

CIEN: a unique research model

Fundación CIEN: un modelo de investigación único



Alberto Rábano

Pascual Sánchez Juan

Fundación CIEN, Instituto de Salud Carlos III

LA REINA SOFÍA Y SU
FUNDACIÓN

LA FUNDACIÓN AL DÍA

NUESTROS PROYECTOS

PROYECTO ALZHEIMER

DOCUMENTACIÓN

COLABORAR

LA ENFERMEDAD

EL CENTRO

NUESTRO TRABAJO

DOCUMENTOS

CAMPAÑAS

FAMILIARES

SIMPOSIUM Y CONGRESOS

HERRAMIENTAS DE
ACCESIBILIDAD



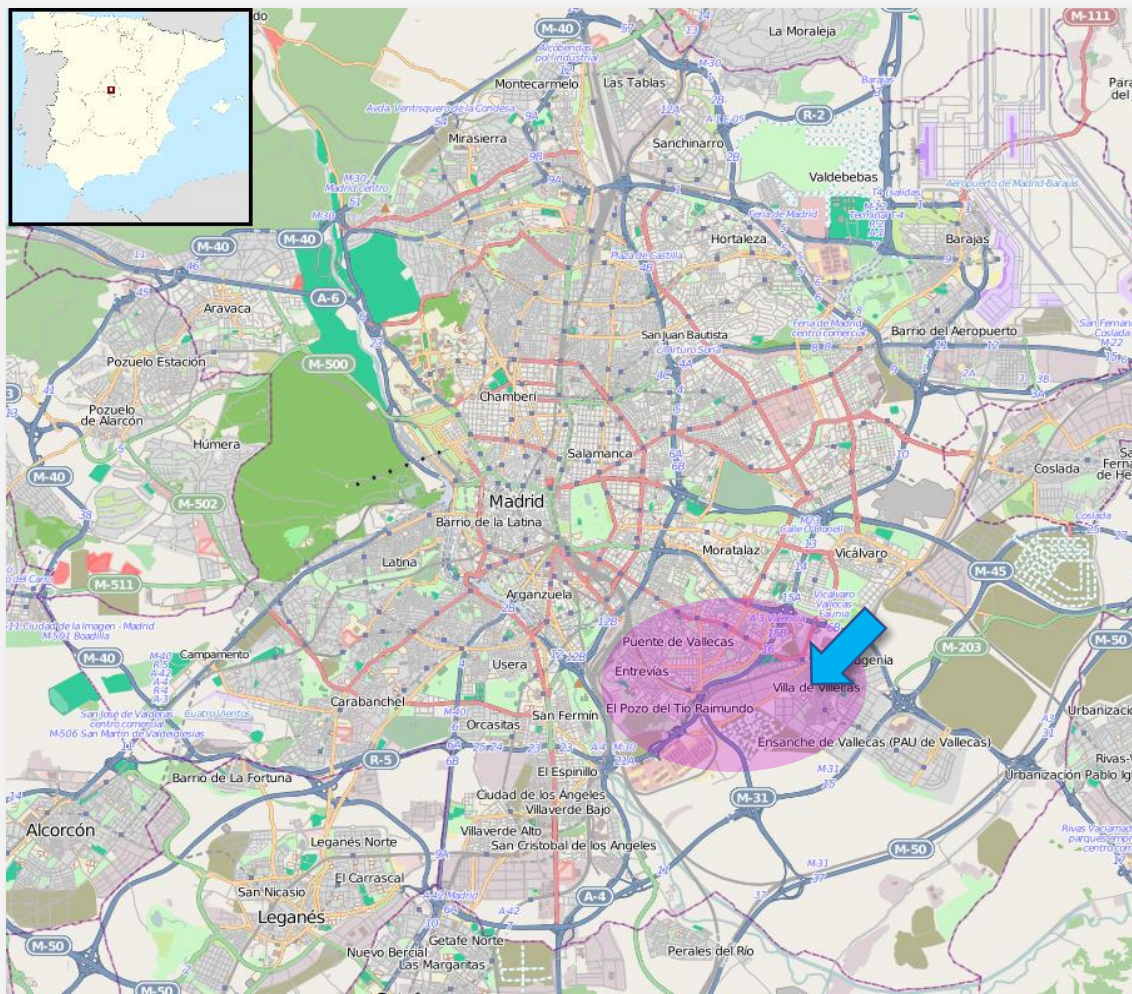
EL
**CENTRO
ALZHEIMER**
FUNDACIÓN
REINA SOFÍA

VER VÍDEO

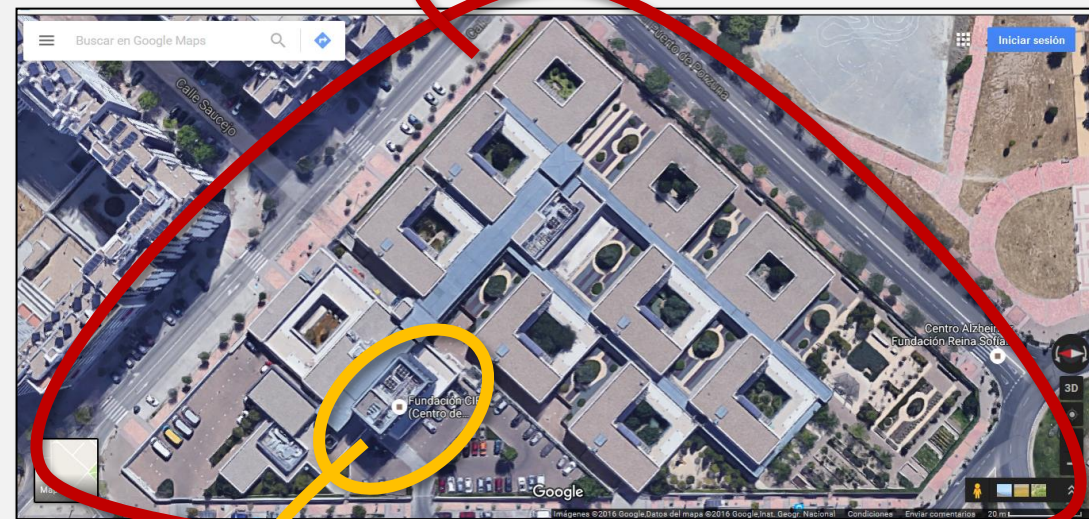
2007



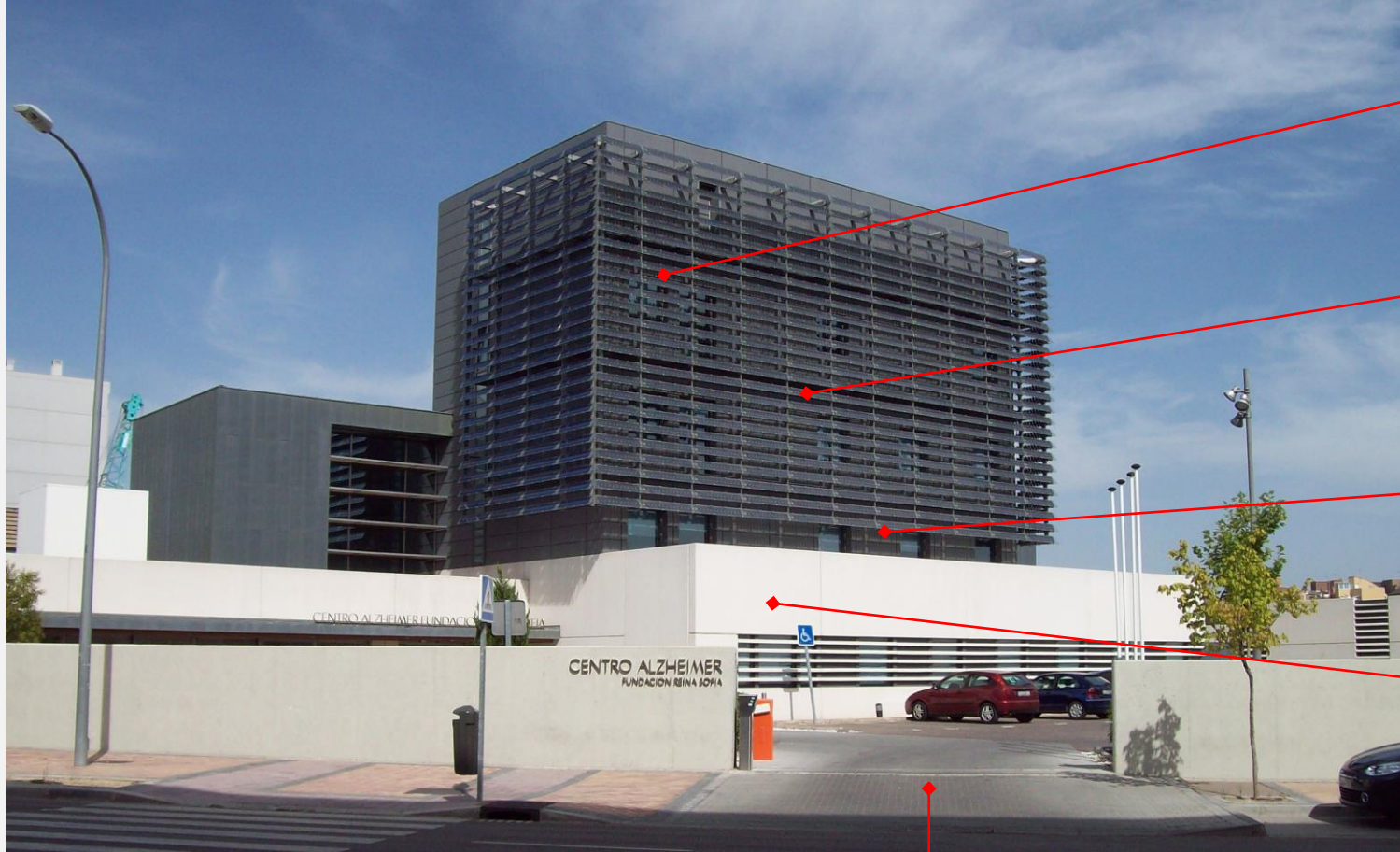
Madrid - Vallecas



Centro Alzheimer Fundación Reina Sofía



Fundación CIEN



Tercera planta:
Laboratorios

Segunda planta:
Despachos, Extracciones

Primera planta:
Despachos clínicos

Planta baja:
Dirección, Administración, Sala de seminarios

Planta sótano:
Neuroimagen, Banco de Tejidos

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.

El Banco de Tejidos CIEN

TODOS PODEMOS
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Instituto de Salud Carlos III
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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

168

Programa de donación externo

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

567

El Proyecto Vallecas

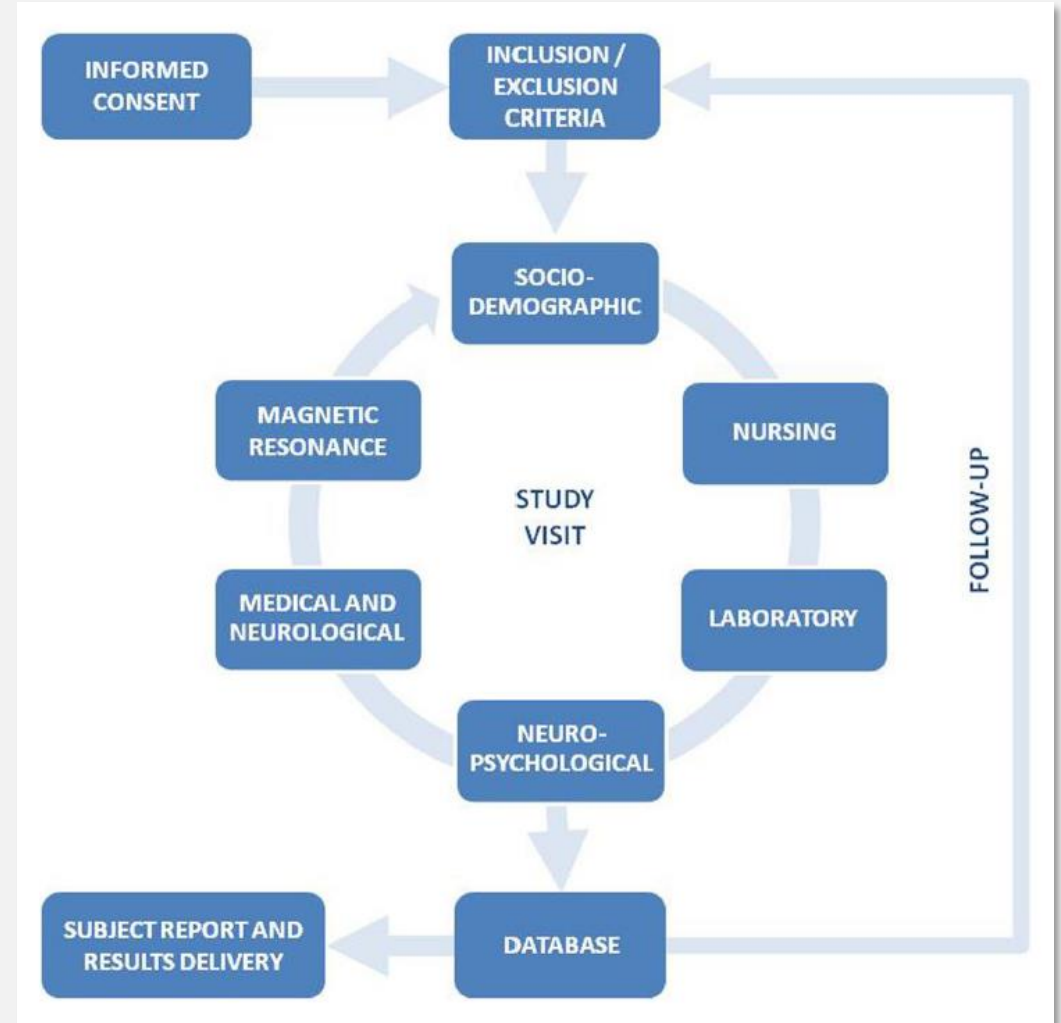
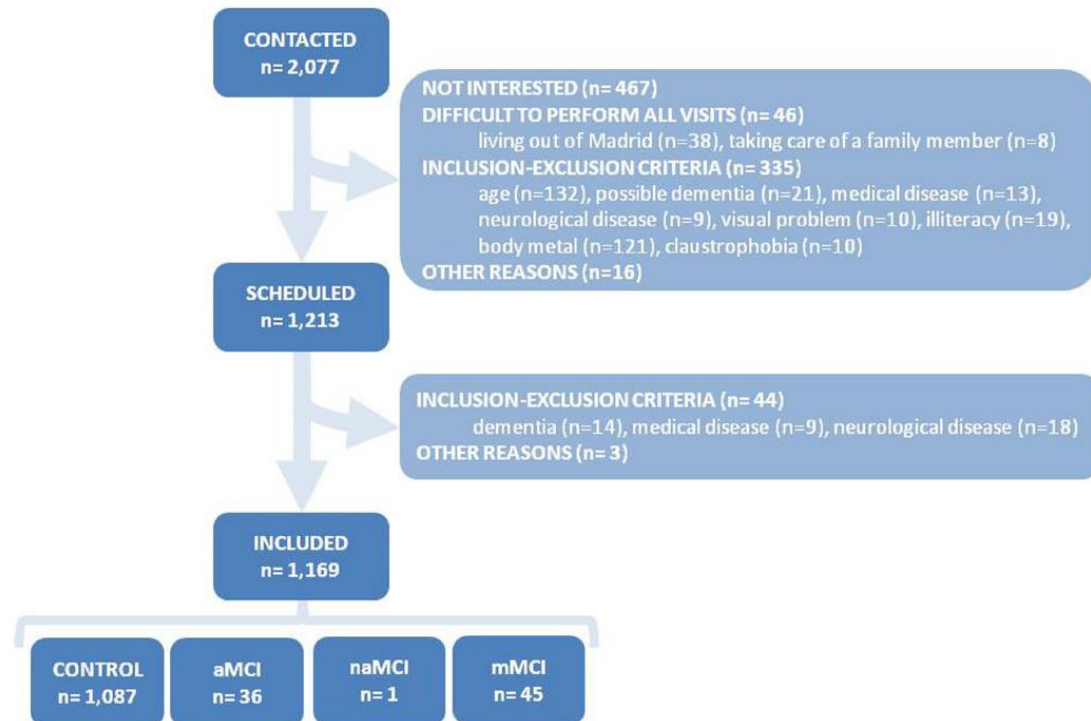




The Vallecas Project: a cohort to identify early markers and mechanisms of Alzheimer's disease

Javier Olazarán^{1*}, Meritxell Valenti², Belén Frades², María Ascensión Zea-Sevilla², Marina Ávila-Villanueva², Miguel Ángel Fernández-Blázquez², Miguel Calero², José Luis Dobato², Juan Antonio Hernández-Tamames³, Beatriz León-Salas², Luis Agüera-Ortiz², Jorge López-Álvarez², Pedro Larrañaga⁴, Concha Bielza⁴, Juan Álvarez-Linera⁵ and Pablo Martínez-Martín⁶

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



El Proyecto Alzheimer Fundación Reina Sofía



El Proyecto Centro Alzheimer: Objetivos

- Crear y mantener una **cohorte de pacientes** con demencia moderada o avanzada en un solo centro, con evaluaciones semestrales, obtención de muestras de sangre, estudios de RM, y donación de tejido cerebral post mortem.
- Contribuir con datos primarios al conocimiento de la evolución de las **fases avanzadas de la demencia**.
- Analizar factores asociados a distintas patologías, y determinantes de **patrones evolutivos diferenciales** (factores de riesgo, comorbilidad, tasa de progresión, cognitivos, funcionales, etc).

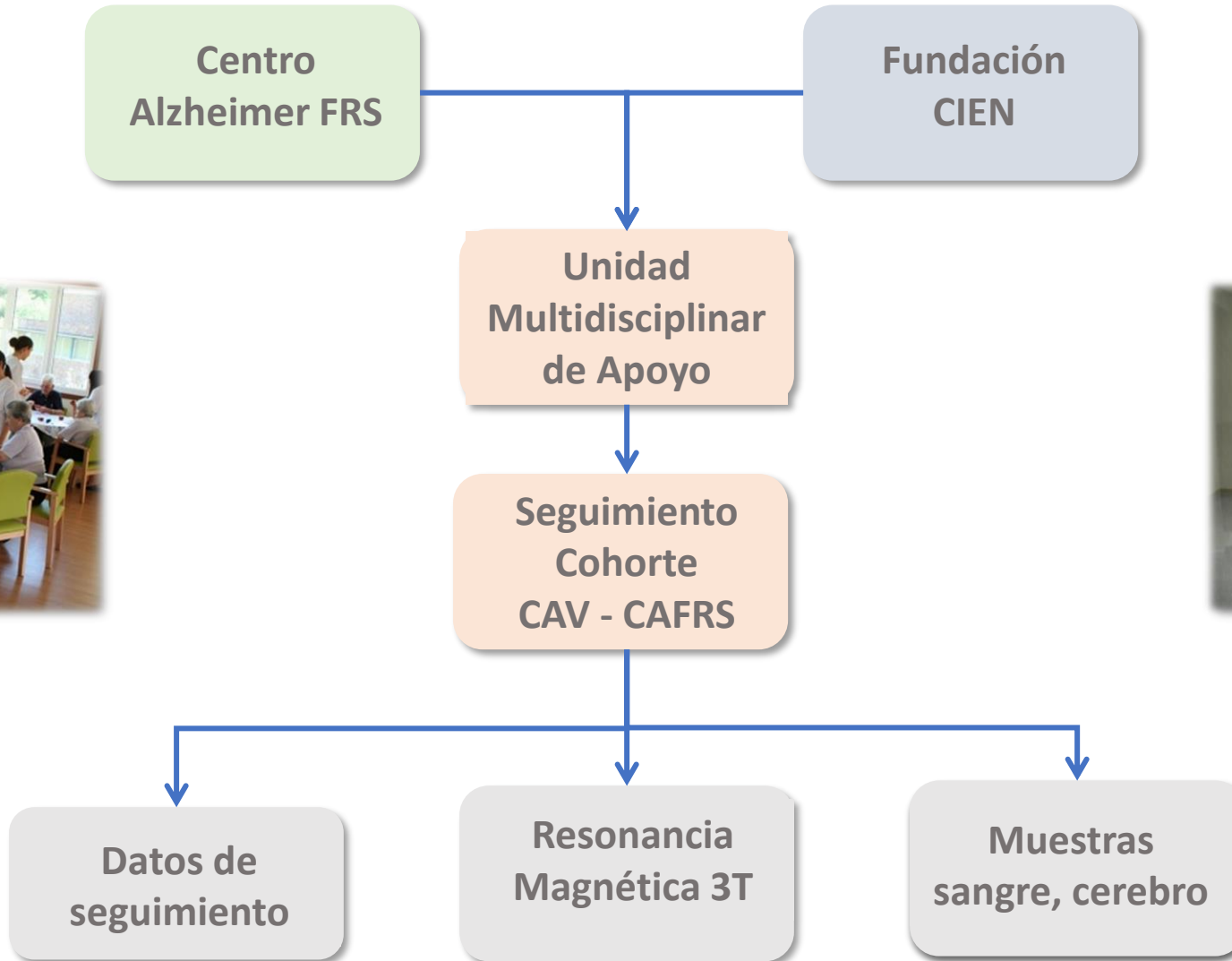


**Comunidad
de Madrid**

CONSEJERÍA DE FAMILIA,
JUVENTUD Y POLÍTICA SOCIAL

Cohorte Alzheimer de Vallecas (CAV – CAFRS)

ISC
Instituto
de Salud
Carlos III



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

^aAlzheimer Disease Research Unit, CIEN Foundation, Carlos III Institute of Health, Alzheimer Center Reina Sofía
 Foundation, Madrid, Spain

^bCIBERSAM, Carlos III Institute of Health, Madrid, Spain

^cCIBERNED, Carlos III Institute of Health, Madrid, Spain

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

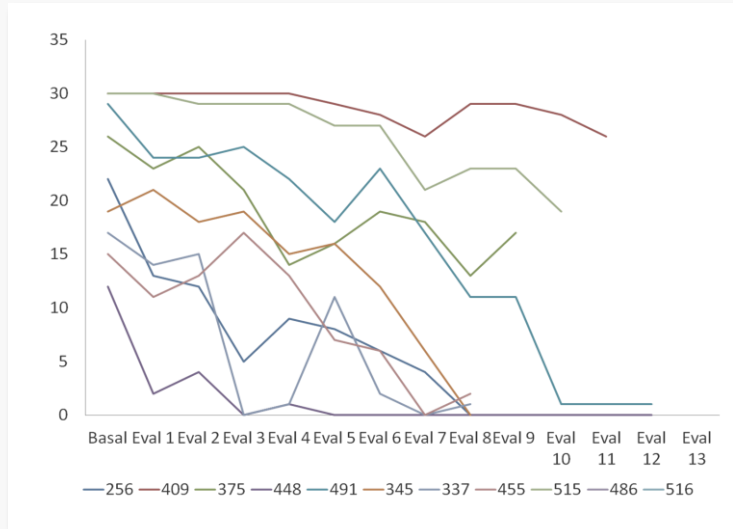
Area	Scale References ²	Objective/Rationale	Observations ¹
Cognition	MMSE	General cognition, universal measurement	B, 6 [17, 18]
	sMMSE	General cognition, advanced dementia	B, 6 [19, 20]
	Animals	Verbal fluency, frontotemporal functions	B, 6 [22, 23]
	SIB	General cognition, avoid floor effect	B, 6 [46, 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]
	SCOPA-motor	Parkinsonism, predictor of gait dysfunction and functional dependence	B, 6 [31, 32]
QoL	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]
	QUALID	QoL in advanced dementia	B, 6, NH [66, 67]
	QoL- AD	QoL as perceived by patient and caregiver	B, 6, DC [41, 42]

¹B: 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.

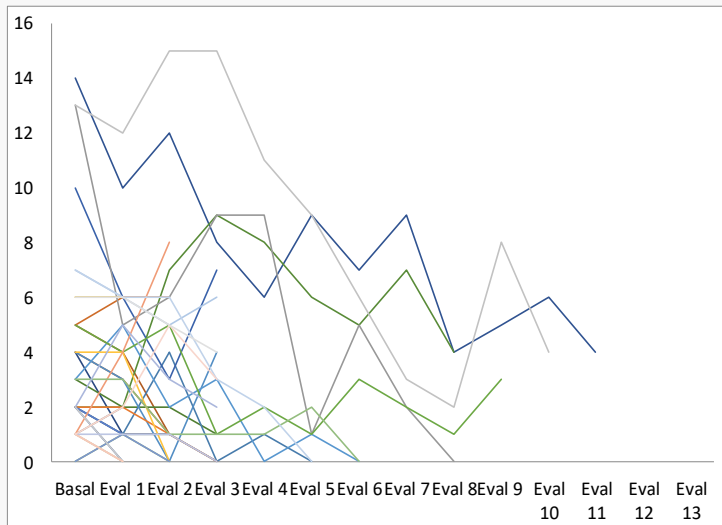
²The original reference appears first, followed by reference of the most relevant validation studies in Spanish samples.

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.

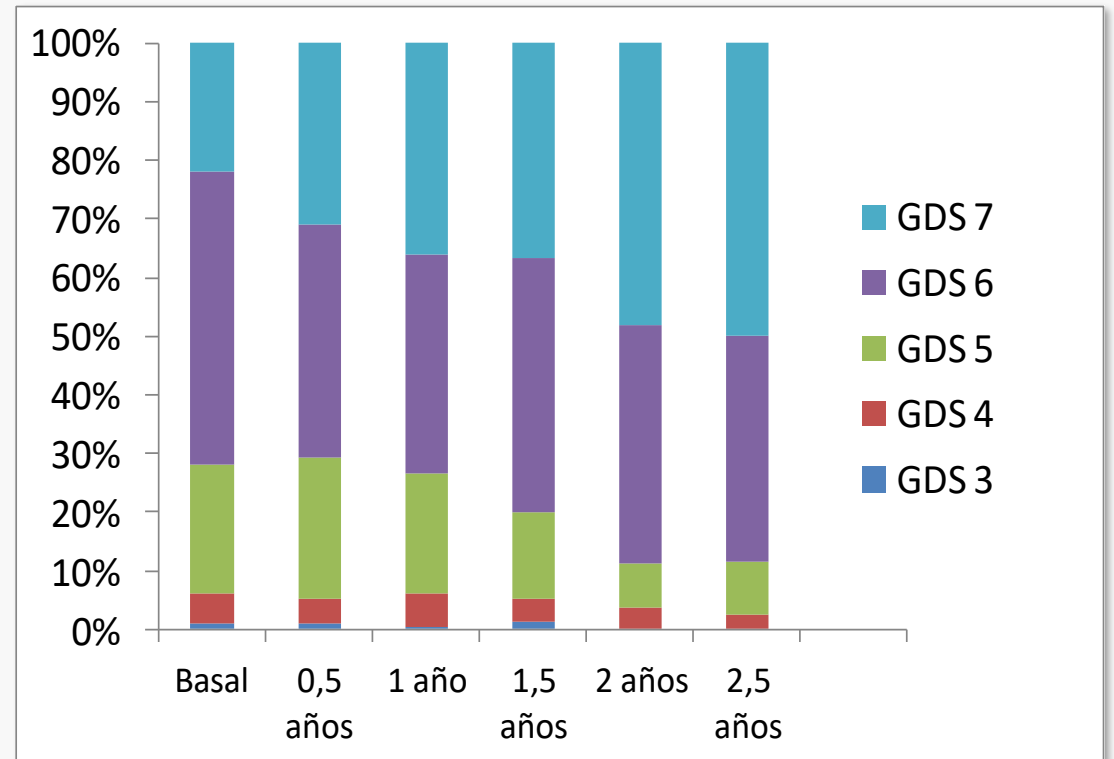
Severe Mini-mental State Examination



Semantic fluency: animals



Global Dementia Scale





ELSEVIER

Contents lists available at [SciVerse ScienceDirect](#)

Archives of Gerontology and Geriatrics



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

A Novel Rating Scale for the Measurement of

Quality of
Alzheimer

Beatriz León-Salas,
José Luis Domercq,
Pablo Martínez-Martín

A

J Neurol

DOI 10.1007/s00415-015-7692-9

ORIGINAL COMMUNICATION

Luis F. Agüera-Ortiz,
Isabel Cruz-Orduña

**Validation of the SIB-s
dementia: a new rating scale for
dementia**

Sloane Heller · C
Laura Carrasco
Pablo Martínez-Martín

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

Pat
Mic
Der



ELSF

Alzheimer's & Dementia ■ (2015) 1-9

Alzheimer's
&
Dementia

Current Topics in Research

Javier
Inmac
Alber

Cerebral Microbleeds in Clinical and Pathological

Inmaculada Boyano, MD, PhD¹,
Jorge López-Alvarez, MD^{2,3}, Carolin
Emma Osa-Ruiz, BSc², Irene Rodríguez
Almudena Pérez, BSc², Eva Alfayate
Laura Fernández, PsyD², Luis Agüer
Alberto Rábano, MD, PhD², and Javi

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

1

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,c,*}

^aNeurology Service, University Hospital Gregorio Marañón, Madrid, Spain

^bPsychiatry Department, University Hospital 12 de Octubre, Madrid, Spain

^cAlzheimer's Center Reina Sofía Foundation - CIEN Foundation and CIBERNED, Carlos III Institute of Health, Madrid, Spain

^dCIBERSAM, Madrid, Spain

^eMemory Disorders Unit, HM Hospitals, Madrid, Spain

Algunas cifras de la CAV-CAFRS...

540 pacientes con demencia incluidos en la cohorte.

3738 evaluaciones realizadas por la UMA.

68% de pacientes con RM (3T).

3058 muestras de sangre (**52812** alícuotas de hemoderivados).

168 cerebros extraídos (**50%** con RM seriadas previas).

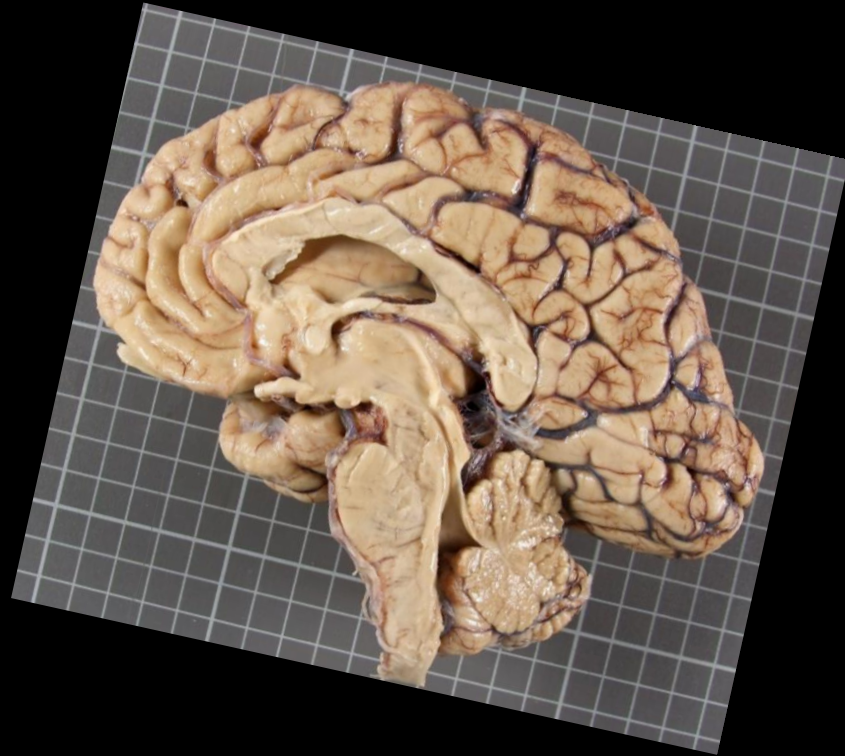


26 exitus (17%) en la primera ola.

64 pacientes con COVID-19 sintomático o asintomático (cohorte actual, 43%).



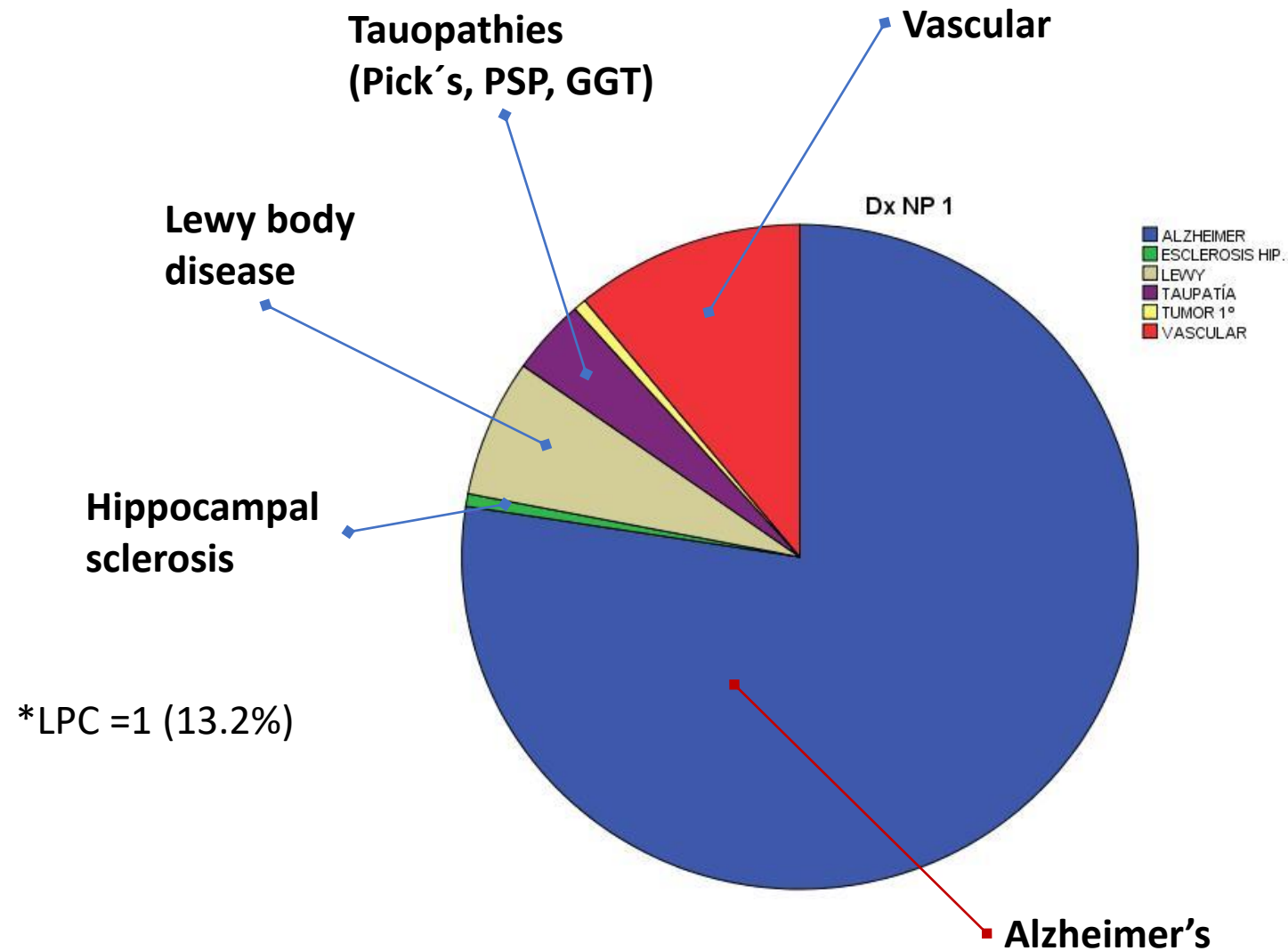
3T magnetic resonance
post mortem pre-extraction

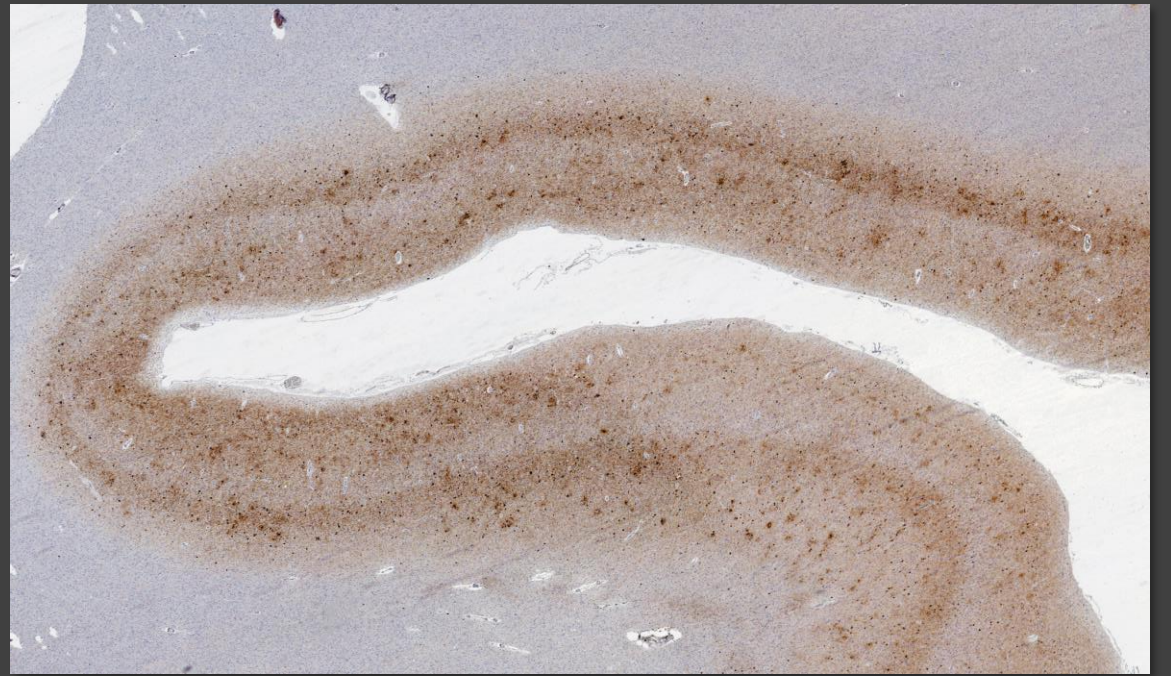
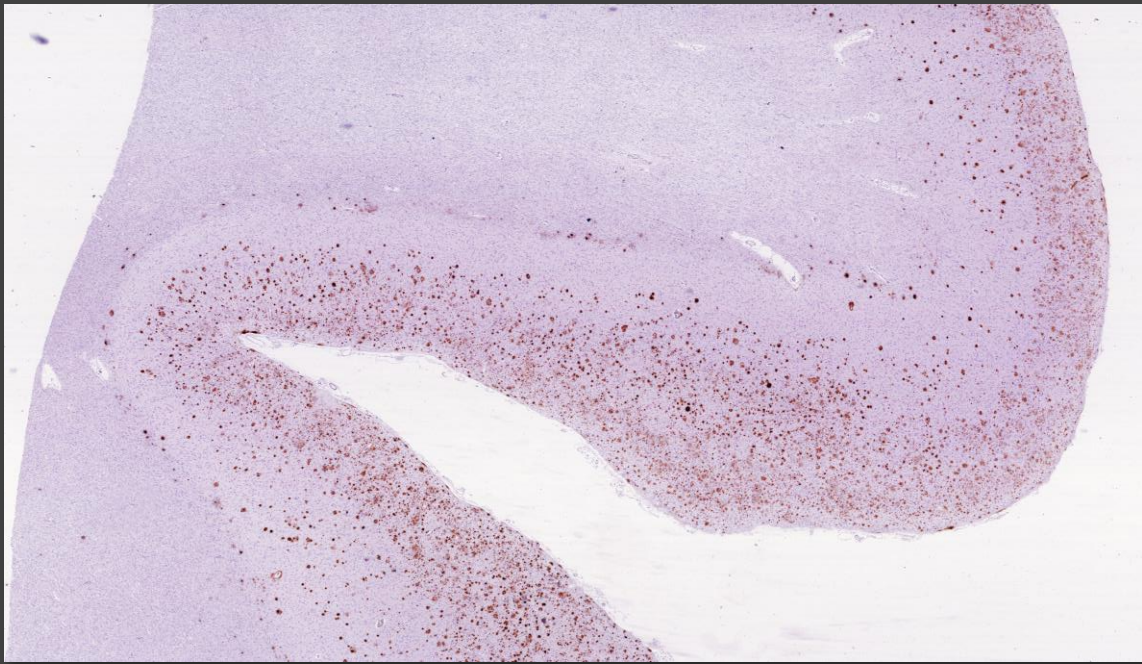


Macroscopy of fixed brain

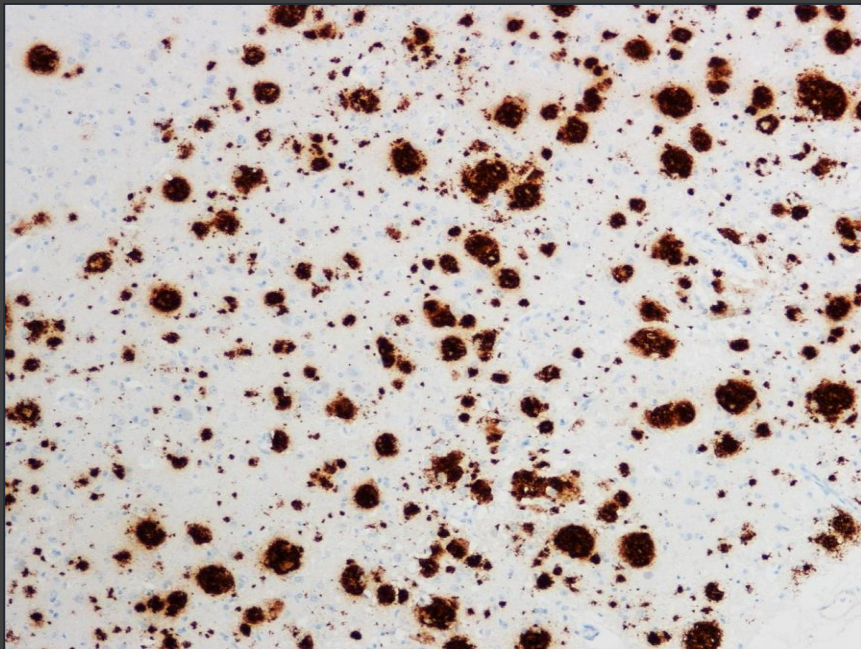
N	167
Sex	79% female
T in CAFRS (mths)	52.9 (38.6)
Age at onset	75.4 (7.3)
Age at death	87.2 (6.5)
Survival time	11.9 (4.4)
PMI (hrs.)	4.5 (2.1)
APOE e4	45.2%
High ADNC	75.8%
High vascular path.	54.5%
Lewy path. (LPC>1)*	37.8%
LATE (HS)	71.2% (45.2%)
ARTAG	52.7%
AGD	12%

Main neuropathological diagnosis

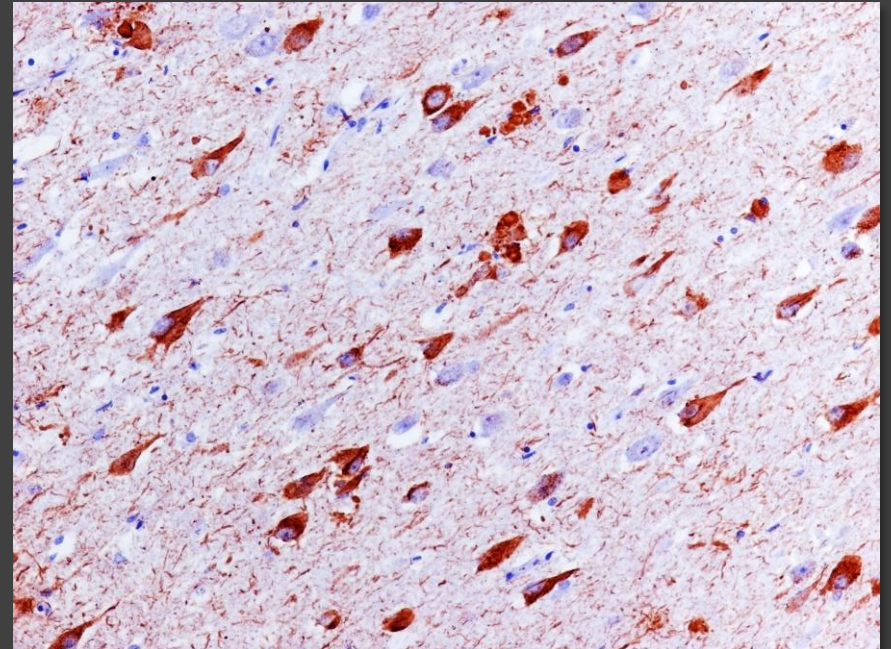




A β



Tau



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

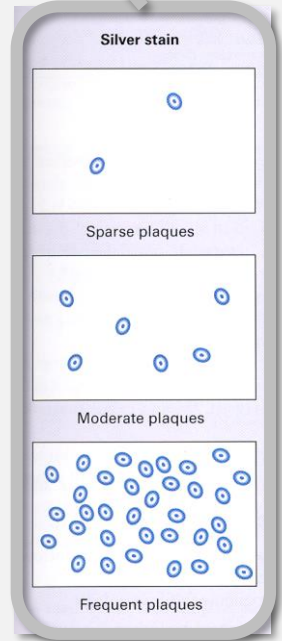
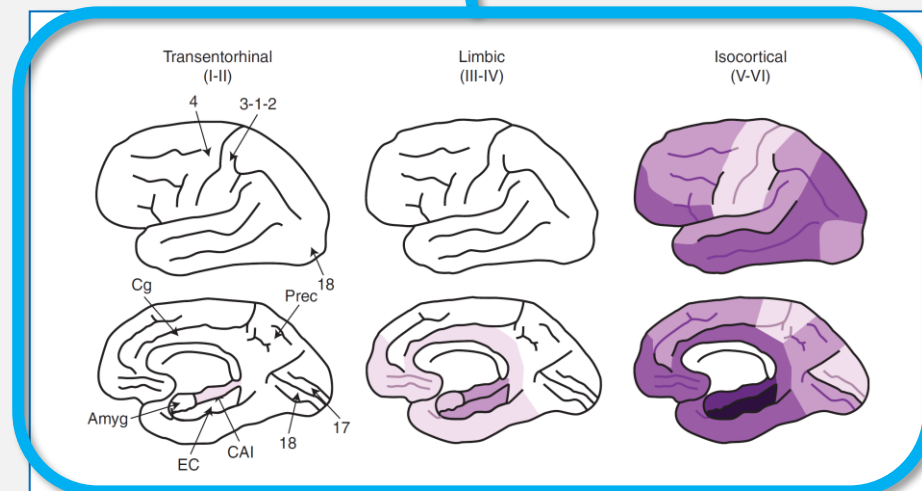
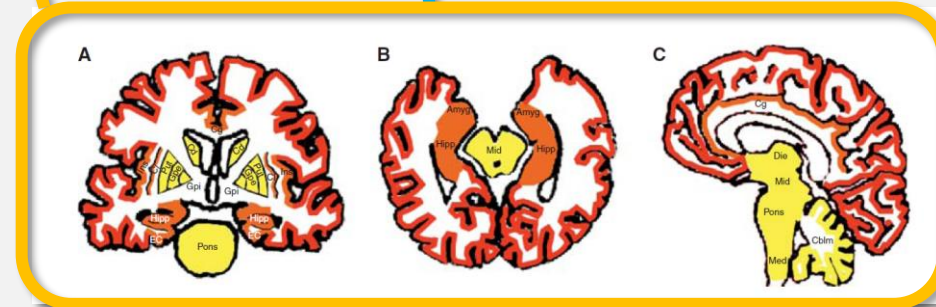
Thomas J. Montine · Creighton H. Phelps · Thomas G. Beach · Eileen H. Bigio · Nigel J. Cairns · Dennis W. Dickson · Charles Duyckaerts · Matthew P. Frosch · Eliezer Masliah · Suzanne S. Mirra · Peter T. Nelson · Julie A. Schneider · Dietmar Rudolf Thal · John Q. Trojanowski · Harry V. Vinters · Bradley 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”	NERAD 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
	0 or 1	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**

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. Bainⁿ, 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. Brenowitz¹, Rebecca A. Hubbard², C. Dirk Keene³, Stephen E. Hawes⁴, W.T. Longstreth Jr^{1,5}, Randy L. Woltjer⁶, and Walter A. Kukull¹

¹National 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. Robinson¹, Maria M. Corrada², Gabor G. Kovacs^{1,3}, Myrna Dominique¹, Carrie Caswell⁴, Sharon X. Xie⁴, Virginia M.-Y. Lee¹, Claudia H. Kawas⁵, and John Q. Trojanowski¹



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

Salvatore Spina^{1,†}, Renaud La Joie^{1,†}, Cathrine Petersen¹, Amber L. Nolan¹, Deion Cuevas¹, Celica Cosme¹, Mackenzie Hepker¹, Ji-Hye Hwang¹, Zachary A. Miller¹, Eric J. Huang², Anna M. Karydas¹, Harli Grant¹, Adam L. Boxer¹, Maria Luisa Gorno-Tempini¹, Howard J. Rosen¹, Joel H. Kramer¹, Bruce L. Miller¹, William W. Seeley^{1,2}, Gil D. Rabinovici^{1,3} and Lea T. Grinberg^{1,2}

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

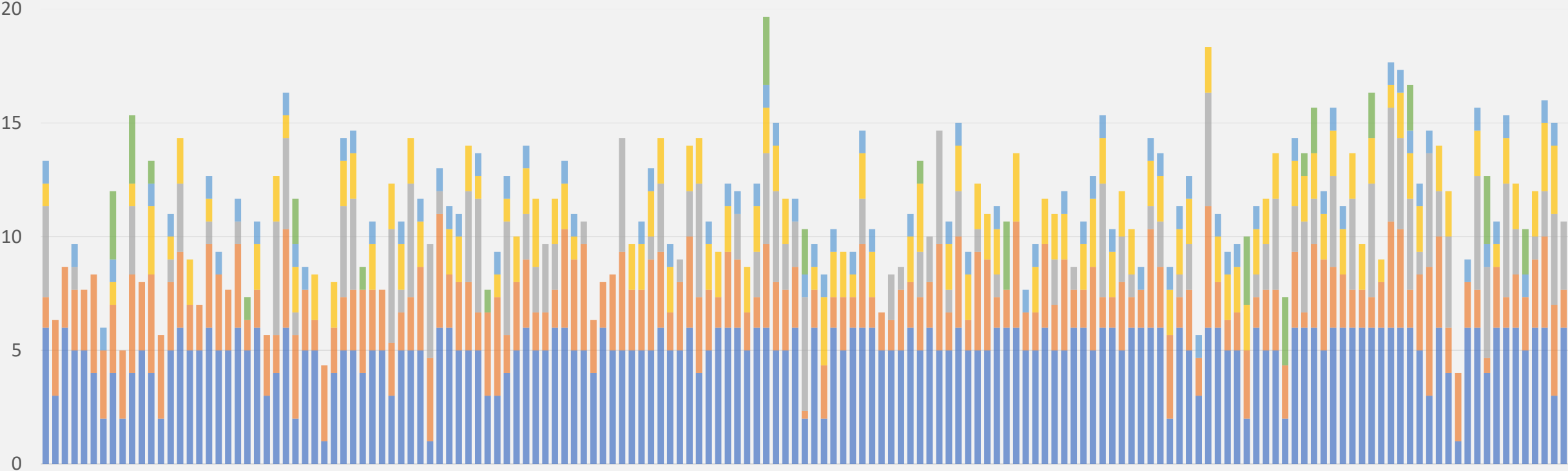
John L. Robinson^{1,2,3,4}, Edward B. Lee^{1,2,3,4}, Sharon X. Xie^{1,2,3,4,5}, Lior Rennert^{1,2,3,4,5}, EunRan Suh^{1,2,3,4}, Colin Bredenberg^{1,2,3,4}, Carrie Caswell^{1,2,3,4,5}, Viviana M. Van Deerlin^{1,2,3,4}, Ning Yan^{1,2,3,4,6}, Ahmed Yousef^{1,2,3,4}, Howard I. Hurtig^{1,2,3,7}, Andrew Siderowf^{1,2,3,7}, Murray Grossman^{1,2,3,7,8}, Corey T. McMillan^{7,8}, Bruce Miller⁹, 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^{1,3}, Johannes Bretschneider¹⁴, Virginia M.-Y. Lee^{1,2,3,4,7} and John Q. Trojanowski^{1,2,3,4,7}

The problem of pathological heterogeneity and comorbidity in dementia

- Alzheimer's disease neuropathology change
- Cerebrovascular pathology
- Lewy type pathology
- Limbic-predominant age-related TDP-43 encephalopathy (LATE)
- Aging-related tau astrogliopathy (ARTAG)
- Argyrophilic grain disease
- Other pathologies



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)

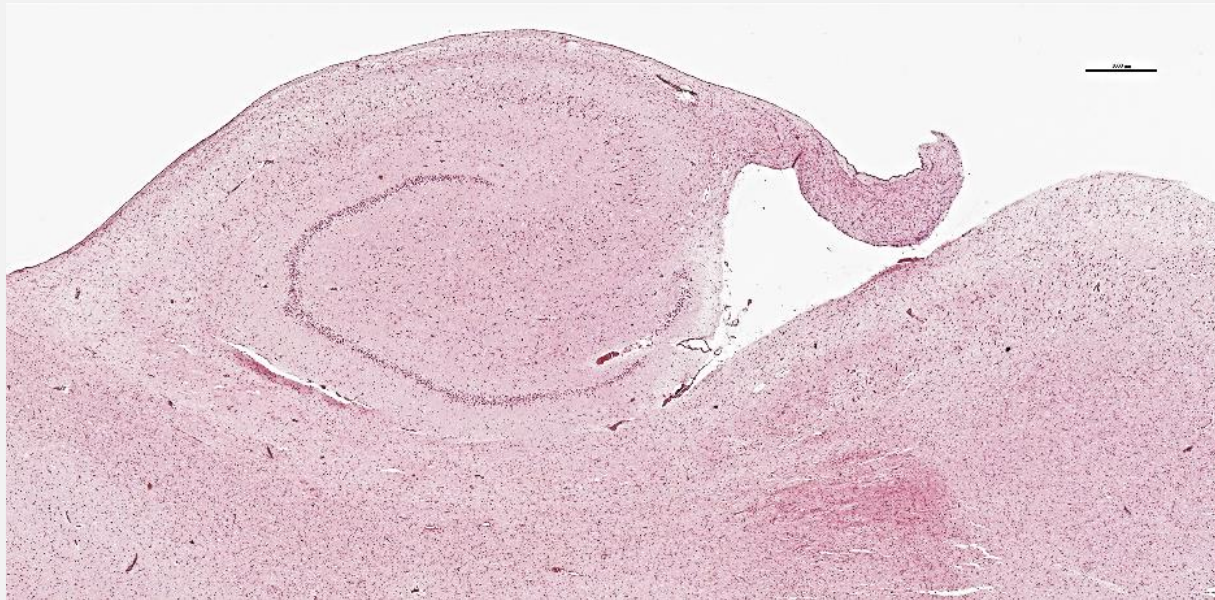


Hippocampal sclerosis



TDP-43



H/E



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

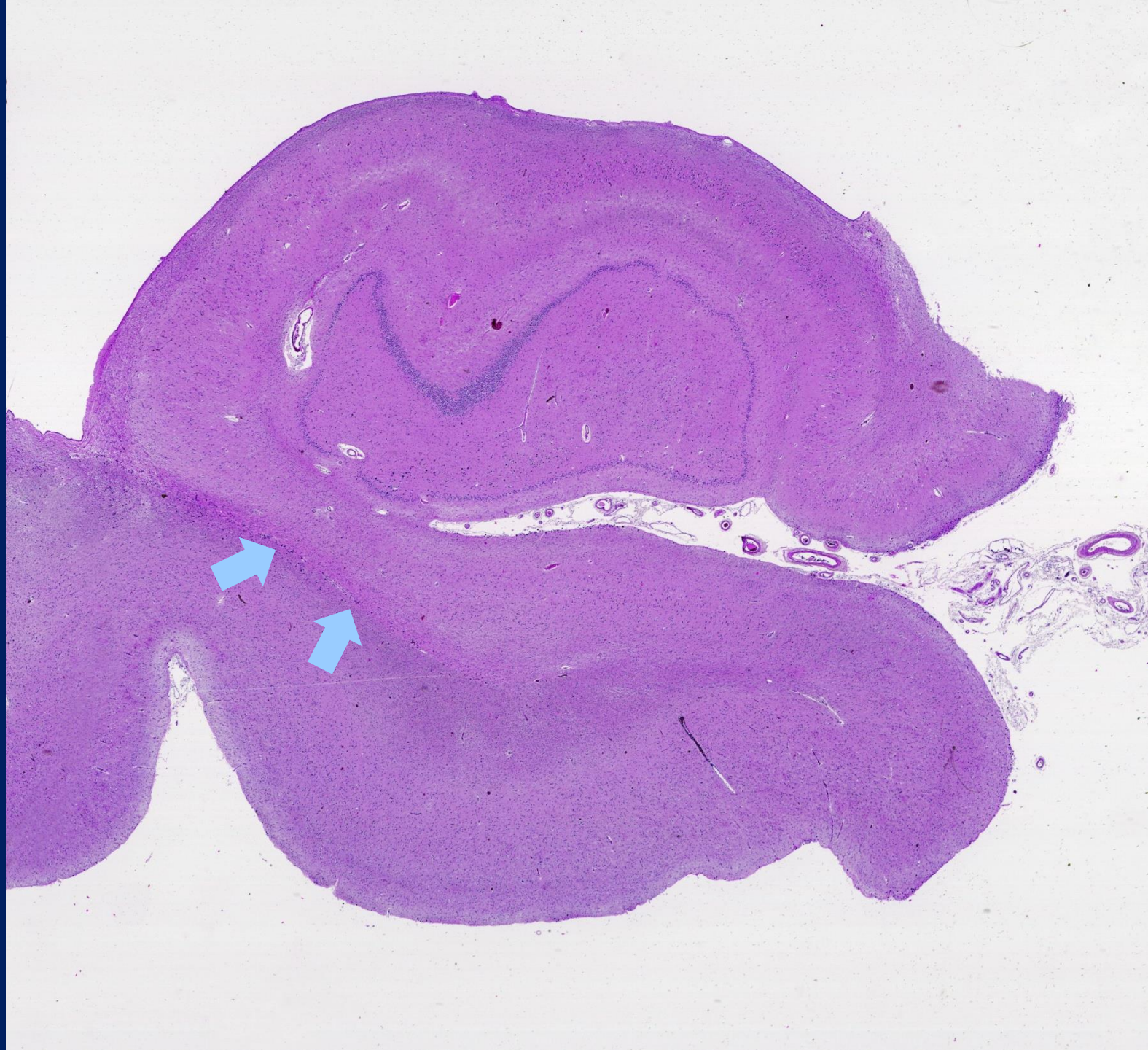
Peter T. Nelson,¹  Dennis W. Dickson,² John Q. Trojanowski,³ Clifford R. Jack Jr.,⁴ Patricia A. Boyle,⁵ Konstantinos Arfanakis,^{5,6} Rosa Rademakers,² Irina Alafuzoff,⁷ Johannes Attems,⁸ Carol Brayne,⁹ Ian T.S. Coyle-Gilchrist,⁹ Helena C. Chui,¹⁰ David W. Fardo,¹ Margaret E. Flanagan,¹¹ Glenda Halliday,¹² 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 Makkejad,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 Yu⁵ and Julie A. Schneider⁵

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

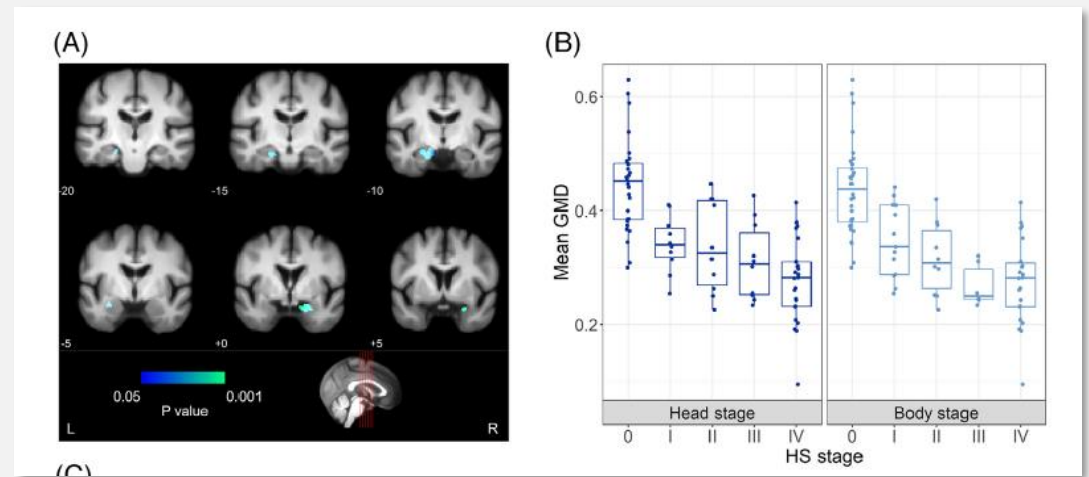
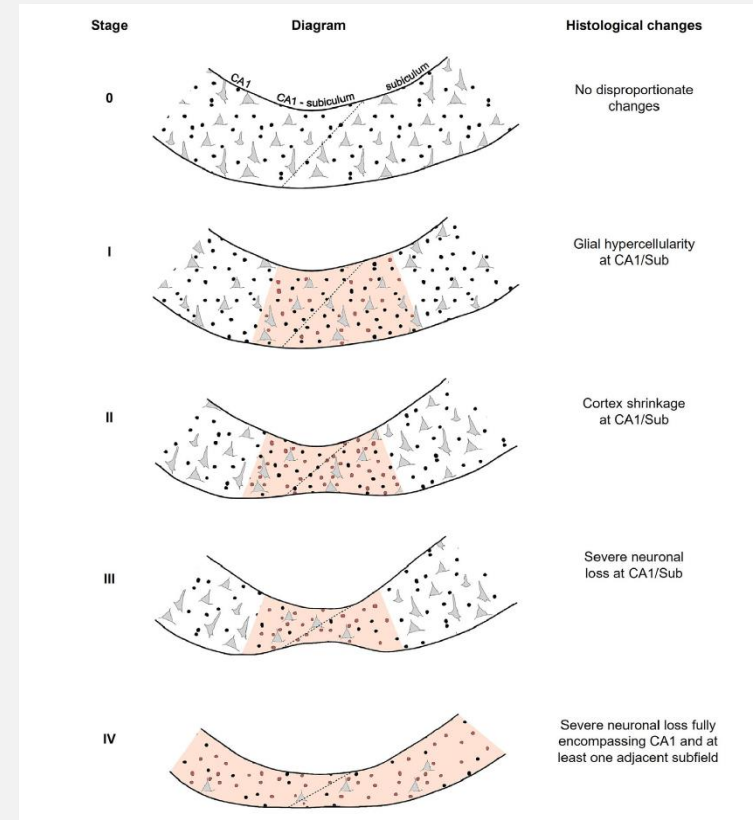
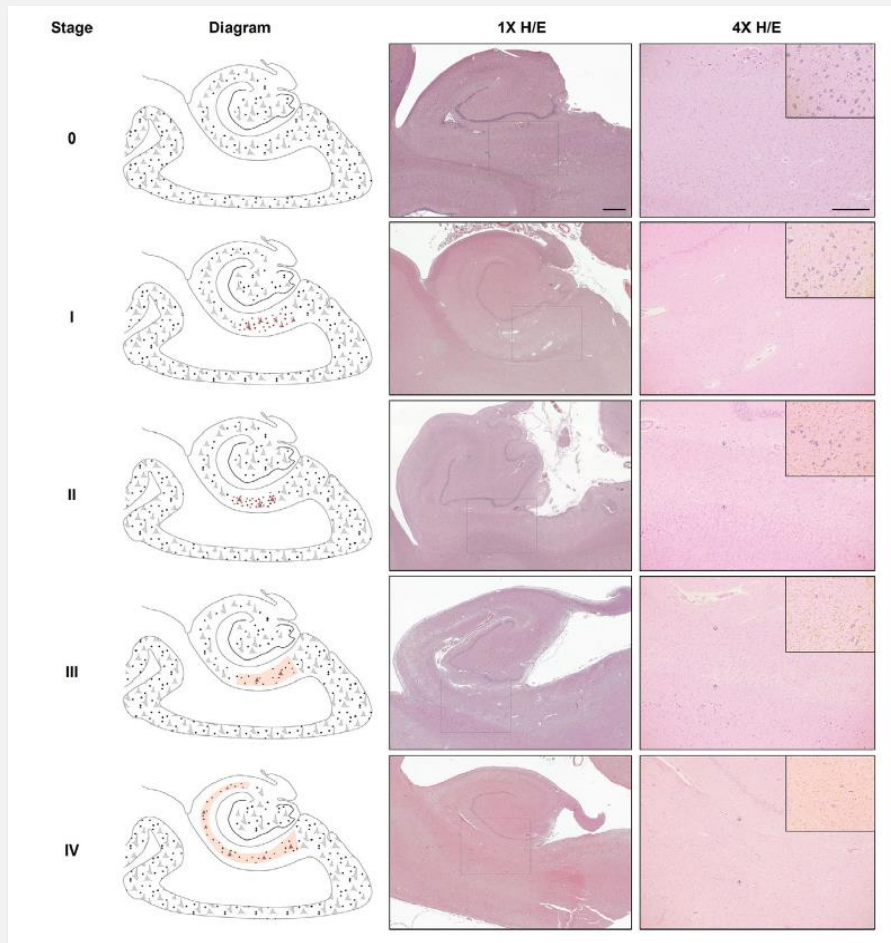
*-Any TDP-43 proteinopathy is seen in that anatomic region



RESEARCH ARTICLE

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

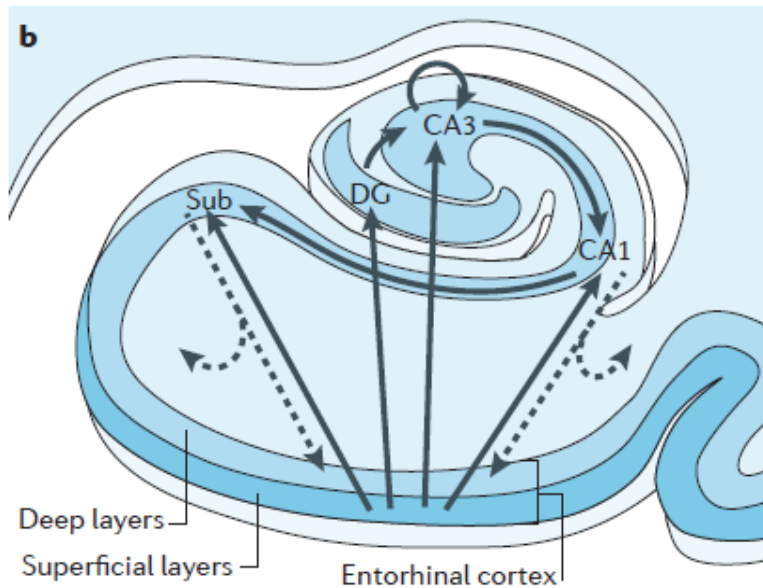
Diana Ortega-Cruz^{1,2} | Alicia Uceda-Heras^{2,3} | Juan Eugenio Iglesias^{4,5} |
María Ascensión Zea-Sevilla² | Bryan Strange^{1,2} | Alberto Rabano²



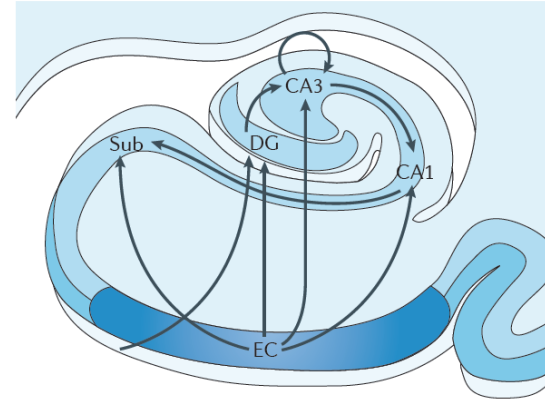
A pathophysiological framework of hippocampal dysfunction in ageing and disease

Scott A. Small*, Scott A. Schobel[‡], Richard B. Buxton[§], Menno P. Witter^{||}
and Carol A. Barnes[¶]

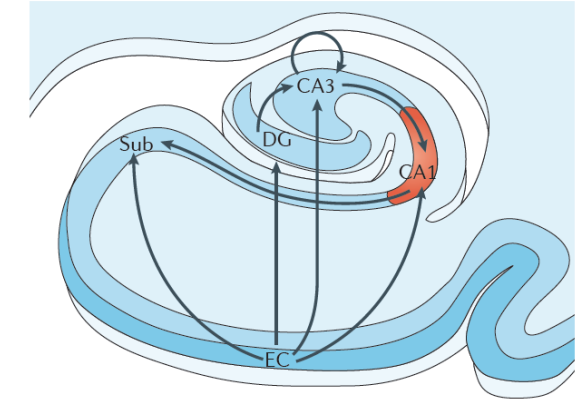
VOLUME 12 | OCTOBER 2011 | 585



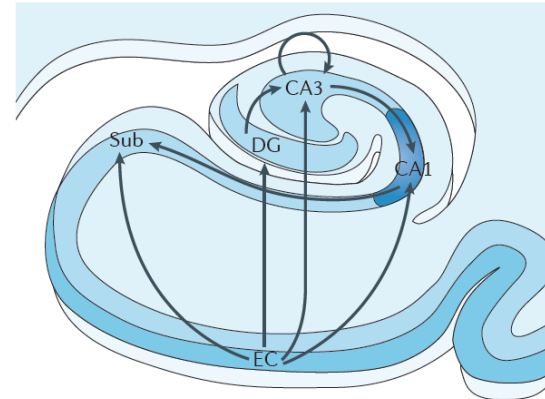
a Alzheimer's disease



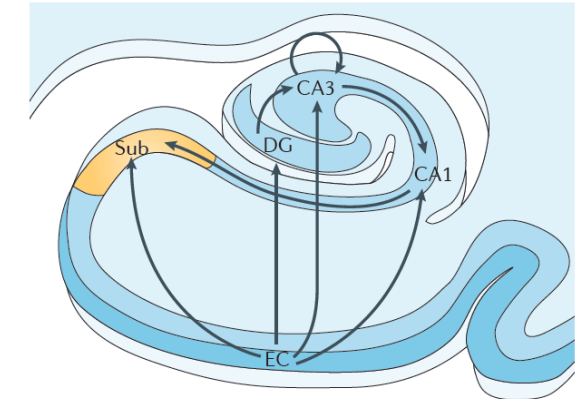
b Schizophrenia



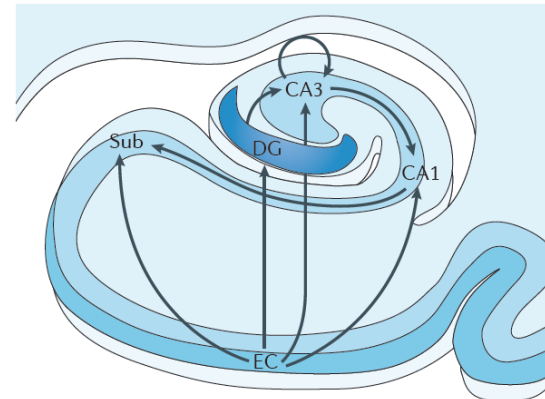
Vascular disease



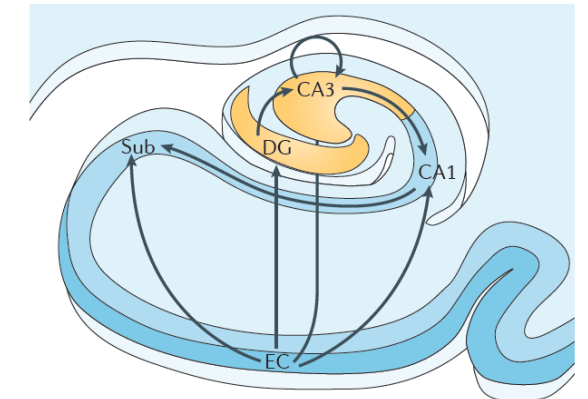
Depression

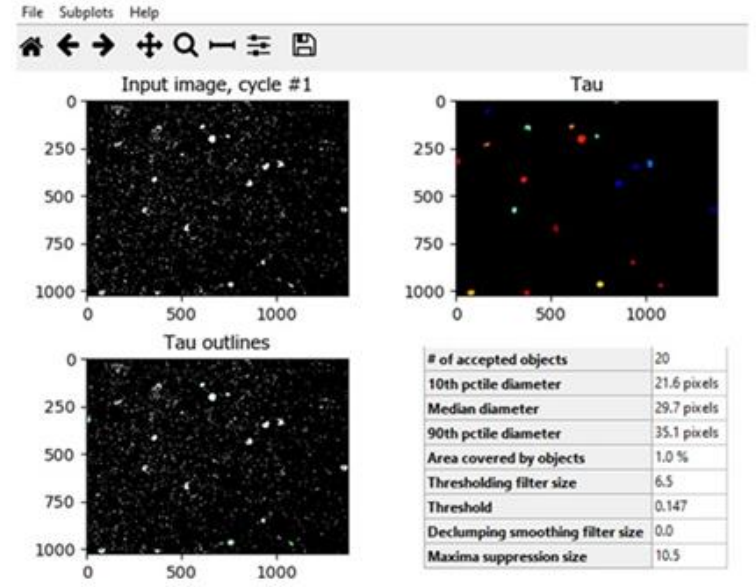
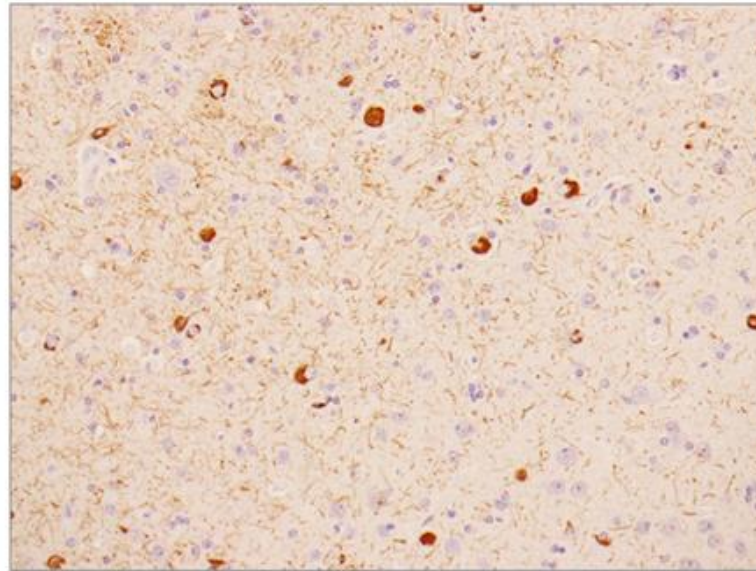


Ageing

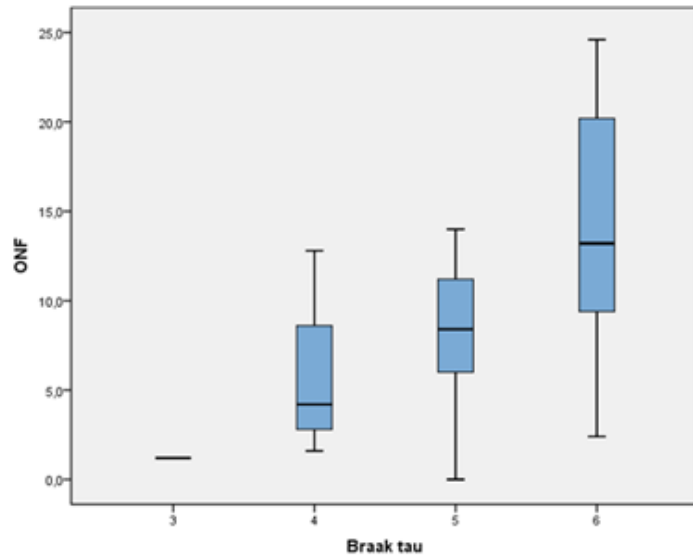


PTSD

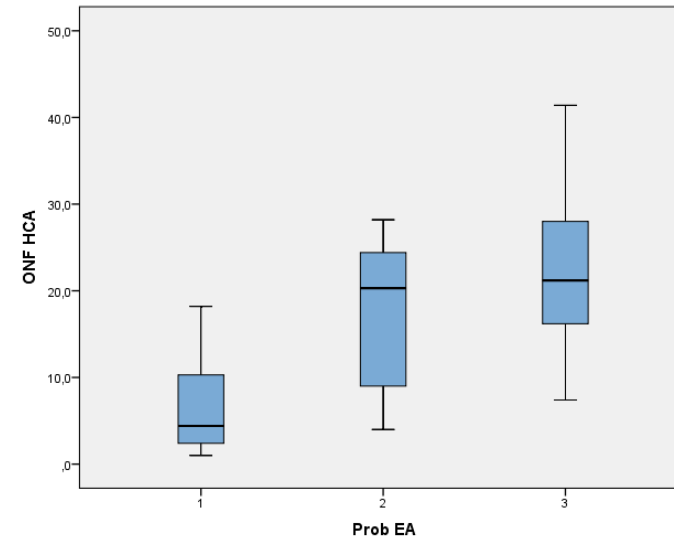




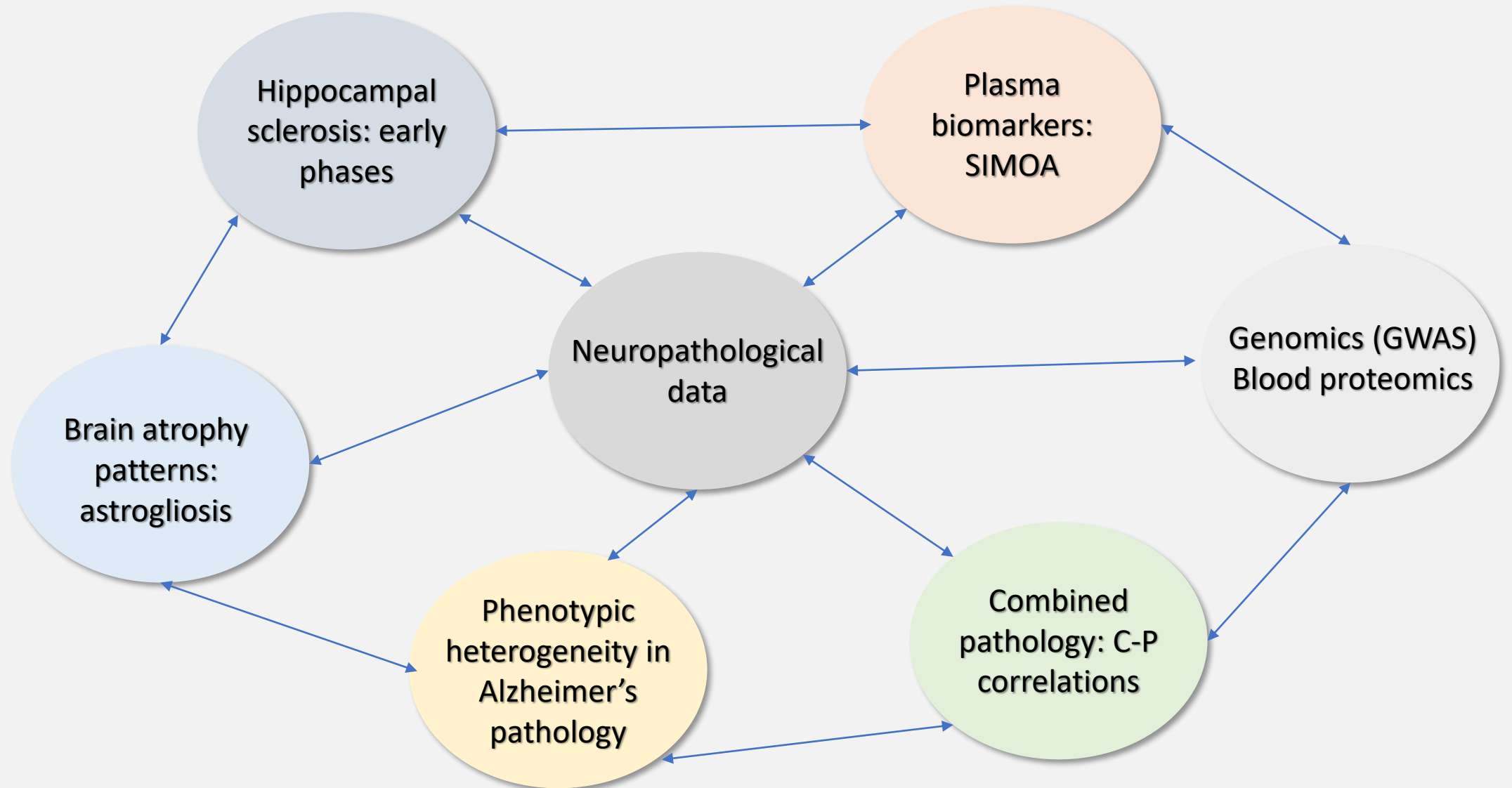
Córtex temporal lateral



Córtex hipocampo



Neuropathological data of the Vallecas Alzheimer's Study: research lines at the CIEN Foundation





29/06/2021

El Dr. Alberto Rábano habla del enigma del Alzheimer en este reportaje de Materia Ciencia de El País

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