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

- Parkinson's disease
- PD caregivers
- Chronic medical conditions
- General population
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 of 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