REVIEW ARTICLE

Understanding the dopaminergic pathway relative to men's sexual dysfunction in patients with Parkinson's disease: a narrative review with implications for future research

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Parkinson's disease (PD) is often most recognized for motor symptoms but associated non-motor symptoms such as sexual dysfunction can significantly impact quality of life. This condition involves a hormonal disruption and has a predilection for male patients, yet there are no formal guidelines for screening or management of sexual health pathology in these patients. While prior publications have addressed the presence of sexual dysfunction (SD) among men with PD, there has been a paucity of work examining the hypothalamic-pituitary-gonadal (HPG) axis and the interplay between dopamine, prolactin (PRL), and testosterone. This review provides an overview of data extracted from the existing peer-reviewed literature regarding hormonal and sexual health changes in men with PD and the impact of dopaminergic and/or androgen replacement therapy. Furthermore, while some research suggests that PD patients are at higher risk for prolactin elevation and testosterone deficiency, heterogeneity of the data limits extrapolation. Additionally, data related to pharmacologic optimization of the HPG axis in this patient population is similarly limited. Prospective studies are needed to better characterize the hormonal pathophysiology of PD as it relates to sexual dysfunction such that men at risk can be effectively identified so as to offer interventions that may improve quality of life.

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INTRODUCTION

Parkinson's Disease (PD) is a debilitating neurodegenerative disorder that stems from the progressive loss of dopaminergic neurons within the substantia nigra [1]. The clinical manifestations are often grouped into motor (e.g., tremor, bradykinesia) and nonmotor categories with the nonmotor elements often less-emphasized in the literature [2]. Dopamine is both a neurotransmitter and hormone, such that PD can also be viewed as a hormonal disorder [3]. Axis disruptions have relevance to both overall health and quality of life [4, 5].

According to the Parkinson's Foundation there are roughly 60,000 people in the United States diagnosed with PD annually with an anticipated prevalence of 1.2 million people living with PD by the year 2030 [6]. PD has a predilection for affecting males more than females, a discrepancy attributed to the neuroprotective properties of estrogen against dopaminergic neuron degradation [2, 7]. Relative to controls, men with PD have nearly twice the risk of sexual dysfunction, most commonly involving erectile dysfunction (ED), premature ejaculation, orgasmic dysfunction, and decreased libido [2]. Each of these components may be related to hormonal axis disruption.

Unfortunately, sexual dysfunction is often overlooked among PD patients, possibly due to tunnel-vision relative to motor symptoms. However, a study by Politis et al. found sexual dysfunction (classified as loss of libido and/or ED) to be the 12th most bothersome symptom (out of 24) in this population [1]. Another cross-sectional study of 113 men with PD found the prevalence of sexual dysfunction to be 68%, but the rate increased to 75% when considering only those patients not on pharmacotherapy [8]. The majority of subjects self-reported PD as having a negative impact upon their sexual health.

Although reports document the noteworthy existence of sexual dysfunction among men with PD, there is a paucity of data relative to the disruption of the hypothalamic-pituitary-gonadal (HPG) axis and the interplay between dopamine, prolactin (PRL), and testosterone (Fig. 1). Likewise, there have been insufficient efforts to fully characterize the hormonal response from PD-related medications and the role for androgen replacement therapy (ART) in men with PD. Thus, we chose to review the peer-reviewed literature relevant to investigations into the underlying pathophysiology and the efforts to optimize the hormonal underpinnings of sexual health among men with PD. In doing so, we hope to create a basis upon which to build working relationships between clinicians and researchers within both urology and neurology, with an ultimate goal of improving understanding of disease and patient quality of life.

Methodology of research

This narrative review was performed by conducting a Medline/Pubmed search. The search was performed using the following word combinations: Parkinson's AND disease AND urology, Parkinson's AND disease AND testosterone, Parkinson's AND disease AND prolactin, Parkinson's AND disease AND testosterone replacement

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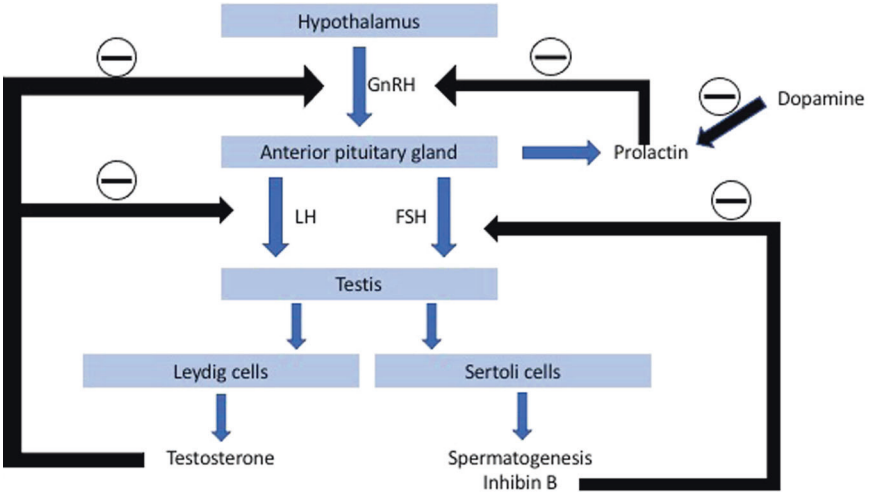

Fig. 1 Anticipated hypothalamic-pituitary-gonadal axis in eugonadal male without PD. Patients with PD may experience hormonal derangements at various points in this axis. GnRH Gonadotropin-releasing hormone, LH Luteinizing hormone, FSH Follicle stimulating hormone. Minus signs represent points of negative regulation/feedback.

therapy, Parkinson's AND disease AND l-dopa AND sexual function, Parkinson's AND disease AND erectile dysfunction. The following exclusion criteria were utilized: non-English language, abstract only or no abstract available. Relevant articles from the bibliographies of chosen manuscripts were added as needed. For consistency, discussions regarding PRL and testosterone levels were reported in the same units (ng/mL and ng/dL respectively). Data from original manuscripts utilizing different units were converted to align with previously mentioned units. Manuscripts selected for review were published between 1972 and 2022. After assessment, 46 manuscripts/works were included for this review.

The dopaminergic pathway to testosterone deficiency

Dopamine is known to inhibit PRL production and release [9]. Thus, degradation of dopaminergic neurons can lead to a rise in serum PRL, which can subsequently inhibit pulsatile GnRH release, resulting in decreased production of luteinizing hormone (LH) and testosterone (Fig. 2). In fact, providers well-versed in evaluation and management of men with low testosterone are quite familiar with the need to rule out hyperprolactinemia as a cause [10]. As many men with PD may be diagnosed after the fourth decade of life, some clinicians may be tempted to assume low testosterone in these patients is purely age-related [6]. However, several groups have noted that men with PD appear to be at increased risk for low testosterone [11]. Okun et al. examined the prevalence of symptomatic testosterone deficiency (TD) in 91 PD patients using prior serum measurements and the St. Louis testosterone deficiency questionnaire [12]. Nearly half were found to have been previously diagnosed with TD. Of the remaining patients, half were found to have low levels of free testosterone. However, interpretation of this latter point is difficult as the diagnosis of TD should not be based purely on free testosterone measurements per the American Urological Association [10]. In a separate study of their PD patient registry, using a testosterone cutoff of <325 ng/dL to define TD, Okun et al. found a prevalence of 35%, which was higher than that for men without PD [13].

Despite data suggesting a higher prevalence, TD does not appear to be ubiquitous amongst men with PD as some studies have shown normal baseline testosterone levels in newly diagnosed patients [14, 15]. In a contemporary analysis, 32 PD patients from the INSPECT trial were examined to determine whether dopaminergic therapy influenced testosterone levels and motor function. At baseline prior to intervention, the mean total testosterone levels per group ranged from 361.06 to 449.55 ng/dL, which is not consistent with TD [3]. However, neither the natural history of hormonal alterations or true prevalence of TD has been effectively characterized. Doing so will require adequately powered, prospective data with long-term follow-up.

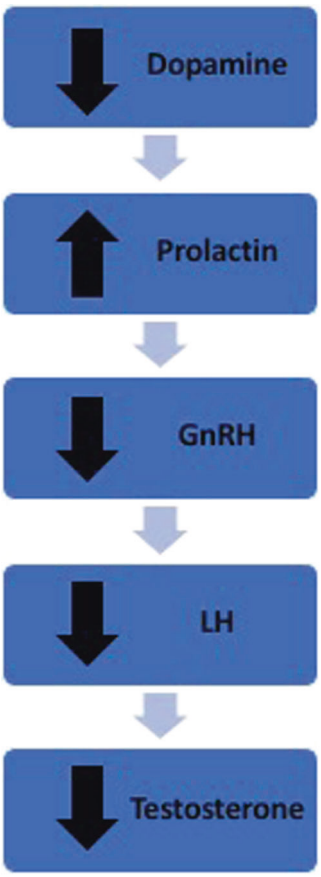

Fig. 2 Anticipated natural history of the male, hypothalamic-pituitary-gonadal axis in Parkinson's Disease. Derangements in each area of the axis may represent an opportunity for further study on pharmacologic intervention as it relates to men's sexual health.

The role of prolactin

It has been demonstrated that PD patients have higher nocturnal PRL levels compared to age-matched controls [16]. Otake et al.

studied ten newly diagnosed, untreated PD patients (men and women) [17]. These individuals were exposed to an L-dopa "test" of 500 mg orally and PRL levels were measured before and after treatment. PD patients were noted to have high mean PRL levels at baseline compared to controls (22.5 vs 9.22 ng/mL, respectively). Following L-dopa administration, mean PRL declined modestly to 18.5 ng/mL. There was no significant correlation between hormone levels and clinical findings. However, this was limited to the Yahr scale which assesses only the motor component of PD [17]. Results of this study are difficult to extrapolate due to the mixture of male and female patients as well as the cross-sectional nature of L-Dopa dosing, PRL measurement and lack of longitudinal follow up. Work by Daniel et al. examined 25 (18 male) PD patients, already on dopaminergic therapy in a cross-sectional fashion to elucidate the effect of therapy on PRL, LH, follicle-stimulating hormone (FSH), and testosterone [18]. There were no significant deviations from the reference ranges for LH, FSH, and testosterone. While 44% of patients had PRL values in normal range, the remainder demonstrated elevated levels. The authors note that 83% of those with "suppressed" PRL levels were on dopaminergic agonists (e.g., pramipexole, ropinirole, rotigotine), whereas these agents were only used by 31% of those with elevated ("non-suppressed") levels ($p < 0.05$).

More recently, Nitkowska et al. examined estradiol, testosterone, sex hormone binding protein, and PRL levels in a cohort of 36 male, PD patients undergoing treatment versus 69 age-matched controls [19]. Evaluations also included the Unified Parkinson's Disease Rating Scale (UPDRS), Abnormal Involuntary Movement Scale (AIMS), Mini Mental Status Exam, Beck.

Depression Inventory (BDI), and Parkinson's Disease Questionnaire (PDQ 39). PRL levels were significantly higher in the PD cohort compared to controls (13.7 ng/mL versus 7.6 ng/mL) and 31% of PD patients had hyperprolactinemia. Additionally, controls demonstrated higher levels of both testosterone (530 vs 420 ng/dL) and estradiol (55.2 vs 30.1 pg/mL) [19]. Although the higher mean testosterone for controls reached statistical significance, both means fell within the normal range, complicating a determination of clinical significance. The data was also hindered by lack of pretreatment testosterone values. When the laboratory data was interpreted alongside the clinical inventories, lower PRL levels were associated with lower BDI scores (better) as well as lower PDQ 39 scores (better). Sub-analysis suggested patients with higher testosterone levels experienced slower disease progression [19].

The existing literature prevents effective characterization of the HPG axis in men with PD, either at baseline or following disease-specific therapy. Many studies are cross sectional in nature, contain males and females, involve various dopaminergic agonists, and fail to examine hormonal profiles prior to treatment. For instance, a recent meta-analysis comparing serum prolactin levels in PD vs. healthy patients failed to show a significant difference [20]. However, the results were limited by analysis of underpowered studies (range: 7–39 patients per study) and significant heterogeneity ($I^2 = 96.7\%$) [20]. Also, some of these investigations were performed in the context of thyrotropin-releasing hormone stimulation [21–24]. Finally, among this population of men with PD, there is a paucity of data correlating hormonal levels to commonly used instruments in men's health, such as the International Index of Erectile Function and the Androgen Deficiency in the Aging Males questionnaire.

Sexual quality of life in men with PD

Rates of sexual dysfunction among men with PD range from 41–82% [25–27]. However, the etiology is likely multifactorial considering the potential for neurological, vascular, and endocrine pathophysiology among these patients. Additionally, psychogenic factors may stem from self-perception/self-esteem issues relative to motor symptoms, emotional state, and partner status [28]. Thus, there are many targets for meaningful research in order to improve upon the reportedly high incidence of poor libido, erectile and orgasmic dysfunction, and avoidance of intercourse [29].

Sexual activity can be impaired by the motor-related symptoms of PD (e.g., rigidity, bradykinesia, clumsiness). These symptoms may worsen in the evening hours when sexual activity is often pursued. Non-motor symptoms of PD can also strain relationships in other ways. Sleep dysfunction in PD patients may result in partners sleeping apart, leading to a decline in intimacy [28]. Depression is commonly noted in men with PD, and this has been associated with poor erectile quality and sexual dysfunction in general. Unfortunately, medications used to treat depression in this population (e.g., selective serotonin reuptake inhibitors) have been shown to aggravate ED [30]. Despite the high prevalence of sexual dysfunction among men with PD, providers managing the neurological symptoms often feel that those issues should be adequately addressed before considering treatment for sexual health, rather than doing so concurrently [25, 30].

Sexual health following dopaminergic therapy

Based on the pathophysiology, dopaminergic agonists are the mainstay of therapy in patients with PD [31, 32]. Following initiation of therapy, patients have reported improvement in sexual dysfunction, and even hypersexuality [33–35]. Bronner et al. investigated this further and noted 8.8% of patients reported increased sex drive, 3.5% developed compulsive sexual behavior, and 2% demonstrated hypersexuality [28]. However, a concrete explanation to tie these symptoms to use of dopaminergic agonists has not been put forth. A case study by Ivanco et al. discussed that lowering dopaminergic drug doses was of minimal behavioral benefit for reduction of hypersexuality [36]. Perhaps conversely, a separate report described fluctuating erections with "peak" doses of levodopa [37]. Finally, other reports have noted that therapy such as Pergolide may improve IIEF metrics in young males with PD [38, 39]. Thus, due to the limited data, it is unknown if there is a dose-dependent effect of dopaminergic-agonist relative to causation of hypersexuality.

Symptoms of TD can mimic non-motor symptoms of PD, which may prevent men from receiving potentially valuable hormonal therapy (Table 1 [10, 40, 41]). In a survey of men with PD, 93% answered positively to 3 or more questions on ADAM, despite only

Table 1. Symptoms of Parkinson's disease and testosterone deficiency.

Parkinson's Disease symptoms		Testosterone deficiency symptoms [7, 8]
Motor Symptoms [33]	**Non-Motor Symptoms [34]**	
•Tremor •Rigidity •Bradykinesia •Akinesia •Gait disturbance •Impaired handwriting/ grip force •Speech deficits •Freezing •Muscle cramps and dystonia	•Fatigue •Sleep disturbance (excessive day time sleepiness, insomnia, REM sleep behavior disorder) •Neuropsychiatry (depression, anxiety, apathy, cognitive impairment) •Dysautonomia (constipation, sexual dysfunction, pain, bladder disturbance, sweating, orthostatic hypotension, blurred vision etc.)	•Fatigue •Reduced energy •Reduced endurance •Diminished work and/or physical performance, •Visual field changes •Anosmia •Depression •Reduced motivation •Poor concentration •Impaired memory •Irritability •Low sex drive •Changes in erectile function

35% having serum levels to support TD [12, 13]. Among men with PD and TD, the use of ART has been shown to significantly improve motor and nonmotor symptoms [13, 42]. However, when ART has been applied to men with PD whose testosterone levels did not quite meet criteria for TD (i.e., "borderline"), symptomatic improvement did not reach statistical significance, but the therapy was well tolerated [43]. To draw an interesting parallel from another area of research, multiple authors have looked at the risk of development of PD in the setting of androgen deprivation therapy for prostate cancer. The data, however, is mixed as some studies suggest an increased risk whereas others do not [13, 44–46].

Future directions

Considering the number of individuals affected by PD (both patients and their loved ones), the male predilection, a clear hormonal pattern, and the detriment to quality of life from sexual dysfunction, well-designed research and organized collaboration is required. Men's health providers should work with colleagues within the neurosciences to develop multidisciplinary pathways for men with PD. New and existing patients should be screened for signs and symptoms of sexual dysfunction and/or testosterone deficiency. Future research efforts should consider (1) establishing the prevalence of TD among men with PD, with efforts to define the natural progression over time, (2) evaluating the impact of ART upon sexual dysfunction and other PD-related symptoms in these patients, and (3) examining the hormonal and sexual health impact of dopaminergic agonists, and whether any such effects are dose-related.

CONCLUSIONS

In addition to the classic motor impairments, men with PD are at increased risk of sexual dysfunction. The loss of dopaminergic suppression of PRL appears to place patients at potentially greater risk of low testosterone. This hormonal pathology has numerous implications for both sexual health and overall wellness, and symptoms can unfortunately be misinterpreted or ignored. Better data to guide clinical practice is required. Effective collaboration between providers specialized in PD and those in men's health may create meaningful clinical algorithms to identify men at risk and to optimize their quality of life and longevity.

DATA AVAILABILITY

No new data was generated in this manuscript. Analysis of preexisting data as part of the review is available in the discussion section (pages 6–11) with original data also available by accessing the citation in the reference section.

REFERENCES

1. Politis M, Wu K, Molloy S, Peter GB, Chaudhuri KR, Piccini P. Parkinson's disease symptoms: the patient's perspective. Mov Disord. 2010;25:1646–51.
2. Zhao S, Wang J, Xie Q, Luo L, Zhu Z, Liu Y, et al. Parkinson's Disease is associated with risk of sexual dysfunction in men but not in women: a systematic review and meta-analysis. J Sex Med. 2019;16:434–46.
3. Okun MS, Wu SS, Jennings D, Marek K, Rodriguez RL, Fernandez HH. Testosterone level and the effect of levodopa and agonists in early Parkinson disease: results from the INSPECT cohort. J Clin Mov Disord. 2014;1:8.
4. Savci C, Sendir M. Evaluation of health related quality of life in patients with Parkinsons disease. Neurosciences. 2009;14:60–66.
5. Kinateder T, Marinho D, Gruber D, Hatzler L, Ebersbach G, Gandor F. Sexual Dysfunctions in Parkinson's Disease and Their Influence on Partnership-Data of the PRISM Study. *Brain Sci* 2022; 12.
6. Marras C, Beck JC, Bower JH, Roberts E, Ritz B, Ross GW, et al. Prevalence of Parkinson's disease across North America. NPJ Parkinsons Dis. 2018;4:21.
7. Ng YF, Chen CY, Chia GT, Tan BBJ, Chan LL, Tan EK. The association between Parkinson's disease and Sexual dysfunction: Clinical correlation and therapeutic implications. Ageing Res Rev. 2022;79:101665.
8. Raciti L, De Cola MC, Ortelli P, Corallo F, Lo Buono V, Morini E, et al. Sexual dysfunction in Parkinson Disease: a multicenter italian cross-sectional study on a still overlooked problem. J Sex Med. 2020;17:1914–25.
9. Ben-Jonathan N, Hnasko R. Dopamine as a prolactin (PRL) inhibitor. Endocr Rev. 2001;22:724–63.
10. Mulhall JP, Trost LW, Brannigan RE, Kurtz EG, Redmon JB, Chiles KA, et al. Evaluation and management of testosterone deficiency: AUA guideline. J Urol. 2018;200:423–32.
11. Bourque M, Soulet D, Di Paolo T. Androgens and Parkinson's Disease: a review of human studies and animal models. Androg Clin Res Ther. 2021;2:294–303.
12. Okun MS, Crucian GP, Fischer L, Walter BL, Testa CM, Vitek JL, et al. Testosterone deficiency in a Parkinson's disease clinic: results of a survey. J Neurol Neurosurg Psychiatry. 2004;75:165–6.
13. Okun MS, McDonald WM, DeLong MR. Refractory nonmotor symptoms in male patients with Parkinson disease due to testosterone deficiency: a common unrecognized comorbidity. Arch Neurol. 2002;59:807–11.
14. Sinhamahapatra SB, Kirschner MA. Effect of L-dopa on testosterone and luteinizing hormone production. J Clin Endocrinol Metab. 1972;34:756–8.
15. Pekkarinen A, Rinne UK, Salokangas R, Siirtola T, Sonninen V. Plasma testosterone content of male patients with Parkinson's disease during L-dopa treatment with or without dopadecarboxylase inhibitor. Acta Neurol Scand Suppl. 1972;51:129–30.
16. Bellomo G, Santambrogio L, Fiacconi M, Scarponi AM, Ciuffetti G. Plasma profiles of adrenocorticotropic hormone, cortisol, growth hormone and prolactin in patients with untreated Parkinson's disease. J Neurol. 1991;238:19–22.
17. Otake K, Oiso Y, Mitsuma T, Hirooka Y, Adachi K. Hypothalamic dysfunction in Parkinson's disease patients. Acta Med Hung. 1994;50:3–13.
18. Daniel JS, Govindan JP, Kamath C, D'Souza C, Adlan MA, Premawardhana LD. Newer dopaminergic agents cause minimal endocrine effects in idiopathic Parkinson's disease. Clin Med Insights Endocrinol Diabetes. 2014;7:13–17.
19. Nitkowska M, Tomasiuk R, Czyzyk M, Friedman A. Prolactin and sex hormones levels in males with Parkinson's disease. Acta Neurol Scand. 2015;131:411–6.
20. Duc Nguyen H, Hoang NMH, Ko M, Seo D, Kim S, Jo WH, et al. Association between serum prolactin levels and neurodegenerative diseases: systematic review and meta-analysis. Neuroimmunomodulation. 2022;29:85–96.
21. Kostic VS, Marinkovic Z, Filipovic S, Momcilovic D. Function of dopamine receptors in young-onset Parkinson's disease: prolactin response. Mov Disord. 1993;8:227–9.
22. Cusimano G, Capriani C, Bonifati V, Meco G. Hypothalamo-pituitary function and dopamine dependence in untreated parkinsonian patients. Acta Neurol Scand. 1991;83:145–50.
23. Lawton NF, MacDermot J. Abnormal regulation of prolactin release in idiopathic Parkinson's disease. J Neurol Neurosurg Psychiatry. 1980;43:1012–5.
24. Eisler T, Thorner MO, MacLeod RM, Kaiser DL, Calne DB. Prolactin secretion in Parkinson disease. Neurology. 1981;31:1356–9.
25. Pfeiffer RF. Autonomic dysfunction in Parkinson's Disease. Neurotherapeutics. 2020;17:1464–79.
26. Elshamy AM, Mohamed ES, Al-Malt AM, Ragab OA. Sexual dysfunction among egyptian idiopathic Parkinson's Disease patients. J Geriatr Psychiatry Neurol. 2022;35:816–22.
27. Hu X, Liu WG, Yan FL. [Male sexual dysfunction and Parkinson's disease: a preliminary investigation]. Zhonghua Nan Ke Xue. 2013;19:518–21.
28. Bronner G, Vodusek DB. Management of sexual dysfunction in Parkinson's disease. Ther Adv Neurol Disord. 2011;4:375–83.
29. Sakakibara R, Shinotoh H, Uchiyama T, Sakuma M, Kashiwado M, Yoshiyama M, et al. Questionnaire-based assessment of pelvic organ dysfunction in Parkinson's disease. Auton Neurosci. 2001;92:76–85.
30. Sakakibara R, Uchiyama T, Yamanishi T, Kishi M. Genitourinary dysfunction in Parkinson's disease. Mov Disord. 2010;25:2–12.
31. Parent M, Parent A. Substantia nigra and Parkinson's disease: a brief history of their long and intimate relationship. Can J Neurol Sci. 2010;37:313–9.
32. Armstrong MJ, Okun MS. Diagnosis and treatment of parkinson disease: a review. JAMA. 2020;323:548–60.
33. Harvey NS. Serial cognitive profiles in levodopa-induced hypersexuality. Br J Psychiatry. 1988;153:833–6.
34. Vogel HP, Schiffter R. Hypersexuality–a complication of dopaminergic therapy in Parkinson's disease. Pharmacopsychiatria. 1983;16:107–10.
35. Uitti RJ, Tanner CM, Rajput AH, Goetz CG, Klawans HL, Thiessen B. Hypersexuality with antiparkinsonian therapy. Clin Neuropharmacol. 1989;12:375–83.
36. Ivanco LS, Bohnen NI. Effects of donepezil on compulsive hypersexual behavior in Parkinson disease: a single case study. Am J Ther. 2005;12:467–8.
37. Jimenez-Jimenez FJ, Tallon-Barranco A, Cabrera-Valdivia F, Gasalla T, Orti-Pareja M, Zurdo M. Fluctuating penile erection related with levodopa therapy. Neurology. 1999;52:210.

38. Pohanka M, Kanovsky P, Bares M, Pulkrabek J, Rektor I. Pergolide mesylate can improve sexual dysfunction in patients with Parkinson's disease: the results of an open, prospective, 6-month follow-up. Eur J Neurol. 2004;11:483–8.
39. Moussa M, Abou Chakra M, Papatsoris AG, Dellis A, Dabboucy B, Peyromaure M, et al. Perspectives on the urological care in Parkinson's disease patients. Arch Ital Urol Androl. 2022;94:107–17.
40. Moustafa AA, Chakravarthy S, Phillips JR, Gupta A, Keri S, Polner B, et al. Motor symptoms in Parkinson's disease: a unified framework. Neurosci Biobehav Rev. 2016;68:727–40.
41. Chaudhuri KR, Healy DG, Schapira AH. National Institute for Clinical E. Non-motor symptoms of Parkinson's disease: diagnosis and management. Lancet Neurol. 2006;5:235–45.
42. Mitchell E, Thomas D, Burnet R. Testosterone improves motor function in Parkinson's disease. J Clin Neurosci. 2006;13:133–6.
43. Okun MS, Fernandez HH, Rodriguez RL, Romrell J, Suelter M, Munson S, et al. Testosterone therapy in men with Parkinson disease: results of the TEST-PD Study. Arch Neurol. 2006;63:729–35.
44. Elshaikh MA, Underwood W, Soto DE. Androgen deprivation therapy for patients with prostate carcinoma and Parkinson's disease: case report and review of literature. Can J Urol. 2009;16:4495–7.
45. Young JWS, Sutradhar R, Rangrej J, Marras C, Fleshner N, Alibhai SMH. Androgen deprivation therapy and the risk of parkinsonism in men with prostate cancer. World J Urol. 2017;35:1417–23.
46. Chung SD, Lin HC, Tsai MC, Kao LT, Huang CY, Chen KC. Androgen deprivation therapy did not increase the risk of Alzheimer's and Parkinson's disease in patients with prostate cancer. Andrology. 2016;4:481–5.

AUTHOR CONTRIBUTIONS

All authors met criteria for authorship as follows: NAD: Conceived and/or designed the work that led to the submission, acquired data, and/or played an important role in interpreting the results, drafted and revised the manuscript, approved the final version, and has agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. KT: Conceived and/or designed the work that led to the submission, acquired data, and/or played an important role in interpreting the results, drafted and revised the manuscript, approved the final version, and has agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. RR: Conceived and/or designed the work that led to the submission, acquired data, and/or played an important role in interpreting the results, drafted and revised the manuscript, approved the final version, and has agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. RPT: Conceived and/or designed the work that led to the submission, acquired data, and/or played an important role in interpreting the results, drafted and revised the manuscript, approved the final version, and has agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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