

BEHAVIORAL CONCERNS RELATED TO PARKINSONISM



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Relevant to the content of this educational activity, I don't have a financial relationship with an ineligible company.

PARKINSON'S DISEASE

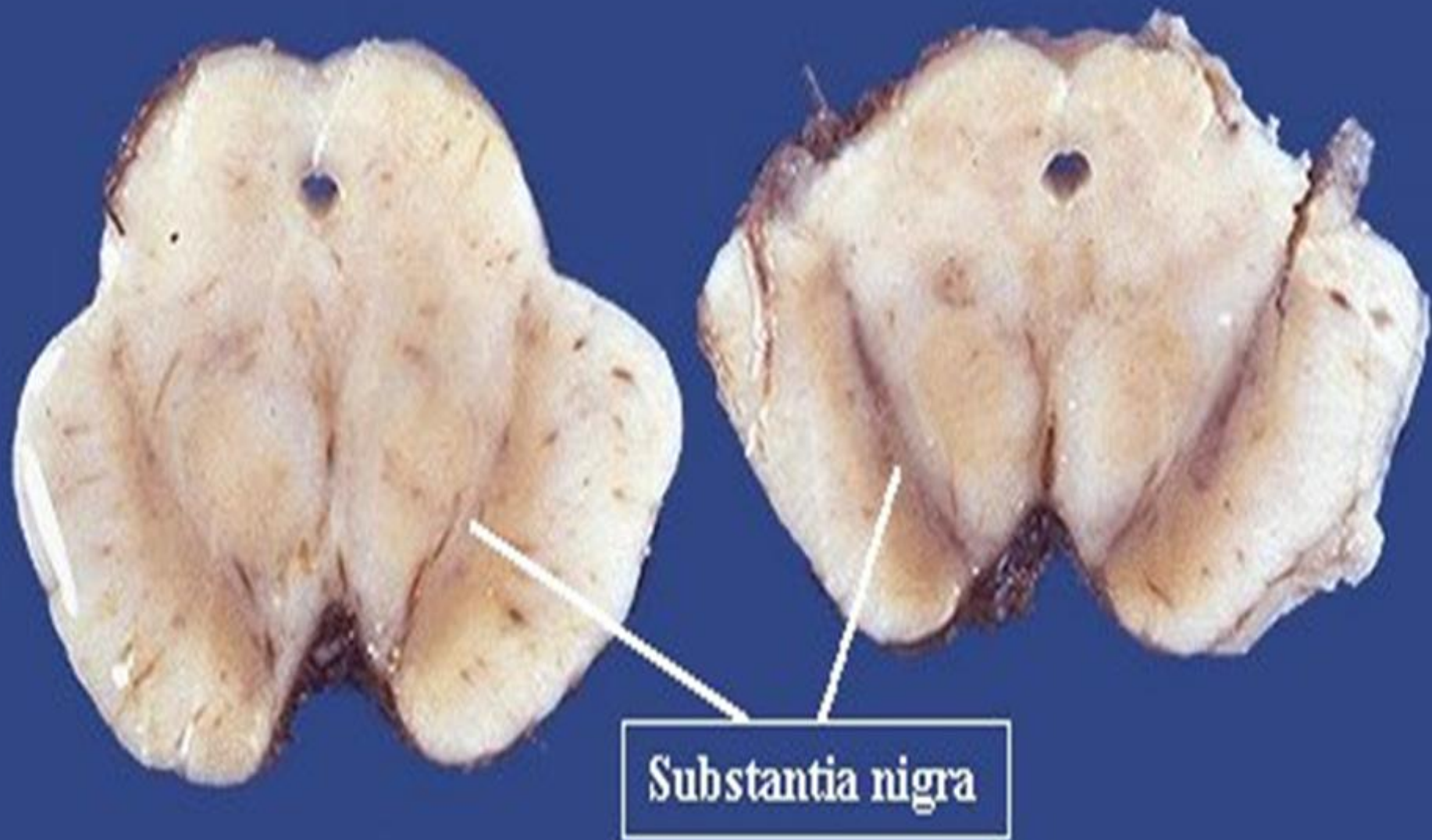


- First described by James Parkinson.
- AKA *paralysis agitans*.
- Cause is unknown (idiopathic).
- Second most common neurodegenerative disorder in people over 60.
 - 1% of people over 65.

PARKINSON'S DISEASE: NEUROPATHOLOGY

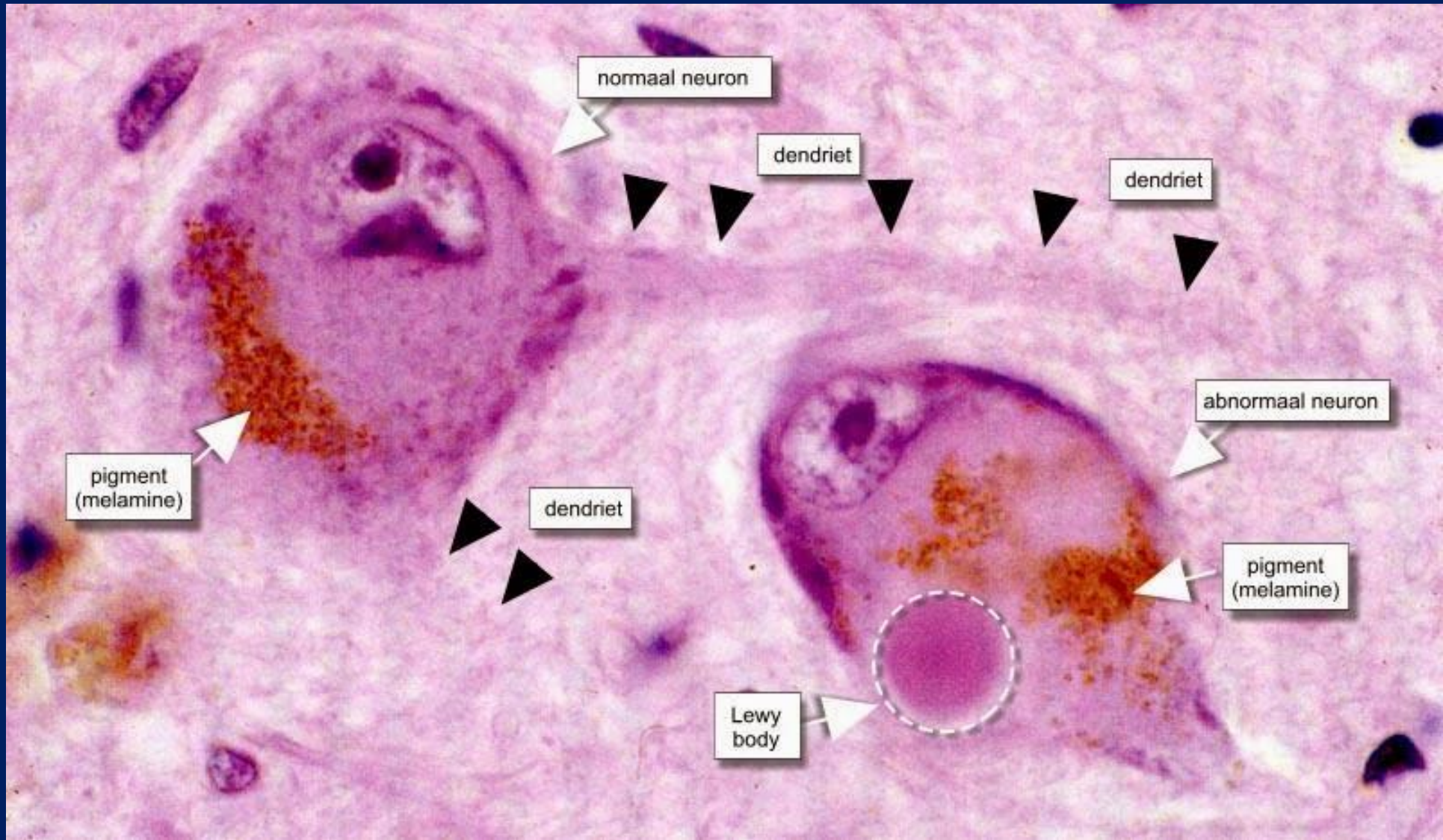


- Dopaminergic neurons in substantia nigra degenerate, which leads to a progressive deficit of dopamine.
- The neurons contain eosinophilic cytoplasmic inclusion bodies known as Lewy Bodies.
- Lewy bodies are made of proteins derived from alpha-synuclein.
- In PD, Lewy Bodies are concentrated primarily in substantia nigra region.



Parkinson's Disease

Normal



PARKINSON'S DISEASE: DIAGNOSIS



- Primarily diagnosed via clinical history and exam.
- Both motor symptoms and non-motor symptoms.
- Dopamine Transporter Scan (DaT Scan) can be useful.

MOTOR SYMPTOMS:



Bradykinesia (slow movement):

- Gait changes including shortened stride and reduced arm swing (“shuffling”)
- Stooped or leaning posture
- Mask-like facial expression
- Lack of dexterity
- Micrographia
- Hypophonia
- Dysphagia

Resting Tremor:

- “Pill rolling”
- Asymmetrical/unilateral
- Worse with position change
- Worse when concentrating

MOTOR SYMPTOMS

(CONT'D)



Rigidity/stiffness:

- “Lead pipe”
- “Cogwheeling”
- Pain

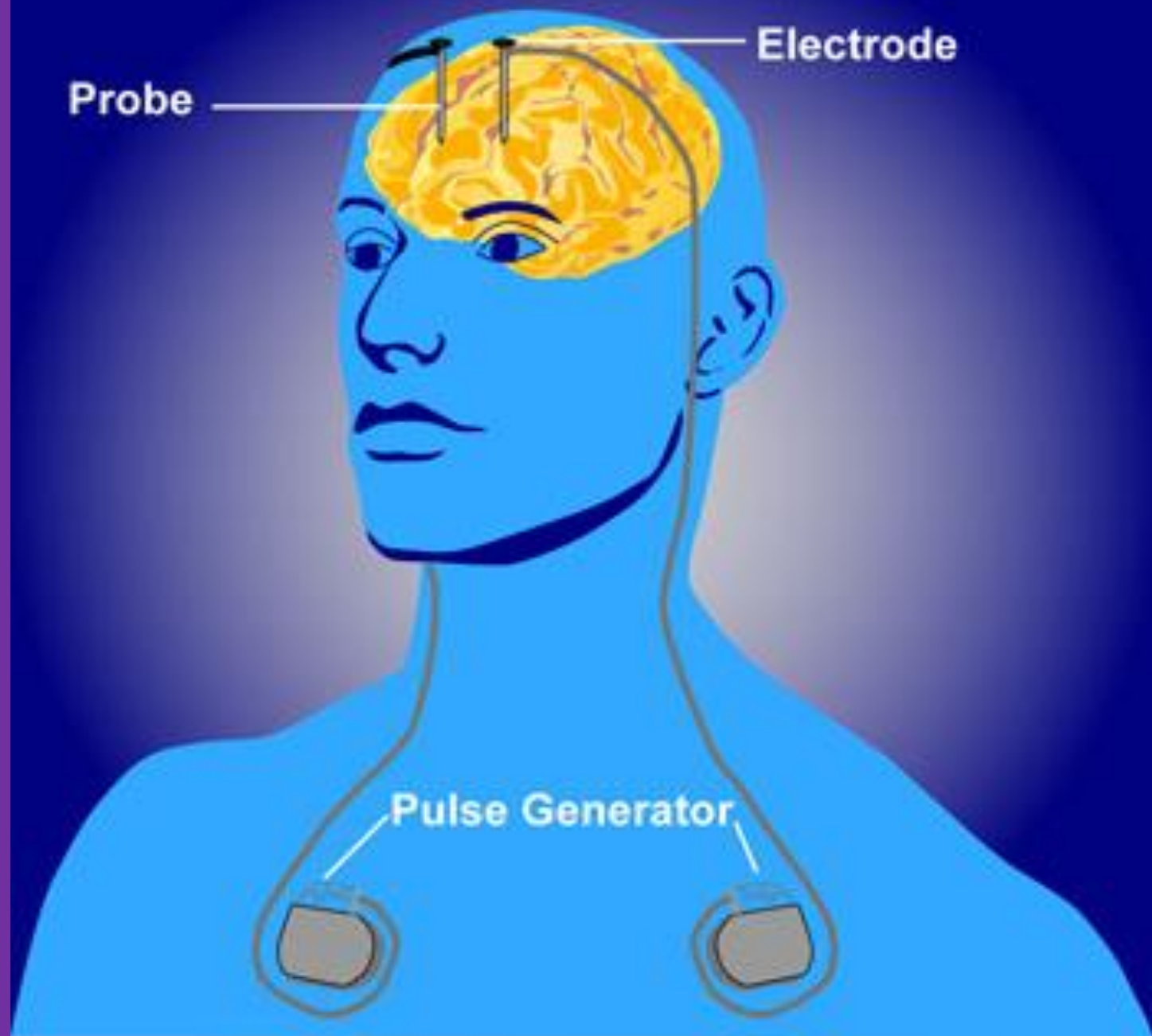
Postural instability:

- Gait changes
- Falls
- Imbalance
- Difficulty with obstacles

TREATMENT OF MOTOR SYMPTOMS:



- **Levodopa** preparations
- Catechol-O-methyltransferase (COMT) inhibitors
- Dopamine agonists
- Monoamine oxidase-B inhibitors
- Amantadine
- Anticholinergics
- Deep brain stimulation (DBS)
- Other



TREATMENT OF MOTOR SYMPTOMS: CHALLENGES



- Responsiveness changes over time
- “Wearing off” or “on-off”
- Dyskinesia

NON-MOTOR SYMPTOMS



➤ Cognitive:

- Mild cognitive impairment (MCI)
- Dementia (neurocognitive disorder)

➤ Mood:

- Depressive disorders
 - Apathy/fatigue/anhedonia
- Anxiety disorders

➤ Psychotic:

- Hallucinations
- Delusions
- Perceptual disturbances

NON-MOTOR SYMPTOMS

(CONT'D)



- Impulse-control disorders
- Punding
- Sleep disorders
- Misuse of medication

MILD COGNITIVE IMPAIRMENT IN PD



- Up to 55% .
- Attention, executive and visuo-spatial often affected.
 - Language and memory less affected.
- MCI increases risk of PD in those who don't have PD.
- MCI increases risk of dementia in those who have PD.
 - However, some remain stable and some improve.
- **Risk factors:** Male, older, more severe/advanced disease, lower premorbid IQ, lower education, depression, anxiety medication, daytime sleepiness.

MILD COGNITIVE IMPAIRMENT IN PD: TREATMENT



- Very few studies, but following have been considered:
 - Cholinesterase inhibitors (ChEIs):
 - Rivastigmine
 - Donepezil
 - Treatments for attention:
 - Amoxetine
 - Methylphenidate
- Limit anticholinergic drugs
- Education
- Cognitive stimulation?

DEMENTIA IN PD



- Lifetime prevalence of at least 75%.
- Occurs an average of 10 years after onset.
- Must differentiate from LBD (“one year rule”).
- Attention, executive and visuo-spatial often affected.
 - Language and memory less affected.
- Can be combined with vascular and Alzheimer's.
- **Risk factors:** Male, more severe/advanced disease, older age, presence of other non-motor symptoms (VH), autonomic symptoms and atypical features.

DEMENTIA IN PD: TREATMENT



- Response to ChEIs often vigorous.
 - Cholinergic deficit may be greater in PD than in AD.
 - **Rivastigmine***
 - May improve cognitive and behaviors symptoms.
 - May improve ADLs/function.
 - Donepezil
 - Galantamine?
- Memantine?
- Limit anticholinergic drugs.
- Education for caregivers and family.

DEPRESSIVE DISORDERS IN PD



- Up to 90%.
- PD affects serotonin and norepinephrine as well as dopamine.
- Depression increases risk of PD.
- PD increases risk of depression.
- **Risk factors:** Severe/advanced disease, motor fluctuations, anxiety, MCI, psychosis, early or late stage, motor disability, younger age, female, et al.

DEPRESSIVE DISORDERS IN PD: DIAGNOSIS



- Depressive symptoms may mimic symptoms of PD.

- Diagnoses: Major depression, persistent depressive disorder, unspecified depressive disorder, depressive disorder due to another medical condition, etc.

- Rating Scales:
 - Hamilton Depression Scale.
 - Beck Depression Inventory.
 - Geriatric Depression Scale.
 - Cornell Scale for Assessment of Depression in Dementia.
 - Others

DEPRESSIVE DISORDERS IN PD: TREATMENT



- Minimal research.
- **TCA may be superior.**
 - Nortriptyline and desipramine preferred TCAs.
- SSRI, SNRI, mirtazapine, bupropion.
- Pramipexole, ropinirole?

DEPRESSIVE DISORDERS IN PD: TREATMENT (CONT'D)



- ECT (improvement of mood and motor symptoms)
- rTMS
- DBS (wanes over time)
- CBT

SUICIDALITY IN PD



- Up to 30%
- **Risk factors:** Depressive/anxiety disorder, education level, age of onset, duration of illness, history of impulse-control problems.
- DBS may cause suicidal thoughts.

APATHY AND FATIGUE IN PD



- Up to 75%.
- Significant cause of disability and caregiver distress.
- Apathy usually observed, while fatigue is usually a subjective complaint.
- Likely due to frontal lobe pathology.
- May be a symptom separate from depression, but the two syndromes frequently co-exist.
- Often predictive of cognitive decline and dementia.
- No specific treatment, but dopamine agonists and stimulants may be beneficial for fatigue.

ANHEDONIA IN PD

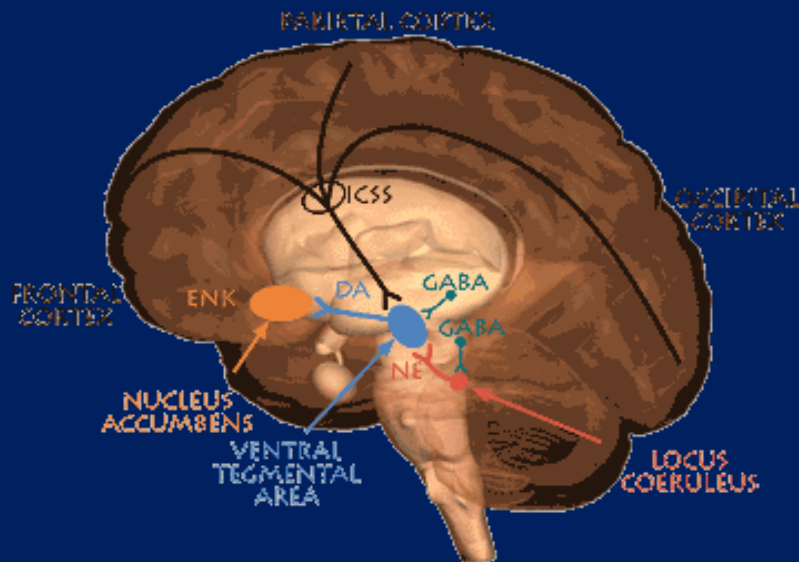


- Up to 45%
- Inability to experience pleasure.
- May be part of a depressive syndrome, or a separate symptom directly related to PD.
- Could be related to disruption of the dopaminergic reward pathway (mesolimbic).

THE REWARD CIRCUIT PATHWAY



- Many substances (or activities) stimulate dopaminergic neurons that project from the ventral tegmental area to the limbic system and the cerebral cortex.



ANXIETY DISORDERS IN PD



- Very common (up to 67%).
- Can be a primary disorder, or can be secondary to other disease complications (depression, psychosis, medications, “on-off” periods)
- Most common types:
 - Panic, GAD, Social phobia, OCD, unspecified.
- **Risk factors:** Female, younger, depression, sleep disturbances, severity of illness, fluctuating motor symptoms.

ANXIETY DISORDERS IN PD: TREATMENT



- **Control motor fluctuations.**
- **Virtually no research on treating anxiety alone.**
 - Only anxiety + depression
- **Medications:**
 - SSRI
 - TCA
 - Benzo (but may worsen other symptoms)
- **Nonpharmacologic:** Relaxation training, massage, psychoeducation, sleep hygiene, socialization.

PSYCHOSIS IN PD



- Hallucinations, delusions, perceptual disturbances.
- Up to 75%
- Is it actually related to the PD disease process?
 - Or a side effect of treatment?
- Psychosis may occur in other dementia syndromes.
- Often occurs at night (vivid dreams).
- Risk factors: Older, more severe/advanced disease, higher doses of dopamine agonists, visual problems, sleep disorder, cognitive impairment,

HALLUCINATIONS IN PD



- Visual hallucinations most common.
- Well formed, people, animals, objects.
- May appear and vanish suddenly.
- Other types of hallucinations possible including:
 - Auditory, tactile, olfactory, gustatory, and somatic.

OTHER PSYCHOTIC SYMPTOMS IN PD



- Delusions:
 - Relatively rare.
 - Paranoid (infidelity).
 - Capgras Syndrome (misidentification).
 - May believe spouse is someone else.

- Other perceptual disturbances:
 - Illusions.
 - Sense of presence or passage.

PSYCHOSIS IN PD: TREATMENT



- Evaluate for delirium.
- Evaluate antiparkinson medication regimen and adjust if possible:
 - Anticholinergics, selegiline, amantadine, dopamine agonists, levodopa.
- Antipsychotics are last resort, as they may worsen motor symptoms:
 - **Clozapine**, quetiapine, olanzapine, risperidone.
- Cholinesterase inhibitors?
- Nonpharmacological: Psychoeducation, cognitive (distraction, redirection), Environmental (lighting, eyeglasses).

IMPULSE CONTROL DISORDERS IN PD



- Up to 60%
- Side effect of dopaminergic medications.
- Excessive sexuality, gambling, shopping, walking, generosity, smoking. Also, hoarding, kleptomania, reckless driving.
- **Risk factors:** Young, single, male, smoker, history of substance use, family history addiction, bipolar.

IMPULSE CONTROL DISORDERS IN PD: TREATMENT



- **Reduction or discontinuation of dopaminergic medication.**
 - Withdrawal syndrome possible (depression, craving, etc.)

- **Pharmacologic:**
 - Zonisamide?
 - Naltrexone?
 - Other meds:
 - Donepezil, divalproex, SSRI, antipsychotics, hormonal.

PUNDING IN PD



- Repetitive, purposeless behavior:
 - Sorting, disassembling, cleaning, grooming, writing, singing, playing an instrument, etc.

- Relatively rare.

- Side effect of dopaminergic medication.

- **Treatment:**
 - Reduce dopaminergic medication.
 - Amantadine?
 - Clozapine?

SLEEP DISORDERS IN PD



- Sleep disorders are risk factors for PD.
- Types:
 - Insomnia (45-50%)
 - REM sleep behavior disorder (25-50%)
 - Excessive daytime drowsiness (15-87%)
 - Restless leg syndrome (0-50%)
 - Obstructive sleep apnea
- **Risk factors:** Older, male, cognitive impairment, hallucinations, higher doses dopaminergic drugs.

REM SLEEP BEHAVIOR DISORDER



- Often associated with Parkinson's Disease or Lewy Body Disease.
- Can be a harbinger of future alpha-synucleinopathy.
- Typically a middle-aged or older male.
- Thrashes around and strikes out during sleep. May injure self or partner.
- Usually good response to low-dose benzodiazepine.

SLEEP DISORDERS IN PD: TREATMENT



- Sleep study (polysomnography).
- Adjustment of dopaminergic medication:
 - Some cause daytime drowsiness.
 - Some can disrupt sleep.
- Sleep hygiene important.

SLEEP DISORDERS IN PD: TREATMENT (CONT'D)



- Modafinil for excessive daytime drowsiness.
- Clonazepam for REM sleep behavior disorder.
- Dopaminergic agents for restless leg syndrome.
- CPAP/BIPAP critical for obstructive sleep apnea.

SLEEP HYGIENE



- Stay on a set sleep schedule.
- Abstain from substances (caffeine/alcohol).
- Avoid daytime naps.
- Don't exercise or eat heavily just before bedtime.
- Don't use bed for anything other than sleep or sex.
- Avoid overstimulation before bed (screens).
- Don't stay in bed if unable to sleep; get up and engage in relaxing activity.
- Relaxation exercises.

MISUSE OF MEDICATION IN PD



- Also known as “**Dopamine Dysregulation Syndrome**”.
- Patients become addicted to dopamine agonists (usually levodopa or apomorphine).
- **Risk factors:** Younger, higher doses of dopaminergic drugs, past drug use, excessive alcohol use, novelty-seeking traits, depression.
- **Treatment:** Reduce or stop rapidly-acting “booster” doses if possible.
- May have worsening psychiatric symptoms after reducing medication.

LEWY BODY DISEASE



- Also known as:
 - “Diffuse Lewy Body Disease”
 - “Lewy Body Dementia”
 - “Lewy Body Variant of Alzheimer’s Disease (AD)”
 - “Senile Dementia of Lewy Body Type”

- 2nd or 3rd most common type of dementia.
 - Prevalence in general population of up to 5%
 - Up to 30% of all dementia cases

- Lewy bodies spread diffusely through cortex of brain.

LEWY BODY DISEASE: DIAGNOSTIC TESTS



- No single “silver bullet” test:
 - Structural imaging (CT, MRI)
 - Functional imaging (SPECT, PET)
 - MIBG-SPECT scan of heart
 - Cerebrospinal fluid
 - EEG
 - Genetic tests
 - Mental status testing (esp. clock drawing)
 - Neuropsychological assessment

LEWY BODY DISEASE: CLINICAL FEATURES



➤ Early:

- Dementia
- Fluctuating cognition
- Psychosis
(hallucin/delusions)
- Autonomic dysfunction
(falls, syncope)

➤ Later:

- Motor symptoms of
Parkinsonism

➤ Other:

- REM sleep behavior
disorder
- Very sensitive to
antipsychotics

DEMENTIA IN LBD



- Memory, attention, visuo-spatial, and executive function affected.
- Agnosia and apraxia possible.
- Aphasia not typically seen, but may confabulate, perseverate and seem incoherent at times.
- **FLUCTUATES**

PSYCHOSIS IN LBD



- Primarily visual hallucinations (up to 80% of LBD)
- Well formed, detailed, 3-dimensional.
- People or animals common.
- Usually provokes a response from patient.
- **FLUCTUATES**



AUTONOMIC DYSFUNCTION IN LBD

- Orthostatic hypotension
- Vertigo
- Dizziness
- Syncope
- Bladder control
- Transient impairment of consciousness
- Falls

DIFFERENTIATING LBD FROM AD



- Many LBD cases have pathological features mixed with AD (up to 80%).
 - About 1/3 of PD have pathological features mixed with AD.
- LBD has more pronounced autonomic dysfunction than AD.
- LBD often has more pronounced psychotic symptoms than AD, especially early on.

DIFFERENTIATING LBD FROM PD



- Average age of LBD onset is 68 (similar to AD).
- “One-year rule” in differentiating LBD from PD:
 - In PD, usually see motor symptoms for years before dementia becomes evident.
 - In LBD, motor symptoms and dementia occur within one year.

DIFFERENTIATING LBD FROM PD



LBD

➤ Early:

- Dementia
- Hallucinations and delusions
- Fluctuating mental status

➤ Late:

- Motor symptoms

PD

➤ Early:

- Motor symptoms

➤ Late:

- Dementia
- Hallucinations

LEWY BODY DISEASE: TREATMENT



- Cholinesterase inhibitors are mainstay:
 - **Rivastigmine**
 - Donepezil
 - Length of treatment?
 - Assess at 6 months and 3 years
 - May improve psychiatric and motor symptoms

- Memantine

LEWY BODY DISEASE: TREATMENT (CONT'D)



- If antipsychotics necessary:
 - Clozapine
 - Quetiapine
 - Pimavanserin

- Antidepressants: Avoid anticholinergic medications.

- Non-pharmacologic: Similar to AD.

OTHER TYPES OF PARKINSONISM



- Drug-induced
 - Medications
 - Antipsychotics
 - Other phenothiazines (GI)
 - Illicit drugs (rare)
 - Cocaine
 - Amphetamines
 - MDMA (“Ecstasy”)
 - Heroin

- Vascular Parkinsonism

- Various encephalopathies (FTD)

AND FINALLY...



➤ David's Story

REFERENCES



1. Aarsland D, Marsh L, Schrag A. Neuropsychiatric symptoms in Parkinson's disease. *Mov Disord.* 2009 Nov 15;24(15):2175-86. doi: 10.1002/mds.22589. Review. PubMed PMID: 19768724; PubMed Central PMCID: PMC2787875.
2. Connolly B, Fox SH. Treatment of cognitive, psychiatric, and affective disorders associated with Parkinson's disease. *Neurotherapeutics.* 2014 Jan;11(1):78-91. doi: 10.1007/s13311-013-0238-x. Review. PubMed PMID: 24288035; PubMed Central PMCID: PMC3899484.
3. Deik, A, et al. Substances of Abuse and Movement Disorders: Complex Interactions and Comorbidities. *Curr Drug Abuse Rev.* 2012 Sept; 5(3); 243-253.
4. Goldman JG, Williams-Gray C, Barker RA, Duda JE, Galvin JE. The spectrum of cognitive impairment in Lewy body diseases. *Mov Disord.* 2014 Apr 15;29(5):608-21. doi: 10.1002/mds.25866. Review. PubMed PMID: 24757110; PubMed Central PMCID: PMC4126402.
5. Grover S, Somaiya M, Kumar S, Avasthi A. Psychiatric aspects of Parkinson's disease. *J Neurosci Rural Pract.* 2015 Jan;6(1):65-76. doi:10.4103/0976-3147.143197. Review. PubMed PMID: 25552854; PubMed Central PMCID: PMC4244792.
6. Kaufman, D. *Clinical Neurology for Psychiatrists.* 6th Ed. Saunders Elsevier, 2007. pp 513-514.
7. Macijauskienė J, Lesauskaitė V. Dementia with Lewy bodies: the principles of diagnostics, treatment, and management. *Medicina (Kaunas).* 2012;48(1):1-8. Review. PubMed PMID: 22481369.
8. Mollenhauer B, Förstl H, Deuschl G, Storch A, Oertel W, Trenkwalder C. Lewybody and parkinsonian dementia: common, but often misdiagnosed conditions. *Dtsch Arztebl Int.* 2010 Oct;107(39):684-91. doi: 10.3238/arztebl.2010.0684. Epub 2010 Oct 1. Review. PubMed PMID: 20963199; PubMed Central PMCID: PMC2957617.
9. Williams DR, Litvan I. Parkinsonian syndromes. *Continuum (Minneapolis, Minn).* 2013 Oct;19(5 Movement Disorders):1189-212. doi: 10.1212/01.CON.0000436152.24038.e0. Review. PubMed PMID: 24092286; PubMed Central PMCID: PMC4234134.