



Overview of LBD Research

Leah K. Forsberg, Ph.D.

Outline

- LBDA Centers of Excellence
- LBD Research and Biomarkers
- Current Research Studies at Mayo

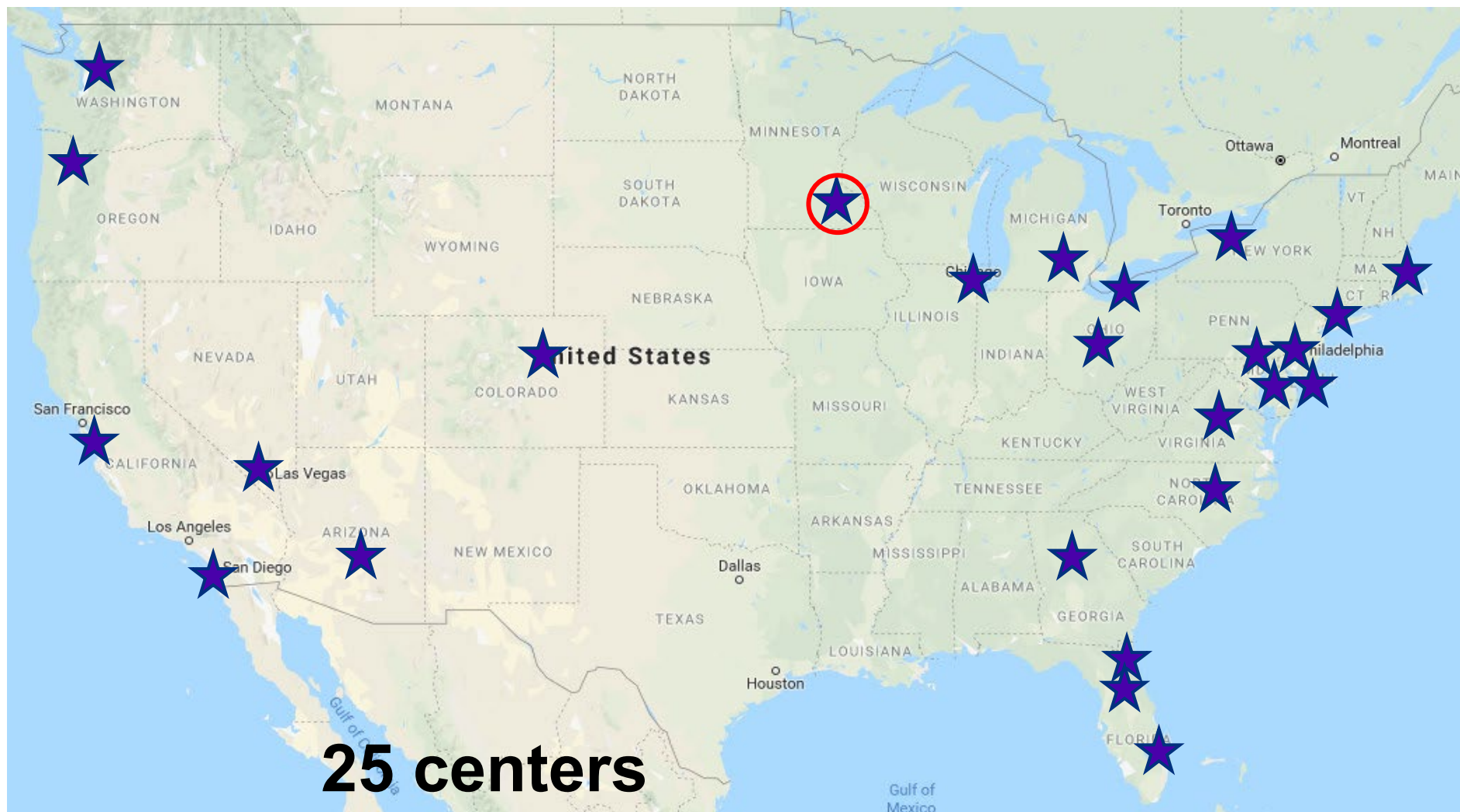
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Research Centers of Excellence

- The LBDA created Research Centers of Excellence (RCOE)
- Primary Goals of the program:
 - 1). Improve LBD Clinical Care
 - 2). Develop a clinical trials-networks and the associated infrastructure
- Currently 25 centers around the United States have been designated Centers of Excellence

LBDA RCOE Program



<https://www.lbda.org/rcoe>

RCOE Objectives

Improving Clinical Care

- 1) identify the optimal tools for clinical diagnosis
- 2) define the standards of care for management throughout the course of the disorder
- 3) promote continuing medical education to health care providers
- 4) operate and maintain LBD-specific resources, support groups and programs

Developing Clinical Trial Ready Network

- 1) review the landscape of clinical measures and biomarkers pertinent to LBD trial methodology
- 2) determine the optimal core and supplemental battery of measures for clinical trials, and develop new measures when needed
- 3) expand relationships with industry partners
- 4) determine core principles for LBD trials
 - (ie, minimize pt/family burden, master trial agreements, data/sample/scan sharing, etc.)

LBDA RCOE Investigators and Staff

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Outline

- LBDA Centers of Excellence
- **LBD Research and Biomarkers**
- Current Research Opportunities at Mayo

Lewy Bodies and Alpha-synuclein

Alpha-synuclein protein is a major component of Lewy Bodies

Lewy bodies affect different parts of the brain:

- Brainstem—important for regulating sleep and maintaining alertness
- Limbic—regulates emotion and behavior
- Cerebral cortex—controls many functions like information processing, perception, thought, and language
- Hippocampus—essential to forming new memories
- Midbrain and basal ganglia—involved in movement



Clinical Features of DLB

Symptom/sign	Manifestation	Frequency (%)
Dementia	Attention, visual spatial > memory	100
Core features		
Fluctuations	Altered levels of attention	60
Visual hallucinations	Recurrent, fully formed	50-75
Parkinsonism	Action > rest tremor	75
REM sleep behavior disorder	Act out dreams	79

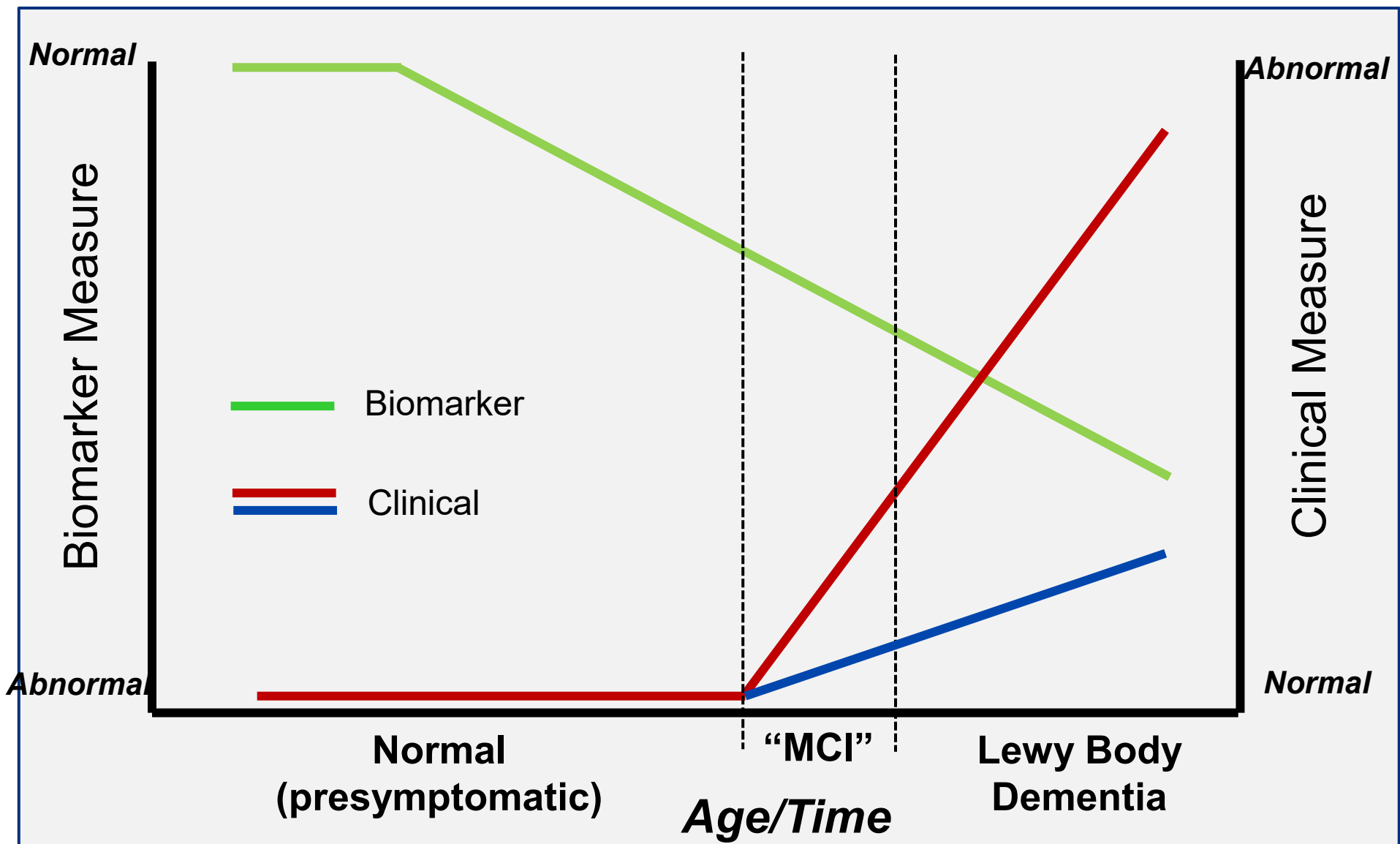
Research Biomarkers

What is a Biomarker?

A biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition.—NCI

A measurable substance in an organism whose presence is indicative of some phenomenon such as disease, infection, or environmental exposure.—
Dictionary.com

Theoretical Biomarker Framework

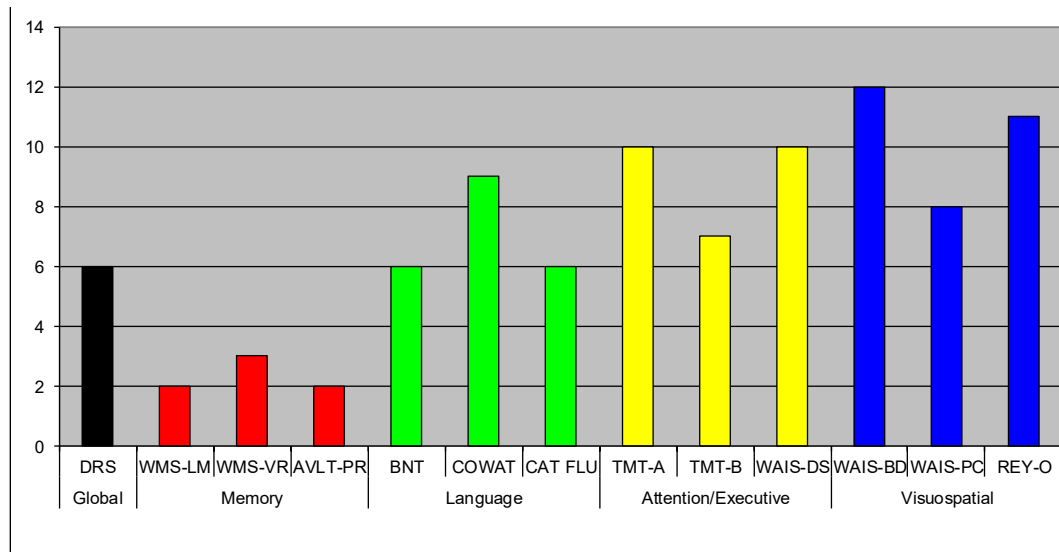


Research Biomarkers for LBD

- Neuropsychology
- Sleep studies
- Blood
- CSF
- Skin/salivary gland biopsy
- MRI
- DaTscan
- Glucose (FDG) PET
- Amyloid (PiB, other) PET
- Tau (AV1451, other) PET
- Brain donation

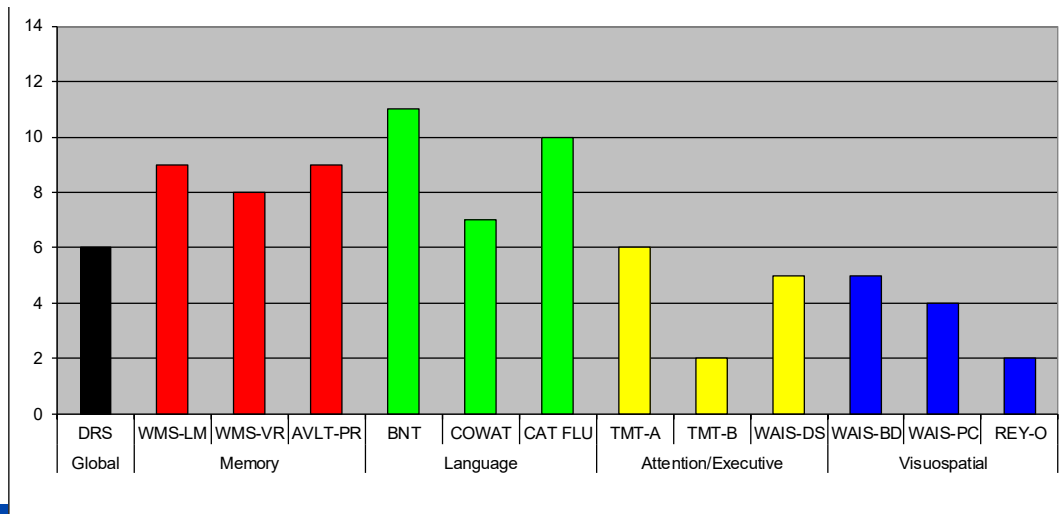
Neuropsychology as a Biomarker

AD



**Impaired on:
Memory measures**

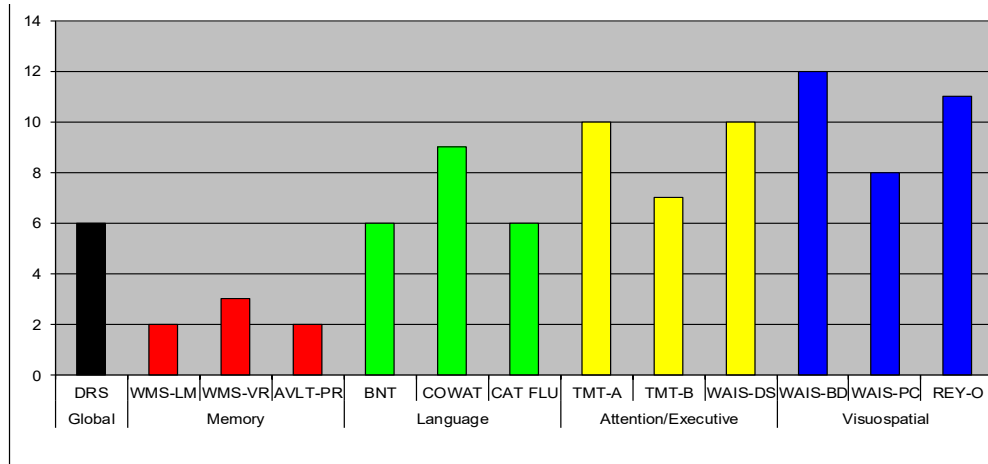
DLB



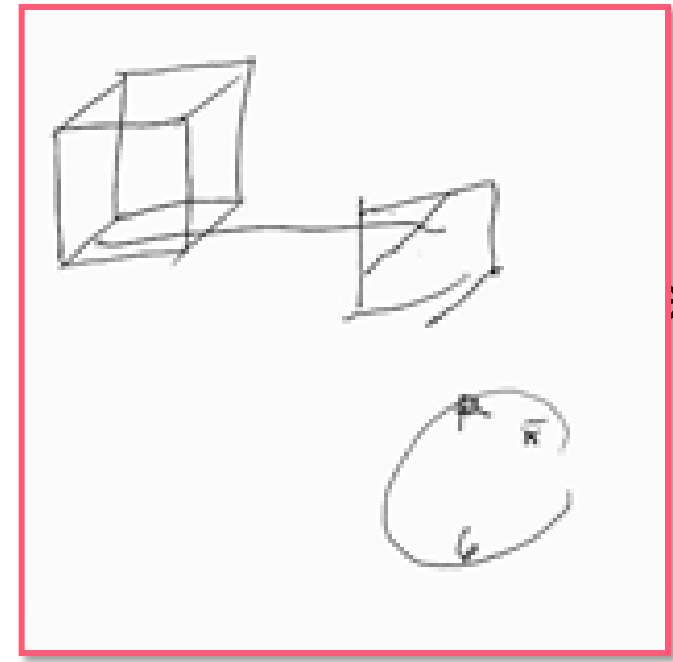
**Impaired on:
Attention/executive
and visuospatial
measures**

Neuropsychology as a Biomarker

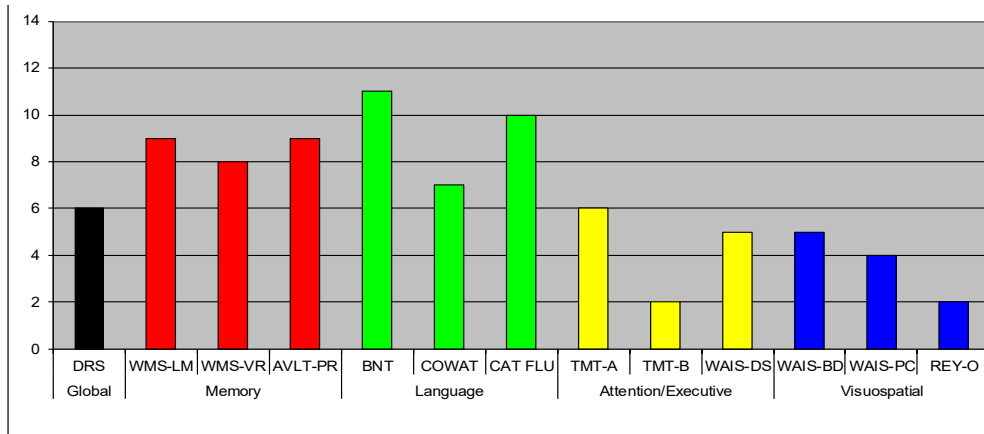
AD



**Impaired on:
Memory measures**



DLB



Bloodwork

- Rule out other systemic cause for cognitive changes
- Blood count, electrolytes, thyroid hormone, B12

Lumbar Puncture

- Sometimes done (particularly in atypical cases)
- Can assess whether there is an infectious, autoimmune, or inflammatory disorder present
- Can detect biomarkers for Alzheimer's disease

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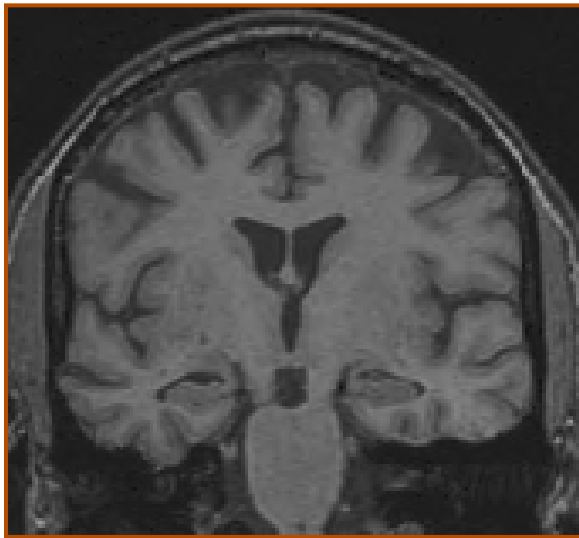
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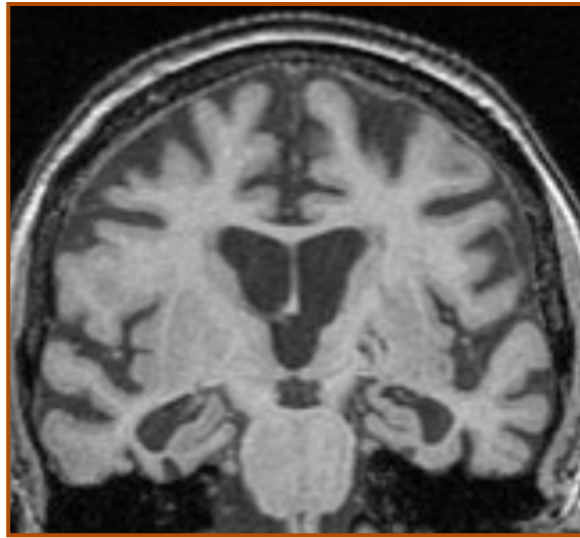
Currently we're looking for proteins in the blood or cerebral spinal fluid that might be related to LBD or LBD progression

Dementia With Lewy Bodies

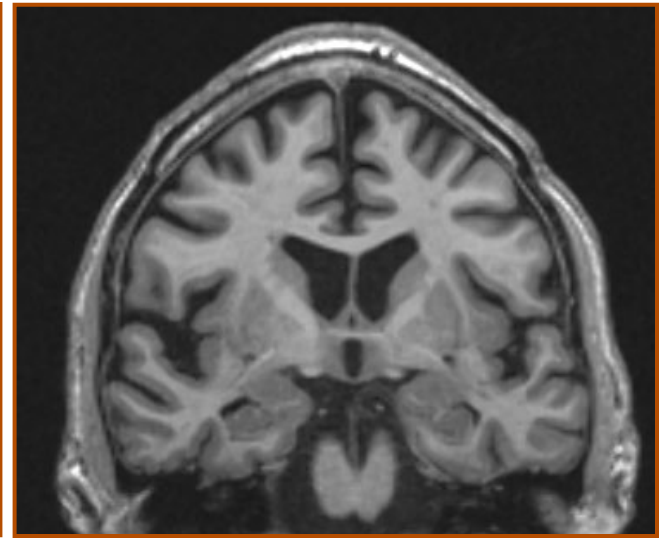
Radiologic Evaluation: MRI



Normal



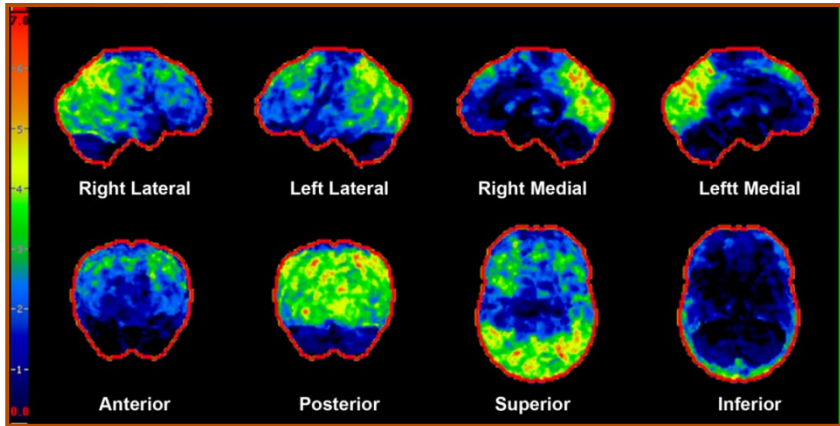
AD



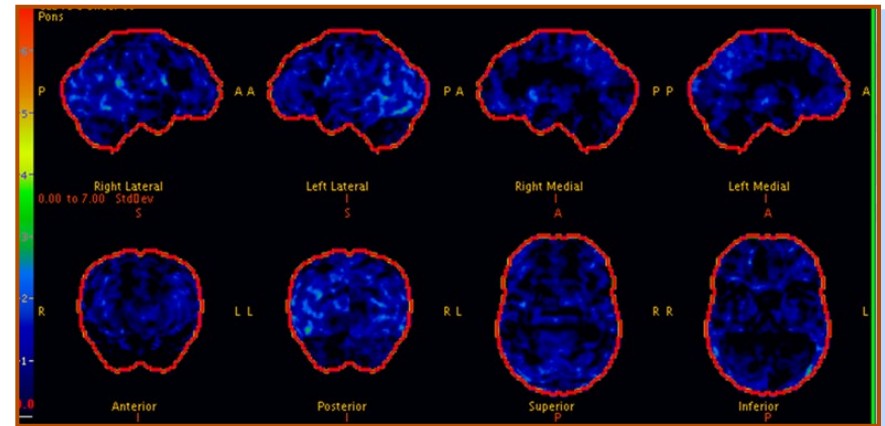
DLB

Dementia With Lewy Bodies

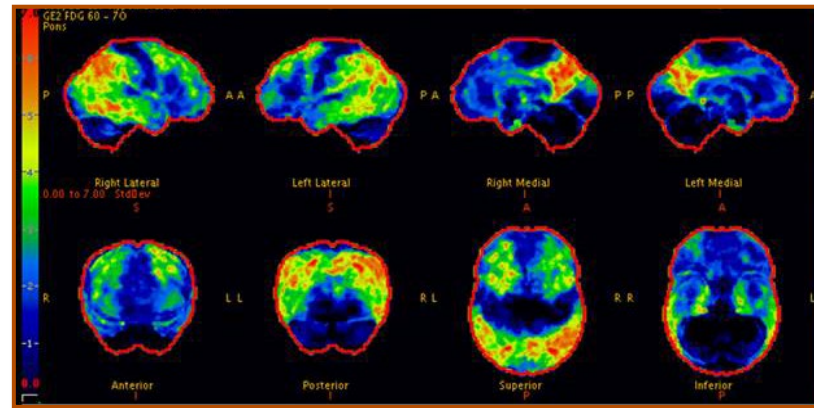
Radiologic Evaluation: FDG PET



DLB



Normal

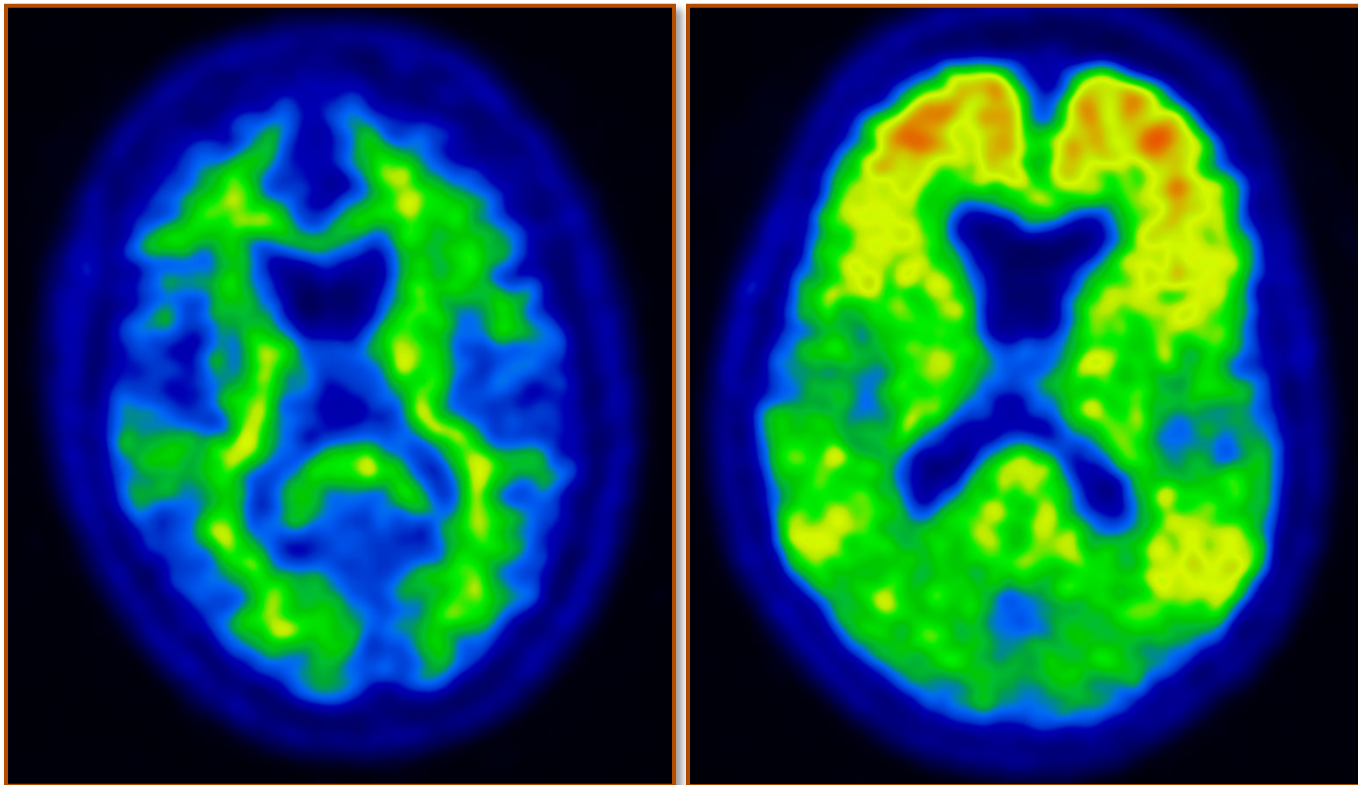


AD

Slide courtesy of Dr. Jon Graff-Radford

Dementia With Lewy Bodies

Radiologic Evaluation: Amyloid PET

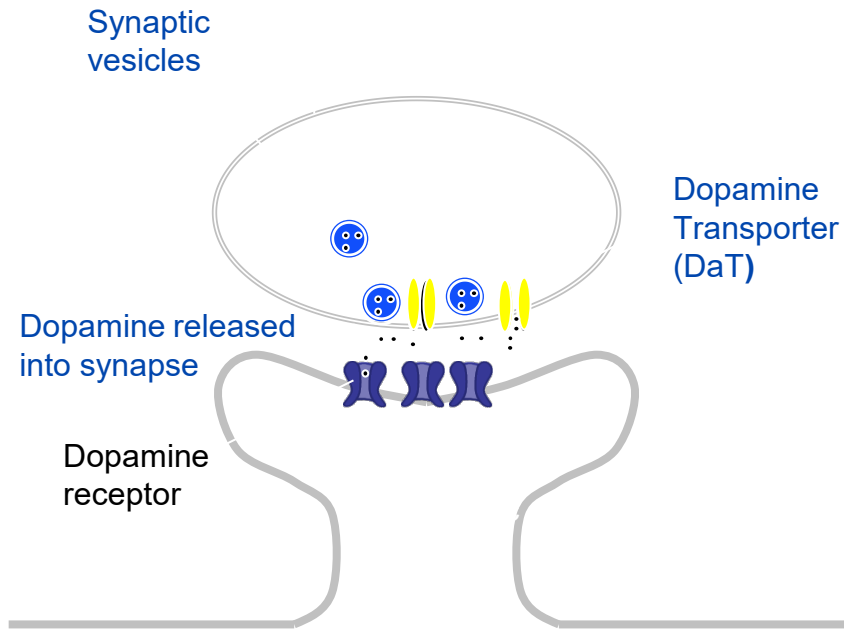


Normal

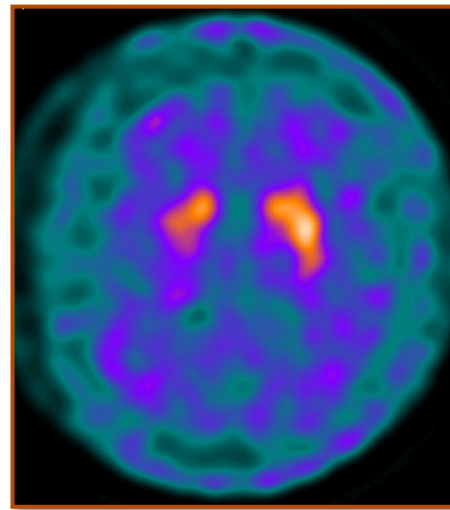
DLB

Dementia With Lewy Bodies

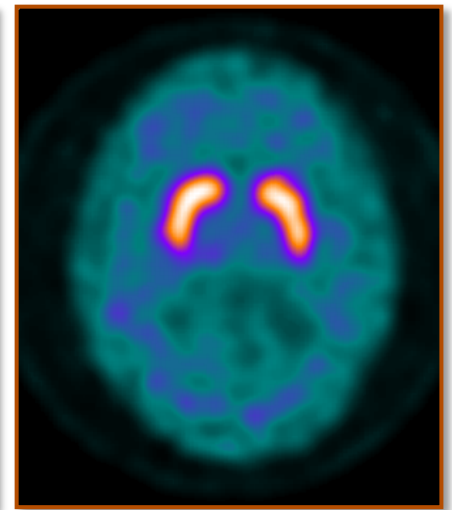
Radiologic Evaluation: DaT Scan



Ioflupane binds presynaptically to the dopamine transporter receptors (DaT)



DLB



Normal

Importance of Biomarker Collection

A better understanding of changes in your body due to disease progression will:

- Improve diagnosis of DLB
- Identify biomarker changes that are linked to certain clinical symptoms
- Inform clinical trials
 - Tests that measure disease change can be used to understand if a therapeutic is working

Importance of Biomarker Collection

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- Improve diagnosis of DLB
- Identify biomarker changes that are linked to certain clinical symptoms
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But....How do we collect biomarkers? How often do we collect biomarkers? Who do we collect biomarkers on?

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Dementia with Lewy Body Related Research Opportunities

Lewy Body Disease

- Mayo Clinic Lewy Body Disease Functional Genomics Program
 - To understand the role genes, proteins, lipids, diet, microbiome, and other lifestyle factors relate to LBD.
 - 1-time visit for those with LBD
 - Clinical Exam, blood draw, stool sample, skin punch

REM Sleep Behavior Disorder (RBD)

- North American Prodromal Synucleinopathy Consortium (NAPS)
 - To collect information on RBD and help plan a future treatment study
 - 2 year study for those with RBD
 - Clinical Exam, Neuropsych Testing, Questionnaires, Blood Draw, LP

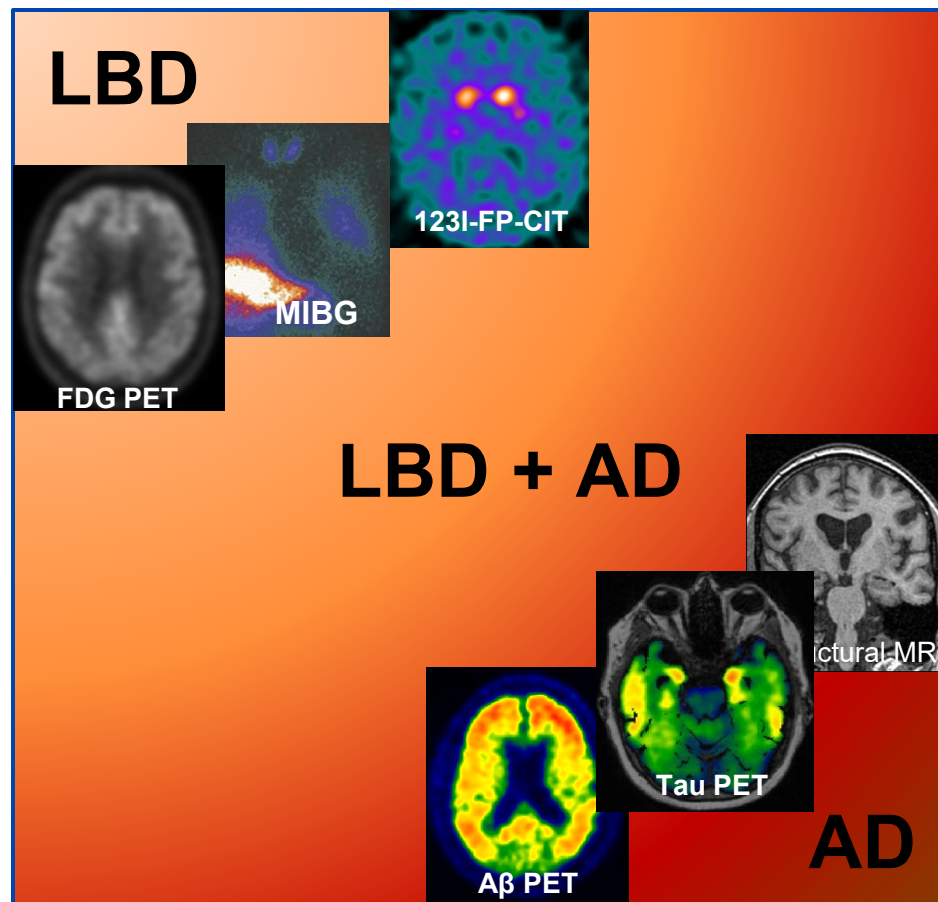
Dementia with Lewy Body Related Research Opportunities Continued

Dementia with Lewy Bodies (DLB)

- Longitudinal Imaging Biomarkers of Disease Progression in DLB (DLBU01)
 - See next series of slides
- Integrated Neurocognitive and Sleep-Behavior Profiler for the Endophenotypic Classification of Dementia Subtypes (INSPECDS)
 - Characterizing neuropsychological biomarkers for progression of neurodegenerative disease
 - Single visit with questionnaires, computerized tasks, sleep profiler device, clinical exam

Highlighted Research Study:

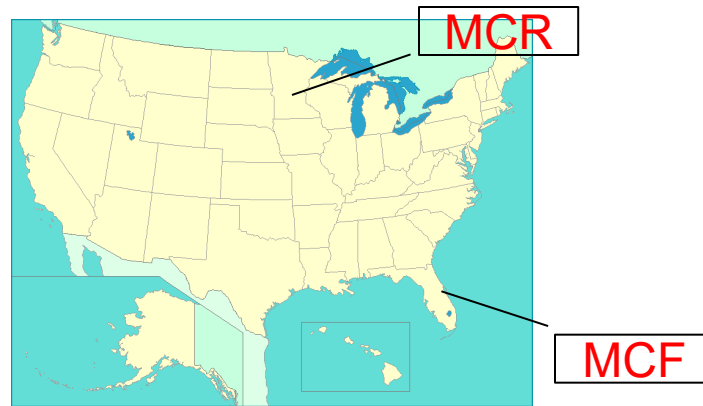
Longitudinal Imaging Biomarkers of Disease Progression in DLB Framework



Purpose: To determine the paths of change in imaging biomarkers of DLB and the associated rates of cognitive and functional decline

Mayo Clinic DLB Research Consortium Cohort

Patients with probable dementia with Lewy bodies (n=90) with baseline and at least a six month and 2 annual follow-up assessments



Mayo Clinic Rochester (currently 46 participants)

Mayo Clinic Florida (currently 12 participants)

Assessments and Procedures

5 Year study, with 6 clinic visits

Visit 1

- Blood draw
- Neuropsych testing
- MRI
- TAU PET
- Amyloid PET
- DaTScan
- Clinical Assessments
- Lumbar puncture (Optional)

6 month Visit

- Blood draw
- Neuropsych testing (brief)
- Clinical Assessments

Annual Visits (years 2-5)

- Blood draw
- Neuropsych testing
- MRI
- Amyloid PET
- DaTScan
- Clinical Assessments
- Lumbar puncture (Optional)

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There are data repositories where many LBD research studies from across the United States send samples for storage. This allows LBD researchers access to the collected samples.

LBD Research at Mayo

- Thank you to everyone participating in research at any institution
- Interested in participating in research at the Mayo Clinic?
 - Call our research center at 507-293-5011
- Coming soon:
 - Phase II study with Neflamapimod (drug) for those with DLB

General LBD Research Resources

- LBDA has information on research studies
 - Find out more: <https://www.lbda.org/rcoe>
- Parkinson's Disease Biomarker Program, supports many research studies (including the large Mayo DLB biomarker study)
 - Find out more: <https://pdbp.ninds.nih.gov/>

Collaborations and Support

Behavioral Neurology

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Neuropathology

Dennis Dickson, MD
Melissa Murray, PhD
Joseph Parisi, MD

Neurogenetics

Owen Ross, PhD

Numerous colleagues in
US, Europe, Asia,
Australia

LBD Research

