

Treatment of Psychiatric Aspects of Parkinson's Disease

Maryland Psychiatric Society

Psychopharmacology Update 2025



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M E D I C I N E

Financial disclosures

- I have no relevant financial disclosures.

Learning objectives

- *I will provide an overview of common psychiatric complications of Parkinson's disease along with first-line strategies for treatment.*

Outline for today's talk

- Parkinson's disease & Non-motor symptoms (NMS)
- Non-motor fluctuations (NMF)
- Prescribing considerations
- Depression & apathy
- Anxiety
- Cognitive impairment
- Psychosis
- Impulse Control Disorders
- Sleep disturbances
- Use of psychotherapy in PD

Parkinson's disease (PD)

MOTOR

- Bradykinesia
- Resting tremor
- Rigidity
- Postural instability

- Carbidopa/Levodopa
- Dopamine Agonists

NON-MOTOR (NMS)

- Autonomic dysfxn
- Sleep disorders
- Mood & Anxiety
- Cognitive dysfunction
- Pain, fatigue, etc.

Non-motor symptoms (NMS) in PD

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- Are common (up to 90% of all patients all stages)
- May precede the development of motor fx of PD
- Often become more pronounced as PD progresses
- Greater neg impact on quality of life than motor sx
- May feel **more impaired by NMS** than motor deficits

Non-motor fluctuations (NMF)

- “Wearing off” phenomena b/c of pulsatile dopaminergic therapy
- NMFs significantly affect well-being & go underrecognized
- Increase in frequency and severity with PD progression
- Typically occur alongside motor fluctuations
- Complex relationship with dopaminergic therapy
- Also involve serotonergic and noradrenergic pathways
- Multidisciplinary care with Neurology = best treatment outcomes
- First step is to optimize the antiparkinsonian regimen

Prescribing considerations in PD

- Falls - postural instability and autonomic dysfunction (orthostatic hypotension) increase the risk of falls
- Confusion – very sensitive to anticholinergic side effects d/t profound reduction in acetylcholine and high prevalence of cognitive decline
- Motor worsening - stiffness and/or tremor can be exacerbated by psychotropic medications
- Sedation – daytime fatigue is already common in PD
- *The evidence is limited – mostly we extrapolate.*

Depression and Apathy in PD

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Presentation of Depression in PD

- Major depression in 17%; depressive sx in 35%
- Overlap between PD sx and depressive sx → overdiagnosis
 - masked facies, psychomotor slowing, fatigue, etc.
- Focus on nonoverlapping / “core” depressive symptoms:
 - inappropriate guilt
 - worthlessness
 - hopelessness
 - suicidal ideation
- Is distinct from (but can co-exist with) demoralization
- Watch out for projection → underdiagnosis
- Can co-exist with Apathy in PD

Treatment of depression in PD

- Several RCTs for pharm treatment of depression
- SSRIs & SNRIs are generally considered first-line treatments
- **Venlafaxine** is classified as clinically useful by the MDS-EBM
- Sertraline, Citalopram, Fluoxetine, Paroxetine, are possibly useful
 - **Sertraline** is the best-tolerated SSRI in PD (2021 Delphi Consensus)
 - all can worsen tremor but typically not clinically significant
 - several large studies have found no increased risk of serotonin syndrome with concomitant use of MAOI-B for motor sx
- Nortriptyline, Desipramine, and Amitriptyline are possibly useful
 - TCAs side effects like orthostatic hypotension limit their use
- **Pramipexole** (DA) is clinically useful
- Mirtazapine and Bupropion are likely to be effective

- Pontone and Mills, 2021; Rodríguez-Antigüedad et al., 2025¹¹

Apathy in PD

- Apathy in upwards of 40% people with PD
- Reduction in goal-directed activity / loss of motivation
- Emotional blunting and lack of engagement in activities
- Can be in association with depression
- Correlated with worsening cognitive impairment
- High caregiver burden – impacts ability to exercise, etc.
- **Rivastigmine** has evidence for reducing apathy

- Heim and Djamshidian, 2025

Anxiety in PD

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Presentation of Anxiety in PD

- Anxiety disorders occur in 31% of people with PD
- Can be the main NMS contributing to impaired quality of life
- Overlap with autonomic dysfxn; often co-morbid with Depression
- GAD, Panic disorder, and Unspecified are most common
- Fluctuation associated anxiety (= NMF)
 - episodes are panic-like with physical complaints
 - worse in off-state; during transition from DA on-state
 - optimizing dopamine replacement therapy *may* be helpful
- Social Phobia is also common; fear of falling (specific phobia)
- Associated with cognitive dysfunction
- Internal tremor

Treatment of Anxiety in PD

- No high quality RCTs of pharmacologic treatments in PD
- Start with monotherapy with **SNRIs** or **SSRIs** or an atypical AD
 - **Venlafaxine ER**
 - **Sertraline**
 - divided dosing may be ideal
- Buspirone - small RCT showed worsening motor function
- Benzodiazepines are sometimes used with caution

- Pontone, AJGP, 2021; Schneider et al., 2020

Cognitive impairment in PD

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Cognitive impairment in PD

- Mild Cognitive Impairment (PD-MCI) in 25%
- Dementia (PDD) is present in 50% at 10 years
- Early on: executive function, attention, visuospatial dysfxn
- Later in the course: memory and language affected
- Lewy bodies +/- Alzheimer's pathology; greater cholinergic deficit
 - more frequent NPS with worsening cognition, esp psychosis
 - higher burden of NPS is associated with dementia conversion
- **Rivastigmine** is the only FDA approved medication
 - insufficient evidence for other acetylcholinesterase inhibitors
 - mixed results with memantine – but we use it
- modifiable risk factors (vascular, orthostatic hypotension, OSA)

Psychosis in PD

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Presentation of Psychosis in PD

- 60% of patients (or more) develop hallucinations or delusions
- Minor phenomena are common, may be a prodromal form*
 - passage phenomena, feeling of presence, illusions
- Well-formed visual hallucinations of people or animals
 - at least partial insight, generally non-distressing
- Delusions are mostly paranoid, typically in dementia
- Can be caused by or worsened by dopaminergic meds

- Schneider et al., 2024; Segal et al., 2021

Treatment of Psychosis in PD

- Clozapine has demonstrated efficacy (6.25-50 mg/d) – no EPS
- **Quetiapine**'s efficacy is less clear but the most frequently prescribed (50-150 mg/d, starting at 12.5mg QHS) – less EPS
- **Pimavanserin**, a selective 5-HT_{2A} inverse agonist (34mg daily)
- Aripiprazole may be used as an alternative in selected patients
- Olanzapine can cause motor worsening – *but we use it*
- Haloperidol and Risperidone are contraindicated
- Rivastigmine is useful and safe, particularly in PD dementia
- Non-pharmacologic management is first-line treatment
 - Circadian rhythms, lighting/vision, causes of delirium
 - Psychoeducation and reassurance

- Rodríguez-Antigüedad et al., 2025; Segal et al., 2021

Impulse Control D/O in PD

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Impulse Control D/O (ICDs) in PD

- Impulse Control Disorders impact 14-45% of PD patients
- Pathological gambling, hypersexual behaviors, excess shopping, binge eating, hoarding, punding
- Dopamine Dysregulation Syndrome (DDS)
- Male sex, younger age at PD onset, and longer PD duration
- Dopamine agonist (DA) treatment is the strongest ICD predictor
 - DDS is most associated with higher levodopa doses
- Mainstay of treatment is to **taper off the offending agent**
- Serotonergic antidepressants increase the probability of ICD

- Morrow et al., 2024; Weintraub et al., 2022

Sleep disorders in PD

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Sleep disorders in PD

- Sleep fragmentation w/ frequent awakenings is common
- REM Sleep Behavior Disorder (RBD)
 - highly associated with neurodegenerative synucleinopathies
 - **Melatonin** (3-12mg in the evening) safe & affective
 - **Clonazepam** (0.25-1mg at bedtime) is modestly effective
- Restless Legs Syndrome (RLS)
 - RLS associated with an increased risk of developing PD
 - dopamine agonist tx is associated with risk of developing PD
- Excessive Daytime Somnolence
 - more common as PD progresses; r/t cognitive fluctuations

- Bang et al., 2025; St Louis et al., 2017

Psychotherapy in PD

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Psychotherapy in PD

- Demoralization and depression often overlap
 - feeling overwhelmed, inability to cope effectively with feeling
 - *“the frustration of enduring persistent and intrusive PD symptoms without relief, coupled with diminishing hope for improvement and the resultant feelings of stigma and isolation”*
- Demoralization typically requires psychotherapy, not ADs alone
- Interpersonal Therapy (IPT) - beneficial for depression in RCT
- CBT – growing support for its efficacy in treating anxiety
 - rumination, catastrophizing, inability to tolerate uncertainty
- Exercise is particularly beneficial for motor symptoms of PD
- Team effort with therapists, PT/OT/SLP, personal trainers, etc.

- Cronin-Golomb A, et al., 2025; Koszycki et al., 2025; McDaniels et al., 2025



Maryland Association for Parkinson Support

DONATE

MAPS ▾

About Parkinson's Disease ▾

Classes ▾

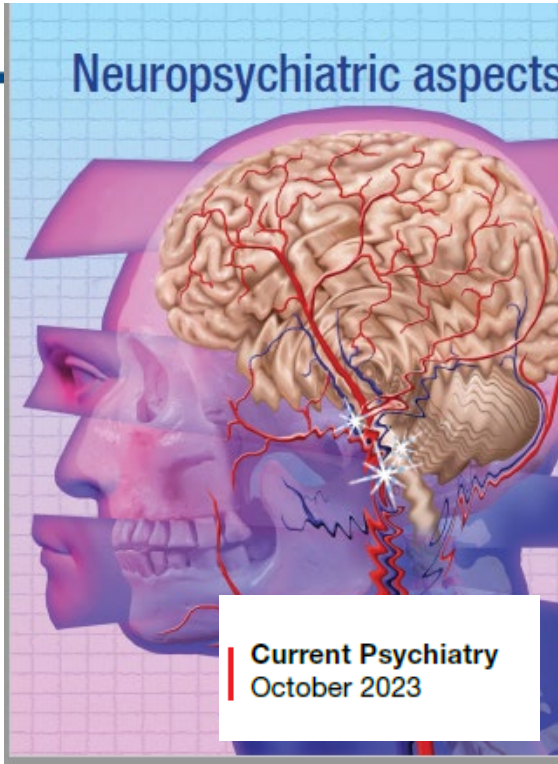
Events ▾

PD Support Groups ▾

STORE



Papers to read



of Parkinson's disease: Practical considerations

How to identify and manage common psychiatric manifestations of PD

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Treatment in Geriatric Mental Health:
Research in Action

Optimal Treatment of Depression and Anxiety in Parkinson's Disease

Gregory M. Pontone, M.D., M.H.S., Kelly A. Mills, M.D., M.H.S.

THERAPEUTIC ADVANCES in
Neurological Disorders

Review

Neuropsychiatric disorders in Parkinson's disease

Beatrice Heim and Atbin Djamshidian 

Ther Adv Neurol Disord

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Movement Disorders

CLINICAL PRACTICE



Using Principles of Cognitive Behavioral Therapy to Treat Anxiety in Parkinson's Disease

Alice Cronin-Golomb, PhD,^{1*} Bradley McDaniels, PhD,² Soania Mathur, MD,² Gregory M. Pontone, MD,⁴ Gretchen O. Reynolds, PhD,⁴ and Indu Subramanian, MD^{3,5}

Movement Disorders

CLINICAL PRACTICE

From Hopelessness to Hope: Addressing Demoralization in Parkinson's Disease

Bradley McDaniels, PhD,^{1*} Ellen R. Bradley, MD,^{2,3} Gregory Pontone, MD,⁴ Kuhan Pushparatnam, BSc,⁵ Soania Mathur, MD,⁶ Rebecca Miller, PhD,⁷ and Indu Subramanian, MD^{3,5}

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Editorial

Reconceptualizing Catatonia as “Psychiatric Parkinsonism”

Jared T. Hinkle, M.D., Ph.D., Gregory M. Pontone, M.D., M.H.S.

Time for questions

**I'm so tired.
Almost time to
crawl into bed
and not be able
to sleep for
three hours.**

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