Dementia with Lewy bodies

OUTLINE

- Introduction
- History
- Epidemiology
- Etiology
- Clinical Features
- Pathology
- Differential Diagnosis
- Treatment

- Dementia of lewy bodies DLB is a neurodegenerative dementia characterized by progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational function

- considered to be the second most common cause of dementia after Alzheimer disease in the elderly

- DLB shares some clinical and pathological features with both Alzheimer disease and Parkinson disease

HISTORY

- Dr Friedrich Lewy identified protein 1912
- intracytoplasmic spherical eosinophilic neuronal inclusion bodies identified originally in subcortical nuclei as one of the hallmarks of idiopathic Parkinson disease
- first described in 1984 by Kosaka distinguished "diffuse" Lewy body disease from "brainstem predominant" Lewy body disease and a "transitional type" which is intermediate between the two

- Several historical terms have been used to describe what is now referred to in general as DLB
- diagnostic criteria were published by the Consortium on Dementia with Lewy bodies in 1996 and revised in 2005
- criteria defines the core clinical features and those clinical features that were supportive of the diagnosis
- The presence of one core feature was required for a diagnosis of possible DLB and at least two core features for probable DLB

- The core features of DLB include
- 1 fluctuating cognition with pronounced variations in attention and alertness
- 2 **recurrent visual hallucinations** which are typically well formed and detailed
- 3 spontaneous motor features of parkinsonism

features that are suggestive of the diagnosis of DLB are

- rapid eye movement REM sleep behaviour disorder
- severe neuroleptic sensitivity
- low dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET imaging

Features supportive of the diagnosis include

- repeated falls and syncope
- transient unexplained loss of consciousness
- severe autonomic dysfunction
- hallucinations in other modalities
- systematized delusions
- depression
- preservation of medial temporal lobe structures on CT MRI scan generalized low uptake on SPECT PET perfusion scan with reduced occipital activity
- prominent slow wave activity on EEG with temporal lobe transient sharp waves

- The distinction between DLB and Parkinson disease with dementia requires evidence of dementia within 1 year of the motor symptoms for a diagnosis of DLB

- criteria **did not exclude patients who simultaneously met clinical and or pathological criteria for a diagnosis of Alzheimer disease**

- criteria **for DLB were revised in 2005** with efforts made to clarify the overlap of DLB with Parkinson disease and Alzheimer disease

- clarified to indicate **DLB should be diagnosed when dementia precedes or is concurrent with parkinsonian symptoms** and should not be diagnosed when dementia arises in the "context of well established Parkinson disease"

- The DSM 5 incorporated the above described criteria in the diagnosis major neurocognitive disorder with Lewy bodies

- For a diagnosis of major neurocognitive disorder with Lewy bodies an individual must have two core features or one suggestive feature with one or more core features

- If only one core feature or one or more suggestive features then a diagnosis of **possible** neurocognitive disorder with Lewy bodies is made

Epidemiology

- The **prevalence** of DLB in populations over 65 has been found to range from 0.1 to 5 percent
- DLB likely accounts for 15 to 35 percent of all dementia patients
- mean age at onset being 75 years old with a range from 50 to 80 years
- incidence of DLB 35 per 100 000 person years with peak incidence in the 70 to 79 year age group
- There is a slight male predominance

Etiology

- Lewy bodies are comprised of **abnormal fibrillar deposits of α synuclein**
- Mutations and copy number variations in the gene **encoding α synuclein *SNCA* result in disorders with Lewy body pathology**
- Mutations in **β synuclein *SNCB*** and in *GBA* resulting in DLB have also been described
- The ***APOE* ε4** allele has also been associated with increased risk of DLB
- The causes of most cases of sporadic DLB remain unknown

Clinical features

- progressive cognitive decline of sufficient magnitude to interfere with normal ADL
- memory impairment may not necessarily be prominent or persistent in early stages
- deficits of attention executive function and visuospatial ability prominent
- fluctuation in cognitive function and pronounced variation in attention and alertness is common in DLB
- exhibit daytime drowsiness lethargy with lengthy naps followed by periods of confusion upon awakening
- may appear to 'switch off' or go blank at times manifest as staring into space

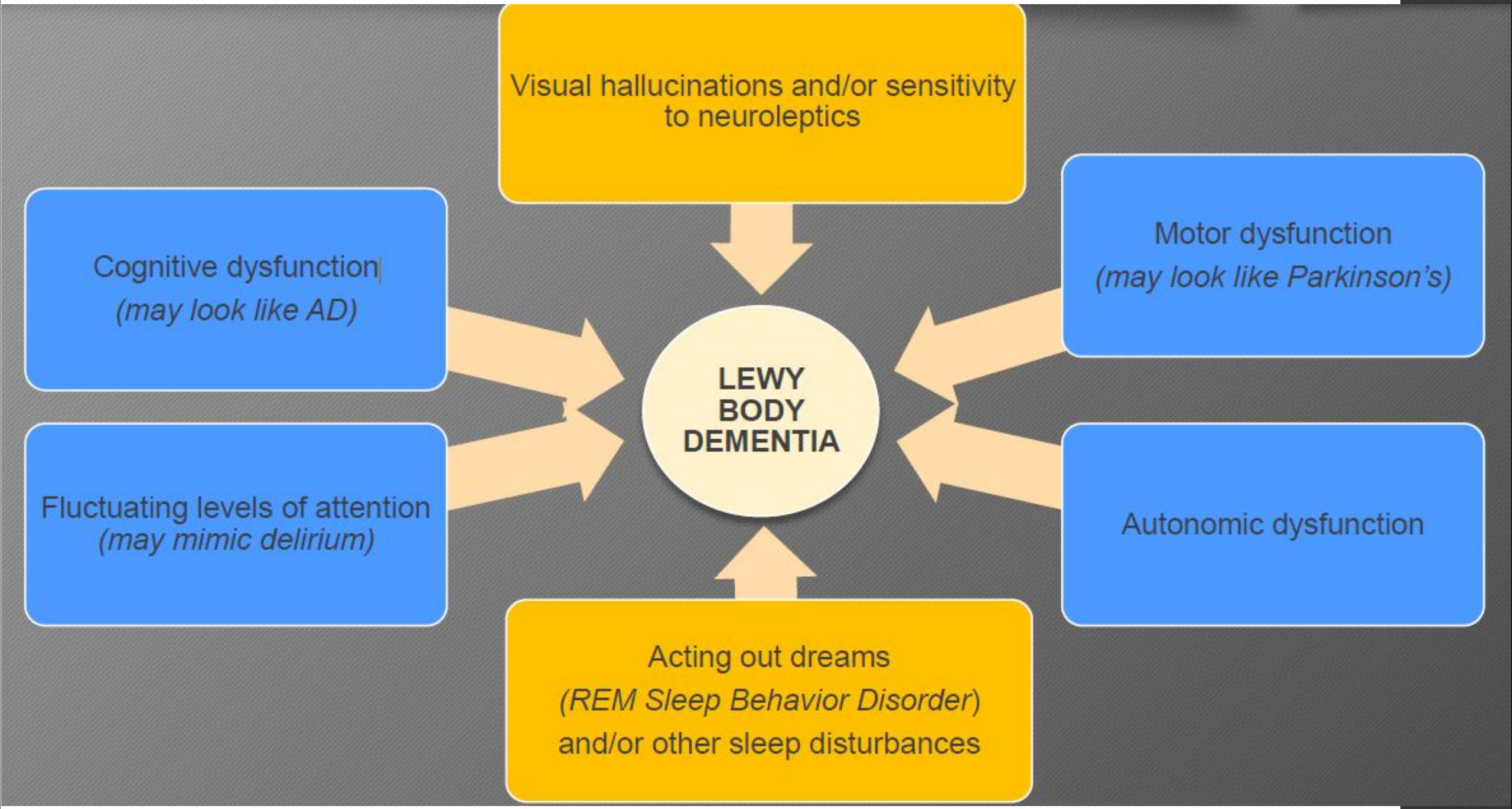
- visual hallucinations occur early in the course
- visual hallucinations usually recurrent formed detailed and tend to persist common theme is animals or people intruding into home
- Patients may have delusional explanations of the hallucinations
- Emotional responses to the hallucinatory experiences can range from indifference to amusement to fear
- Correlate with a higher density of Lewy bodies in anterior and inferior temporal lobe and amygdala and reduced occipital perfusion in primary and secondary visual cortex

- Extrapyramidal symptoms noted in DLB are **rigidity and bradykinesia hypophonic speech masked facies stooped posture slow and shuffling gait**

- The parkinsonism seen in DLB tends to include greater postural instability gait impairment and facial immobility compared to patients with Parkinson disease

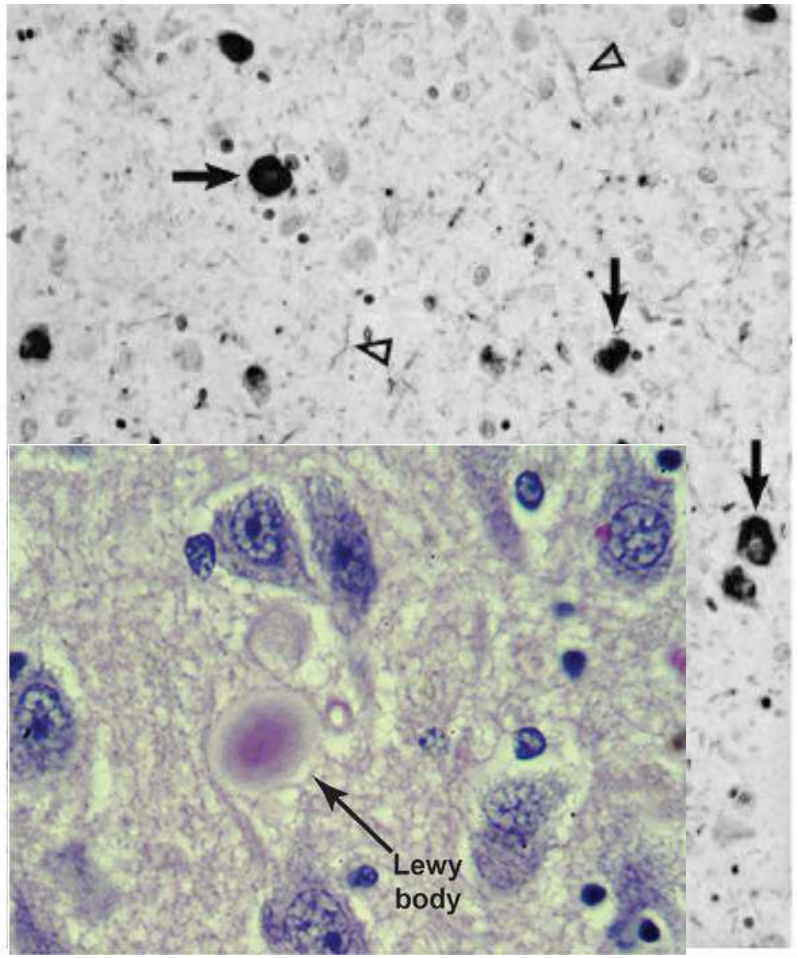
- other clinical features suggestive of a diagnosis of DLB include REM sleep behavior disorder
- vivid and often frightening dreams during REM sleep with lack of muscle atonia allowing for "acting out of dreams"
- have little or no recall of their dreams or these episodes
- diagnosis can be confirmed by polysomnography
- REM sleep behaviour disorder may predate the emergence of parkinsonism or dementia by many years

- Severe neuroleptic sensitivity is present in about half of patients
- demonstrate acute onset or exacerbation of parkinsonism and impaired consciousness with even a low dose of a first or second generation antipsychotic agent
- Sensitivity to antipsychotics has profound treatment implications in DLB
- most common **delusions in DLB are persecution and theft television characters in the room spousal infidelity and Capgras syndrome delusional misidentification syndrome**

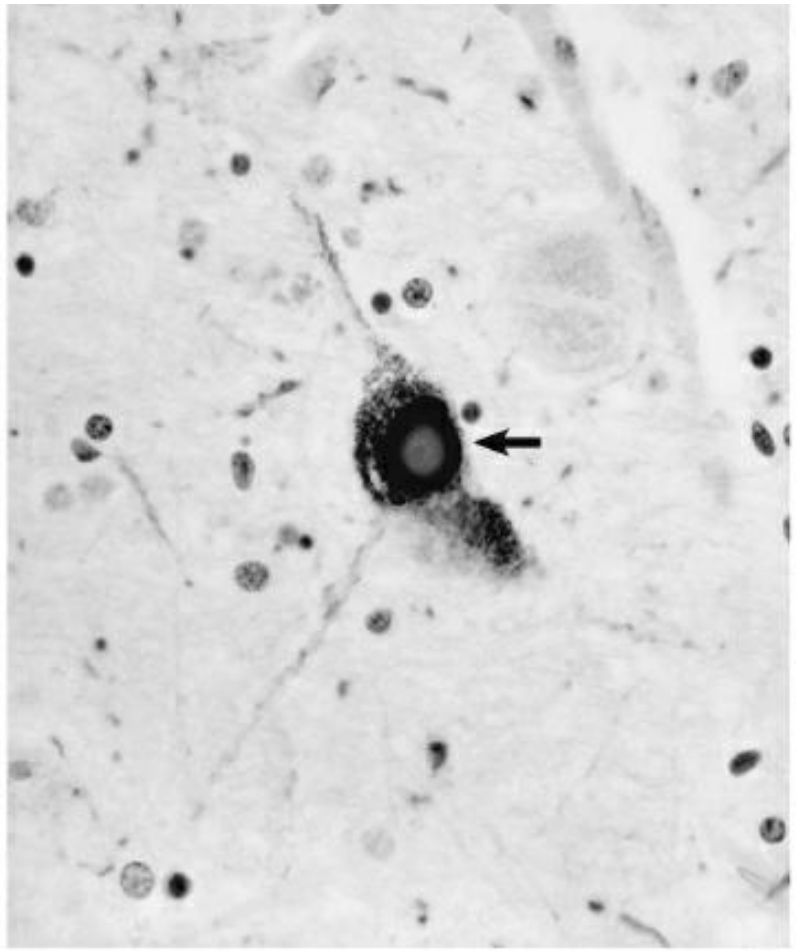

Visual hallucinations and/or sensitivity to neuroleptics
Cognitive dysfunction
(may look like AD)
Motor dysfunction
(may look like Parkinson's)
LEWY BODY DEMENTIA
Fluctuating levels of attention
(may mimic delirium)
Autonomic dysfunction
Acting out dreams
(REM Sleep Behavior Disorder)
and/or other sleep disturbances

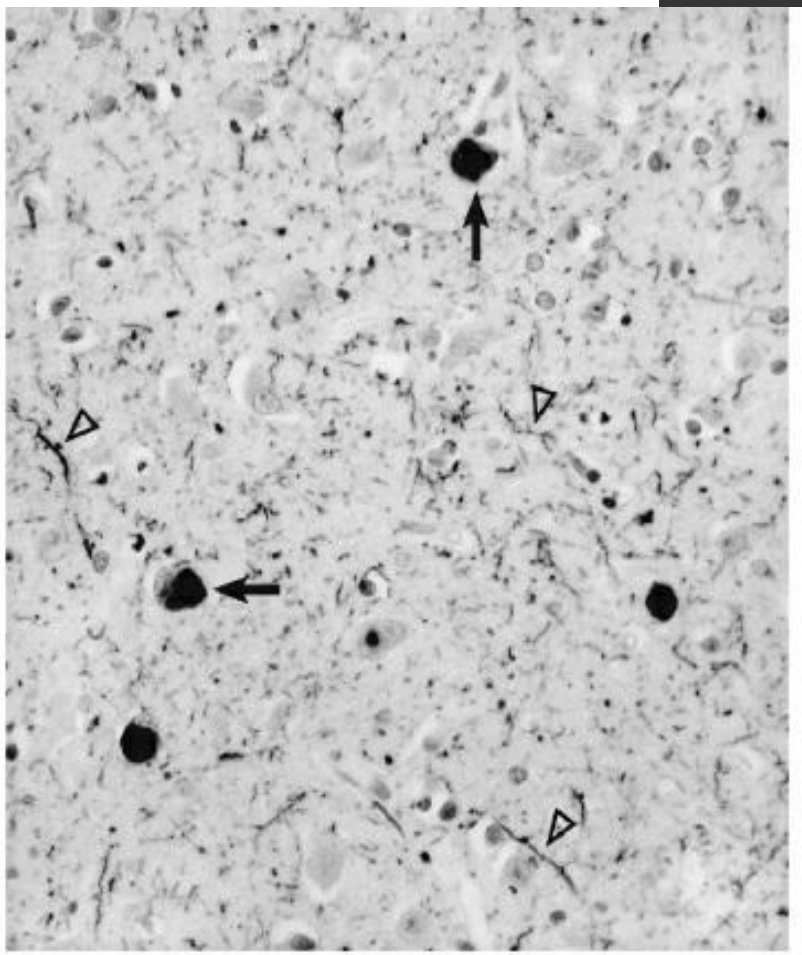
Pathology

- Lewy bodies are only essential finding in the pathological diagnosis of DLB
- spherical intracytoplasmic eosinophilic neuronal inclusion bodies
- Classical Lewy bodies are inclusions with a hyaline core and pale halo
- Cortical Lewy bodies less well defined spherical inclusions
- bodies are composed predominantly of fibrillar deposits of α synuclein and can also include neurofilament proteins and ubiquitin
- aggregates of α synuclein occur in neuronal processes called Lewy neurites
- Alzheimer disease pathology particularly amyloid containing plaques is also a common feature in most cases of DLB



A, B





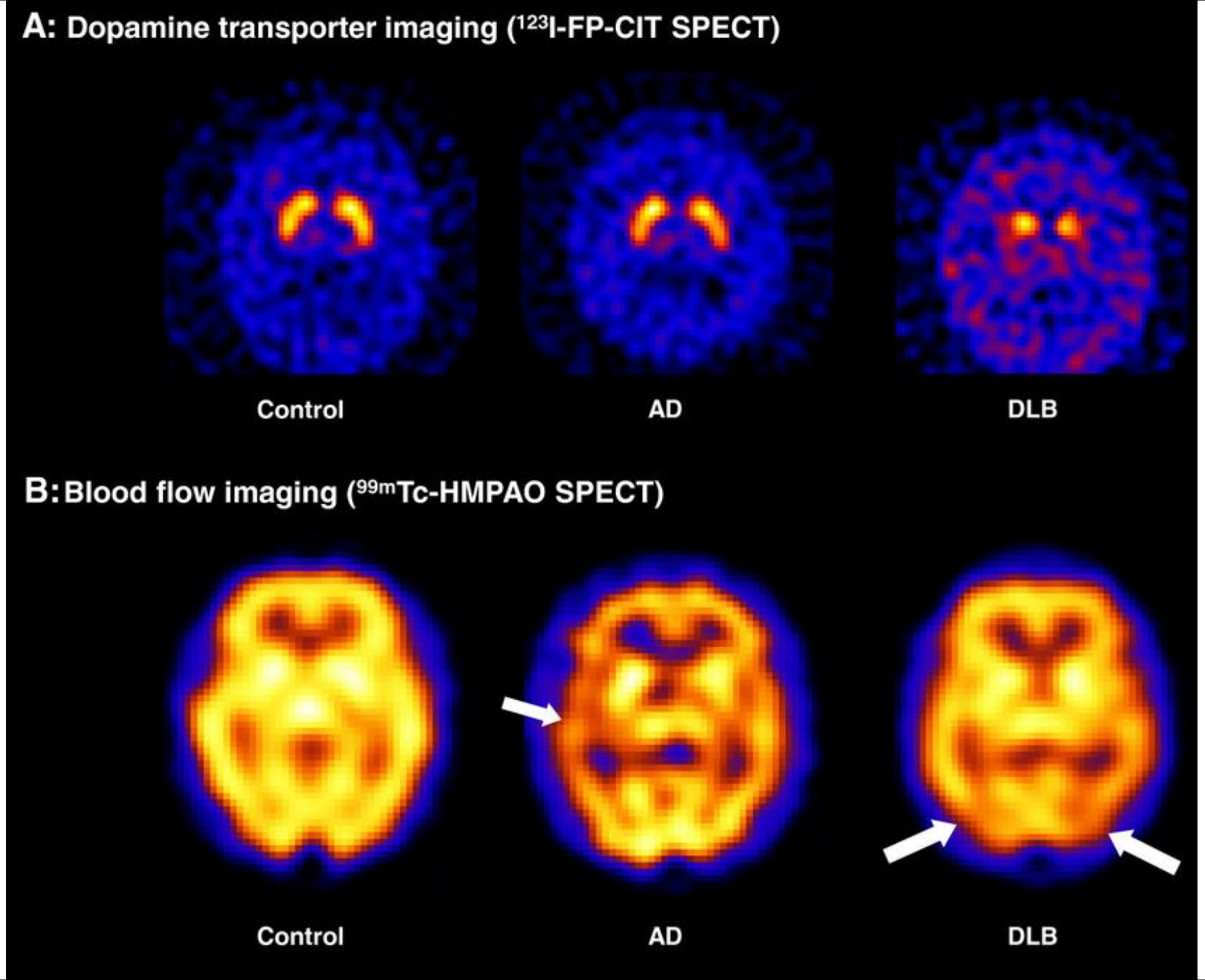
C

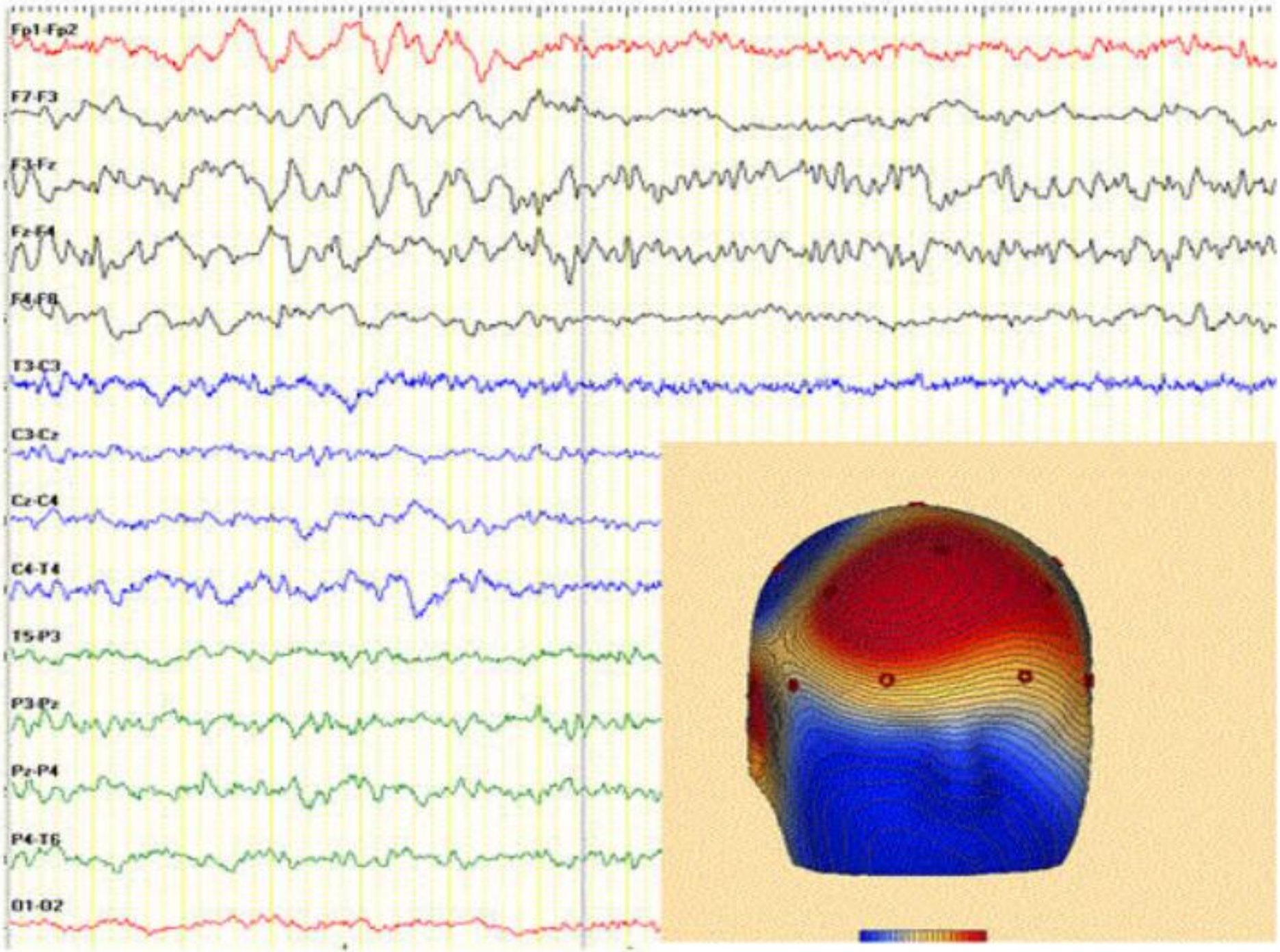
- Structural imaging studies CT and MRI are not able to effectively differentiate Alzheimer disease from DLB

- **SPECT and PET imaging are better tool for distinguishing between Alzheimer disease and DLB**

- Imaging the presynaptic dopaminergic terminals using 123I-IP CIT SPECT or 18-F dopa PET shows marked **loss of presynaptic dopaminergic terminals in the corpus striata in DLB whereas no change in these terminals in normal individuals and in patients with Alzheimer disease**

- EEG shows early generalized background slowing with abnormal transient sharp waves in the temporal lobes or frontally dominant burst patterns


A: Dopamine transporter imaging (^{123}I-FP-CIT SPECT)
Control
AD
DLB
B: Blood flow imaging (^{99m}Tc-HMPAO SPECT)
Control
AD
DLB

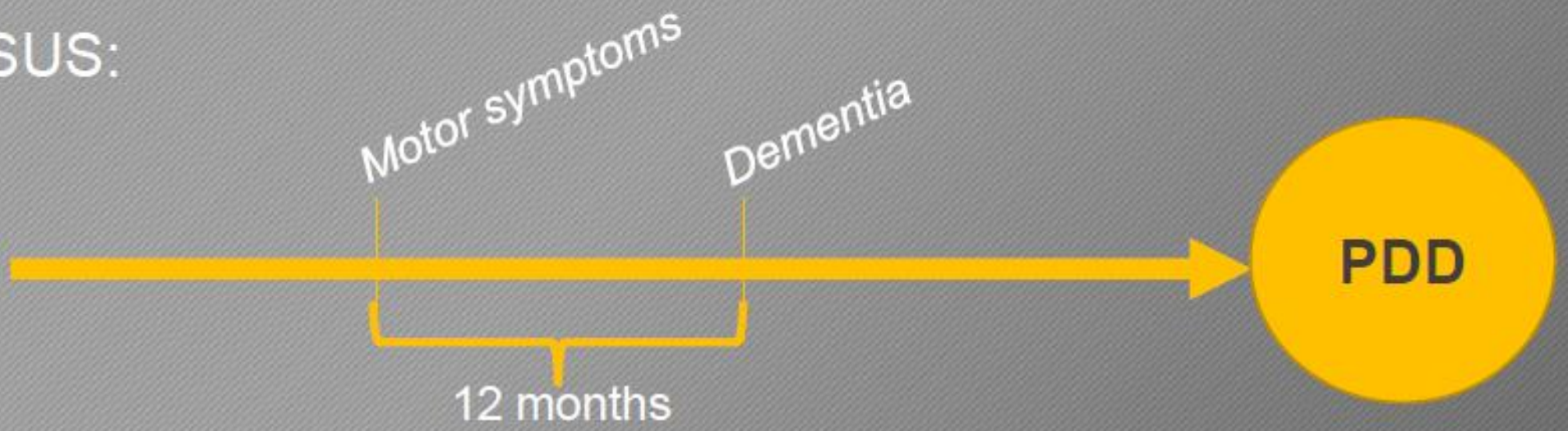

Fp1-Fp2
F7-F3
F3-Fz
Fz-F4
F4-F8
T3-C3
C3-Cz
Cz-C4
C4-T4
T5-P3
P3-Pz
Pz-P4
P4-T6
O1-O2

Differential Diagnosis

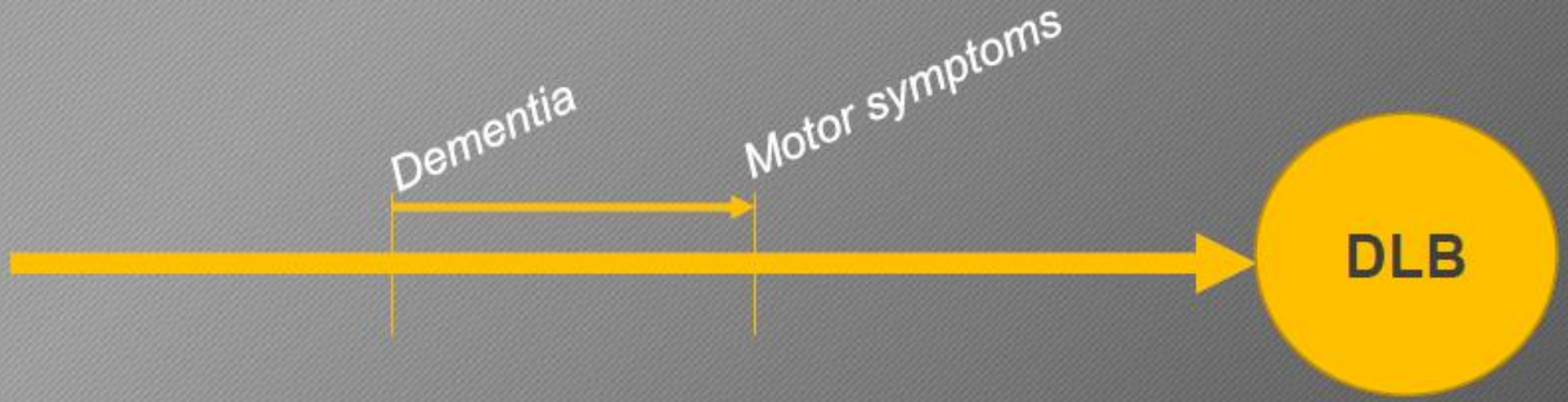
- DLB overlaps with Alzheimer disease both in terms of clinical presentation and neuropathological changes
- The clinical symptoms are overlapping and no specific cut off based on number or pattern of core suggestive and supportive features present is definitive
- presence of at least two of the core features in the early disease course fluctuating attention prominent visual hallucinations and parkinsonism indicates DLB with high specificity

- also considerable clinical and pathological overlap and comorbidity between DLB and Parkinson disease
- The primary diagnosis should be made based on the temporal relationship of the onset of cognitive and motor symptoms
- Dementia develops in at least 30 percent of patients with Parkinson disease and up to 78 percent when patients are followed over 8 years
- cases where there is not a clear temporal relationship between the motor and cognitive symptoms the term Lewy body disease may be useful
- For research purposes the "1 year rule" should be used between the onset of parkinsonism and dementia to distinguish between these two entities

BY CONSENSUS:



IF



- **Multiple system atrophy MSA also has a synuclein involvement**
  - Clinical symptoms of MSA include parkinsonism cerebellar ataxia pyramidal symptoms and autonomic dysfunction
  - Autonomic dysfunction is necessary for a diagnosis of MSA and includes orthostatic hypotension erectile dysfunction in males constipation and urinary symptoms
  - Dementia is much less common in MSA and is a non supporting feature of the diagnosis

- Distinguishing between delirium and DLB can be challenging
- The fluctuating level of alertness and consciousness in DLB is also a hallmark of delirium
- Visual hallucinations also common in both
- DLB like other dementias also increases the risk for a superimposed delirium due to medications medical illness and after hospitalization for any reason
- Delirium however should typically have an acute or subacute onset and a duration limited to the period of exposure to the underlying causal agent
- CJD may be considered in patients who develop myoclonus which is also characteristic of a rapidly progressive form of DLB

Treatment

- PHARMACOLOGICAL TREATMENT
- **Cholinesterase Inhibitors** the mainstay of treatment for the cognitive impairment of DLB
- randomized placebo controlled trial showed that **donepezil was associated with improvements in cognition behavior and global functioning as well as reductions in caregiver burden**
- randomized placebo controlled trial **of rivastigmine demonstrated significant improvement in apathy anxiety delusions hallucinations and cognitive functioning**

- **Memantine** Data in regard to the usage of memantine is mixed Some studies that have shown that memantine is associated with improved quality of life and improvements in global clinical status a recent systematic review found that there was no benefit

- reports of worsening hallucinations and delusions

- **Antipsychotics First generation antipsychotics are generally not well tolerated in DLB and should be avoided**

- A placebo controlled study **of olanzapine** in psychosis in Alzheimer disease looked at a subgroup of patients retrospectively diagnosed with DLB **demonstrated a decrease in positive symptoms of psychosis without worsening of parkinsonism or cognition** Cummings et al 2002

- no controlled trials involving the use of clozapine in the treatment of neuropsychiatric symptoms of DLB
- given utility in treating psychosis in Parkinson disease shows clinical value in its treatment of psychotic symptoms in DLB as well
- open label study of quetiapine for psychosis and agitation in DLB found a clinically significant reduction in symptoms in about half the patients Takahashi et al 2003

- Antidepressants not systematically studied in DLB SSRIs and selective and norepinephrine reuptake inhibitors SNRIs are probably preferred and antidepressants with anticholinergic properties should be avoided
- Benzodiazepines Clonazepam may have benefit for the treatment of REM sleep behavior disorder but like all long half life benzodiazepines must be used cautiously in the elderly
- Antiparkinsonian Medications L dopa and direct dopamine agonists may be tried in DLB Responses are variable Given their increased potential for neuropsychiatric complications initial doses should be small
- Anticholinergic medications are generally not recommended because of the associated cognitive side effects

- NONPHERMACOLOGICAL TREATMENT
- Physical therapy Can improve gait strength training and flexibility
- Occupational therapy Works with fine motor skills and independence training continence hygiene
- Speech therapy Swallowing issues voice volume

references

- Sadock Benjamin J Sadock Virginia A Ruiz Pedro Kaplan Sadock's Comprehensive Textbook of Psychiatry 10th Edition 2017 Wolters Kluwer
- Kaplan and Sadock's Synopsis of Psychiatry Behavioral Sciences Clinical Psychiatry Eleventh North American Edition by Benjamin J Sadock Virginia A Sadock
- McKeith IG Dickson DW Lowe J Emre M O'Brien JT Diagnosis and management of dementia with Lewy bodies Third report of the dementia with Lewy bodies Consortium Neurology2005 65 1863 1872
- Rabins PV Rovner BW Rummans T Schneider LS Tariot PN Guideline watch October 2014 Practice guideline for the treatment of patients with Alzheimer's disease and other dementias American Psychiatric Association
- Seitz DP Adunuri N Gill SS Gruneir A Herrmann N Rochon P Antidepressants for agitation and psychosis in dementia Cochrane Database Syst Rev 2011 2Art No CD008191
- Google Images

THANK YOU


Now, what did I come in here for?
MEMORY CLINIC
RECEPTION
CARTOONSTOCK .com
Search ID: enan637