

# Mental Health and Parkinson's Disease

Assessing and addressing mental health in patients and care partners improves quality of life.

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Parkinson's disease (PD) is a disorder defined and diagnosed by its disabling motor symptoms of bradykinesia, rigidity, and tremor. However, the nonmotor neuropsychiatric symptoms associated with PD, including depression, anxiety, apathy, impulse control disorders, and psychosis, have an even greater adverse effect on quality of life and the risk of nursing home placement. Despite the burden neuropsychiatric symptoms bring, they often go unrecognized and untreated. Similarly, although there are a number of evidence-based drug treatments, physical and occupational therapies, and assistive devices to address motor impairments of PD, most neuropsychiatric symptoms are treated off-label with drugs that have little or no evidence for efficacy or safety when used in this population. At least two-thirds of individuals with PD will have a clinically significant neuropsychiatric disorder during the course of their disease, and most will have more than 1 disorder concurrently (Table).

## Anxiety and Depression

Anxiety and depression co-occur frequently, and these disorders will affect approximately 50% of patients with PD.<sup>1</sup> Anxiety and depression are more common in persons with PD than in other similarly disabling conditions like diabetes, rheumatoid arthritis, or multiple sclerosis. This suggests that the pathological process of PD overlaps with the mechanisms underpinning anxiety and depression.

## Apathy

Apathy affects up to one-third of patients but is often unrecognized.<sup>2</sup> Apathy, characterized by loss of motivation, lack of concern, diminished interests, and flat affect, is common in patients with PD and other neurodegenerative disorders. Apathy can occur as an isolated neuropsychiatric phenomenon or as part of a depressive disorder. Although

the patient is often too unmotivated to complain, apathy is associated with diminished quality of life and greatly increased burden and distress for care partner(s).

## Impulse-Control Disorders

Impulse-control disorders are associated with the use of dopamine-agonist medications that are often used to treat motor symptoms in patients with PD.<sup>3</sup> Compulsive behaviors and impulse-control disorders, most commonly pathologic gambling, hypersexuality, and uncontrolled spending, can be triggered by dopaminergic therapies. Impulse-control disorders are particularly prevalent (>10%) in patients receiving dopamine agonists. Despite the serious psychosocial and financial consequences of impulse-control disorders, they frequently go unrecognized as many physicians are not accustomed to inquiring about gambling, sexual behavior, or spending patterns.

TABLE. TIMING OF BEHAVIORAL CHANGES IN PARKINSON'S DISEASE

AT ANY STAGE OF THE DISEASE	Anxiety
	Apathy
	Depression
	Fatigue
	Sleep disorders
LATER IN THE COURSE OF THE DISEASE <sup>a</sup>	Cognitive decline
	Delirium
	Dementia
	Hallucinations
	Psychosis

<sup>a</sup>Consider alternate diagnoses (eg, dementia with Lewy bodies) if these symptoms occur early in the disease course.

## Psychosis

Visual hallucinations and illusions are common in patients with PD. Fortunately, severe psychosis—one of the most feared psychiatric disturbance in PD—which also includes delusions and behavioral disturbances, affects only about 5% to 10% of patients.<sup>4,5</sup> There are several factors that predispose patients with PD to psychosis. So-called intrinsic factors include underlying cognitive decline, dementia (dementia with Lewy bodies or Parkinson's disease dementia), advanced age, long-standing PD, sleep deprivation, and visual processing abnormalities. So-called extrinsic factors include the use of dopamine agonists, amantadine, anticholinergics, or higher doses of carbidopa–levodopa combinations. The motor symptoms of patients with psychosis and PD should be managed with monotherapy, if possible, using carbidopa–levodopa combinations at the lowest doses required to control symptoms. Avoiding polypharmacy will decrease the risk of psychotic symptoms. Adjunctive treatment with an antipsychotic is indicated only when psychosis persists despite lowered doses of carbidopa–levodopa therapy or when impaired motor function does not permit lower doses of combined carbidopa and levodopa.

## The Role of Dopaminergic Treatments

Complications of PD treatment, especially on-off fluctuations, can affect mental health in patients with PD (Box 1). Physicians are generally aware that after several years of PD the motor responses to dopaminergic therapies often begin to fluctuate. Initially, patients can experience wearing off of the motor benefits of levodopa therapy (eg, increased bradykinesia, tremor, gait disturbance, or rigidity) at the end of the dosing period. In more advanced PD, the fluctuating motor symptoms worsen, becoming more intense and less predictable in relation to the timing of medication. Significant nonmotor fluctuations, including marked anxiety, panic attacks, and severely altered mood may occur in addition to

### Box 1. Treatment-Induced Symptoms

- Compulsive behaviors
- Excessive daytime sleepiness
- Hallucinations
- Impulse control disorders
- Psychosis

motor fluctuations. Optimizing dopaminergic therapies can reduce motor and nonmotor fluctuations. If not judiciously prescribed, the polypharmacy often needed to diminish motor and nonmotor fluctuations can trigger serious iatrogenic problems, including hallucinations, psychosis, or impulse control disorders. Unfortunately, some patients might surreptitiously overmedicate themselves due to the fear of experiencing the unpleasant off-period anxiety and dysphoria. Frequent dosing and medication overuse often results in addiction-like behavior known as the *dopamine dysregulation syndrome*, which is characterized by increased dopaminergic drug craving and use despite serious medication-induced side effects. Comorbid impulse-control disorders, psychosis, and panic attacks are common in dopamine dysregulation syndrome.<sup>6</sup> Patients often use motor terminology to describe a need related to their craving of more medication, and this often results in misdiagnosis.

## Screening

The high prevalence of neuropsychiatric symptoms in patients with PD underscores the importance of routine screening for neuropsychiatric symptoms. However, finding time in a busy clinical practice for this type of evaluation can be challenging. While several scales for detecting depression, anxiety, impulse control disorders, and apathy have been validated for use in PD, there are currently no definitive rating tools for PD psychosis. Despite these barriers, this is a vitally important task as the consequences of failing to recognize and treat neuropsychiatric disorders can be severe. Data from a large multicenter NIH clinical trial showed that at least 40% of participants with depression were untreated. Left untreated, even mild depressive symptoms predict development of more severe symptoms, increased impairment in activities of daily living, and the need for antiparkinson's drug therapy. Similarly, untreated anxiety has been shown to worsen freezing of gait and the on-off fluctuations related to dopaminergic treatment. Failing to recognize a patient's impulse-control disorders can lead to her or his financial ruin, divorce, and legal problems. Psychosis is associated with agitation and a broad range of behavioral problems that can make daily life at home unmanageable.

## Treatment of Neuropsychiatric Conditions

Drug treatments for neuropsychiatric symptoms are available, but most have limited evidence for safety and efficacy when used to treat patients with PD.<sup>7</sup>

### Anxiety and Depression

Antidepressants are among the best studied, and recent systematic reviews suggest that selective serotonin reup-

take inhibitors (SSRIs) are the most effective and well-tolerated in patients with PD.<sup>8</sup> However, other classes of antidepressants such as selective serotonin and norepinephrine reuptake inhibitors (SS/NRIs) and tricyclics may be equally effective, although with a slight increase in potential side effects. While there are currently no evidence-based drug treatments for anxiety in persons with PD, antidepressants are likely useful, and cognitive-behavioral therapy has demonstrated efficacy across several trials for both anxiety and depression.<sup>9</sup>

### Apathy

Treatment of apathy is a major unmet need. Optimizing dopaminergic management for the motor symptoms of PD can improve the patient's level of activity but does not eliminate apathy.

### Impulse-Control Disorders

Treatment of impulse-control disorders includes eliminating the triggering agent, which is usually a dopamine agonist, and obtaining appropriate psychiatric consultation.

### Psychosis

Treating psychosis is a bit more problematic because first- and second-generation antipsychotics can worsen the motor symptoms of PD and may increase the risk of mortality.<sup>10</sup> Therefore, few are considered safe for use in patients with PD; according to a 2011 Movement Disorder Society review, only clozapine, quetiapine, and pimavanserin are recommended.<sup>7</sup> Even among these, the choice of treatment may be fraught with tradeoffs. For instance, although proven effective, clozapine requires weekly blood monitoring and has a host of serious potential side effects. Quetiapine is deemed to have acceptable risk without monitoring but is sedating and lacks evidence for efficacy. The newest agent, pimavanserin, is approved by the Food and Drug Administration (FDA) for psychosis in patients with nondemented PD. However, pimavanserin has not yet been proven to work in patients with PD psychosis with dementia.

### Mental Health Considerations for Caregivers

An important and yet often overlooked aspect of neuropsychiatric symptoms is that the patient is not the only person to bear the burden of these comorbidities. Family members, spouses, and friends increasingly assume the role of care partner as a patient's course of illness progresses. Ideally, as a patient's disability becomes more severe, this partnership helps the patient better manage symptoms, comply with treatment, and remain in the home. Yet the ability of a care partner to provide help is more often confounded by the presence of neuropsychi-

atric symptoms in the patient than the overall severity of his or her physical impairment. Therefore, best management should include not only treatments for the neuropsychiatric symptoms in the patient with PD but also awareness and support for the patient's care partners.<sup>11</sup>

Providing assistance for a person with PD sometimes evolves into an overwhelming burden, upending lives and creating serious levels of family dysfunction. The mental health and coping skills of care partners has a major impact on their lives and the quality of life of the patient with PD. Interviewing care partners to assess their concerns, problems, and ability to effectively serve in this capacity is an important, although often neglected, aspect of patient care.

It is well documented that patients with PD who are experiencing significant depression, anxiety, dementia, or psychosis with severe motor fluctuations are likely to cause an increased burden of care for care partners. There are also many other symptoms that can insidiously affect the coping abilities of the care partner. Apathy is a major source of frustration, stress, and conflict between patients and care partners. The lack of motivation, indifference, and diminished interests of a patient with PD who also has significant apathy is frequently misinterpreted by family and care partners as willful laziness or depression.

Patients with insomnia and frequent nocturnal awakenings, whether due to frequent nocturia, REM-sleep behavioral disorder, sleep fragmentation, nocturnal immobility, or the need for medication administration in the middle of the night, can severely disrupt sleep for the care partner. A sleep-deprived care partner is unlikely to function well throughout the day.

The fear of leaving the patient alone for a few hours, or the patient's fear of being left alone, founded or not, can enslave the care partner for 24 hours per day, 7 days per week. The resulting social isolation severely impairs the quality of life of the care partner. Care partners commonly experience anger, denial, guilt, resentment, irritability, depression, anxiety, fatigue, exhaustion, and the sense of being overwhelmed. Patients may sense that they are being ignored, neglected, or abused—emotionally, verbally, or physically. These are unpleasant feelings that care partners and patients may not want to divulge to each other. Therefore, it is important that the care partner and patient have an opportunity to speak to the physician privately, allowing them to vent their emotions without fear of embarrassment or recrimination.

Care partners must be reminded that their health is at stake, and that they are entitled to have some free time to recharge their emotional batteries. Recommendations for alleviating the burden for the primary care partner are listed in Box 2. Care partners should all be encouraged to

## Box 2. Tips for alleviating the care partner's burden

**Do something nice for yourself every day!**

**Do not drop out of the mainstream of life!**

- Enlist other family members to assist on a regularly scheduled basis
- Hire aides at home for several hours on a regular basis
- Participate in exercise programs
- Participate in education seminars and support groups
- Consult with a mental health professional
- Have a home safety evaluation
- Make use of adult day-care programs

participate in PD support groups and educational programs, as they will benefit from the advice and experience of others who have had to cope with similar situations. Consultation with a mental health professional is important for care partners who are becoming overwhelmed or depressed.

Family members or friends often say they are willing to pitch in and help the primary care partner without committing to a specific schedule. The assistance of other family members should be arranged on a predictable and regular basis. This might enable the primary care partner to make plans in order to re-engage in the mainstream of life (eg, take a class, socialize with friends, exercise, attend church). The assistance of family members on a haphazard basis or only during emergency situations does not ease the ongoing daily burdens for the care partner.

If family members are unavailable to provide consistent help, hiring aides on a regular basis is a helpful option. Care partners often resist this recommendation, saying “no one can care for my loved one like I can.” Although that may be true, hiring aides does help prevent burnout for someone providing care. Care partners should be reassured that patients often benefit from the variety of interacting with an aide, and having a more relaxed and refreshed care partner. Hiring an aide allows the care partner to preserve his or her role as a spouse or family member rather than as an unpaid servant.

Participation in adult day care programs several times a week is particularly appropriate for patients with PD and dementia, providing mental stimulation for the patient and predictable respite for the care partner. Community programs, philanthropies, or faith-based groups might provide assistance with transportation or companion care for those who cannot afford these options. Relocating to a continuing care retirement center may be appropriate, although it is often a difficult decision emotionally and financially. Care partners should be encouraged to consult a social worker, an elder-law specialist, or the local department of aging for additional recommendations.

The health of patients with PD and their care partners are intertwined. Physicians treating the patient with PD must discuss these issues with family members and request permission to forward their observations and concerns to the physicians caring for the care partner. ■

1. Pontone GM, Williams J, Anderson K, et al. Prevalence of anxiety disorders and anxiety subtypes in patients with Parkinson's disease. *Mov Disord*. 2009;24(9):1333-1338.
2. Pagonabarraga J, Kulisevsky J, Strafella AP, Krack P. Apathy in Parkinson's disease: clinical features, neural substrates, diagnosis, and treatment. *Lancet Neurol*. 2015;14:518-531.
3. Weiss H, Marsh L. Impulse control disorders and compulsive behaviors associated with dopaminergic therapies in Parkinson disease. *Neural Clin Practice*. 2012;2:267-274.
4. Flýtche DH, Creese B, Politis M, et al. The psychosis spectrum in Parkinson disease. *Nat Rev Neurol*. 2017;13:81-95.
5. Mack J, Rabins P, Anderson K, et al. Prevalence of psychotic symptoms in a community-based Parkinson's Disease sample. *Am J Geriatr Psychiatry*. 2012;20(2):123-132.
6. Warren N, O'Gorman C, Lehn A, Siskind D. Dopamine dysregulation syndrome in Parkinson's disease: a systematic review of published cases. *J Neural Neurosurg Psychiatry*. 2017;88:1060-1064.
7. Seppi K, Weintraub D, Coelho M, et al. The movement disorder society evidence-based medicine review update: treatments for the non-motor symptoms of Parkinson's disease. *Mov Disord*. 2011;26:42-80.
8. Mills KA, Greene MC, DeZube R, et al. Efficacy and tolerability of antidepressants in Parkinson's disease: A systematic review and network meta-analysis. *Int J Geriatr Psychiatry*. 2018;33(4):642-651.
9. Pontone GM, Williams J, Anderson K, et al. Pharmacologic treatment of anxiety disorders in Parkinson's disease. *Am J Geriatr Psychiatry*. 2013;21(6):520-528.
10. Weiss HD, Adler S. The management of psychosis in Parkinson's disease. *Psychiatry Times*. 2014;31:19-22.
11. Mosley PE, Moodie R, Dissanayaka N. Caregiver burden in Parkinson disease: a critical review of recent literature. *J Geriatr Psychiatry Neurol*. 2017;30:235-252.

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