

Anxiety in Parkinson's Disease: a neglected disorder

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Concern about the future is a natural response to having a chronic condition so:

What do we mean by anxiety?

- **Generalized anxiety:**
 - Excessive and constant worry and nervousness greater than usual –
 - Feeling of being out of control
 - Physical symptoms including restlessness, sleep disturbance, poor concentration, racing heart, excessive sweating, fluttering stomach, trouble breathing

What do we mean by anxiety?

- **Panic attacks** (most common type):
 - Discrete period of intense fear or discomfort associated with severe emotional and physical distress
 - Begin abruptly and peak within 10 minutes, then last about an hour
 - Other symptoms include palpitations, sweating, shaking, dizziness, and fear of dying
 - May be associated with “off” periods in Parkinson’s disease

What do we mean by anxiety?

- **Social avoidance**

- Avoiding social situations due to an excessive fear of embarrassment
 - May be directly related to having PD symptoms such as tremor or trouble walking
 - May predate the diagnosis of PD
 - Goes away when person is removed from the social situation

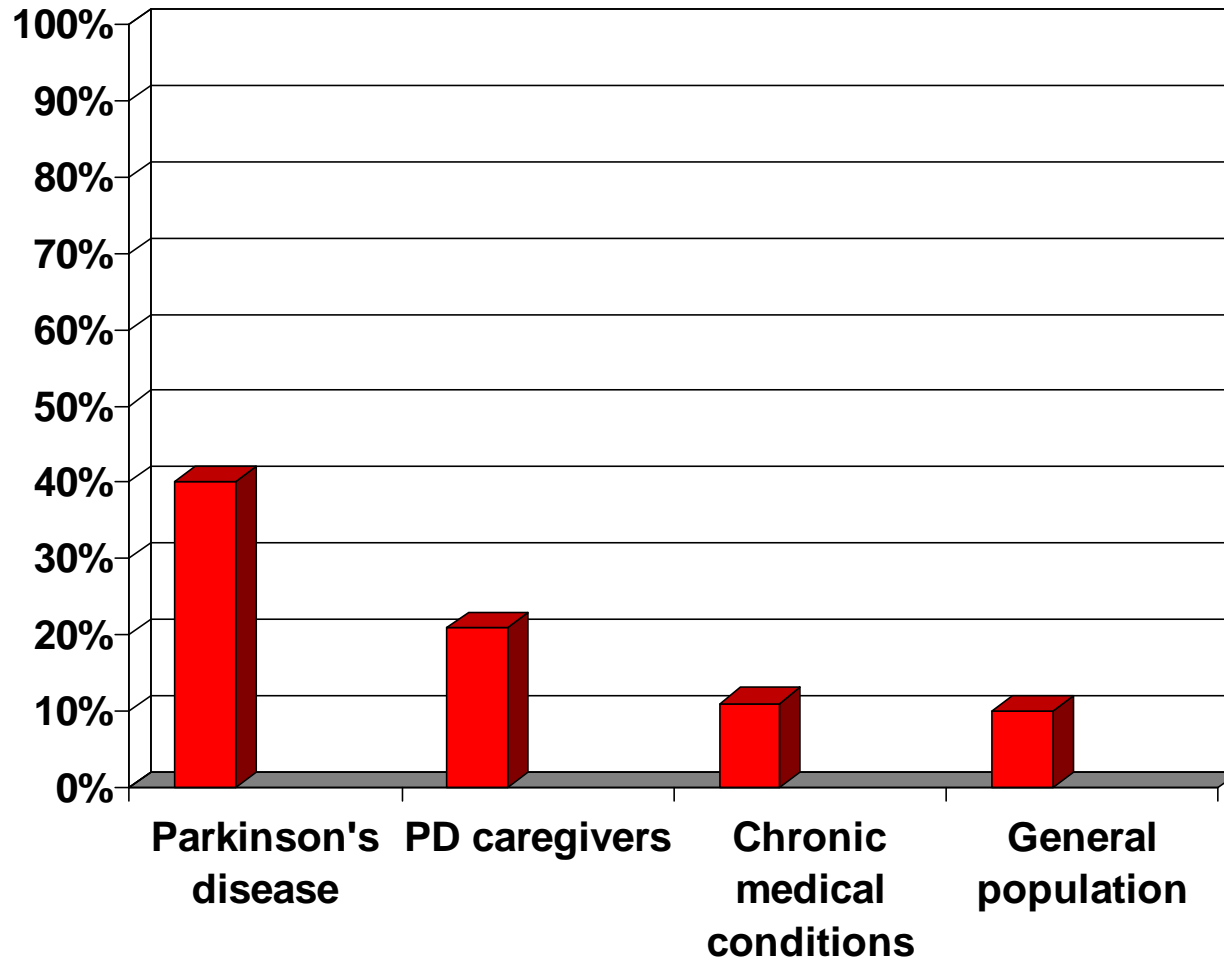
- **Obsessive-compulsive disorder;**

- Repetitive and intrusive thoughts and behaviors that are disturbing to the patient

How common is anxiety?

- Anxiety associated with PD is understudied
- Likely occurs in at least 40% of PD patients in some stage of their illness
 - 30% suffer from panic attacks
 - At least 10% suffer from generalized anxiety
 - Up to 15% have social avoidance

Frequency of anxiety



Why be concerned about anxiety in PD?

- **Anxiety is a major determinant of quality of life in persons with PD even when accounting for**
 - **the presence of depression**
 - **the severity of the movement disorder**

Anxiety and Depression in PD

- **Major depression and anxiety commonly occur together in persons with Parkinson's disease.**

Diagnostic criteria for depression

- **Five or more of the symptoms below present every day, for most of the day, for at least two weeks.**
- **At least one of:**
 - Depressed mood or
 - Anhedonia – loss of interest in usual activities
- **Other symptoms may include:**
 - Changes in appetite or weight
 - Too little or too much sleep
 - Fatigue or loss of energy
 - Feelings of guilt or worthlessness
 - Difficulty thinking, or making decisions
 - Recurrent thoughts of death or suicidal thoughts

Depression in PD: symptoms

- Compared to non-PD depressed patients:
 - **More:**
 - anguish, anxiety, irritability,
 - pessimism regarding the future,
 - suicidal ideation
 - **Less:**
 - guilt, self blame,
 - feelings of failure,
 - suicide

Anxiety in PD – associated symptoms

- **More severe motor symptoms**
- **More severe walking difficulties**
- **Gait Freezing**
- **On/Off fluctuations - ???**
 - **Most studies suggest that anxiety tends to occur during the “off” phase in those who experience “on off” phenomenon.**

Anxiety Rating Scales in PD:

Beck Anxiety Inventory

The Hospital Anxiety and Depression Scale

Hamilton Anxiety Rating Scale

The Neuropsychiatric Inventory-anxiety subscale

- **Assist with identifying anxiety in PD**
- **Helpful for measuring severity and response to therapy**
- **Completed by the patient or administered by health care providers**
- **None are perfect**

What causes anxiety in PD?

- Research suggests that anxiety is not just a reaction to the motor symptoms of PD, but a manifestation of the disease itself.
- Anxiety may precede the onset of motor symptoms of PD by years.
- Abnormalities in PD patients of certain brain chemicals involved in nerve transmission may also be responsible for anxiety
 - Norepinephrine
 - Serotonin
 - Dopamine

Important aspects of managing anxiety in PD

- Maximize treatment of motor symptoms of PD – minimize “off” time
- Assessment for depression including suicidal thoughts or plan
- Assessment for medications that may cause anxiety
- Association of other conditions that may cause anxiety or have symptoms in common with anxiety such as thyroid problems, urinary tract infection or constipation
- Assessment of prior history of anxiety and response to treatment

Treatment of Anxiety in PD

Caution:

- There are few good treatment studies of anxiety in PD.
- The following recommendations are based mostly on small studies and on studies of depression where anxiety was measured.

Selective serotonin reuptake inhibitors (SSRI)

- Effective for all types of anxiety including obsessive compulsive disorder
- Considered first line by most VA physicians
- May take several weeks to work
- Start at low dose and increase slowly

Selective Serotonin reuptake inhibitors

- Fluoxetine (Prozac) and sertraline (Zoloft) -
 - tend to be activating
 - Side effects – nausea, insomnia, anxiety, and sexual dysfunction
- Paroxetine (Paxil) –
 - Mildly sedating and may lessen anxiety
 - Side effects – nausea, dry mouth, and sexual dysfunction
- Citalopram (Celexa)
 - Helpful for anxiety
 - Less potential for drug interactions due to milder p450 inhibition
 - May cause less sexual dysfunction
- Escitalopram (Lexapro)
 - Profile similar to citalopram, but more potent

Atypical antidepressants

- **Mirtazapine (Remeron)**
 - Useful for depression with anxiety and insomnia. May increase appetite as well.
 - Side effects include sedation (greater at lower doses), weight gain, dry mouth.
 - Less sexual dysfunction
- **Venlafaxine (Effexor)**
 - Has anti-anxiety properties
 - Side effects include nausea, dizziness, constipation and sweating
 - Blood pressure monitoring recommended

Potential interactions of antidepressants with rasagiline (Azilect) / selegiline (Deprenyl)

- There are case reports of serious interactions known as the serotonin syndrome but frequency is very low (estimated to be 0.24%).
- Symptoms / signs include fever, confusion, agitation, stupor, sweating, diarrhea, delusions, mania, tremor, rigidity
- Manufacturer recommendations:
 - Selegiline (Deprenyl) – avoid combined use of selegiline with antidepressants
 - Rasagiline (Azilect) – mirtazapine is contraindicated; “seems prudent to avoid combining rasagiline and all antidepressants”. A 14 day wash out is recommended

Potential interactions of antidepressants and rasagiline / selegiline

- Rasagiline clinical trials allowed use of antidepressants. No serious interactions were reported among 250 treated patients.
- Conclusion: Risk is low. Careful monitoring and good patient education are important if combining these medications with antidepressants.

Medical Treatment of Anxiety

- **Benzodiazepines**

- Include diazepam, clonazepam, lorazepam, and alprazolam
- Effective for panic, generalized anxiety, and social phobia
- Work quickly after one dose
- Side effects include sedation, confusion, fatigue, and impaired memory and these symptoms are worse in older and cognitively impaired patients
- Falls more common in PD patients taking benzodiazepines

- **Buspirone**

- Effective for generalized anxiety but not for panic or social phobia

Treatment of Anxiety in PD

- **Cholinesterase inhibitors** – donepezil, rivastigmine, galantamine
 - May be useful for anxiety in patients with dementia
- **Deep brain stimulation** has been reported to be associated with decreased anxiety in PD patients
 - There are case reports of unmasking of anxiety with DBS

Medical Treatment of Anxiety

- **Psychotherapy or talk therapy is poorly studied in PD but is likely to be effective**
- **Exercise including walking, yoga, relaxation techniques, meditation,**
- **Qigong**
 - **Ancient Chinese practice to restore energy to the body, mind, and spirit**
 - **May reduce depression and anxiety in PD patients**

Alternative therapy for depression

- poorly studied in PD patients

Please discuss use of these over the counter remedies with your health care provider due to potential for significant side effects and harmful interactions.

- Valerian extract
 - From the roots of the Valerian plant native to Europe and Asia
 - May be helpful for anxiety
- Rhodiola rosea
 - Herbal supplement
 - May alleviate anxiety and insomnia

Conclusions

- Anxiety disorders are common in Parkinson's disease and affect quality of life
- Anxiety commonly occurs with depression
- Treatments are available to alleviate anxiety in patients with Parkinson's disease although more studies are needed .
- Good reference: Parkinson's Disease: the First Year by Jackie Hunt Christensen