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Paraphilias and paraphilic disorders in Parkinson's disease: a systematic review of the literature

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Abstract

Paraphilias are intense urges or behaviors involving non-normative sexual interests. The newly approved diagnostic criteria in the DSM-5 have established that, while paraphilias should not be regarded as inherently pathological, they ought to be qualified as paraphilic disorders if resulting in distress, impairment or harm to the affected individual or others. Recent evidence documents that both phenomena can emerge as relatively uncommon iatrogenic consequences in Parkinson's disease (PD) patients. To outline the clinical characteristics of paraphilias and paraphilic disorders in PD patients, we summarized the available evidence on these phenomena. The review encompasses all studies on paraphilias in PD patients identified by a search on the Pubmed and Scopus online databases through May 2014. Twenty-two case reports on a total of 31 PD patients with paraphilias and/or paraphilic disorders were identified. These phenomena were typically associated with dopaminomimetic treatment (with a mean levodopa-equivalent daily dose of 1303±823 mg/day) in male patients with motor complications, young age at PD onset and long disease duration. Paraphilias were highly concomitant with impulse-control disorders and/or dopamine dysregulation syndrome. Although evidence on paraphilias and paraphilic disorders in PD patients remains anecdotal, available data point to these phenomena as likely sequelae of high-dose dopaminomimetic treatment. Accordingly, the intensity of paraphilic urges is typically attenuated by the reduction of dopaminomimetic doses, sometimes in association with atypical antipsychotics. Failure to recognize paraphilic disorders may significantly impair the relational

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functioning of the affected PD patients. Practitioners should routinely inquire about paraphilias during their clinical assessment of PD patients.

Keywords

Parkinson's disease; Paraphilias; Paraphilic disorders; Impulse control disorders; Dopamine dysregulation syndrome

Introduction

Converging lines of evidence have shown that, in a subset of Parkinson's disease (PD) patients, administration of dopaminomimetic agents induces a broad range of abnormal sexual manifestations[1], including hypersexuality[2,3] and paraphilias.

While a final consensus is yet to be reached on the definition of hypersexual behaviors (described in the ICD-10 as satyriasis in men and nymphomania in women), these manifestations are generally intended as characterized by maladaptive preoccupation with (or indulgence in) erotic acts and sexual thoughts. Paraphilias are also described as recurrent urges, fantasies or behaviors, resulting in intense sexual arousal; in contrast with hypersexuality, however, these responses are typically evoked by non-normative (and sometimes illicit) sexual stimuli. Given the flexibility of sexual norms across time and different cultural milieux, the exact definition of paraphilias and their classification as pathological conditions remains a highly contentious issue. In response to these concerns, the fifth edition of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-5)[4] has recently provided a final definition of paraphilias as “any intense and persistent sexual interest other than a sexual interest in general stimulation or preparatory fondling with phenotypically normal, physically mature, consenting human partners”. The classification of paraphilias as atypical, yet not inherently pathological behaviors, contrasts with that of *paraphilic disorders*, in which the presence of deviant, maladaptive erotic urges results in a significant threat to the psychological and physical well-being of the affected individual or others. Specifically, the current diagnosis of paraphilic disorders requires that: 1) the patient experiences personal distress over persistent (at least 6 months) and troubling sexual fantasies, urges or behaviors (and not simply distress from society's disapproval), and that 2) such behaviors entail distress, injury or death of another individuals, or involve unwilling persons or persons unable to give legal consent.[4]

While neurologists have become increasingly aware of the highly negative impact of sexual dysfunctions and paraphilic disorders in PD patients, the lack of systematic diagnostic descriptions of these conditions limits the ability to prevent or attenuate their impact. Thus, the present study was aimed at conducting a review of the available peer-reviewed publications on case reports, and highlighting the current evidence on PD-associated paraphilias, including their clinical phenomenology, concurrence with other drug-induced complications, as well as therapeutic prospects.

Literature search strategy

We conducted a detailed Internet-based literature search on all available articles on paraphilic behaviors and disorders in PD through May 2014, using PubMed and Scopus databases. Paraphilia and paraphilic disorders were defined in line with the DSM-5 criteria[4]. The DSM-5 lists eight specific types of paraphilic disorders, namely exhibitionistic disorder; fetishistic disorder; frotteuristic disorder; pedophilic disorder; sexual masochism disorder; sexual sadism disorder; transvestic disorder; and voyeuristic disorder. A ninth residual category, described as other specified paraphilic disorders, includes telephone-scatologic disorder, necrophilic disorder, zoophilic disorder, coprophilic disorder, klismaphilic disorder urophilic disorder, etc. Given that the definitions of the DSM5 do not correspond with the legal definition of sex offending, the literature research was also extended to other cases of PD associated with illegal behaviors such as rape, sex offence, sex abuse, sexual crimes etc.

For each patient, the following criteria were recorded: gender; age at onset of paraphilias; age at onset of PD; disease duration; dopaminomimetic drugs used; total levodopa equivalent daily dose (LEDD); the number and type of paraphilias; presence or absence of other hypersexual behaviors, sex offences and psychiatric comorbid entities, including dopamine dysregulation syndrome (DDS) and impulse control disorders (ICDs).

LEDDs were either based on the values reported in the articles, or calculated as previously described[5], with the following formula: Levodopa dose + levodopa dose×1/3 if on entacapone + bromocriptine (mg)×10 + cabergoline or pramipexole (mg) × 67 + ropinirole or rotigotine (mg) × 20 + pergolide (mg) × 100 + apomorphine (mg) × 8.

Characteristics of Paraphilias in PD

Twenty-two case reports on a total of 31 PD patients affected by paraphilias and/or paraphilic disorders were identified[3, 6-26]. The individual characteristics of each patient are reported in Table 1. Patients were all males, with the exception of two females. Paraphilias included exhibitionism, frotteurism, pedophilia, sexual masochism, transvestism and voyeurism, as well as other specified paraphilias such as telephone scatology, zoophilia, klismaphilia, etc. None of the studies measured and/or estimated the prevalence of paraphilia and/or paraphilic disorders in PD. Exhibitionism was the most commonly described paraphilia (10 cases), followed by tranvestism (6 cases), zoophilia (5 cases), voyeurism and pedophilia (4 cases each). In five patients, multiple paraphilias were reported. Mean age at onset of paraphilias was 57.5 ±12.6 years, mean age at PD onset was 45.5±12.2 years, while mean duration of PD at onset of paraphilic behaviors was 12.2 ± 8.5 years, ranging from 3 to 37 years. Eighteen patients were classified as early-onset PD patients with disease onset at or before age 45.

In all patients, paraphilias were developed following treatment with dopaminomimetic agents; moreover, three of them were also under concomitant treatment with Deep Brain Stimulation (DBS). Levodopa treatment was reported in at least 27 patients; dopamine agonists were used by 22 patients, including pergolide (8), pramipexole (6), ropinirole (4), bromocriptine (3) and lisuride (1). Six patients were treated with the monoamine oxidase (MAO) B inhibitor selegiline. Five of these patients were on levodopa monotherapy

(although two of them were under concomitant DBS), while only a single patient was assuming a dopamine agonist in monotherapy. Mean LEDD was 1303±823 mg/day, with at least nine patients taking more than 1500 mg daily.

Two patients underwent a previous pallidotomy and other two patients underwent a previous unilateral thalamotomy several years before developing paraphilic behaviors and/or disorders. A search for comorbidity issues revealed that, although not every article reported the presence of motor complications, a large proportion of the patients (Table 1) was also affected by motor fluctuations and dyskinesias. In eight patients, paraphilic behavior was accompanied by at least another ICD or punding. Nine patients were affected by dopamine dysregulation syndrome. Clinical history of presence of previous premorbid paraphilic symptoms was reported in 3 patients.

Pharmacological management of paraphilic disorders in PD patients was mainly based on the reduction in the dose of dopaminergic medications (23 patients). The employment of atypical neuroleptic drugs, often in association with dopaminergic treatment reduction, was reportedly useful in 13 patients, with satisfactory control of the disorder in a large proportion of patients. However, at least eight cases were brought to court with penal consequences. Cognitive or learning deficits were reported only in three patients (7, 11 and 30).

Discussion

To date, this is the most detailed review of the clinical features and correlates of paraphilias in PD. The results of our systematic review indicate that aberrant sexual behaviors in PD may include paraphilic behaviors and/or disorders such as exhibitionism, frotteurism, pedophilia, sexual masochism, transvestism and voyeurism, as well as other specified types of paraphilias such as telephone scatology, zoophilia, klismaphilia, etc. Given that the nosological distinction between paraphilias and paraphilic disorders was formally introduced only in 2013, it is sometimes difficult to retrospectively discern and define the pathological nature of the manifestations reported in the relevant literature. Nevertheless, most case reports underscored the egodystonic nature of paraphilias in PD, and described how these phenomena resulted in distress as well as social and functional impairments, thereby meeting the main diagnostic criteria for paraphilic disorders.

The under-reporting of paraphilias in PD patients limits potential comparisons with non-normative sexual behaviors in the general population[27-30]. Nevertheless, our results indicate that iatrogenic and idiopathic paraphilias may share a number of critical features. First, three of the paraphilias most commonly described in PD patients (exhibitionism, transvestism and voyeurism) overlap with the most frequent sexual deviances in the general population. Second, in both conditions, paraphilic behaviors are highly concurrent with mental disorders[31-34]. Third, these phenomena are predominantly observed in male individuals, although some female cases have also been reported[35-36].

Similarly to previous data on PD-associated hypersexuality[37], paraphilic behaviors and disorders are more likely encountered in patients with younger-onset PD. The average age of PD onset is reportedly lower in patients affected by paraphilias (45.5 ± 12.2 years) than in

those with hypersexuality[38] (50.2 ± 3.0 yrs). The low age of onset for paraphilic disorders may reflect the influence of different neurobiological or genetic conditions. It should be noted, however, that the inception of paraphilias was typically observed after an average of 10 years from PD onset, in a stage in which PD motor complications become typical and may require higher doses of dopaminomimetic therapies. All PD patients who developed paraphilias were treated with levodopa (in monotherapy for 15% of the reported cases) or, less frequently, with dopamine receptor agonists (in monotherapy for 5% of the reported cases). Interestingly, also three patients under concomitant DBS developed paraphilic disorders. Thus, unlike ICDs, the development of aberrant sexual behaviors in PD does not appear to be tightly associated with the use of direct dopamine receptor agonists[39-40].

In particular, the high comorbidity rate between DDS and paraphilic disorders suggests that the latter may be triggered by states of excessive activation of dopamine receptors consequent to very high doses of dopamine-replacement therapies (DRTs). This possibility is supported by the observation that most paraphilic behaviors reportedly ceased following dose reduction of DRTs[3,7,8,11,12,14,15,17-19, 21,23-25]. Of note, Nielsen and colleagues showed that these conditions ceased after withdrawal of dopaminergic drugs and resumed soon after DRT reinstatement[12]. However, the use of lower doses of dopaminomimetics did not result in a relapse of paraphilias, suggesting a specific relation of these conditions with high doses of DRTs[12]. This perspective is suggested by the efficacy of dopamine receptor antagonists with intermediate potency (such as atypical antipsychotics) in the management of these disorders.

In all cases of paraphilic behaviors associated with dopamimetics, symptom severity and/or pervasiveness was attenuated reduced by tapering down the dosage of these drugs or using dopaminergic antagonists. However, this treatment typically resulted in the exacerbation of PD manifestations. Notably, the only two cases in which paraphilic behaviors developed after DBS alone were not responsive to any pharmacological intervention; however, both patients had a history of drug dependence and, more importantly, had developed addiction to levodopa (with features of DDS) before and after neurosurgery. This complicated clinical scenario may have contributed to the development of treatment-refractory paraphilic manifestations; thus, the specific etiological role of DBS vis-à-vis these phenomena remains unclear. It is worth noting that, in one of these patients, sexually deviant fantasies were present before surgery, but were acted upon only after DBS, suggesting that the full expression of the paraphilic behavior may have been facilitated by the improvement of motor symptoms.

Whereas paraphilic behaviors in PD have been only described in the past few years - following the recognition that these entities affected 3% of all PD patients[41]-, hypersexuality was one of the earliest neuropsychiatric complications described in PD, with the first report dating to 1969[42]. The most typical hypersexual behaviors induced by dopaminergic treatments in PD encompass excessive requests for sex from a spouse or a partner, increased interest in pornography, compulsive masturbation, etc. Similar sequelae have also been observed in patients receiving dopaminergic agonists for other conditions, such as restless leg syndrome and hyperprolactinemia due to pituitary dysfunction[43-46].

Although the relationship between dopamine signaling and the regulation of sexual behavior and urges is quite complex, hypersexuality and paraphilias may be the phenotypical expressions of different degrees of a common pathophysiological process. Accordingly, Voon et al.[38] have included paraphilic behaviors in the spectrum of pathological hypersexuality associated to PD treatment. Indeed, both hypersexuality and paraphilias have been associated with agonists for D2/D3 dopamine receptors, such as pramipexole, ropinirole and pergolide[10]. This background suggests that, in some predisposed individuals, paraphilias may arise as the epiphenomena of an underlying impulsivity disorder characterized by sexual compulsivity and hypersexuality[47], which may be compounded by dysfunctions of the frontal lobe[48,49]. Future neuropsychological and brain-imaging studies on PD patients affected by paraphilic disorders are warranted to understand the neurobiological bases and relationship of hypersexuality and paraphilias.

An important aspect of paraphilias concerns the mechanisms supporting the preference of non-normative targets for sexual arousal within the sphere of hypersexuality. It is well established that, among the general population, the enactment of erotic fantasies is generally limited, in view of cultural and moral constraints. Similarly, it is conceivable that a subgroup of PD patients may have sexual fantasies related to paraphilic preferences. In some of these patients, the shift from fantasy to behavioral manifestation may be due to high doses of dopamine-replacement therapies, likely in combination with concurrent biological predispositions. In addition to the existence of genetic vulnerability and premorbid personality traits, the individual susceptibility of a patient is largely influenced by ethno-cultural and moral convictions, and can be precipitated by specific environmental contingencies. For instance, one of our patients exhibited paraphilic behaviors following his wife's death, as he was reportedly unable to have regular sexual intercourse[18]. Future studies with large populations of PD patients will be required to examine these complex interactions among genetic, environmental and pharmacological variables with respect to the incidence of paraphilic disorders.

Neurobiological bases of paraphilic behaviors and disorders in PD

The available data on the pharmacological modifications of paraphilic behaviors and disorders in PD can provide critical elements of insights to elucidate the neurobiological bases of these manifestations; these mechanisms, however, remain largely speculative. In consideration of the key role of nucleus accumbens in reward, it is possible that the excessive dopaminergic stimulation in this brain region may reflect a dysregulated recruitment of dopaminergic signaling pathways in this region[50]. An abnormal stimulation of this region has also been described in patients with DDS and is in agreement with the “neural sensitization” theory, which posits that the intermittent administration of dopaminomimetic agents may lead to neuronal sensitization of the mesolimbic dopaminergic system[51-52]. The chronic stimulation of dopamine receptors by DRTs has been postulated to lead to receptor hypersensitivity as the basis for these behavioral side effects[15,50]. According to Robinson and Berridge's incentive sensitization theory, progressive and persistent neuroadaptations induced in dopamine projections to the accumbens-related circuitry are closely related to compulsive drug use[53,54]. More recently, a PET study in PD patients affected by a compulsive medication use, showed an increased

ventral striatal dopamine release in response to an acute levodopa challenge, thus suggesting a crucial neuronal sensitization of such chronic levodopa use in this particular class of vulnerable individuals[55].

It is conceivable that, similarly to DDS, overuse of dopaminergic agents could result in paraphilic behaviors by driving aberrant “novelty seeking” behaviors and excessive risk taking, or promoting disinhibition mechanism in control pathways[15]. Taken together, these data suggest that an excessive load of dopaminergic drugs could overtake the classical features of hypersexuality and lead to the expression of paraphilic disorders.

In addition to the accumbal involvement, other dopaminergic pathways may be involved in the genesis of paraphilic behaviors. For example, dopamine may increase sexual functions by reducing the secretion of prolactin, which exerts a major inhibitory function on sexual functions[19,56]. Furthermore, nigral dopaminergic projections are known to govern the activity of the medial preoptic area (MPOA) and paraventricular nucleus (PVN) of the hypothalamus, which are known to regulate libido and masculine sexual behavior[57-59]. Specifically, dopaminergic drugs may enhance sexual responses by increasing oxytocin release from the PVN[60].

In addition to dopamine, paraphilic disorders in the general population have been associated with changes in other neurochemical factors, including serotonin and androgens. Accordingly, the therapy of these conditions is often based on serotonin reuptake inhibitors, antiandrogens and GnRH analogues, among others[61].

Conclusions

Paraphilic disorders can lead to harmful conduct against themselves, their partners or others, sometimes resulting in criminal actions, such as in the case of pedophilia[61]. Indeed, a wealth of reports highlight the potentially devastating psychological, social, and/or legal, consequences of paraphilic disorders, including pedophilic, frotteuristic and exhibitionistic disorders in PD patients[6,7,18,20,21]. An interesting issue related to paraphilic disorders revolves around the question as to whether DRT-treated individuals should be considered responsible for harmful or criminal behaviors related to their erotic urges. Irrespective of these bioethical issues, the presence of premorbid signs for these disorders should be adequately investigated and monitored since early stages of PD. Once paraphilic disorders are suspected, dosage readjustments for antiparkinsonian drugs should always be considered. Future prospective and multicentric studies will hopefully provide improved diagnostic tools for the early detection of paraphilic behaviors in PD, as well as the identification of susceptibility factors and the quantification of the incidence and prevalence of these conditions.

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Table 1

Characteristics of PD patients described in literature with development of paraphilic disorders/behaviors

Patient #	Gender	Age at onset PD	Age at onset Paraphilia	PD duration	Hoehn and Yahr Stage	Paraphilic Disorder/Behaviors	Therapy, mg/daily	LEDD (mg/daily)	Motor fluctuations	Dyskinesias	Other hypersexual behavior	Other impulse control and repetitive behaviors	Other neuropsychiatric disorders	Previous aberrant sexual behavior	Treatment of paraphilic behaviors (if any)	Outcome	Sex offences/ Legal problem	References
1	M	35	51	16	NR	Sexual Masochism	L-dopa (no dosage) Bromocriptine 120-280 mg Unilateral thalatomy at the age of 40	>2800	NR	NR	YES	None	Compulsion to undress and exhibit in public	Masochistic fantasies	Neuroleptics Bromocriptine discontinuation	Resolution	NR	3
2	M	44	47	3	NR	Exhibitionistic Sexual masochism	L-dopa 4000 mg Selegiline 10 mg	4000	YES	YES	YES	DDS	None	Attraction to bondage since age 14	Pergolide discontinuation L-dopa reduction	Resolution	NR	3
3	M	46	57	11	NR	Pedophilic	L-dopa (no dosage) Bromocriptine overuse	NA	NR	NR	YES	DDS	None	NR	NR	NR	YES	6
4	M	25	45	20	NR	Exhibitionistic	L-dopa 800 mg Ropinirole 36 mg	1520	YES	YES	YES	None	None	NR	Olanzapine	NR	YES	6
5	M	44	49	5	2.5	Frotteuristic	Pergolide 3 mg	300	YES	NO	YES	None	Anxiety Irritability Depression Insomnia	NR	Pergolide reduction to 1.5 mg Quetiapine (100 mg/day)	Resolution	YES	7
6	M	42	52	10	3	Exhibitionistic	L-dopa 800 mg Pergolide 3,5 mg	1150	YES	YES	YES	None	None	NR	Clozapine Ropinirole reduction	Resolution	NR	8
7	M	59	65	6	3	Voyeuristic	L-dopa 400 mg Ropinirole 9 mg	580	YES	YES	YES	None	Cognitive impairment Depression	NR	Clozapine Pergolide reduction	Resolution	NR	8
8	M	60	81	21	NR	Zoophilic	L-dopa 400 mg Pergolide 1 mg	500	YES	NO	NR	Pathological gambling	Heavy alcohol abuse	NR	Clozapine 100 mg	Complete resolution	NR	9
9	M	54	64	10	2	Exhibitionistic	L-dopa 1875 mg Pergolide 1.5 mg Selegiline	2025	NO	NO	YES	Gambling	None	NR	DA Washout Olanzapine Lithium	Resolution	NR	10
10	M	52	60	8	NR	Transvestic	L-dopa 300 mg Ropinirole 21 mg	720	YES	NS	YES	None	None	NR	Ropinirole reduction to 12 mg	Complete resolution	NR	11
11	M	18	29	9	NR	Exhibitionistic Transvestic Telephone scatologia	L-dopa (no dosage)	NA	YES	YES	YES	Risk-seeking behaviors	Aggressivity Learning problems	NR	Cyproterone acetate 150 mg Citalopram 40 mg Quetiapine 100 mg L-dopa reduction	Resolution	NR	12
12	M	33	42	9	NR	Transvestic	L-dopa (no dosage) Lisuride 2 mg	NA	NO	NO	YES	Compulsive shopping; risk-seeking behavior	None	NR	L-dopa monotherapy	No recurrence	NR	13
13	M	38	58	20	NR	Zoophilic	L-dopa 1150 mg Pramipexole 8 mg	1686	YES	YES	YES	Gambling	None	NR	Quetiapine 50 mg Clonazepam 2 mg Pramipexole discontinuation	Marked improvement	NR	14
14	M	34	72	37	4	Transvestic	L-dopa 300 mg Selegiline 10 mg Right Thalamotomy	300	YES	YES	YES	None	Anxiety	NR	Selegiline suspension	Complete resolution	NR	15
15	M	26	29	3	1	Transvestic	Selegiline Ropinirole 12 mg Pramipexole 3 mg	201	NO	NO	YES	Gambling; punding	None	NR	Shift to DAs	Persistency of disorder	NR	16
16	M	45	51	6	2	Voyeristic	Selegiline Pramipexole 4.5 mg	301	NO	NO	YES	Punding	Anxiety Depression Mild OC symptoms	NR	Shift to ropinirole 12 mg	Urges improved significantly	NR	16
17	M	42	48	6	3	Transvestic	L-dopa 2000 mg Pergolide 3 mg	2300	YES	YES	YES	DDS	None	NR	Pergolide suspension L-dopa reduction	Resolution	NR	17
18	F	55	67	12	4	Klismaphilic	L-dopa 2000 mg	2000	YES	YES	NO	DDS	Depression Anxiety	NR	L-dopa reduction	Resolution	NR	17
19	M	58	62	6	3	Zoophilic Paedophilic	L-dopa 1000 mg Pergolide 7 mg	1700	YES	YES	YES	DDS	None	NR	Dopaminergic drugs reduction Clozapine 100 mg	Resolution	NR	18
20	M	37	64	27	NR	Exhibitionistic	L-dopa 1000 mg	1000	NR	NR	YES	DDS	None	NR	L-dopa reduction	Complete resolution	NR	19

Patient #	Gender	Age at onset PD	Age at onset Paraphilia	PD duration	Hoehn and Yahr Stage	Paraphilic Disorder/Behaviors	Therapy, mg/daily	LEDD (mg/daily)	Motor fluctuations	Dyskinesias	Other hypersexual behavior	Other impulse control and repetitive behaviors	Other neuropsychiatric disorders	Previous aberrant sexual behavior	Treatment of paraphilic behaviors (if any)	Outcome	Sex offences/ Legal problem	References
21	M	45	61	16	NR	Exhibitionistic	L-dopa (no dosage) Subthalamic nucleus DBS	NA	YES	YES	YES	DDS, gambling	Previous bipolar disorder and alcohol misuse	NR	Lithium and modifications of the stimulation parameters failed, Clozapine administration and supportive psycho-therapy were not effective	No resolution	NR	20
22	M	45	58	13	NR	Exhibitionistic	L-dopa (no dosage) Subthalamic nucleus DBS	NA	YES	YES	YES	DDS, Gambling	None	NR	NR	No resolution	YES	20
23	M	54	59	5	2	Pedophilic, Voyerirstic	L-dopa Entacapone Pramipexole	NR	NO	NO	YES	NO	Depression	NR	Discontinuation of the pramipexole	Resolution	YES	21
24	M	43	59	16	3	Pedophilic, Voyerirstic	Right pallidotomy L-Dopa Pramipexole	NR	YES	NO	YES	NO	None	NR	Dopaminergic drugs reduction	Gradual decrease	YES	21
25	F	NR	58	NR	NR	Exhibitionistic	Dopaminergic therapy (neither dosage or drugs cited) DBS	700	YES	YES	YES	Compulsive eating	None	NR	Clozapine (no dosage)	Controlled	NO	22
26	M	41	63	22	NR	Zoophilic	Pallidotomy (57ys) L-dopa 600 mg Entacapone 600 mg Selegiline 15 mg.	950	YES	NR	YES	NO	Depression, panic attack	NR	Selegiline removal, decreasing dosage of levodopa/bnserazide 300/75 mg	Resolution	NO	23
27	M	60	67	7	NR	Other Paraphilic behaviors	L-dopa 400 mg Pramipexole 4,5 mg.	700	YES	NR	YES	NO	None	Paraphilic fantasies	Discontinuation of pramipexole, addition of entacapone	Resolution	NO	24
28	M	54	74	20	NR	Zoophilic	L-dopa 750 mg Bromocriptine 15 mg.	900	YES	YES	YES	NO	None	NO	Reduction of levodopa/ carbidopa to 500/50 mg, reduction bromocriptine to 12.5 mg	Resolution	NO	25
29	M	NR	40	NR	NR	Exhibitionism	L-dopa 2125 mg Apomorphine 110 mg	3005	YES	YES	NR	DDS	Depression	NR	Tried continuous apomorphine infusion	NR	NO	26
30	M	75	79	4	3	Sexual sadism disorders	L-dopa 500 mg Pergolide 3 mg	800	YES	YES	YES	NO	NR	NR	Clozapine introduction, pergolide suspension	Resolution	YES	8
31	M	56	62	6	3	Sexual sadism disorders	L-dopa 800 mg Pergolide 3,5 mg	1150	YES	YES	YES	NO	NR	NR	Clozapine introduction, pergolide suspension	Resolution	YES	8

Legend: PD, Parkinson's disease; M, male; F, female; NR, not reported; NA; Not available; DDS; Dopamine dysregulation syndrome; OC, Obsessive Compulsive; >, shifted to; DA, dopamine agonists; DBS, Deep Brain Stimulation.