

Update on Diagnosis and Therapeutics in Alzheimer's Disease and Related Disorders

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VA



U.S. Department of Veterans Affairs
Veterans Health Administration
Geriatric Research, Education, and Clinical Centers

UW Medicine
SCHOOL OF MEDICINE

Disclosures

- NIH/NINDS/NIA
- Lewy Body Dementia Association
- Michael J Fox Foundation
- In Kind Support
 - GE Healthcare



VA



U.S. Department of Veterans Affairs
Veterans Health Administration
Geriatric Research, Education, and Clinical Centers

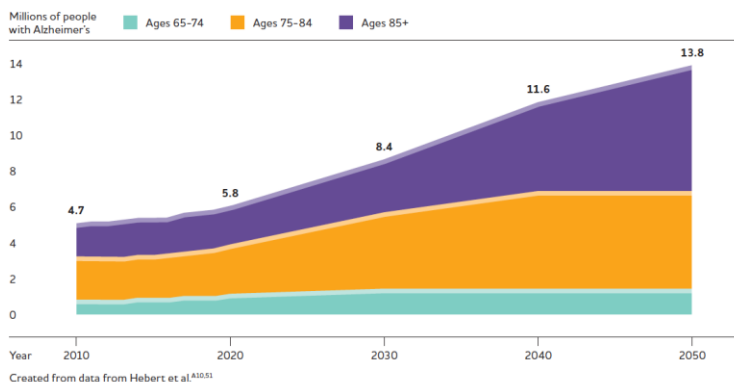
UW Medicine
SCHOOL OF MEDICINE

Overview

- Dementias
 - Definitions/Terms
 - Biology (pathology) of dementia
- Diagnostics
 - Clinical, Imaging, Biomarkers
- Treatments
 - Symptomatic
 - Disease modifying
- Challenging Case

FIGURE 4

Projected Number of People Age 65 and Older (Total and by Age)
in the U.S. Population with Alzheimer's Dementia, 2010 to 2050

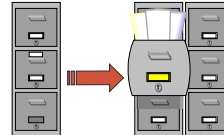


"Facts and Figures 2019, Alzheimer's Association.

What is “Normal” Aging?

- **Memory**

- “Working”
 - Attention, retrieval
- Short term
 - Encoding for storage
- Long term
 - Retrieval



Working ⇒ **Short Term** ⇒ **Long Term**

Mild Cognitive Impairment (MCI)

NIA-AA Core Clinical Criteria:

- Concern regarding a **change in cognition**
 - Patient, informant, clinician
- **Impairment** in one or more cognitive/behavioral domains
 - Memory, executive function, attention, language, visuospatial
- **Preservation of independence in functional abilities**
 - May take more time, be less efficient, make more errors
 - “...generally maintain their independence of function in daily life with minimal aids or assistance”

Albert et al., *Alzheimer's & Dementia*, 1-10, 2011.

Dementia

NIA/AA:

“Dementia is diagnosed when there are cognitive or behavioral (neuropsychiatric) symptoms that: ”

- ...a **decline from previous levels** of functioning...
- ...Cognition/behavior involve at least two cognitive domains:
 - Memory, executive function, visuospatial, language, behavior
- Interferes with **ability to function** at work or at usual activities

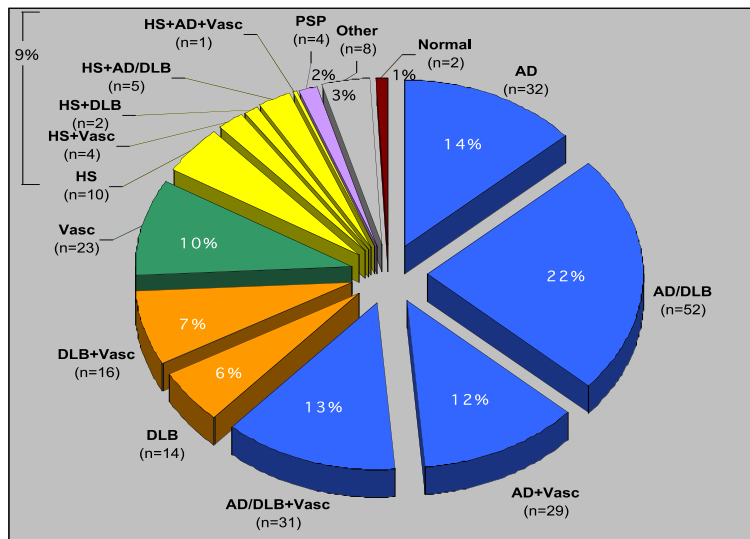
McKhann et al., *Alzheimer's & Dementia*, 1-7, 2011.

Definitions and Nomenclature

Syndrome does not equal Disease

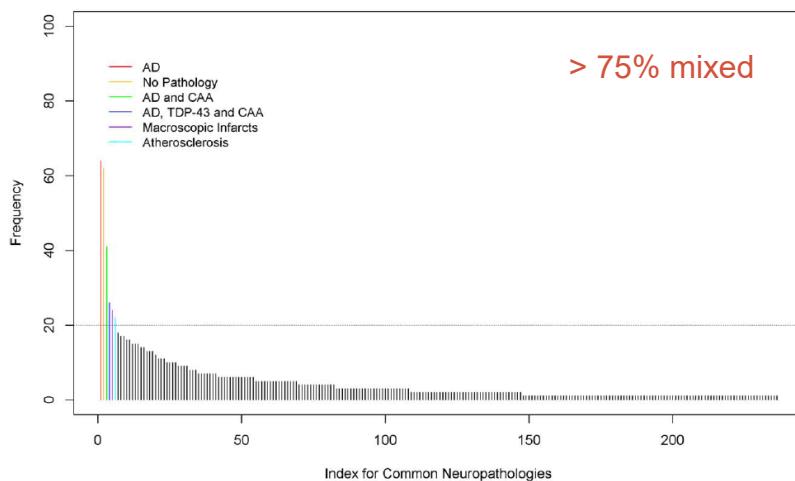
- Headache, cancer, pain, etc.
- Why should brain disease be different?
- Most neurologic aging syndromes driven by “where not what”
 - Mixed brain pathology the rule in dementia

Dementia is usually mixed



Leverenz et al, JAMA Neurol, 2002; Riekse et al JAGS, 2004; Leverenz et al, Brain Path, 2008

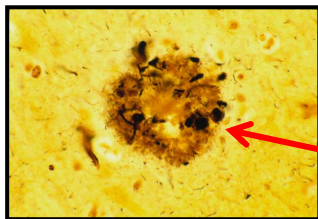
Dementia is more commonly mixed



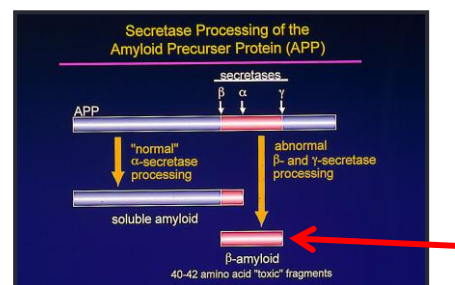
Boyle PA et al, Ann Neurol, 83:74-83, 2018.

What is Alzheimer's Disease?

Alzheimer's Disease- Pathology



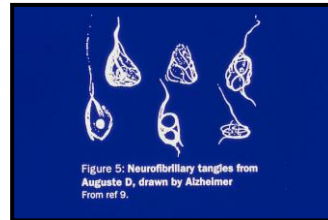
*Beta-Amyloid Protein
"Plaque"*



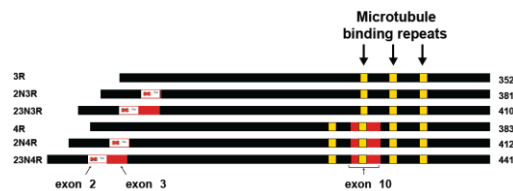
Chromosome 21

Alzheimer's Disease - Pathology

*Neurofibrillary Tangles
“Tangles”*



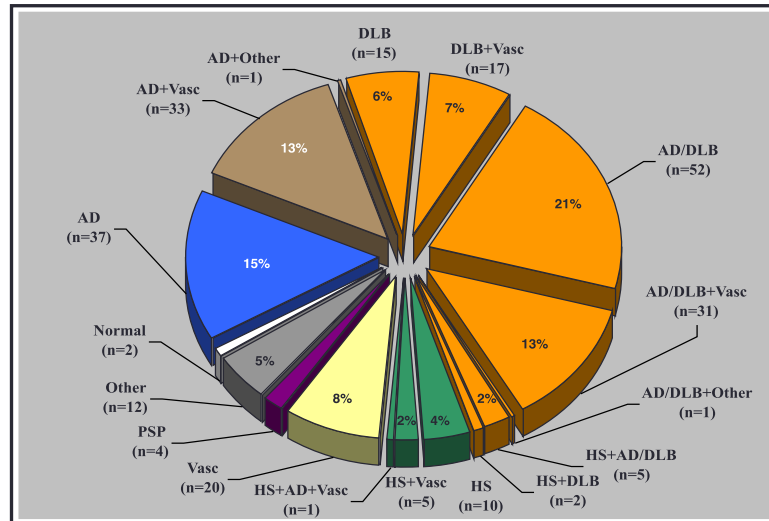
*Tau Protein
Chromosome 17*



The Lewy Body Dementias

*Parkinson's Disease Dementia
Dementia with Lewy Bodies*

Neuropathology of Community Based Dementia



Leverenz et al, JAMA Neurol, 2002; Riekse et al JAGS, 2004; Leverenz et al, Brain Path, 2008



Lewy Body Dementias

- 1.4 Million Americans
 - DLB, PDD, and LBV-AD
- Clinical care
 - Multiple visits before diagnosis, misdiagnosis
 - Inappropriate care (e.g., antipsychotics)
 - Patient and family distress
 - Access to long term care
- Research
 - Consistent and coordinated research and funding (DLBC)



Consensus Criteria for Dementia with Lewy Bodies

1. Dementia
2. Core features (2 = “probable”, 1 = “possible”)
 - a. fluctuating cognition, attention, alertness
 - b. recurrent visual hallucinations
 - c. spontaneous features of parkinsonism
 - d. *REM sleep behavior disorder*
3. *Indicative Biomarkers* (plus one core = “probable” DLB)
 - a. Low dopamine transporter uptake (PET/SPECT)
 - b. Abnormal MIBG myocardial scintigraphy
 - c. PSG confirmation of RBD
4. One year rule for PDD vs. DLB

McKeith et al, Neurology, 2017.

Formed Visual Hallucinations



Parkinson's Disease

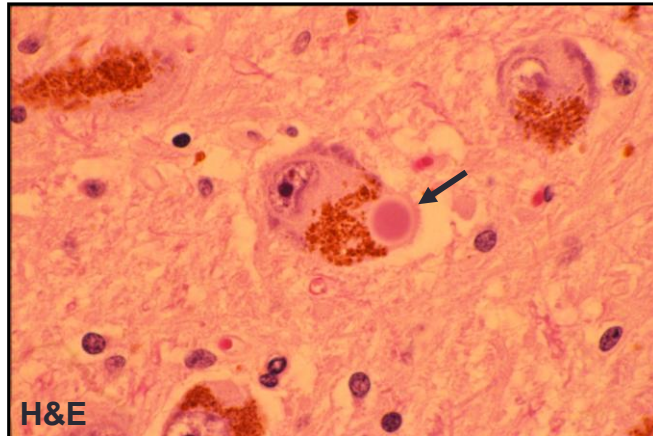
- Tremor (resting)
- Rigidity
- Bradykinesia
- Postural instability



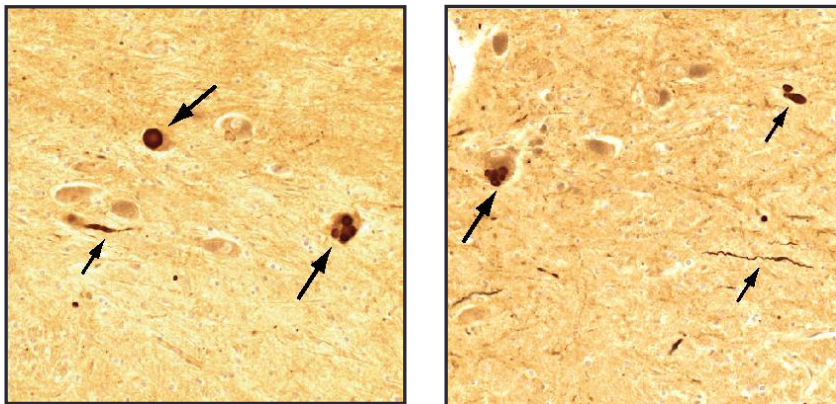
Sleep - RBD

- **REM Sleep Behavior Disorder (RBD)**
 - strongly associated with Lewy body pathology
 - “acting out dreams”
 - responds to clonazepam, melatonin
- **Other sleep disturbance**
 - excessive daytime sleepiness
 - sleep apnea, periodic leg movements, restless leg
- **Frequently more than one disorder**

Pathology in Parkinson's Disease



Pathology in Parkinson's Disease



α -synuclein IHC

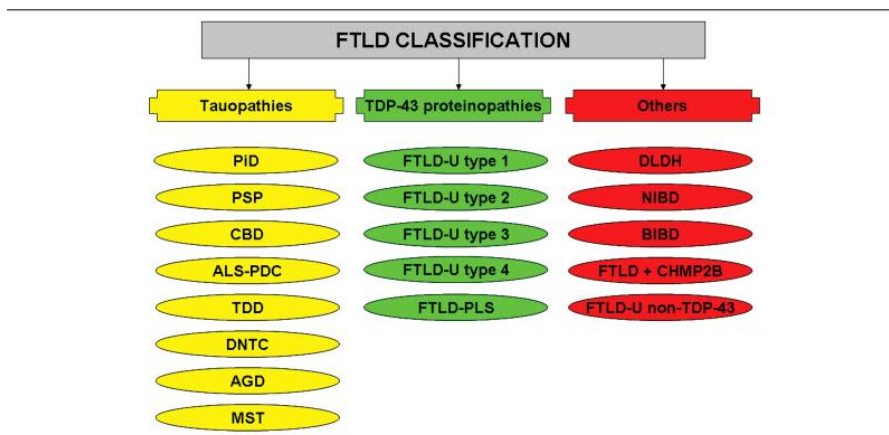
“Frontotemporal Dementia”

Current (2008) Proposed Clinical Syndromes

- **bvFTD**
- **Language syndromes**
 - Semantic
 - Progressive nonfluent aphasia
 - Logopenic aphasia
- **FTD – MND**
- **Parkinsonian disorders**

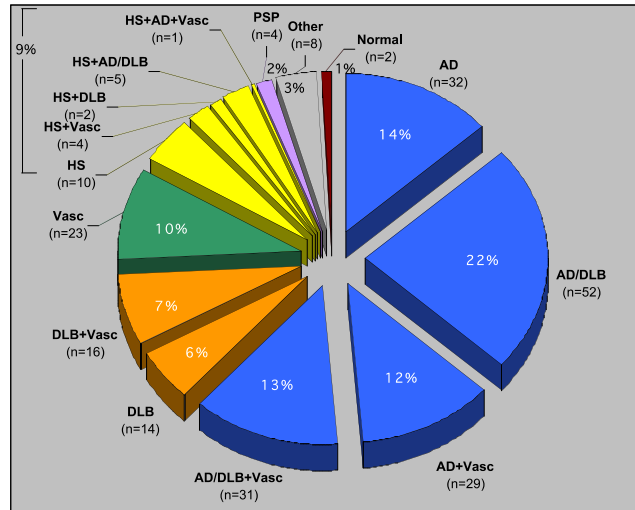
“Frontotemporal Lobar Degeneration”

Current (2008) Proposed Neuropathologic Types



Josephs KA, Ann Neurol, 64:4-14, 2008

Community Based Dementia



Hippocampal Sclerosis (LATE)

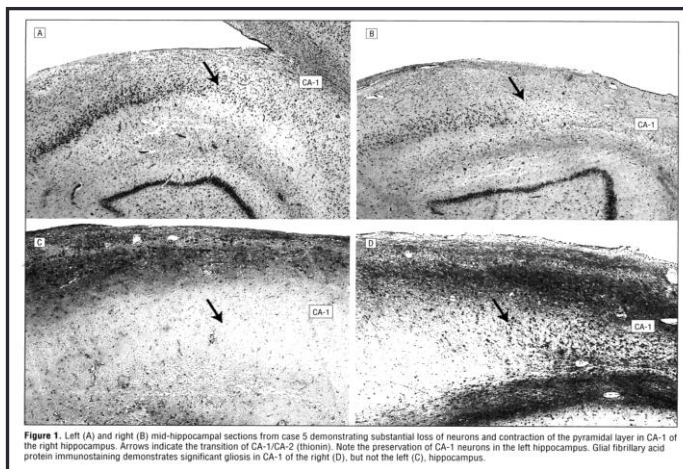
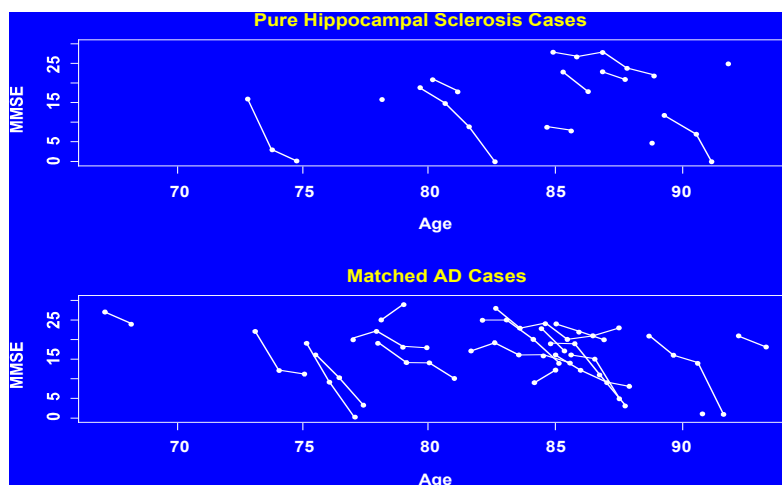


Figure 1. Left (A) and right (B) mid-hippocampal sections from case 5 demonstrating substantial loss of neurons and contraction of the pyramidal layer in CA-1 of the right hippocampus. Arrows indicate the transition of CA-1 to CA-2 (rhombus). Note the preservation of CA-1 neurons in the left hippocampus. Glial fibrillary acid protein immunostaining demonstrates significant gliosis in CA-1 of the right (D), but not the left (C), hippocampus.

Leverenz et al, Arch Neurol, 2002

Hippocampal Sclerosis



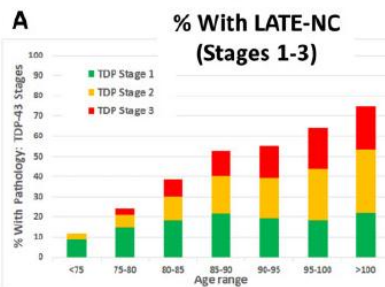
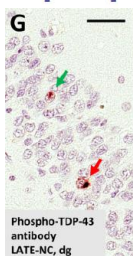
doi:10.1093/brain/awz099

BRAIN 2019; 142; 1503–1527 | 1503

BRAIN
A JOURNAL OF NEUROLOGY

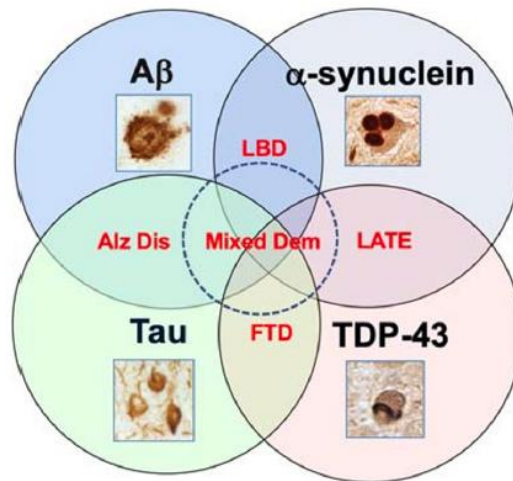
REVIEW

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



Nelson PT et al, Brain, 2019

Laboratory Testing for Mixed Pathology?



Kwon S, Iba M, Kim C, Masliah E, Review, Immunotherapeutics, 2020

Laboratory Testing - CSF/Plasma

TABLE 1 Biomarkers for Alzheimer's disease-related pathologies

Biomarker	Matrix	Methods	Process
A β 42/40 ratio	CSF and plasma	Mass spectrometry assays Immunoassays	Cerebral A β pathology
p-tau	CSF and plasma/serum	Mass spectrometry assays Immunoassays	Neuronal tau phosphorylation and secretion
NfL	CSF and plasma/serum	Immunoassays	Neurodegeneration
GFAP	CSF and plasma/serum	Immunoassays	Astrocytic activation
α -Synuclein seeds	CSF	Assays based on seeded amplification	α -Synuclein pathology
TDP-43 seeds	CSF	Assays based on seeded amplification	TDP-43 pathology

Abbreviations: A β , amyloid beta; CSF, cerebrospinal fluid; GFAP, glial fibrillary acidic protein; NfL, neurofilament light; p-tau, phosphorylated tau; TDP-43, TAR DNA-binding protein 43.

Zetterberg H, Review, Alzheimer's & Dementia, 2022

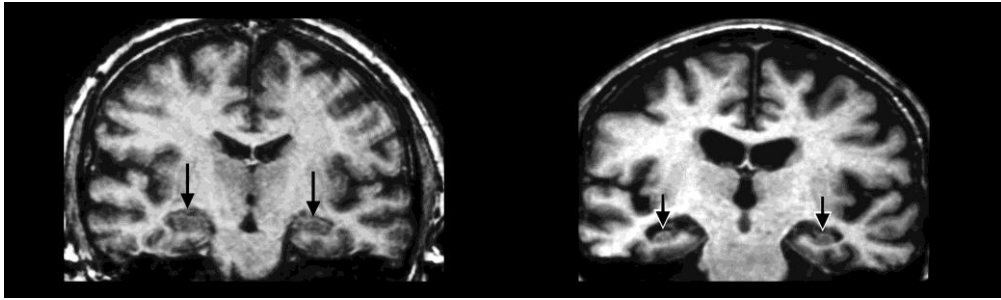
The Office Assessment of Dementia

- A careful history from family member or other informed source.
- Quantified assessment of cognitive function
 - MMSE, MoCA, neuropsychological testing
- Neurological exam
- Laboratory/Imaging/Biomarkers
- Repeat assessments

Laboratory Testing

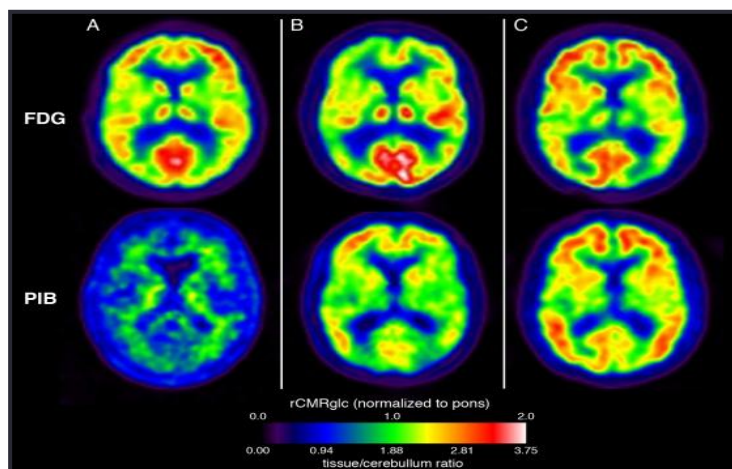
- **Blood**
 - CBC, chemistry, TSH
 - B12, folate, syphilis serology, inflammatory markers
 - Plasma A β , tau, p-tau
 - *Genetic testing* (genetic counseling), APOE, PS1, PS2, APP*
- **Cerebrospinal fluid**
 - A β _{42/40}, tau, p-tau, 14-3-3, inflammatory markers, autoimmune markers
 - Aggregated proteins (RT-QuIC): synuclein, (*TDP-43 or tau?*)
- **Imaging**
 - Structural (CT, MRI with hippocampal volumetrics)
 - SPECT, FDG-PET (where not what)
 - Amyloid imaging
 - Tau, alpha-synuclein, inflammatory – under development

Laboratory Testing - Imaging



Hippocampus - Volume

Laboratory Testing-Imaging

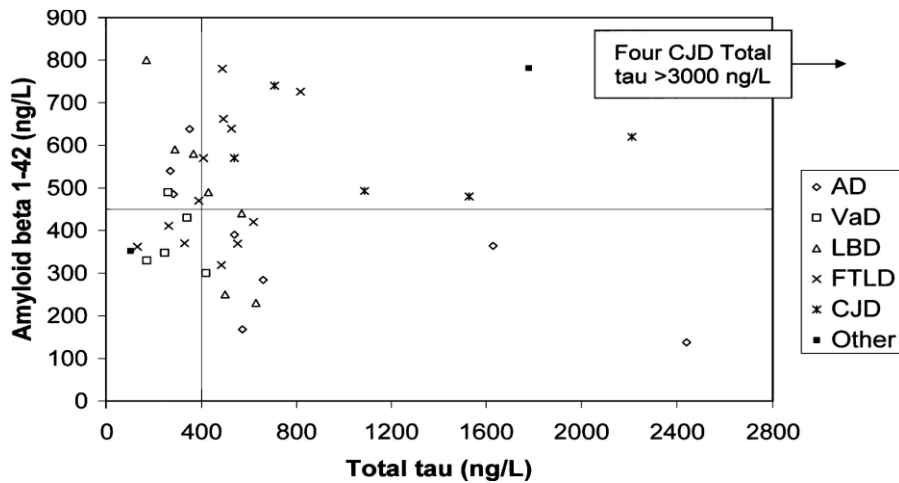


Glucose
(FDG-PET)

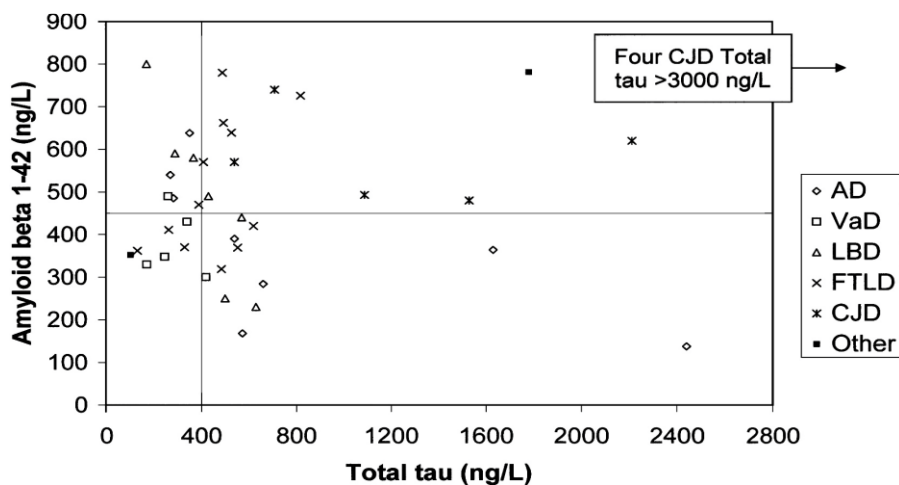
Amyloid

Foster NL Neuroimaging in Weiner and Lipton., 2009: p. 105-136.

Laboratory Testing - CSF



Laboratory Testing-CSF



BRIEF COMMUNICATION

Alpha-synuclein RT-QuIC in the CSF of patients with alpha-synucleinopathies

Graham Fairfoul¹, Lynne I. McGuire¹, Suvankar Pal^{1,2}, James W. Ironside¹, Juliane Neumann³, Sharon Christie⁴, Catherine Joachim⁴, Margaret Esiri⁴, Samuel G. Evetts³, Michal Rolinski³, Fahd Baig³, Claudio Ruffmann³, Richard Wade-Martins⁵, Michele T. M. Hu³, Laura Parkkinen³ & Alison J. E. Green¹

Groveman et al. *Acta Neuropathologica Communications* (2018) 6:7
DOI: 10.1186/s40478-018-0508-2

Acta Neuropathologica
Communications

METHODOLOGY ARTICLE

Open Access

Rapid and ultra-sensitive quantitation of disease-associated α-synuclein seeds in brain and cerebrospinal fluid by αSyn RT-QuIC

Bradley R. Groveman^{1†}, Christina D. Orr^{1†}, Andrew G. Hughson¹, Lynne D. Raymond¹, Gianluigi Zanuso², Bernardino Ghetti³, Katrina J. Campbell¹, Jiri Safar⁴, Douglas Galasko^{5*} and Byron Caughey^{1*}



Fairfoul G et al, *Ann Clin Transl Neurol*, 3:812-18, 2016
Groveman BR et al, *Acta Neuropath Comm*, 2018

Laboratory Testing-CSF/Plasma

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α-Synuclein seeds	CSF	Assays based on seeded amplification	α-Synuclein pathology
TDP-43 seeds	CSF	Assays based on seeded amplification	TDP-43 pathology

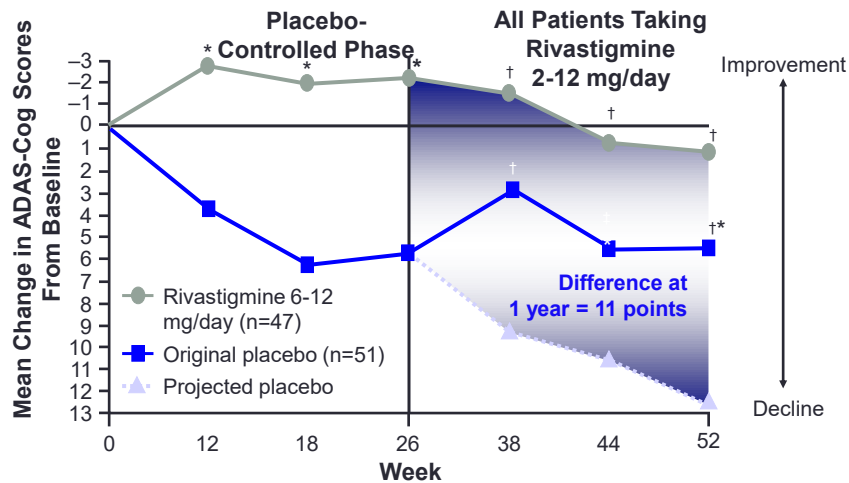
Abbreviations: Aβ, amyloid beta; CSF, cerebrospinal fluid; GFAP, glial fibrillary acidic protein; NfL, neurofilament light; p-tau, phosphorylated tau; TDP-43, TAR DNA-binding protein 43.

Treating the Dementias

Approved Treatments for Dementia Cholinergic Therapy

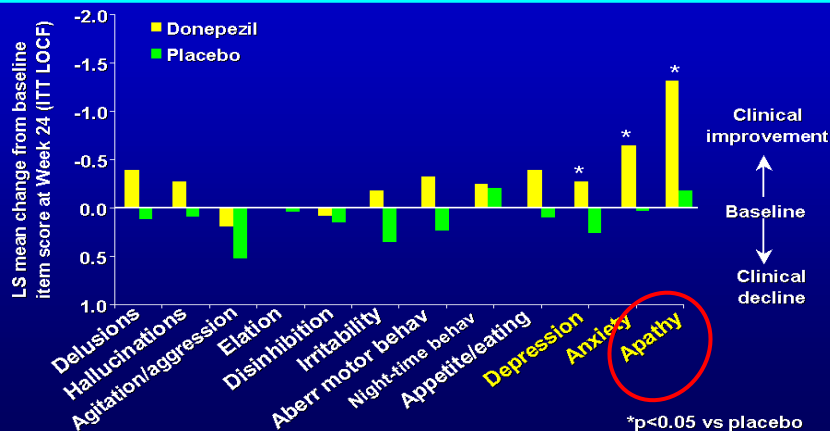
- **Cholinesterase inhibitors**
 - donepezil (Aricept)
 - rivastigmine (Exelon)
 - galantamine (Razadyne)

Approved Treatments for Dementia Cholinergic Therapy



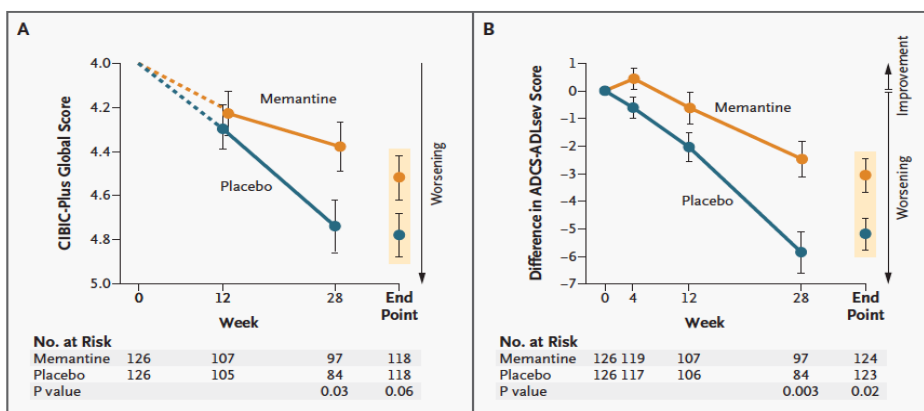
$P < 0.001$ vs placebo; $^{\dagger}P < 0.001$ vs projected placebo; $^{\ddagger}P < 0.05$ vs projected placebo. Observed-case analysis.
ADAS-Cog = Alzheimer's Disease Assessment Scale-Cognitive Subscale. (MMSE 10-17)

MSAD Behavior: NPI Domains



Approved Treatments for Dementia

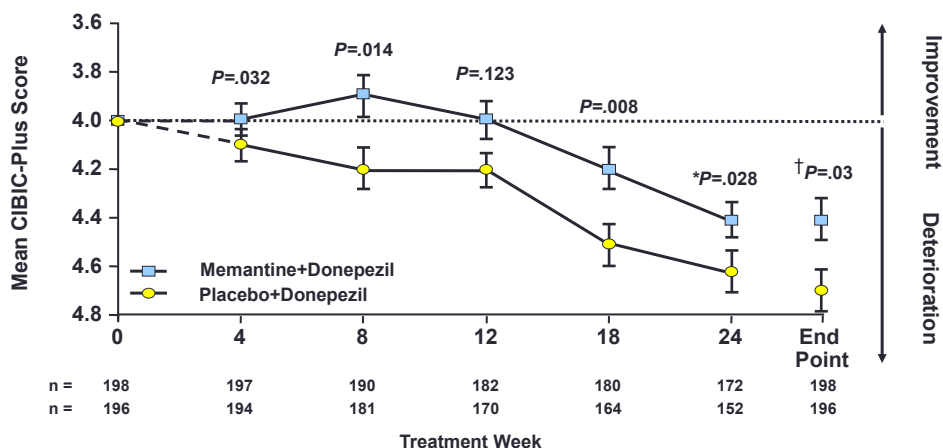
Memantine (Namenda)



Reisberg, et al, NEJM, 1333-41, 2003.

Approved Treatments for Dementia

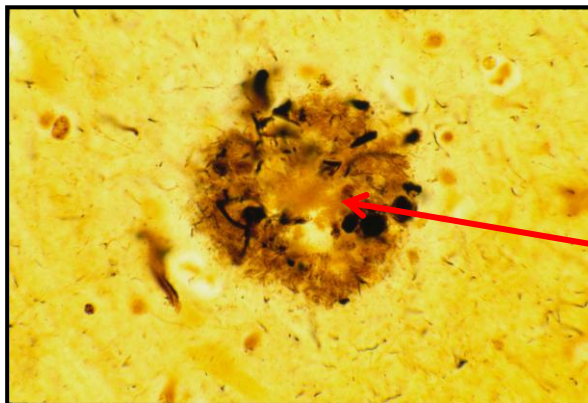
Memantine (Namenda) & Donepezil (Aricept)



*OC analysis. †LOCF analysis.
Source: Data on file, Forest Laboratories, Inc.

The New Disease Modifying Therapies for Alzheimer's Disease

Alzheimer's Disease – Pathology



*Silver Stain:
"Neuritic Plaques"*

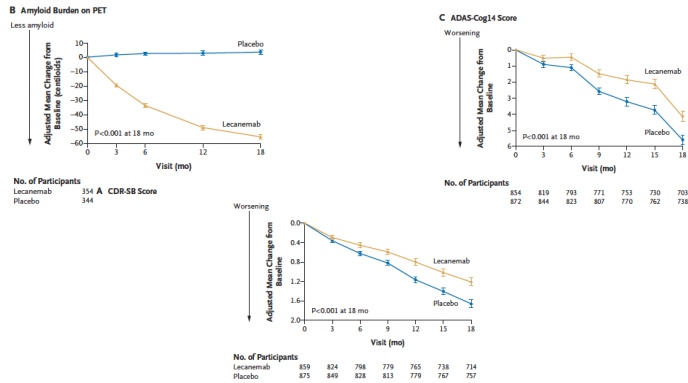
*Beta Amyloid Protein
"BAP"*

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 5, 2023 VOL. 388 NO. 1

Lecanemab in Early Alzheimer's Disease

C.H. van Dyck, C.J. Swanson, P. Aisen, R.J. Bateman, C. Chen, M. Gee, M. Kanekiyo, D. Li, L. Reyderman, S. Cohen, L. Froelich, S. Katayama, M. Sabbagh, B. Vellas, D. Watson, S. Dhadda, M. Irizarry, L.D. Kramer, and T. Iwatsubo



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Table 3. Adverse Events.*

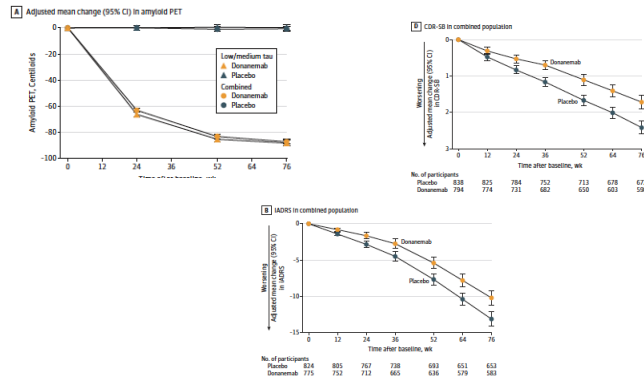
Event	Lecanemab (N=898)	Placebo (N=897)
Overall — no. (%)		
Any adverse event	798 (88.9)	735 (81.9)
Adverse event related to lecanemab or placebo†	401 (44.7)	197 (22.0)
Serious adverse event	126 (14.0)	101 (11.3)
Death	6 (0.7)	7 (0.8)

ARIA-E according to ApoE ε4 genotype — no./total no. (%)

ApoE ε4 noncarrier	15/278 (5.4)	1/286 (0.3)
ApoE ε4 carrier	98/620 (15.8)	14/611 (2.3)
ApoE ε4 heterozygote	52/479 (10.9)	9/478 (1.9)
ApoE ε4 homozygote	46/141 (32.6)	5/133 (3.8)
ARIA-H — no. (%)		
Microhemorrhage	155 (17.3)	81 (9.0)
Superficial siderosis	126 (14.0)	68 (7.6)
Macrohemorrhage	50 (5.6)	21 (2.3)
Symptomatic ARIA-H‡	5 (0.6)	1 (0.1)
Isolated ARIA-H: no concurrent ARIA-E	6 (0.7)	2 (0.2)
	80 (8.9)	70 (7.8)

Donanemab in Early Symptomatic Alzheimer Disease The TRAILBLAZER-ALZ 2 Randomized Clinical Trial

John R. Sims, MD; Jennifer A. Zimmer, MD; Cynthia D. Evans, PhD; Ming Lu, MD, MS, MPH; Paul Ardayfio, PhD; JonDavid Sparks, PhD; Alette M. Wessels, PhD; Sergey Shcherbinin, PhD; Hong Wang, PhD; Emel Serap Monkul Nery, MD; Emily C. Collins, PhD; Paul Solomon, PhD; Stephen Salloway, MD; Liana G. Apostolova, MD; Oskar Hansson, MD, PhD; Craig Ritchie, MD, PhD; Dawn A. Brooks, PhD; Mark Mintun, MD; Daniel M. Skovronsky, MD, PhD; for the TRAILBLAZER-ALZ 2 Investigators



Donanemab in Early Symptomatic Alzheimer Disease The TRAILBLAZER-ALZ 2 Randomized Clinical Trial

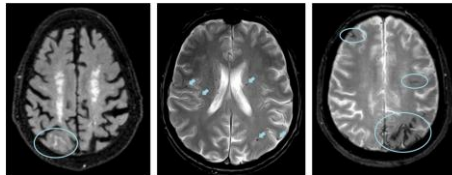
John R. Sims, MD; Jennifer A. Zimmer, MD; Cynthia D. Evans, PhD; Ming Lu, MD, MS, MPH; Paul Ardayfio, PhD; JonDavid Sparks, PhD; Alette M. Wessels, PhD; Sergey Shcherbinin, PhD; Hong Wang, PhD; Emel Serap Monkul Nery, MD; Emily C. Collins, PhD; Paul Solomon, PhD; Stephen Salloway, MD; Liana G. Apostolova, MD; Oskar Hansson, MD, PhD; Craig Ritchie, MD, PhD; Dawn A. Brooks, PhD; Mark Mintun, MD; Daniel M. Skovronsky, MD, PhD; for the TRAILBLAZER-ALZ 2 Investigators

Table 3. Summary of Adverse Events (AEs) by Treatment Group

Event	Donanemab (n = 853) ^a	Placebo (n = 874) ^a
Overview of AEs, No. (%)		
Death ^b	16 (1.9) ^c	10 (1.1)
Death considered related to treatment ^d	3 (0.4)	1 (0.1)
Participants with ≥1 serious AE ^e	148 (17.4)	138 (15.8)
Treatment discontinuations due to AEs	112 (13.1)	38 (4.3)
Study discontinuations due to AEs	69 (8.1)	32 (3.7)
Participants with ≥1 treatment-emergent AE ^f	759 (89.0)	718 (82.2)
Overview of ARIA ^g		
Microhemorrhage or superficial siderosis present at baseline, No. (%)	124 (14.5)	161 (18.4)
ARIA-E by APOE ε4 allele status, No./total No. (%)		
Noncarrier	40/255 (15.7)	2/250 (0.8)
Heterozygous carrier	103/452 (22.8)	9/474 (1.9)
Homozygous carrier	58/143 (40.6)	5/146 (3.4)

Disease Modifying Therapies

- **Mild Cognitive Impairment or Mild Dementia**
- **Confirmed Alzheimer's Pathology**
 - *Amyloid imaging or CSF amyloid/tau*
- **Genetic Testing**
 - *APOE ϵ 2/3/4 associated risks for ARIA*
 - *Amyloid-Related Imaging Abnormalities risk*
- **Management decisions based on MRI for ARIA E/H, symptoms**



ten Kate M, et al, *Alz Res Therapy*, 2018.

A Challenging Case

Clinical Presentation

- **Clinical Presentation**

- 70 y.o. male presented with one to two years of neurologic symptoms:
 - Difficulty using TV remote, some recall issues and a slower gait and stooped posture
 - Progression included VH (seeing his mother and others, some visual misperceptions)
 - Question of acting out dreams

Dementia with Lewy
Bodies Consortium

Clinical Presentation

- **Examination**

- Masked facies, reduced eyeblink
- Mild increased tone, slowed symmetric RAMs
- Gait - Slow, stooped, decreased left arm swing

- **Cognition**

- MoCA - 14/30

- **Imaging**

- Outside MRI with mild atrophy and WM changes

- **Plan**

- Start donepezil
- Enrolled in research observational studies

Dementia with Lewy
Bodies Consortium

Dementia with Lewy Bodies Consortium

READING Passages of texts subject to test ATTENTION Read each of the text in 10 minutes	READING Passages of texts subject to test ATTENTION Read each of the text in 10 minutes	READING Passages of texts subject to test ATTENTION Read each of the text in 10 minutes	READING Passages of texts subject to test ATTENTION Read each of the text in 10 minutes
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	Person	Gender	Age	Marriage
1	Dr. ...	...	...	...
2	Dr. ...	...	...	...
3	Dr. ...	...	...	...
4	Dr. ...	...	...	...
5	Dr. ...	...	...	...
6	Dr. ...	...	...	...
7	Dr. ...	...	...	...
8	Dr. ...	...	...	...
9	Dr. ...	...	...	...
10	Dr. ...	...	...	...
11	Dr. ...	...	...	...
12	Dr. ...	...	...	...
13	Dr. ...	...	...	...
14	Dr. ...	...	...	...
15	Dr. ...	...	...	...
16	Dr. ...	...	...	...
17	Dr. ...	...	...	...
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Dementia with Lewy Bodies Consortium

21	
22	
Total: 7	Total: 9

Present and Past Events	
Current president	"he just died" → (H.W. Bush) ^{meaning}
Previous president	"he did Mr. Bush"
President during Watergate	?
9/11/01	?
12/7/41	X
Score:	0.5 (5)

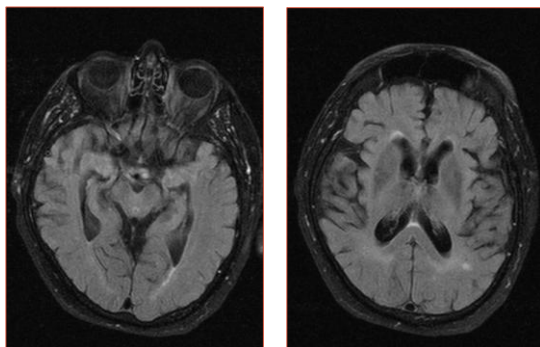
Judgment	
"Those who live in glass houses shouldn't throw stones."	They're wrong, & that's not the answer
"Rome wasn't built in a day."	unusable

A Challenging Case

Thoughts?
Next Steps?

Dementia with Lewy
Bodies Consortium

Imaging - MRI



Initial

Dementia with Lewy
Bodies Consortium

6 Month Visit

- **Interval History**
 - Increased fluctuations and confusion, apathy, no VH
 - No RBD-like sxs, hypersomnia (up to 17 hours every 24)
 - Gait
 - Slow, stooped, decreased left arm swing
- **Evaluation**
 - *UPDRS, Cognitive assessments, blood/CSF/MRI*

Dementia with Lewy
Bodies Consortium

6 Month Visit

- **UPDRS III**
 - **Score 23, L>R, no resting tremor**
 - Slight/Mild
 - Speech, facial expression, rigidity and hand movements (UE, symmetric), gait, posture, bradykinesia, postural tremor, kinetic tremor
 - finger tapping/pronation-supination, toe tapping L only
 - H&Y 2 (bilateral involvement)
 - Schwab & England ADL 70 of 100
 - Not completely independent, takes four times as long, large part of day with chores

Dementia with Lewy
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6 Month Visit

- **Delusions – frequent**
- **Hallucinations – mild**
- Agitation – minimal
- Depression – absent
- Anxiety – absent
- Elation/Euphoria – absent
- **Apathy/Indifference – severe**
- Disinhibition – minimal
- Irritability/Lability – minimal
- Aberrant motor behavior – minimal
- **Sleep – moderate**
- Appetite/Eating disorder – minimal

Dementia with Lewy
Bodies Consortium

6 Month Visit

- Noise Pareidolia – normal (20/20)
- RBD Sleep Questionnaire – negative
- **U Penn Smell Identification Test (UPSIT)**
 - 16 (normal 34 or higher in males)
- **CDR Global 2.0**
- **Craft Story**
 - **Immediate 8/8**
 - **Delayed 4/5**

Dementia with Lewy
Bodies Consortium

DLBC Baseline Visit - Neuropsych

- Noise Pareidolia – normal (20/20)
- Trails A - 41 sec
- **Trails B – unable to perform**
- **MINT – 27 (max 32)**
- **Fluency**
 - “Animals” 13; “Vegies” 5; “L” 6/F 5
- **Digit span forward 4/backward 3**
- **Benson**
 - **Immediate 15**
 - **Delayed 2**

Dementia with Lewy
Bodies Consortium

Consensus Criteria for Dementia with Lewy Bodies

1. **Dementia**
2. **Core features** (2 = “probable”, 1 = “possible”)
 - a. **fluctuating cognition, attention, alertness**
 - b. **recurrent visual hallucinations**
 - c. **spontaneous features of parkinsonism**
 - d. **REM sleep behavior disorder - ?**
3. **Indicative Biomarkers** (plus one core = “probable” DLB)
 - a. **Low dopamine transporter uptake (PET/SPECT)**
 - b. **Abnormal MIBG myocardial scintigraphy**
 - c. **PSG confirmation of RBD**
4. **One year rule for PDD vs. DLB**

McKeith et al, *Neurology*, 2017.

Dementia with Lewy
Bodies Consortium

DLBC 6 Month Visit

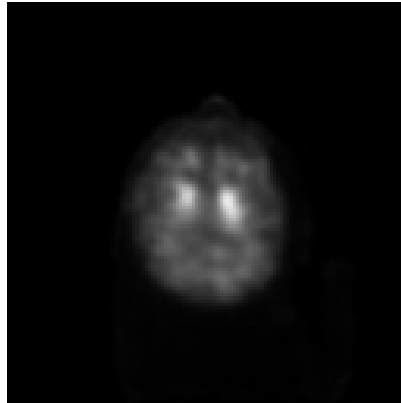
- **UPDRS III**
 - **Score 23 → 46, mild LUE resting tremor**
 - Driven by
 - Rigidity, bilateral bradykinesia (still L>R)
 - **H&Y 2 → 3**

Dementia with Lewy
Bodies Consortium

A Challenging Case

Thoughts?
Next Steps?

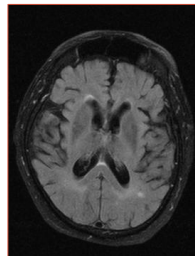
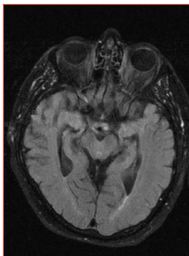
Imaging - DaTscan



2 years after initial evaluation

Dementia with Lewy
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Imaging-MRI



Initial



2 years later

Dementia with Lewy
Bodies Consortium

Lumbar Puncture – 2 years

- **CSF Findings**

- 1 RBC/1 WBC
- Protein 48* (15-45 mg/dL); Glucose 63 (40-70 mg/dL)
- *Research CSF*
 - **$A\beta_{42/40}$ - 0.097 (Low)**
 - *p tau* - 84.5 pg/ml, *t tau* - 327.7 pg/ml (high normal)
 - **SAA - “Detected”**
 - **α -synuclein - 1576 pg/ml** (low, 4095 – 8238)
 - **NFL – 26,379.9 pg/ml** (elevated, 2940.7 – 7944.5)

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Dementia with Lewy
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A Challenging Case

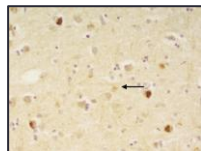
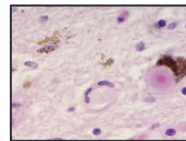
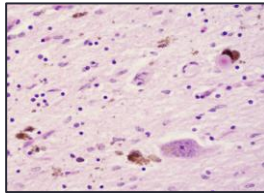
Thoughts?
Underlying Pathology

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Dementia with Lewy
Bodies Consortium

Pathology

Dementia with Lewy
Bodies Consortium

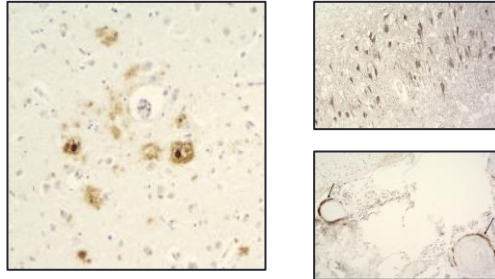
Pathology – Lewy Body Pathology



Neocortical Lewy Body Disease

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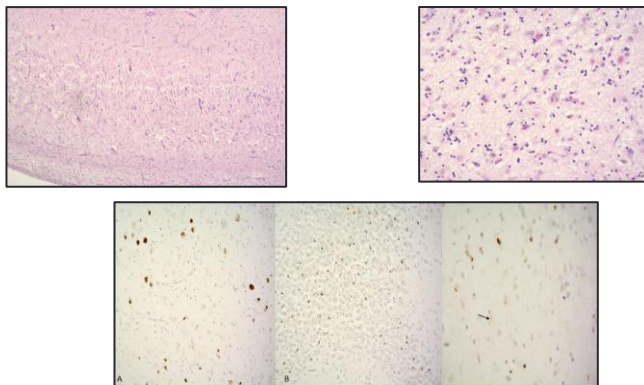
Pathology – Alzheimer's Disease



**Alzheimer's Disease Neuropathologic
Change
Moderate Plaques, Tangles and Mild CAA**

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Pathology – HS/LATE



**LATE Stage 3 with Hippocampal
Sclerosis**

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Pathology - Summary

- **Neocortical Lewy Body Disease**
 - *Consistent with history, biofluid biomarkers and dopamine imaging*
- **LATE (Limbic-predominant Age-associated TDP-43 Encephalopathy)**
 - *Consistent with atrophy observed on imaging, CSF NFL*
- **Alzheimer's Disease/CAA (intermediate)**
 - *Consistent with AD CSF biomarkers*

Dementia with Lewy Bodies Consortium

Thank You

Questions?

Dementia with Lewy Bodies Consortium

VA



U.S. Department of Veterans Affairs
Veterans Health Administration
Geriatric Research, Education, and Clinical Centers

UW Medicine
SCHOOL OF MEDICINE

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