RESEARCH ARTICLE

Sexual Dysfunction in Women With Parkinson's Disease

Sara Varanda, MD,¹* Joana Ribeiro da Silva, MD,² Ana Sofia Costa,³ Cristiana Amorim de Carvalho, MD,⁴ José Nuno Alves, MD,¹ Margarida Rodrigues, MD,¹ and Gisela Carneiro, MD¹

¹Neurology Department, Hospital de Braga, Braga, Portugal ²Psychiatry Department, Centro Hospitalar de Tondela-Viseu, Viseu, Portugal ³Neurocognition Unit, Neurology Department, Hospital de Braga, Braga, Portugal ⁴USF Gualtar, AceS Cávado I, Braga, Portugal

ABSTRACT: Background: Sexual dysfunction in women with Parkinson's disease is poorly understood and research in this area is scarce. The objectives of this study were sexual function characterization in female Parkinson's disease patients, description of sexual dysfunctions, correlation with disease characteristics, and comparison with matched healthy controls.

Methods: Social and demographic data from consecutive female patients with Parkinson's disease and matched healthy controls were collected. The following instruments were used: UPDRS, the Hoehn and Yahr scale, the Beck Depression Inventory-II, the Female Sexual Function Index, and the Sexual Dysfunction Inventory. The only exclusion criterion was cognitive deterioration precluding comprehension of the study scope and its instruments.

Results: Of the 95 patients identified, 61 were included. Mean age was 66 years (range 40-89 years), and mean disease duration was seven years (range 1-18 years). Twenty-nine presented an akinetic-rigid syndrome, 25 tremoric disease, and, the remaining, a

mixed type of disease. Mean "on" total/part III UPDRS scores were 46 ± 15.0 and 31 ± 8.9 . Sexual dysfunction was present in 86.9% of patients and 79.0% of controls, according to the Female Sexual Function Index (p < .01), and in 57.4% of patients and 22.6% of controls, according to the Sexual Dysfunction Inventory (p < .001). Multivariate binary logistic regression identified age and depressive symptoms as positive predictors in the severity of sexual dysfunction. Disease duration, UPDRS part III score, Hoehn and Yahr stage, and antiparkinsonian medication did not show significant predictive value.

Conclusions: Sexual dysfunction is more prevalent in women with Parkinson's disease than in controls and is predicted by older age and severity of depressive symptoms. © 2016 International Parkinson and Movement Disorder Society

Key Words: Parkinson's disease; sexual dysfunction; women

Nonmotor symptoms are relevant contributors to disability and quality-of-life deterioration in Parkinson's disease (PD) patients.¹ However, they remain frequently underrecognized and inadequately treated.² Sexual complaints are usually included in the broader category of autonomic nonmotor symptoms, although their etiology is suspected to be multifactorial.^{3,4}

*Correspondence to: Sara Varanda, Neurology Department, Hospital de Braga, Sete Fontes, São Víctor, 4710-243 Braga, Portugal. E-mail: svaranda@gmail.com

Relevant conflicts of interest/financial disclosures: None.

Funding agencies: None.

Received: 14 January 2016; Revised: 15 June 2016; Accepted: 26 June 2016

Published online 00 Month 2016 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.26739

Apart from dysautonomia, it is believed that motor disability, fatigue, apathy, depression, anxiety, and antiparkinsonian medication play important roles in sexual dysfunction genesis.⁵⁻⁸ There is a lack of research at the pathological level, although it has recently been demonstrated that α -synuclein inclusions are present in axons in the anterolateral funiculus of the spinal cord of PD patients, with an increasing density from cervicothoracic to lumbosacral segments, which leads to the argument that this type of α synuclein axonopathy may also contribute to sexual dysfunction.⁹ Underrecognition of sexual dysfunction in PD patients is reinforced by the lack of appropriate assessment tools. The available instruments assessing nonmotor symptoms only devote two questions to sexual symptoms, rendering a very reductive perspective

of this issue.¹⁰ In clinical practice, management of PD patients tends to be focused on motor symptoms, whereas sexual function is an issue rarely raised, both by neurologists and patients.^{11,12} There may be an erroneous assumption that PD patients, being generally middle-aged or elderly, are not concerned about sexual dysfunction.⁵ Also, the subject of sexuality in older people remains a taboo in many cultures, particularly among women.¹³ There is, indeed, a decline in sexual activity with aging.¹⁴ However, despite this, among women who still have a partner and within the age classes of 65 to 74 and 75 to 85, there are about 40% and 17%, respectively, still sexually active.¹⁵ Both men and women who rate their health as poor are less likely to be sexually active and report sexual problems more frequently.^{14,15} Nevertheless, sexual issues are seldom discussed with physicians, and women are less likely than men to do so.¹⁴ Moreover, physician-patient communication concerning sexuality is generally poor. Reasons pointed out for this include the unwillingness of both patients and physicians to talk about the subject, sex and age differences between patients and their doctors, and social prejudices and stereotypes regarding women's and older people's sexuality.^{11,16}

In line with the scarcity of attention given to sexuality and sexual dysfunction in the general female population, the investigation of sexual dysfunction in PD patients is limited to a few published studies, which generally do not present a standardized methodology and tend to include both male and female patients, ignoring sex differences in sexual functioning.¹⁷⁻¹⁹ There is only one published article focusing specifically on women with PD, which included 27 patients, and concluded that female PD patients were more likely to be dissatisfied with their sexual life, when compared with age- and marital status-matched controls. In addition, they suffered more from a decrease in libido, vaginal tightness, and involuntary urination during intercourse.²⁰ Another study examined a group of 103 PD patients of both sexes, using separate questionnaire sets for each sex, concluding that depression and anxiety play important roles in sexual function of female PD patients.²¹ Because our knowledge of sexual dysfunction in women with PD is so scarce, the approved measures for its treatment are virtually nonexistent.²² The American Academy of Neurology published a guideline concerning nonmotor symptoms treatment, but the only recommendation for sexual dysfunction treatment is sildenafil for men with erectile dysfunction.²³

Objectives

The objectives of this study were to provide a better understanding of sexual function in female PD patients and to establish predictive factors for sexual dysfunction.

Methods

Study Design and Population

The local ethics committee approved the study. Written informed consent was obtained from all participants, and the principles outlined in the Declaration of Helsinki were followed. Female PD patients, diagnosed according to UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria,²⁴ were consecutively recruited from an outpatient movement disorders clinic by two physicians who were not involved in the management of their illness. Of 95 eligible patients, 12 were excluded because of cognitive deterioration precluding study comprehension, and 22 declined participation citing lack of time (n = 12), lack of interest (n = 9), or celibacy (n = 1). Assessments were conducted on the same day following routine neurological consultation. Motor evaluation was performed by the consulting neurologist, who was unaware of the patients' participation. After the consultation, the study's objectives were explained and consent was obtained by a neurologist and a psychiatrist, who gathered the remaining data to maintain confidentiality and anonymity. The control group was recruited from the waiting room of an orthopedics outpatient clinic (n = 62) and was matched to the subjects for social and demographic characteristics. They were either patients being followed for nondisabling hand or shoulder problems (n = 11) or were otherwise healthy women accompanying relatives in the waiting room (n = 51).

Measures

Social and demographic information was collected, including age, ethnic background, residency (rural or urban), educational level, religion, and marital status. Clinical variables, retrospectively obtained from clinical records, included age of onset, disease duration, disease subtype (akinetic-rigid, tremoric, or mixed), current antiparkinsonian medication, "on" total Unified Parkinson's Disease Rating Scale (UPDRS) score,²⁵ and Hoehn and Yahr (H&Y) stage.^{26,27} Comorbidities, other current medication and menopausal status were also obtained from patients and controls.

Instruments

Sexual function was characterized in patients and controls using two instruments: the Female Sexual Function Index (FSFI) and the Sexual Dysfunction Inventory (SDI). The FSFI is a brief multidimensional self-report questionnaire concerning female sexual function. It includes 19 questions, assessing six domains of female sexual function (desire, arousal, lubrication, orgasm, satisfaction, and pain) pertaining to the previous month. Each answer is given between 0/1 and 5. Scores of individual items that comprise a

domain are added, and the sum is multiplied by the domain factor. The sum of the six domain scores results in the full scale score, which ranges between 2 and 36, the latter meaning no sexual dysfunction, as increasing scores indicate better sexual function.²⁸ Although validated for the Portuguese population, no cutoff has yet been identified in this population.²⁹ Therefore, the original > 26.5 cutoff was used.³⁰ The female version of the SDI is a semistructured interview that specifically evaluates each of the sexual dysfunction dimensions included in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV).31 It also provides data regarding sexual orientation, current and past relationships, frequency of sexual behaviors (intercourse, outercourse, and masturbation), and past unwanted sexual experiences.³² This instrument facilitates the assignment of consistent and valid clinical diagnoses, based on criteria defined by the DSM-IV.³¹ As with the FSFI, this interview is translated into the Portuguese language.³³ Severity of depression was assessed, both in patients and controls, using the Beck Depression Inventory-II (BDI-II), which is a 21-question self-report questionnaire, comprising symptoms of depression (such as sadness), cognitions (such as guilt), and physical symptoms (such as fatigue). In this last category, a question is included (item 21) related to "loss of interest in sex." Every question has a set of at least four possible answers, ranging in intensity. Each is assigned a value from 0 to 3, and a total score is calculated through the sum of all individual values.^{34,35} For the Portuguese population, a score of 0 to 11 indicates minimal depression, 12 to 17 indicates mild depression, 18 to 23 indicates moderate depression, and 24 to 63 corresponds to severe depression.³⁶

Statistical Analysis

Distribution normality was assessed through the Kolmogorov-Smirnov test. Independent-sample *t*, Mann-Whitney, chi-square, or Fisher tests were used to determine group differences in demographic and clinical variables, depending on the comparison and test assumption. Multivariate binary logistic regression was used to calculate predictive factors of sexual dysfunction in PD patients. The dependent variable was defined as sexual dysfunction, as determined by a FSFI total score less than 26.5. As covariates, we included clinical and demographic variables, either flagged as significant in the univariate group analysis or considered biologically meaningful. All statistical analyses were performed using SPSS, version 20 (IBM), with the statistical threshold for significance set at 0.05.

Results

As shown in Table 1, mean age of the 61 female PD patients included was 66 years (range 40-89 years). The

TABLE 1. Demographic characteristics of PD patients and controls

Demographic	Patients $(n = 61)$	Controls (n = 62)	Group comparison p value
	(1 - 01)	(11 – 02)	p value
Age (years), mean \pm SD	66.4 ± 11	63.3 ± 11	.140
Habitation area, % rural	60.7	53.2	.405
Educational level, %			.100
Illiteracy	4.9	11.3	
1 to 4 years	75.4	61.3	
5 to 9 years	13.1	22.6	
10 to 12 years	1.7	1.6	
College degree	4.9	3.2	
Marital status, %			.712
Married	67.3	72.6	
Widow	18.0	16.2	
Divorced	6.6	3.2	
Single	4.9	1.6	
Domestic partnership	1.6	3.2	
Dating	1.6	3.2	

SD, standard deviation.

majority lived in rural areas (60.7%) and had an elementary education (75.4%). Most patients were married (67.3%). Mean age of the 62 controls was 63 years (range 35-84 years). The majority lived in rural areas (53.2%) and had an elementary education (61.3%). Most of them were married (72.6%). All subjects and controls were white, and the majority were Catholics.

Clinical characteristics are shown in Table 2. Mean age at PD onset was 59 years, and mean disease duration was seven years. Patients were evenly distributed among different types of disease. All but one, having undergone deep brain stimulation, were currently taking dopaminergic medication. Most patients were in H&Y stage two or three H&Y stage 2 or 3 (n = 53). Concerning comorbidities, 36 patients (59.0%) had a diagnosis of depression or were being treated at a psychiatric outpatient clinic because of depressive symptoms, whereas 28 (45.9%) were taking antidepressants, mostly selective serotonin reuptake inhibitors or serotonin and norepinephrine reuptake inhibitors. Seven controls (11.3%) had also been diagnosed with major depression and were taking antidepressants (p < .001). Patients' mean BDI-II score was 8.5 ± 7.2 (range 0-34). Sixteen patients (26.2%) presented a total score of at least 12, indicating the presence of mild to severe depressive symptoms. Regarding item 21 from the BDI-II, "loss of interest in sex," 27 patients (44.3%) answered they had not noticed any recent change in interest in sex, seven (11.5%) said they were less interested in sex than they used to be, five (8.2%)were much less interested in sex, and 22 (36.1%) had completely lost interest in sex. Therefore, 56% of our subjects reported less interest in sex on BDI-II. Control population mean BDI-II score was 6.2 ± 4.0 (range 0-20), and six controls (9.7%) scored 12 or

Clinical characteristics	Patients (n = 61)	Controls (n = 62)	Group comparison <i>p</i> value
Disease duration (years), mean + SD	7.3 ± 4.5	-	
PD clinical phenotype, %			
Akinetic-rigid-dominant	47.6	-	
Tremor-dominant	40.9	-	
Mixed	40.9	-	
Dopaminergic drugs, %	11.5	-	
	88.5	-	
Levodopa Dopamine agonists	00.0 57.4	-	
Monoamine oxidase inhibitors	57.4 21.3	-	
	21.3 11.0 ± 6.4	-	
UPDRS II score, mean ± SD		-	
On UPDRS III score, mean \pm SD	30.8 ± 9.0	-	
Median H&Y stage	2.0	-	. 001
Physical comorbidities, %	85.3	64.5	<.001
Depression	59.0	11.3	<.001
Cardio- or cerebrovascular disease	13.1	32.3	<.01
Gynecological	3.2	38.7	<.001
Neoplastic	9.8	4.8	.179
Degenerative osteoarticular	6.6	9.7	.447
Antidepressants, %	45.9	12.9	<.001
BDI-II total score, mean \pm SD	8.5 ± 7.2	6.2 ± 4.0	.155
Postmenopausal, %	91.8	88.7	.098

TABLE 2. Clinical characteristics of PD patients and controls

SD, standard deviation; PD, Parkinson's disease; UPDRS, Unified Parkinson's Disease Rating Scale; H&Y, Hoehn and Yahr; BDI-II, Beck Depression Inventory-II.

more, which indicated mild to moderate depressive symptoms. With respect to item 21, 47 controls (75.8%) claimed less interest in sex. Both severity of depressive symptoms and answers to item 21 did not significantly differ between patients and controls.

Table 3 shows overall sexual function of patients and controls. All patients defined themselves as exclusively heterosexual, and most had a current partner (70.5%). At the time the study was conducted, according to SDI, the majority of PD patients did not have regular intercourse with their partner (60.7%). Of these, two (5.4%) had outercourse (or nonpenetrative sexual activities), and none practiced masturbation. All controls were exclusively heterosexual. Most had a current partner (77.4%). The majority had regular intercourse with the partner (64.5%). Of those who did not, eight (36.4%) had outercourse, and none practiced masturbation. Hence, PD patients were less likely to be sexually active, either regarding intercourse (p = .007) or outercourse (p = .001).

Sexual dysfunction assessment tools revealed the following: 52 patients (86.9%) had total scores less than 26.5 on the FSFI, indicating the presence of sexual dysfunction; 35 patients (57.4%) met diagnostic criteria for at least one type of sexual dysfunction, according to the SDI; and 20 (32.8%) met diagnostic criteria for more than one. Furthermore, the SDI identified the following subtypes of sexual dysfunction in PD patients (not mutually exclusive): hypoactive sexual desire disorder in 16 (26.2%), sexual aversion disorder in three (4.9%), sexual arousal disorder in 17 (27.9%), orgasmic disorder in 16 (26.2%), dyspareunia in 11 (18.0%), and vaginismus in one (1.6%). In turn, controls scored significantly higher in total FSFI (p < .01) and in individual domains of arousal orgasm (p = .018),(p = .041),and satisfaction

TABLE 3. Sexual characterization of PD patients and controls

Sexual characteristics	Patients (n = 61)	Controls (n = 62)	Group compariso <i>p</i> value
Current relationship, yes %	70.5	77.4	.466
Monthly sexual activity with partner, %			.007
0	60.7	35.5	
1-5 times	23.0	37.1	
6-10 times	11.5	19.3	
More than 10 times	4.8	8.1	
Monthly outercourse activity with partner, %			.001
0	68.8	32.2	
1-5 times	6.6	21.0	
6-10 times	8.2	21.0	
More than 10 times	16.4	25.8	
FSFI, mean \pm SD	10.2 ± 10.3	14.7 ± 11.3	.006
Sexual dysfunction diagnosis on SDI, %	57.4	22.6	<.01
Sexual dysfunction subtypes, % of total			
Hypoactive sexual desire disorder	26.2	8.1	
Sexual aversion disorder	4.9	4.8	
Sexual arousal disorder	27.9	11.3	
Orgasmic disorder	26.2	9.7	
Dyspareunia	18.0	11.3	
Vaginismus	1.6	0	

SD, standard deviation; FSFI, Female Sexual Function Index; SDI, Sexual Dysfunction Inventory.

Demographic, clinical, and sexual characteristics	Without sexual dysfunction (n = 8)	With sexual dysfunction $(n = 53)$	Group comparisor <i>p</i> value
Age (years), mean \pm SD	58 ± 12	67 ± 10	.029
Disease duration (years), mean \pm SD	6.4 ± 3.8	8.1 ± 4.6	.304
PD clinical phenotype, %	0.4 = 0.0	0.1 = 4.0	.420
Akinetic-rigid-dominant	44.4	47.1	.120
Tremor-dominant	55.6	39.2	
Mixed	0	13.7	
Dopaminergic drugs, %	Ũ	10.1	.218
Levodopa	77.7	80.5	.210
Dopamine agonists	88.8	54.9	.099
Monoamine oxidase inhibitors	22.2	11.7	
UPDRS II score, mean \pm SD	7.2 ± 3.8	11.7 ± 6.5	.053
On UPDRS III score, mean \pm SD	28.8 ± 8.5	31.2 ± 9.1	.626
Median H&Y stage	2.0	2.0	.810
Physical comorbidities, %			.675
Depression	55.6	58.8	.712
Cardio- or cerebrovascular disease	25.0	11.3	
Gynecological	0	3.7	
Neoplastic	0	11.3	
Degenerative osteoarticular	12.5	5.6	
Antidepressants, %	22.2	49.0	.033
BDI-II total score, mean \pm SD	2.4 ± 3.2	9.6 ± 7.2	.001
Postmenopausal, %	11.5	80.3	.517
FSFI, mean \pm SD	31.3 ± 3.7	6.5 ± 5.6	<.001
Current relationship, yes %	100	66.0	.048
Monthly sexual activity with partner, %			.001
0	0	69.8	
1-5 times	50	18.9	
6-10 times	37.5	7.5	
More than 10 times	12.5	3.8	
Monthly outercourse activity with partner, %			.271
0	50	71.7	
1-5 times	0	7.6	
6-10 times	25	5.7	
More than 10 times	25	15.1	

TABLE 4. Group differences analysis of PD patients with and wit	thout sexual dysfunction
--	--------------------------

SD, standard deviation; PD, Parkinson's disease; UPDRS, Unified Parkinson's Disease Rating Scale; H&Y, Hoehn and Yahr; BDI-II, Beck Depression Inventory-II; FSFI, Female Sexual Function Index.

(p = .001). Individual scores in desire, lubrication, and pain domains were not different from those of the patients. Forty-nine controls (79.0%) had a total FSFI score less than 26.5, which was not significantly different from PD patients (p = .482). Fourteen met diagnostic criteria for at least one type of sexual dysfunction in SDI (22.6%), and eight received a diagnosis of more than one dysfunction (12.9%). Therefore, according to the SDI, sexual dysfunction was significantly more prevalent in PD patients than in controls (p < .01). We have not found any case of hypersexuality.

Group differences analysis of PD patients with and without sexual dysfunction (see Table 4) showed that patients with sexual dysfunction were significantly older, had higher UPDRS-II and BDI-II scores, and were more frequently taking antidepressants. Comparisons of patients with and without sexual dysfunction regarding other demographic (habitation area, educational level, marital status) and clinical variables did not show any significant differences. We next looked to what degree demographic and clinical variables predicted the presence of sexual dysfunction in women with PD, as defined by the FSFI. Multivariate binary regression results showed that older age (OR, 1.14; 95% CI, 1.02-1.27: p < .05) and higher frequency of depressive symptoms (OR, 1.54; 95% CI, 1.03-2.29; p < .05) significantly predicted sexual dysfunction (see Table 5).

Discussion

Our results show that sexual dysfunction is highly prevalent in female PD patients and more frequent than in controls. To our knowledge, this is the first study approaching sexuality in female PD patients with different but complementary instruments, specifically developed to assess sexual function in women. Because of the lack of validated instruments for sexual function assessment in female PD patients, most

Variables included in the model	Odds ratio	95% CI	p value
Sexual dysfunction — FSFI < 26.5			
Age (for each increment of 1 year)	1.14	1.02-1.27	.026
BDI-II total score (for each increment of 1 point)	1.54	1.03-2.29	.035
Antidepressants (none as reference group)	0.64	0.03-13.6	.777
UPDRS II score (for each increment of 1 point)	1.11	0.84-1.48	.458
On UPDRS III score (for each increment of 1 point)	0.88	0.75-1.03	.112
Disease duration (for each increment of 1 year)	1.04	0.78-1.39	.788

TABLE 5. Female Parkinson's disease patients with sexual dysfunction — multivariate analysis using binary logistic regression

CI, confidence interval; FSFI, Female Sexual Function Index; BDI-II, Beck Depression Inventory-II; UPDRS, Unified Parkinson's Disease Rating Scale.

published studies used divergent methodologies, rendering comparison of results very difficult. In addition to being a female-specific instrument, the FSFI is brief and easy to apply, and offers the possibility of selfassessment, facilitating patient compliance and bypassing potential constraints related to this topic. Our study is further strengthened by the use of the female version of the SDI, a more detailed instrument, which provides a complementary qualitative approach to female sexual function. We decided to use both tests to suppress their individual liabilities. Alternative assessment instruments, namely, those used in previous studies, focus on both male and female aspects of sexuality and/or are not validated for the Portuguese population.^{37,38}

As expected, the prevalence of sexual dysfunction found with each instrument was uneven, resulting in a difference of almost 30% in patients (87% with the FSFI, 57% with the SDI) and 60% in controls (79% with the FSFI, 23% with the SDI). Such discrepancy may be explained by the nature of each instrument. Given that with the SDI the identification of a sexual dysfunction rests on clinical criteria, the diagnosis is much stricter. To diagnose a particular dysfunction, according to the DSM-IV, the disturbance is required to cause marked distress or interpersonal difficulty.³¹ In fact, it has been demonstrated in previous studies concerning the general female population that only a small proportion of sexually dysfunctional women report distress resulting from this issue.³⁹ Accordingly, some of the women we studied, patients and controls, who scored less than 26.5 on the FSFI, experienced no marked distress and could not have been formally diagnosed with a sexual dysfunction via the SDI. Moreover, if a woman, for any reason, has not had intercourse in the previous month, questions 3 to 14 and 17 to 19, which relate to arousal, lubrication, orgasm, and pain domains, will all have a score of 0 (no sexual activity or did not attempt intercourse). Hence, she will have a maximum of 12 on total FSFI, scoring for sexual dysfunction,²⁸ although she may not verbalize any signs of sexual dysfunction in a semistructured interview approach such as the SDI. This may be the reason why, based on the FSFI cutoff, there were differences concerning current relationship status and monthly sexual activity between PD patients with and without sexual dysfunction (see Table 4).

The first published study evaluating female PD patients with a specific female sexuality questionnaire revealed a 36% prevalence of sexual dysfunction in 11 patients.⁵ Kummer and colleagues also approached this issue by analyzing answers to item 21 of the BDI, and they found loss of libido in 65.6% of the 90 PD patients included (of both sexes),¹⁸ which is comparable to our results. As in this study, we have demonstrated the predictive value of depression and older age in sexual dysfunction. In fact, age and depression have been identified as important predictors of sexual dysfunction in other previous studies.^{19-21,40}

According to the SDI results, despite most PD patients having a partner, a large proportion were not sexually active, unlike controls of the same age and with the same menopausal and marital status. Although Patients sexual dysfunction was found to be independent of PD-related clinical variables (except UPDRS II score), the fact that matched controls were significantly more sexually active and had less sexual dysfunction points to a possible causal role of disease in sexual dysfunction. Previous studies have suggested higher UPDRS score¹⁸ and H&Y stage⁴¹ as relevant predictors of sexual dysfunction. The relation of sexual dysfunction to PD clinical variables may not have been shown in our analysis of differences in disease groups, probably, because there are too many variables for a relatively small cohort. It is also possible that age and depression are much more significant than other variables, as they are known to affect the sexual function of women in general^{39,42-45} and with other chronic neurological diseases.⁴⁶⁻⁴⁸ For instance, female multiple sclerosis patients also seem to have a high prevalence of sexual dysfunction (32% in a recent study of 85 subjects, also using the FSFI).⁴⁸ As in our study and others in PD patients, in multiple sclerosis patients, no correlations have been found between sexual dysfunction and disease duration,

lesion burden, and disability, although a link between depression and sexual dysfunction in these patients has also been suggested.⁴⁹ In fact, a previous diagnosis of depression was meaningfully more frequent in female PD patients when compared with controls. However, the assessment of depressive symptoms through the BDI-II score did not significantly differ between groups. Furthermore, previous studies in depressed female patients revealed a lower prevalence of sexual dysfunctions compared with what we found in our cohort of PD patients - in 100,000 depressed women, 17.7% had hypoactive sexual desire disorder, 3.4% sexual aversion disorder, 5.8% sexual arousal disorder, and 7.7% orgasmic disorder.50 Almost half of our patients were taking antidepressants, which is also an important aspect, given that some of these drugs, especially serotoninergic ones, may cause sexual side effects, such as decreased libido, arousal difficulties, delayed orgasm, and anorgasmia.⁵¹ Still, only six patients had total BDI scores compatible with moderate to severe depressive symptoms (range 18-63), four of whom had a previous diagnosis of depression. We can argue that, although there was a high prevalence of depression and antidepressant medication in PD patients, their psychiatric disease was well managed, and, accordingly, most patients had a lower BDI score, in the mild depression range. Our study did not identify antidepressants as predictors of sexual dysfunction. However, when deciding to treat depression in PD patients, the potential of aggravating sexual dysfunction of several antidepressants must be taken into account.^{51,52} Whenever possible, nonpharmacological measures should be recommended to enable arousal, including sex counseling,⁴ scheduling regular sexual activity, and exercise.^{53,54} The addition of bupropion may also play a beneficial role when antidepressant therapy is needed.⁵⁵ A prospective followup of this patients subgroup and an intervention aimed at reviewing the effects of changing to drugs with less sexual side effects could give us more information concerning the complex relation among PD, antidepressants, and sexuality. Regarding other physical comorbidities, we found a higher prevalence of vascular and gynecological diseases in controls than in patients. Considering these are known contributors to sexual dysfunction,⁵⁶ we would expect a higher prevalence of sexual dysfunction in controls. This appears to reinforce the major influence of depression in sexual dysfunction among female PD patients.

We believe our findings are of significant clinical relevance because sexual dysfunction has an important impact on patients quality of life.⁵⁷

Limitations

Although our sample is larger than others previously studied, it may not be large enough to provide a complete identification of sexual dysfunction determinants in female PD patients.

We decided to exclude cognitively impaired patients, given the nature of the sexual dysfunction measures used. The inclusion of these patients would not guarantee reliable data, although it would possibly disclose different results.

Given that more than 50% of the total population only had an elementary education, it was necessary, in some, to apply the FSFI by direct interview. This may have induced some bias in the FSFI results.

There are other shortcomings related to the sexuality assessment instruments. As described above, the FSFI evaluates women with a current partner and with regular intercourse, only providing a superficial characterization of non-sexually active patients, who represent a substantial percentage of our sample. Not having had intercourse in the last month is sufficient to put the subject into the sexual dysfunction group. Another disadvantage of the FSFI is its exclusive reference to intercourse, ignoring other types of sexual activity (for example, oral or manual). Nevertheless, the SDI also entails certain disadvantages, being time consuming, on the one hand, and, given its openquestion format, possibly more prone to the emergence of constraints, on the other hand. Accordingly, we believe the FSFI is a good screening tool, whereas the SDI appears to be the best instrument to diagnose specific sexual dysfunctions. However, further studies using both the FSFI and the SDI in PD patients are needed, to allow us to fully confirm their validity in this population.

We did not find any case of hypersexuality in our sample, nor did we observe an increase in sexual fantasies accompanying disease progression, as was suggested in another study.⁵⁸ Nevertheless, the complaints related to hypersexuality are expressed by partners, not reported by patients.^{4,59} As we did not interview partners, we cannot assure the entire validity of results regarding this issue. Moreover, many patients may feel heightened sexual drive and do not experience hypersexual behaviors, which is part of the impulse control disorder,⁶⁰ and this may not have been assessed with the instruments used.

Conclusions

Sexual dysfunction is more common in women with PD than in the general population, being predicted by older age and depression. It appears independent of PD-related clinical variables. Clinicians should systematically and thoroughly assess nonmotor symptoms in PD patients, keeping in mind that, when assessing possible sexual dysfunction, older and depressed female patients may be particularly vulnerable.

References

- 1. Schrag A, Jahanshahi M, Quinn N. What contributes to quality of life in patients with Parkinson's disease? J Neurol Neurosurg Psychiatry 2000;69(3):308-312.
- 2. Gallagher DA, Lees AJ, Schrag A. What are the most important nonmotor symptoms in patients with Parkinson's disease and are we missing them? Mov Disord 2010;25(15):2493-2500.
- 3. Chaudhuri KR, Healy DG, Schapira AH; National Institute for Clinical Excellence. Non-motor symptoms of Parkinson's disease: diagnosis and management. Lancet Neurol 2006;5(3):235-245.
- 4. Bronner G, Aharon-Peretz J, Hassin-Baer S. Sexuality in patients with Parkinson's disease, Alzheimer's disease, and other dementias. Handb Clin Neurol 2015;130:297-323.
- Brown RG, Jahanshahi M, Quinn N, Marsden CD. Sexual function in patients with Parkinson's disease and their partners. J Neurol Neurosurg Psychiatry 1990;53(6):480-486.
- 6. den Brok MG, van Dalen JW, van Gool WA, Moll van Charante EP, de Bie RM, Richard E. Apathy in Parkinson's disease: A systematic review and meta-analysis. Mov Disord 2015;30(6):759-769.
- Rutten S, Ghielen I, Vriend C, et al. Anxiety in Parkinson's disease: Symptom dimensions and overlap with depression and autonomic failure. Parkinsonism Relat Disord 2015;21(3):189-193.
- Ozcan T, Benli E, Demir EY, Ozer F, Kaya Y, Haytan CE. The relation of sexual dysfunction to depression and anxiety in patients with Parkinson's disease. Acta Neuropsychiatr 2015;27(1):33-37.
- 9. Del Tredici K, Braak H. Spinal cord lesions in sporadic Parkinson's disease. Acta Neuropathol 2012;124(5):643-664.
- Chaudhuri KR, Martinez-Martin P, Schapira AH, et al. International multicenter pilot study of the first comprehensive selfcompleted nonmotor symptoms questionnaire for Parkinson's disease: the NMSQuest study. Mov Disord 2006;21(7):916-923.
- Gott M, Hinchliff S, Galena E. General practitioner attitudes to discussing sexual health issues with older people. Soc Sci Med 2004;58(11):2093-2103.
- 12. Bronner G. Practical strategies for the management of sexual problems in Parkinson's disease. Parkinsonism Relat Disord 2009; 15(Suppl 3):S96-S100.
- 13. Lusti-Narasimhan M, Beard JR. Sexual health in older women. Bull World Health Organ 2013;91(9):707-709.
- Lindau ST, Schumm LP, Laumann EO, Levinson W, O'Muircheartaigh CA, Waite LJ. A study of sexuality and health among older adults in the United States. N Engl J Med 2007; 357(8):762-774.
- 15. Lindau ST, Gavrilova N. Sex, health, and years of sexually active life gained due to good health: evidence from two US population based cross sectional surveys of ageing. BMJ 2010;340:c810.
- 16. Nusbaum MR, Singh AR, Pyles AA. Sexual healthcare needs of women aged 65 and older. J Am Geriatr Soc 2004;52(1):117-122.
- 17. Celikel E, Ozel-Kizil ET, Akbostanci MC, Cevik A. Assessment of sexual dysfunction in patients with Parkinson's disease: a case-control study. Eur J Neurol 2008;15(11):1168-1172.
- Kummer A, Cardoso F, Teixeira AL. Loss of libido in Parkinson's disease. J Sex Med 2009;6(4):1024-1031.
- 19. Sakakibara R, Shinotoh H, Uchiyama T, et al. Questionnaire-based assessment of pelvic organ dysfunction in Parkinson's disease. Auton Neurosci 2001;92(1-2):76-85.
- Welsh M, Hung L, Waters CH. Sexuality in women with Parkinson's disease. Mov Disord 1997;12(6):923-927.
- Kotkova P, Weiss P. Psychiatric factors related to sexual functioning in patients with Parkinson's disease. Clin Neurol Neurosurg 2013;115(4):419-424.
- 22. Bronner G, Vodusek DB. Management of sexual dysfunction in Parkinson's disease. Ther Adv Neurol Disord 2011;4(6):375-383.
- 23. TA, Sullivan KL, Arnulf I, et al. Practice Parameter: treatment of nonmotor symptoms of Parkinson disease: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2010;74(11):924-931.
- Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 1992;55(3): 181-184.

- Goetz CG, Tilley BC, Shaftman SR, et al. Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): scale presentation and clinimetric testing results. Mov Disord 2008;23(15):2129-2170.
- Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. Neurology 1967;17(5):427-442.
- 27. Goetz CG, Poewe W, Rascol O, et al. Movement Disorder Society Task Force report on the Hoehn and Yahr staging scale: status and recommendations. Mov Disord 2004;19(9):1020-1028.
- Rosen R, Brown C, Heiman J, et al. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. J Sex Marital Ther 2000; 26(2):191-208.
- Pechorro P, Diniz A, Almeida S, Vieira R. Validação de uma versão feminina do índice de satisfação sexual (ISS). Laboratório de Psicologia 2009;7(1):11.
- Wiegel M, Meston C, Rosen R. The female sexual function index (FSFI): cross-validation and development of clinical cutoff scores. J Sex Marital Ther 2005;31(1):1-20.
- Association AP. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Washington, DC; 2000.
- 32. Sbrocco T, Weisberg R, Barlow D. Sexual Dysfunction Inventory (SDI). Boston: Boston University; 1992.
- Nobre P, Carvalheira A, Fonseca L. Entrevista de avaliação de disfunções sexuais (SDI). 2003.
- Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4: 561-571.
- Levin BE, Llabre MM, Weiner WJ. Parkinson's disease and depression: psychometric properties of the Beck Depression Inventory. J Neurol Neurosurg Psychiatry 1988;51(11):1401-1404.
- Vaz Serra AS, Pio Abreu JL. Aferição dos quadros clínicos depressivos. II — estudo preliminar de novos agrupamentos sintomatológicos para complemento do inventário depressivo de Beck. Coimbra Médica; 1973;XX:19.
- Taylor JF, Rosen RC, Leiblum SR. Self-report assessment of female sexual function: psychometric evaluation of the Brief Index of Sexual Functioning for Women. Arch Sex Behav 1994;23(6): 627-643.
- McGahuey CA, Gelenberg AJ, Laukes CA, et al. The Arizona Sexual Experience Scale (ASEX): reliability and validity. J Sex Marital Ther 2000;26(1):25-40.
- Shifren JL, Monz BU, Russo PA, Segreti A, Johannes CB. Sexual problems and distress in United States women: prevalence and correlates. Obstet Gynecol 2008;112(5):970-978.
- 40. Wielinski CL, Varpness SC, Erickson-Davis C, Paraschos AJ, Parashos SA. Sexual and relationship satisfaction among persons with young-onset Parkinson's disease. J Sex Med 2010;7(4 Pt 1): 1438-1444.
- 41. Wermuth L, Stenager E. Sexual problems in young patients with Parkinson's disease. Acta Neurol Scand 1995;91(6):453-455.
- 42. Kuffel SW, Heiman JR. Effects of depressive symptoms and experimentally adopted schemas on sexual arousal and affect in sexually healthy women. Arch Sex Behav 2006;35(2):163-177.
- 43. Frohlich P, Meston C. Sexual functioning and self-reported depressive symptoms among college women. J Sex Res 2002;39(4):321-325.
- Gracia CR, Sammel MD, Freeman EW, Liu L, Hollander L, Nelson DB. Predictors of decreased libido in women during the late reproductive years. Menopause 2004;11(2):144-150.
- Atlantis E, Sullivan T. Bidirectional association between depression and sexual dysfunction: a systematic review and meta-analysis. J Sex Med 2012;9(6):1497-1507.
- Zelena V, Kuba R, Soska V, Rektor I. Depression as a prominent cause of sexual dysfunction in women with epilepsy. Epilepsy Behav 2011;20(3):539-544.
- Eraslan D, Yalinay Dikmen P, Ilgaz Aydinlar E, Incesu C. The relation of sexual function to migraine-related disability, depression and anxiety in patients with migraine. J Headache Pain 2014; 15:32.
- Scheepe JR, Alamyar M, Pastoor H, Hintzen RQ, Blok BF. Female sexual dysfunction in multiple sclerosis: results of a survey among Dutch urologists and patients. Neurourol Urodyn 2015.

- 49. Calabro RS, Russo M. Sexual dysfunction and depression in individuals with multiple sclerosis: is there a link? Innov Clin Neurosci 2015;12(5-6):11-12.
- 50. Fabre LF, Smith LC. The effect of major depression on sexual function in women. J Sex Med 2012;9(1):231-239.
- 51. Montejo AL, Montejo L, Navarro-Cremades F. Sexual side-effects of antidepressant and antipsychotic drugs. Curr Opin Psychiatry 2015;28(6):418-423.
- 52. Waldinger MD. Psychiatric disorders and sexual dysfunction. Handb Clin Neurol 2015;130:469-489.
- Lorenz TA, Meston CM. Acute exercise improves physical sexual arousal in women taking antidepressants. Ann Behav Med 2012; 43(3):352-361.
- 54. Lorenz TA, Meston CM. Exercise improves sexual function in women taking antidepressants: results from a randomized crossover trial. Depress Anxiety 2014;31(3):188-195.
- 55. Taylor MJ, Rudkin L, Bullemor-Day P, Lubin J, Chukwujekwu C, Hawton K. Strategies for managing sexual dysfunction induced by

antidepressant medication. The Cochrane database of systematic reviews 2013;5:CD003382.

- 56. McCabe MP, Sharlip ID, Lewis R. et al. Risk Factors for Sexual Dysfunction Among Women and Men: A Consensus Statement From the Fourth International Consultation on Sexual Medicine 2015. J Sex Med 2016;13(2):153-67.
- Davison SL, Bell RJ, LaChina M, Holden SL, Davis SR. The relationship between self-reported sexual satisfaction and general wellbeing in women. J Sex Med 2009;6(10):2690-2697.
- Yu M, Roane DM, Miner CR, Fleming M, Rogers JD. Dimensions of sexual dysfunction in Parkinson disease. Am J Geriatr Psychiatry 2004;12(2):221-226.
- Bronner G, Hassin-Baer S. Exploring hypersexual behavior in men with Parkinson's disease: is it compulsive sexual behavior? J Parkinsons Dis 2012;2(3):225-234.
- 60. Giladi N, Weitzman N, Schreiber S, Shabtai H, Peretz C. New onset heightened interest or drive for gambling, shopping, eating or sexual activity in patients with Parkinson's disease: the role of dopamine agonist treatment and age at motor symptoms onset. J Psychopharmacol 2007;21(5):501-506.