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ISTAART

alzheimer's association

Atypical Alzheimer's Disease: *2022 in review*

Dr Maura Malpetti

Race Against Dementia & Alzheimer's Research UK Fellow

Department of Clinical Neurosciences
Cambridge Centres for FTD and Parkinson-Plus

@AtypicalPIA

18th January 2023

Disclosure and policies

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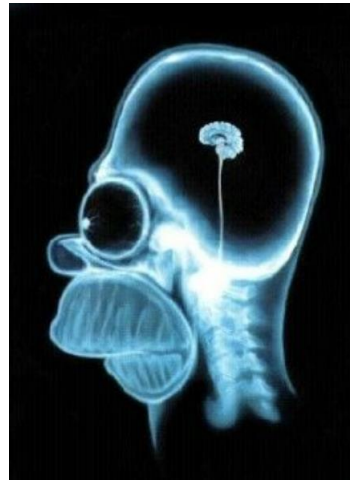
Nothing to disclose.

The information included in this presentation may be shared on other platforms.

RACE AGAINST DEMENTIA

Alzheimer's Research UK



Biased toward biomarkers!

Atypical AD: initial dominant difficulties

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A MEMORY

Typical AD

B LANGUAGE

- Impaired single-word retrieval, sentence repetition, phonologic errors
- Spared single-word comprehension, motor speech

C VISUAL/SPATIAL

- Space and/or object perception difficulties, simultanagnosia, face perception and reading difficulties….

D EXECUTIVE

- Predominant decline in core executive cognitive function

E MOTOR

- Parkinsonism, Myoclonus, Apraxia…
- Executive, visuospatial, and language dysfunction

F BEHAVIOURAL

- Deterioration of behaviour ~bvFTD
- Executive deficits with relative sparing of memory and visuospatial functions

Early onset
< 65 yo

Atypical AD: clinical diagnosis

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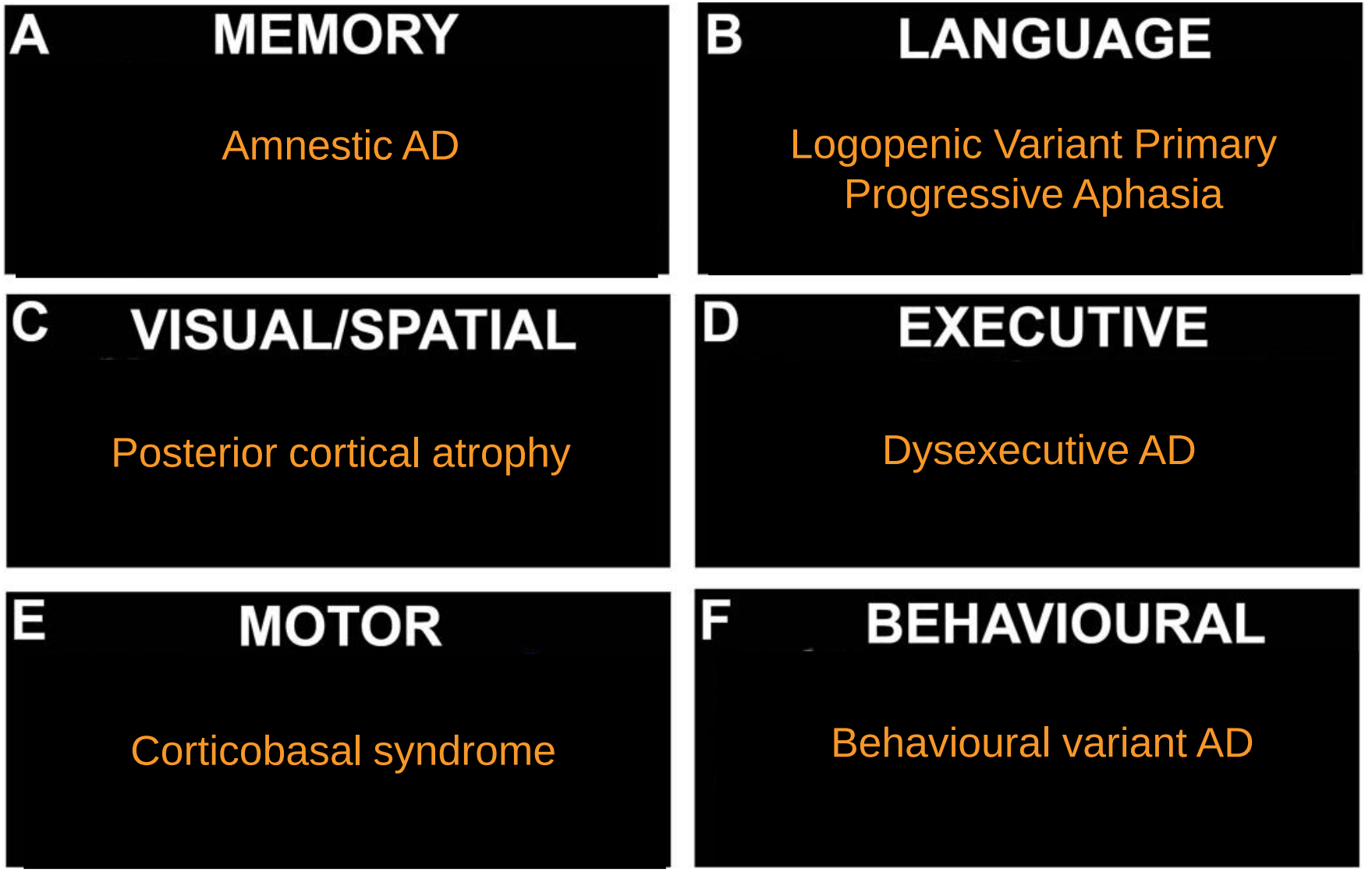

Early onset
< 65 yo

Atypical AD: clinical (mis)diagnosis

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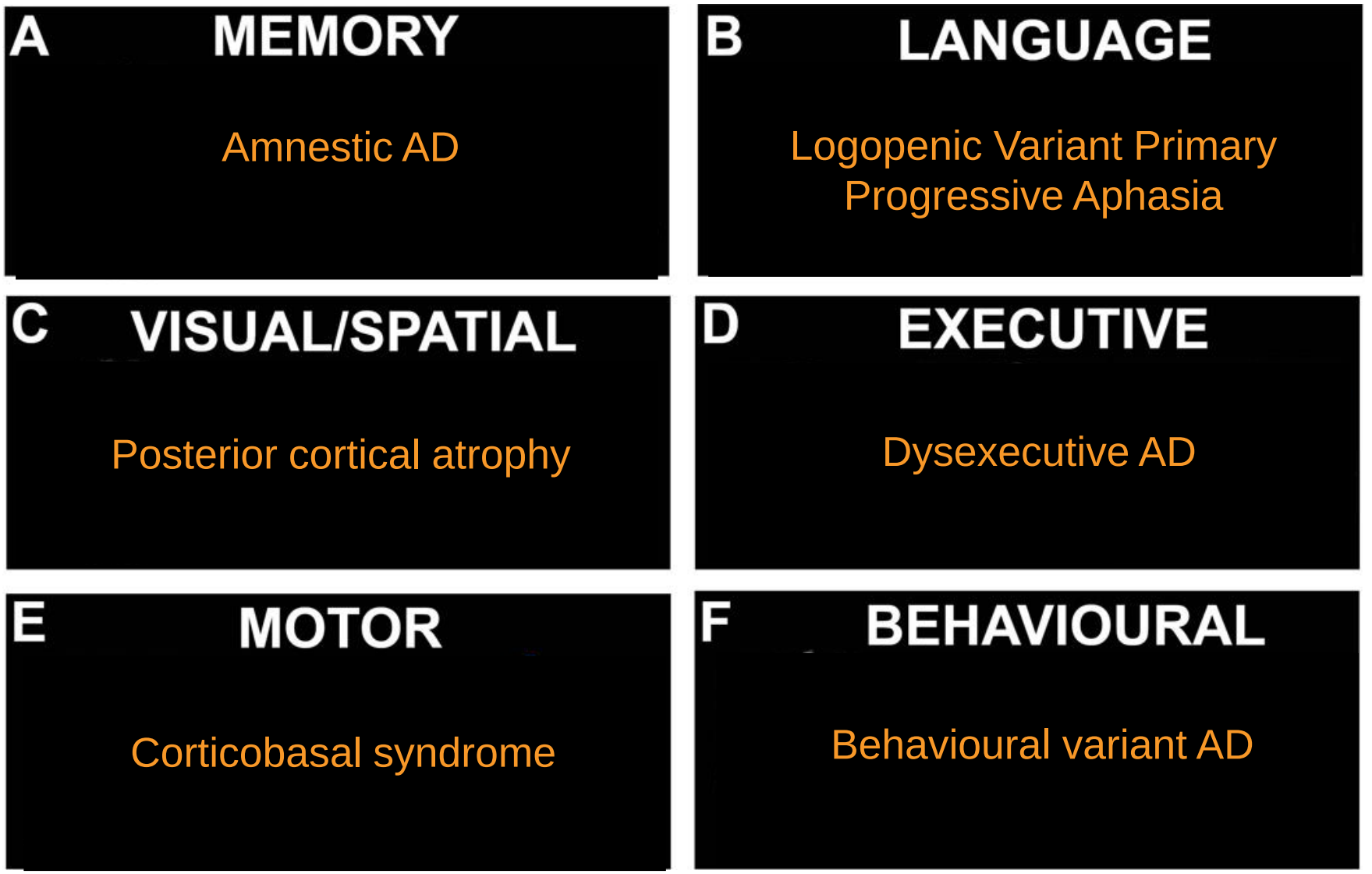

Other PPA, stroke…

Dementia with Lewy Body, or ocular conditions…

Vascular dementia, psychiatric diagnoses…

CBS due to CBD, PD…

bvFTD, psychiatric diagnoses…

Graff-Radford et al Lancet Neurol 2021

Atypical AD: localised brain changes

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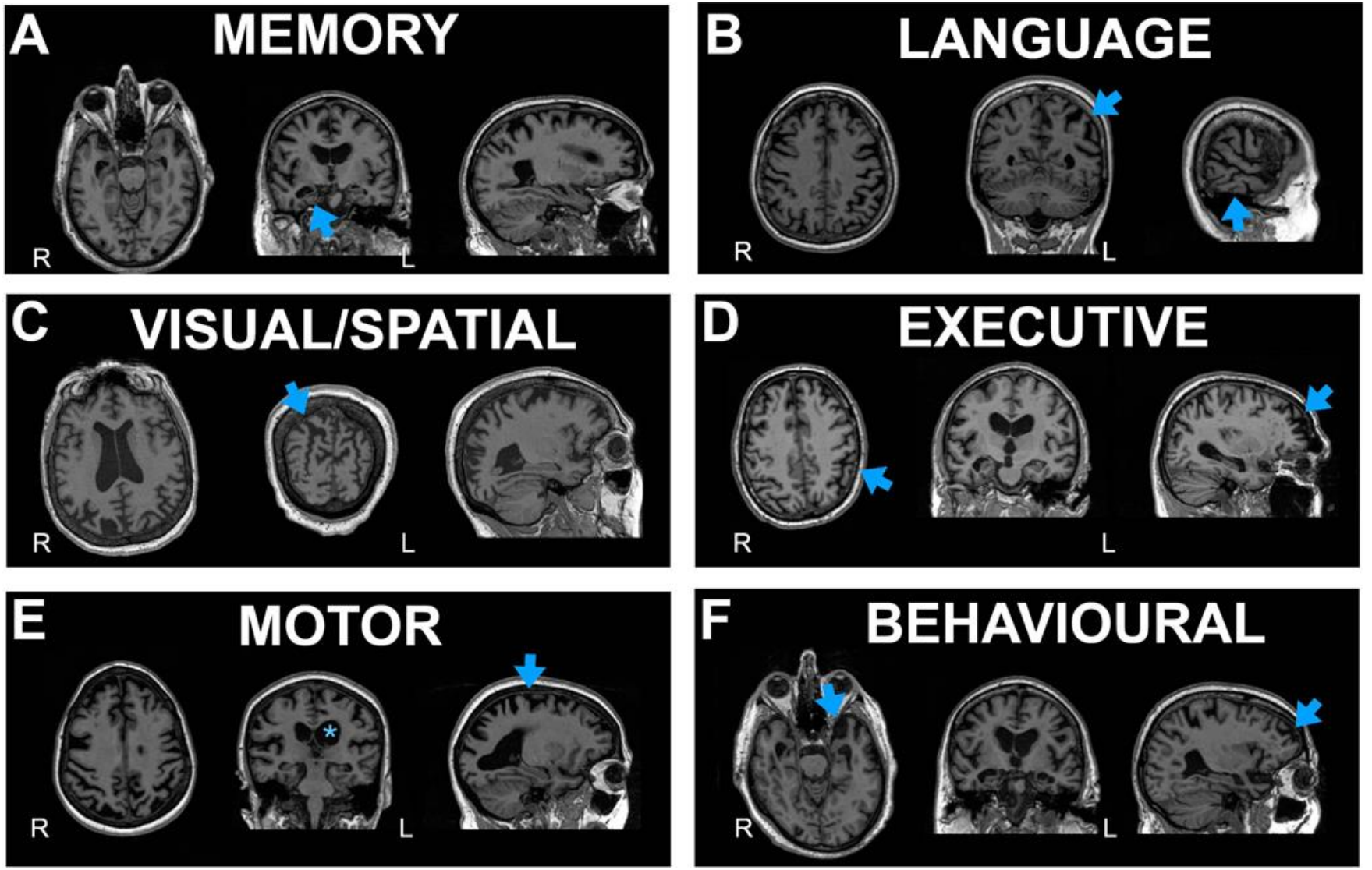

Similar patterns with Tau PET and FDG PET

Graff-Radford et al Lancet Neurol 2021

What's new?

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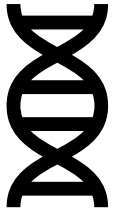
BIOMARKERS

Diagnosis
Prognosis
Tau spreading

GENETICS



Influencing factors
Risk factors

PATHOLOGY

Regional vulnerability
Clinico-path correlations

APOLOGIES: too many good discoveries and results in 2022 to be discussed in 30 minutes!

What's new?

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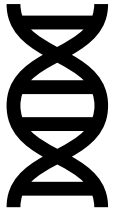
BIOMARKERS

Diagnosis
Prognosis
Tau spreading

GENETICS



Influencing factors
Risk factors

PATHOLOGY

Regional vulnerability
Clinico-path correlations

Biomarkers: what's new?

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RESEARCH ARTICLE

Investigating Heterogeneity and Neuroanatomic Correlates of Longitudinal Clinical Decline in Atypical Alzheimer Disease

Jennifer L. Whitwell, PhD, Peter R. Martin, MS, Jonathan Graff-Radford, MD, Mary M. Machulda, PhD, Irene Sintini, PhD, Marina Buciuc, MD, Matthew L. Senjem, MS, Christopher G. Schwarz, PhD, Hugo Botha, MD, Minerva M. Carrasquillo, PhD, Nilufer Ertekin-Taner, PhD, Val J. Lowe, MD, Clifford R. Jack, MD, and Keith A. Josephs, MD, MST, MSc

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Neurology® 2022;98:e2436-e2445. doi:10.1212/WNL.0000000000200336

Journal of Neurology (2022) 269:4110–4128
https://doi.org/10.1007/s00415-022-11025-x

ORIGINAL COMMUNICATION

Phenotypic subtypes of progressive dysexecutive syndrome due to Alzheimer's disease: a series of clinical cases

Nick Corriveau-Lecavalier[1] · Mary M. Machulda[2] · Hugo Botha[1] · Jonathan Graff-Radford[1] · David S. Knopman[1] · Val J. Lowe[3] · Julie A. Fields[2] · Nikki H. Stricker[2] · Bradley F. Boeve[1] · Clifford R. Jack Jr[3] · Ronald C. Petersen[1] · David T. Jones[1,3]

Journal of Alzheimer's Disease
DOI 10.3233/ADR-220010
IOS Press

Research R

Temporal Cortical Thickness and Cognitive Associations among Typical and Atypical Phenotypes of Alzheimer's Disease

Alissa M. Butts[a,b], Mary M. Machulda[c], Peter Martin[d], Scott A. Przybelski[d], Joseph R. Duffy[e], Jonathan Graff-Radford[e], David S. Knopman[e], Ronald C. Petersen[e], Clifford R. Jack Jr.[f], Val J. Lowe[f], Keith A. Josephs[e] and Jennifer L. Whitwell[f,*]

diagnostics
MDPI
Article

Recognizing Atypical Presentations of Alzheimer's Disease: The Importance of CSF Biomarkers in Clinical Practice

George P. Paraskevas [1,2,*], Vasilios C. Constantinides [1], Fotini Boufidou [1], Ioanna Tsantzali [2], Efstratios-Stylianos Pyrgelis [1], Georgios Liakakis [1] and Elisabeth Kapaki [1]

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

ALZHEIMER'S DISEASE

Intrinsic connectivity of the human brain provides scaffold for tau aggregation in clinical variants of Alzheimer's disease

Joseph Therriault[1,2,3], Tharick A. Pascoal[1,2,3], Mélissa Savard[1], Sulantha Mathotaarachchi[1], Andréa L. Benedet[1,2,3], Mira Chamoun[1,2], Cécile Tissot[1,2,3], Firoza Z. Lussier[1,2,3], Nesrine Rahmouni[1,2,3], Jenna Stevenson[1,2,3], Muhammad Naveed Iqbal Qureshi[1,2,3], Min [illegible], Para[illegible]

Neuroimage Clin. 2022; 36: 103161.
Published online 2022 Aug 22. doi: 10.1016/j.nicl.2022.103161
PMCID: PMC9428862
PMID: 36029670

Distinct brain iron profiles associated with logopenic progressive aphasia and posterior cortical atrophy

Neha Atulkumar Singh,[a] Arvin Arani,[b] Jonathan Graff-Radford,[a] Matthew L. Senjem,[b] Peter R. Martin,[c] Mary M. Machulda,[d] Christopher G. Schwarz,[b] Yunhong Shu,[b] Petrice M. Cogswell,[b] David S. Knopman,[a] Ronald C. Petersen,[a] Val J. Lowe,[b] Clifford R. Jack, Jr.,[b] Keith A. Josephs,[a] and Jennifer L. Whitwell[b,*]

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DOI: 10.1002/alz.12456
Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION
FEATURED ARTICLE

Rates of longitudinal change in ^{18}F-flortaucipir PET vary by brain region, cognitive impairment, and age in atypical Alzheimer's disease

Jeffrey S. Phillips[1] | Frederick J. Nitchie IV[1] | Fulvio Da Re[2] | Christopher A. Olm[1] | Philip A. Cook[1] | Corey T. McMillan[1] | David J. Irwin[1] | James C. Gee[1] | Jacob G. Dubroff[1] | Murray Grossman[1] | Ilya M. Nasrallah[1] | for the Alzheimer's Disease Neuroimaging Initiative[#]

Neuro | Published: 26 July 2022

Quantitative susceptibility mapping demonstrates different patterns of iron overload in subtypes of early-onset Alzheimer's disease

Grégory Kuchcinski, Lucas Patin, Renaud Lopes, Mélanie Leroy, Xavier Delbeuck, Adeline Rollin-Sillaire, Thibaud Lebouvier, Yi Wang, Pascal Spincemaille, Thomas Tourdias, Lotfi Hacein-Bey, David Devos,

Validity of cingulate–precuneus–temporo-parietal hypometabolism for single-subject diagnosis of biomarker-proven atypical variants of Alzheimer's Disease

Valeria Isella[1,5] · Cinzia Crivellaro[2] · Anna Formenti[1] · Monica Musarra[2] · Sara Pacella[2] · Sabrina Morzenti[3] · Francesca Ferri[1] · Cristina Mapelli[1] · Francesca Gallivanone[4] · Luca Guerra[2] · Ildebrando Appollonio[1] · Carlo Ferrarese[1]

Tau and the fractionated default mode network in atypical Alzheimer's disease

Deepti Putcha,[1,2] Ryan Eckbo,[1] Yuta Katsumi,[1] Bradford C. Dickerson,[1,2,] Alexandra Touroutoglou[1,2,*] and Jessica A. Collins[1,*]

nature › nature communications › articles › article

Article | Open Access | Published: 05 August 2022

Multi-cohort and longitudinal Bayesian clustering study of stage and subtype in Alzheimer's disease

Konstantinos Poulakis, Joana B. Pereira, J.-Sebastian Muehlboeck, Lars-Olof Wahlund, Örjan Smedby, Giovanni Volpe, Colin L. Masters, David Ames, Yoshiki Niimi, Takeshi Iwatsubo, Daniel Ferreira, Eric Westman, Japanese Alzheimer's Disease Neuroimaging Initiative & Australian Imaging, Biomarkers and Lifestyle study

Nature Communications **13**, Article number: 4566 (2022) | Cite this article

Biomarkers: what's new?

UNIVERSITY OF CAMBRIDGE

RESEARCH ARTICLE

Investigating Heterogeneity and Neuroanatomic Correlates of Longitudinal Clinical Decline in Atypical Alzheimer Disease

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Neurology® 2022;98:e2436-e2445. doi:10.1212

Atrophy

Received: 29 January 2021 | Revised: 24 June 2021 | Accepted: 30 July 2021

DOI: 10.1002/alz.12456

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THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

FEATURED ARTICLE

Rates of longitudinal change in ^{18}F-flortaucipir PET vary by brain region, cognitive impairment, and age in atypical Alzheimer's disease

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Jacob G. Dubroff[1] | Murray Grossman[1] | Ilya M. Nasrallah[1]
Disease Neuroimaging Initiative[#]

Tau

RESEARCH ARTICLE

Discordance and Concordance Between Cerebrospinal and [^{18}F]FDG-PET Biomarkers in Assessing Atypical and Early-Onset AD Dementia Cases

Kely Mónica Quispialaya, MD,* Joseph Therriault, BSc,* Antonio Aliaga, MSc, Maria Zimmermann, BSc, Jaime Fernandez-Arias, MSc, Firoza Lussier, MSc, Gassan Massarweh, PhD, Tharick Pascoal, MD, PhD, Jean-Paul Soucy, MD, MSc, Serge Gauthier, MD, Bertrand Jean-Claude, PhD, Brian Gilfix, MD, PhD, Paolo Vitali, MD, PhD, and Pedro Rosa-Neto, MD, PhD

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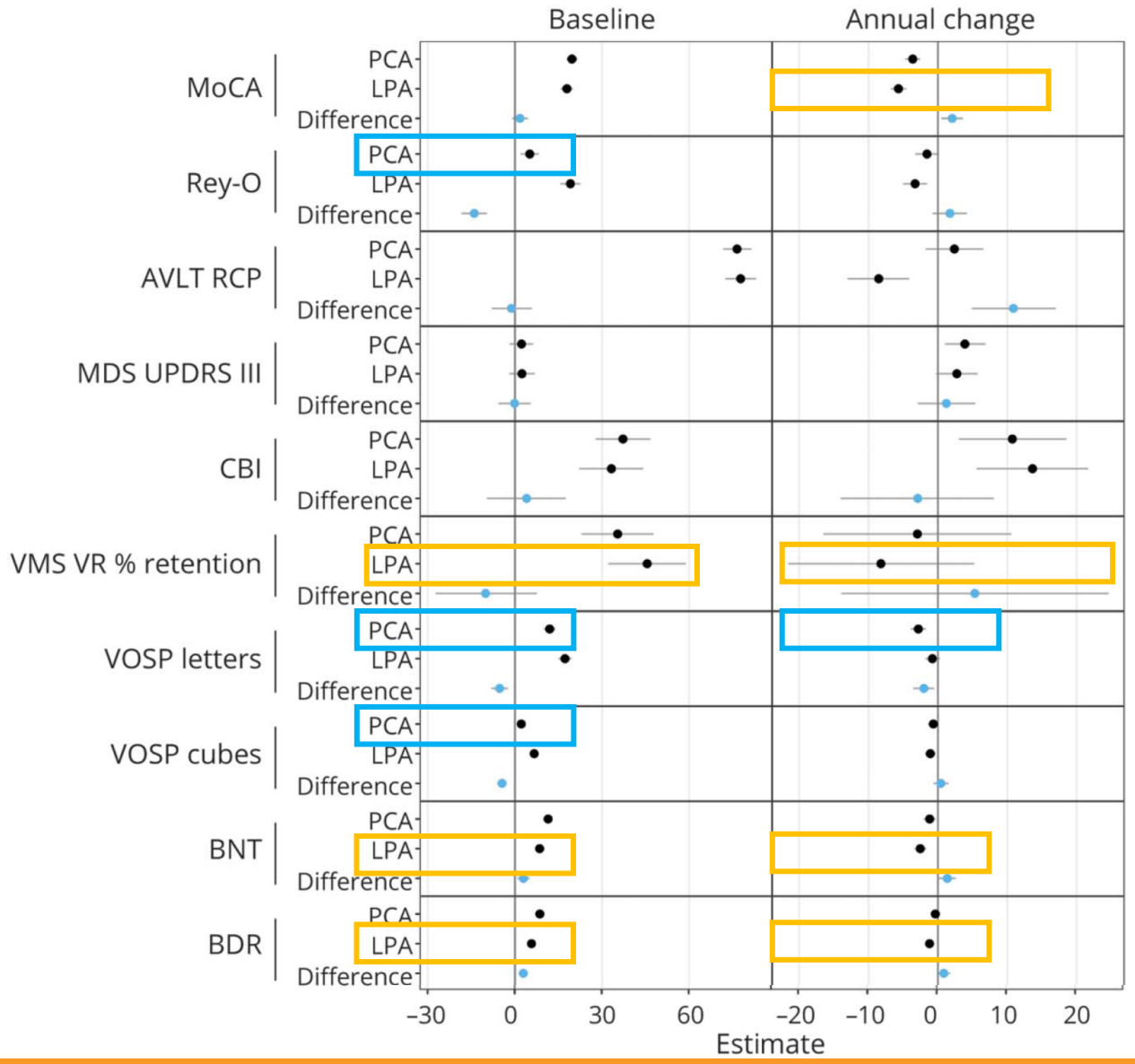
Neurology® 2022;99:e2428-e2436. doi:10.1212/WNL.0000000000201198

Hypometabolism + CSF

Biomarkers: clinical outcomes vs atrophy

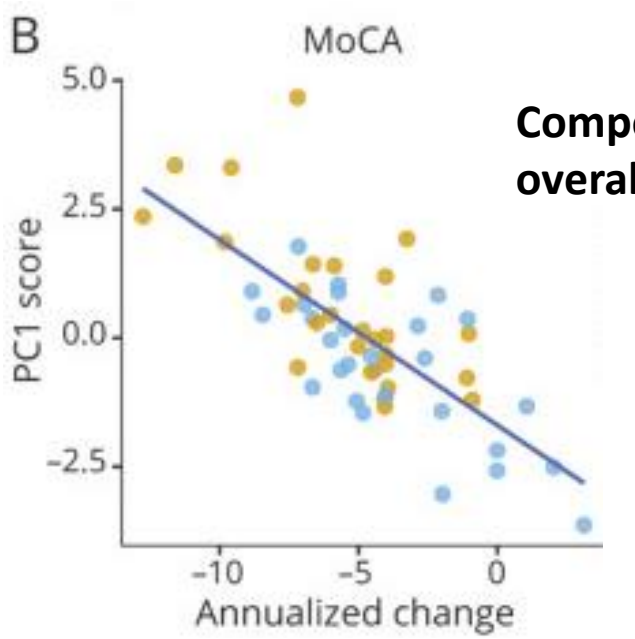
Clinical decline in atypical AD:
heterogeneity in patterns of change and relationships to concurrent brain atrophy?

Biomarkers: clinical outcomes vs atrophy



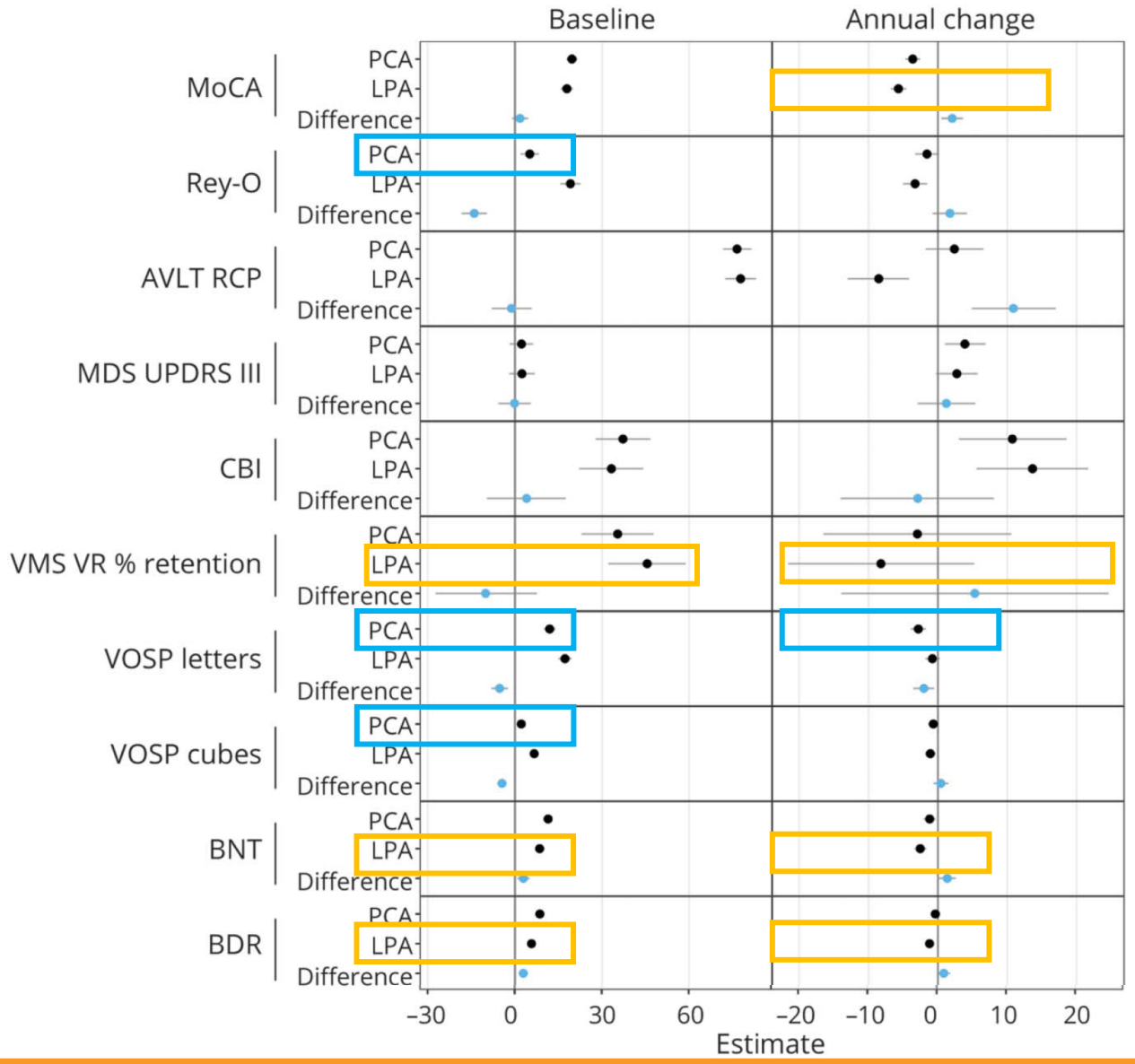
Rates of change in 13 clinical measures in patients with **PCA** and **LPA**

Principal component analysis



Component 1 = overall severity

Biomarkers: clinical outcomes vs atrophy



Rates of change in 13 clinical measures in patients with **PCA** and **LPA**

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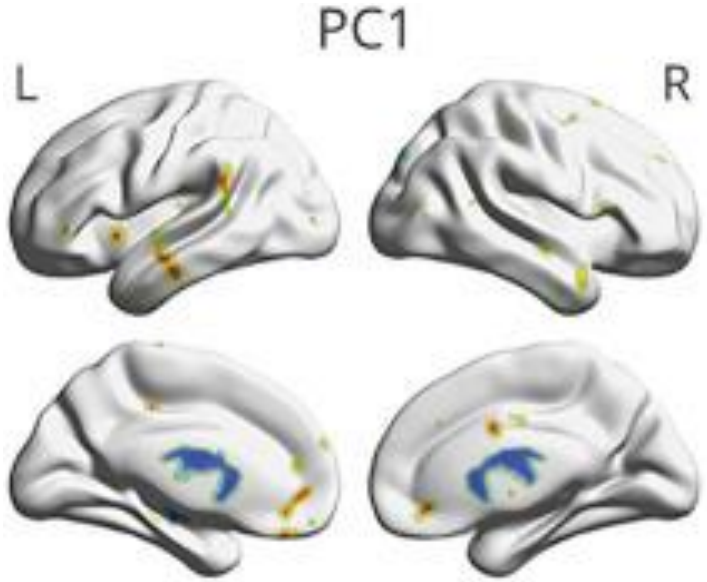

Associated with faster rates of atrophy in temporal lobe and supramarginal gyrus, and faster rates of ventricular expansion

Whitwell et al Neurology 2022

Biomarkers: tau progression

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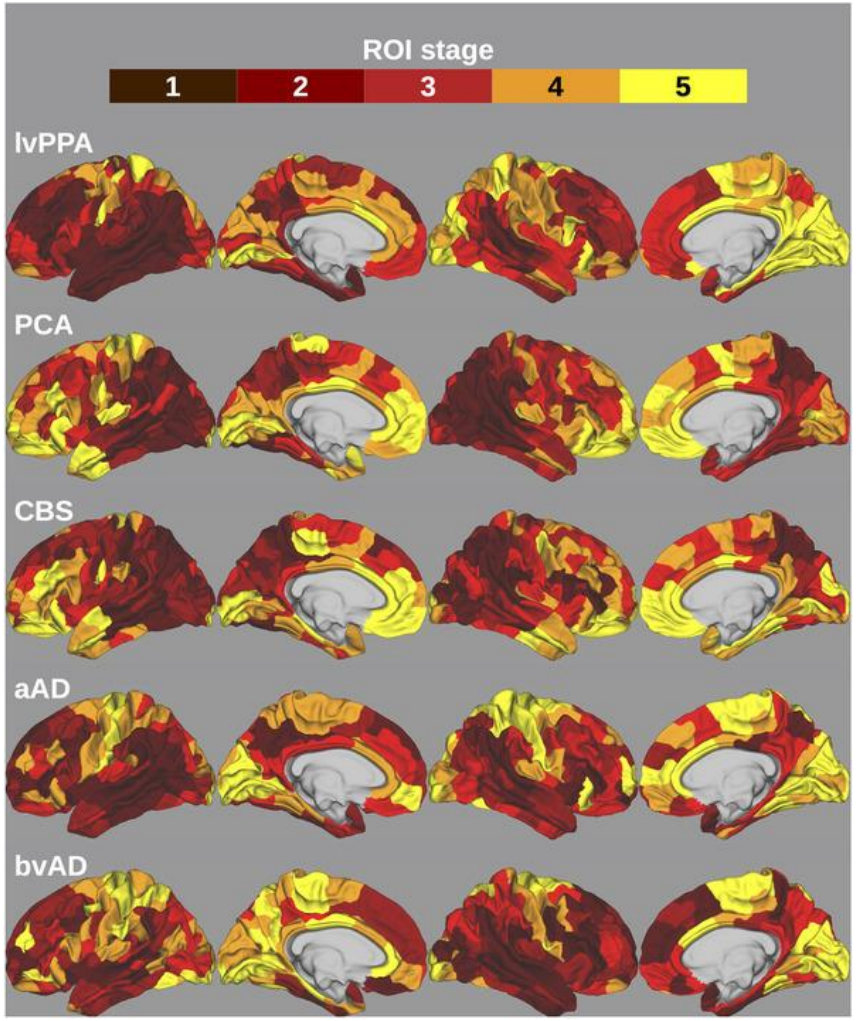
Tau progression over time in atypical AD:
regional specific rate of change and influencing factors?

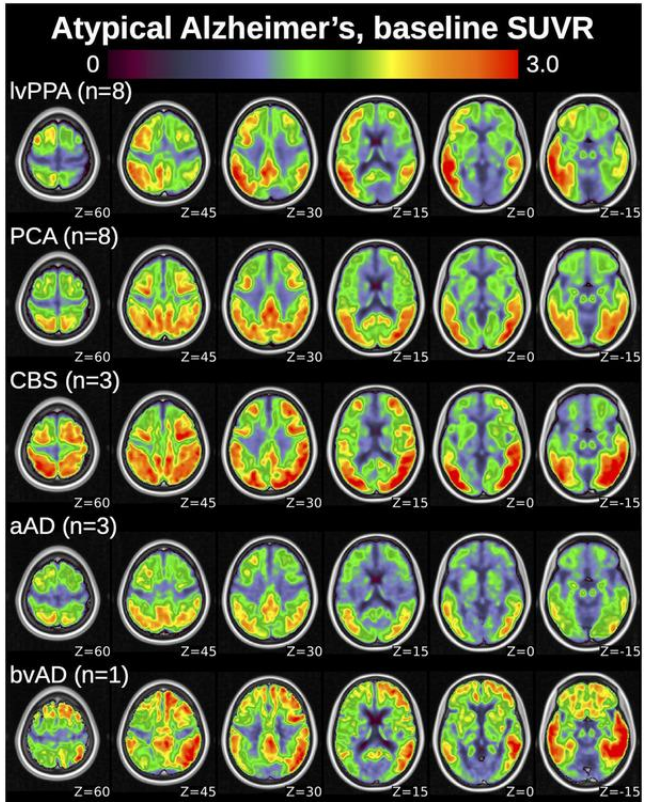
Biomarkers: tau progression



Models of neocortical disease progression in atypical AD, based on frequency of gray matter atrophy in an independent sample of patients.

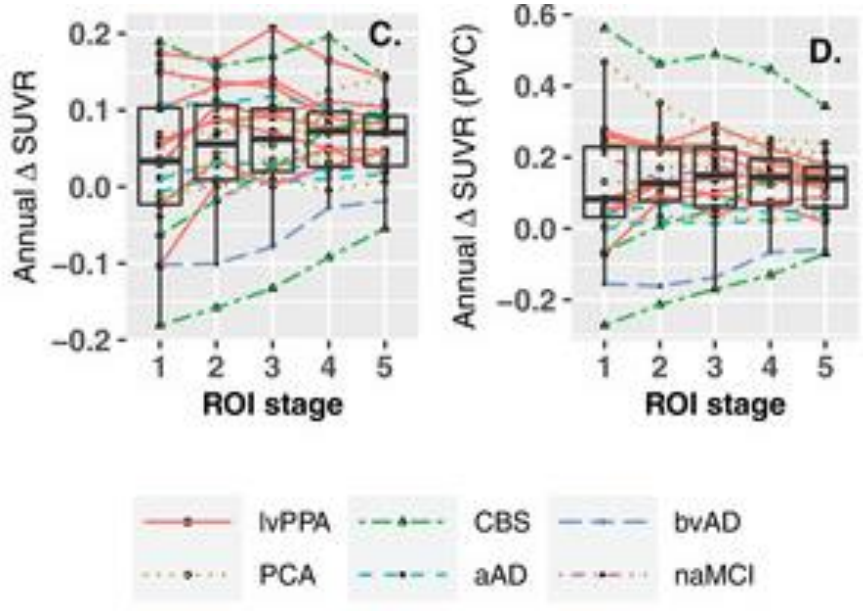
Stage 1 = earliest areas of disease

Stage 5 = latest areas of disease

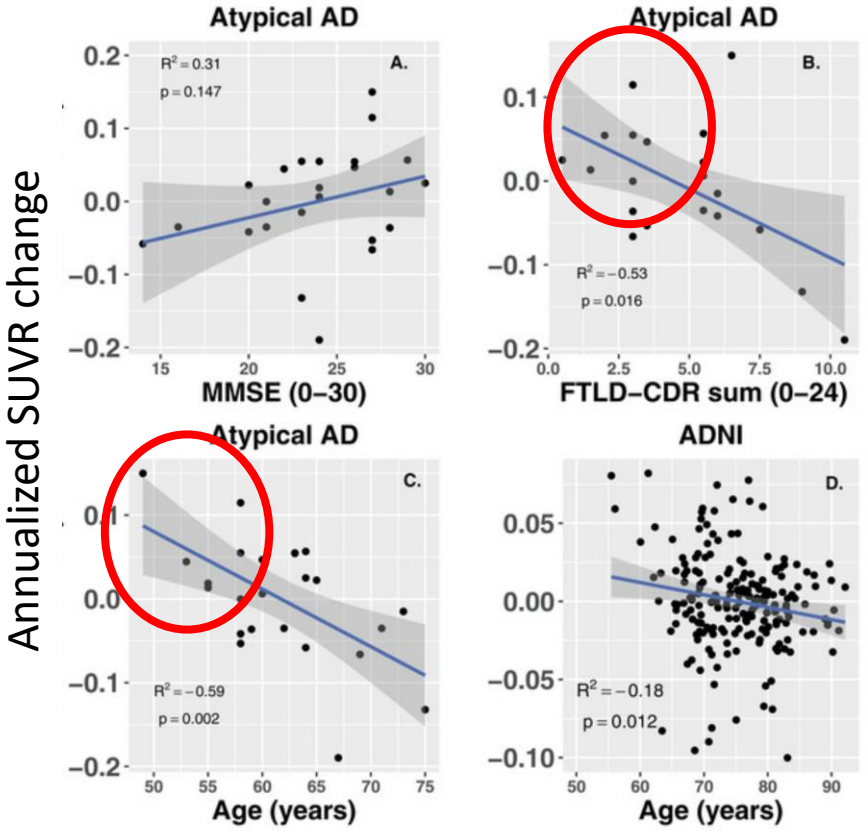


Phillips et al Alzh & Dem 2022

Biomarkers: tau progression



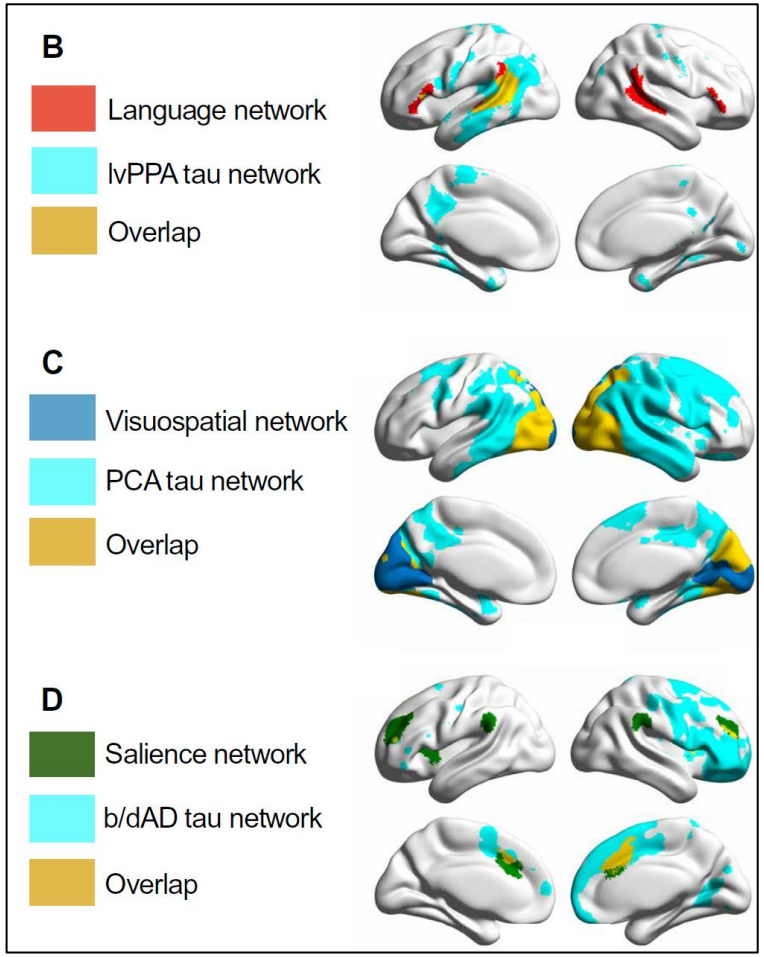
Areas of early disease higher tau at baseline and reduced changes over time relative to late-stage disease regions.



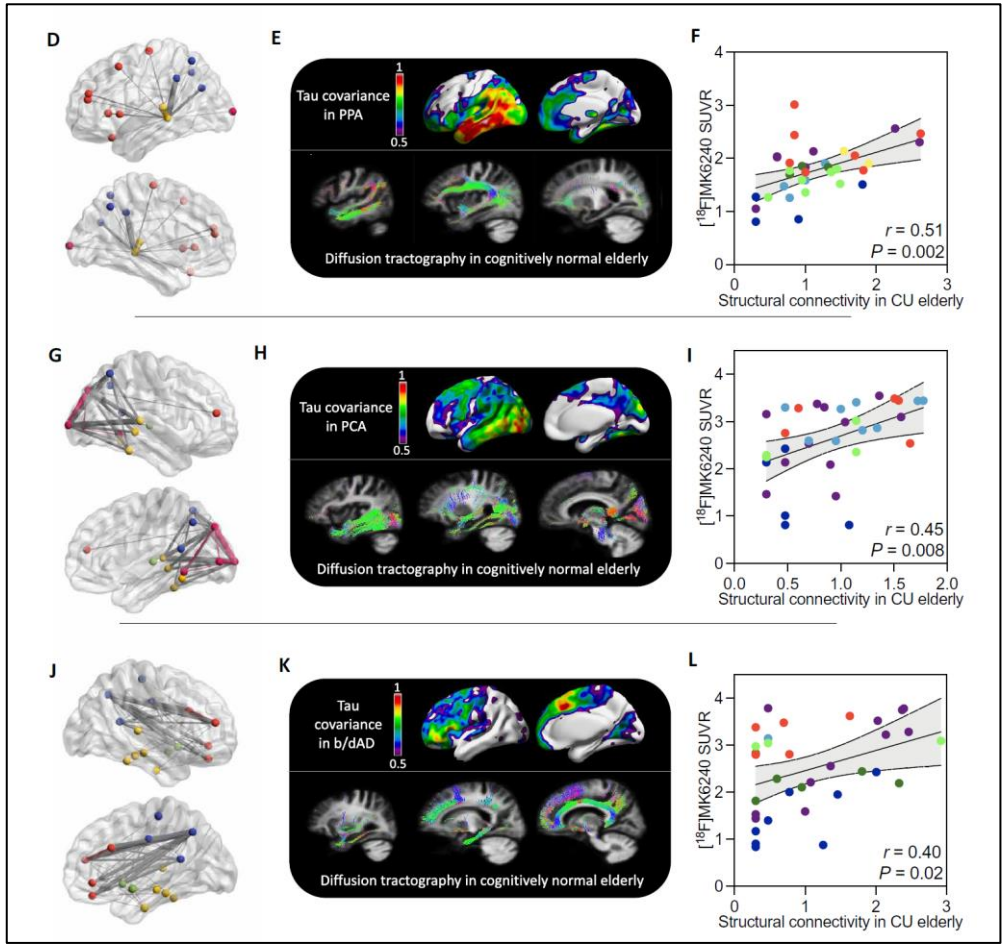
Younger and less impaired patients had greater SUVR increases.

Biomarkers: connectivity and tau propagation

Functional networks



Structural connectivity



AD phenotypes are associated with distinct network-specific patterns of tau aggregation and longitudinal progression

Biomarkers: FDG PET vs CSF

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Complementary biomarkers in atypical AD:

concordance between CSF and FDG PET in atypical and early-onset AD?

Biomarkers: FDG PET vs CSF

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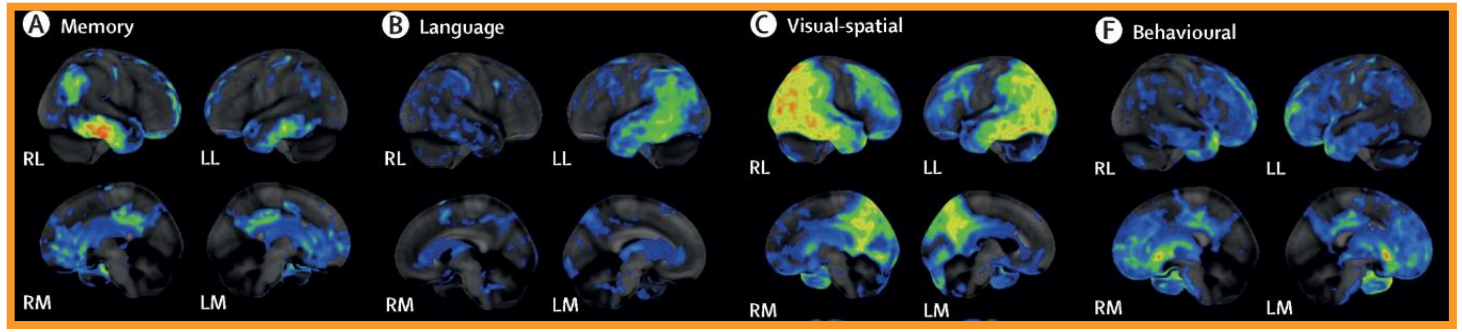
INCLUSION:

- Patients with early onset dementia OR late onset atypical AD
- FDG PET AND CSF



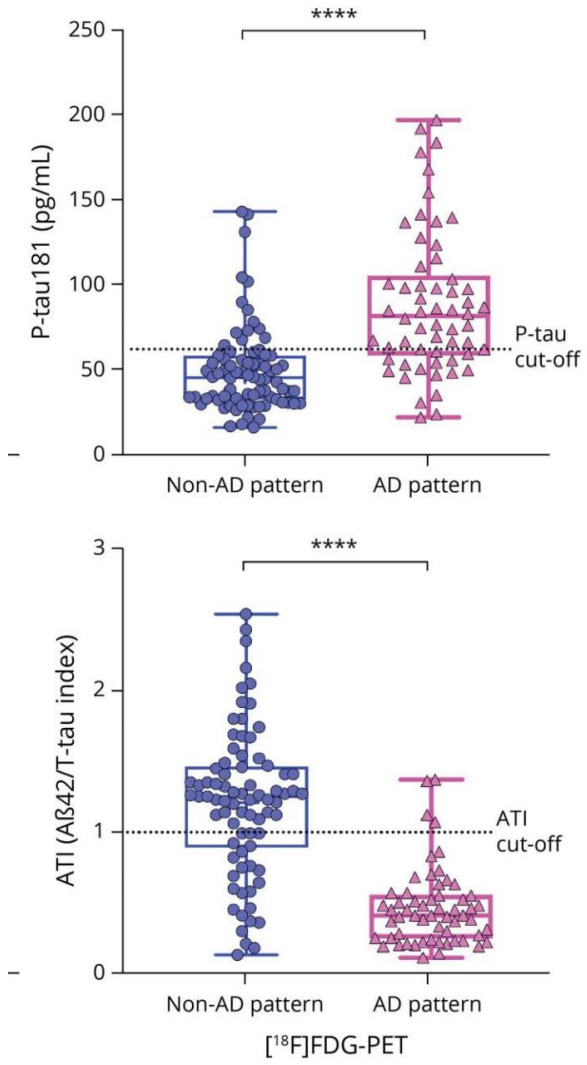
Graff-Radford et al *Lancet Neurol 2021*

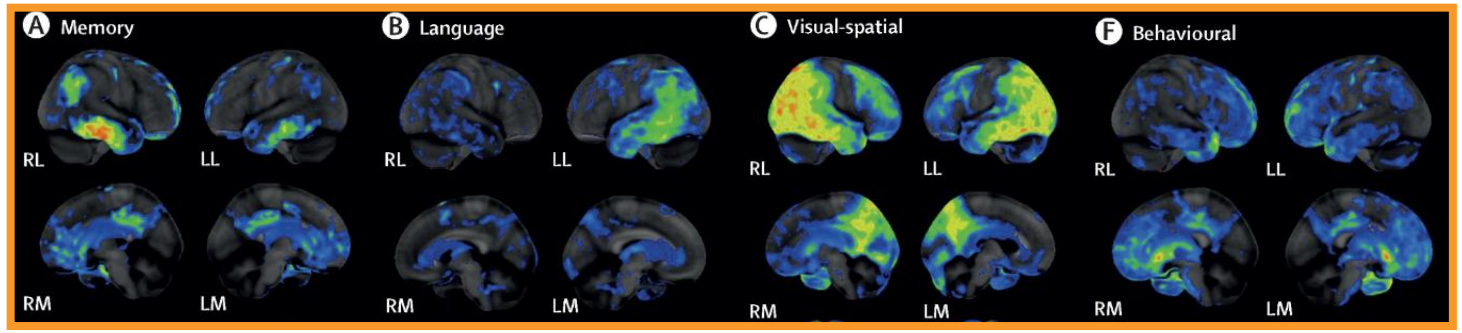
Aβ42to T-tau ratio <1.0
P-tau181 > 61 pg/mL

		[^{18}F] fdg-PET		
		Non-AD pattern	**AD pattern**	**Subtotal**
CSF	Non-AD			
	AD			
	Subtotal			136

Quispialaya, Therriault et al Neurology 2022

Biomarkers: FDG PET vs CSF





Graff-Radford et al *Lancet Neurol 2021*

		[18F] fdg-PET		
		Non-AD pattern	**AD pattern**	**Subtotal**
CSF	Non-AD	68	16	84
	AD	10	42	52
	Subtotal	78	58	136

[18F]FDG-PET and CSF biomarkers were discordant in nearly 20% of cases: extreme atypical presentations of AD or mixed pathologies.

Quispialaya, Therriault et al Neurology 2022

What's new?

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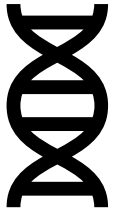
BIOMARKERS

Diagnosis
Prognosis
Tau spreading

GENETICS



Influencing factors
Risk factors

PATHOLOGY

Regional vulnerability
Clinico-path correlations

Genetics: 2021

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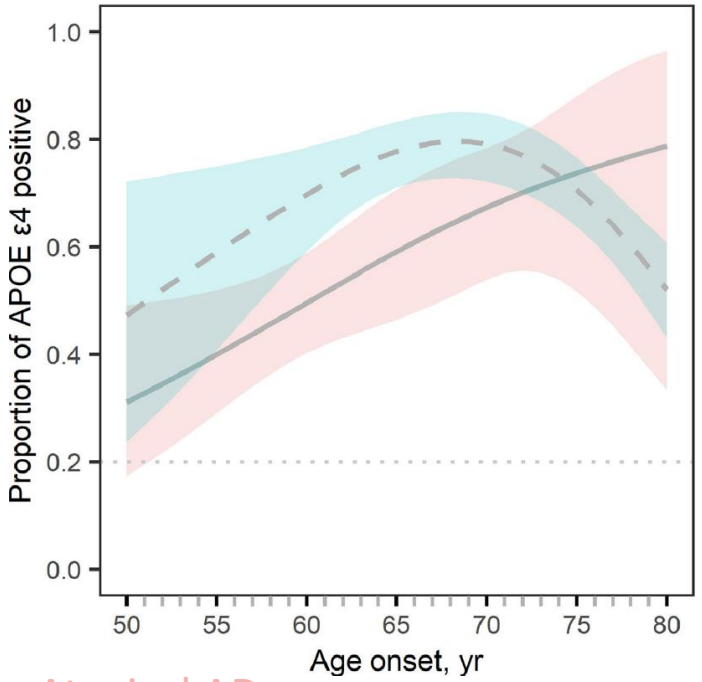
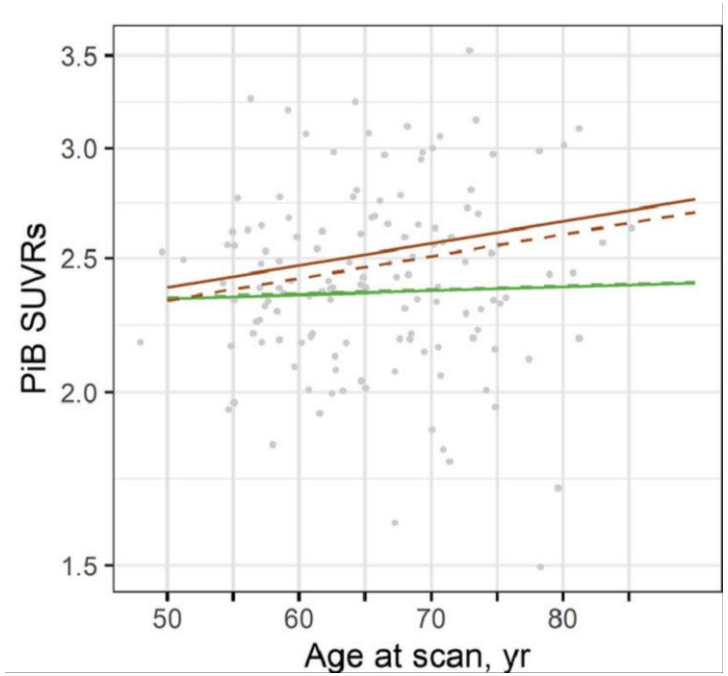
APOE ε4 frequency increases with **age at onset** in atypical AD



Atypical AD

Typical AD

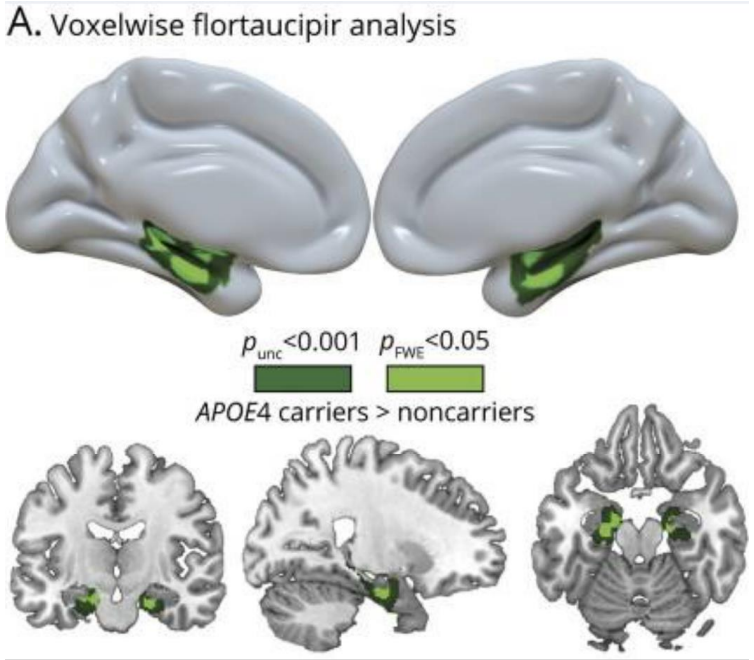
Global Aβ standard uptake value ratios does not differ according to *APOE* e4 status



PCA

lvPPA

The presence of *APOE4* is associated with focal medial temporal **flortaucipir-SUVR** increases



La Joie et al Neurology 2021, Whitwell et al Neurobio Aging 2021

Genetics: what's new?

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DOI: 10.1002/alz.12711

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FEATURED ARTICLE

APOE ε4 influences medial temporal atrophy and tau deposition in atypical Alzheimer's disease

Neha Atulkumar Singh[1] | Nirubol Tosakulwong[2] | Jonathan Graff-Radford[1] | Mary M. Machulda[3] | Nha Trang Thu Pham[4] | Irene Sintini[4] | Stephen D. Weigand[2] | Christopher G. Schwarz[4] | Matthew L. Senjem[4] | Minerva M. Carrasquillo[5] | Nilufer Ertekin-Taner[5] | Clifford R. Jack Jr.[4] | Val J. Lowe[4] | Keith A. Josephs[1] | Jennifer L. Whitwell[4]

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DOI: 10.1002/alz.12831

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FEATURED ARTICLE

APOE ε4 carrier status and sex differentiate rates of cognitive decline in early- and late-onset Alzheimer's disease

Angelina J. Polsinelli[1,2] | Paige E. Logan[1,2] | Kathleen A. Lane[3] | Mohit K. Manchella[4] | Sára Nemes[1] | Apoorva Bharthur Sanjay[1] | Sujuan Gao[2,3] | Liana G. Apostolova[1,2]

Link to Biomarkers

Acta Neuropathologica (2022) 144:1085–1102
https://doi.org/10.1007/s00401-022-02495-4

ORIGINAL PAPER

Check for updates

TREM2 risk variants are associated with atypical Alzheimer's disease

Boram Kim[1] · EunRan Suh[2] · Aivi T. Nguyen[1] · Stefan Prokop[5] · Bailey Mikytuck[1] · Olamide A. Olatunji[1] · John L. Robinson[2] · Murray Grossman[3] · Jeffrey S. Phillips[3] · David J. Irwin[3] · Dawn Mechanic-Hamilton[4] · David A. Wolk[4] · John Q. Trojanowski[2] · Corey T. McMillan[3] · Vivianna M. Van Deerlin[2] · Edward B. Lee[1]

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Link to Pathology

Genetics: APOE and brain changes

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APOE ε4 effects on brain changes in atypical AD:

regional association of APOE ε4 with gray matter volume loss and tau?

Genetics: APOE and brain changes

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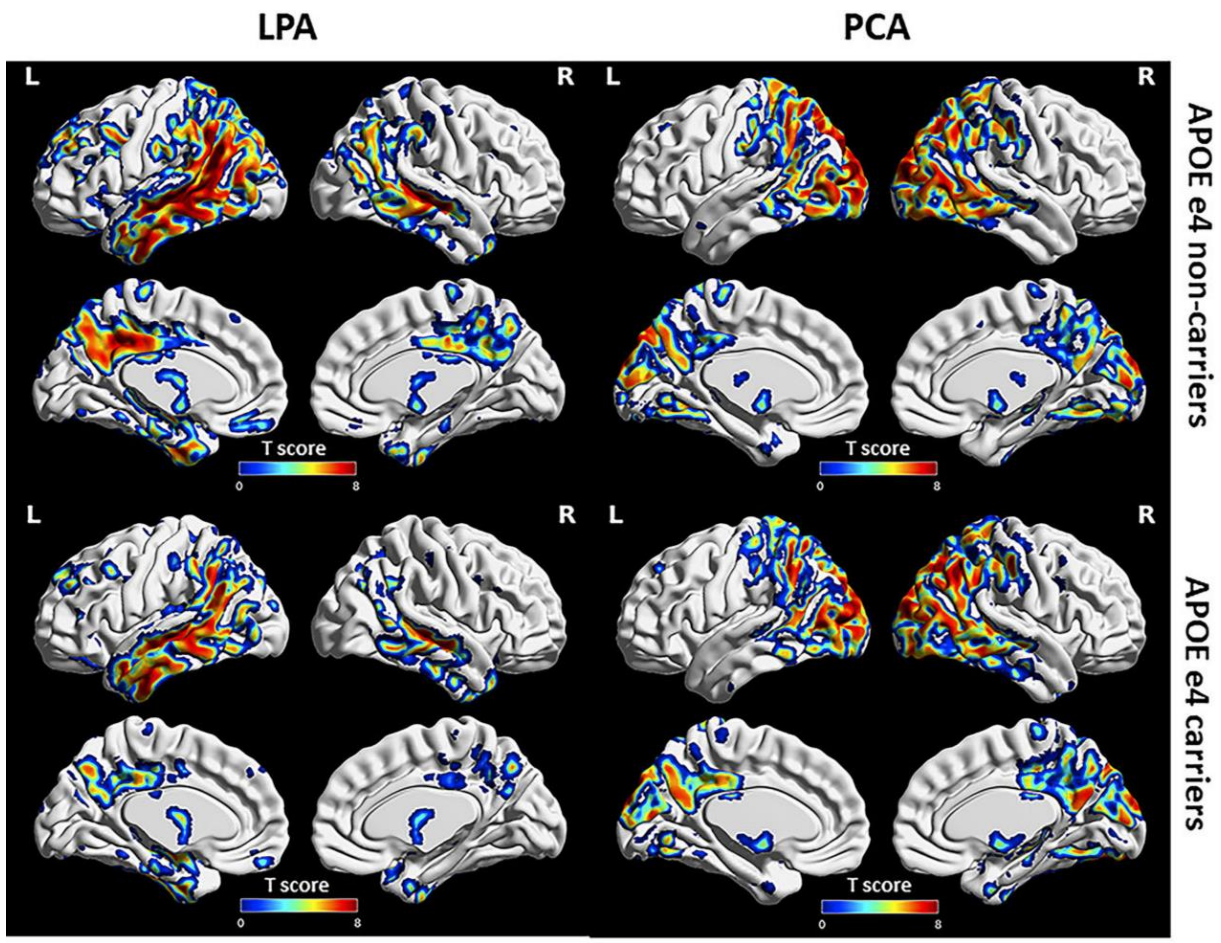
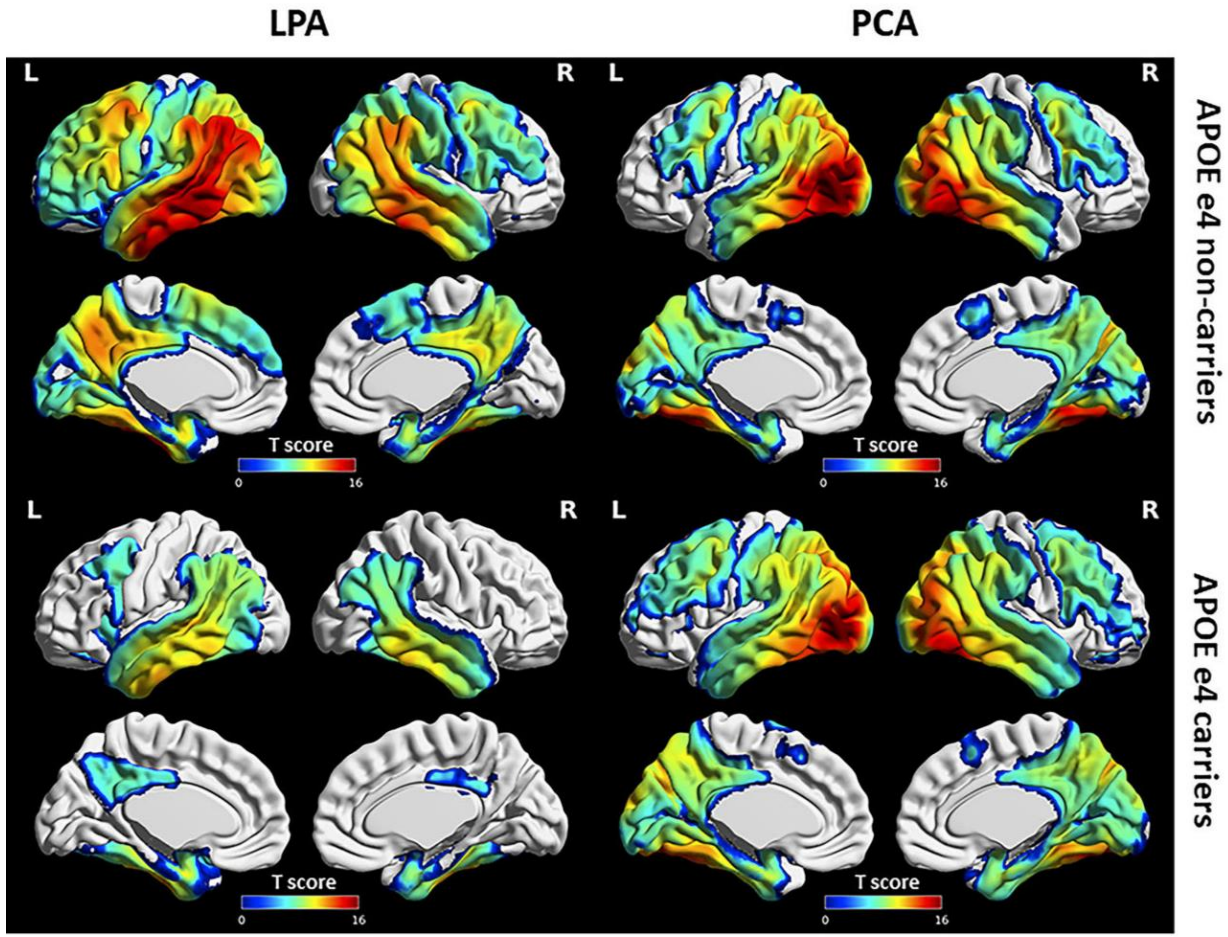
Grey matter loss



Tau pathology



Singh et al Alzh & Dem 2022

Genetics: APOE and brain changes

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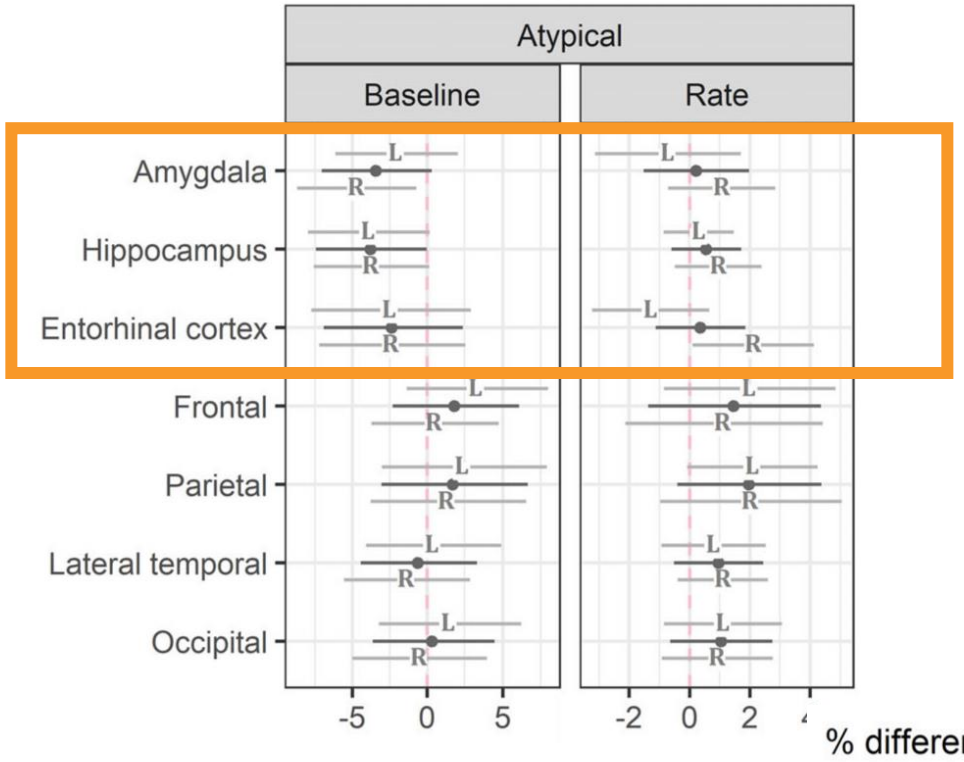
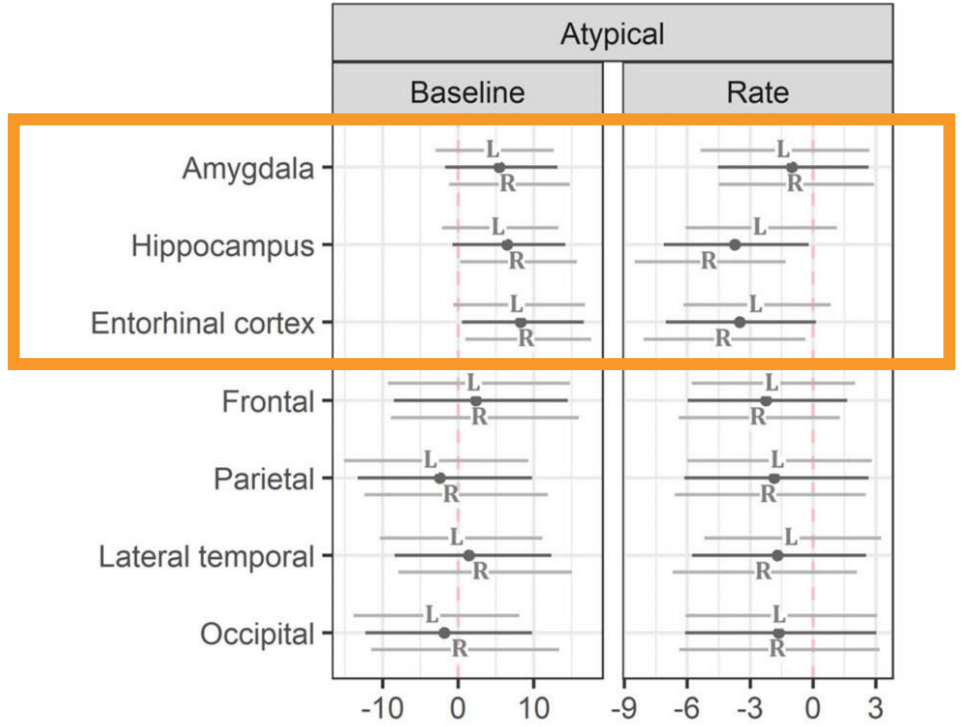
Grey matter loss

Negative values = ε4 carriers with more loss



Tau pathology

Positive values = ε4 carriers with more uptake



% difference (APOE ε4+ minus APOE ε4-)

APOE ε4 was associated with more medial temporal involvement at baseline, while over time non-carriers show faster progression

Singh et al Alzh & Dem 2022

Genetics: APOE and cognitive changes

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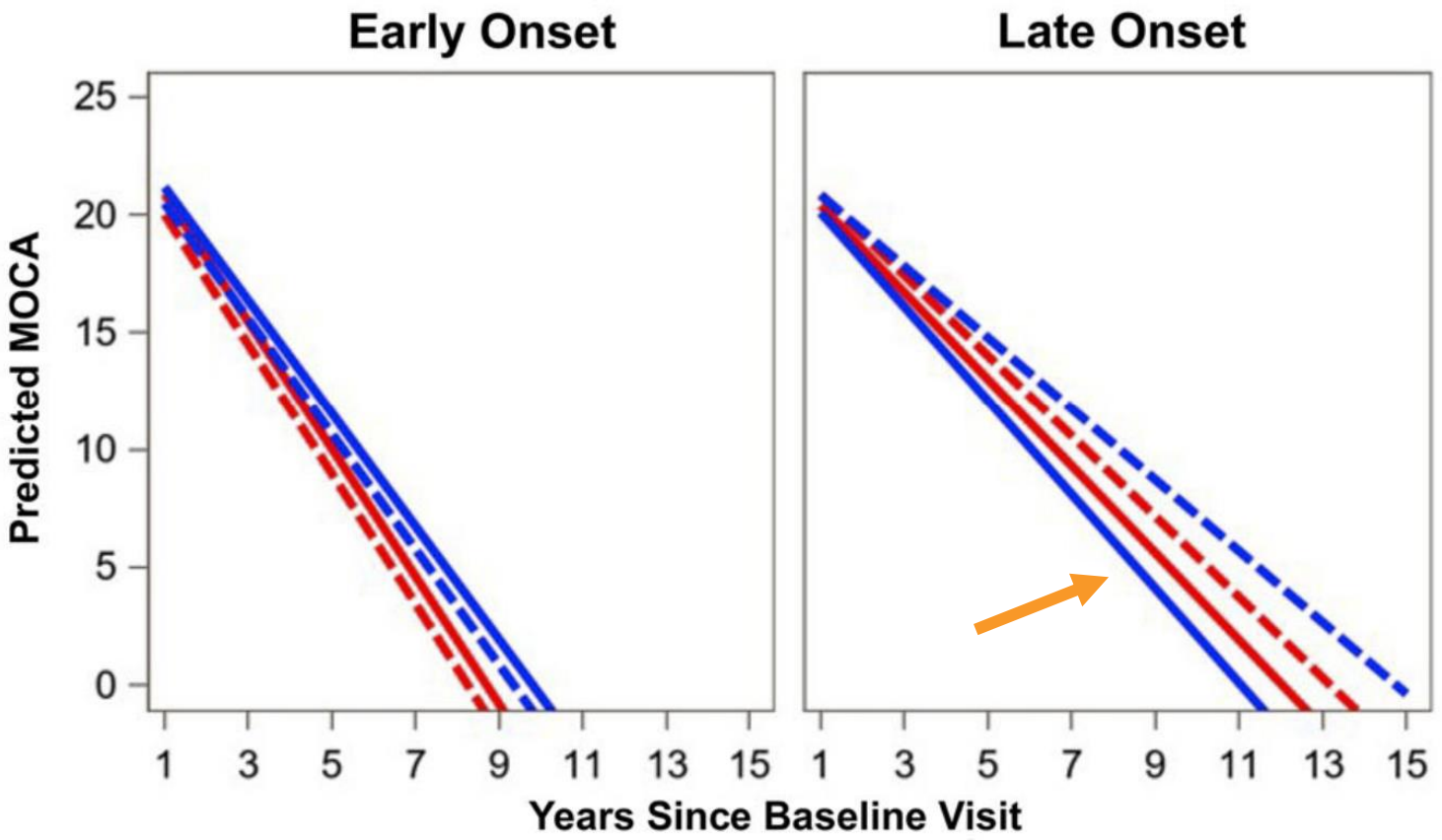
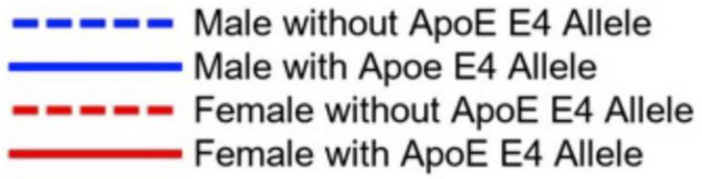
APOE ε4 and sex effects in early onset AD:

different effects on cognitive decline in early- vs late-onset AD?

Genetics: APOE and cognitive changes





Global measure of cognition: APOE ε4 affected the rate of decline in LOAD (sex no effect)

Polsinelli et al Alzh & Dem 2022

Genetics: APOE and cognitive changes

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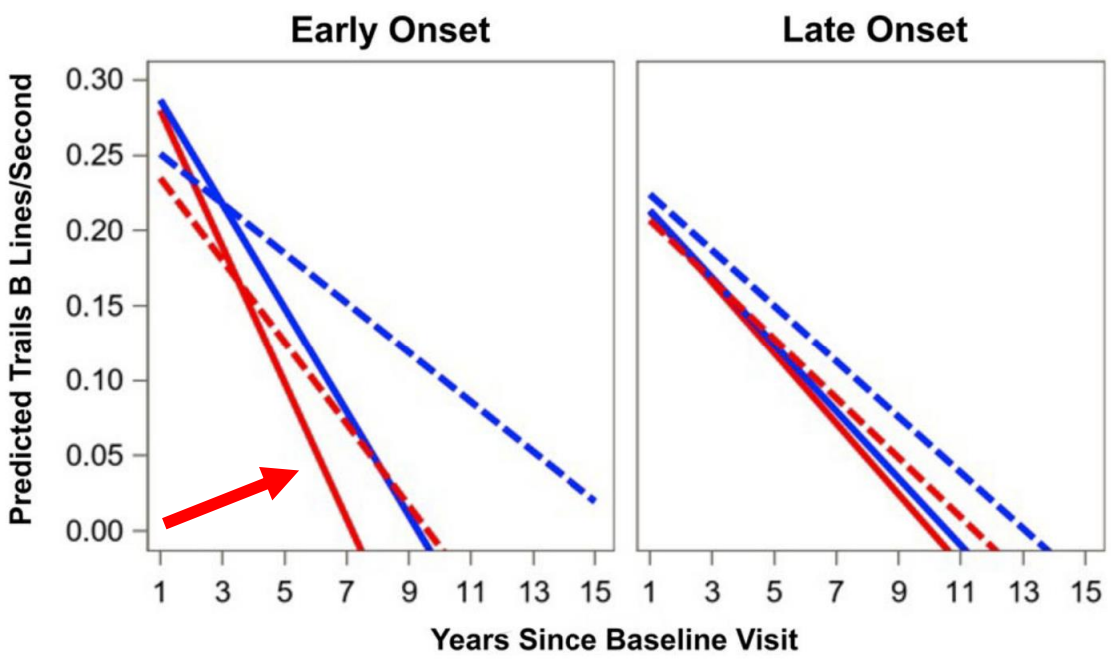
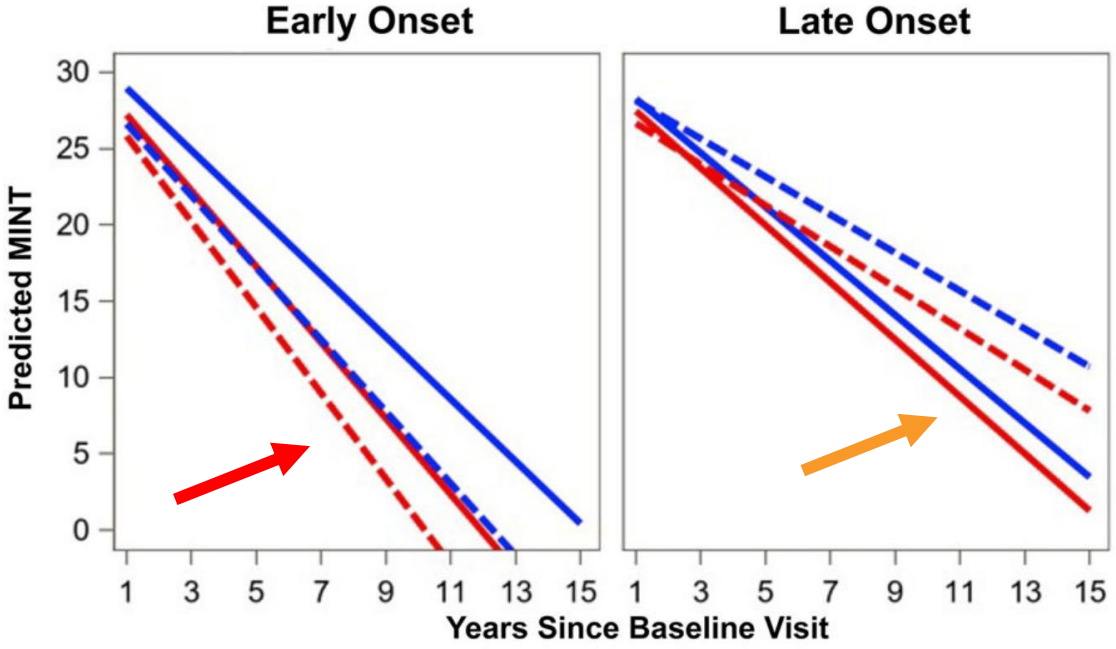
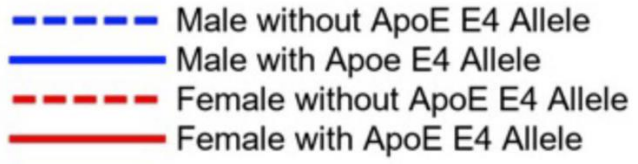
In the EOAD group, the presence of *APOE ε4* and female sex accelerated cognitive decline.





The effect of *APOE ε4* was greater in EOAD for **executive functioning** and greater in LOAD for **language**.



Polsinelli et al Alzh & Dem 2022

Genetics: TREM2 and atypical AD

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TREM2 and increased risk in atypical AD:

TREM2 variants associated with atypical clinical and pathology AD?

Kim et al Acta Neuropath 2022

Genetics: TREM2 and atypical AD

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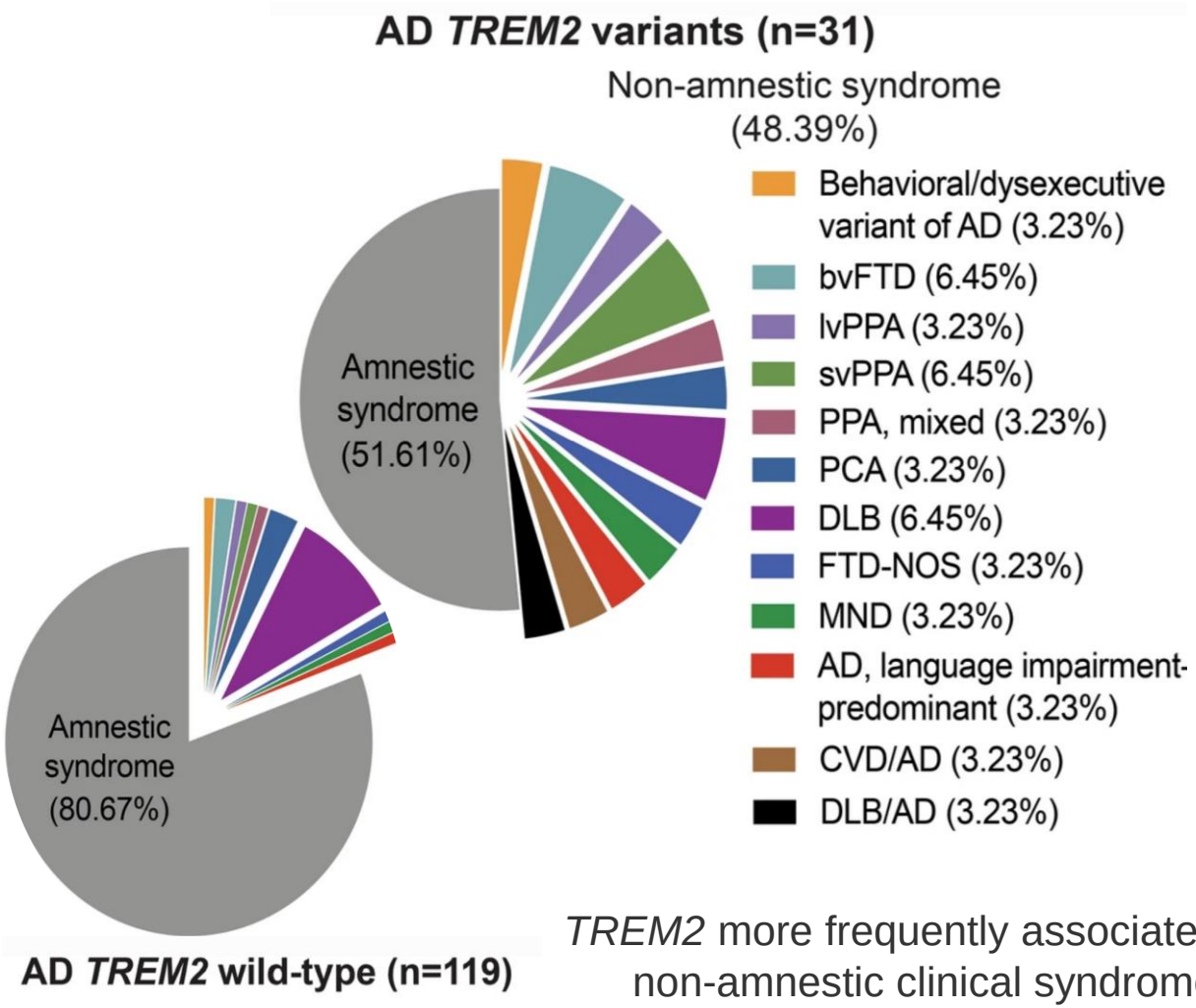
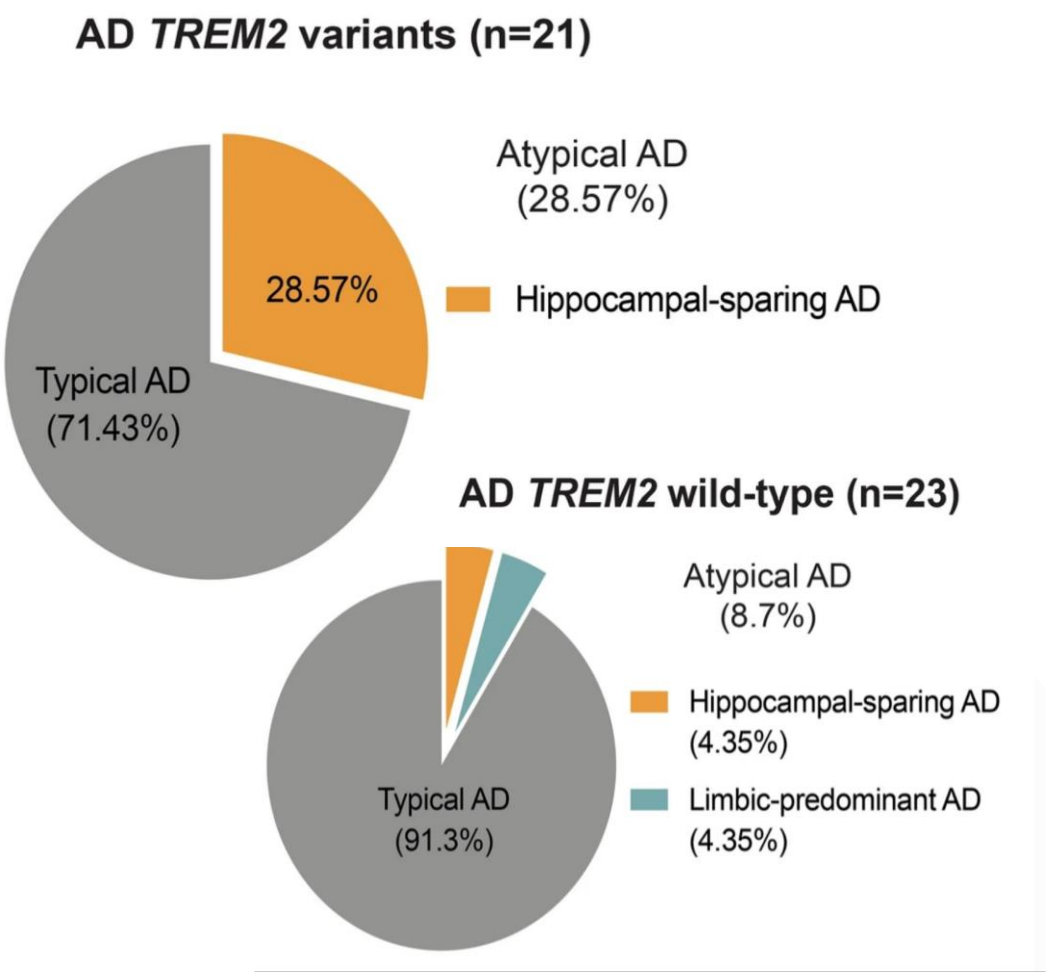
Clinical variants



TREM2 more frequently associated with non-amnestic clinical syndromes

Pathology



TREM2 associated with an atypical distribution of neurofibrillary tangle density

Kim et al Acta Neuropath 2022

Genetics: TREM2 and atypical AD

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Co-pathologies

c AD *TREM2* variants (n=31) AD *TREM2* wild-type (n=119)

Kim et al Acta Neuropath 2022

Genetics: TREM2 and atypical AD

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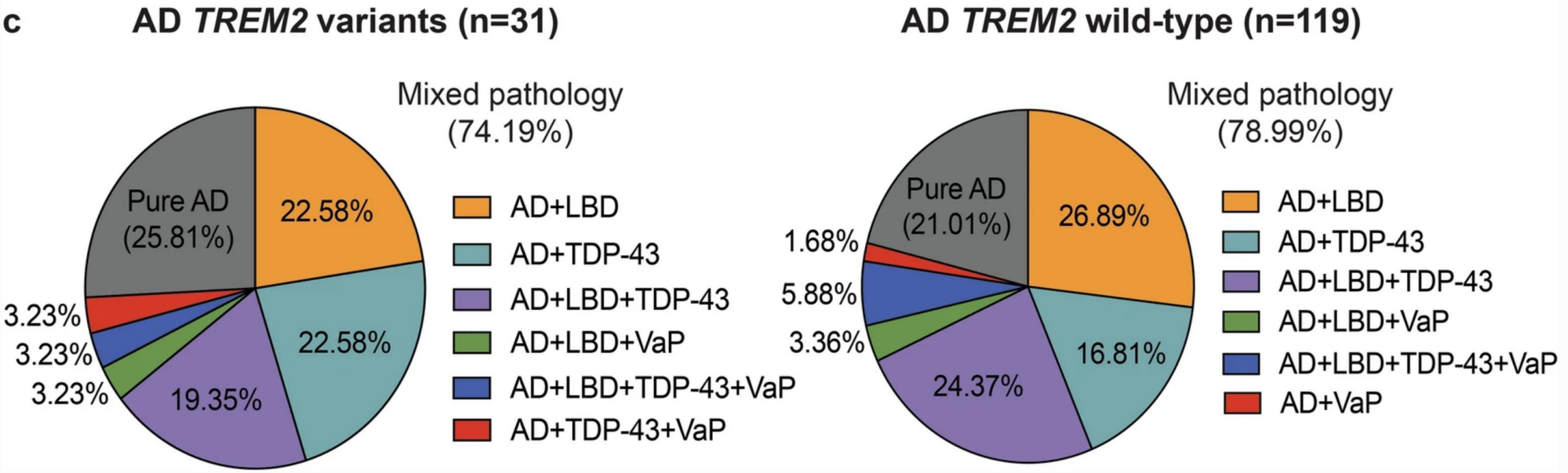
Co-pathologies



TREM2 variant cases were **not** associated with an increased prevalence, extent, or severity of co-pathologies.

Kim et al Acta Neuropath 2022

What's new?

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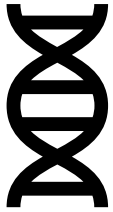
BIOMARKERS

Diagnosis
Prognosis
Tau spreading

GENETICS

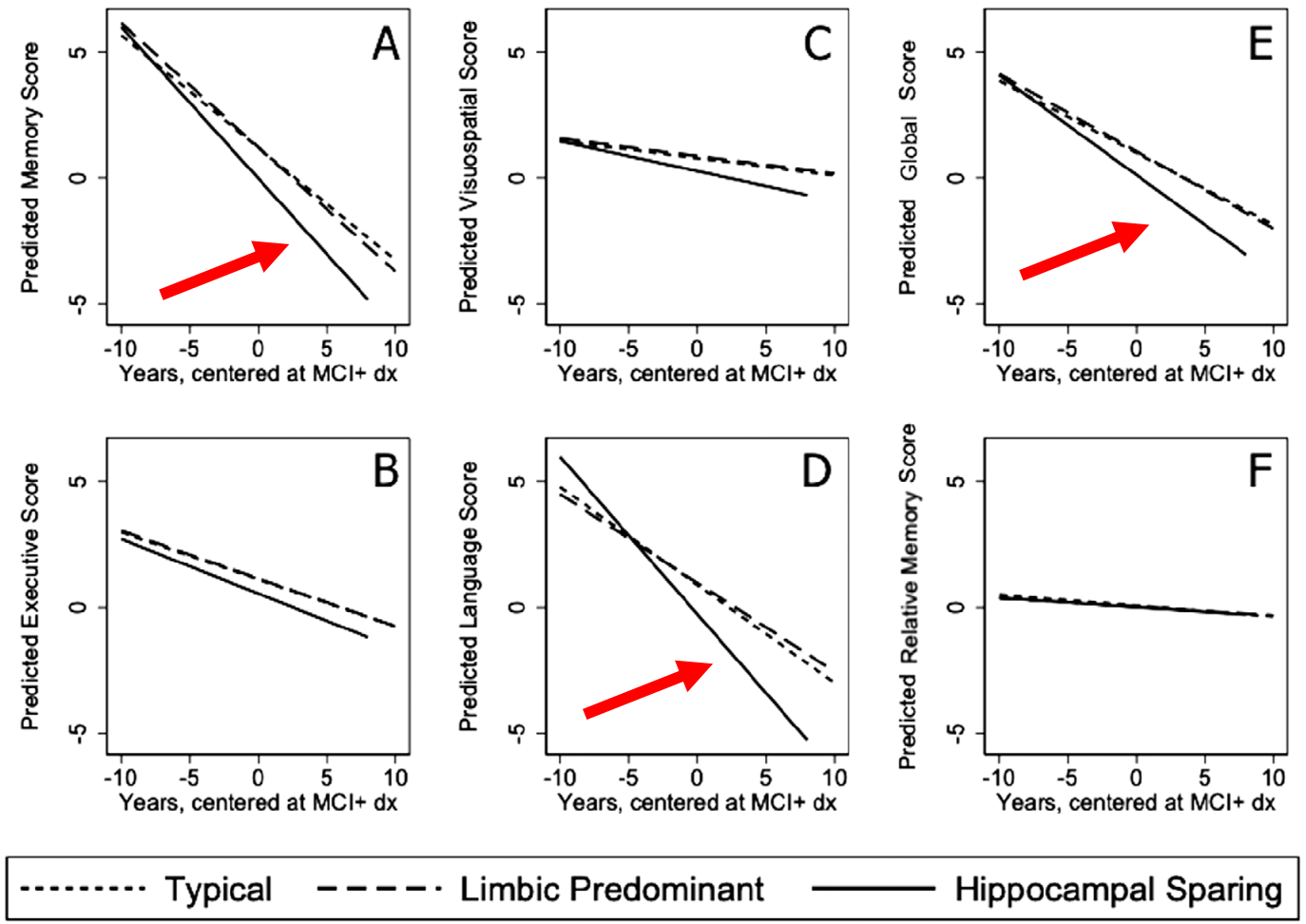


Influencing factors
Risk factors

PATHOLOGY

Regional vulnerability
Clinico-path correlations

Pathology: 2021



Hippocampal Sparing AD cases but not Limbic predominant cases performed worse and declined faster

NumCopath	EOAD	LOAD
6	1	2
5	2	4
4	9	7
3	26	14
2	31	18
1	25	3
0	2	0
Total	96	48

Non-AD pathological diagnoses play an important role in the clinical phenotype of **early onset AD**

Pathology: what's new?

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Acta Neuropathologica (2022) 144:1103–1116
https://doi.org/10.1007/s00401-022-02472-x

ORIGINAL PAPER

Check for updates

Regional distribution and maturation of tau pathology among phenotypic variants of Alzheimer's disease

Sanaz Arezoumandan[1,2] · Sharon X. Xie[3] · Katheryn A. Q. Cousins[2] · Dawn J. Mechanic-Hamilton[4,5] · Claire S. Peterson[1,2] · Camille Y. Huang[1] · Daniel T. Ohm[1,2] · Ranjit Ittyerah[6] · Corey T. McMillan[2,5] · David A. Wolk[4,5] · Paul Yushkevich[5,6] · John Q. Trojanowski[5,7] · Edward B. Lee[5,7,8] · Murray Grossman[2] · Jeffrey S. Phillips[2] · David J. Irwin[1,2]

J Neuropathol Exp Neurol
Vol. 81, No. 3, March 2022, pp. 158–171
doi: 10.1093/jnen/nlac008

OXFORD

ORIGINAL ARTICLE

Hemispheric Asymmetry and Atypical Lobar Progression of Alzheimer-Type Tauopathy

Cécilia Tremblay, PhD, Geidy E. Serrano, PhD, Anthony J. Intorcia, BS, Jasmine Curry, BS, Lucia I. Sue, BS, Courtney M. Nelson, BS, Jessica E. Walker, BS, Michael J. Glass, BS, Richard A. Arce, BS, Adam S. Fleisher, MD, MAS, Michael J. Pontecorvo, PhD, Alireza Atri, MD, PhD, Thomas J. Montine, MD, PhD, Kewei Chen, PhD, and Thomas G. Beach, MD, PhD

Neurology | American Academy of Neurology

Neurology. 2022 Jul 26; 99(4): e323–e333.
doi: 10.1212/WNL.0000000000200573
PMCID: PMC9421777
PMID: 35609990

Neuropathologic Features of Antemortem Atrophy-Based Subtypes of Alzheimer Disease

Rosaleena Mohanty, PhD, Daniel Ferreira, PhD, Simon Frerich, MSc, J-Sebastian Muehlboeck, MSc, Michel J. Grothe, PhD, Eric Westman, PhD, and on behalf of the Alzheimer's Disease Neuroimaging Initiative

Link to Biomarkers

Pathology: tau distribution & maturation

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Regional tau pathology in atypical AD:
differences in regional distribution and burden of tau?

Pathology: tau distribution & maturation

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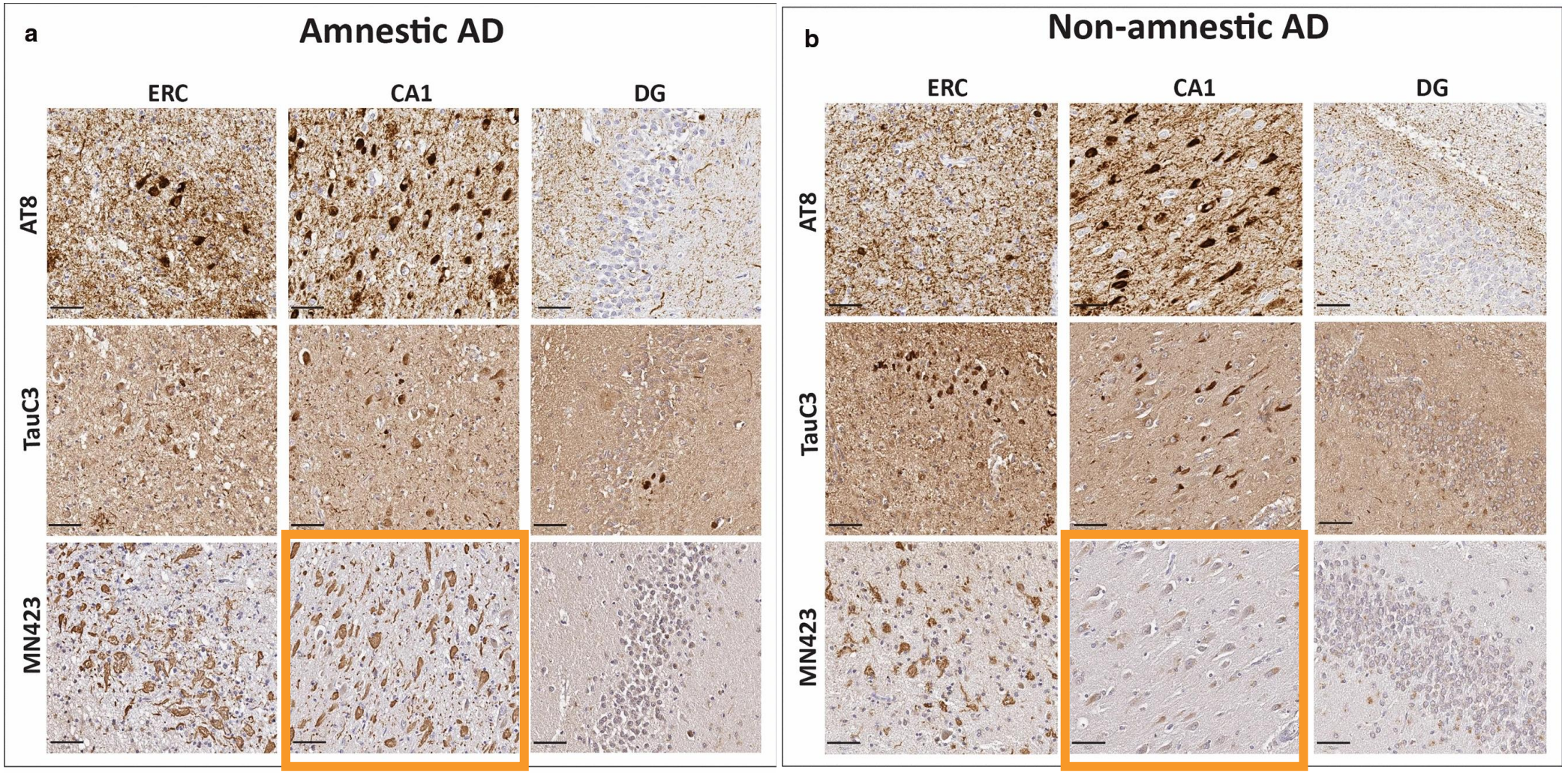
phosphorylated -tau

mature tangles

ghost tangles



Subcortical and cortical regions: QuPath for percentage of staining-positive pixels

Pathology: tau distribution & maturation

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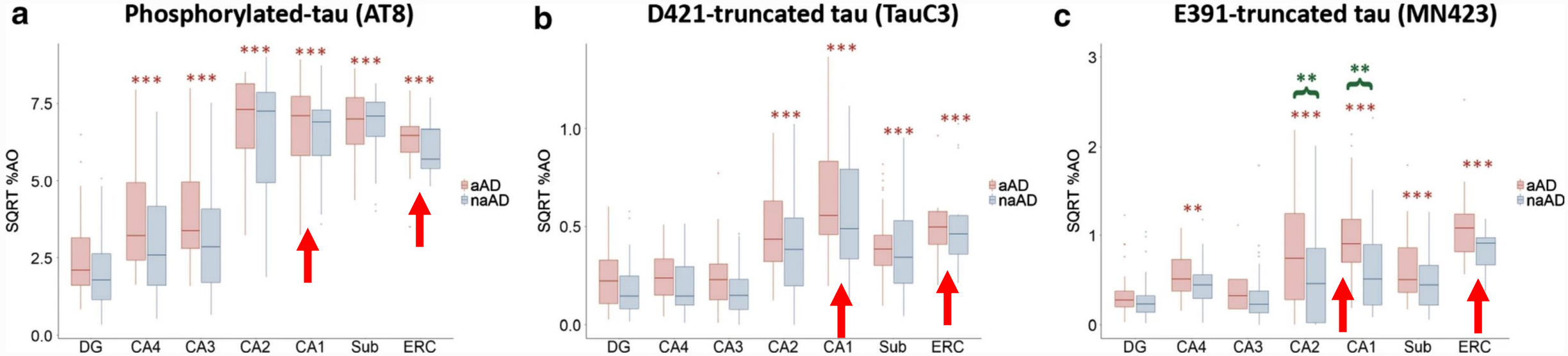

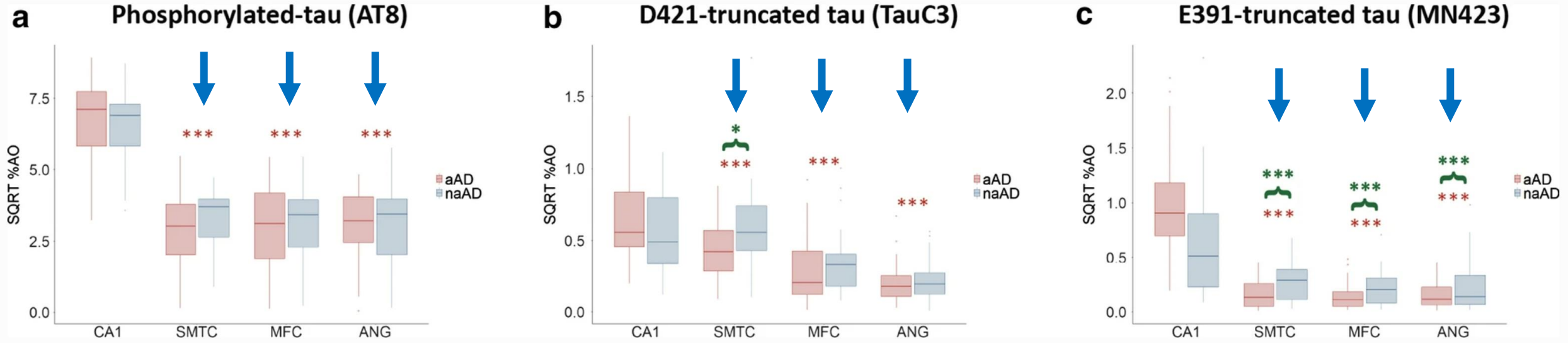

Pathology: tau distribution & maturation

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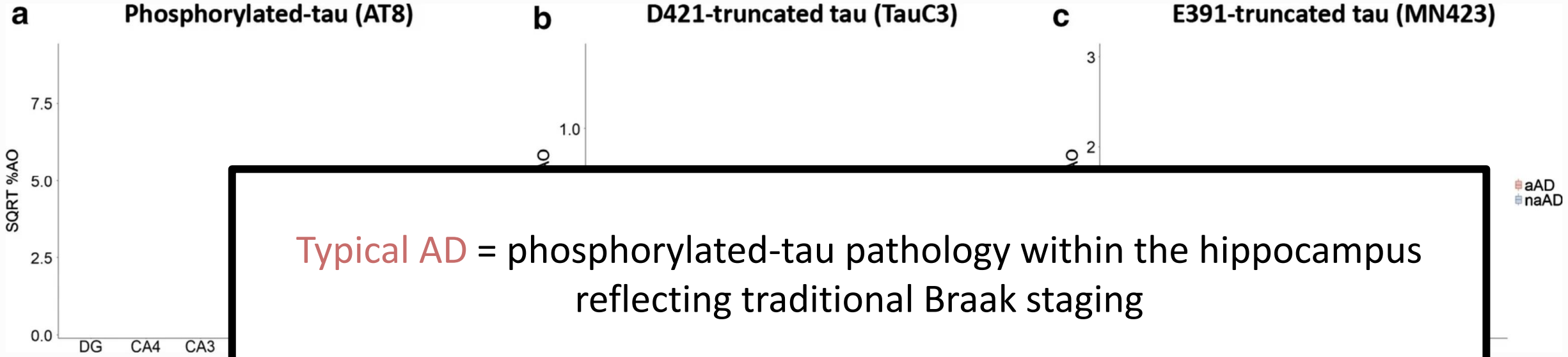
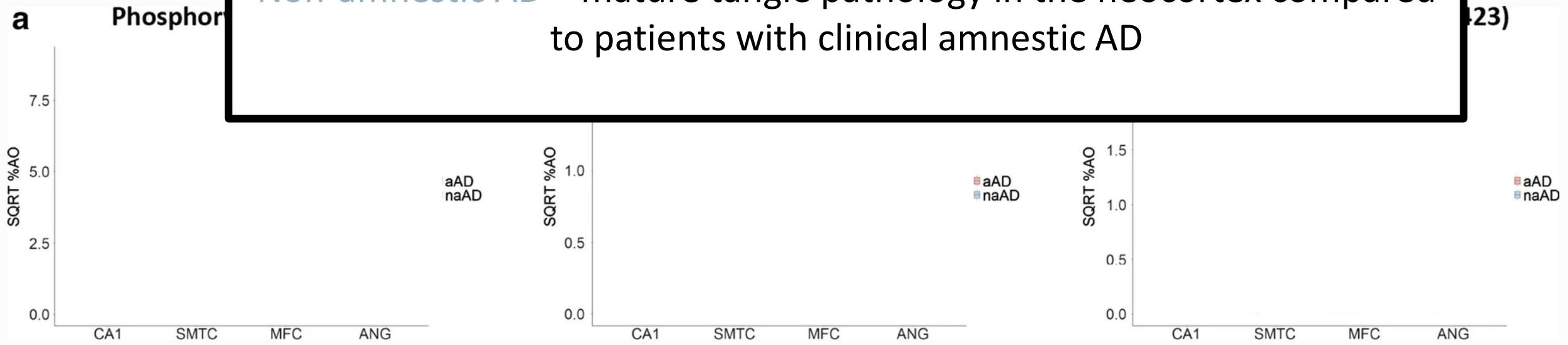


Typical AD = phosphorylated-tau pathology within the hippocampus reflecting traditional Braak staging

Non-amnestic AD = mature tangle pathology in the neocortex compared to patients with clinical amnestic AD



Pathology: topographical progression

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Tau spreading in atypical AD:

interhemispheric tau differences and atypical spreading patterns?

Pathology: topographical progression

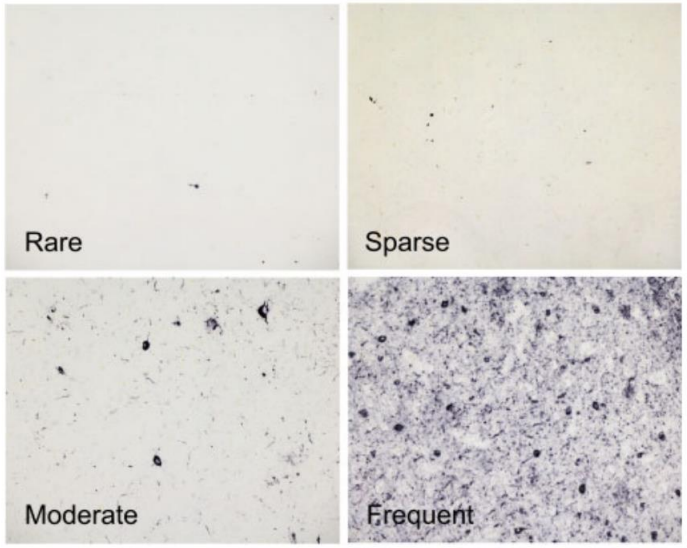
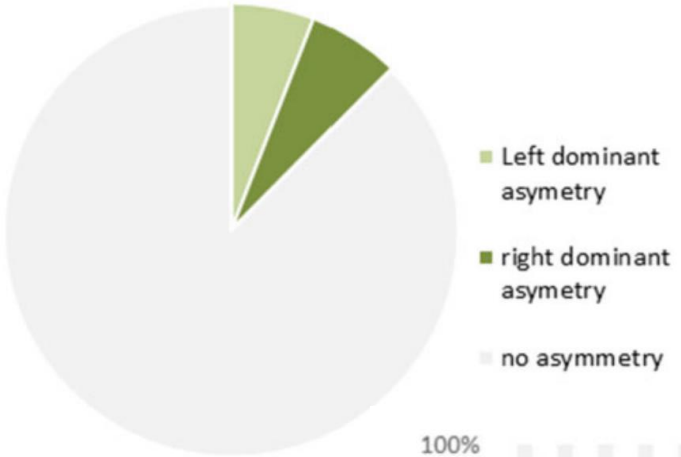
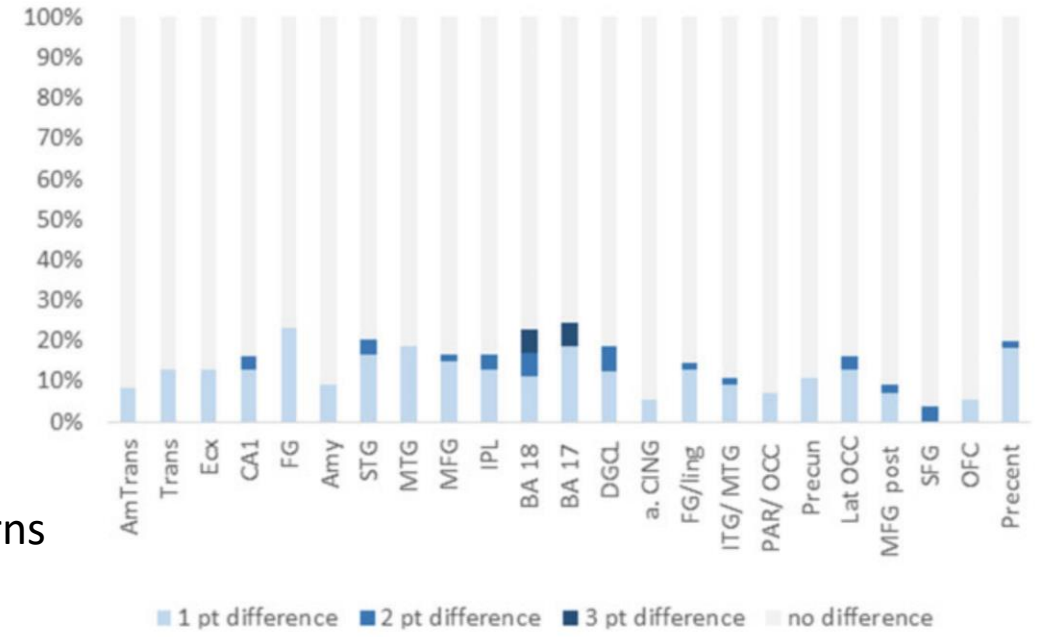


FIGURE 1. Density template for AT8 tau pathology density scoring. Each region of interest was graded for the density of tau NFT pathology as being either absent (Score 0), uncommon (Score 1), sparse (Score 2), moderate (Score 3), or frequent (Score 4).



Frequent mild (82% of cases) and occasional moderate (32%) interhemispheric density discrepancies were observed



Asymmetry and atypical tau topographical progression patterns may be associated with atypical AD clinical presentations

Tremblay et al J Neuropathol Exp Neurol 2022

Pathology: antemortem-to-postmortem

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MRI-to-postmortem correlations in atypical AD:

MRI-based atrophy subtypes differ in neuropathologic features?

Pathology: antemortem-to-postmortem

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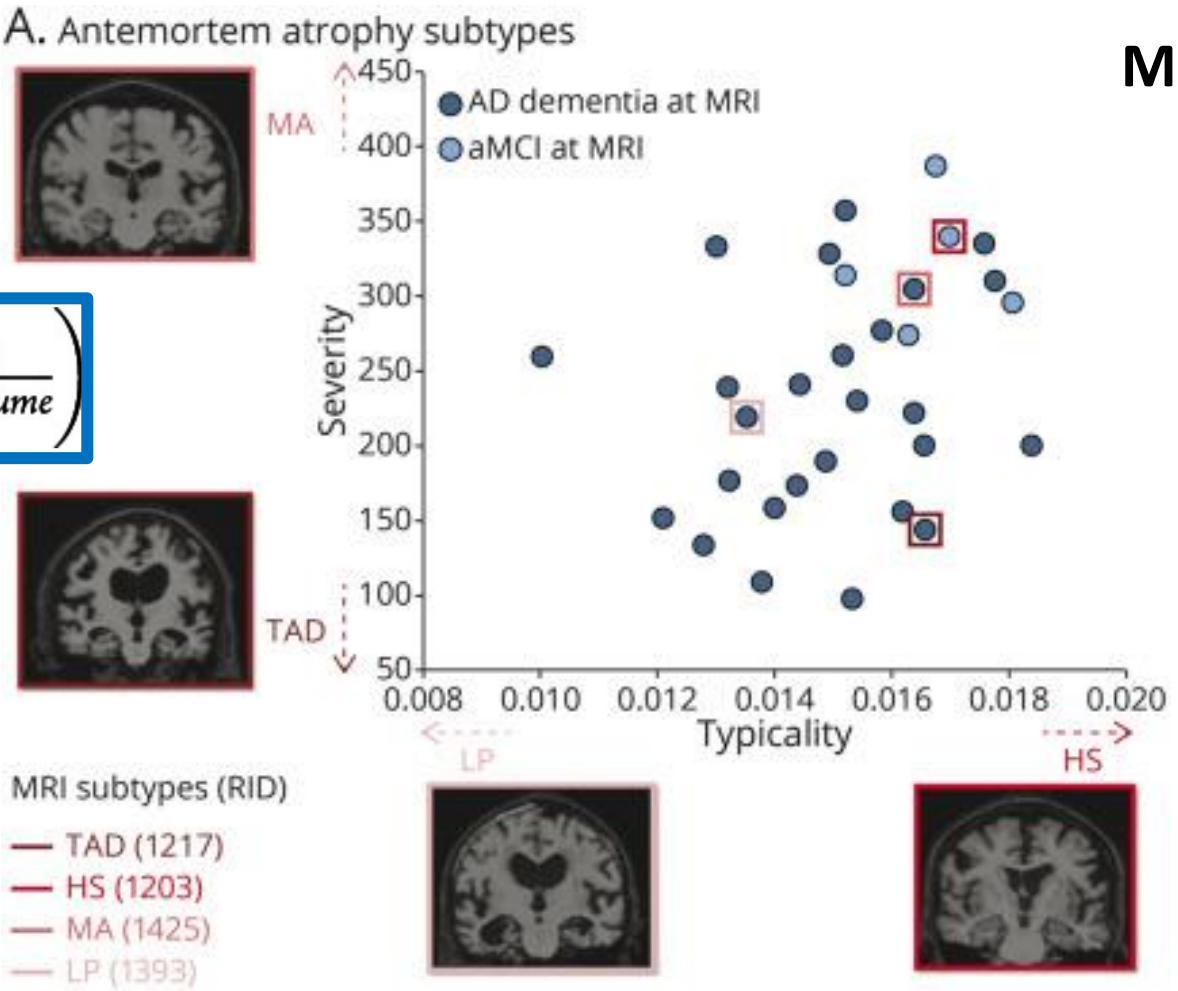
MINIMAL ATROPHY

$$\left(\frac{\textit{total brain volume}}{\textit{cerebrospinal fluid volume}}\right)$$

TYPICAL AD



MRI-Based Heterogeneity

Severity vs. Typicality

$$\left(\frac{\textit{hippocampal volume}}{\textit{cortical volume}}\right)$$

LIMBIC PREDOMINANT ⟷ **HIPPOCAMPAL SPARING**

Pathology: antemortem-to-postmortem

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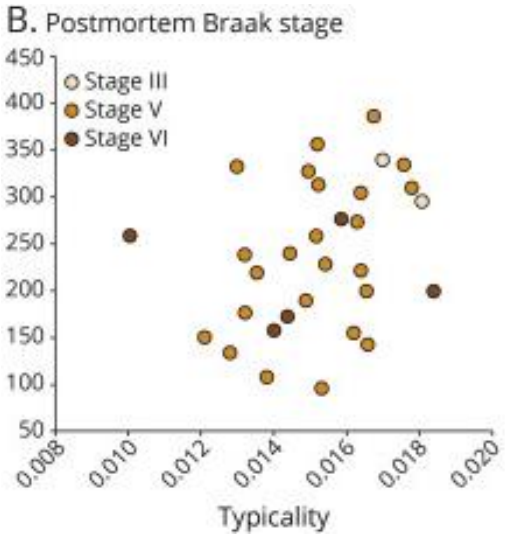
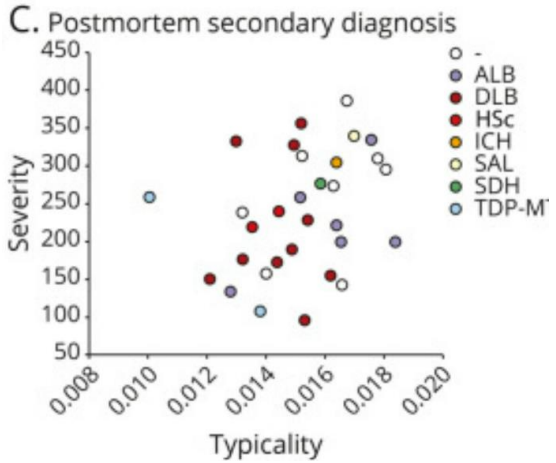
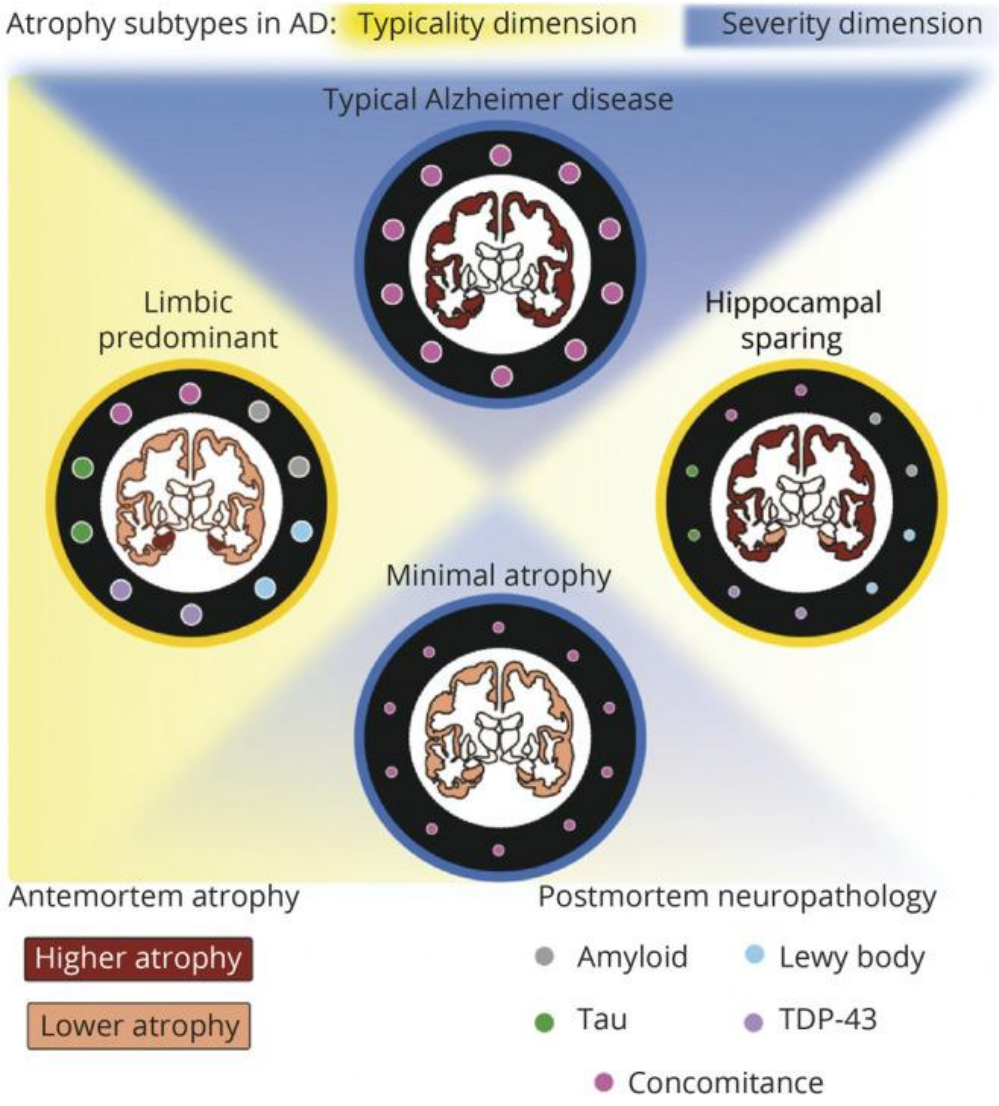
Postmortem: Amyloid, Tau, Alpha syn, TDP-43 Concomitance





Antemortem **typicality** = **negatively** associated with neuropathology severity and concomitance of pathologies

Antemortem **severity** = **negatively** associated with pathologies concomitance



Pathology: antemortem-to-postmortem

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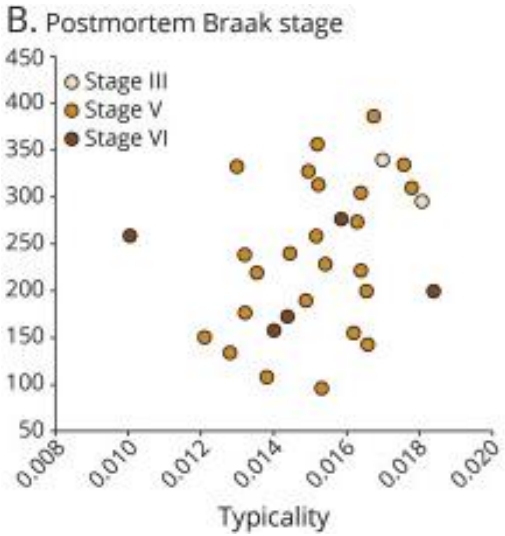
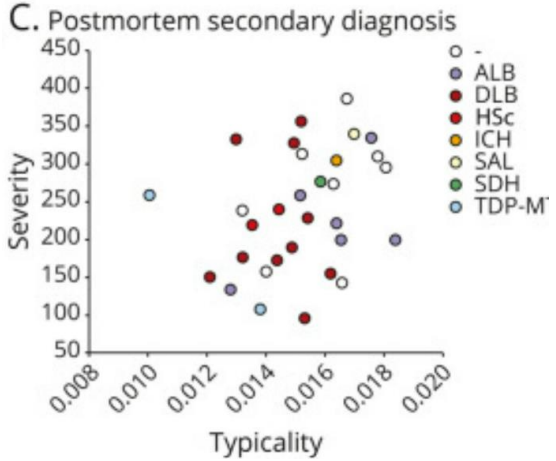
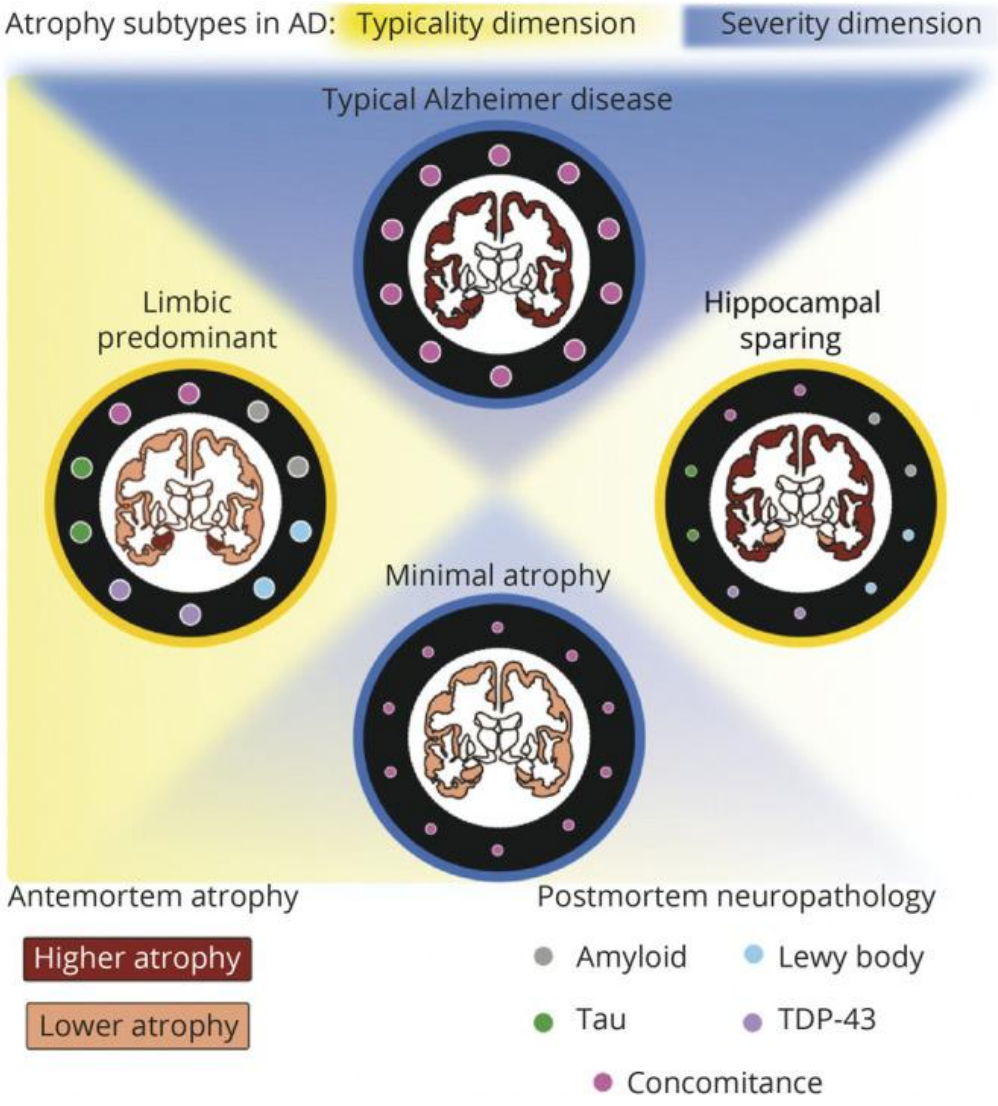
Postmortem: Amyloid, Tau, Alpha syn, TDP-43 Concomitance







Limbic-predominant AD and typical AD subtypes with similar pathways, more vulnerable than **hippocampal-sparing** patterns

Mohanty et al Neurology 2022

2022 Summary

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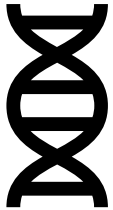
BIOMARKERS

- Identification of neurodegeneration-specific clinical outcome
- In vivo tracking of tau progression
- Complementary diagnostic biomarkers

GENETICS



- APOE effects on brain changes and clinical outcome
- Interaction effects with sex
- TREM2 associated with different clinical variants and pathology

PATHOLOGY

- Regional-specific vulnerability
- Differential tau spreading
- Postmortem validation of in vivo patterns

Next challenges…

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1. Fluid markers in atypical AD

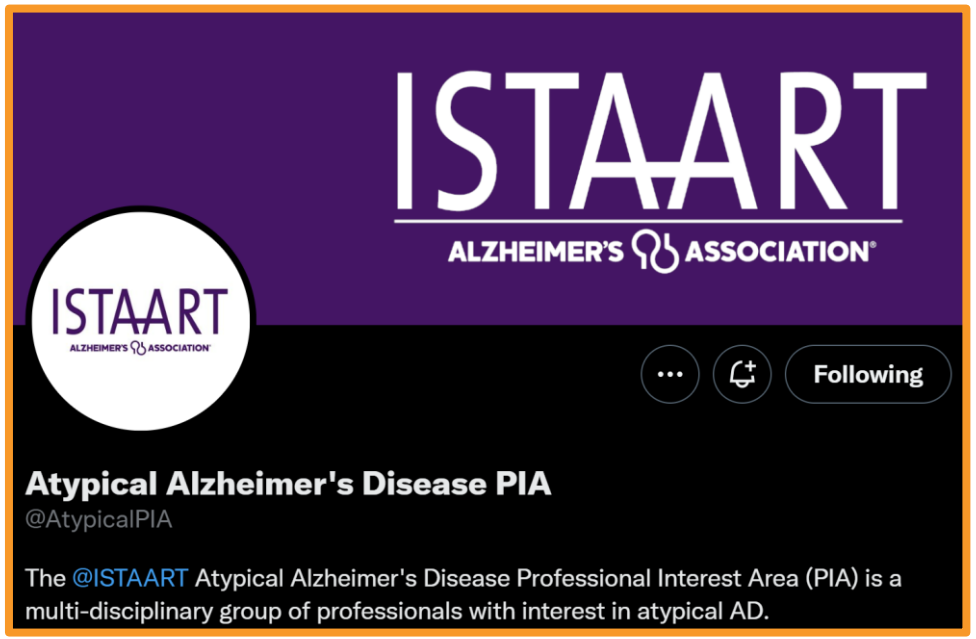
2. Differential regional vulnerability (i.e. networks, inflammation)

3. Under-investigated influencing factors (i.e. brain development)

4. Clinical trials involving atypical AD: stratification and outcomes

Thank you!

mm2243@cam.ac.uk
@M_Malpetti



Baayla Boon
Eduardo Zimmer
Gil Rabinovici
James Rowe
Jennifer Whitwell
John O'Brien
Jonathan Schott
Keir Yong
Matthias Brendel
Michael Ewers
Michael Scholl
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Renaud La Joie
Rik Ossenkopele
Rosaleena Mohanty

RACE AGAINST DEMENTIA

Alzheimer's Research UK

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Ask the experts!

Baayla Boon

Jennifer Whitwell

Rosaleena Mohanti

Keir Yong