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Review article

# 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 = 268-3090). 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.

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## 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

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their families [12].

Compulsive sexual behaviour, including both pathological and conventional forms of sexual behaviour, has an estimated prevalence of 3.0%–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 Fig. 1.

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.

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 3090 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].

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