REGISTER TODAY – www.alzheimers.emory.edu

Emory Goizueta ADRC
19th Brain Health Virtual Forum
Tuesday, October 27
1:00 p.m.–3:00 p.m.

Distingishing the Different Dementias

Attend this free educational program to hear from Emory, Boston and Florida Atlantic University experts. Alzheimer’s disease (AD) is the most common and most studied cause of dementia. During the program you will learn how to distinguish Alzheimer’s disease from other major forms of dementia. Be sure to invite a friend, colleague or loved one to this comprehensive, interdisciplinary program.

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<table>
<thead>
<tr>
<th>What</th>
<th>Who</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introductions and types of dementia</td>
<td>Monica Parker, MD</td>
<td>Emory Goizueta Alzheimer’s Disease Research Center, Director, Minority Engagement Core (MEC)</td>
</tr>
<tr>
<td>Exercise <strong>Demo</strong></td>
<td>John Lewis</td>
<td>Energy Fitness of America</td>
</tr>
<tr>
<td>Welcome</td>
<td>Allan Levey, MD, PhD</td>
<td>Chair, Emory University, Department of Neurology</td>
</tr>
<tr>
<td>Lewy Body Dementia: diagnosis and screening</td>
<td>James Galvin, MD, MPH</td>
<td>Professor of Clinical Biomedical Science and Associate Dean for Clinical Research at Charles E. Schmidt College of Medicine, Florida Atlantic University</td>
</tr>
<tr>
<td>Chronic Traumatic Encephalopathy: CTE</td>
<td>Robert Stern, PhD</td>
<td>Professor of Neurology, Neurosurgery, and Anatomy &amp; Neurobiology</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Director of Clinical Research, BU CTE Center</td>
</tr>
<tr>
<td>Stroke and Vascular Dementia overview</td>
<td>Karima Benameur, MD</td>
<td>Associate Professor in Neurology at Emory University</td>
</tr>
</tbody>
</table>

**Stretch break**
<table>
<thead>
<tr>
<th>What</th>
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<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-Dementia</td>
<td>Lenora Higginbotham, MD</td>
<td>Senior Associate, Emory University, Parkinson's disease and Movement Disorders</td>
</tr>
<tr>
<td>Therapeutic Neuro-interventions</td>
<td>Suzette Binford, M.Ed.</td>
<td>Therapeutics Program Manager, Emory Brain Health Center</td>
</tr>
<tr>
<td>LBDA</td>
<td>Todd Graham</td>
<td>Vice President, Institutional Advancement Lewy Body Dementia Association</td>
</tr>
<tr>
<td>EHAS/EHBS</td>
<td>Whit Morgan</td>
<td>Communications Specialist, Emory Healthy Aging/Brain Study</td>
</tr>
<tr>
<td>Closing</td>
<td>Monica Parker, MD</td>
<td>Emory Goizueta Alzheimer’s Disease Research Center, Director, MEC</td>
</tr>
</tbody>
</table>
John Lewis
Exercise Demo
Monica Parker, MD
Director, Minority Engagement Core
Topic: Dementia 101
The Goizueta Foundation Endowed Chair for Alzheimer’s Disease Research
Betty Gage Holland Chair
Professor and Chair, Department of Neurology
Director, Emory Alzheimer’s Disease Research Center

Allan I. Levey MD, PhD
James Galvin, MD, MPH
Professor of Clinical Biomedical Science and Associate Dean for Clinical Research at Charles E. Schmidt College of Medicine, Florida Atlantic University

Topic: Lewy Body Dementia
Robert Stern, PhD

Professor of Neurology, Neurosurgery, and Anatomy & Neurobiology
Director of Clinical Research, BU CTE Center | Senior Scientist, BU Alzheimer’s Disease Center | Boston University School of Medicine

Topic: CTE
Karima Benameur, MD

Associate Professor in Neurology at Emory University

Topic: Vascular Dementia
Lenora Higginbotham, MD
Senior Associate, Emory University, Parkinson's disease and Movement Disorders
Thank You Volunteers
Suzette Binford, M.Ed.

Therapeutics Program Manager, Emory Brain Health Center | Cognitive Empowerment Program
THANK YOU FOR YOUR SUPPORT
Vice President, Institutional Advancement
Lewy Body Dementia Association

Todd Graham
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Emory Healthy Aging Study
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Dementia 101

Monica W. Parker, MD
Director, Minority Engagement Core
Emory Alzheimer’s Disease Research Center
... 5.6 million today ... nearly 50% over age 85 have AD ... 
... 70 million baby boomers turning 65 – ~10,000 per day thru 2030
Alzheimer’s Disease in Georgia is Rapidly Increasing
Georgians with Alzheimer’s will increase by 45% from 2000 to 2025.

Percentage Change in Number with Alzheimer’s Disease Compared to 2000

~150,000 Georgians Have Alzheimer’s Disease
## Alzheimer’s Projections*

<table>
<thead>
<tr>
<th>STATE</th>
<th>2019</th>
<th>2025</th>
<th>2019-2025% inc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Georgia</td>
<td>150,000</td>
<td>190,000</td>
<td>26.7%</td>
</tr>
<tr>
<td>Alabama</td>
<td>94,000</td>
<td>110,000</td>
<td>17.0%</td>
</tr>
<tr>
<td>Florida</td>
<td>560,000</td>
<td>720,000</td>
<td>28.6%</td>
</tr>
<tr>
<td>Tennessee</td>
<td>120,000</td>
<td>140,000</td>
<td>16.7%</td>
</tr>
<tr>
<td>Illinois</td>
<td>230,000</td>
<td>260,000</td>
<td>13%</td>
</tr>
</tbody>
</table>

What Is Dementia or NCD?

Dementia or Neurocognitive Disorders (NCD), IS NOT NORMAL aging!

- Symptoms and behaviors interfere with normal social or occupational function
- No effective treatment
- May overlap with delirium, a treatable medical problem
Neurocognitive Disorders in DSM-5: Impairment Across 6 Key Domains

<table>
<thead>
<tr>
<th>Domain</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complex attention</td>
<td>Ability to attend to and process multiple stimuli</td>
</tr>
<tr>
<td>Executive function</td>
<td>Ability to plan, organize, and complete tasks/projects</td>
</tr>
<tr>
<td>Learning and memory</td>
<td>Acquiring, manipulating, and remembering items, facts, words and their meanings, events, people, procedures, skills, etc.</td>
</tr>
<tr>
<td>Perceptual-motor</td>
<td>Identification and manipulation of figures, maps and items; motor tasks; recognition of faces and colors</td>
</tr>
<tr>
<td>Language</td>
<td>Expressive and receptive language skills</td>
</tr>
<tr>
<td>Social cognition</td>
<td>Socially appropriate behaviors and decision-making; empathy</td>
</tr>
</tbody>
</table>

Symptoms of Dementia

- Memory Loss
- Repetition of words, stories, phrases
- Loss of bowel and bladder function
- Inability to independently dress, groom, toilet, feed or manage finances or meals
- Gait instability- falls
- Personality Changes- belligerent, apathy
- Psychoses- paranoia
30% of all dementia is preventable.

- Increase education through secondary school
- Manage hypertension
- Prevent obesity
- Smoking cessation
- Treat diabetes
- Hearing loss assessment and management
- Reduce physical inactivity
- Treat depression
- Reduce social isolation
- Treat Sleep Disorders
## Dementia or Neurocognitive Disorder

<table>
<thead>
<tr>
<th>Protection Factors</th>
<th>Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Education</td>
<td>- Age</td>
</tr>
<tr>
<td>- Chronic Disease Management</td>
<td>- Gender</td>
</tr>
<tr>
<td>- Hypertension</td>
<td>- Traumatic Brain Injury</td>
</tr>
<tr>
<td>- T2D</td>
<td>- APOE4</td>
</tr>
<tr>
<td>- Statins</td>
<td>- Tobacco use</td>
</tr>
<tr>
<td>- Daily aerobic exercise</td>
<td>- Hypertension</td>
</tr>
<tr>
<td>- Mediterranean/Dash Diet</td>
<td>- T2D</td>
</tr>
<tr>
<td>- Red Wine (1)</td>
<td>- Obesity</td>
</tr>
<tr>
<td>- BMI &lt;25</td>
<td>- Cardiovascular Disease</td>
</tr>
<tr>
<td></td>
<td>- Sleep Disorders</td>
</tr>
<tr>
<td></td>
<td>- Hearing Loss</td>
</tr>
</tbody>
</table>
There is no available cure for brain degenerative disease... Yet!

Research is being done to find effective treatments and diagnostic tools.
Websites

- [www.alzu.org](http://www.alzu.org) Tutorial about the disease
- [www.alz.org](http://www.alz.org) Resources for caregivers
- [http://www.alzheimers.emory.edu](http://www.alzheimers.emory.edu) Emory Alzheimer’s Disease Research Center
Lewy Body Dementia

James E. Galvin, MD, MPH
Comprehensive Center for Brain Health
Lewy Body Dementia Research Center of Excellence
University of Miami Miller School of Medicine
Acknowledgements

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  • Magdalena Tolea, PhD
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  • Amie Rosenfeld, DPT
  • Iris Cohen, MSW
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  • Michael Kleiman, PhD
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  • Claudia Moore, CCRC
  • Judy Simon
  • Conor Galvin

• University of Miami
  • David Loewenstein, PhD
  • Peggy Pericak-Vance, PhD
  • Karen Nuytemans, PhD

• New York University
  • Ab Brody, PhD
  • Els Fieremans, PhD
  • Ricardo Osorio, MD

• Weil-Cornell University
  • Tracy Butler, MD

• Washington University
  • Anne Fagan, PhD

• Washington State University
  • Dedra Buchwald, MD

• University of Colorado
  • Manson Spero, PhD

• Penn State University
  • Marie Boltz, PhD

• Mt Sinai Icahn School of Medicine
  • Alison Goate, PhD

• Newcastle University
  • Ian McKeith, MD

• Florida Atlantic University
  • Elan Barenholtz, PhD
  • Behnaz Ghoraani, PhD
  • JuYoung Park, PhD
  • Lilah Besser, PhD
  • Lisa Wiese, PhD
  • Lun-Ching Chang, PhD

• Cleveland Clinic
  • James Leverenz, MD

• Simon Frasier University
  • Faisal Beg, PhD

• University of Wisconsin
  • Craig Atwood, PhD

• University of Florida
  • Melissa Armstrong, MD

• Industry Partners
  • MagQu Ltd Inc.
  • CogRx
  • Life Molecular Imaging

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The Most Common Disease You Never Heard Of

• 2nd most common cause of dementia after AD
  • Causes 10-12% of irreversible dementia
• Includes Dementia with Lewy Bodies (DLB) and Parkinson’s Disease Dementia (PDD)
  • PDD: Movement Disorder begins 1st, at least 1 year before cognitive problems
  • DLB: Any other pattern
• At least 75% of PD patients who live 10 years will develop dementia
• More common in men
• May have faster decline than AD
• The combined sum of patients Lewy body dementia is **1.4 million**
• Often significant delay to diagnosis and treatment

Other Neurologic Diseases
• Multiple Sclerosis: 1,000,000
• Stroke: 800,000
• Brain Tumors: 700,000
• Muscular dystrophy: 250,000
• Huntington’s disease: 30,000
• Amyotrophic Lateral Sclerosis: 12,000

Lewy Body Dementia Association (LBDA.org)
Important Individuals with LBD

Robin Williams  
Estelle Getty  
Al Arbour  
Ted Turner  
Jerry Sloan  
Bill Buckner  
Casey Kasem  
Dina Merrill  
Donald Featherstone
MY Important Person with LBD
## Symptoms Associated With LBD

### MOTOR
- Slowness
- Stiffness
- Imbalance and Falls
- Tremor
- Shuffling Gait
- Myoclonus

### PSYCHIATRIC/BEHAVIORAL
- Visual Hallucinations
- Other Hallucinations
- Delusions
- Depression, Anxiety, Apathy
- REM Sleep behavior disorder
- Cognitive fluctuations

### CONSTITUTIONAL
- Loss of Smell
- Constipation
- Urinary Incontinence
- Drooling, Runny Nose
- Dizziness, Lightheaded, Fainting
- Abnormal Sweating
- Sexual Dysfunction

### COGNITION
- Visual Tracking and Attention
- Visual Perception
- Verbal Initiation
- Timed Attention
- Executive Tasks
- Slowed Thinking
- Slowed Processing Speed

### MOTOR Symptoms

<table>
<thead>
<tr>
<th>Motor symptom</th>
<th>Image A</th>
<th>Image B</th>
<th>Image C</th>
<th>Image D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slowness</td>
<td><img src="imageA.png" alt="Image A" /></td>
<td><img src="imageB.png" alt="Image B" /></td>
<td><img src="imageC.png" alt="Image C" /></td>
<td><img src="imageD.png" alt="Image D" /></td>
</tr>
<tr>
<td>Stiffness</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imbalance and Falls</td>
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<td>Myoclonus</td>
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</table>

### PSYCHIATRIC/BEHAVIORAL Symptoms

<table>
<thead>
<tr>
<th>Psychiatric symptom</th>
<th>Image A</th>
<th>Image B</th>
<th>Image C</th>
<th>Image D</th>
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</thead>
<tbody>
<tr>
<td>Visual Hallucinations</td>
<td><img src="imageA.png" alt="Image A" /></td>
<td><img src="imageB.png" alt="Image B" /></td>
<td><img src="imageC.png" alt="Image C" /></td>
<td><img src="imageD.png" alt="Image D" /></td>
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<tr>
<td>Other Hallucinations</td>
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<tr>
<td>Delusions</td>
<td></td>
<td></td>
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<tr>
<td>Depression, Anxiety, Apathy</td>
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<tr>
<td>REM Sleep behavior disorder</td>
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<tr>
<td>Cognitive fluctuations</td>
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</table>

### CONSTITUTIONAL Symptoms

<table>
<thead>
<tr>
<th>Constitutional symptom</th>
<th>Image A</th>
<th>Image B</th>
<th>Image C</th>
<th>Image D</th>
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<tr>
<td>Loss of Smell</td>
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<td><img src="imageB.png" alt="Image B" /></td>
<td><img src="imageC.png" alt="Image C" /></td>
<td><img src="imageD.png" alt="Image D" /></td>
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<td>Constipation</td>
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<td>Drooling, Runny Nose</td>
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<tr>
<td>Sexual Dysfunction</td>
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</table>
Neurodegeneration in DLB vs AD

Dopaminergic cell loss is observed in the substantia nigra of a DLB patient (black arrows, A) compared with AD (B) and control (C).

In the same patients, atrophy of the medial temporal lobe is evident in AD (black arrows, E), whilst it is relatively spared in DLB (D) and control (F). Both scale bars represent 1 cm.

Outeiro et al. Mol Neurodegener. 2018;14:5.
Propagation of LB Pathology

Schematic representation of $\alpha$-synuclein pathology spreading routes in Lewy body disorders. 

a. Caudorostral route in PD

b. Hypothetical olfactory route in DLB

Light red arrows = weak incursions of $\alpha$-synuclein pathology; dark red arrows = aggressive incursions of $\alpha$-synuclein pathology.

Am = amygdala; DMV = dorsal motor nucleus of the vagus; ENS = enteric nervous system; Ent = anterior entorhinal cortex; LC = locus coeruleus; OB = olfactory bulb; SN = substantia nigra.

DLB Criteria

Revised criteria for the clinical diagnosis of probable and possible DLB

**Essential** for a diagnosis of DLB is dementia, defined as a progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational functions, or with usual daily activities. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention, executive function, and visuoperceptual ability may be especially prominent and occur early.

**Core clinical features (the first 3 typically occur early and may persist throughout the course)**

- Fluctuating cognition with pronounced variations in attention and alertness
- Recurrent visual hallucinations that are typically well-formed and detailed
- REM sleep behaviour disorder, which may precede cognitive decline
- One or more spontaneous cardinal features of parkinsonism: bradykinesia (defined as slowness of movement and decrement in amplitude or speed), rest tremor, or rigidity

**Supportive clinical features**

- Severe sensitivity to antipsychotic agents
- Postural instability
- Repeated falls
- Syncope or other transient episodes of unresponsiveness
- Hypersomnia
- Hyposmia
- Severe autonomic dysfunction, eg, constipation, orthostatic hypotension, urinary incontinence
- Hallucinations in other modalities
- Systematized delusions
- Apathy, anxiety, and depression

DLB Criteria: Biomarkers

• Indicative Biomarkers
  • Reduced dopamine transporter uptake in basal ganglia by PET or SPECT
  • Abnormal (low) uptake MIBG myocardial scintigraphy
  • Polysomnographic confirmation of REM sleep without atonia

• Supportive Biomarkers
  • Relative preservation of medial temporal lobe structures on MRI/CT
  • Generalized low upatake on SPECT/PET with reduced occipital activity +/- cingulate island sign on FDG-PET
  • Prominent posterior slow wave activity on EEG

McKeith et al, Neurology (2017)
Imaging in LBD

AD

DLB

Control

DLB

H/M 2.58
H/M 1.44
H/M 1.41
H/M 1.3
H/M 1.34
H/M 2.26
H/M 2.54
H/M 2.43
H/M 2.87
H/M 2.6
H/M 2.67
H/M 2.68
# Cognitive Profiles

<table>
<thead>
<tr>
<th>Cognitive Domain</th>
<th>AD</th>
<th>LBD</th>
<th>bvFTD</th>
<th>VaD</th>
<th>Depression</th>
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</thead>
<tbody>
<tr>
<td><strong>Episodic Memory</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Free recall</td>
<td>+++</td>
<td>++</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Recognition</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Prompting</td>
<td>x</td>
<td>(\checkmark)</td>
<td>(\checkmark)</td>
<td>(\checkmark)</td>
<td>(\checkmark)</td>
</tr>
<tr>
<td>Intrusions</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Semantic memory</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
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<tr>
<td>Procedural memory</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Working memory</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>+/-</td>
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<tr>
<td>Insight</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Attention</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Executive functions</td>
<td>++ typical AD</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>+++ frontal variant</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visuospatial skills</td>
<td>++ typical AD</td>
<td>+++</td>
<td>-</td>
<td>+</td>
<td>+</td>
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<tr>
<td></td>
<td>+++ PCA</td>
<td></td>
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</tbody>
</table>

+++ Early and severe impairment; ++ moderate impairment; + mild impairment; +/- impairment in some studies but not others; - no significant impairment; x not helpful; \(\checkmark\) helpful.

Karantzoulis and Galvin, Neurotherapeutics 2014; Galvin JE Practical Neurology 2019
Plasma Alpha-Synuclein

Data from MagQu Inc, Taiwan
Plasma Biomarkers

Lin et al. Front Aging Neurosci 2018
Caregiver Experience With Diagnosis

78% of patients had been diagnosed with something else first
- 53% AD or other dementia
- 39% PD or other movement disorder
- 24% Primary psychiatric disorder

62% of diagnosing physicians were neurologists, and only 6% were PCPs

2/3 of patients saw at least 3 physicians before LBD diagnosis

Median time to diagnosis was 12-18 months

PD = Parkinson's disease.
Caregiver Perception of Physician Knowledge

- 70% had difficulty finding a physician knowledgeable about diagnosing LBD
- After diagnosis, 53% of patients returned to primary care for management
- 77% had difficulty finding a physician knowledgeable about treating LBD

How useful it is to get a diagnosis?

- **DLB causes significantly greater functional disability than AD**
- **Care costs of DLB are twice those for AD**
- **Quality of life for people with DLB is significantly worse than for those with AD, with 1 in 4 caregivers rating DLB as worse than death.**
- **A correct DLB diagnosis increases the chances of correct management.**

Research Criteria for Prodromal LBD

• One or more core clinical features may develop years before dementia
  • Spontaneous parkinsonism
  • REM sleep behavior disorder
  • Autonomic complaints (orthostasis, constipation, olfaction)

• Three defined presentations for prodromal phases
  • Mild Cognitive Impairment
  • Delirium-onset Presentation
  • Psychiatric-onset Presentation

McKeith et al, *Neurology* 2020
MCI with Lewy Bodies

- Concern by patient, informant, or clinician
- Objective evidence of impairment in 1 or more cognitive domains
- Preserved or minimally affected ADLs
- Core features
  - Fluctuating cognition
  - Visual hallucinations
  - RBD
  - Parkinsonism

McKeith et al, Neurology 2020
Delirium-Onset LBD

- Patients with underlying LBD more susceptible that underlying AD
- Provoked by multiple factors (surgery, infections, fever, medications)
- Prodromal DLB should be suspected
  - Other provoking factors not found
  - Prolonged or recurrent delirium
  - Later develop progressive cognitive decline
- Core features have limited diagnostic weight
  - Can occur with other causes of delirium

McKeith et al, *Neurology* 2020
Psychiatric-Onset LBD

• Characterized by predominant psychiatric symptoms
  • Visual hallucinations
  • Systematized delusions (Capgras)
• May present with apathy, anxiety, and depression
• May be severe enough to require hospitalization
• Core features may mimic other psychiatric presentations or be due to treatment of symptoms
  • Bradykinesia mimicked by psychomotor retardation
  • Parkinsonism induced by medications
  • RBD induced by antidepressants

McKeith et al, Neurology 2020
# Lewy Body Composite Risk Score (LBCRS)

Please rate the following symptoms as being present or absent for at least 3 times over the past 6 months. Does the patient...

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have slowness in initiating and maintaining movement or have frequent hesitations or pauses during movement?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have rigidity (with or without cogwheeling) on passive range of motion in any of the 4 extremities?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have a loss of postural stability (balance) with or without frequent falls?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have a tremor at rest in any of the 4 extremities or head?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have excessive daytime sleepiness and/or seem drowsy and lethargic when awake?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have episodes of illogical thinking or incoherent, random thoughts?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have frequent staring spells or periods of blank looks?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have visual hallucinations (see things not really there)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appear to act out his/her dreams (kick, punch, thrash, shout or scream)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have orthostatic hypotension or other signs of autonomic insufficiency?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**TOTAL SCORE**
### LBCRS Performance

<table>
<thead>
<tr>
<th>LBCRS Variable</th>
<th>Control</th>
<th>AD</th>
<th>DLB</th>
<th>Overall p-value</th>
<th>Post-hoc AD vs DLB</th>
<th>MCI-AD</th>
<th>MCI-DLB</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradykinesia</td>
<td>11.1</td>
<td>33.3</td>
<td>98.6</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>17.2</td>
<td>73.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Rigidity</td>
<td>2.2</td>
<td>7.1</td>
<td>38.9</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>5.2</td>
<td>26.7</td>
<td>.01</td>
</tr>
<tr>
<td>Postural Instability</td>
<td>11.1</td>
<td>26.2</td>
<td>69.4</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>19.0</td>
<td>46.7</td>
<td>.03</td>
</tr>
<tr>
<td>Rest Tremor</td>
<td>2.2</td>
<td>2.4</td>
<td>27.8</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>3.4</td>
<td>26.7</td>
<td>.04</td>
</tr>
<tr>
<td>Daytime Sleepiness</td>
<td>22.2</td>
<td>54.8</td>
<td>80.6</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>37.9</td>
<td>66.7</td>
<td>.05</td>
</tr>
<tr>
<td>Illogical Thoughts</td>
<td>6.7</td>
<td>31.7</td>
<td>75.0</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>8.6</td>
<td>26.7</td>
<td>.06</td>
</tr>
<tr>
<td>Staring</td>
<td>2.3</td>
<td>19.0</td>
<td>60.6</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>12.1</td>
<td>33.3</td>
<td>.05</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>0.0</td>
<td>0.0</td>
<td>47.9</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>0.0</td>
<td>6.7</td>
<td>.05</td>
</tr>
<tr>
<td>RBD</td>
<td>15.6</td>
<td>21.4</td>
<td>61.1</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>12.1</td>
<td>26.7</td>
<td>.16</td>
</tr>
<tr>
<td>Orthostatic</td>
<td>11.1</td>
<td>7.1</td>
<td>36.1</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>1.7</td>
<td>13.3</td>
<td>.04</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>0.8 (1.2)</td>
<td>1.9 (1.2)</td>
<td>6.0 (1.7)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>1.2 (1.1)</td>
<td>3.8 (1.4)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>
### DIAMOND LEWY Toolkit

#### Assessment Toolkit for Dementia with Lewy Bodies

**Name:**

**Date of testing:**

**Date of birth:**

**NHS No.:**

**Informant:**

Please use this Assessment toolkit in all people with cognitive decline. Below are the diagnostic features of dementia with Lewy bodies (DLB) at two levels of confidence (probable DLB and possible DLB) and on the following pages are specific questions to assist in the identification of the core and suggestive features of DLB.

#### DLB Diagnostic Criteria

1. Clinician diagnosis of dementia (cognitive decline sufficient to interfere with social/occupational function).

2. Use screening questions below to cover the four domains of: cognitive fluctuation, visual hallucinations, RBD and Parkinsonism.

   - **Tick**

   - **Cross**

3. Core clinical features
   - Fluctuation in cognition
   - Recurrent visual hallucinations
   - REM sleep behaviour disorder
   - One or more features of spontaneous Parkinsonism

4. Indicative Biomarkers
   - Dopaminergic abnormalities in basal ganglia on SPECT/PET
   - Low uptake on MIBG myocardial scintigraphy
   - Polysomnography (PSG): confirmation of REM sleep without atonia

Diagnose Probable DLB if either 2 core features are identified or 1 core and 1 indicative biomarker feature.

Diagnose Possible DLB if any one feature is present. In such circumstances consider whether to refer subject for a dopaminergic SPECT scan (DaTSCAN), or MIBG or PSG, depending on local availability.

#### Other Diagnoses

Parkinson’s Disease Dementia (PDD) (PD >1yr before cognitive symptoms)

Alzheimer’s Disease

Other Dementia

MCI

Patient informed of diagnosis.  Yes  No

#### Questions to Identify Symptoms of DBL

Please respond to each of the questions below, asking carer or patient as appropriate.

**Cognitive Fluctuation (to carer)**

- If two or more of these are answered “Yes” the subject is highly likely to have cognitive fluctuation.

  1. Does the patient show moderate changes in their level of functioning during the day?  Yes  No

  2. Between getting up in the morning and going to bed at night, does the patient spend more than one hour sleeping?  Yes  No

  3. Is the patient drowsy and lethargic for more than one hour during the day, despite getting their usual amount of sleep the night before?  Yes  No

  4. Is it moderately difficult to arouse the patient so they maintain attention through the day?  Yes  No

**REM Sleep Disorder**

(to carer = bed partner)

- Have you ever seen the patient appear to “act out his/her dreams” while sleeping (punched or flailed arms in the air, shouted or screamed)?  Yes  No

- If answered affirmatively, then RBD is highly likely to be present.

**REM Sleep Disorder**

(to patient only if no bed partner and they have sufficient cognitive ability to be confident their answer is reliable)

- Have you ever been told that you seem to “act out your dreams” while sleeping (punched or flailed arms in the air, shouted or screamed)?  Yes  No

**Visual Hallucinations**

For the participant: Some people see things that other people cannot see.

- 1. Do you feel like your eyes ever play tricks on you?  Yes  No

- 2. Have you ever seen something (or things) that other people could not see?  Yes  No

**For the carer:**

- 1. Does the patient have hallucinations such as seeing false visions?  Yes  No

- 2. Does he/she seem to see things that are not present?  Yes  No

If, according to clinical judgement, visual hallucinations are present, determine as far as possible their frequency and recurrence. As a guide, visual hallucinations associated with DLB should not only occur during delirium, and are often recurrent over a period of months.

**Assessment of Parkinsonism (5-item UPDRS)**

- Parkinsonism in DBL requires the presence of at least one of bradykinesia, rest tremor or rigidity. The 5-item UPDRS is a brief and validated scale to identify parkinsonism in DLB. (See below for further details).

<table>
<thead>
<tr>
<th>POSTURAL TREMOR OF THE HANDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Slight</td>
</tr>
<tr>
<td>Mild</td>
</tr>
<tr>
<td>Moderate</td>
</tr>
<tr>
<td>Severe</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>KINETIC TREMOR OF THE HANDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Slight</td>
</tr>
<tr>
<td>Mild</td>
</tr>
<tr>
<td>Moderate</td>
</tr>
<tr>
<td>Severe</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FACIAL EXPRESSION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Slight</td>
</tr>
<tr>
<td>Mild</td>
</tr>
<tr>
<td>Moderate</td>
</tr>
<tr>
<td>Severe</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GLOBAL SPONTANETY OF MOVEMENT (BODY BRADYKINESIA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Slight</td>
</tr>
<tr>
<td>Mild</td>
</tr>
<tr>
<td>Moderate</td>
</tr>
<tr>
<td>Severe</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>RIGIDITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Slight</td>
</tr>
<tr>
<td>Mild</td>
</tr>
<tr>
<td>Moderate</td>
</tr>
<tr>
<td>Severe</td>
</tr>
</tbody>
</table>

**Total 5-item UPDRS Score =**

**Is Parkinsonism present?** (Use clinical judgement but for guidance a score >7 suggests significant parkinsonism is present, though a high score (>2) in a single domain may be sufficient to meet criteria.)

---

LBD Module for NIA-Alzheimer Center Program

Goals

• Develop a companion module to the Uniform Data Set (UDS) to improve characterization of DLB and PDD
• Harmonize efforts with those of the Movement Disorder Society efforts to characterize the non-motor features of Parkinson’s disease
• Capitalize on previous efforts to create a FTD module
• Standardize battery of clinical and cognitive tools for DLB and PDD that can be databased at NACC and shared amongst investigators.

Requirements

• Choose instruments and measurements from each workgroup
• Harmonize new data with variables captured as part of UDS 3.0
• Capture prodromal symptoms
• Instruments or measurements selected should be free of licensing fees or that an agreement is in place to make their use free
• Not burden sites
# DLB Module

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>AD</th>
<th>DLB</th>
<th>p-value</th>
<th>Post-hoc AD vs DLB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Autonomic Features</td>
<td>1.9 (2.7)</td>
<td>3.6 (2.4)</td>
<td>6.7 (3.6)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>SCOPA-Sleep, Nighttime</td>
<td>3.6 (3.1)</td>
<td>3.8 (3.1)</td>
<td>3.9 (4.0)</td>
<td>.90</td>
<td>.99</td>
</tr>
<tr>
<td>SCOPA-Sleep, Sleep Quality</td>
<td>2.6 (1.4)</td>
<td>2.8 (1.5)</td>
<td>3.1 (1.8)</td>
<td>.236</td>
<td>.41</td>
</tr>
<tr>
<td>SCOPA-Sleep, Daytime Sleepiness</td>
<td>2.1 (2.0)</td>
<td>3.4 (3.4)</td>
<td>6.4 (4.6)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mayo Sleep: RBD, %</td>
<td>17.3</td>
<td>20.5</td>
<td>64.5</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mayo Sleep: PLMS, %</td>
<td>2.0</td>
<td>15.4</td>
<td>29.1</td>
<td>&lt;.001</td>
<td>.03</td>
</tr>
<tr>
<td>Mayo Sleep: RLS, %</td>
<td>9.6</td>
<td>9.1</td>
<td>22.7</td>
<td>.02</td>
<td>.01</td>
</tr>
<tr>
<td>Mayo Sleep: Snort, %</td>
<td>16.0</td>
<td>15.4</td>
<td>37.3</td>
<td>.001</td>
<td>.001</td>
</tr>
<tr>
<td>Mayo Sleep: Apnea, %</td>
<td>14.9</td>
<td>19.4</td>
<td>27.3</td>
<td>.21</td>
<td>.26</td>
</tr>
<tr>
<td>Alertness</td>
<td>9.3 (1.1)</td>
<td>8.1 (1.6)</td>
<td>6.4 (2.1)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mayo Fluctuations Total</td>
<td>0.3 (0.6)</td>
<td>1.2 (0.9)</td>
<td>2.7 (1.3)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Noise Pareidolia – Correct Faces</td>
<td>6.9 (0.4)</td>
<td>6.0 (1.4)</td>
<td>5.9 (1.4)</td>
<td>&lt;.001</td>
<td>.79</td>
</tr>
<tr>
<td>Noise Pareidolia – Correct Noise</td>
<td>12.7 (0.8)</td>
<td>11.7 (1.8)</td>
<td>9.0 (3.7)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Noise Pareidolia – Total Correct</td>
<td>19.6 (1.0)</td>
<td>17.3 (3.1)</td>
<td>15.4 (4.3)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Noise Pareidolia – Total Pareidolia</td>
<td>0.3 (0.7)</td>
<td>2.2 (2.9)</td>
<td>4.0 (3.9)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>
Noise Pareidolia
Noise Pareidolia

Correct Face
Correct Noise
Total Correct
Pareidolia

Control
AD
DLB

<.001
.006
<.001
<br>.004
<br>.001
<br>.001
<br>.001
<br>.001
<br>.001

<.001
<.001
Current Treatment Options

**Pharmacology**¹-⁴
(nearly all options are off-label use of medication for DLB)

- **Cognitive Symptoms**
  - Donepezil (approved for DLB in Japan/Philippines)⁵
  - Other cholinesterase inhibitors
  - Memantine (?)

- **Motor Symptoms**
  - Carbidopa
  - Levodopa

- **Fluctuation Attention**
  - Modafinil
  - Armodafinil

- **Behavior**
  - Antidepressants
  - Atypical antipsychotics
  - Prazosin (?)
  - Antiepileptics (?)

- **Sleep**
  - Melatonin
  - Clonazepam

- **Autonomic**
  - Fludrocortisone
  - Midodrine
  - Drospirenone
  - Trospium

---

Optimizing Clinical Trial Design

- Clinicaltrial.gov search
  - 94 registered studies
    - 67 interventional
    - 27 observational
  - 16 interventional studies are active
    - 6 drug
    - 1 procedure
    - 3 imaging agent
    - 6 non-pharmacologic
LBD Research Centers of Excellence

- 24 research centers across the country
  - 17 States and District of Columbia
- Excellence in Clinical Care and Research
- Form Clinical Trials Network
- Mayo Clinic – Rochester is the Coordinating Center

Summary

• The Lewy body dementias
  • PDD and DLB differ only by timing of movement disorder
  • While clinical criteria lack sensitivity, they are highly specific and correlated strongly with pathology

• For the present time, treatments are largely symptomatic

• We are spearheading novel research
  • Improving clinical practice
  • Improving diagnosis
  • Improving lives of patients and their caregivers
  • Developing new medications
Chronic Traumatic Encephalopathy (CTE)

Robert A. Stern, PhD
Professor of Neurology, Neurosurgery, and Anatomy & Neurobiology
Co-Founder and Director of Clinical Research, BU CTE Center
Senior Investigator, BU Alzheimer’s Disease Research Center
Boston University School of Medicine
Punch Drunk and Dementia Pugilistica

• We have known about the long-term neurological consequences of boxing (including dementia) for almost 100 years

• **Punch Drunk:**
  • Martland, *Journal of American Medical Association*, 1928
  • “goofy,” “slug-nutty”
  • Later on, “institutionalized in an asylum”…for dementia

• **Dementia Pugilistica:**
  • Millspaugh, 1937

• **Chronic Traumatic Encephalopathy:**
  • Bowman & Blau, 1940; Critchley, 1957
Chronic Traumatic Encephalopathy (CTE) is often referred to as Dementia Pugilistica.

- Neurodegenerative disease, similar to Alzheimer’s disease, but it is a unique disease.
- Associated with a history of repetitive head impacts, including concussions and subconcussive trauma.
- The repetitive trauma appears to start a cascade of events in the brain that eventually leads to progressive destruction of brain tissue and associated cognitive decline, dementia, and problems with emotional and behavioral control.
CTE from Repetitive (Subconcussive) Brain Trauma

• Although a history of a **single moderate-to-severe traumatic brain injury (TBI)** can increase risk for later-life cognitive decline in some people, it does **not** seem to lead to Alzheimer’s disease or to CTE.

• **Concussion** = mild TBI with some symptoms. Single or multiple concussions do not seem to increase risk for CTE.

• **Subconcussive Trauma** = blow to head resulting in very mild brain injury BUT without any symptoms. Cumulative amount of repetitive subconcussive trauma appears to lead to CTE.
Dave Duerson – Age 50
November 28, 1960 – February 11, 2011
Dave Duerson’s History

• Successful businessman post NFL
• Starting at age 45, he had worsening short-term memory difficulties and other cognitive changes
• Increasingly out of control:
  • Short fuse, hot tempered, physically abusive, verbally abusive; lost business, marriage
• Committed suicide Feb 2011, shooting self in chest to avoid hurting brain.
Clinical Features Associated with CTE

• Changes in Emotional and Behavioral Control
  • Agitation
  • Rage
  • Short Fuse
  • Impulsivity
  • Aggression
  • *This “Neurobehavioral Dysregulation” often occurs earlier in life, i.e., ages 30’s-50’s*

• Changes in Cognitive Functioning
  • Poor Short-Term Memory
    • cannot make new memories, rapid forgetting, repeating stories
  • Executive Function Impairment
    • poor judgment and decision-making, impaired organizational and planning skills, poor multi-tasking
    • Other areas of cognitive functioning can also be impaired
  • *Cognitive changes often begin later in life, i.e., 50’s-70’s*

• Dementia
  • Dementia = cognitive impairment bad enough to impact daily functioning, independence
  • Not “Alzheimer’s disease”
    • Dementia from CTE can easily be misdiagnosed as Alzheimer’s disease dementia
CTE – NOT just former pro football players and boxers

- CTE has been diagnosed in post-mortem examinations in the following:
  - College football players
  - High school football players
  - Soccer players (pro and semi-pro)
  - Ice hockey players (pro and semi-pro)
  - Rugby players
  - Military veterans exposed to blast trauma
  - Developmentally disordered “headbanger” (woman)
  - Victim of years of repetitive brain trauma from domestic violence (woman)
Traumatic Encephalopathy Syndrome (TES)

• We cannot yet confirm the diagnosis of CTE during life; it is a neuropathological diagnosis

• But, there are now Diagnostic Criteria for “Traumatic Encephalopathy Syndrome” (TES) which describes the clinical features associated with underlying CTE brain pathology
Similar to Alzheimer’s disease, objective biological tests (i.e., Biomarkers), in addition to a good clinical evaluation, will lead to accurate early detection and diagnosis of CTE during life.
Tau Positron-Emission Tomography in Former National Football League Players

Robert A. Stern, Ph.D., Charles H. Adler, M.D., Ph.D., Kewe Chen, Ph.D., Michael Navitsky, M.S., Ji Luo, M.S., David W. Dodick, M.D., Michael L. Alosco, Ph.D., Yorghos Tripodis, Ph.D., Dhruvan D. Goradia, Ph.D., Brett Martin, M.S., Diego Mastroeni, Ph.D., Nathan G. Fritts, B.A., Johnny Jarnagin, B.A., Michael D. Devous, Sr., Ph.D., Mark A. Mintun, M.D., Michael J. Pontecorvo, Ph.D., Martha E. Shenton, Ph.D., and Eric M. Reiman, M.D.
We now have Potential CTE biomarkers

• Fluid biomarkers
  • Blood
  • Spinal fluid

• Neuroimaging biomarkers
  • Advanced MRI scans
  • PET scans
$17 Million grant funded by the National Institute of Neurological Disorders & Stroke

**7-Year Multicenter Study**

**Principal Investigators**
- Robert Stern, Ph.D., Boston University
- Jeffrey Cummings, M.D., Cleveland Clinic
- Eric Reiman, M.D., Banner Alzheimer’s Institute
- Martha Shenton, Ph.D., Brigham & Women’s Hospital

- **Males between 45-74 years old**
- **Three groups**
  - 120 Former NFL Players (43% Black)
    - No Symptoms
    - Mild Symptoms
    - Dementia
  - 60 Former College Football Players (no other contact sports) (17% Black)
    - No Symptoms
    - Mild Symptoms
    - Dementia
  - 60 Controls (no contact sports, TBI, Military) (40% Black)
    - All No Symptoms

**Biomarkers**
- Fluid: CSF & Blood, Saliva
- Neuroimaging: MRI, DTI, fMRI, MRS, PET-amyloid, & PET-tau

**Clinical Diagnosis**
- Traumatic Encephalopathy Syndrome
  - Behavior/Mood, Cognitive, Mixed, Dementia Subtypes
  & Chronic Traumatic Encephalopathy
  - Probable, Possible, Unlikely

**Clinical Exams**
- Neurocognitive, Mood, Behavior, & Motor Tests

**Baseline Examinations Completed**
February 26, 2020 !!!!!!!!

**Baseline Evaluations and Three-Year Follow-Ups**
Prevention

• Once we can diagnose CTE during life, we will be able to begin clinical trials for treatment
• And, if we can detect it early in the disease course, prior to symptoms, we can conduct clinical trials for prevention!
“I read that story about dementia in former NFL players. Maybe we should reconsider this.”
Please Stay Safe
Vascular Dementia

Karima Benameur, MD
Emory University
Dementia

An “umbrella” term used to describe a range of symptoms associated with cognitive impairment.

Alzheimer’s 50%-75%

Vascular 20%-30%

Lewy Bodies 10%-25%

Frontotemporal 10%-15%

Mixed Dementia = >1 neuropathology - prevalence unknown
CENTRAL ILLUSTRATION: Vascular Cognitive Impairment and Dementia

Risk Factors
- Lifestyle

Genetic Variants

Large and Small Vessel Disease
- White Matter Disease
- Microinfarcts Microhemorrhages
- Large Infarcts
- Brain Atrophy

Vascular Cognitive Impairment

Hypertension  
Diabetes

Vascular dementia

Alzheimer’s disease

Cerebrovascular impairment

Amyloid plaque

Neurofibrillary tangle

Cognitive impairment

Dementia

Understanding Root Causes

Symptoms
- Result or outcome of the problem
- What you see as a problem (Obvious)
  - Achy, weak, tired

The Problem
- Gap from goal or standard
  - Fever

Causes
- “The Roots” – system below the surface, bringing about the problem (Not Obvious)
  - Infection
Understanding Root Causes

Symptoms
- Stroke
- Vascular Cognitive Impairment/Dementia

The Problem
- Metabolic Syndrome

Causes
- Diabetes
- Hypertension
- Dyslipidemia
- Poor Quality Diet
- Physical Inactivity
- Smoking

*Age adjusted by direct standardization to the 2000 U.S. Census population by using age groups 20–39, 40–59, and 60–74 years.
From: Increased consumption of refined carbohydrates and the epidemic of type 2 diabetes in the United States: an ecologic assessment
Am J Clin Nutr | © 2004 American Society for Clinical Nutrition
Age-adjusted Prevalence of Obesity and Diagnosed Diabetes Among US Adults

**Obesity (BMI ≥ 30 kg/m²)**
- **1994**
- **2000**
- **2015**

**Diabetes**
- **1994**
- **2000**
- **2015**

CDC's Division of Diabetes Translation, United States Surveillance System available at http://www.cdc.gov/diabetes/data
At last, something's going to change
What impact will this have? How will it affect me?
Can I cope?

Denial
Change? What change?
This is bigger than I thought
I'm off! This isn't for me!

Disillusionment
I can see myself in the future

Moving forward

This can work and be good

Anxiety
Happiness
Fear
Threat
Guilt
Depression
Hostility

Who am I?
Did I really do that?
Effects of SAD Diet on Calorie intake and satiety

Diets were presented in random order and matched for provided calories, sugar, fat, fiber, and macronutrients.

Ad Libitum Intake (kcal/d)

Body Weight Change (kg)

Days on Diet

Ultra-processed Diet

Unprocessed Diet

Cell Metabolism Volume 30, Issue 1, 2 July 2019, Pages 67-77.e3
Be Culturally Cognizant
The greatest medicine of all is teaching people how not to need it

~ Hippocrates
Parkinson’s Disease Dementia

Lenora Higginbotham, MD
Movement Disorders Neurology
Emory 19th Brain Health Forum
The Lewy Body Dementias include Parkinson’s disease dementia (PDD) and Dementia with Lewy bodies (DLB).

Both diseases feature the abnormal accumulation of the protein \textit{alpha-synuclein} in the brain in the form of \textit{Lewy bodies}.
The Lewy Body Dementias

However, these two diseases can be distinguished by the **timing of cognitive decline** relative to motor symptoms.
Parkinson’s Disease (PD)
Motor syndrome of bradykinesia and rigidity +/- rest tremor

Levodopa Responsiveness
Improvement with dopamine replacement therapy and mimics (e.g. DBS) is a hallmark of PD

PD Dementia (PDD)
Dementia is a late finding of PD, occurring years and even decades after onset of motor symptoms
The core diagnostic criteria for PDD require a diagnosis of Parkinson’s disease first!

Unlike Alzheimer’s disease, primary memory loss may not be the most prominent symptom in PDD.

***Inattention***
Focus, Concentration, Train of Thought

***Executive Dysfunction***
Planning, Problem Solving, Organization, Time Management

***Neuropsychiatric Deterioration***
Hallucinations, Delusions, Apathy, Anxiety

***Visuospatial Dysfunction***
Navigation, Pattern Detection
Early Complaints in PDD

• Easily losing the thread of conversations
• Trouble with multi-tasking, organizing, or planning
• Difficulty switching tasks
• Occasionally getting lost while driving or increasing dependence on GPS devices
• Visual hallucinations
Memory loss in PDD, if present, is often the result of impaired retrieval of stored information and improves with cueing.
Detailed neuropsychological testing is often necessary to tease out these patterns of cognitive decline.
Neurologic Work-Up to Consider...

- Lab studies
- Bedside psychiatric assessment
- Detailed neuropsychological testing
- MRI brain w/wo contrast*
- Amyloid or FDG PET Scan*

*Optional depending on presentation and other circumstances.
Pharmacological Treatment of PDD

- Acetylcholinesterase Inhibitors
  - Donepezil, rivastigmine*, galantamine
- NMDA Antagonists
  - Memantine
- Atypical Antipsychotics
  - Quetiapine, clozapine, pimavanserin
- Dopaminergic Therapy Adjustments

*Rivastigmine is the only drug FDA approved for the treatment of Parkinson’s disease dementia.
Maintaining Brain Health

• Maintaining a variety of healthy social interactions
• Exercising intentionally and regularly
• Adopting a healthy diet (e.g. Mediterranean, DASH)
Any Questions?
Therapeutic Neuro-Interventions

Suzette Binford, M.Ed.
What are Therapeutic Neuro-Interventions?

• The term therapeutic neuro-interventions refers to things we can do to protect and preserve our brain cells (neurons)
• One of the goals of these interventions is to promote neuroplasticity of the brain (ability of the neurons to reorganize and make new connections) and maintain brain function
Is there anything I can do to reduce my risk of Alzheimer’s?

1. Aging!
2. Genes
3. Gender
4. Head injury
5. Vascular disease
6. Lifestyle

Mostly out of our control

Opportunity!
Neuroprotective Factors

- Maintain a healthy diet to support brain health, such as the MIND diet
- Increase exercise to recommended 30 minutes 5 days/week
- It is recommended older adults average 7-9 hours of consolidated sleep per night.
- Treat depression or other mood disorders and reduce stress.
- Maintain regular social interactions
- Increase cognitive stimulation through targeted practice or learning new skills.
How does Exercise benefit the brain?

- **What’s good for the heart is good for the brain.**
  - 25% of every heartbeat’s blood flow goes to the brain!

- Exercise *increases blood flow* to the brain, which results in better overall brain health.
- Enhances functional connectivity in frontal, posterior, and temporal brain regions important for reasoning, visual analysis, and memory.
- Can support neural systems involved in memory.
- There is also evidence that physical exercise increases neuronal connection density.
Vascular Risk Factors

- Disrupt blood flow to the brain, and over time can affect cognition
  - Hypertension
  - Hyperlipidemia
  - Diabetes
  - Heart Disease
  - Sleep Apnea

- Stroke
- MCI
- Dementia
Vascular Risk Factors: Cognitive Onset and Progression

Cognitive Functioning vs Age

- Normal Aging
- Vascular Risks
  - Hypertension
  - Plus Diabetes
  - Plus Hyperlipidemia
Metabolic Syndrome: a cluster of conditions that increases the risk of heart disease, stroke, and diabetes

1) High blood sugar levels
2) Hypertension
3) High cholesterol levels
4) Excess abdominal body fat
In patients with Metabolic Syndrome, the rate of progression from mild cognitive impairment to dementia was 8 times higher than in MCI patients without Metabolic Syndrome.
What can I do today?

• **Long-Term Goal:** Engage in regular exercise of moderate intensity 5 days per week for 30 minutes OR 20 minutes vigorous activity 3 days/week; follow the MIND diet or similar heart-healthy diet

• **Small changes to make today:**
  - Improve management of vascular risk factors
  - Incorporate exercise into your daily routine
  - Do some form of exercise most days of the week (even if you don’t hit the recommended amount).
  - Find a fitness partner
  - Eat 5 servings of fruits and vegetables every day and reduce processed sugar and high-fat foods
• Cognitive stimulation throughout life (and in late life) leads to lower incidence of dementia.
• Encourages social engagement
• Improves mood, reduces boredom
• Related to greater brain volume, density, and functional connectivity.
• More cognitive activity increases our “cognitive reserve.”
How much should I do?

- The most important thing is to engage in **regular** cognitive activity that is challenging and fun.
- Try to engage in cognitively stimulating activities for **at least 30 minutes 3 or more days per week.**
What counts as cognitive stimulation?

- Learn something new!
- Take a cooking, art, or computer class
- Learn a new language or how to play a musical instrument
- Engage your brain with someone else
- Choose activities that involve mental and physical engagement
Formal Cognitive Training

- **Computerized programs** that utilize structured practice on cognitively challenging tasks (e.g., Brain HQ)

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Formal Cognitive Training

- **Compensatory strategy training** which involves learning strategies to support everyday cognition.

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• Visually Appealing
• Can be fun!
• Adapts to individual performance levels

• Can be expensive
• Effectiveness is mixed
• Can be difficult to engage with
What can I do today?

• **Long-Term Goal:** Engage in cognitively stimulating activities 3 or more days per week for at least 30 minutes at a time.

• **Small changes to make today:**
  – Identify a new skill you’d like to learn or a hobby you want to be more involved in and try it out!
  – Join a group or club through the
  – Pursue opportunities for Lifelong Learning, like OLLI
  – Start a weekly card game with a friend
  – Call a loved one to chat
Manage modifiable risk factors and increase physical and cognitive activity.

Small changes can make a big difference!

It's important to find things that work for you, brain health is not one-size-fits-all.

Key Take-Aways
WHO WE ARE

FOUNDING GROWTH MISSION
• Founded by care partners in 2003 who saw a need for an organization dedicated solely to LBD.
• Serve approximately 1.4 million people living with Lewy body dementia (LBD), their families and carepartners
Since 2003, LBDA has developed and leads the nation’s largest network of over 130 LBD-specific support groups. Headquartered in Atlanta with staff of 15 and nationwide support network. Expanded efforts from providing support and resources to funding research and advancing advocacy.
MISSION

LBDA will be the leading authority on Lewy body dementias, relentless in the search for a cure, while providing quality support for those living with the disease and their caregivers.
EFFORTS

EDUCATION  ADVOCACY  RESEARCH
October is LBD Awareness Month

Get Started

Those Living with LBD  Caregivers  Healthcare Professionals  Donors
EDUCATION
ADVOCACY

• We advocate for the need of the LBD community across the healthcare, government and corporate sectors.
• LBDA’s advocacy impacts national and international funding initiatives on Lewy body dementias.
• We serve as a bridge between federal agencies and lawmakers, LBD experts, biotech and pharmaceutical industry, to LBD advocates.
The top national research priorities for Lewy body dementia are to find better ways to diagnose and find treatments for symptoms that have the greatest impact on those with LBD and their caregivers.

The LBDA established the Research Centers of Excellence program in 2017 and is comprised of 26 of the top academic medical research centers in the US.

The LBDA RCOE program was established to address a common problem many LBD families face – finding a physician with experience in LBD clinical management.
LBDA RCOE sites provide LBD specific care, they conduct clinical research, provide support to those with LBD and their families and caregivers and educate healthcare professionals associated with the disease.
SUPPORT

LEWY BUDDIES

GROUPS

DIGITAL HELP
LEWY BUDDIES

• Lewy Buddies are LBDA volunteers who help address challenges faced by those with LBD and their families.
• When someone calls the “Lewy Line,” a 1-800 number for the LBD community, they are then put in contact with a Lewy Buddy.
• Lewy Buddies are well informed through personal experience and training.
GROUPS

• LBDA provides the nation’s largest network of LBD support groups with over 130 locations nationally.
• Groups are operated by trained Support Group Facilitators.
• Groups are available for both caregivers and those with LBD.
LBDA maintains online support groups for care partners and those living with LBD – and have proven invaluable during the pandemic.

- Recurring meetings are held in LBDA’s various Facebook groups.
- Webinars and the video library provide resources for the LBD community to find guidance and information.
IMPORTANT

Phone: 800-539-9767
Email: support@lbda.org
THANK YOU
Healthy Aging Study
Introducing the Emory Healthy Aging Study

What is it?
- The Emory Healthy Aging Study is a longitudinal study focused on helping us better understand how we age and age-related disease through the creation of a large database of health history information provided by participants.

Who can participate?
- Participation is open to anyone over the age of 18 who lives in the U.S. (or U.S. territories), can read and understand English, and have access to an internet capable device.

How does it work?
- Participating in the Emory Healthy Aging Study is done entirely online. We ask each participant to complete an online health history questionnaire and to update it once a year.
Emory Healthy Aging Study: Data Collected

The Emory Healthy Aging Study collects participant data on:

- Demographics
- Exercise
- Diet
- Activities and habits
- Medical history

The EHAS Health History Questionnaire (HHQ) can be completed through the following mediums:

- Computer
- Tablet
- Mobile device (iOS, Android, etc.)
Emory Healthy Aging Study: Participant Demographics

Age:
- 18-35: 7%
- 36-55: 7%
- 56-75: 25%
- >76: 61%

Gender:
- Male: 29%
- Female: 71%

Race:
- Caucasian: 80%
- African American: 14%
- Asian: 2%
- Multi-racial: 2%
- Other: 2%
How to Participate in the Emory Healthy Aging Study

To join the study:

• Visit our website, healthyaging.emory.edu
• Click the yellow “Join The Study” button
Introducing the Emory Healthy Brain Study

What is it?
- The Emory Healthy Brain Study is a longitudinal sub-study of the Emory Healthy Aging Study focused on identifying the biomarkers of Alzheimer’s disease and other forms of dementia.

Who can participate?
- We are looking for healthy individuals between the ages of 50-75 years old.
- Data collected from the Emory Healthy Aging Study health history questionnaire helps us identify individuals who are eligible for participation.

How does it work?
- Study participants complete a remote visit, and two short in-clinic visits every two years. During these visits we perform a variety of tests, collect biospecimens, and conduct an MRI scan.
Questions?

healthyaging@emory.edu

Jefferson.morgan@emory.edu
Dementia

Distinguishing the Different Dementias

Emory Goizueta ADRC
19th Brain Health Virtual Forum
Tuesday, October 27
1:00 p.m.-3:00 p.m.

Attend this free educational program to hear from Emory, Boston and Florida Atlantic University experts. Alzheimer's disease (AD) is the most common and most studied cause of dementia. During the program you will learn how to distinguish Alzheimer's disease from other major forms of dementia. Be sure to invite a friend, colleague or loved one to this comprehensive, interdisciplinary program.

Registration required. www.alzheimers.emory.edu