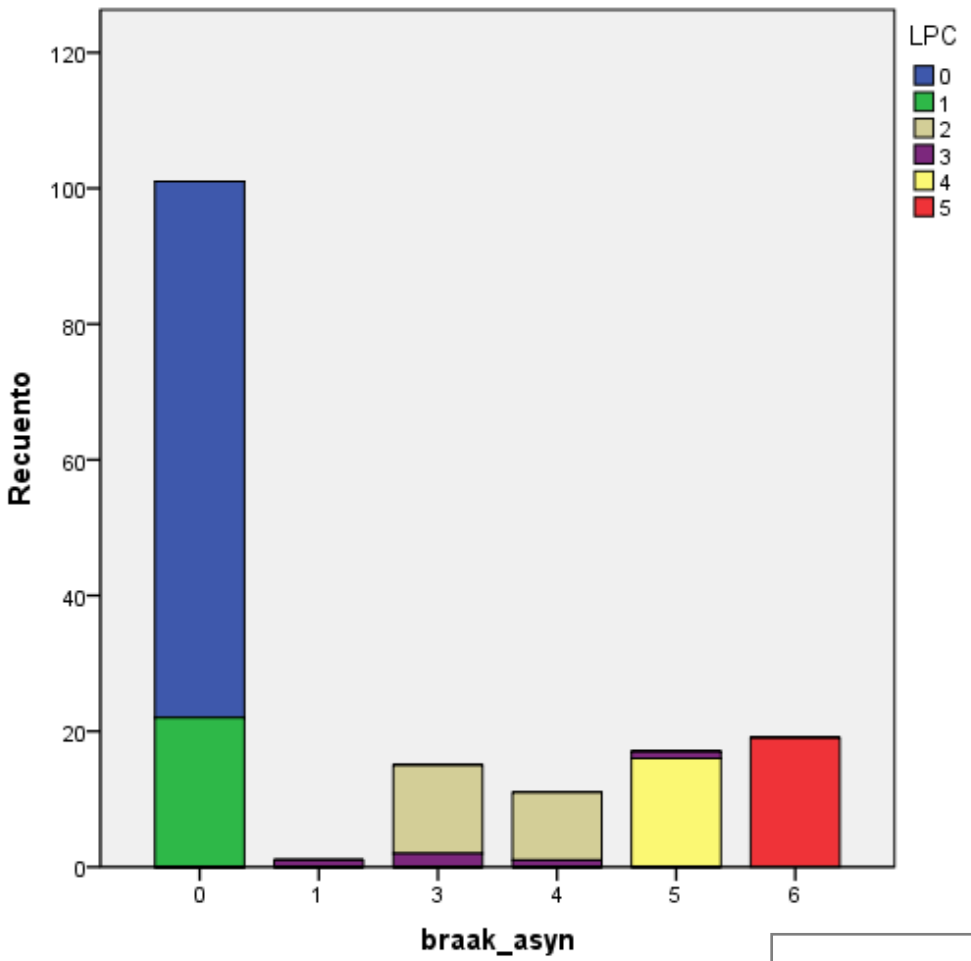
Braak


braak_asyn
Frecuencia
120
100
80
60
40
20
0
0
1
3
4
5
6

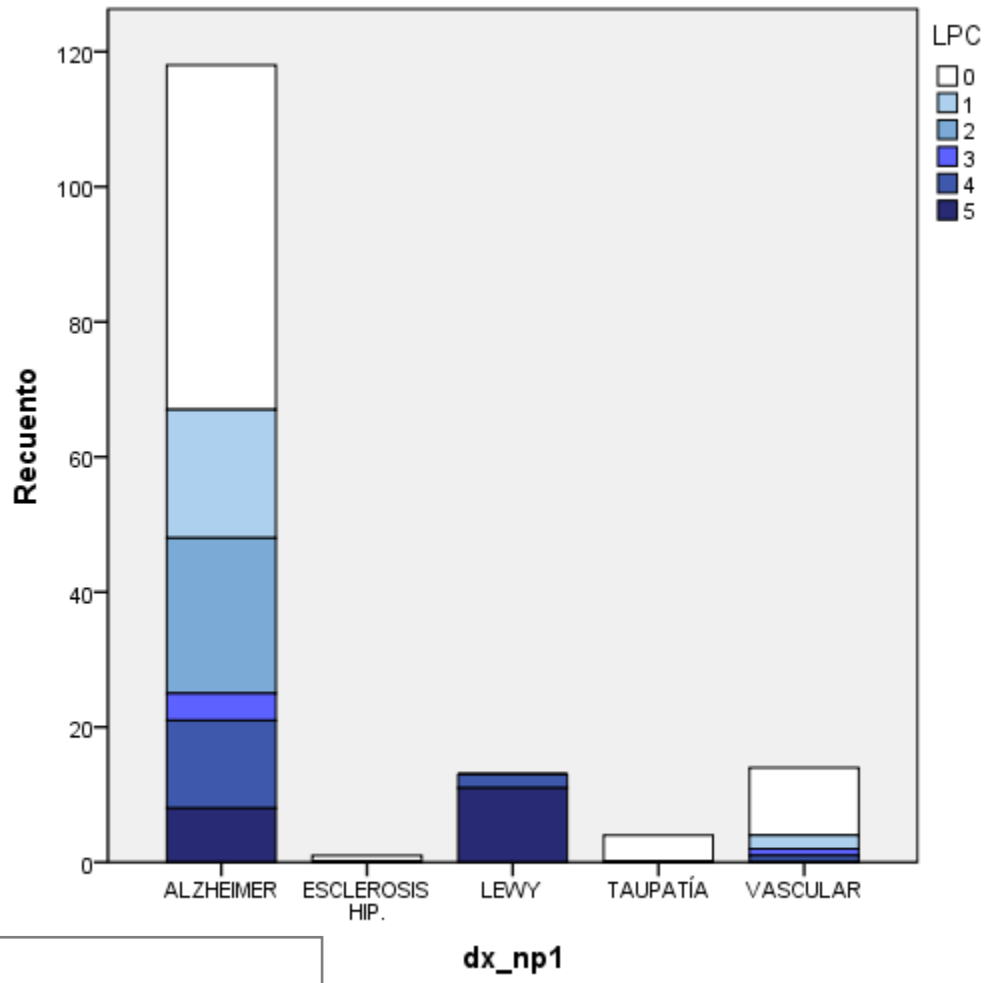
LPC


LPC
Frecuencia
60
40
20
0
Solo olfatorio
Predominio amígdala
Predominio tronco
Límbico
Neocortical

LPC / Braak



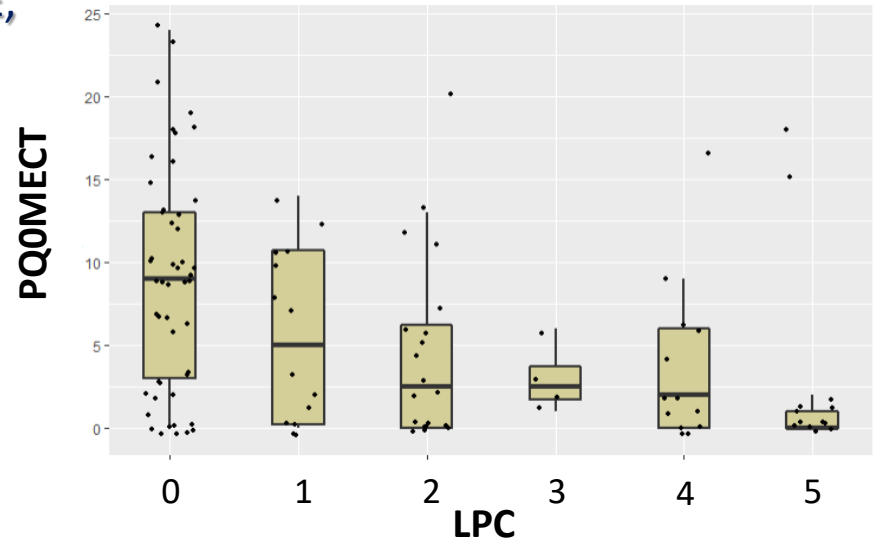
LPC / Diagnóstico NP principal



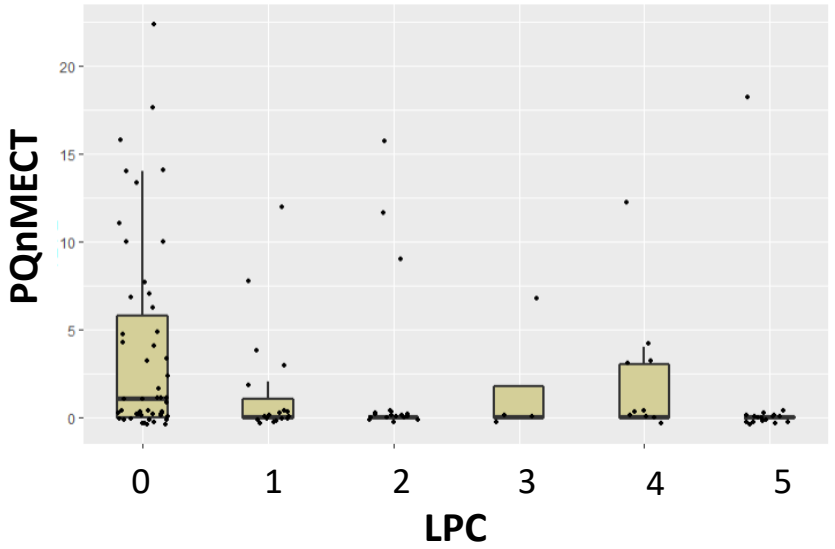
LPC

0 = Negativo	3 = Tronco
1 = Olfatorio	4 = Límbico
2 = Amígdala	5 = Neocortical

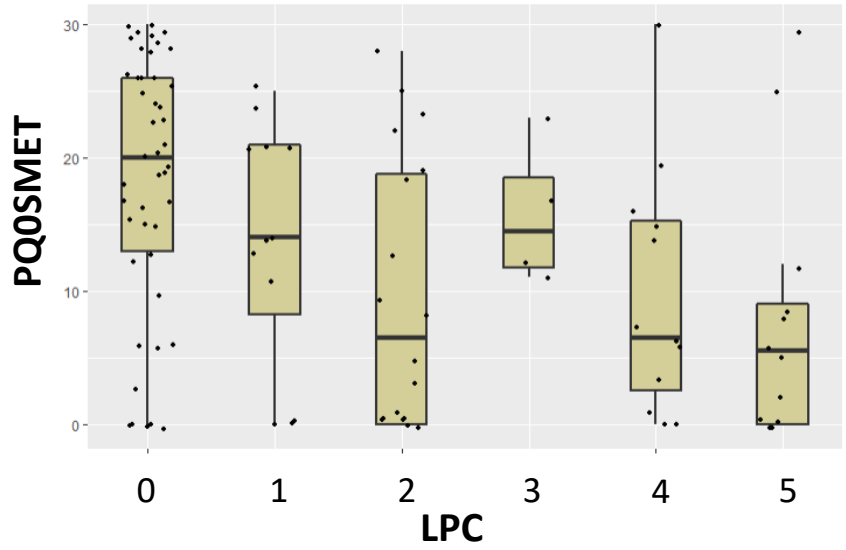
Total score, severe MMSE, basal



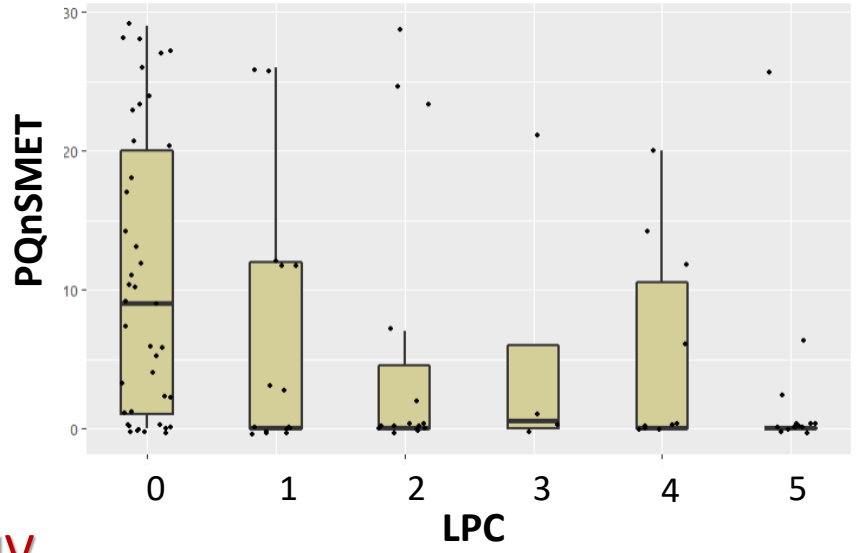
Total score, severe MMSE, penultimate



Total score, MEC (Lobo), basal



Total score, MEC (Lobo), penultimate



Braak stage > IV

Kruskal-Wallis, $p < 0.05$

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

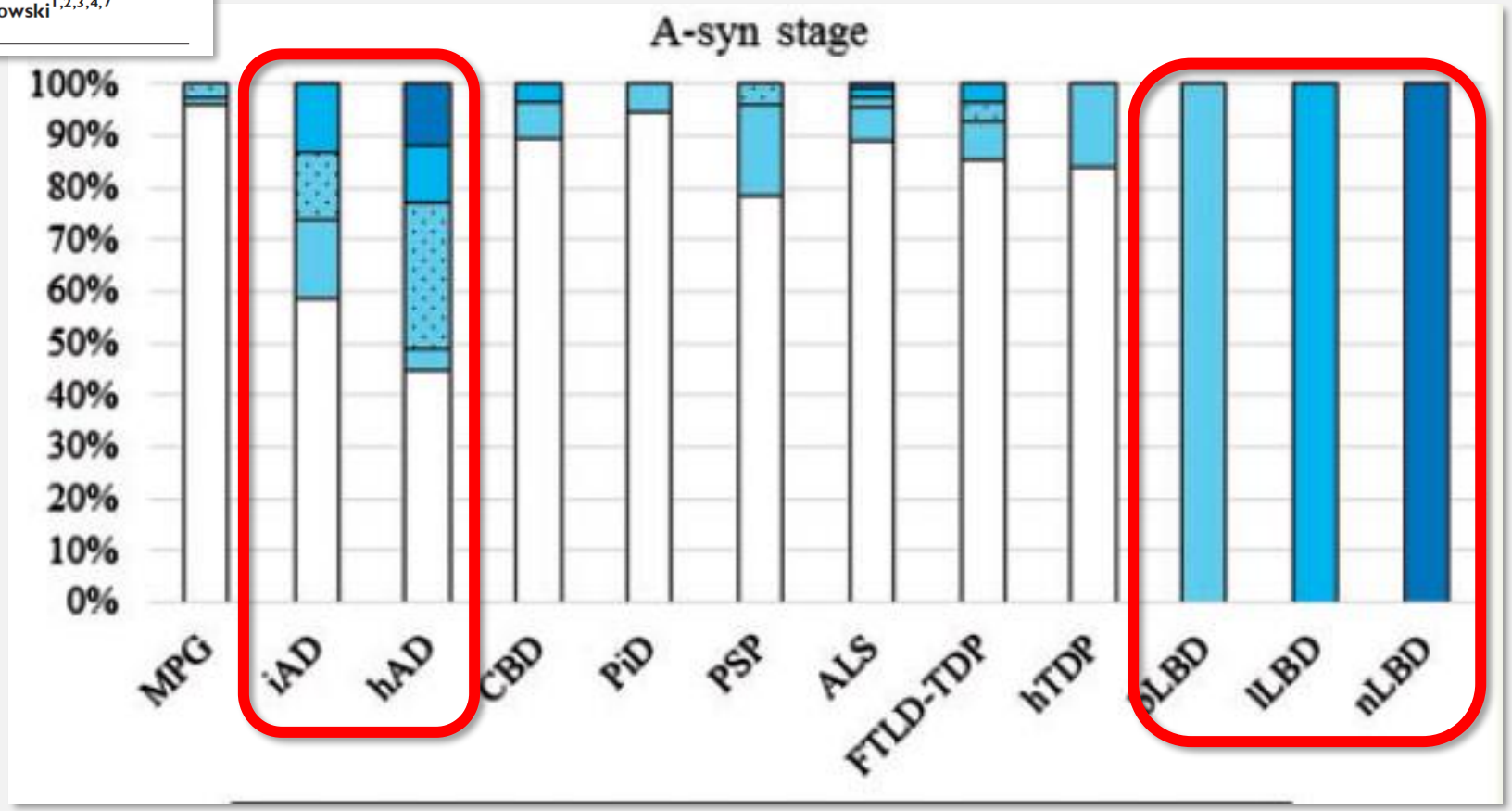
John L. Robinson,[1,2,3,4] Edward B. Lee,[1,2,3,4] Sharon X. Xie,[1,2,3,4,5] Lior Rennert,[1,2,3,4,5] EunRan Suh,[1,2,3,4] Colin Bredenberg,[1,2,3,4] Carrie Caswell,[1,2,3,4,5] Vivianna M. Van Deerlin,[1,2,3,4] Ning Yan,[1,2,3,4,6] Ahmed Yousef,[1,2,3,4] Howard I. Hurtig,[1,2,3,7] Andrew Siderowf,[1,2,3,7] 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]

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]

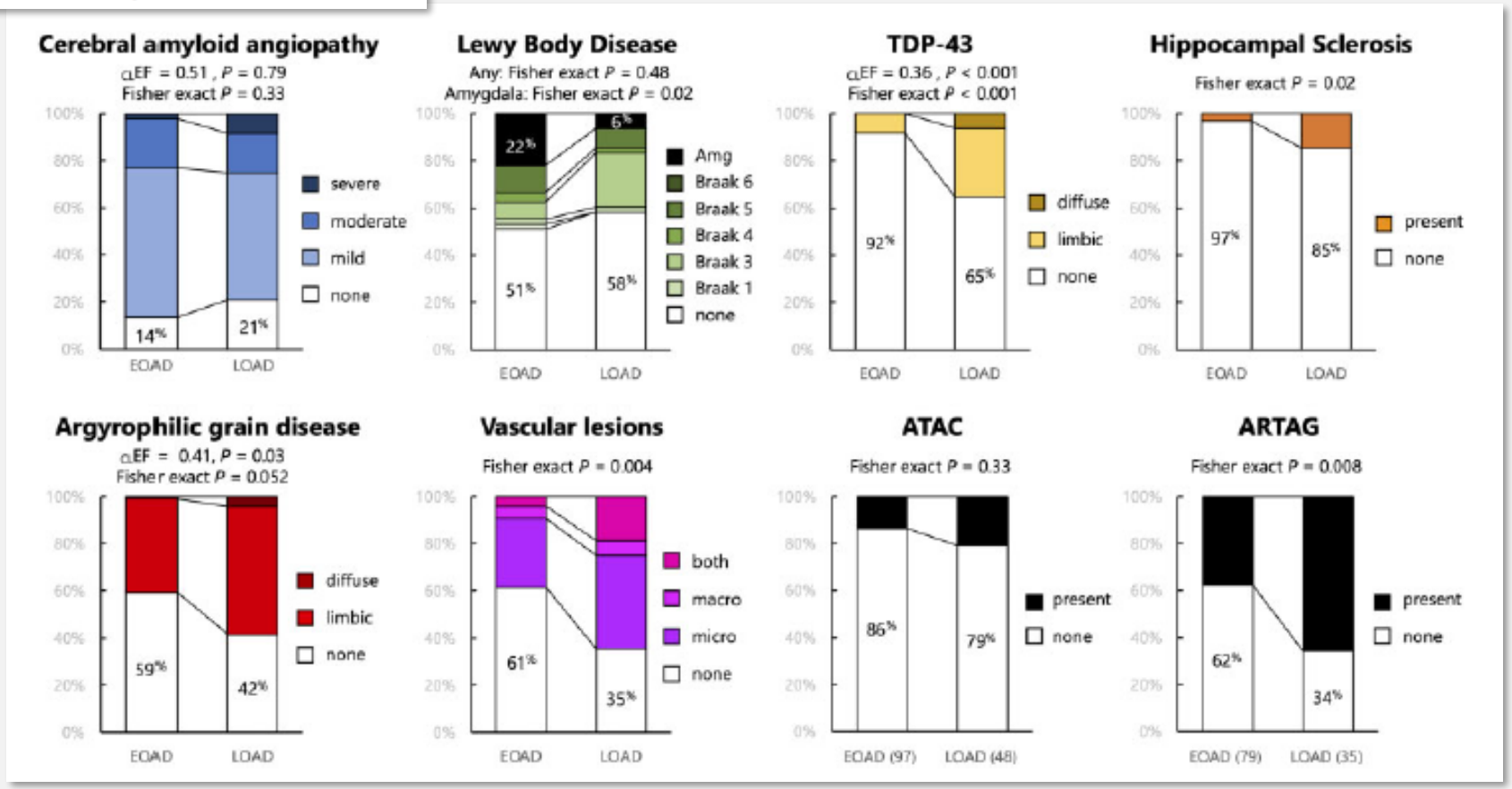


doi:10.1093/brain/awab099 BRAIN 2021: 144; 2186–2198 | 2186

BRAIN
ORIGINAL ARTICLE

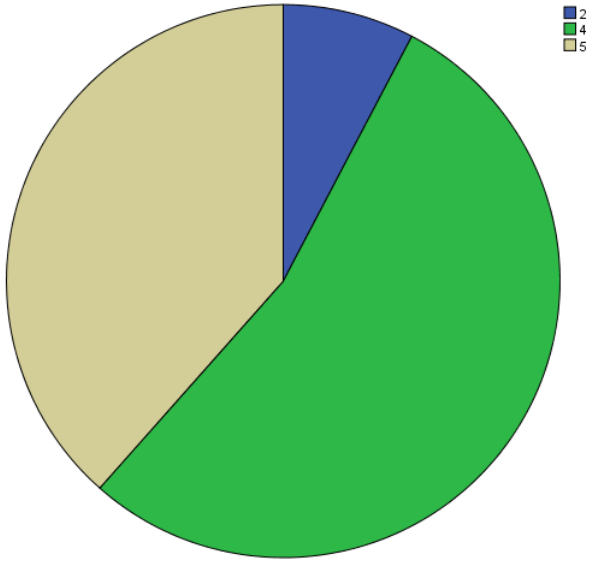
Comorbid neuropathological diagnoses in early versus late-onset Alzheimer's disease

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]

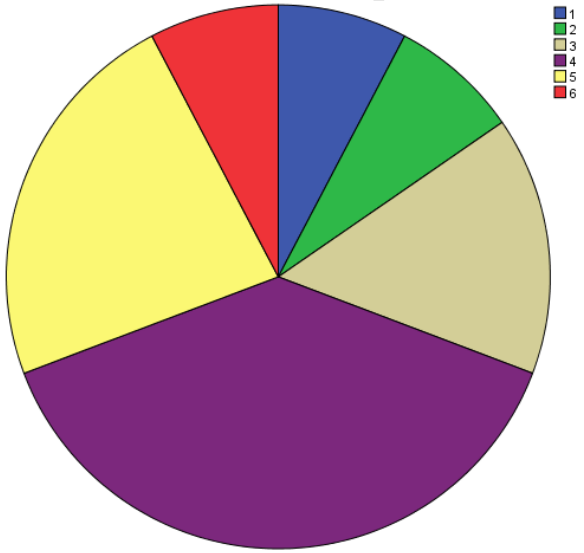


Patología combinada en demencia con cuerpos de Lewy [N = 13, Mujeres = 69%, edad al exitus = 87,5 años (6,7)]

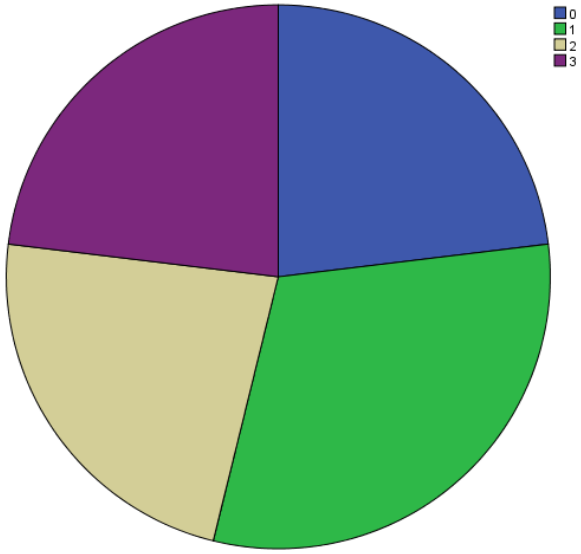
Thal (Aβ)



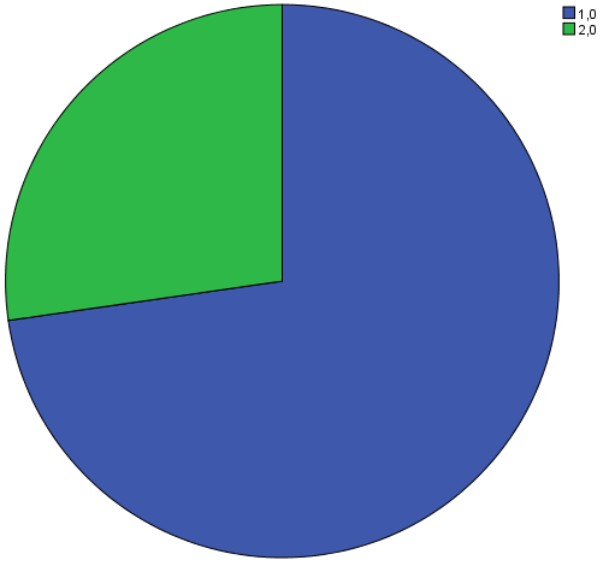
Braak tau



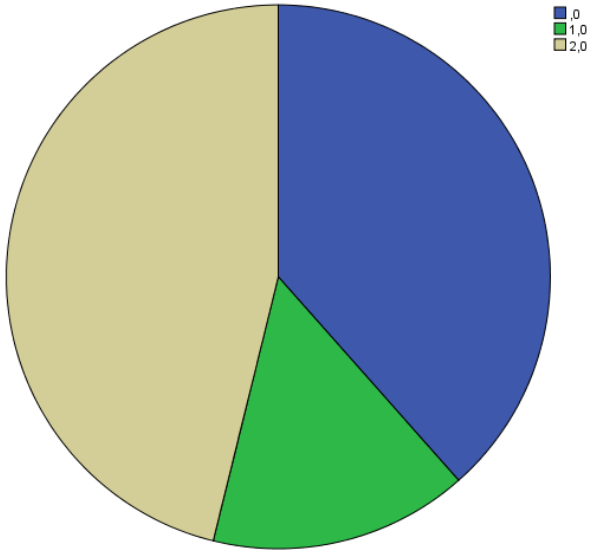
NIA C



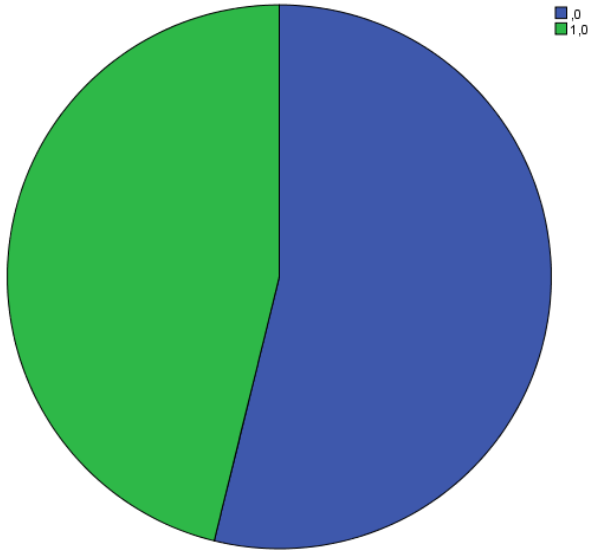
VCING



LATE (TDP-43)



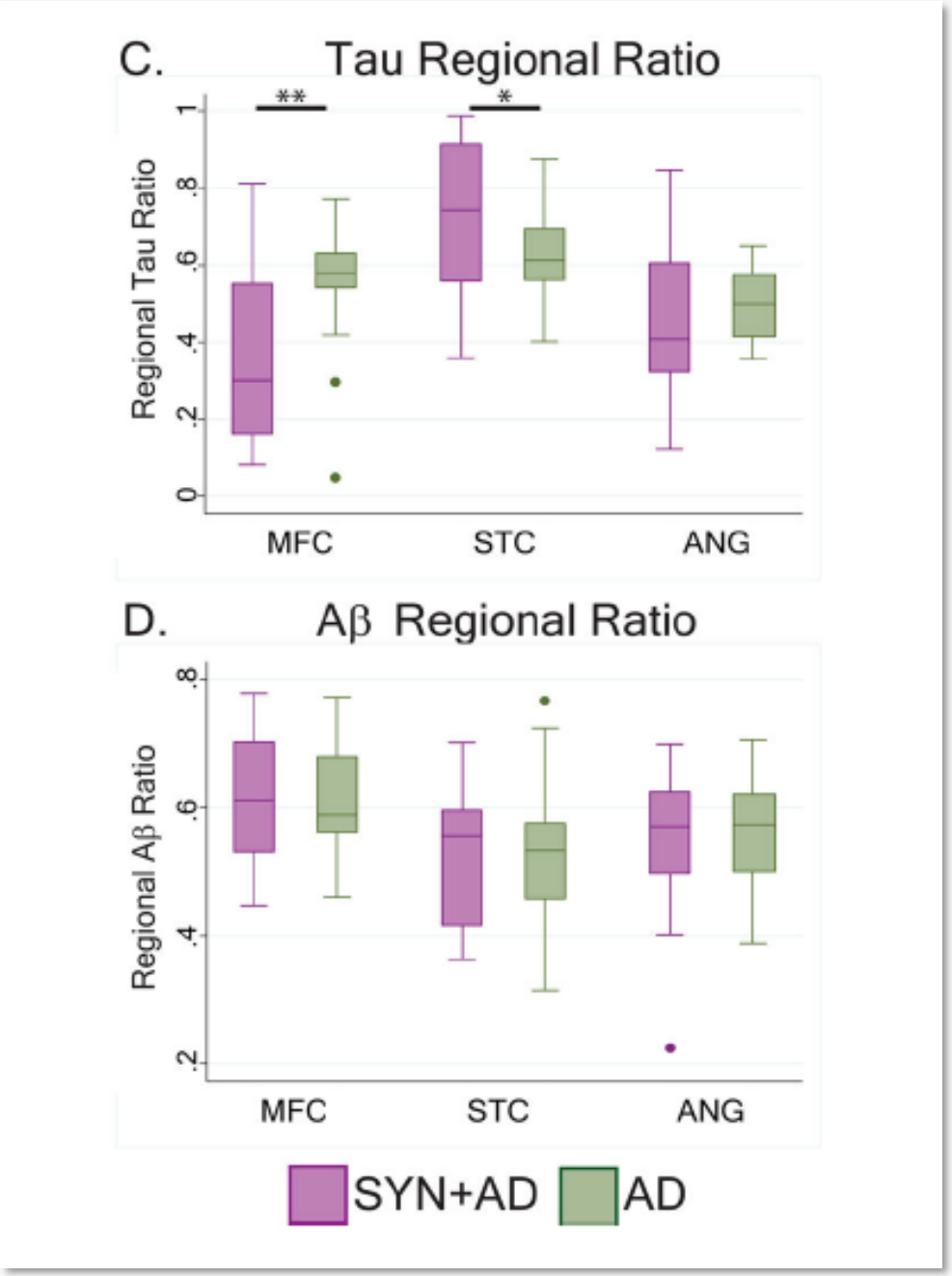
ARTAG



Published in final edited form as:
Ann Neurol. 2019 February ; 85(2): 259–271. doi:10.1002/ana.25392.

Cognitive and Pathological Influences of Tau Pathology in Lewy Body Disorders

David G. Coughlin, MD[1,2,7], **Sharon X. Xie, PhD**[7,8,9], **Mendy Liang, BS**[1,2], **Andrew Williams, BS**[1,2], **Claire Peterson, BS**[1,2], **Daniel Weintraub, MD**[1,4,7,10], **Corey T. McMillan, PhD**[1,3], **David A. Wolk, MD**[1,8], **Rizwan S. Akhtar, MD PhD**[1,6,7], **Howard Hurtig, MD**[1,7], **H. Branch Coslett, MD**[1,8], **Roy Hamilton, MD MS**[1,8], **Andrew Siderowf, MD MSCE**[1,4,7], **John E. Duda, MD**[4,10], **Katya Rascovsky, PhD**[1,3], **Edward B. Lee, MD PhD**[5,7,8], **Virginia M.-Y. Lee, PhD**[5,6,7,8], **Murray Grossman, MD**[1,3,7], **John Q. Trojanowski, MD PhD**[1,5,6,7,8], and **David J. Irwin, MD MSTR**[1,2,3,4,7,8]



Gracias!

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

Twitter: @banco_tx_CIEN