Psychological Issues in Parkinson’s Disease

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Aims

- Discuss the importance of recognizing psychological issues in Parkinson’s Disease (PD)
- Explain the specific kinds of emotional, behavioral, and thinking problems that can affect persons with PD
- Highlight possible causes/factors that contribute to these symptoms
- Review available treatments for the neuropsychiatric symptoms of PD
- Answer questions ???

Parkinson’s Disease

- 2\textsuperscript{nd} most common neurodegenerative disorder, after Alzheimer’s disease
- Affects about 1.5 million Americans
- Average age of onset around 60 years old
- 1 in 100 have PD in the >65 year old age group
- However, 15% diagnosed before age 50 years old
- Male to female ratio 3:2
- The exact cause of PD remains unknown
James Parkinson- 1817

AN ESSAY ON THE SHAKING PALSY.

CHAPTER I. DEFINITION—HISTORY—ILLUSTRATIVE CASES.

SHAKING PALSY (Paralysis Agitans.)
Involuntary tremulous motion, with lessened muscular power, in part 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 intellect being unimpaired.

He described the classic motor symptoms of PD...

• Resting tremor
• Bradykinesia (slowed movements)
• Muscle Rigidity
• Shuffling gait
• Stooped posture

• But...
“... the senses and intellect being uninjured”

- He did not fully appreciate the psychological symptoms that might manifest in PD
- He did briefly mention “melancholy,” or depression in the full essay

In recent years, psychological symptoms have been increasingly recognized as manifestations of PD...

“The Quintessential Neuropsychiatric Disorder”

- Depression
- Anxiety
- Psychosis
- Apathy
- Impulse Control Disorders
- Cognitive Impairment/Dementia
- Disorders of sleep and wakefulness

Weintraub and Burn, 2011, Movement Disorders
Basal Ganglia

- Caudate
- Putamen
- Globus Pallidus
- (Nucleus Accumbens)

Basal Ganglia Anatomy
Basal Ganglia Motor Function:

BG involved in automatic execution of learned motor plans

- Implicated in action selection → which of several possible behaviors to execute at a given time

- Allows for initiation, termination and scaling of movement

- Hypodopaminergic state → bradykinesia, freezing, etc

Dopamine in Normal Movement
Activated receptor
Striatal dopamine receptors
Striatal neuron
Dopamine
Nigrostriatal nerve terminals
Dopamine in PD
PD with levodopa treatment
Striatal dopamine receptors

Dopamine made from levodopa

Striatal neuron

Activated receptor
Unactivated receptor
Normal neuronal function

Cortico-striatal-pallido-thalamo-cortical Loops

Krack et al, 2010, Trends in Neuroscience
<table>
<thead>
<tr>
<th>Low dopamine (PD)</th>
<th>High dopamine (levodopa, dopamine agonists)</th>
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<tbody>
<tr>
<td>Motor</td>
<td></td>
</tr>
<tr>
<td>- Bradykinesia</td>
<td>- Dyskinesia</td>
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<tr>
<td>- Apathy (motor component)</td>
<td>- Motor Impulsivity</td>
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<tr>
<td>Cognitive/Associative</td>
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<tr>
<td>- Bradyphrenia</td>
<td>- Cognitive impulsivity</td>
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<tr>
<td>- Empty brain (absence of ideas)</td>
<td>- Flight of ideas</td>
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<tr>
<td>- Apathy (cognitive component)</td>
<td>- Novelty seeking</td>
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<tr>
<td>Emotional (Limbic)</td>
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<tr>
<td>- Depression</td>
<td>- Euphoria, mania</td>
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<tr>
<td>- Apathy (emotional component)</td>
<td>- Emotional impulsivity/Behavioral addictions</td>
</tr>
<tr>
<td>- Anhedonia</td>
<td>- Hedonism, creativity, pleasure seeking, risk-taking behavior</td>
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<tr>
<td>- Anxiety, harm avoidance</td>
<td>- Feeling on or “high”</td>
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<td>- Drug withdrawal syndrome</td>
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**Depression**

- Up to 50% of PD patients will experience depression at some point in the course of the disease
  - Major depression in 5-20%
  - Minor depression in another 10-30%
- Can lead to worsening function and poorer quality of life
- Increases difficulty for caregivers
- May come on even before the onset of motor symptoms (about 5 years)
- Under-recognized and Under-treated!!!
Depression Symptoms

- Depressed mood
- Diminished interest or pleasure
- Change in appetite (and weight)
- Sleep problems (insomnia or hypersomnia)
- Fatigue
- Feelings or worthlessness or guilt
- Psychomotor slowing or agitation
- Poor concentration
- Recurrent thoughts of death or suicide

Depression Causes

- **Psychological Causes**
  - Sadness, Helplessness, and Hopelessness may stem from having a chronic illness
  - Isolation because of physical disability or embarrassment about PD symptoms
- **Biological Factors**
  - History or mental illness
  - Genetics/Family History
  - Brain changes (serotonin, norepinephrine and dopamine change in both PD and depression)
  - Some patients experience depressive symptoms during medication “off” periods
Depression Treatment

- *Selective Serotonin Reuptake Inhibitors* (SSRIs - Celexa, Zoloft, Paxil, Prozac)
- Some studies indicate that older antidepressants might be more effective in PD - *Tricyclic Antidepressants* (Nortriptyline, Desipramine)
- *Pramipexole* (a Dopamine agonist) has been shown to be helpful in some cases
- Treating “off” periods may be helpful
- A recent study showed that antidepressants do not necessarily make motor symptoms worse
- Electroconvulsive (“shock”) therapy

Anxiety

- Anxiety is common in PD - 40% have anxiety disorders
- Men and women affected equally
- May consist of *Generalized Anxiety, Panic Attacks*, or *Social Anxiety*
- In some cases, anxiety is directly related to changes in motor symptoms or “off” periods (may have fear of not being able to function)
- Anxiety disturbances may develop in a “prodromal” period up to 20 years before motor symptoms develop
Generalized Anxiety Symptoms

- Feelings of apprehension
- Restlessness or feeling on edge
- Being easily fatigued
- Difficulty concentrating
- Irritability
- Muscle tension
- Difficulty falling asleep

***Worrying about one’s physical condition is a natural reaction in PD, but excessive anxiety causing disability should not be accepted as “normal”!***

Panic Attacks

- Palpitations, rapid heart rate
- Sweating
- Trembling
- Shortness of breath
- Feeling of choking
- Chest discomfort
- Nausea
- Fear of losing control or going crazy
- Feelings of unreality
- Fear of dying
- Numbness or tingling sensations
- Chills or Hot flushes
Anxiety Treatments

- Same medications as used for depression (SSRIs, tricyclic antidepressants)
  * These medications may take weeks to have their effect
- There are more rapid-acting anxiety medications, benzodiazepines (Clonazepam, Lorazepam, Alprazolam) that help with anxiety quickly, but...
  These medications can be troublesome because:
  - May cause confusion
  - Increased risk of falls
  - Sedation
  - Can lead to dependence/withdrawal if stopped

Psychosis

- A loss of touch with reality
- Characterized by:
  - Hallucinations
  - Delusions
  - “Minor” Psychotic Symptoms
- Affects up to 60% of those with PD
- Too much dopamine! (the problem in schizophrenia)
Psychosis- Hallucinations

- A perception in any of the five sensory modalities without a real stimulus
- **Visual** Hallucinations are by far the most common
- Typical visual hallucination is a complex visual image such as a person or an animal
- **Auditory** and **tactile** (and **olfactory** and **gustatory**) hallucinations may also occur, but are less common and usually coexist with visual hallucinations
- Initially have insight (*the recognition that the perceptions are not real*), but this can be lost over time

Psychosis- Delusions

- *A fixed, false, idiosyncratic belief*
- Less common than hallucinations (about 10% of patients)
- They are not deliberate or “made up”
- Different types of delusions:
  - **Persecutory**- believing one is being harassed, wronged, attacked, or conspired against
  - **Jealousy**- belief that one’s partner is being unfaithful
Psychosis- “Minor Symptoms”

- **Illusion** - A distorted sensory perception of a real stimulus (i.e. garden hose seen as a snake)
- **Sense of Presence** - Vivid sensation that someone is nearby, including behind the person, when no one is there and no one is seen
- **Passage Hallucination** - a brief vision of a person, animal or other object that passes sideways in the peripheral visual fields

Psychosis-Risk Factors

- Older age
- Longer duration of disease
- Cognitive impairment
- Sleep disturbance (vivid dreaming)
- Depressed mood
- Vision Problems (macular degeneration, glaucoma, etc)

PD Psychosis can persist and worsen with time, resulting in:

- Increased caregiver burden
- Nursing home placement
- Mortality
Psychosis- Treatment

- Taper antiparkinsonian medications in following order:
  1- Anticholinergics (Trihexyphenidyl, Benztropine)
  2- Amantadine and Selegiline
  3- Dopamine agonists (Pramipexole, Ropinirole)
  4- COMT inhibitors (Entacapone, Tolcapone)
  5- Managed PD with $L$-dopa therapy, in lowest dose possible to maintain motor function

Psychosis- Treatment 2

- Antipsychotic medications
  - Work by blocking dopamine
  - May help reduce psychotic symptoms, but most cause a significant deterioration in motor function
  - Quetiapine and Clozapine the only two recommended in PD because they do not worsen motor symptoms
PD Psychosis

Is diminished motivation and goal-directed behavior
- Up to 40% of PD patients
- Although often related to depression (25%), it can be found in patients without mood disorder
- Associated with cognitive dysfunction related to dysfunction of Frontal dopamine systems in the brain
Impulse Control Disorders

- A failure to resist an impulse, drive, or temptation to perform an act that is harmful to the person or others
- Increasingly recognized as problems in PD
- Related to the dopaminergic medications used to treat PD
- Has also been reported in some patients following deep brain stimulation surgery

Impulse Control Disorders in PD

Pathological gambling
Compulsive shopping
Compulsive hypersexuality
Compulsive eating
Punding
Levodopa dependence
ICD Prevalence

Study of 3090 PD patients

- Any ICD 13.6%
- Four main types
  - Pathological Gambling 5.0%
  - Compulsive sexual behavior 3.5%
  - Compulsive buying 5.7%
  - Binge eating 4.3%
  - More than one ICD 3.9%

Weintraub et al, 2010, Arch Neurol

Patient Perspectives

- “I’m the wife of one of these patients. He had never overeaten, gambled, sought out pornography or been unfaithful — until he started pramipexole three years ago.
- Our marriage has crumbled, our family life has been destroyed, our children are in therapy and so are we.
- I have taken away his ATM and credit cards multiple times — the last time was earlier this week — because he was unable to tell me what happened to all the money.
- He will now stop taking it, but there is no question that he functions better physically with it than another other drug.”
ICD associated characteristics

- Dopamine agonist (DA) treatment
- Younger age, younger-age of PD onset, being unmarried, a family history of gambling or alcohol problems, and a novelty-seeking personality
- Some characteristics associated with particular ICD-types, such as male gender in the case of Pathological Gambling and Hypersexuality
- Higher levels of depressive, anxiety and obsessive-compulsive symptoms

ICD Treatments

- Attempt to remove the offending dopaminergic medication...
- The problem is the medication that brought on ICD behaviors also is often the one that best treats motor symptoms
- Benefit from other medications is minimal
- Amantadine has been shown to be helpful, but has also been shown to cause ICDs
- Deep brain stimulation has been associated with both improvement and new onset of ICD behavior
PD Cognitive Impairment/Dementia

- Most persons with PD will experience some degree of cognitive (“Thinking”) impairment during the course of their illness
- Deficits are often subtle in the earlier stages and not all will experience full dementia
- Dementia is diagnosed when thinking problems begin to impact functional abilities
- Up to 70% may experience dementia in the later stages
- Pattern of deficits is different than those seen in Alzheimer's Disease
- Can be the most troubling symptoms of PD

Risk Factors for Dementia

- Increasing age
- Older age at PD onset
- Longer disease duration
- Family history of dementia
- Greater severity of motor symptoms
- Depression
- Hypertension
PD vs. Alzheimer’s Dementia

<table>
<thead>
<tr>
<th>PD Dementia</th>
<th>Alzheimer’s Disease</th>
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<tr>
<td>Main deficits in:</td>
<td>Main deficits in:</td>
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<tr>
<td>- Attention</td>
<td>- Memory</td>
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<tr>
<td>- Speed of thinking processes</td>
<td>- Language</td>
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<tr>
<td>- Memory retrieval</td>
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<tr>
<td>- Visuospatial Ability</td>
<td></td>
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<tr>
<td>- Executive Function</td>
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Diagnosing Cognitive Impairment/Dementia in PD

- Interview patient and family members or caregivers
- Cognitive screening tests such as the *Mini Mental State Exam (MMSE)* or the *Montreal Cognitive Assessment (MOCA)*
- Assess the patient’s functional ability (Activities of daily living)
- Neuropsychological testing (more in depth testing of different areas of thinking)
- Brain imaging (MRI or CT scan) may be helpful in ruling out other causes of cognitive impairment (such as a stroke)
Dementia Treatments

- *Acetylcholinesterase inhibitors (Donepezil, Rivastigmine, Galantamine)* → Do not produce marked improvements in cognition but may help slow the progression
- Other medications (antipsychotics, antidepressants, etc) may be used to treat some of the behavioral disturbances that may accompany dementia
- Occupational and Behavioral therapy may be beneficial in using non-pharmacologic interventions for behavior issues

Conclusions

- Psychological symptoms are common in PD and it is best thought of as a “Neuropsychiatric” disorder
- These psychological symptoms are under-recognized and under-treated in PD
- Bring psychological problems up with your doctor if you or someone close to you notices changes in your mood, thinking or behavior
- There are a number of treatments that can be helpful for the psychological symptoms of PD!
Thank you…

Any Questions???