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.

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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.

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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.

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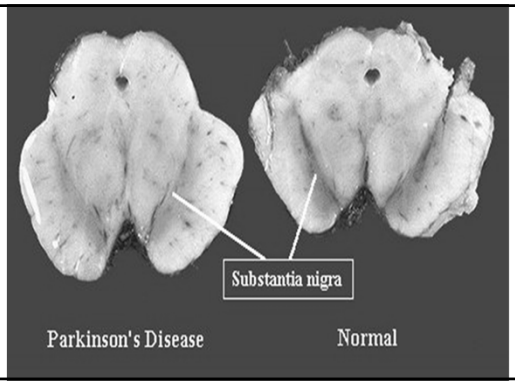
Slide 3

dfs1 dsteenblock, 4/30/2015



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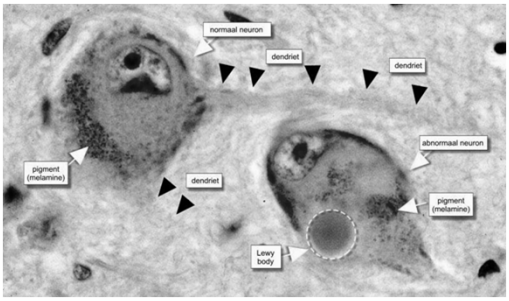

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PARKINSON'S DISEASE: DIAGNOSIS

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

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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

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MOTOR SYMPTOMS
(CONT'D)

Rigidity/stiffness:

- "Lead pipe"
- "Cogwheeling"
- Pain

Postural instability:

- Gait changes
- Falls
- Imbalance
- Difficulty with obstacles

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TREATMENT OF MOTOR SYMPTOMS:

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

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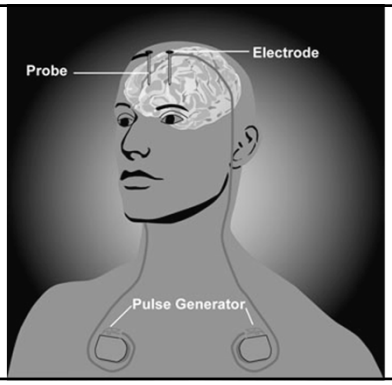

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TREATMENT OF MOTOR SYMPTOMS: CHALLENGES

- Responsiveness changes over time
- "Wearing off" or "on-off"
- Dyskinesia

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NON-MOTOR SYMPTOMS

- Cognitive:
  - Mild cognitive impairment (MCI)
  - Dementia (neurocognitive disorder)
- Mood:
  - Depressive disorders
    - Apathy/fatigue/anhedonia
  - Anxiety disorders
- Psychotic:
  - Hallucinations
  - Delusions
  - Perceptual disturbances

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NON-MOTOR SYMPTOMS (CONT'D)

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

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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.

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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?

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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.

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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.

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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.

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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

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DEPRESSIVE DISORDERS IN PD: TREATMENT

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

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DEPRESSIVE DISORDERS IN PD: TREATMENT (CONT'D)

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

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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.

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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.

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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).

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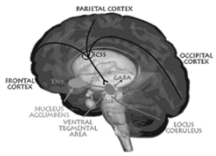
THE REWARD CIRCUIT PATHWAY

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



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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.

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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.

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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,

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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.

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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.

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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).

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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.

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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.

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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?

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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.

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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.

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SLEEP DISORDERS IN PD: TREATMENT

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

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SLEEP DISORDERS IN PD: TREATMENT (CONT'D)

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

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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.

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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.

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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.

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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

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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

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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

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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

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AUTONOMIC DYSFUNCTION IN LBD

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

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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.

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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.

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DIFFERENTIATING LBD FROM PD

LBD

- **Early:**
  - Dementia
  - Hallucinations and delusions
  - Fluctuating mental status
- **Late:**
  - Motor symptoms

PD

- **Early:**
  - Motor symptoms
- **Late:**
  - Dementia
  - Hallucinations

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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

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LEWY BODY DISEASE: TREATMENT (CONT'D)

- If antipsychotics necessary:
  - Clozapine
  - Quetiapine
  - Pimavanserin
- Antidepressants: Avoid anticholinergic medications.
- Non-pharmcologic: Similar to AD.

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OTHER TYPES OF PARKINSONISM

- Drug-induced
  - Medications
    - Antipsychotics
    - Other phenothiazines (GI)
  - Illicit drugs (rare)
    - Cocaine
    - Amphetamines
    - MDMA ("Ecstasy")
    - Heroin
- Vascular Parkinsonism
- Various encephalopathies (FTD)

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AND FINALLY…

- David's Story

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