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

- 2nd 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 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.

He described the classic motor symptoms of PD…

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

Classic Triad

- 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

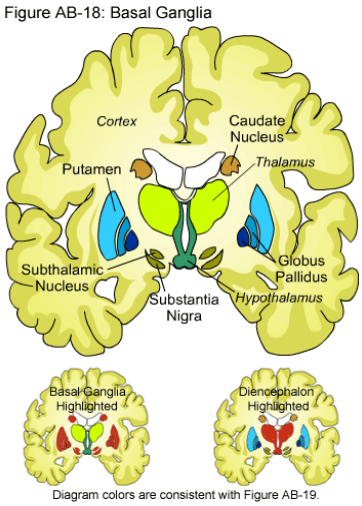
Weintraub and Burn, 2011, *Movement Disorders*

Basal Ganglia

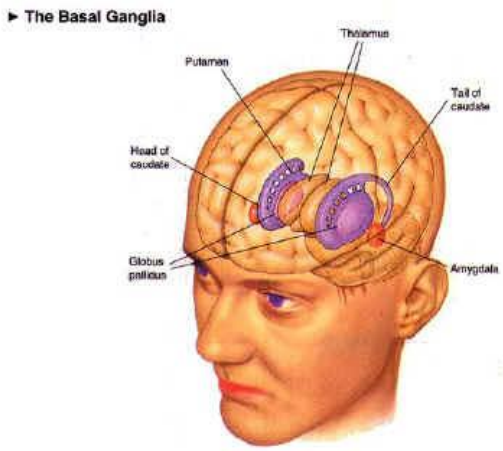
- Caudate
- Putamen

} Striatum

- Globus Pallidus
- (Nucleus Accumbens)



Basal Ganglia Anatomy



Basal Ganglia Motor Function:

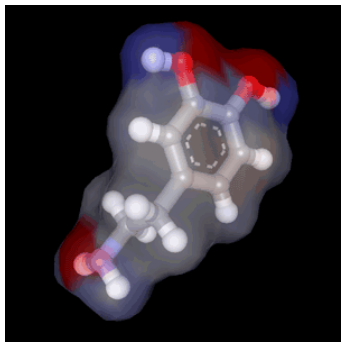
BG involved in automatic execution of learned motor plans

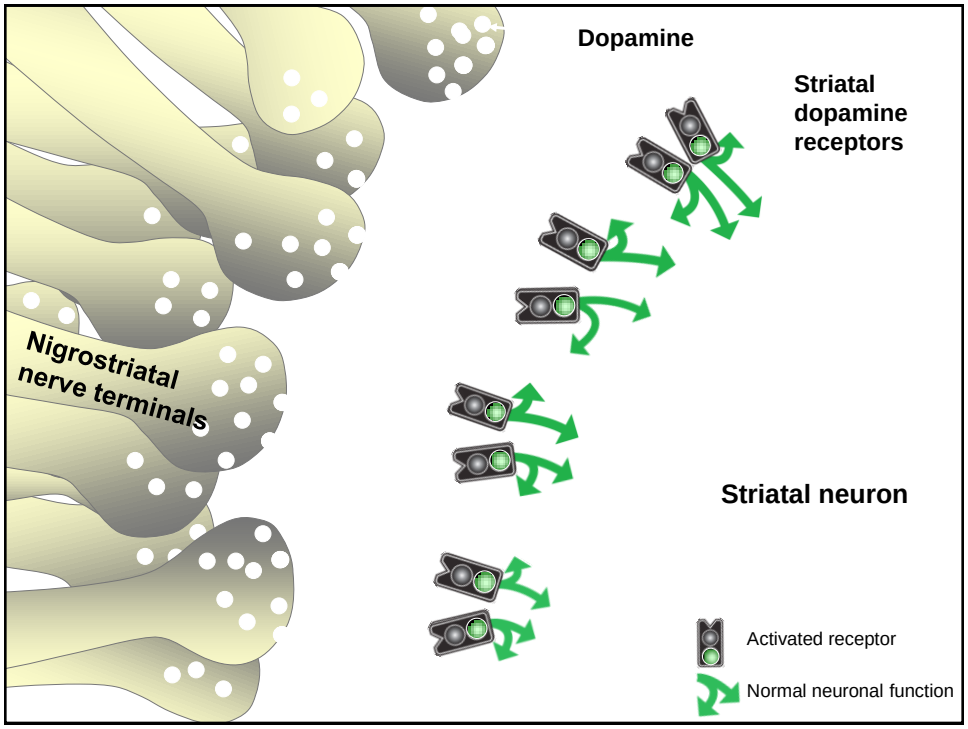
Implicated in action selection→which of several possible behaviors to execute at a given time

Allows for initiation, termination and scaling of movement

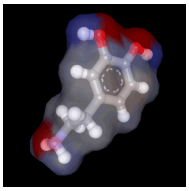
Hypodopaminergic state→ bradykinesia, freezing, etc

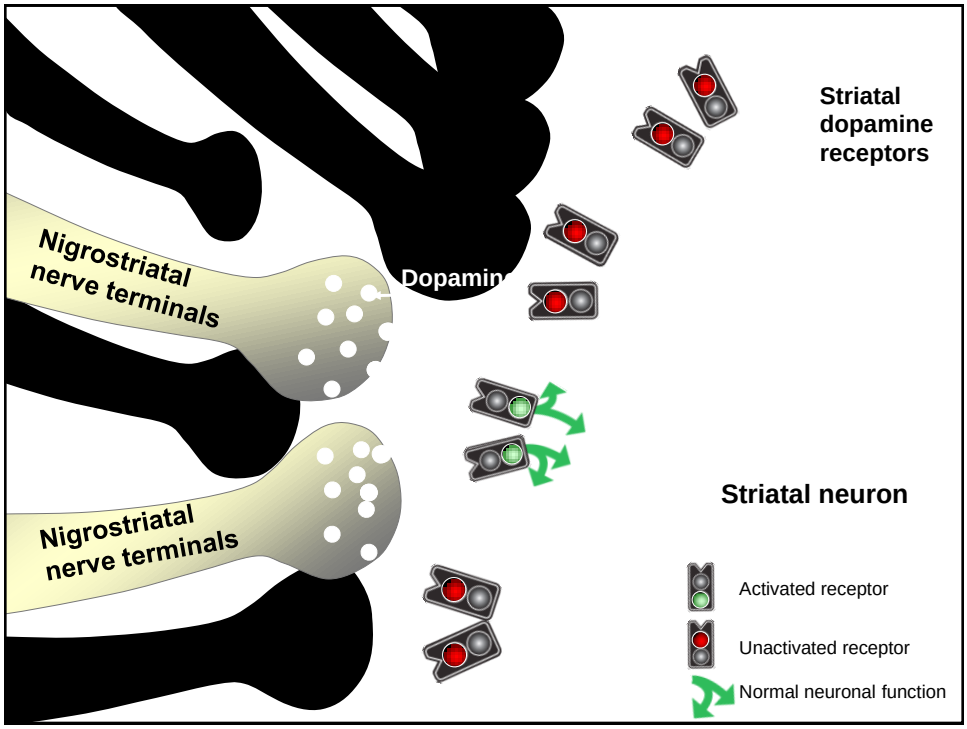
Dopamine in Normal Movement



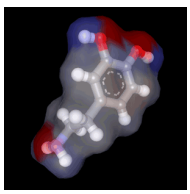
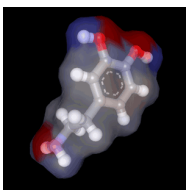
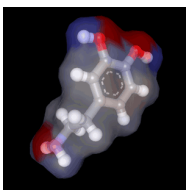


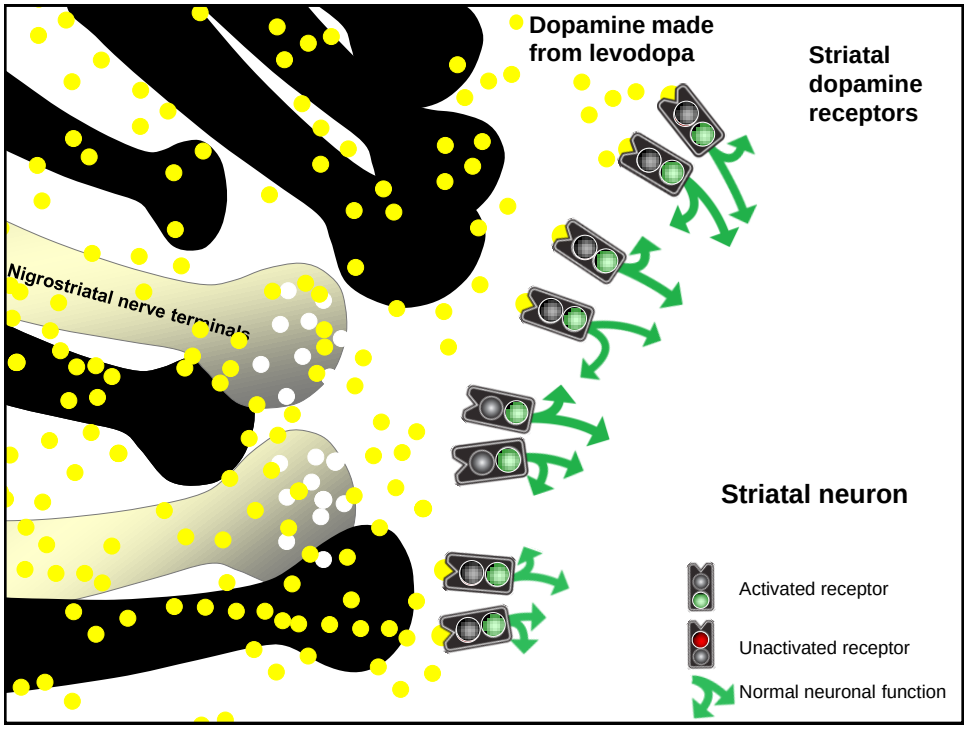
Dopamine in PD



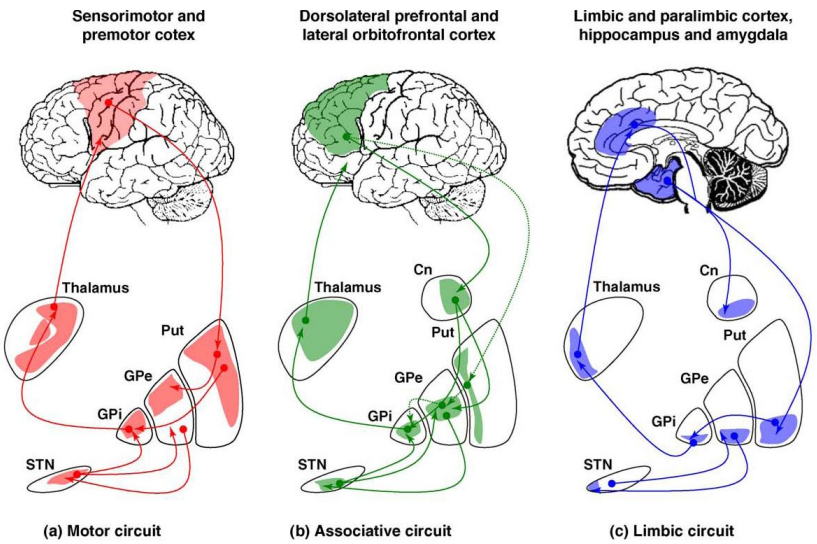


PD with levodopa treatment



Cortico-striatal-pallido-thalamo-cortical Loops



Krack et al, 2010, *Trends in Neuroscience*

	Low dopamine (PD)	High dopamine (levodopa, dopamine agonists)
Motor	- Bradykinesia - Apathy (motor component)	- Dyskinesia - Motor Impulsivity
Cognitive/ Associative	- Bradyphrenia - Empty brain (absence of ideas) - Apathy (cognitive component)	- Cognitive impulsivity - Flight of ideas - Novelty seeking
Emotional (Limbic)	- Depression - Apathy (emotional component - Anhedonia - Anxiety, harm avoidance - Drug withdrawal syndrome	- Euphoria, mania - Emotional impulsivity/Behavioral addictions - Hedonism, creativity, pleasure seeking, risk-taking behavior - Feeling on or "high"

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
- Psychmotor slowing or agitation
- Poor concentration
- Recurrent thoughts of death or suicide

Depression Causes

- *Psychological Causes*
  - Sadness, Helplessness, and Hopelessness may stem form 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)

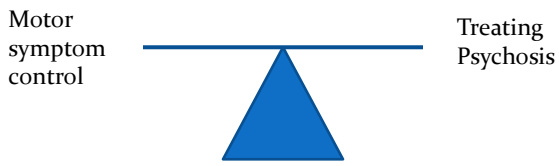
4- COMT inhibitors (Entacapone, Tolcapone)

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

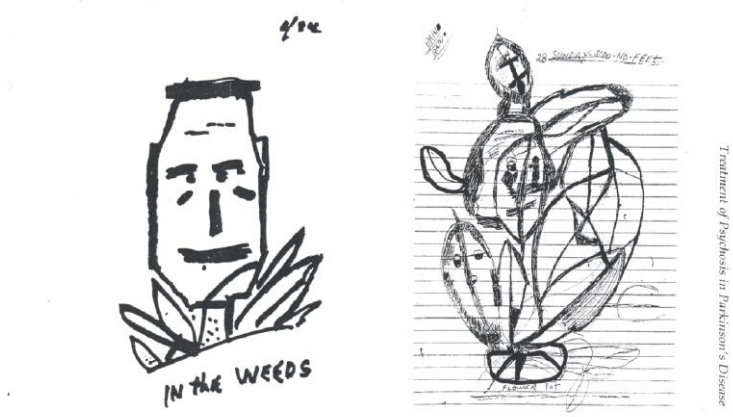
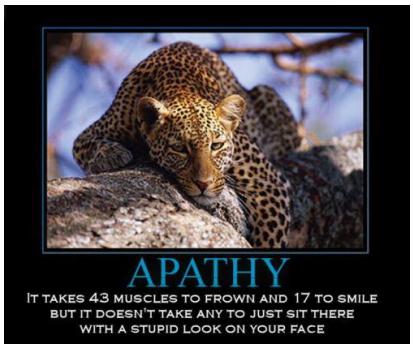


Figure 3–2. Illustrations by a man with Parkinson's disease of hallucinations induced by levodopa and selegiline.

Treatment of Psychosis in Parkinson's Disease 177

PD - Apathy

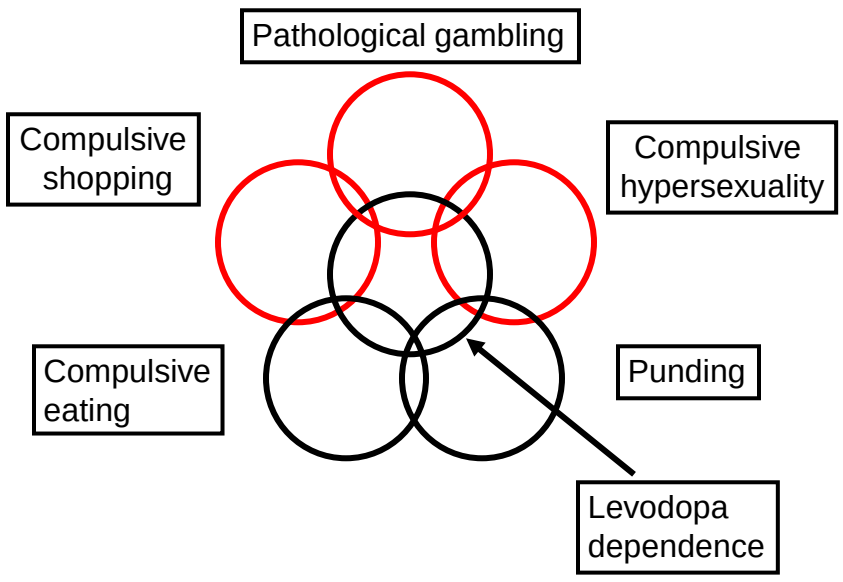


- Is diminished motivation and goal-directed behavior
- Up to 40% of PD patients
- Although often related to depression (25%), it can be found in patients without mood disorder
- Associated with cognitive dysfunction related to dysfunction of Frontal dopamine systems in the brain

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



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 over-eaten, 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

PD Dementia	Alzheimer's Disease
Main deficits in: - Attention - Speed of thinking processes - Memory retrieval - Visuospatial Ability - Executive Function	Main deficits in: - Memory - Language

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 bur may help slow the progression
- Other medications (antipsychotics, antdepressants, 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???