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The PRIAMO study: active sexual life is associated with better motor and non motor outcomes in men with early Parkinson's disease

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Abbreviations: ANOVA: analysis of variance; EQ-VAS: EuroQol visual analogue scale; HAM: Hamilton Depression scale; HRQol: health-related quality of life; H&Y: Hoehn and Yahr; MMSE: Mini Mental State examination; NMS: non motor symptoms; OR: odds ratio; PD: Parkinson's disease; PD-NSA: Parkinson's disease patients without sexual activity; PDQ-39: 39 items Parkinson's disease questionnaire; Priamo: PaRkinson dIseAse non MOtor symptoms; PD-SA: Parkinson's disease patients with sexual activity; SD: standard deviation; UPDRS-III: Unified Parkinson's Disease Rating Scale part III; RR: relative risk.

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Abstract

Background and purpose. Data suggest a relationship between sexual dysfunction, mainly erectile dysfunction in men, and worse disease progression in Parkinson's disease (PD). There is a scant of evidence on the correlates of sexual activity in PD patients. By involving a subgroup of 355 patients from the PRIAMO (PaRkinson dIseAse non MOtor symptoms) study, the present 24-month longitudinal prospective analysis aims to demonstrate that the presence of active sexual life is associated with disease progression in early PD.

Methods and results. Multivariable mixed-effect logistic regression models showed that gastrointestinal (OR 0.56, 95% CI 0.39 – 0.82, P = 0.003) and apathy (OR 0.42, 95% CI 0.29 – 0.63, P < 0.001) were less likely to be associated with sexual activity in men. Analysis also demonstrated that sexual activity in men was associated with lower motor disability (coefficient -2.881, 95%CI -4.732 to -1.030, p=0.002), better quality of life (coefficient -24.196, 95%CI -44.884 to -3.508, p=0.022; coefficient 0.083, 95% CI 0.023 to 0.143, P = 0.006), lower depression scores (coefficient -1.245, 95%CI -2.104 to -0.387, p=0.004). No association was shown in women.

Conclusions: This is the first prospective longitudinal study involving a large cohort of PD patients suggesting that sexual is associated with lower motor and non-motor disability as well as with better quality of life in men. These findings should prompt movement disorders specialists to periodically inquiry their patients' sexual life.

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Introduction

Sexual activity is a complex process requiring a coordinated functioning of the person's mental, autonomic, sensory and motor systems and relies on proper function of the neurologic, vascular and endocrine system as well as a healthy emotional state [1]. Indeed chronic diseases have an impact on sexual function through both direct and indirect mechanisms [1].

As patients with Parkinson's disease (PD) have to cope with important changes in their sexual function, achieve a satisfying intimate and sexual relationship is often a challenge [2]. On the other hand, evidence shows that quality of sexual expression improves general satisfaction of life in PD patients [3].

Psychosocial (religion, cultural background and role changes) and individual factors have diverse impact on sexuality and sexual functioning determining the high gender-specificity of the topic [1,4]. From the clinician's perspective, examination of the patient's sexual life is often neglected during the clinical interview. Likewise, the most commonly used tools to evaluate non-motor symptoms (NMS) as well as health-related quality of life (HR-QoL) in PD contain either a few or none item related to sexual function. Yet, as effective pharmacologic and behavioral therapies for sexual problems are available, sex life should be proactively investigated [5].

Data available so far show a relationship between sexual dysfunction, mainly erectile dysfunction in men, and worse disease progression in PD [6]. Though, active sexual life rather than sexual function is considerate a surrogate of general health [1]. Notwithstanding, there is a scant of evidence on the correlates of sexual activity in PD patients.

By further analyzing prospective data from a subset of patients of the PRIAMO (PaRkinson dIseAse non MOtor symptoms) study [7,8], the present work aims to demonstrate that the presence of active sexual life is associated with disease progression in early PD. In detail, our goals were to evaluate (1) whether an active sexual life is associated with better motor and non-motor outcomes

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as well as quality of life and (2) the prevalence of sexual dysfunction in a cohort of sexually active PD patients.

Patients and methods

Patients and assessments

This study involves a subgroup of patients from the PRIAMO study. The PRIAMO study is a large Italian multicentre observational study designed to assess the prevalence and evolution of NMS in patients affected by different parkinsonian syndromes and including a cross sectional and a longitudinal prospective 24-month phase [7-10].

Study methods and patient baseline features have been extensively described elsewhere [7,8]. The study has been conducted between July 2005 and June 2006 [7]. Each patient underwent a baseline (T1) and two follow-up visits, at 12 months (±4) after the baseline visit (T2) and 9-16 months after the first follow-up visit (T3), respectively. Diagnosis of idiopathic PD was based on Gelb et al. criteria [11]. Enrolled patients were administered a semistructured interview exploring 12 NMS domains (gastrointestinal, urinary, pain, cardiovascular, sleep, fatigue, apathy, attention/memory, skin, psychiatric, respiratory and other symptoms including smell and taste impairment, diplopia, weight change), each one including 2 to 10 specific questions with dichotomus (yes/no) answers (see supplemental material online)[7,8].

Patients were asked whether they had been sexually active in the past 12 months. Only those reporting being sexually active were administered a semi-structured gender-tailored interview, specifically investigating the occurrence of several genital symptoms during the past month (see supplemental material online).

The Unified Parkinson's Disease Rating Scale-part III (UPDRS-III) was used to evaluate motor disability, while cognitive abilities were investigated with the Mini-Mental State Examination

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(MMSE). Depressive symptoms were evaluated with the Hamilton Depression scale (HAM). HR-QoL was investigated using the 39-item Parkinson's disease questionnaire (PDQ-39) and the EuroQol visual analogue scale (EQ-VAS) [7,8]. All those scales are available for the Italian population.

All the clinicians involved were expert in movement disorders and participated in a training session before starting enrolment for the PRIAMO study.

For this subanalysis, only patients with early stage PD [namely, Hoehn and Yahr (H&Y) stage≤2] at baseline and with no missing answers to the gateway question on sexual activity for at least two assessments were considered. The study was approved by the ethic committees of the participating centres and all patients provided written informed consent.

Statistical analysis

Of 1142 PD patients enrolled in the PRIAMO study, 355 (238 men and 117 women) PD patients had H&Y stage≤2 at baseline and with no missing answers to the gateway question on sexual activity for at least two assessments, and, thus, were eligible for the present study. Given the high gender specificity of the topic as well as the lower number of included women, all the following analyses were performed separately for men and women.

Included subjects were divided in PD with (PD-SA) and without active sexual life (PD-NSA) over a follow-up of 24 months and were confronted for demographics and clinical assessments.

After checking normal distribution of variables, comparisons between groups were performed using χ^2, t-test and analysis of variance (ANOVA) as appropriate. Accordingly, descriptive statistics are presented as proportions, or mean and standard deviation (SD). In order to test a possible association between NMS and active sexual life (i.e., the outcome) over time multivariable mixed-effect logistic regression models were computed controlling for age and disease duration. To test whether active sexual life is associated with lower motor and cognitive impairment as well as better

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mood and HR-QoL, multivariable mixed-effect linear regression models were used, considering UPDRS-III, MMSE, HAM, PDQ-39 and EQ-VAS as outcome variables and age and disease duration as covariates. All covariates used for the adjusted analyses were tested for multicollinearity. The multicollinearity diagnostics (VIF) were all less than 5, indicating an assumption of reasonable independence among predictor variables. Results are presented as adjusted odds ratio (OR), regression coefficients (coeff.), as appropriate, and 95% confidence intervals (95%CI) and considered statistically significant if $p \leq 0.05$. Statistical analyses were performed with STATA software (version 14.0; Stata-Corp LP, College Station, TX).

Results

Demographic and clinical features of the included cohort at T1, T2 and T3 are displayed in Table 1 and supplemental material online. The prevalence of sexual activity presented a reduction over the longitudinal phase in the whole group (T1: 56.3%; T2: 53.7%; T3: 50.8%). Men were more likely to be sexually active at all time points (Figure 1A).

As for men, PD-SA were younger and had earlier onset of symptoms, lower UPDRS-III, better HR-QoL and lower frequency of gastrointestinal symptoms compared to PD-NSA. Moreover, PD-SA presented lower apathy rates and depression scores in at least two assessments. At T3, PD-SA were less frequently on L-dopa and presented lower fatigue and attention/memory symptoms rates (Table 1 and supplemental material online).

As for women, PD-SA were younger and had earlier onset of symptoms compared to PD-NSA. Moreover, PD-SA presented less frequently urinary symptoms at T2 and better HR-QoL at T3 (Table 1 and supplemental material online).

Multivariable mixed-effects logistic models showed that, among NMS domains, gastrointestinal (OR 0.56, 95% CI 0.39 – 0.82, P = 0.003) and apathy (OR 0.42, 95% CI 0.29 – 0.63, P < 0.001) were less

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likely to be associated with PD-SA in men. In addition, sexual activity was less frequently associated with treatment with L-dopa (OR 0.65, 95% CI 0.43 – 0.97, P = 0.037). No association emerged for women.

Multivariable mixed-effects linear models showed that sexual activity in men was associated with less severe motor disability (UPDRS-III, coefficient -2.881, 95%CI -4.732 to -1.030, p=0.002) (Figure 1B), better HR-QoL (PDQ-39, coefficient -24.196, 95%CI -44.884 to -3.508, p=0.022; EQ-VAS, coefficient 0.083, 95% CI 0.023 to 0.143, P = 0.006) (Figure 1C), lower depression scores (HAM, coefficient -1.245, 95%CI -2.104 to -0.387, p=0.004) (Figure 1D). No association was shown in women (UPDRS-III, coefficient -2.921, 95%CI -6.663 to 0.821, p=0.126, PDQ-39, coefficient -17.671, 95% CI -59.599 to 24.256, p=0.409; EQ-VAS, coefficient 0.028, 95% CI -0.069 to 0.126, p = 0.573; HAM, coefficient -0.767, 95%CI -2.228 to 0.693, p=0.303).

MMSE was associated with PD-SA neither in men (coefficient -0.268, 95%CI -0.794 to 0.257, p=0.317) nor women (coefficient -0.523, 95%CI -1.543 to 0.499, p=0.316).

The results of the gender-tailored semi-structured interview administered to PD-SA as well as the reasons for lack of sexual activity in PD-NSA are shown in Table 2 and supplemental material online. Briefly, men complained of loss of erection, impotence and orgasmic disorder as well as sexual dissatisfaction, while women had reduced sexual drive and arousal and orgasmic dysfunction as well as sexual dissatisfaction. The majority of patients, both men and women, failed to provide a response for not being sexually active.

Discussion

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This is the first prospective longitudinal study involving a large cohort of PD patients demonstrating the relationship between the presence of sexual activity and less severe motor and non-motor disability as well as better HR-QoL in men.

Patients of our cohort presented a progressive reduction of sexual activity from 56.3% to 50.8% over the 2-year follow up. In line with previous literature, men were sexually active twice as much as women (67% versus 33%) (Figure 1A) [2].

The most novel finding of our analysis was that, irrespective of disease severity as evaluated by the H&Y, sexually active men displayed distinctive demographic and clinical features compared to sexually non-active men. As such, sexually active men had younger age at examination and at onset and lower rates of treatment with L-dopa at the end of the follow up reflecting a milder motor impairment and disease progression. Furthermore, sexual activity was not related with apathy or gastrointestinal symptoms, while it was significantly associated with better HR-QoL as well as with lower motor and depression scores all over the 2-year observation period (Figure 1B-D). Notwithstanding, nearly half of sexually active men complained about erectile dysfunction (ie, loss of erection and impotence) and orgasm disorders at every timepoint (Table 2). Our results were confirmed after excluding those patients reporting clear symptoms of sexual dysfunction with the gender-tailored semistructured interview (supplemental material online).

This is in line with several data showing a close relationship between sexual health and general health both in healthy individuals and in patients with chronic disease [1,12]. The World Health Organization has declared that sexual health is a pivotal aspect of life, irrespective of the presence of sexual dysfunction, and that each individual has the right to conduct intimate relationships and personal control over sexual and reproductive behavior with appropriate information and treatment [12]. Yet, psychosocial factors may hamper sexual communication between couples, and clinicians rarely proactively inquire patients' sexual issues. Chronic diseases are associated with a

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profound change in sexual activity and sexual dysfunction is one of the commonest NMS in PD [8]. The goal of treatment of sexual function in PD should not be limited to maintain full genital functions but, rather, to achieve pleasure and satisfaction, reduce anxiety and concerns, increase intimate couple communication and reduce relationship tension [1,5]. Our data would confirm these theories and should prompt clinicians to broadly address sexual issues in PD patients not limited to sexual dysfunction.

However, in our analysis no such a relationship emerged for women. Several explanations may account for such gender discrepancy. As a matter of fact, specific gender differences exist in motor and non-motor symptoms in early PD [13-15]. Then, women are less prone to talk about sexual and genital issues due to societal attitudes [5]. Finally, women were much less represented in our cohort (33% versus 67%).

The majority of the patients partecipating in the gender-tailored semistructured interview (Table 2) dir not report reduced sexual drive over the longitudinal follow up. Although impulse control disorders were not carefully evaluated in this cohort, it could be speculated that those patients present increased impulsivity. Though, we did not find a specific association with treatment with dopamine agonists.

Our study has limitations. First, the lack of a longer longitudinal observation precludes the possibility of describing the complete natural history of PD men with active sexual life. Notwithstanding, this is the largest study to date evaluating prospectively both motor and non-motor burden in patients with sexual activity compared to those without. Secondly, the lack of a control group from the general population represents another drawback as lack of sexual activity is a common finding in the general elderly population. However, a large amount of literature reports sexual inactivity as more prevalent in PD patients compared to healthy controls [1-3,4]. In addition, the large sample size of our study should attenuate this bias. We also recognize the lack of assessment of severity of

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NMS in our study. However, the Priamo study was designed before the release of the Non-Motor Symptoms Scale [17]. Furthermore, we used a non-validated gender-tailored semi-structured interview to specifically explore sexual issues in sexually active patients. Then, we acknowledge our data may be affected by a recall bias. Finally, we recognize reduced sexual activity can simply reflect reduced motivation as well as increased apathy, which in turn may be associated to reduced dopamine levels [16]. However, the lack of a formal assessment of apathy (ie, the Apathy Scale) and molecular imaging to assess dopamine striatal function prevent us from drawing any conclusion on such hypothesis.

In conclusion, our 24-month longitudinal prospective analysis suggests that sexual activity might be associated with reduced motor and non-motor burden and milder disease progression in men with early PD. These findings should prompt movement disorders specialists to periodically inquiry their patients' sexual life. Further studies are needed to confirm such data in men and explore such a relationship in women with PD.

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Tables legend

Table 1

Data are in mean (standard deviation) unless otherwise specified. Abbreviations: EQ-VAS = the EuroQol visual analogue scale; HAM = Hamilton Depression scale; MMSE = Mini-mental state examination; PD-NSA = Parkinson's disease without active sexual life; PD-SA = Parkinson's disease with active sexual life; PDQ-39 = the 39-item Parkinson's disease questionnaire; T1 = baseline visit; T2 = first follow up visit; T3 = second follow up visit; UPDRS-III = the Unified Parkinson's disease rating scale part III.

Table 2

Abbreviations: *The remaining patients failed to provide a response; T1 = baseline visit; T2 = first follow up visit; T3 = second follow up visit.

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Figure 1 legend

Figure 1A. Sexual activity according to gender for all time points.

Figure 1B. Motor disability according to UPDRS-III in men (PD-NSA compared with PD-SA).

Figure 1C. Health-related quality of life according to the EQ-VAS in men (PD-NSA compared with PD-SA).

Figure 1D. Depression according with the Hamilton scale in men (PD-NSA compared with PD-SA).

Abbreviations: *=significant differences between gender, p<0.001; EQ-VAS = the EuroQol visual analogue scale; F = female gender; HR-QoL = Health-related quality of life; M = male gender; PD-NSA = Parkinson's disease without active sexual life; PD-SA = Parkinson's disease with active sexual life; UPDRS-III = the Unified Parkinson's disease rating scale part III.

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Table 1. Demographic and clinical features of the enrolled patients at T1, T2 and T3

T1	Women			Men		
	PD-SA (45)	PD-NSA (72)	p	PD-SA (155)	PD-NSA (83)	p
Age	61.27 (8.57)	68.06 (6.48)	<0.001	62.51 (9.77)	70.84 (7.24)	<0.001
Age at onset	56.38 (8.46)	62.78 (9.84)	<0.001	57.39 (10.61)	64.82 (11.37)	<0.001
Disease duration	4.89 (3.96)	6.08 (8.19)	0.363	5.1 (3.6)	5.15 (4.4)	0.928
UPDRS-III	19.6 (9.59)	19.56 (9.95)	0.983	17.46 (8.78)	20.84 (10.98)	0.011
MMSE	27.2 (4.7)	27 (2.79)	0.773	27.43 (3.89)	26.67 (5.19)	0.206
HAM	6.3 (4.08)	7.01 (5.66)	0.465	5.52 (4.47)	6.26 (4.98)	0.688
L-dopa, n (%) yes/no	28/18 (60/40)	46/26 (63.9/36.1)	0.699	86/69 (55.5/44.5)	58/25 (69.9/30.1)	0.037
PDQ-39 Total	179.9 (108.4)	213.6 (129.8)	0.141	153.5 (93.4)	164.9 (123.8)	0.254
EQ-VAS	64.9 (14.8)	64.5 (14.9)	0.887	66.91 (15.13)	61.87 (18.7)	0.030
T2	**Women**			**Men**		
	PD-SA (33)	PD-NSA (82)	p	PD-SA (149)	PD-NSA (80)	p
UPDRS-III	19.34 (9.43)	19.44 (10.59)	0.960	18.25 (10.12)	22.83 (9.8)	0.001
MMSE	26.46 (6.57)	27.39 (2.98)	0.286	27.38 (3.94)	25.68 (6.19)	0.012
HAM	6.35 (4.23)	5.95 (4.55)	0.651	5.04 (3.66)	6.49 (5.19)	0.016
L-dopa, n (%) yes/no	29/10 (74.4/25.6)	59/23 (72/28)	0.830	99/50 (66.4/33.6)	59/21 (73.8/26.3)	0.295
PDQ-39 Total	175.1 (109.6)	159.5 (119.3)	0.707	149.8 (100.5)	167 (105.2)	0.158
EQ-VAS	64.23 (17.67)	61.59 (17.33)	0.437	67.04 (15.78)	61.77 (18.25)	0.025
T3	**Women**			**Men**		
	PD-SA (28)	PD-NSA (80)	p	PD-SA (137)	PD-NSA (79)	p
UPDRS-III	19.25 (9.52)	25.06 (9.79)	0.139	20.37 (10.61)	25.75 (11.85)	0.001
MMSE	26.29 (7.57)	24.08 (8.46)	0.225	26.08 (7.13)	26 (5.19)	0.930
HAM	5.65 (4.73)	6.51 (5.84)	0.503	4.67 (4.34)	6.30 (5.29)	0.016
L-dopa, n (%) yes/no	20/8 (71.4/28.6)	61/19 (76.3/23.8)	0.619	97/40 (70.8/29.2)	71/9 (88.8/11.3)	0.001
PDQ-39 Total	162.7 (104.9)	201 (137)	0.141	151.5 (101)	184.2 (106.3)	0.036
EQ-VAS	65.1 (19.5)	58.1 (18.3)	0.09	67.1 (15.4)	62.1 (16.6)	0.028

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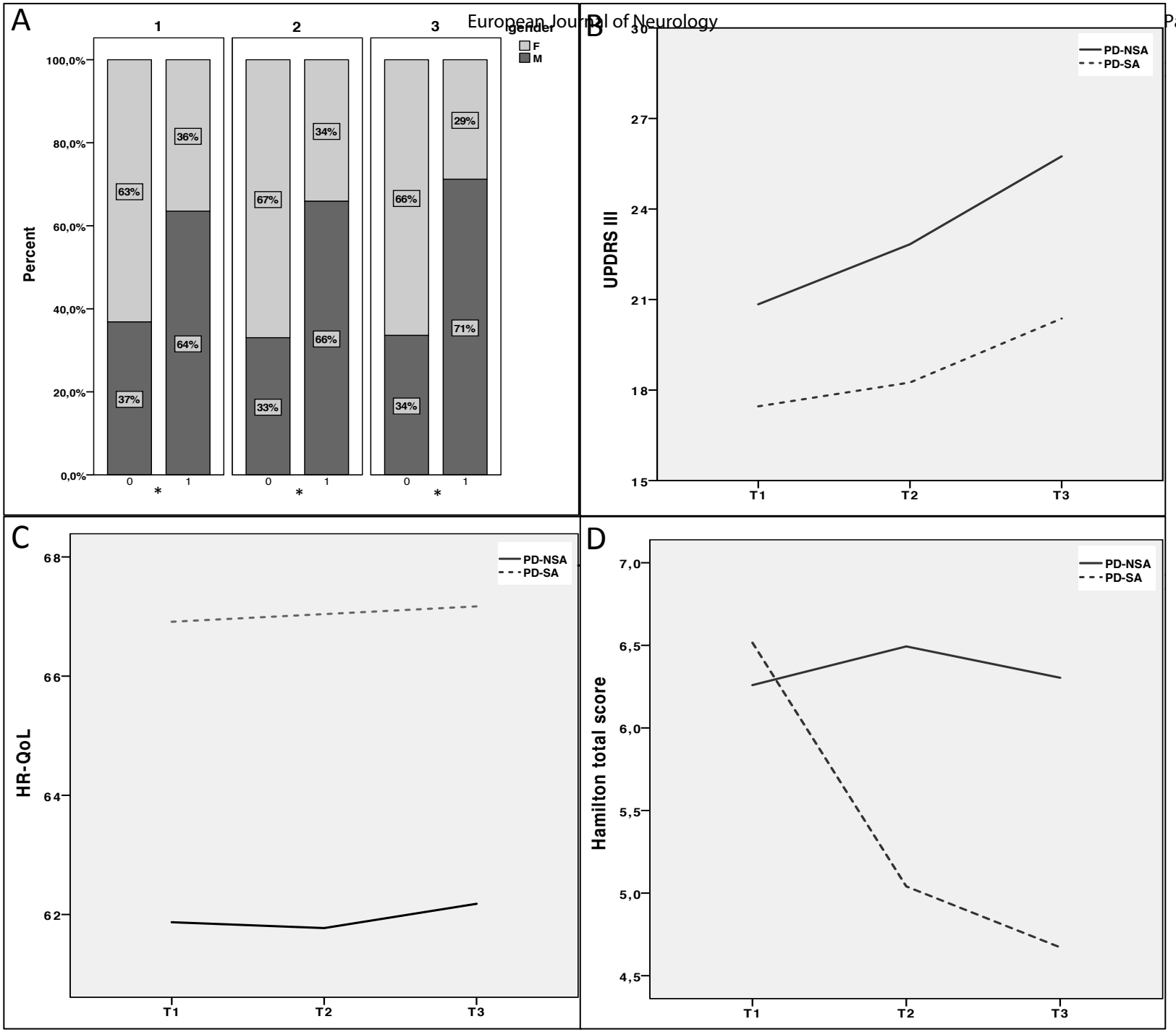
Abbreviations: EQ-VAS: EuroQol visual analogue scale; MMSE: Mini Mental State examination; PD-NSA: Parkinson's disease patients without sexual activity; PDQ-39: 39 items Parkinson's disease questionnaire; PD-SA: Parkinson's disease patients with sexual activity; UPDRS-III: Unified Parkinson's Disease Rating Scale part III.

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Table 2. Prevalence of specific genital issues according to the gender-tailored semistructured interview

Men	**T1 (155)**	**T2 (149)**	**T3 (137)**	**p**
1.Reduced sexual drive, n (%) yes/no	25/49* (33.7/66.2)	16/57* (22/78)	19/50* (27.5/72.4)	0.20
2.Increased sexual drive, n (%) yes/no	24/43* (35.8/64.1)	25/51* (33/67)	20/50* (28.5/71.5)	0.65
3.Orgasmic dysfunction, n (%) yes/no	24/41* (36.9/63)	30/39* (43/57)	28/36* (51.8/48.2)	0.80
4.Sexual dissatisfaction, n (%) yes/no	21/45* (31.8/68.1)	28/44* (39/61)	22/43* (33.8/66.1)	0.66
5.Impotence, n (%) yes/no	31/37* (45.5/54.5)	28/42* (40/60)	33/33* (50/50)	0.50
6.Premature ejaculation, n (%) yes/no	12/54* (18.7/81.2)	8/60* (11.7/88.2)	7/55* (11.2/88.8)	0.44
7.Lack of ejaculation, n (%) yes/no	13/53* (19.6/80.3)	12/56* (17.6/82.4)	9/53* (14.5/85.4)	0.73
8.Loss of erection, n (%) yes/no	40/28* (58.8/41.1)	33/37* (47.1/52.9)	29/35* (45.3/54.6)	0.23
9.Use of Sildenafil/Tadalafil, n (%) yes/no	7/60* (10.4/89.5)	5/65* (7.1/92.8)	7/58* (10.7/389.2)	0.72
Women	**T1 (45)**	**T2 (39)**	**T3 (28)**	
1.Reduced sexual drive, n (%) yes/no	7/3* (70/30)	6/5* (54.5/45.4)	1/7* (12.5/87.5)	0.05
2.Increased sexual drive, n (%) yes/no	3/7* (30/70)	2/9* (18.1/81.8)	3/4* (42.8/57.2)	0.02
3.Orgasmic dysfunction, n (%) yes/no	5/3* (62.5/37.5)	2/6* (25/75)	1/5* (16.6/83.4)	0.14
4.Sexual dissatisfaction, n (%) yes/no	5/3* (62.5/37.5)	2/6* (25/75)	1/5* (16.6/83.4)	0.14
5.Low sexual arousal, n (%) yes/no	5/3* (62.5/37.5)	2/6* (25/75)	1/5* (16.6/83.4)	0.14
6.Anorgasmia, n (%) yes/no	3/5* (37.5/62.5)	2/6* (25/75)	6/3* (66.6/33.3)	0.20
7.Dispareunia, n (%) yes/no	3/5* (37.5/62.5)	1/7* (12.5/87.5)	6/3* (66.6/33.3)	0.07

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A
1
2
3
gender
F
M
100,0%
80,0%
60,0%
40,0%
20,0%
0,0%
Percent
63%
36%
37%
64%
67%
34%
33%
66%
66%
29%
34%
71%
0
1
*
B
PD-NSA
PD-SA
UPDRS III
30
27
24
21
18
15
T1
T2
T3
C
PD-NSA
PD-SA
HR-QoL
68
66
64
62
T1
T2
T3
D
PD-NSA
PD-SA
Hamilton total score
7,0
6,5
6,0
5,5
5,0
4,5
T1
T2
T3

Supplemental material

PRIAMO semistructured interview exploring NMS domains (dichotomus answers, yes/no)

Patients were asked to report each specific symptom as affected/not affected with reference to the month before the visit. Both patients and their caregivers contributed to the completion of the interview.

1)Does the patient have the following gastrointestinal disturbances?

-drooling

-swallowing difficulties

-nausea/vomit

-constipation

-anorectal dysfunction

-incomplete bowel emptying

-fecal incontinence

2)Does the patient have the following pain symptoms?

-undefinied pain

-lower limbs pain

-abdominal pain

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-pain (after assumption of antiparkinsonian medications)

-shoulder pain

3)Does the patient have the following urinary symptoms?

-urgency

-frequency (need of voiding every 2 hours or less)

-nocturia

4)Does the patient have the following cardiovascular symptoms?

-dizziness, lightheadness during postural changes

-falls after syncope

5)Does the patient have the following sleep disturbances?

-RBD (talking or moving while sleeping)

-difficulties in falling asleep

-diurnal somnolence

-restless legs syndrome

6)Does the patient have fatigue severe enough to limit activities of daily living?

7)Does the patient have apathy?

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-lost of interest for sorroundings, activities of daily living or new activities

8)Does the patient have impared attention/memory?

-difficulties in sustaining attention

-forgetful for recent events/talks or activities of daily living

9)Does the patient have the following skin problems?

-seborrhea

-hyperhidrosis

10)Does the patient have the following psychiatric disturbances?

-anhedonia

-anxiety

-panic attacks

-aggressiveness

-suicide ideas

-irritability

-unexplained worry

-sadness/depression

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-psychotic thinking

-hallucinations

11)Does the patient have the following respiratory disturbances?

-dyspnoea

-stridor

-cough

12)Does the patient have the following other non motor symptoms?

-smell disturbances

-taste disturbances

-weight changes

-diplopia

-sexual disturbances

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Semi-structured gender-tailored interview on genital symptoms

Men

1) Do you have reduced sexual desire?
2) Do you have increased sexual desire?
3) Do you have sexual dissatisfaction?
4) Do you have impotence?
5) Do you have premature eiaculation?
6) Do you have lack of eiaculation?
7) Do you have lloss of erection?
8) Do you use Sildenafil/Tadalafil?

Women

1) Do you have reduced sexual desire?
2) Do you have increased sexual desire?
3) Do you have sexual dissatisfaction?
4) Do you have low sexual arousal?
5) Do you have anorgasmia?

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6) Do you have dispareunia?

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Non motor features of enrolled patients at T1, T2 and T3

T1	Women			Men		
	PD-SA (45)	PD-NSA (72)	p	PD-SA (155)	PD-NSA (83)	p
Gastrointestinal, n (%) (yes/no)	28/17 (62.2/37.8)	43/29 (59.7/40.3)	0.847	83/72 (52.3/46.5)	56/27 (67.5/32.5)	0.040
Pain, n (%) (yes/no)	32/13 (71.1/28.9)	43/29 (59.7/40.3)	0.239	81/74 (52.3/47.7)	42/41 (50.6/49.4)	0.892
Urinary, n (%) (yes/no)	19/26 (42.2/57.8)	37/35 (51.4/48.6)	0.349	90/65 (58.1/41.9)	49/34 (59/41)	0.885
Postural hypotension, n (%) (yes/no)	10/35 (22.2/77.8)	9/63 (12.5/87.5)	0.201	16/139 (10.3/89.7)	14/69 (16.9/83.1)	0.156
Sleep, n (%) (yes/no)	29/16 (64.4/33.3)	39/33 (54.2/45.8)	0.337	93/62 (60/40)	46/37 (55.4/44.6)	0.581
Fatigue, n (%) (yes/no)	30/15 (66.7/33.3)	49/23 (68.1/31.9)	0.876	66/89 (42.6/57.4)	31/52 (37.3/62.7)	0.490
Apathy, n (%) (yes/no)	12/32 (28.9/71.1)	24/48 (33.3/66.7)	0.685	32/123 (20.6/79.4)	30/53 (36.1/63.9)	0.013
Attention/Memory, n (%) (yes/no)	17/28 (37.8/62.2)	24/48 (33.3/66.7)	0.692	62/93 (40/60)	41/42 (49.4/50.6)	0.172
Skin, n (%) (yes/no)	7/38 (15.6/84.4)	3/69 (4.2/95.8)	0.053	39/116 (25.2/74.8)	17/66 (20.5/79.5)	0.522
Mental health, n (%) (yes/no)	32/13 (71.1/28.9)	41/31 (56.9/43.1)	0.170	101/54 (65.2/34.8)	45/38 (54.2/45.8)	0.089
Respiratory, n (%) (yes/no)	6/39 (13.3/86.7)	11/61 (15.3/84.7)	0.771	23/132 (14.8/85.2)	14/69 (16.9/83.1	0.709
Other symptoms, n (%) (yes/no)	23/22 (51.1/48.9)	34/38 (47.2/52.8)	0.708	94/61 (60.6739.4)	51/32 (61.4/38.6)	0.904
T2	**Women**			**Men**		
	PD-SA (39)	**PD-NSA (82)**	**p**	**PD-SA (149)**	**PD-NSA (80)**	**p**
Gastrointestinal, n (%) (yes/no)	23/16 (59/41)	53/29 (64.6/35.4)	0.055	87/62 (58.4/41.6)	58/22 (72.5/27.5)	0.044
Pain, n (%) (yes/no)	27/12 (69.2 /30.8)	53/29 (64.6/35.4)	0.684	72/77 (48.3/51.7)	52/28 (65/35)	0.018
Urinary, n (%) (yes/no)	13/26 (33.3/66.7)	46/36 (56.1/43.9)	0.021	94/55 (63.1/36.9)	56/24 (70/30)	0.311

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Postural hypotension, n (%) (yes/no)	9/30 (23.1/76.9)	14/68 (17.1/82.9)	0.463	17/132 (11.4/88.6)	15/65 (18.8/81.3)	0.161
Sleep, n (%) (yes/no)	22/17 (56.4/43.6)	41/41 (50/50)	0.562	97/52 (65.1/34.9)	52/28 (65/35)	0.988
Fatigue, n (%) (yes/no)	24/15 (61.5/38.5)	50/32 (61/39)	0.558	67/82 (45/55)	41/39 (51.2/48.8)	0.406
Apathy, n (%) (yes/no)	8/31 (20.5/79.5)	26/56 (31.7/68.3)	0.279	31/118 (20.8/79.2)	30/50 (37.5/62.5)	0.008
Attention/Memory, n (%) (yes/no)	12/27 (30.8/69.2)	32/50 (39/61)	0.250	64/85 (43/57)	42/38 (52.5/47.5)	0.211
Skin, n (%) (yes/no)	7/32 (17.9/82.1)	9/73 (11/89)	0.389	41/108 (27.5/72.5)	16/64 (20/80)	0.262
Mental health, n (%) (yes/no)	29/10 (74.4/25.6)	47/35 (57.3/42.7)	0.075	82/67 (55/45)	46/34 (57.5/42.5)	0.781
Respiratory, n (%) (yes/no)	8/31 (20.5/79.5)	16/66 (19.5/80.5)	0.089	29/120 (19.5/80.5)	18/62 (22.5/77.5)	0.609
Other symptoms, n (%) (yes/no)	90/52 (60.4/39.6)	49/31 (61.3/38.8)	0.900	21/18 (53.8/46.2)	40/42 (48.8/51.2)	0.698
T3	**Women**			**Men**		
	PD-SA (28)	**PD-NSA (80)**	**p**	**PD-SA (137)**	**PD-NSA (79)**	**p**
Gastrointestinal, n (%) (yes/no)	17/11 (60.7/39.3)	48/32 (60/40)	0.947	79/58 (57.7/42.3)	62/18 (77.5/22.5)	0.003
Pain, n (%) (yes/no)	22/6 (78.6/21.4)	55/25 (68.8/31.3)	0.467	68/69 (49.6/50.4)	44/36 (55/45)	0.483
Urinary, n (%) (yes/no)	16/12 (57.1/42.9)	42/38 (52.5/47.5)	0.826	83/54 (60.6/39.4)	57/23 (71.3/28.7)	0.141
Postural hypotension, n (%) (yes/no)	2/26 (7.1/92.9)	7/72 (8.9/91.1)	0.775	10/127 (7.3/92.7)	12/67 (15.2/84.8)	0.100
Sleep, n (%) (yes/no)	18/10 (64.3/35.7)	51/28 (64.6/35.4)	0.979	87/50 (63.5/36.5)	57/23 (71.3/28.7)	0.297
Fatigue, n (%) (yes/no)	15/13 (53.6/46.4)	46/33 (58.2/41.8)	0.825	60/77 (43.8/56.2)	49/31 (61.3/38.8)	0.017

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Apathy, n (%) (yes/no)	4/24 (14.3/85.7)	27/53 (33.8/66.3)	0.056	28/109 (20.4/79.6)	31/49 (38.8/61.3)	0.004
Attention/Memory, n (%) (yes/no)	9/19 (32.1/67.9)	42/37 (53.2/46.8)	0.078	51/86 (37.2/62.8)	44/36 (55/45)	0.016
Skin, n (%) (yes/no)	3/25 (10.7/89.3)	9/70 (11.4/88.6)	0.922	39/98 (28.5/71.5)	15/65 (18.8/81.3)	0.143
Mental health, n (%) (yes/no)	18/10 (64.3/35.7)	45/34 (57/43)	0.655	70/67 (51.1/48.9)	48/32 (60/40)	0.258
Respiratory, n (%) (yes/no)	3/25 (10.7/89.3)	10/69 (12.7/87.3)	0.784	18/118 (13.2/86.8)	13/67 (16.3/83.8)	0.552
Other symptoms, n (%) (yes/no)	15/13 (53.6/46.4)	40/39 (50.6/49.4)	0.829	84/53 (61.3/38.7)	54/25 (68.4/31.6)	0.308

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Reasons for lack of sexual activity in PD-NSA

	T1		T2		T3	
	W (72)	**M (83)**	**W (82)**	**M (80)**	**W (80)**	**M (79)**
By choice, n (%)	5 (7)	1 (1.2)	6 (7.3)	1 (1.2)	4 (5)	6 (7.5)
Age, n (%)	5 (7)	6 (7.2)	4 (4.8)	10 (12.5)	6 (7.5)	8 (10.1)
Widow/Widower, n (%)	12 (16.6)	7 (8.4)	15 (18.2)	10 (12.5)	8 (10)	11 (13.9)
Issues with parkinsonism, n (%)	3 (4.1)	9 (10.8)	1 (1.2)	16 (20)	11 (13.7)	6 (7.5)
Issues with the partner, n (%)	0 (0)	3 (3.6)	0 (0)	3 (3.7)	2 (2.5)	2 (2.5)
Issues of the partner, n (%)	0 (0)	1 (1.2)	4 (4.8)	5 (6.2)	6 (7.5)	3 (3.7)
Other reasons, n (%)	2 (2.7)	11 (13.2)	5 (6)	13 (16.2)	15 (18.7)	0 (0)
Non reponders, n (%)	50 (69.5)	45 (54.2)	47 (57.3)	22 (27.5)	28 (35)	43 (54.4)

More than one answer possible. Abbreviations: M = men; PD-NSA = Parkinson's disease without active sexual life; W = women; T1 = baseline visit;

T2 = first follow up visit; T3 = second follow up visit.

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Results

Since we do not have a specific measure for sexual dysfunction to be added as a covariate, we repeated all the analysis excluding all those patients replying “yes” to any related questions of the gender-tailored semistructured interview detailed in Table 2 (questions from 3 to 9 for men and from 3 to 7 for women). This process determined the exclusion of 10 women and 57 men.

Multivariable mixed-effects logistic models showed that, among NMS domains, gastrointestinal (OR 0.65, 95% CI 0.25 – 0.96, P = 0.007) and apathy (OR 0.62, 95% CI 0.18 – 0.73, P = 0.002) were less likely to be associated with PD-SA in men. In addition, sexual activity was less frequently associated with treatment with L-dopa (OR 0.75, 95% CI 0.23 – 0.95, P = 0.027). No association emerged for women.

Multivariable mixed-effects linear models showed that sexual activity in men was associated with less severe motor disability (UPDRS-III, coefficient -2.312, 95%CI -3.879 to -1.521, p=0.009), better HR-QoL (PDQ-39, coefficient -22.789, 95%CI -40.632 to -2.006, p=0.029; EQ-VAS, coefficient 0.080, 95% CI 0.023 to 0.138, P = 0.007), lower depression scores (HAM, coefficient -1.329, 95%CI -2.678 to -0.408, p=0.008). No association was shown in women (UPDRS-III, coefficient -4.44, 95%CI -9.595 to 0.696, p=0.090, PDQ-39, coefficient -11.0901, 95% CI -67.858 to 45.67, p=0.702; EQ-VAS, coefficient 0.022, 95% CI -0.149 to 0.104, p = 0.737; HAM, coefficient -0.654, 95%CI -2.643 to 1.335, p=0.519).

MMSE was associated with PD-SA neither in men (coefficient -0.367, 95%CI -0.954 to 0.431, p=0.517) nor women (coefficient -0.678, 95%CI -1.987 to 0.401, p=0.213).

The associations between sexual activity and motor, non motor outcomes as well as with quality of life were confirmed for men when excluding patients reporting sexual dysfunction.

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