DEMENTIA IN PARKINSON`S DISEASE

DR C PADMAKUMAR

MD FRACP FRCP(Edin)

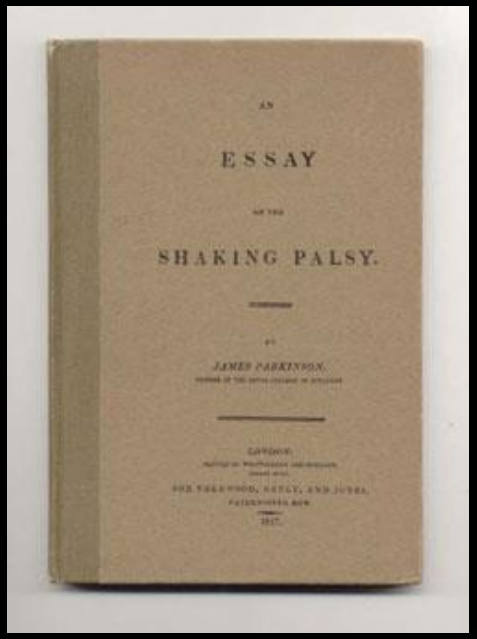
Director-Parkinson`s Disease Service for the Older Person

HNELHD

DEMENTIA IN PD

- The concept of Non Motor Symptoms in PD
- Dementia in Parkinson`s Disease (PDD)
- How is PDD different from Alzheimer`s Dementia
- Management of Dementia in PD

DR JAMES PARKINSON 1817



- *Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forward, and to pass from a walking to a running pace:* ***the senses and intellects being uninjured***

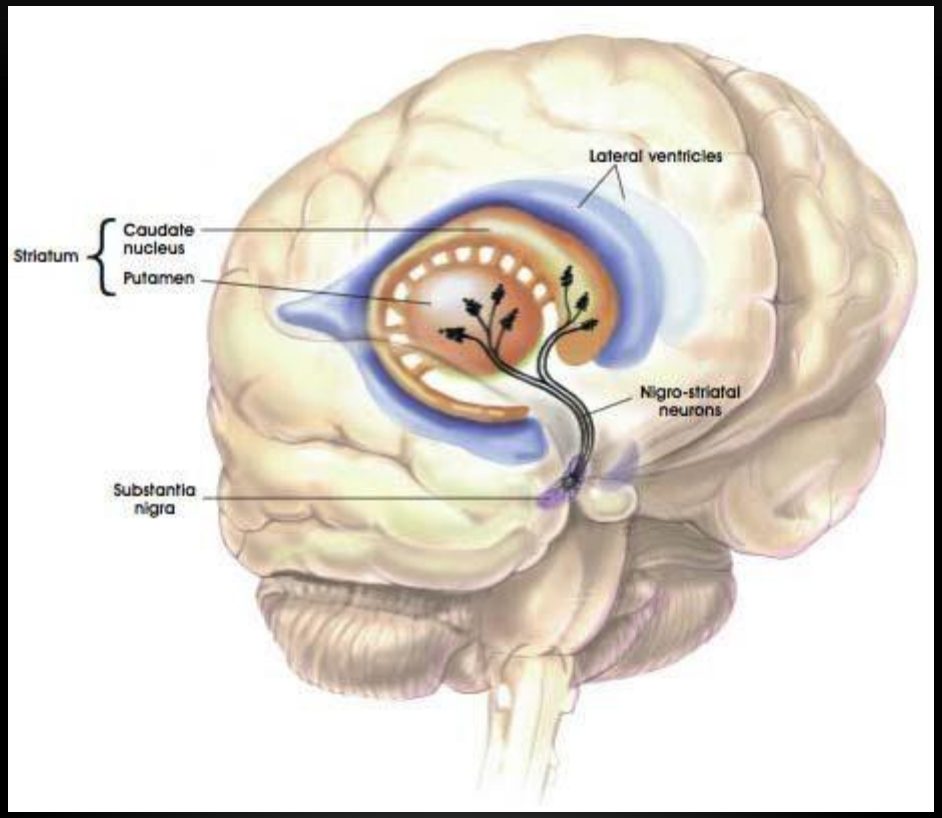
- Mov Disord. 2008 Apr 30;23(6):837-44. doi: 10.1002/mds.21956.
- **The Sydney multi center study of Parkinson's disease; the inevitability of Dementia at 20 years**
- Hely MA, Reid WG, Adena MA, Halliday GM, Morris JG.
- **Source**
- Department of Neurology, Westmead Hospital, Westmead, New South Wales, Australia.

BRAIN FAILURE

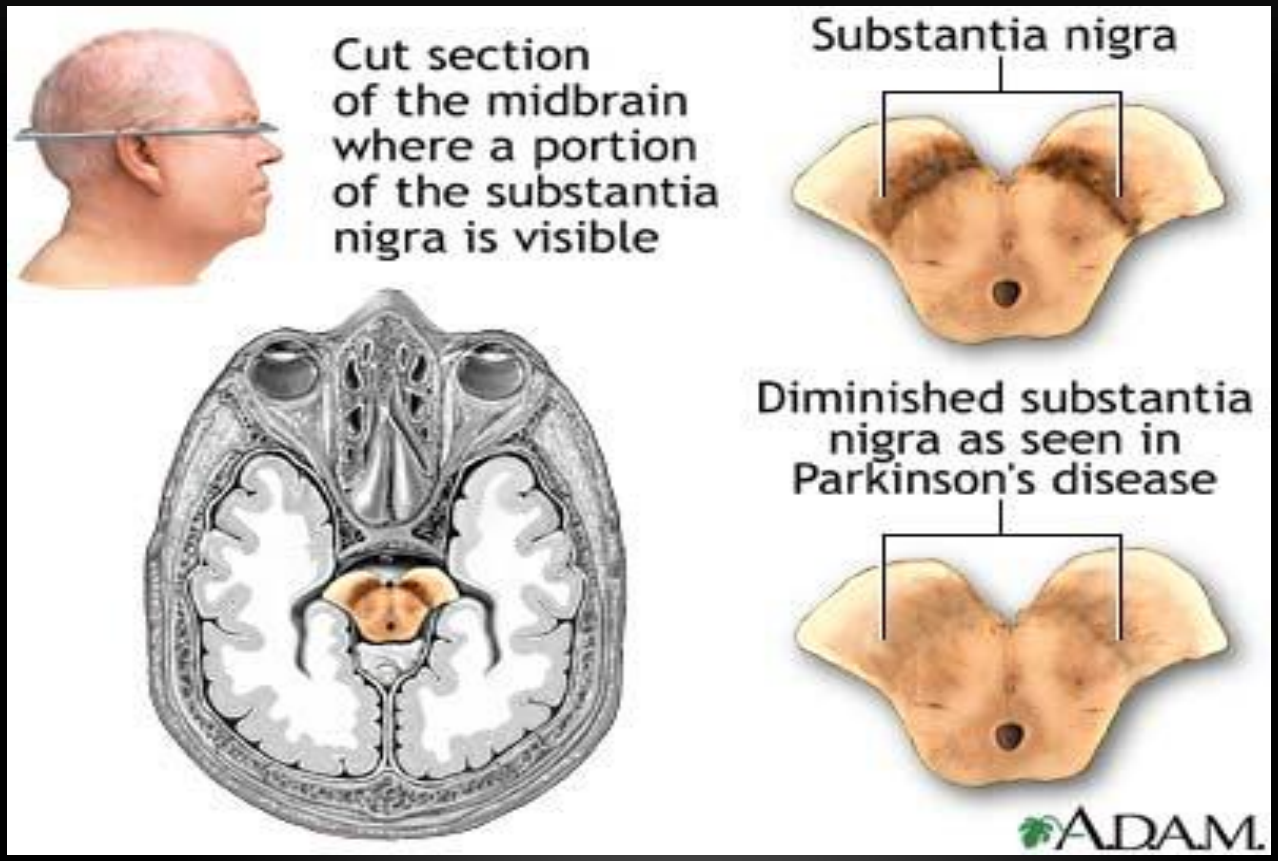
- The common denominator for disease burden in Elderly

- Stroke/ Dementia/Parkinson`s Disease

IDIOPATHIC PARKINSON`S DISEASE



IDIOPATHIC PARKINSONS DISEASE

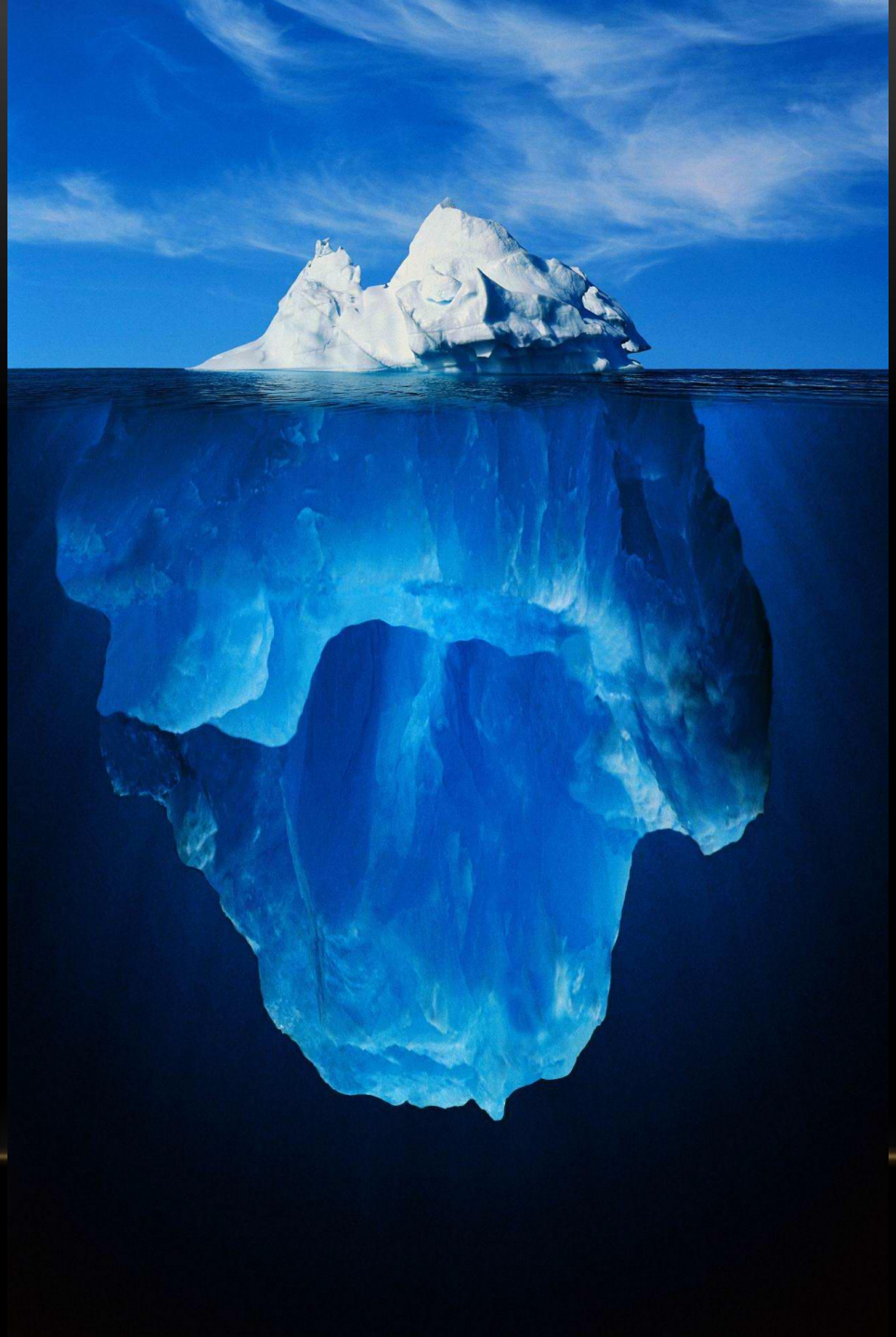


PARKINSON`S DISEASE DIAGNOSIS

- The **4 S !**

- **S**LOWNESS
- **S**TIFFNESS
- **S**HAKES
- **S**TUMBLES

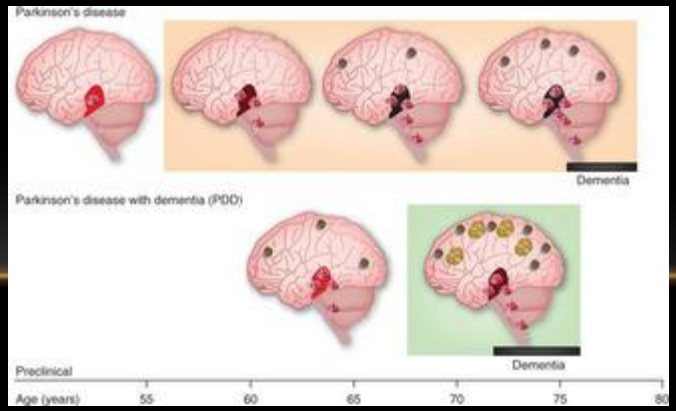
- 2 out 4 diagnostic of Idiopathic PD
- **Bradykinesia Must be present**



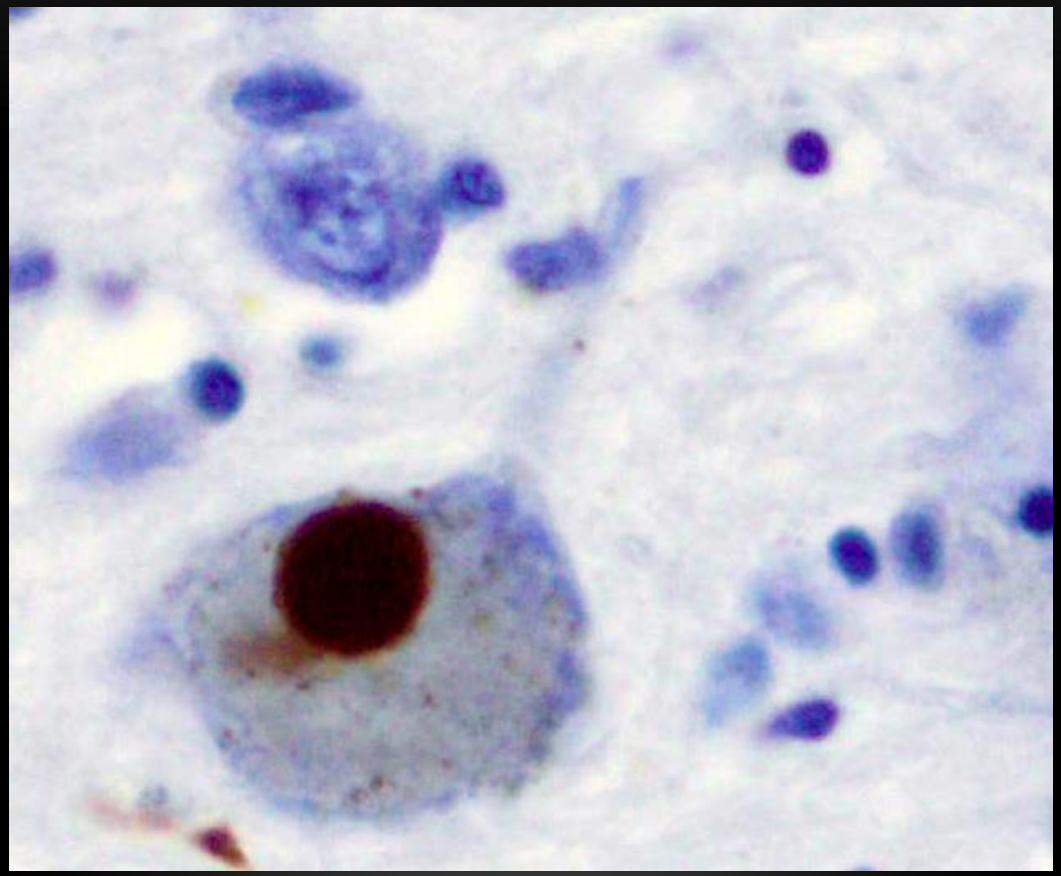
BRAAK`S HYPOTHESIS

- Challenging the conventional wisdom….

- Staging of Brain Pathology related to Parkinson's Disease .
- Neurobiology of Aging 2003 : 24;197-210.



ALPHA SYNUCLEIN



EARLY NMS

- Loss of Smell
- Urinary Incontinence
- Sexual dysfunction
- Orthostatic & Post Prandial Hypotension
- Depression ,Anxiety ,Apathy
- Sleep : RBD, Increased day time sleep, Insomnia

LATE NMS

- DEMENTIA
- DEPRESSION
- POSTURAL HYPOTENSION
- URINARY INCONTINENCE
- PAIN
- FALLS
- NEUROPSYCHIATRIC SYMPTOMS

HOW TO DIAGNOSE NMS ?

- **PD NMS QUESTIONNAIRE**

PD IS NOT JUST A MOVEMENT DISORDER…IT`S A MOOD DISORDER

- The Tremulous Mind

- Anxiety, Apathy, Depression, Anhedonia.
- Dementia

DEMENTIA

- DSM 1V edition
- Multiple cognitive deficits that affect
- Memory
- Aphasia
- Apraxia
- Agnosia
- Executive dysfunction

WHERE IS THE PROBLEM?

- Degeneration of Limbic & Neo-cortex in addition to Corpus Striatum changes.
- Motor – Putamen
- Cognition – Caudate Nucleus & Cortico striate fibres.

COGNITION PROFILE IN PD

- Executive dysfunction : Dopaminergic fibres
- Attention deficits : Nor Adrenergic fibres
- Mnemonic deficits : Cholinergic fibres

DEMENTIA IN PD

- PD carries a 6 fold risk of getting Dementia
- Point prevalence of 30%-40%
- Increasing longevity may explain the increase incidence
- PDD represents 3-4% of Dementias
- Age , more than 70 ,increases Dementia risk
- Severe motor features ,axial rgidity and postural instability –gait disorder (PGID) increases the risk

EXECUTIVE FUNCTION

- Ability to plan initiate complex, goal directed behaviour
- Difficulty processing information
- Shifting focus….difficult to concentrate
- Struggle to solve multiple step problems
- Difficulty in actively retrieving information

- **Relies heavily on the integrity of Pre Frontal Cortex**

PATIENT DESCRIPTION

- `I do well , if I`m doing things that are routine and if I do them slowly. I have always been a clear thinker ,with good attention to detail. I can still do that , but not if I have to think of more than one thing at a time.

- Today I have been helping my 2 grandchildren learn to play a board game. Just the teaching of things like this me makes me irritable and frustrated , The 7 year old can`t sit still and spills and knocks things onto the floor all the time ;while the 10 year old knows everything .I was also trying to put dirty dishes into my daughter`s dishwasher at the same time.

- By the time the game was over I was at the end of my tether .I have now decided that I can play a game with the kids one at a time , even if I have to play twice in a row…and then wash the dishes !`

KEY PROBLEM

- Difficulty in **resisting cognitive interference**
- Trivial tasks become important; difficulty ignoring them
- 2 or 3 things cannot happen at the same time together

DEMENTIA IN PD

- **1. Dopaminergic dysfunction**
- Lack of dopamine
- Disruption of striatal-frontal connections
- Anatomical substrate : Frontal lobe
- Functional deficit : Executive impairment

DEMENTIA IN PD

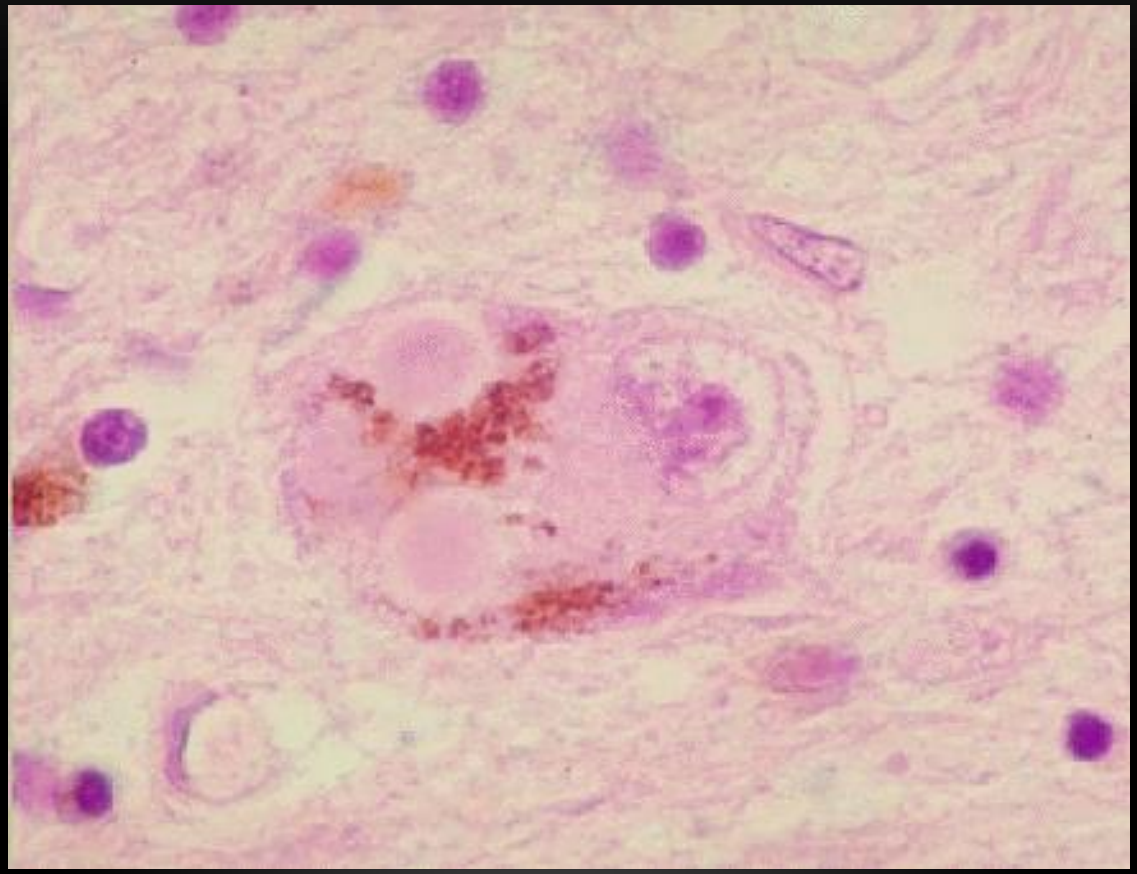
- **2.Cortical Cholinergic deficit**
- Nucleus Basalis of Meynert situated in the basal forebrain …full of cholinergic neurons that project into the cortex
- Significant loss of basal forebrain in PDD
- Critical threshold of forebrain loss (60-80%)

CRITICAL ASSOCIATION

- **3. LEWY BODIES in Cortex and Limbic system**
- LB in Cortex 91%sensitive and 90% specific for PDD

- Lewy Bodies : can be found in normal patients ; hence `where` it is found is more important than it`s actual presence

LEWY BODY



DEMENTIA IN PD

- APOE increases risk of AD
- MAPT gene increases risk of Dementia in PD
- H1/H1 genotype of MAPT gene is an independent predictor of Dementia in PD

DIFFERENCE BETWEEN AD & PDD

- Subcortical v Cortical dementia

- Slowing of the mind (Bradyphrenia)
- Changes in personality & mood
- Inability to use acquired knowledge
- Diminished ability to retrieve learned information
- forgetfulness
- PDD

CORTICAL DEMENTIAS

- Frank amnesia
- Aphasia
- Apraxia
- Agnosia

- AD

- These are absent in PDD
- Also INSIGHT IS RELATIVELY INTACT in PDD.

DIAGNOSIS

- MMSE not suitable ,since executive symptoms are affected.
- ACE-R
- Frontal Assessment Battery
- MOCA

DEMENTIA LEWY BODY DLB

- Second commonest type of Dementia 15%
- Extensive overlap between the pathological features of both AD & PD
- Dementia
- Fluctuations in attention and arousal
- Visual Hallucinations
- Parkinsonism
- **1 -2 year rule in Diagnosis**

DLB

- PDD and DLB not 2 separate entities but represent a spectrum of same pathological process ; difference because of parts of the brain affected

- No single pathological feature separating PD & DLB
- **Early involvement of Amygdala** – cognitive changes and Temporal lobe - Hallucinations

PD MILD COGNITIVE IMPAIRMENT (PD MCI)

- PD MCI now a well described clinical entity
- Compared to MCI in AD, Non amnestic type more common in PD
- PD MCI is a risk factor for getting PDD
- Memory loss or difficulty concentrating , but functioning well otherwise ; good scores on cognitive assessment

AD

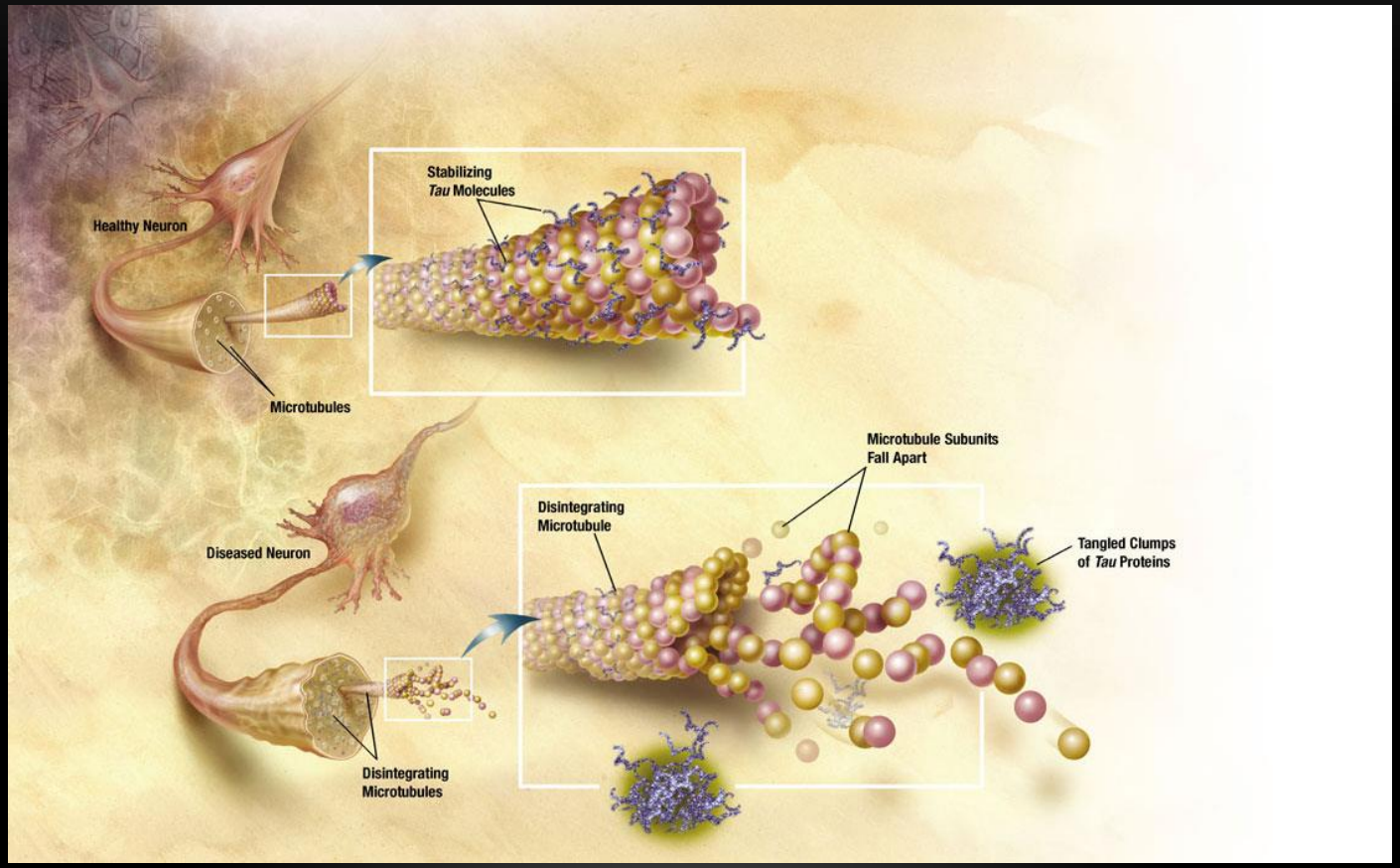
- Gross pathology

- Brain atrophy
- Loss of neurons
- Gliosis
- Loss of Synapses

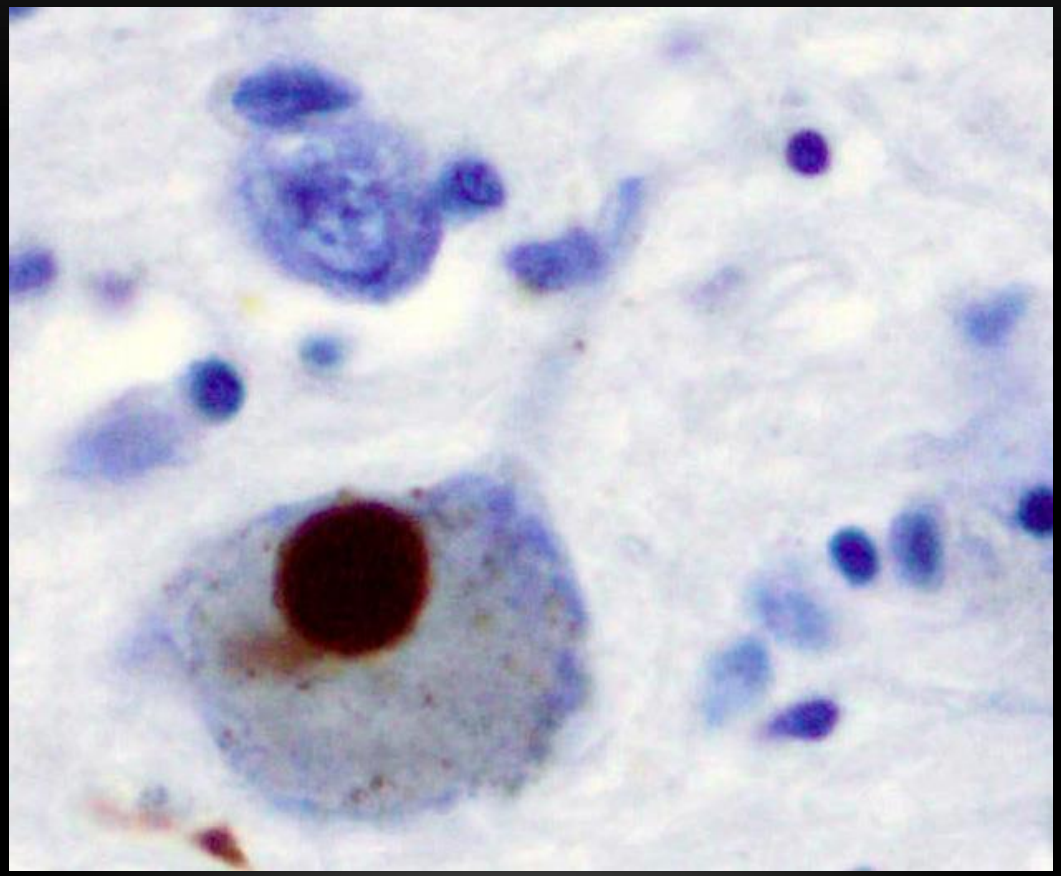
AD

- Abnormally phosphorylated TAU protein present in surviving neurons as paired helical filaments….NFT
- NFT within the cell body
- Neuropil threads NT in the dendritic processes
- Specific to AD

TAU & AD


Healthy Neuron
Stabilizing
Tau Molecules
Microtubules
Diseased Neuron
Microtubule Subunits
Fall Apart
Disintegrating
Microtubule
Tangled Clumps
of *Tau* Proteins
Disintegrating
Microtubules

ALPHA SYNUCLEIN

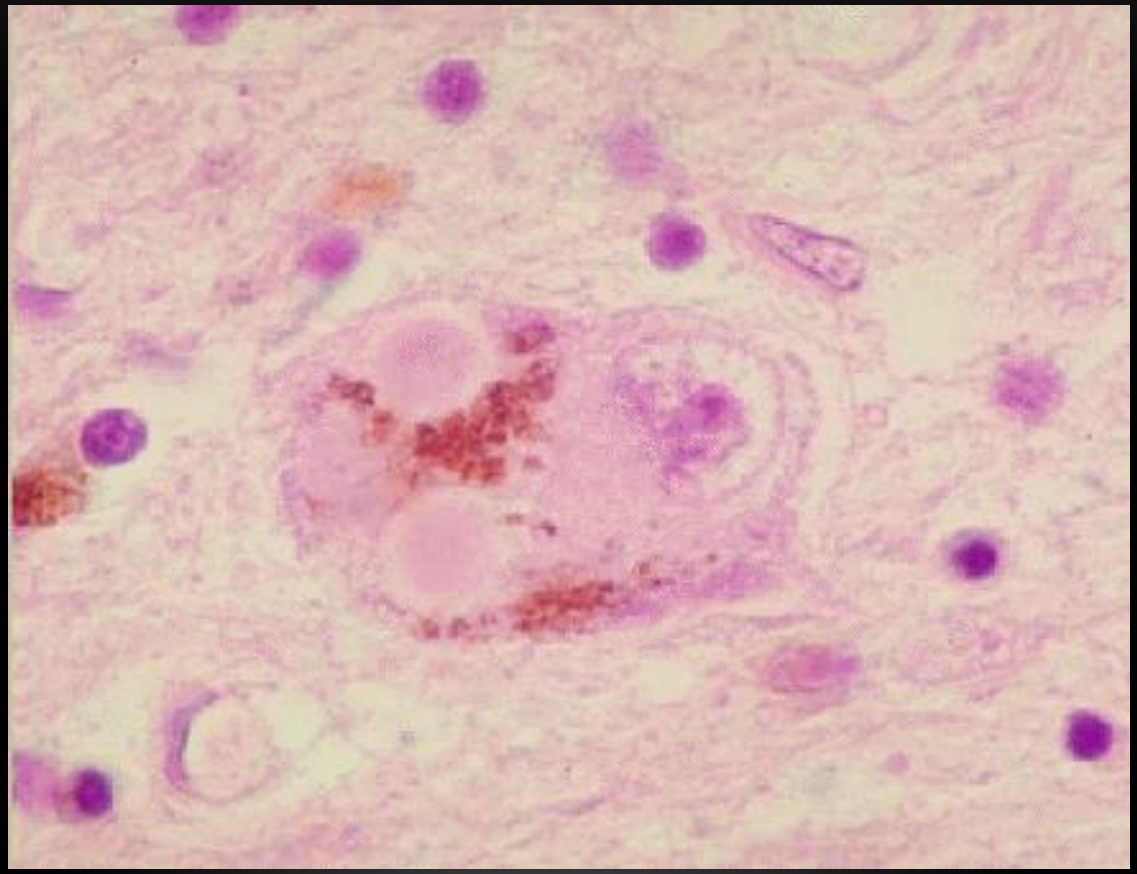


PD

- Gross

- Neuronal loss
- Gliosis
- Presence of Lewy Bodies
- LB : Eosinophilic inclusions found in the nerve cells made up of Ubiquitin and Aggregations of Alpha Synculein
- Lewy Neurites : Thread like inclusions within neurites

LEWY BODY



TREATMENT OF DEMENTIA IN PD

- Important for family members and carers **to realise , acknowledge and adapt** to patient`s limitations , which may not be just physical.
- Tremors of the Mind need looking after as well.

TREATMENT OF PDD

- Aerobic exercise – evidence based
- WALKING …..the best treatment for Dementia

TREATMENT OF DEMENTIA

- FOOD !
- REGULAR MEALS
- 1 HOT MEAL PER DAY, MINIMUM !!

- Attention to Nutrition reduces risk of infection and mortality
- Gil Gregolino P et al
- J Nutr Health Aging 2003: 7:304-8

TREATMENT

- Mind the Mind !
- Nintendo (Mind-Gym)
- **Avoid distractions….especially while driving**
- Pro actively planning for the future
- POA& EG.
- Social support
- Improving interactions

MEDICAL TREATMENT OF PDD

- Not which tablet to start but….**which tablet to stop !**
- Reduce the dose / eliminate medications which will worsen cognition
- Dopa agonists
- MAO –B inhibitors
- Anticholinergic drugs like trihexyphenidyl
- Amantadine
- Never Stop suddenly in PD !

MEDICAL TREATMENT OF PDD

- Maintaining the patient on lowest possible dose of monotherapy with L-Dopa, without leading to unacceptable immobility

CHOLINE ESTERASE INHIBITORS

- Used in AD
- Cholinergic transmission is reduced
- Cholinergic neurons depleted

- Similar pathology in PDD ; especially in DLB
- Hence should be useful

EXPRESS

- Rivastigmine
- 541 patients randomised to
- Placebo or Rivastigmine daily
- Followed for 26 weeks
- Modest but statistically significant improvement in ADAS-Cog scores

EDON

- Donepezil in PDD
- 549 patients studied
- 24 weeks
- Dose dependent benefit with Donepezil

TREATMENT

- PDD patients doesn`t tolerate Dopaminergic treatment as well those without Dementia
- Hence motor symptoms suffer because of restriction in the use of L-Dopa doses
- PDD is a contraindication for DBS

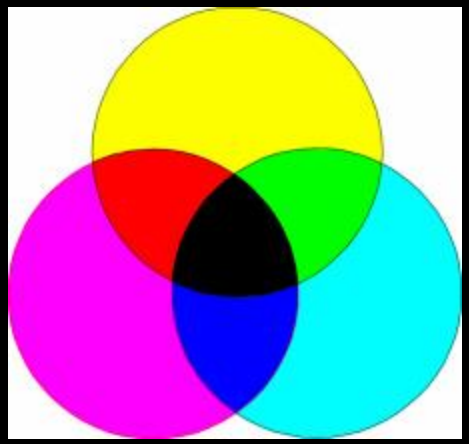
CHOLINE ESTERASE INHIBITOR IN PDD

- A trial with choline esterase inhibitor is reasonable and should be offered to any patient with cognitive dysfunction serious enough to impair QOL.

THE FUTURE

- Disease modifying agents for PD.
- Inhibition of Alpha Synuclein accumulation in susceptible brain cells.
- Drugs which stimulate cholinergic receptors rather than ChEIs needed.

GP,GERIATRICIAN ,NEUROLOGIST NEUROPSYCHIATRIST & PD SPECIALIST NURSE




RANKIN PARK
CENTRE

1 HOXTON SQUARE , SHOREDITCH


JAMES
PARKINSON
1755-1824
Physician and
Geologist
lived here

THE ALE HOUSE SERMON

SHOREDITCH CHAPEL

200 YEARS OF PARKINSON'S DISEASE: 1817- 2017

International Conference

Newcastle, Australia

MAY 5- 7, 2017