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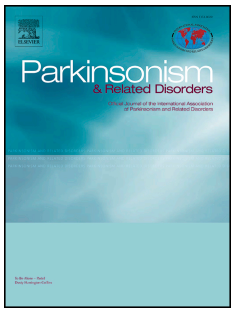

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The prevalence and clinical characteristics of hypersexuality in patients with Parkinson's disease following dopaminergic therapy: A systematic literature review

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Abstract

Introduction: A range of impulse control disorders have been identified as possible behavioural effects of brain dopamine replacement therapy (DRT) in patients with Parkinson's disease (PD). Among the behavioural problems associated with dysregulation of dopaminergic pathways underlying reward processing, hypersexuality carries significant social and legal repercussions, in addition to embarrassment for the patient with PD and his/her family. The present article evaluates the prevalence and characteristics of hypersexuality in the context of PD, focusing on the best available evidence.

Methods: We conducted a systematic literature review according to the Prisma guidelines on large-scale epidemiological studies (n>250) assessing hypersexuality in patients with PD treated with DRT.

Results: Our systematic literature review identified 10 relevant studies characterised by medium–to-large sample sizes (n=268-3,090). Average lifetime prevalence of hypersexuality in patients with PD on DRT was found to be 2.7% (7.4% in patients on dopamine agonists). In general, hypersexuality was associated with male gender and higher doses of dopamine agonists. Other clinically relevant associations included younger age, earlier PD onset and history of behavioural symptoms prior to dopamine agonist use.

Conclusion: Hypersexuality is not rare in patients with PD treated with DRT, particularly in those on dopamine agonists. These findings indicate that PD specialists should regularly screen and monitor for hypersexuality, paying particular attention to younger male patients, with an early PD onset and previous history of behavioural problems.

Key words: Parkinson's disease; Hypersexuality; Impulse control disorders; Dopamine replacement therapy; Levodopa; Dopamine agonists.

1. Introduction

Parkinson's disease (PD) is increasingly recognised as a neuropsychiatric disorder characterised by both motor and non-motor clinical manifestations, encompassing autonomic, cognitive and behavioural symptoms [1]. Although behavioural problems may precede the onset of typical motor symptoms by years [2] and are important predictors of health-related quality of life in patients with PD [3-5], these symptoms are frequently unrecognised and undertreated. Over the last few years, the study of impulsivity in PD has been of particular interest, since it has been observed that dopamine replacement therapy (DRT) may lead to the development or worsening of specific impulse control disorders (ICDs),ranging from pathological gambling to compulsive shopping and punding [6]. ICDs are characterised by repetitive behaviours aimed at reward seeking [7] and occur in approximately 13.6% of patients with PD [8], suggesting that they are not a rare occurrence in specialist PD clinics. Specifically, hypersexuality was among the first PD-related ICDs to be recognised, since the early 1980s [9,10]. Hypersexuality can be clinically defined as "a preoccupation with sexual gratification outside the accepted social and personal bounds, despite the harm that may be incurred" [11]. It is often an underreported issue and has been demonstrated to be potentially problematic from both social and medico-legal perspectives for patients with PD and their families [12].

Compulsive sexual behaviour, including both pathological and conventional forms of sexual behaviour, has an estimated prevalence of 3.0% to 6.0% in the US adult population [13]. In PD, early prevalence estimates have shown considerable disparity, ranging from 1.7% to 8.8% [14-17]. However, most epidemiological studies have focussed on convenience samples of patients recruited at single sites, therefore providing limited evidence. In recent years, hypersexuality has been increasingly reported in association with hyperdopaminergic state in patients with PD; specifically, different studies have identified the association of hypersexuality with dopamine agonists [18,19] and levodopa treatment [8]. Approximately 2.2-8.3% of patients with PD taking Levodopa, Pramipexole, or Selegiline can develop hypersexuality according to preliminary studies [7,20-24]. It is important that treating clinicians are aware of the extent of these pathological behaviours in the PD population and are able to correctly recognise them in order to implement appropriate management strategies and therefore limit potential harm to patients and society. Thus, we set out to conduct a systematic review focussing on the prevalence and clinical characteristics of hypersexuality in patients with idiopathic PD treated with DRT.

2. Methods

We conducted a systematic literature review according to the methodology described in the PRISMA guidelines [25] to assess the prevalence and clinical characteristics of hypersexuality in patients with PD on DRT. Our searches were carried out across the Medline, Embase and PyscInfo databases using the search terms 'Parkinson*' and 'hypersexual*' with the latter being expanded, as appropriate, to include all related terms, such as 'sexual deviation', 'erotomania', 'sexual addiction' and 'psychosexual behaviours'.

The searches were limited to original studies published in the English language since 1983. No limits were applied to the demographic characteristics of participants or the study type, in order to allow generalisation of the data to the entire PD population. We included only study on patients diagnosed with idiopathic PD and treated with any form of DRT. Our review targeted studies with a sample size larger than 250 and excluded articles focussing solely on paraphilias, as these conditions do not necessarily accompany hypersexuality. The primary outcome measures were the point and/or lifetime prevalence of hypersexuality and the description of any clinical correlates for these patients.

The selection process of this systematic literature review is illustrated by the flow chart in **Figure 1**.

[PLEASE INSERT FIGURE 1 HERE]

Titles and abstracts were initially reviewed; full texts were retrieved for all identified relevant articles and were then further assessed for possible inclusion. Finally, the reference lists of pertinent articles and the online Tables of Contents of relevant journals (including 'Movement Disorders', 'Parkinsonism and Related Disorders', 'Journal of Parkinson's Disease' and 'Parkinson's Disease') were manually scanned to ensure that any other potentially relevant studies had not been missed out. After contacting the authors of unavailable material, it was found that three potentially eligible studies were conference abstracts with unpublished full texts and therefore had to be excluded from the present review.

3. Results

3.1. Prevalence

This systematic literature review identified six original studies on the prevalence of hypersexuality in PD that met our inclusion criteria. All were carried out since 2006 and took place in specialist centres for movement disorders, apart from two large postal surveys conducted in Scandinavia [26,27]. The main findings from these studies are summarised in **Table 1**.

[PLEASE INSERT TABLE 1 HERE]

The study by Voon et al. [7] included a specifically designed questionnaire to screen for hypersexuality based on DSM-IV criteria. This questionnaire was to be completed by patients or their carer and consisted of five items assessing the possible links between increased sex drive and medication, preoccupation with sexual thoughts, inappropriate behaviour, use of explicit material and complaints by spouse. Additionally, diagnostic criteria for 'pathologic hypersexuality' were proposed focussing on the frequency and quality of these aberrant behaviours. This questionnaire has since been used in other studies investigating hypersexuality in PD. All pathological behaviours captured in the study by Voon et al. [7] had onset after starting dopaminergic medication.

Weintraub et al. [24] used the Modified Minnesota Impulsive Disorders Interview (MIDI), which contains questions aimed at identifying various DSM-IV-defined ICDs, including clinically significant hypersexuality, in patients who screened positive for ICDs. This study used a screening process which was systematic yet unstructured and focussed on patients treated with Pramipexole, Ropinirole and Pergolide.

Fan et al. [28] adopted Voon's questionnaire (7) followed by telephone interview for patients who screening positive for increased sex drive. Hypersexuality was the most common ICD identified in this study, with 6 patients reported as fulfilling diagnostic criteria for pathological hypersexuality. All of these patients were being treated with Piribedil; five were also on Levodopa and one on Pramipexole.

Weintraub et al. [8] conducted a large case-control study on 3,090 patients (of whom 98.1% were taking either levodopa or dopamine agonists) to assess the point prevalence of ICDs, including hypersexuality.

Hassan et al. [29] investigated the frequency of ICDs by retrospectively assessing the medical records of all patients on DA therapy in a specialist PD clinic. With regard to DA doses, 64.0% of patients reached the defined therapeutic dosage and 33.0% reached the defined target dose. The authors of this study defined sexual behaviours as pathological in line with the DSM-IV-TR definition of "failure to resist […] despite severe personal, family, or vocational consequences" [11].

Chiang et al. [30] employed Voon's criteria [7] for hypersexuality and found the highest lifetime prevalence of hypersexuality (3.0%) among the reviewed studies which used this set of diagnostic criteria.

In the Scandinavian surveys [26,27] and the large single-centre study conducted in Italy [31] and Mexico [32], the frequency of ICDs was assessed using the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP), a self-administered screening questionnaire for ICDs and other compulsive behaviours in PD [33]. In the two single-centre studies, the QUIP was complemented by diagnostic interviews [31,32].

3.2. Relationship to drug therapy

All studies found a significantly increased risk of developing hypersexuality and other ICDs with the use of DAs. When comparing patients on DAs and patients not on DAs, Weintraub et al. [8] found that the frequency of hypersexuality was significantly different: 90.0% *versus* 18.0%; OR 2.59 (CI 1.6-4.3; p<0.001). Both Weintraub et al. [8] and Hassan et al. [27] reported that a combination of DA and Levodopa further increased the odds of having an ICD compared to DAs alone by 50.0% [8], although individually DAs were more causative [7].

3.3. Clinical characteristics

The study by Weintraub et al. [8] found that men were more likely than women to be diagnosed with compulsive sexual behaviour (5.2% vs. 0.5%; OR, 11.98; CI, 4.87-29.48; p<0.001). These findings were in line with the results of the studies by Voon et al. [7] and Chiang et al. [28], which reflect gender patterns in the general population [13,29,30]. Voon et al. [7] also found that 6 of the 7 patients diagnosed with hypersexuality had co-morbid depression and that hypersexuality was associated with early PD onset (p<0.001). A univariate analysis carried out by Weintraub et al. [24] found that younger age, longer PD duration, history of ICD symptoms prior to PD diagnosis and use of DAs or Amantadine were associated with the presence of an active ICD. After using a multivariate model, these authors showed that DA use (p=0.01) and history of ICD symptoms prior to PD onset (p=0.02) were the only significant predictors of an active ICD. Fan et al. [26] found that alcohol consumption was an independent risk factor for ICD in the Chinese population. Living in the US, being unmarried and current cigarette smoking were additional demographic variables independently associated with ICDs according to the findings of the study by Weintraub et al. [8].

4. Discussion

4.1. Prevalence and demographic characteristics

This systematic literature review set out to determine the prevalence of hypersexuality in patients with idiopathic PD treated with DRT and to assess the clinical characteristics associated with hypersexuality in the largest studies conducted to date. The combined results of the six identified studies indicate an average lifetime prevalence of hypersexuality of 2.7% (7.4% in patients on DAs). Based on the results of three studies, the average active prevalence of hypersexuality was also 2.7%. The higher prevalence estimates for risk of both ICDs and hypersexuality in the Scandinavian studies [26,27] are not prevalence rates of clinical diagnosis, because these postal surveys relied solely on a self-report instrument (QUIP) which also identifies subclinical syndromes. In addition to male gender, younger age has been associated with ICDs in the general population. The study by Weintraub et al. [8] confirmed these observations by showing that the age effect remained even after controlling for DA exposure. However this association may also reflect differences in prescribing patterns, since younger patients are more likely to be prescribed a dopamine agonist [8,24,29]. Finally it has been argued that although younger patients may be inherently more susceptible ICDs, they may also be better able to act on their impulses than older patients [29].

4.2. Clinical phenomenology

Apart from touching on the use of pornography, the prevalence studies included in the present review did not formally discuss the clinical phenomenology of hypersexuality in PD, which has been mainly reported in single case reports or case series [18,21,34-36]. Reported hypersexual behaviours encompass excessive masturbation, compulsive pornography use, extramarital affairs, and plain increased libido. A recently published systematic literature review with focus on the clinical manifestations of paraphilias or paraphilic disorders in PD identified 22 case reports on a total of 31 patients [37]. These reports mainly described middle-aged male patients with motor complications, young age at PD onset, and long disease duration, reporting a range of altered sexual behaviours concomitant to either initiation or dose escalation of different forms of DRT (the majority being DAs). Exhibitionism was the most commonly described paraphilia, followed by transvestism, zoophilia, voyeurism, and pedophilia. Of note, both hypersexual behaviours and paraphilias were commonly reported in association with other ICDs, including pathological gambling, delusional jealousy, hyperphagia and other repetitive behaviours, such as compulsively sweeping or playing video games.

4.3. Role of dopaminergic stimulation

The causative role of dopaminergic medications was established by the concordant findings of the reviewed studies: Voon et al. [7] clearly showed that all behaviours had onset after medication onset and none of the patients had excessive medication use, and Weintraub et al. [24] found that all patients were taking DAs (Pramipexole, Ropinirole, or Pergolide) while symptomatic. Interestingly, almost one-third (30.0%) of patients had developed pathological behaviours at target doses of drugs.

The findings of the reviewed studies demonstrated a strong class association [24,38-40], but no statistically significant correlation with individual DA type or dose. Weintraub et al. [24] found that daily doses of DAs were higher for those screening positive for ICDs when concerning Pergolide, but not Pramipexole or Ropinirole. Weintraub et al. [8] also reported an independent, dose-dependent association of Levodopa therapy and active ICDs. The Levodopa monotherapy effect had previously been suggested by other authors [18] and was supported by the results of the study by Voon et al. [7], although its significance was questioned because of the limited sample size.

Of note, the only study [26] which reported no difference between agonist and nonagonist treatment groups in ICD risk was conducted after the role of DAs in compulsive behaviours had become apparent to the scientific community, and the clinical practice might have changed regarding the optimal treatment of patients with early PD. Indeed, a number of patients might not have been given DAs because they had been considered at risk for developing ICDs and the daily doses of DAs in this sample were small compared to the doses used by other studies.

Patients with ICDs often report being psychologically driven to engage in rewarding behaviours [29]. There is evidence of a distinct mechanism of action, as opposed to an additive effect, for DAs in the development of ICDs. A possible neurophysiological explanation revolves around dopamine-receptor binding profiles [8]. Dopamine 1 (D1) and D2 receptors, which are abundant in the dorsal striatum [41], are thought to mediate the motor effects of dopamine replacement therapies. In contrast, D3 receptors are abundant in the ventral striatum [41], a region associated with both behavioural addictions [42] and substance abuse disorders [43]. Second generation non-ergot DAs, such as Pramipexole and Ropinirole, demonstrate higher selective affinity for D3 receptors [44] compared to D1 and D2 receptors [44]. The less robust association between ICDs and Levodopa could reflect the fact that its physiologically active metabolite dopamine shows greater selectivity to D1 and D2 receptors [44]. Overall, behavioural changes in patients with PD appear to be associated with abnormal dopamine stimulation caused by a combination of disease progression, dopaminergic medications and environmental and genetic factors [1]. There is high inter-individual variability in the predisposition to develop impulsive behaviours, with genetic burden, character traits and pre-morbid mental state all playing a part [35,45].

The pharmacological approach for patients experiencing ICDs in the context of hyperdopaminergic treatment is simply dose reduction, discontinuing or switching the DA [9]. Hassan et al. [29] found that following cessation or dose reduction of the DA, almost all patients had complete or partial resolution of their compulsive behaviours at follow-up. Weintraub et al. [24] found similar results, with 7/18 patients becoming completely asymptomatic with the recommended changes in pharmacotherapy, further suggesting that impulsive behaviours are time-locked to dopamine agonist use. It is important to reach an agreement with the patient and his/her family about the optimal compromise between motor benefits and non-motor adverse effects resulting from DA pharmacotherapy. Thus, sound clinical judgement is crucial and close monitoring is required, particularly when initiating and titrating medication [9].

4.4. Ascertainment of sexual behaviours

In consideration of the lack of a standardised set of diagnostic criteria for hypersexuality, clinical researchers have used a pragmatic approach based on the use of questionnaires encompassing a range of hypersexual behaviours. One of the main problems with the commonly used questionnaire approach is under-ascertainment of prevalence. This approach may fail to capture patients who are reluctant to disclose sensitive behaviours of sexual nature due to associated stigma, shame and embarrassment, as well as possible legal implications. Not surprisingly, it has been found that behaviours are often reported by the patient's partner, after initial denial by the patient [29]. Indeed spousal assistance may be deemed crucial in providing a collateral history, although this in itself may introduce a bias in terms of accuracies and insight. Patients with PD and cognitive problems are at particularly high risk of returning either inaccurately or inadequately completed questionnaires. Moreover, questionnaires alone do not allow for a reliable differential diagnosis between behaviours which are clearly excessive and pathological and behaviours which could represent benign variants of accepted sexuality. The importance of a thorough clinical assessment cannot be underestimated. Studies conducted by mail and telephone interview [24, 29] may not pick up or assess conditions such as depression, anxiety and diminished cognitive function that are likely to confound the results of self-reports [29]. The accuracy of screening instruments for the detection of neuropsychiatric disorders in patients with PD was recently reviewed [46] and the Parkinson's Disease-Sexual Addiction Screening Test (PD-SAST) [47] was found to be a valid instrument for hypersexuality specifically. The PD-SAST is a short (5-item) and reliable measure of hypersexuality that was developed and validated in 2013 to be used in everyday practice in patients with PD as a screening instrument for multidimensional aspects of hypersexuality [47].

A common problem with the studies on hypersexuality in PD is loss to follow up: for example, in the study by Voon et al. [7], 4 patients with hypersexuality could not be reached, 14 patients misinterpreted the questionnaire and 2 patients with likely hypersexuality refused assessment. Similarly, Fan et al. [28] found that 12 patients screening positive for ICDs refused a telephone interview. Another factor making hypersexuality difficult to diagnose is the inter-individual variability which characterises the sex life. Changes from baseline sexual behaviours may not be regarded as abnormal even in the presence of a clear deviation from the patient's habitual behaviour. Likewise, patients with excessive sexual thoughts who deny distress or interference with their daily life may be diagnosed as 'subclinical' and therefore not captured in epidemiological studies. In general, prevalence rates may have been influenced by differences in culture and ethnicity, social and environmental factors and medication practices (both dosage and types of drugs used) across different centres. For example, the relatively lower frequency of ICD behaviours in China may reflect less widespread use of Levodopa and DAs (45.8% in the Chinese population *versus* 50.4-68.0% in Western Countries) [24,28,48,49].

4.5. Limitations

There are several limitations to consider when appraising the results of our review. Despite the efforts made, coverage of relevant literature could be incomplete. Extensive hand-searching of further scientific journals and translations of foreign material may have yielded additional studies. Moreover, our search strategy did not capture unpublished material, resulting in publication bias.

Finally, there was heterogeneity in the methodology of the reviewed epidemiological studies, with some studies assessing point prevalence and others focusing on lifetime prevalence: the cumulative lifetime prevalence of hypersexuality in PD is likely to be higher than point prevalence estimates. The overall quality of the studies varied depending on both assessment methods and setting/target population. It is important to note that patients were recruited from specialist centres located in selected regions, thus limiting the generalisability of any findings: movement disorder referral centres are likely to have higher rate of DA use as compared to general neurology clinics or district hospitals. The fact that the total number of hypersexuality cases identified across the reviewed studies was relatively small further limited any conclusions about the exact nature of the association between DA treatment and ICDs in PD.

Although prospective studies are considered most ideal to study any causative role of DRT, they may not be feasible due to fact that PD patients frequently undergo changes in medication over time and that there may be a significant lag time between initiation of DRT and onset of ICD behaviours [8]. Ideally, multicentre studies involving larger random samples of patients, with established diagnostic and inclusion criteria are needed to definitively determine the prevalence and clinical correlates of ICDs in PD.

4.6. Conclusions

The results of this literature review show that hypersexuality is not rare in patients with PD treated with DRT, particularly in those taking DAs. It has been shown that hypersexual behaviours and ICDs in general are an under-reported phenomenon in the PD population: for example, in the study by Weintraub et al. [24], the problem was only documented in 27.3% of patients with an active ICDs. These findings indicate that PD specialists should regularly screen and monitor for hypersexuality, paying particular attention to younger male patients, with an early PD onset and previous history of behavioural problems. Those patients shown to have an increased risk should be screened and it is paramount that they are educated on the risk of developing such pathological behaviours as potential side effects of their medication. Since patients are unlikely to volunteer their symptoms [50], it is important for the physician to recognise the early manifestations of hypersexuality, in order to diagnose and manage the patients accordingly before harm is brought upon relationships and the law [51]. This will help prevent the significant psychosocial implications hypersexuality carries for patients with PD and their families. There is a need for further investigations into hypersexuality and other ICDs as adverse behavioural effects of deep brain stimulation in patients with PD who underwent this increasingly common procedure [52]. Finally, as DAs are increasingly being used for other indications (restless legs syndrome and other neuropsychiatric conditions), it is important for future research to assess the prevalence and risk of hypersexuality in other clinical populations treated with dopaminergic agents.

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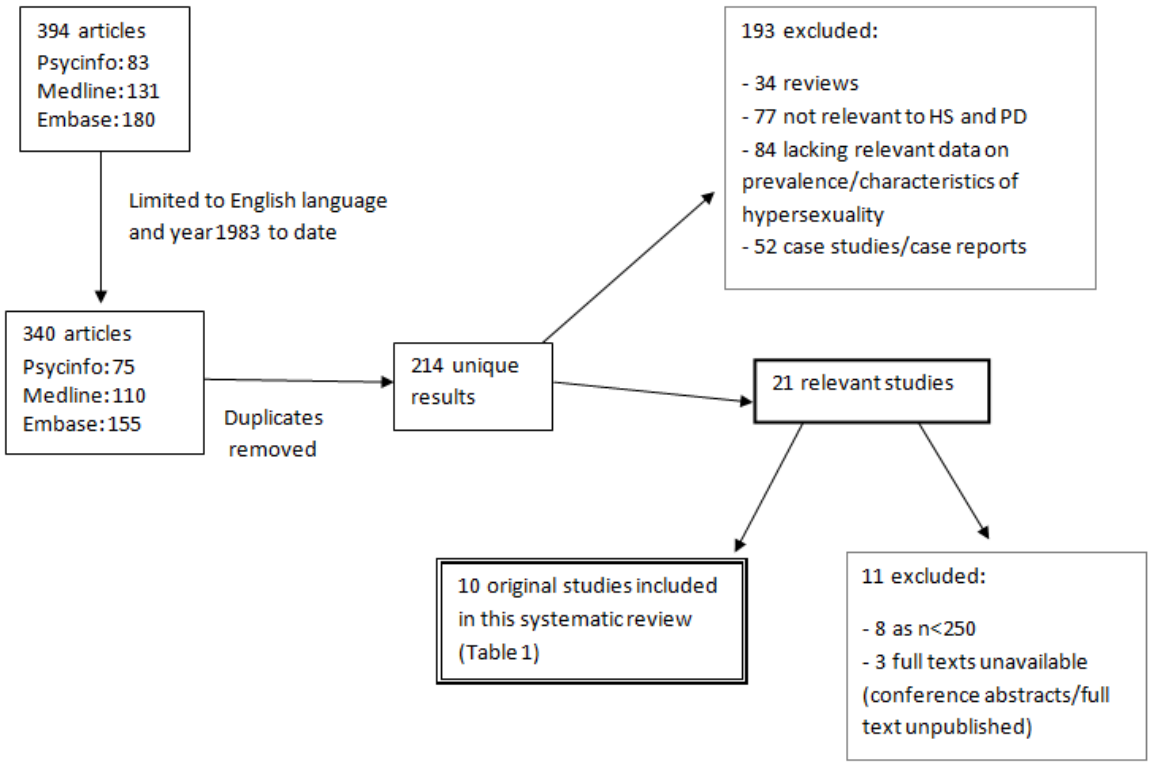
Table 1. Studies on the prevalence of hypersexuality in Parkinson's disease (PD).

Figure 1. Selection process for the studies on hypersexuality In Parkinson's disease included in this systematic literature review.

Table 1: Studies on the prevalence of hypersexuality in Parkinson's disease (PD).

Study	Voon et al. (7)	Weintraub et al. (24)	Fan et al. (28)	Weintraub et al. (8)	Hassan et al. (29)	Chiang et al. (30)	Joutsa et al. (26)	Poletti et al. (31)	Rodríguez-Violante et al. (32)	Callesen et al. (27)
Year	2006	2006	2009	2010	2011	2011	2012	2013	2014	2014
Setting	Outpatient clinic, movement disorders centre, Canada	Two university-based movement disorder centres, Philadelphia, USA	Centre of neurodegenerative disorders, Xuanwu Hospital, China	46 movement disorder centres in the United States and Canada	Mayo clinic, USA	Outpatient clinic, Taiwan	Postal survey of members of the Finnish Parkinson Association, Finalnd	Movement disorders outpatient clinic, Viareggio, Italy	Movement Disorders Clinic at the Neurology and Neurosurgery National Institute in Mexico City, Mexico	Postal survey of outpatients identified through the Danish National Patient Registry, Denmark
Study population	293 of 396 (75.0%) consecutive patients with PD	272 patients with PD. Active prevalence of ICDs 4.0%; lifetime prevalence of ICDs 6.6%	312 of 400 (78.0%) patients with PD on medication. Lifetime prevalence of ICDs 3.5%	3090 patients with PD. Active prevalence of ICDs 13.6%	321 patients with PD on dopamine agonists. Lifetime prevalence of compulsive behaviours 22% (of whom 16% defined as 'pathologic')	268 of 278 (96.4%) consecutive patients with PD. Lifetime prevalence of ICDs 5.6%	575 of 1000 (57.5%) patients with PD (stratified random sample from the patient register). Lifetime prevalence of ICDs 34.8%	805 consecutive patients with PD. Lifetime prevalence of ICDs 8.1%	300 consecutive patients with PD. Lifetime prevalence of ICDs 10.6%	490 patients with PD. Active prevalence of ICDs 14.9%; lifetime prevalence of ICDs 35.9%
Type of study	Case-control	Cross-sectional	Case-control	Cross-sectional	Cross-sectional	Cross-sectional	Cross-sectional	Cross-sectional	Case-control	Cross-sectional
Study duration (months)	3	11	-	6	24	3	9	17	-	-
Relevant inclusion/exclusion criteria	Excluded patients with atypical parkinsonism, cognitive impairment, and ≤1 year motor symptom onset	Excluded patients with secondary parkinsonism and cognitive impairment	Excluded patients with atypical parkinsonism, secondary parkinsonism, and cognitive impairment	Included patients on medication for ≤1 year with a demonstrated response (DA treatment not initiated or terminated in prior 6 months).	Included patients with idiopathic PD on Ropinirole/Pramipexole for ≥3 months and seen at least once by specialist in clinic during the study period	Excluded patients with cognitive impairment	Excluded patients reporting other primary diagnoses and patients without appropriate medication data	Excluded patients with newly diagnosed drug-naïve Parkinson's disease and patients with secondary or atypical Parkinsonism	Included only patients belonging to level 1 and 2 (average household income of 500 USD/monthly or lower and no social security)	Excluded patients with a diagnosis of dementia or other neurological or neurodegenerative disease (including atypical PD and Parkinson plus), patients with previous history of strokes or brain tumors, and patients with personality disorders
Assessment	Questionnaire, psychiatric assessment	Minnesota Impulsive Disorders Interview (MIDI)	Questionnaire, telephone interview. Voon's criteria for hypersexuality	Minnesota Impulsive Disorders Interview (MIDI)	Assessment based on DSM-IV criteria	Questionnaire, psychiatric assessment. Voon's criteria for hypersexuality	Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP)	Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP) followed by semistructured diagnostic interview	Structured interview (Minnesota Impulsive Disorders Interview (MIDI), assessment based on DSM-IV criteria), neurological evaluation, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP)	Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP)
Active prevalence	2.0%	2.6%	-	3.5%	-	-	-	-	-	-
Lifetime prevalence	2.4%	2.6%	1.9%	-	-	3.0%	22.8%	3.0%	3.0%	9.0%
Lifetime prevalence on DAs	7.2%	-	-	-	7.5%	-	-	-	-	-
Main strengths	Systematic screening using set criteria,	Use of multivariate model to determine predictors of active	High response rate, controlled study	Systematic screening, large sample size, blinding	Large recruitment window, multi-level assessment of compulsive	Limited referral bias	Large sample size, not limited to specialist clinics	Two-stage assessment, large sample size from	Multi-stage assessment	Large sample size, not limited to specialist clinics

	controlled study	ICDs		of raters	behaviours			single centre		
Main limitations	Referral bias	Referral bias, lack of structured diagnostic interviews, long interval between screening and follow-up	Potential heterogeneity across research sites	Referral bias, lack of structured diagnostic interviews	Referral bias, small assessment window	Loose inclusion/exclusion criteria	Sample derived, from PD association (support group) rather than general community, no physician verification of PD diagnosis, self-report tool which also identifies subclinical syndromes	Referral bias, underdetection of impulse control disorders in cognitively preserved patients	Cross-sectional design, population with a low socio-economic level from a single tertiary medical centre	Sample derived, from PD registry rather than general community, no physician verification of PD diagnosis, self-report tool which also identifies subclinical syndromes



The prevalence and clinical characteristics of hypersexuality in patients with Parkinson's disease following dopaminergic therapy: A systematic literature review

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Highlights

- Patients with Parkinson's disease (PD) on pharmacotherapy can develop hypersexuality

- Hypersexuality has social and legal repercussions for the patients and their families

- We conducted a systematic literature review on the prevalence of hypersexuality in PD

- Data from 8 large studies (n=268-3,090) yielded a lifetime prevalence figure of 2.7%

- Hypersexuality was associated with male gender and higher doses of dopamine agonists