

Lewy Body Dementia (LBD)

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Lewy Body Dementia (LBD)

Second most common neurodegenerative dementia

- Second only to Alzheimer's disease
- About 5% (1-25%) of all dementias



Clinical Features

LBD causes both cognitive and motor changes

- **Can be confused with both Alzheimer's and Parkinson's disease**
- Will focus on how to differentiate each one
 - 1) cognitive changes
 - 2) motor changes



Lewy Body Dementia – Cognitive changes

Dementia

Progressive cognitive decline leading to functional impairment



Prominent Patterns of Cognitive Changes

LBD

Executive Function
Visuospatial
Memory usually later

Other features

Fluctuating consciousness

Hallucinations

- Usually well-formed (people, animals)

Illusions also

Alzheimer's disease

Memory

Language, executive function

Hallucinations, fluctuations less common



Lewy Body Dementia

Cognitive Changes

Dementia

Changes in alertness

Hallucinations

Parkinsonism

“Motor” Symptoms:

- Rest tremor
- Slowness of movement
- Stiffness (Rigidity)
- In LBD, usually symmetric, unlike PD
- Balance difficulty
- Shuffling gait
- Stooped posture
- Softer voice; less facial expression
- Can be prominent or extremely subtle





Rest tremor
Turning 'en bloc'
Stooped posture

Medlink Neurology
www.medlink.com



Postural instability



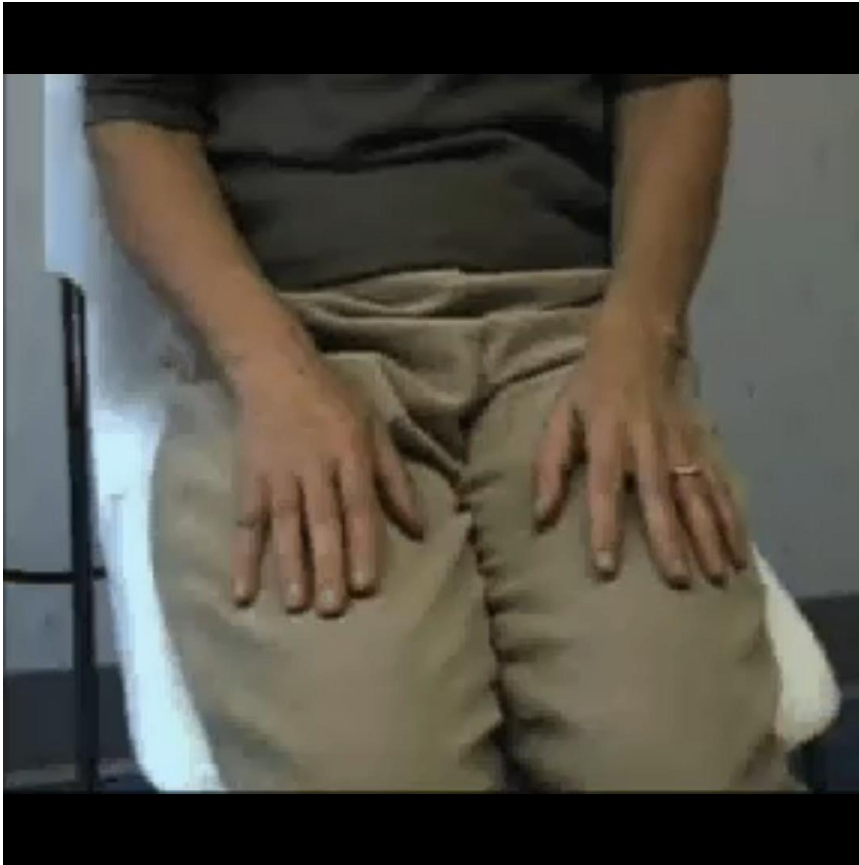
Medlink Neurology
www.medlink.com



Freezing of gait



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Signs can be subtle

- Rest tremor
- Bradykinesia



Signs can be subtle

- Rest tremor
- Bradykinesia



Nutt JG and Wooten GF. Diagnosis and Initial Management of Parkinson's Disease. N Engl J Med 2005;353(10):1021-7.



Lewy Body Dementia (LBD)

Cognitive Changes

Dementia

Changes in alertness

Hallucinations

Parkinsonism

REM sleep disorder

“Motor” Symptoms:

- Rest tremor
- Slowness of movement
- Stiffness (Rigidity)
- Balance difficulty
- Shuffling gait
- Stooped posture
- Softer voice; less facial expression
- Smaller writing



REM Sleep Behavior Disorder (RBD)

During REM sleep, when dreams occur, the body is normally paralyzed (atonia)

In RBD, the paralysis doesn't occur

- Act out dreams
- Talking in sleep
- Can be violent

RBD symptoms might start many years before any other symptoms



Lewy Body Dementia (LBD)

Cognitive Impairment

Dementia

Hallucinations

Changes in alertness

Parkinsonism

REM sleep disorder

Supportive Features

Autonomic nervous system dysfunction

- Lightheadedness when standing
- Constipation
- Frequent urination

Loss of sense of smell

Anxiety/depression/delusions

Sensitivity to certain antipsychotic medications

- e.g. haloperidol



Why is it called Lewy Body Dementia?

In certain brain cells (neurons), there are “clumps” of specific proteins, called Lewy Bodies

- ubiquitin and α -synuclein

Lewy Body Diseases

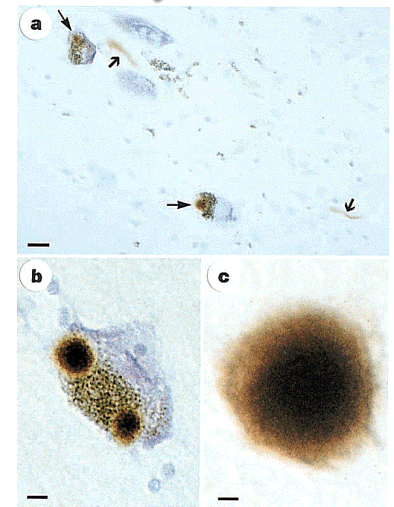
Dementia with Lewy Bodies

Parkinson’s Disease and Parkinson’s Disease Dementia

Multiple Systems Atrophy (MSA)

These are also termed “synucleinopathies” because of the accumulation of the protein synuclein

Lewy Bodies



Spillantini et al., Nature 1997

Very common for people with LBD to also have Alzheimer’s disease pathology in the brain



Dementia with Lewy Bodies Diagnosis

Cognitive changes
consistent with dementia

Dementia should start within 1
year of Parkinsonian motor signs
or else classified as Parkinson's disease
dementia

At least 2 of these features

Parkinsonism

Visual Hallucinations

REM sleep disorder

Fluctuating consciousness



Biomarkers:

Measurable characteristics (from brain imaging, blood test, spinal fluid, etc.) that can indicate an underlying condition

Used in diagnosis of LBD

Dopamine transporter SPECT (DaTscan)

- Motor symptoms of LBD due to loss of specific neurons that make the neurotransmitter dopamine
- Measures loss of dopamine neurons

Cardiac MIBG scintigraphy

- Measures loss of autonomic sympathetic neurons

Polysomnography (sleep study)

- Documents RBD (REM sleep without atonia)
- Most typical sleep studies (e.g. for sleep apnea) do not assess for this

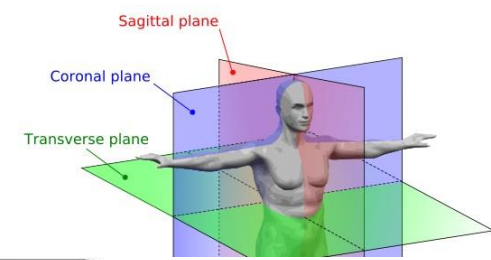
Supportive

Brain PET or SPECT scan - decreased metabolism in “occipital” region of brain

New spinal fluid and skin biomarkers – looks for synuclein “clumping”

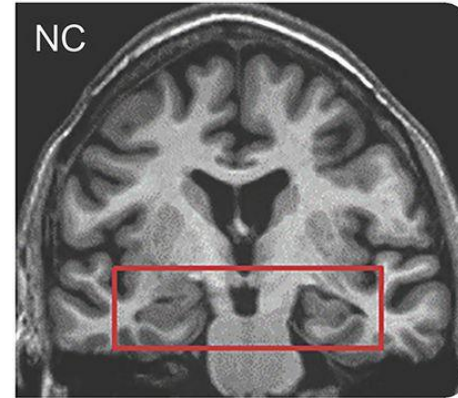
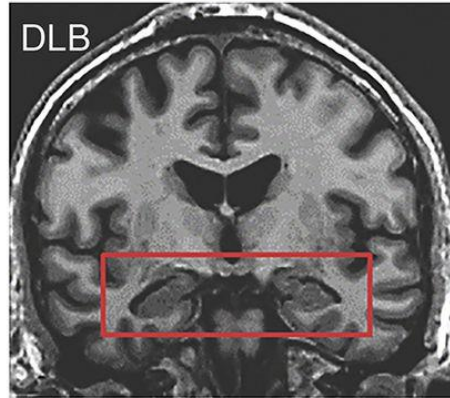
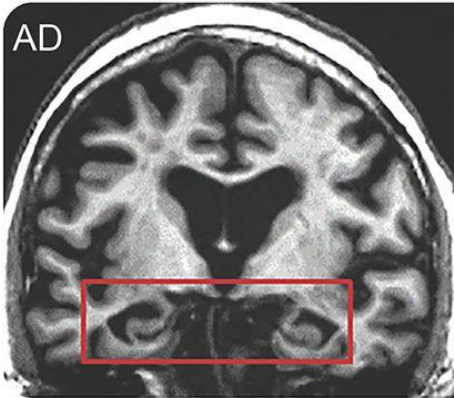


Brain Imaging in LBD

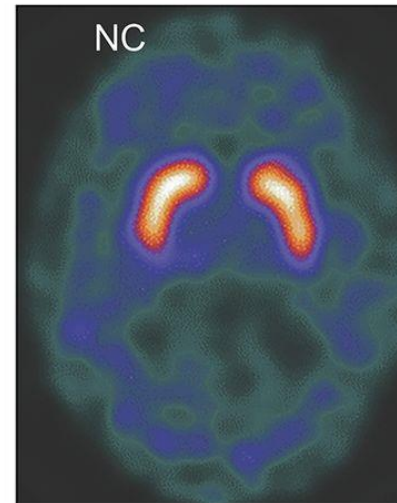
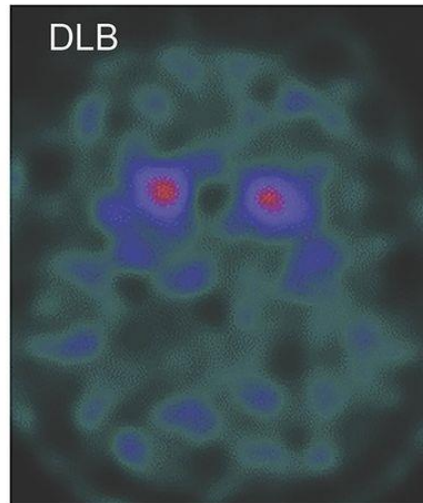
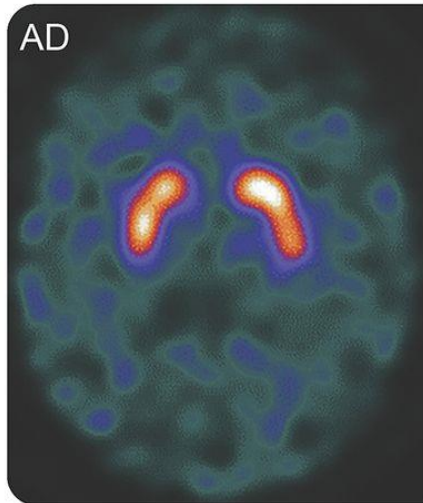


My-ms.org

A. MRI

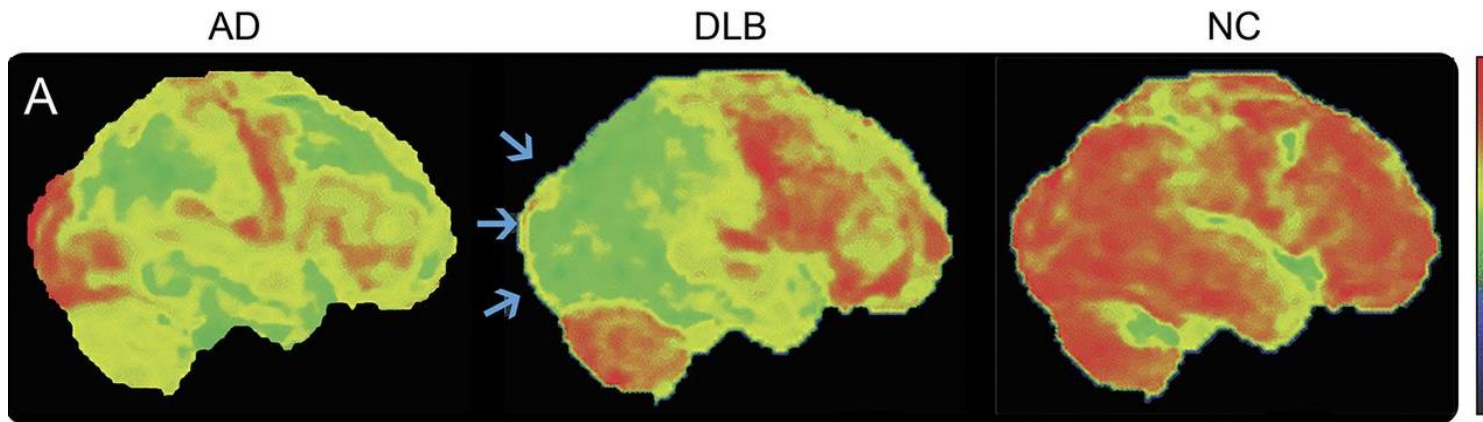


B. FP-CIT SPECT



Modified from McKeith et al. *Neurology* 2017;89:88-100

Brain Imaging in LBD

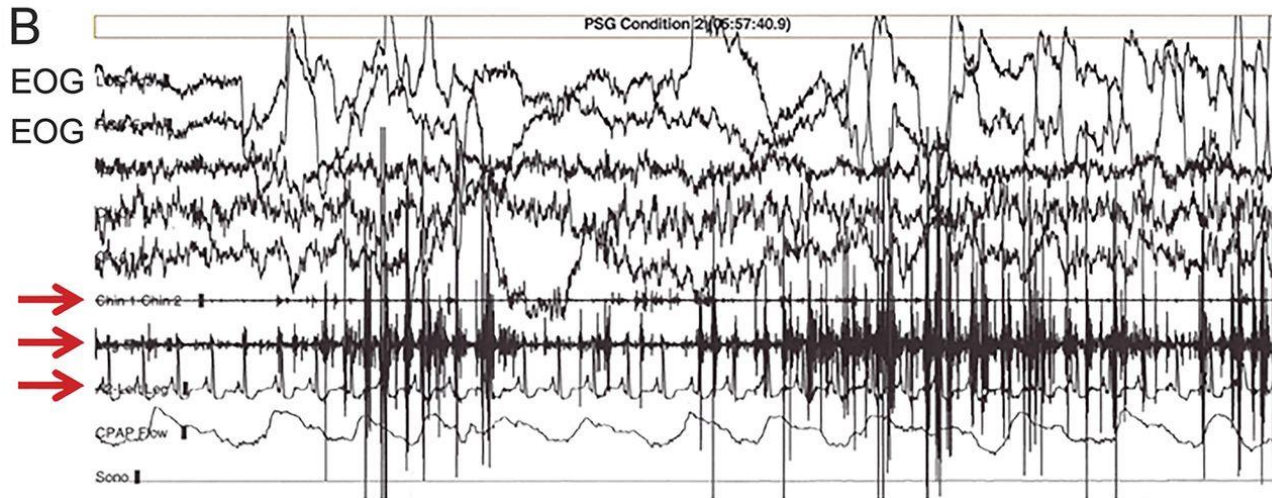
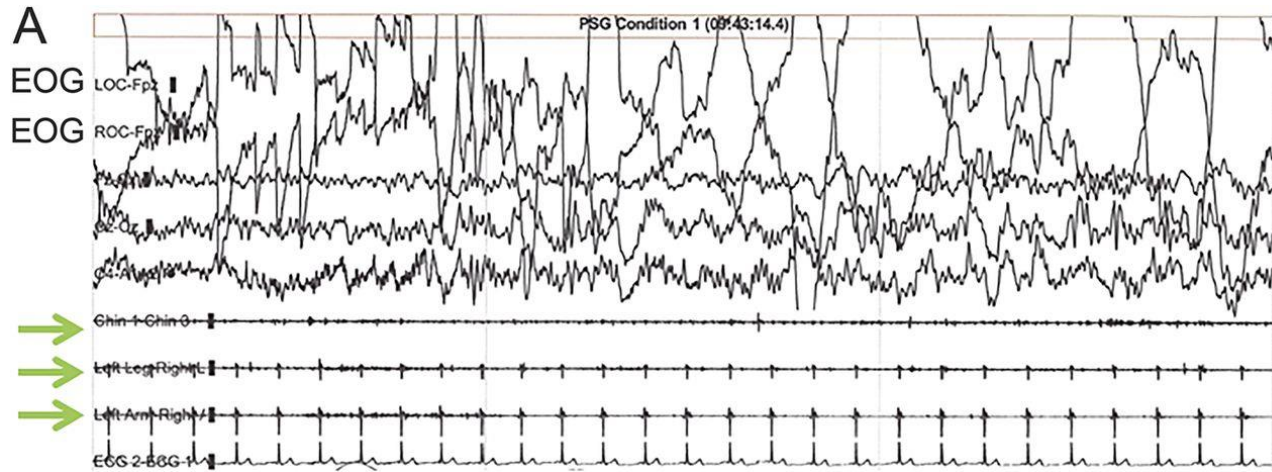


PET Imaging: Metabolic activity

Modified from McKeith et al. *Neurology* 2017;89:88-100

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SLEEP STUDY: Polysomnographic (PSG) recordings RBD



Ian G. McKeith et al. *Neurology* 2017;89:88-100



LBD Treatment Strategies

Multifactorial and individualized

- No disease-modifying therapy available
- Address specific symptoms
 - Complexities of treatment interactions



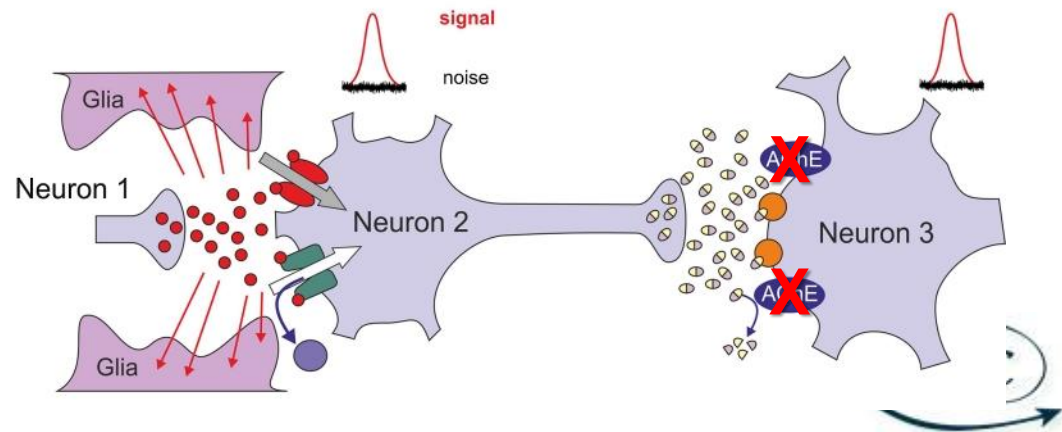
Treatment Strategies

Cognitive changes

Acetylcholinesterase inhibitors

- Donepezil
- Rivastigmine (oral or transdermal)
- Galantamine

Often more noticeable benefit in LBD than in AD



(Modified from Parsons et al.,
Neurotox Res, 2013)



Treatment Strategies

Psychosis (hallucinations, delusions)

Cholinesterase inhibitors might be helpful (e.g. donepezil)

AVOID typical antipsychotics (e.g., haloperidol)

- If necessary, the atypical antipsychotic quetiapine is a better choice
 - Less motor side effects
 - Or clozapine (but requires weekly blood monitoring)

Future targets?



Treatment Strategies

Parkinsonism (motor symptoms)

PT/OT/Speech

- Specific programs for parkinsonism-related motor symptoms can be helpful (e.g. “BIG” and “Loud” programs, Lee Silverman Voice therapy)

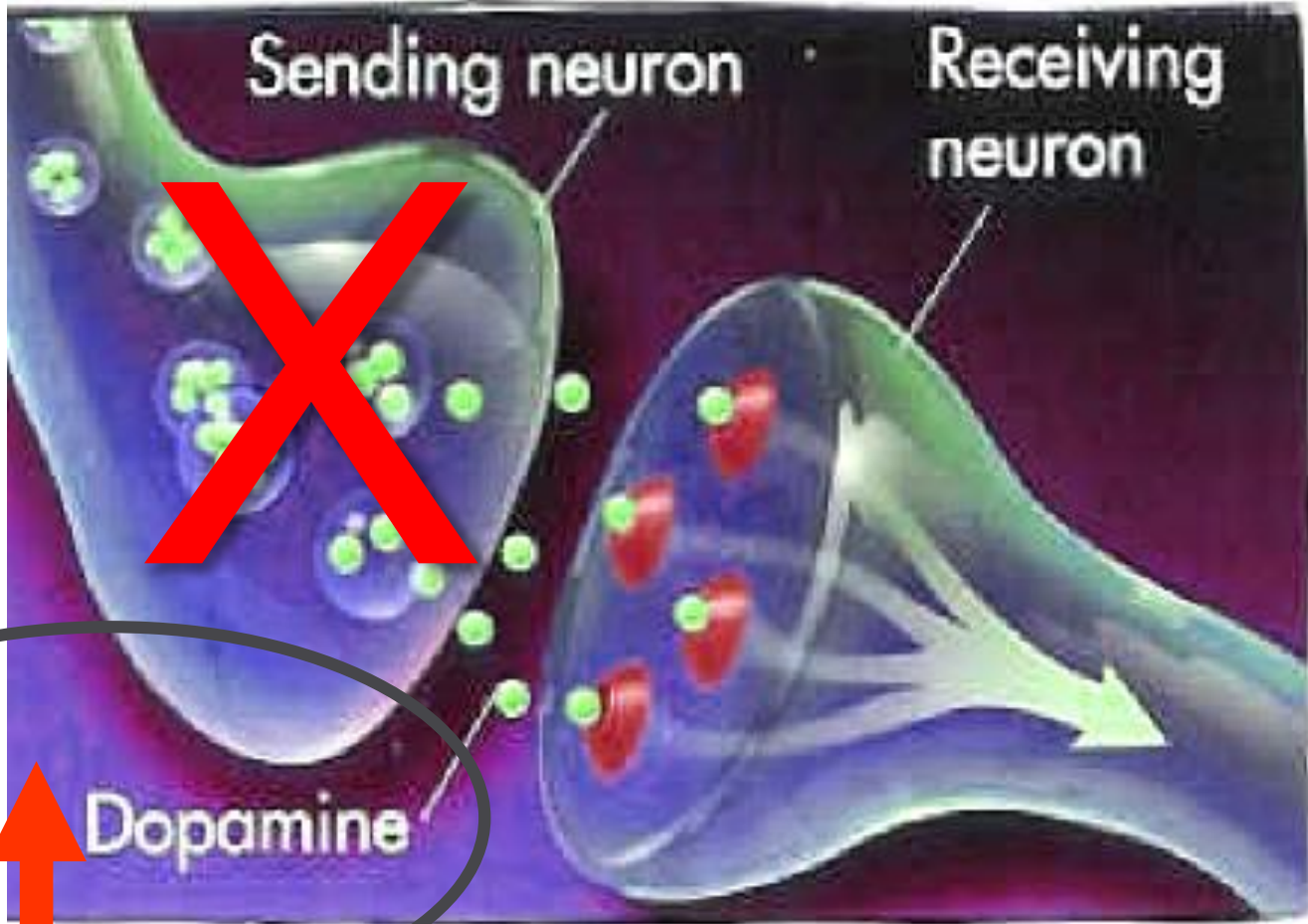
Exercise!

- May slow disease process down

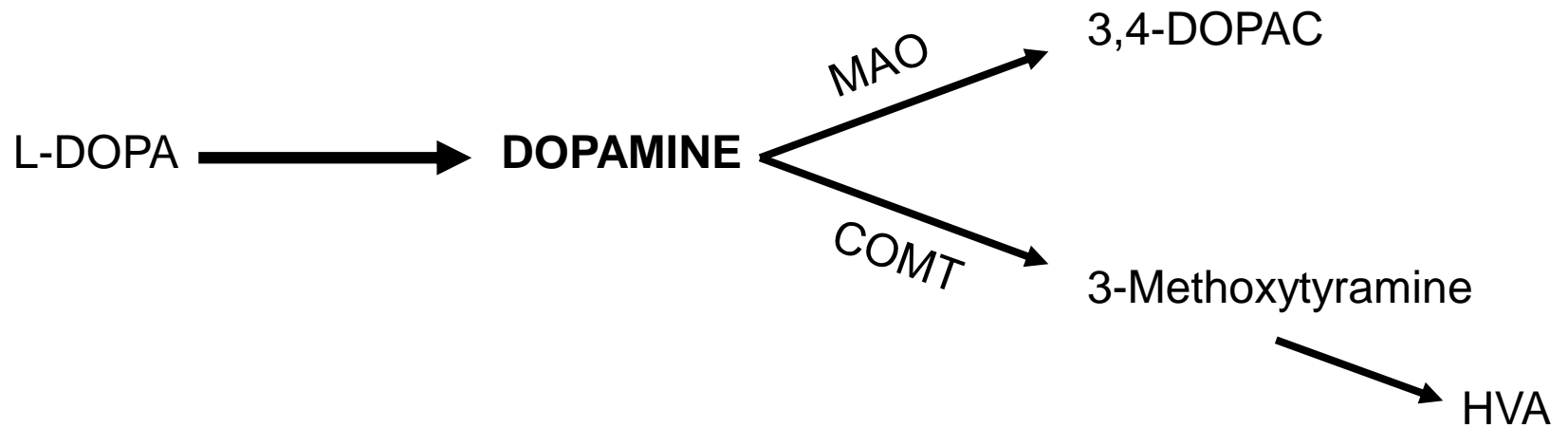
Medications

- Levodopa/carbidopa
 - How it works
 - Risks in DLB

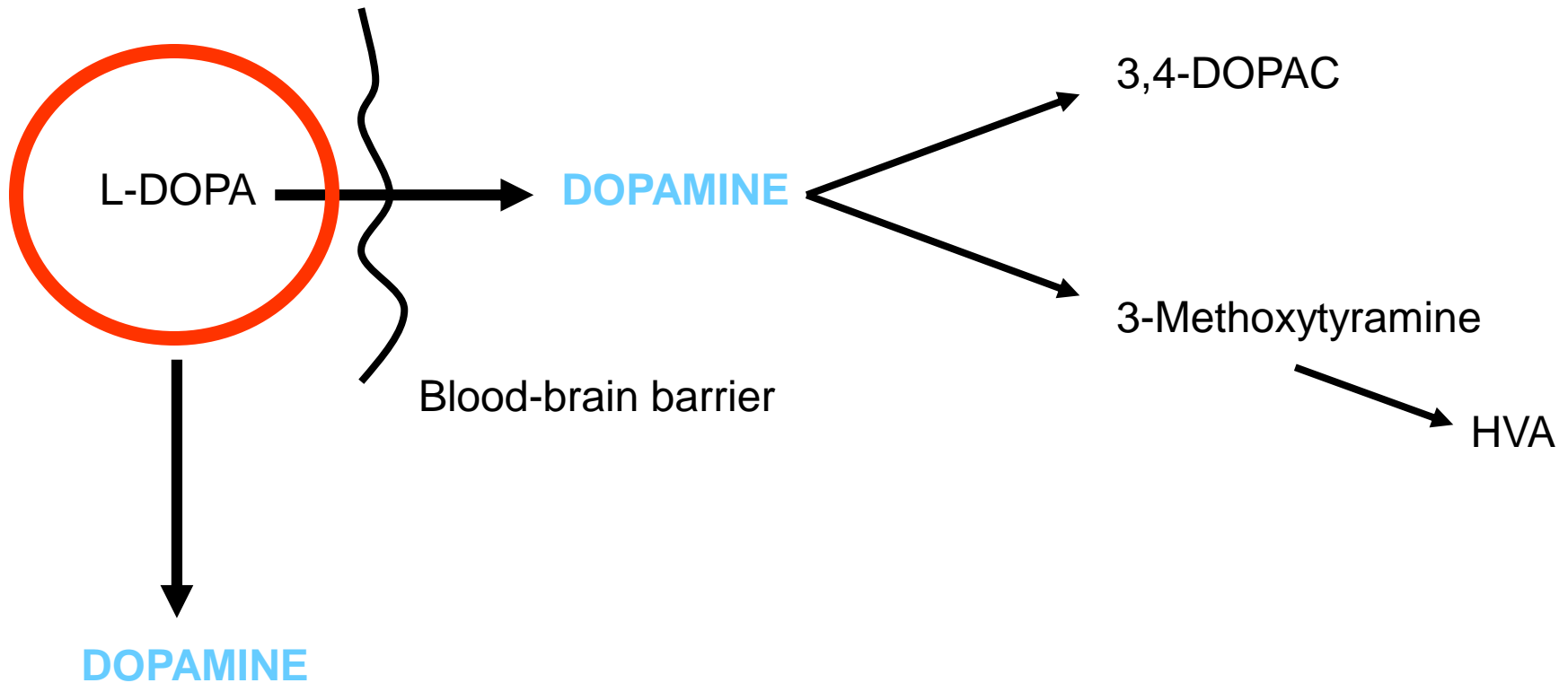




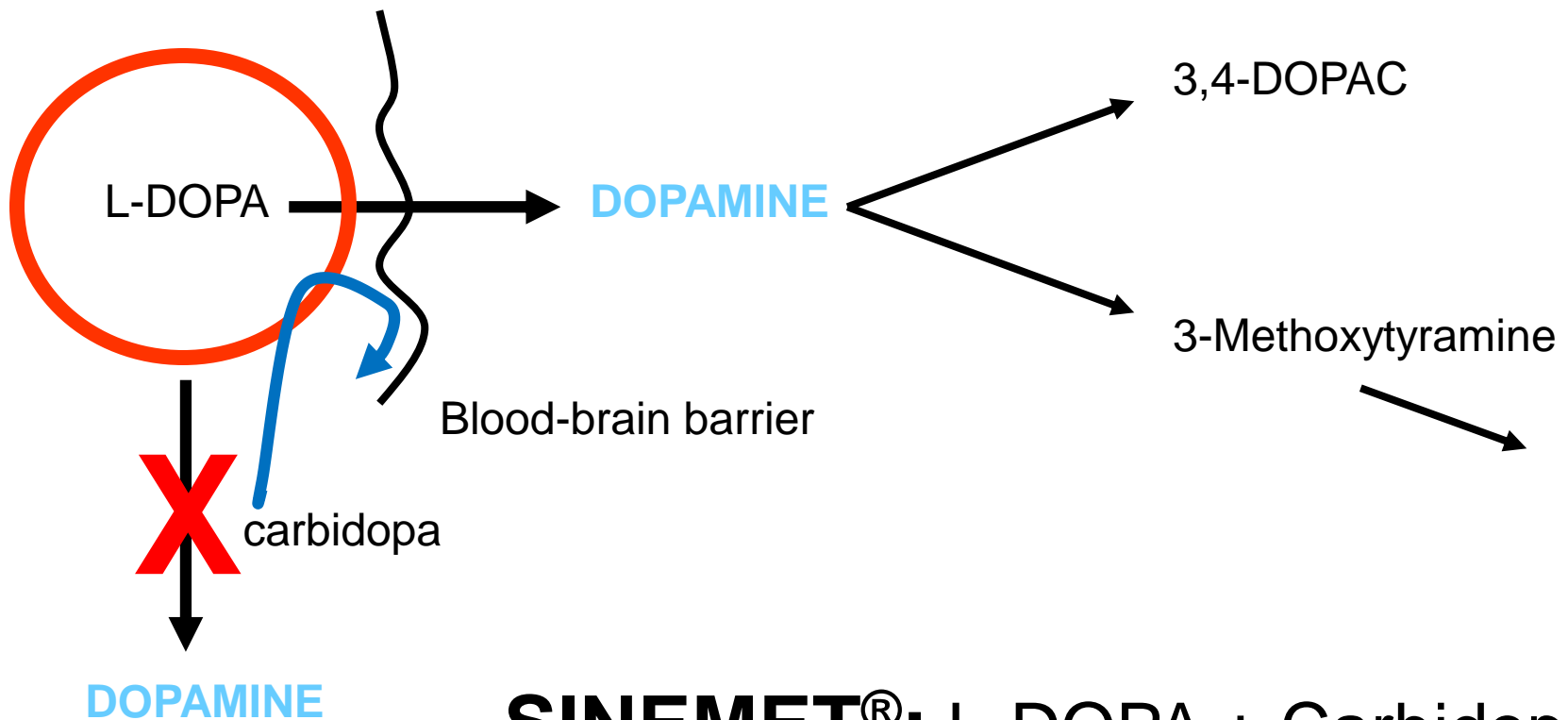
Dopamine metabolism



Dopamine metabolism



Dopamine metabolism



SINEMET[®]: L-DOPA + Carbidopa



Carbidopa/Levodopa

Can help with

- Slowness
- Stiffness
- Shuffling walk/freezing
- Tremor

Not as useful as in Parkinson's disease

- Potential side effects
 - Worsening hallucinations



LBD Complexities

Dopamine-related treatments

Hallucinations, Delusions

Levodopa

DOPAMINE LEVELS

Quetiapine
Other anti-psychotics

Parkinsonian motor sx



Treatment Strategies

Sleep Disturbance

- REM sleep behavior disorder (RBD)
 - Melatonin, Low-dose clonazepam

Depression/Anxiety

SSRIs

- e.g., sertraline, escitalopram

SNRIs

- e.g., venlafaxine



Treatment Strategies

Apathy

Lack of interest, initiative motivation

- Different than depression; biologically driven

Can be very frustrating

- Can impede participating in healthful activities

Can be difficult to treat

Involves several different brain pathways

- Treatments try to target those areas
 - SSRIs (serotonin medications); cholinesterase inhibitors (e.g. donepezil); dopamine-related medications



Treatment Strategies

Apathy

Exercise

Schedule activities

Set small goals each day

Keep social/family connections

New learning/new hobby?

For family:

- Encouragement and praise
- Try to avoid being critical
- Plan things to do together



Treatment Strategies

Autonomic disturbances

Orthostatic hypotension (lightheadedness on standing)

- Compression stockings, staying hydrated, fludrocortisone, midodrine

Urinary incontinence

- Try to avoid anti-cholinergics for urinary symptoms

Constipation

- Diet, miralax or other agents



Treatments to AVOID

Dopamine antagonists

- Such as MOST antipsychotics (haloperidol, risperidone)
- If needed, consider Clozaril or Seroquel
- **Includes some anti-nausea medications to avoid: Reglan, Compazine**

Anticholinergics

- Such as Benadryl, over the counter sleep aids

Dopamine “agonists” – activate dopamine receptors

- Pramipexole, ropinirole, rotigotine
- Frequently worsen hallucinations, can cause encephalopathy, behavioral changes
- Frequently used if misdiagnosed as Parkinson’s disease



PIND



Therapeutic Challenges

We can ONLY treat the symptoms

We don't yet know how to stop or slow the disease

Neuroprotective therapies

- What causes the pathology?
- How do we stop the progression?



Research/Future Directions

Basic science research studies

- Genetics
- Animal models/Cell studies
- To elucidate the mechanisms/causes of the disease

Clinical studies

- Multiple studies underway to characterize clinical progression and biomarkers
- Critical for outcomes for future neuroprotective therapy trials
- Clinical trials for potential neuroprotective therapies being developed

Goals:

- Develop effective neuroprotective therapies to slow/prevent progression
- Develop better symptomatic therapies



FOR MORE INFORMATION



About LBDA

www.lbda.org

- National non-profit founded 20 years ago by care partners seeking answers and support
- Mission: Through outreach, education and research, we support those affected by Lewy body dementias
 - Information on LBD, support groups, research

