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# Determinants of Sexual Dysfunction in Male and Female Patients with Parkinson's Disease

Murat İlhan Atagün[1], Birgül Atmaca[2], Feriha Özer[3], Serkan Özben[2], Raziye Tıraş[2], Sibel Çetin[2], Mehmet Fazıl Genç[2]

[1]*Assist. Prof. Dr., Namık Kemal University, Medical School, Department of Psychiatry, Tekirdağ - Turkey*
[2]*Neurologist, Haseki Training and Research Hospital, Department of Neurology, Istanbul - Turkey*
[3]*Assoc. Prof. Dr., Haseki Training and Research Hospital, Department and Movement Disorders Outpatient Clinic, Istanbul - Turkey*

**ABSTRACT**

Determinants of sexual dysfunction in male and female patients with parkinson's disease

**Objective:** Due to the complex nature of Parkinson's disease (PD) and distinct sexual physiologies, male and female patients might have different patterns of sexual dysfunction (SD) in PD. The aim of this study was to assess determinants of SD in female and male patients with PD.

**Methods:** Seventy nine outpatients with idiopathic PD (46 male, 33 female; mean age: 67.51±8.27) were recruited between December 2007 and February 2011. Unified Parkinson's Disease Rating Scale and Hoehn–Yahr stages, Hamilton depression and anxiety scales, Mini-Mental State Examination and Arizona Sexual Experiences scale were the measures.

**Results:** Determinants of SD in the whole group were age and anxiety. Age at disease onset and anxiety designated SD in female group, while age and severity of motor symptoms designated SD in male group.

**Conclusion:** Both in males and females, gonadal steroids decline with advancing age. Dopamine has role in desire, erection, reward-seeking behavior phases of sexuality. Dopamine depletion may cause SD with its dual effects, including erectile dysfunction as well as motor disturbances in PD in male patients. Anxiety effect females more than males due to affected body image and perception of the self.

**Key words:** Parkinson's disease, sexual dysfunction, dopamine, old age

**ÖZET**

Parkinson hastalığında cinsel işlev bozukluklarının kadın ve erkek hastalarda belirleyicileri

**Amaç:** Parkinson hastalığının (PH) karmaşık doğası ve farklı cinsel fizyolojileri nedeni ile kadın ve erkek hastalar, farklı biçimlerde cinsel işlev bozukluğu yaşıyor olabilirler. Bu çalışmada amaç, Parkinson hastası kadın ve erkeklerde cinsel işlev bozukluklarının belirleyicilerinin araştırılmasıdır.

**Yöntem:** İdiyopatik PH olan ve ayakta tedavi gören 79 hasta (yaş ortalaması 67.51±8.27 olan 46 erkek, 33 kadın) Aralık 2007 ile Şubat 2011 tarihleri arasında çalışmaya alındı. Bileşik Parkinson Hastalığı Derecelendirme Ölçeği, Hoehn-Yahr Evrelemesi, Hamilton Depresyon ve Anksiyete Derecelendirme Ölçekleri, Kısa Akıl Muayenesi ve Arizona Cinsel Yaşantılar Ölçekleri ölçüm aygıtlarıydı.

**Bulgular:** Yaş ve anksiyete çalışmaya dahil edilen tüm hastalarda, hastalık başlangıç yaşı ve anksiyete kadın hastalarda, yaş ve motor semptomların şiddeti erkek hastalarda cinsel işlev bozukluklarının belirleyicileriydi.

**Sonuç:** Gonadal steroidler yaşın ilerlemesiyle birlikte, hem erkeklerde hem kadınlarda azalır. Dopamin cinselliğin; istek, sertleşme ve ödül arama davranışı gibi birimlerinde görev alır. Dopamin azalması, erkek hastalarda sertleşme bozukluğuna neden olur ve motor işlevleri etkileyerek, cinsel işlev bozukluğuna yol açar. Anksiyete, kendini algılama ve etkilenmiş beden imajına bağlı olarak gelişir ve erkeklere göre kadınları daha fazla etkiler.

**Anahtar kelimeler:** Parkinson hastalığı, cinsel işlev bozukluğu, dopamin, yaşlılık

Address reprint requests to / Yazışma adresi:
Assist. Prof. Dr. Murat İlhan Atagün,
Medical School of Namık Kemal University,
Department of Psychiatry, Tekirdağ - Turkey

Phone / Telefon: +90-282-250-5730

E-mail address / Elektronik posta adresi:
miatagun@nku.edu.tr

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## INTRODUCTION

Neurodegenerative process of Parkinson's Disease (PD) spreads to affect the mesocortical, mesolimbic, and autonomic central nervous system regions with progression of the disease, and patients frequently develop non-motor disabling symptoms, including sexual dysfunction (SD), which has been only limitedly studied (1). Neurological diseases including PD may deteriorate sexual functions in elderly population (2-8). Sexuality is coordinated by neurologic, vascular and endocrine systems (9), thus neurological disorders can change the processing of sexual stimuli to preclude arousal and to increase desire. Advance in age, severity of the disease and depression were the major determinants in previous studies (5-8).

Sexual physiology differs between genders and advance in age affects genders in different ways. The difference between men and women in ageing and sex is that women experience a quick transition with menopause in which hormonal changes will occur in a short period; and in men hormone changes occur gradually during a longer period. Distinct hormonal physiologies may also influence pathophysiology of PD. In females there is general agreement that gonadal steroids and exogenous estradiol promote striatal adaptation in the partially injured nigrostriatal dopaminergic pathway to protect against striatal dopaminergic neuron loss. In contrast, the body of evidence suggests that in males gonadal factors have negligible or even harmful effects (10-14). These protective effects of gonadal hormones may be the reason of the lower incidence of PD in women (15).

Moreover, male and female patients show different patterns of SD in PD (5,16-19). In females, SD manifests mainly as decreased arousal, difficulty in reaching orgasm and low orgasm satisfaction (5,16); whereas in males predominant signs are erectile dysfunction, premature ejaculation or loss of capacity to ejaculate (18,20). Welsh and colleagues (5) compared 27 female patients with PD with a healthy control group (age and marital status matched) and found that patients were less satisfied with their sexual activities. In a study designed to assess SD in Turkish patients with PD, Çelikel and colleagues (16) found reduced sexual drive and satisfaction with orgasm in women, but no difference in men. On the contrary, some studies reported a higher frequency of sexual problems in male patients (19,21). For instance, according to Brown and his colleagues (19), prevalence of SD in male patients was 65%, while 36% of female patients had SD.

Due to the complex nature of the disease, there are still ambiguities regarding SD in PD. It is aimed to investigate determinants of SD in male and female patients with PD in this study.

## METHODS

Seventy-nine outpatients (46 male, 33 female; mean age: 67.51±8.27, range: 46-85) with idiopathic PD were enrolled between December 2007 and February 2011. The local ethical committee approved the study and each participant has given a written informed consent. After initially obtaining socio-demographic data, Unified Parkinson's Disease Rating Scale (UPDRS) and Hoehn–Yahr (H&Y) stage during the on phase (22,23) were the tools to assess clinical characteristics of the disease. Hamilton Depression Scale (HAM-D) (24), Hamilton Anxiety Scale (HAM-A) (25) and standard Mini-Mental State Examination (MMSE) (26,27) were also used to assess depression, anxiety and cognitive impairments which may affect sexual functions. Due to insufficient motor ability to perform sexual activity and to obtain homogeneous groups, patients with H&Y stage 4 and 5 were excluded. Patients scoring less than 23 points on the MMSE were also excluded. Patients reporting urological or gynecological problems and patients ever used exogenous estrogen replacement therapy were excluded too.

Sexual functions were assessed with Turkish version of the Arizona Sexual Experiences Scale (ASEX), which has two parallel forms for both genders (28,29). ASEX is a 5-item, Likert-type self rating scale. Each item could be rated from 1 to 6 and total scores range between 5-30. Higher scores mean worse sexual functions. Two parallel forms differ in the third item: penile erection/vaginal lubrication (drive, arousal, penile erection/vaginal lubrication, ability to reach orgasm and satisfaction with orgasm).

For statistical analysis, SPSS for windows (version 13.0) was used. $p<0.05$ was accepted as significant. For categorical variables t test for continuous and Chi-square test for categorical variables were applied. Correlations between clinical and demographic characteristics and ASEX scores were evaluated with Pearson's correlation test. Three sets of linear regression analyses were run to obtain determinants of SD measured by ASEX total scores in the whole group, in female and male groups.

## RESULTS

Sociodemographic and clinical characteristics are presented in Table 1 and 2. Age (p=0.259), education (p=0.342, $\chi^2$=2.15), duration of the disease (p=0.319) and age at disease onset (p=0.099) did not differ between groups. Great majority of the participants had sexually active spouse, only four participants were single.

Sixty five patients were receiving levodopa medication and groups did not differ in terms of levodopa use rates (m/f: 36/29, p=0.27, $\chi^2$=1.21). Mean daily dose of levodopa was 416.7 milligrams (sd: ±335.4). 49 patients were receiving agonists and no difference was detected between groups (m/f: 30/19; p=0.49, $\chi^2$=0.48). Six male patients were receiving neuroleptic medications. 14 patients had benign prostate hypertrophy, 3 had malignancies, 1 had osteoporosis and 1 had hyperthyroidism. All of the female participants were postmenopausal and all disease onsets were after menopause. Nine patients

**Table 1: Socio-demographic and Clinical Characteristics of the Patients (Mean±SD)**

| | Whole Group (n=79) | Female Group (n=33) | Male Group (n=46) |
|---|---|---|---|
| **Age** | 67.41±8.12 | 66.18±7.04 | 68.28 ±8.78 |
| **Duration of the disease** | 7.3±4.77 | 7.94±4.8 | 6.85±4.75 |
| **Age at disease onset** | 60.1±8.46 | 58.24±7.57 | 61.43±8.89 |
| **UPDRS** | | | |
| Motor | 14.82±9.18 | 18.41±9.96 | 20.98±9.79 |
| Daily life | 6.18±4.52 | 8.18±4.8 | 9.61±4.51 |
| Cognition | 2.82±1.93 | 2.91±2.01 | 2.98±2.22 |
| Complications | 1.12±1.56 | 1.7±1.98 | 2.11±2.16 |
| Total | 24.85±13.84 | 31.04±15.2 | 35.48±14.69 |
| **MMSE** | 26.59±2.16 | 26.15±2.59 | 26.91±1.76 |
| **HAM-D** | 6.97±5.47 | 6.73±4.79 | 7.15±5.96 |
| **HAM-A** | 7.41±5.36 | 9.39±4.29 | 5.98±5.63 |
| **Levodopa dose** | 416.7±335.4 | 379.6±240.6 | 443.3±389.9 |
| **ASEX** | | | |
| Desire | 4.91±1.26 | 3.75±1.77 | 2.91±1.62 |
| Stimulation | 4.85±1.3 | 3.92±1.73 | 3.26±1.71 |
| Erection/Lubrication | 4.64±1.69 | 4.13±1.64 | 3.76±1.51 |
| Orgasm | 4.91±1.38 | 3.97±1.7 | 3.30±1.6 |
| Orgasm satisfaction | 4.88±1.45 | 4.04±1.71 | 3.43±1.64 |
| Total | 24.36±6.62 | 19.89±7.69 | 16.67±6.78 |

UPDRS: Unified Parkinson's Disease Rating Scale. MMSE: Mini Mental State Examination. HAM-D: Hamilton Depression Rating Scale. HAM-A: Hamilton Anxiety Rating Scale. ASEX: Arizona Sexual Experiences Scale

**Table 2: Socio-demographic and Clinical Characteristics (categorical variables)**

| | Whole Group (n=79) | Male Group (n=46) | Female Group (n=33) |
|---|---|---|---|
| **Education** | | | |
| Uneducated | 18 | 8 | 10 |
| Primary school | 48 | 29 | 19 |
| High school and university | 13 | 9 | 4 |
| **Marital status** | | | |
| Married/Single | 75/4 | 43/3 | 32/1 |
| **Number of patients using medications of** | | | |
| Levodopa | 65 | 36 | 29 |
| Agonist | 49 | 30 | 19 |
| **Hoehn-Yahr Stage** | | | |
| HY 1 | 21 | 12 | 9 |
| HY 2 | 45 | 26 | 19 |
| HY 3 | 13 | 8 | 5 |

reported family history of PD and 6 reported family history of essential tremor. Patients with prostate hypertrophy (n=14) were compared to patients without prostate hypertrophy (n=32) in terms of ASEX scores. No difference was detected between groups (for the total ASEX score, p=0.82, z=-0.23).

Arizona sexual experiences scale total score correlated with age (r=0.31, p=0.005), age at disease onset (r=0.25, p=0.027) and HAM-A score (r=0.36, p<0.001) in the whole group (Table 3). HAM-A score significantly correlated with HAM-D in the whole group (r=0.62, p<0.01). Cognition subscore UPDRS significantly correlated to HAM-A (r=0.36, p<0.01) and HAM-D (r=0.6, p<0.01) scores. Treatment complication subscore of UPDRS correlated with HAM-D score (r=0.28, p=0.014). No other significant correlation was detected between HAM-A and HAM-D scores to any subscore of UPDRS.

In the female group, ASEX total score correlated with age (r=0.41, p=0.018), age at disease onset (r=0.48, p=0.004) and anxiety score (r=0.49, p=0.004); whereas in the male group, ASEX total score correlated with age (r=0.46, p=0.001), age at disease onset (r=0.35, p=0.017), UPDRS total (r=0.5, p<0.001), motor (r=0.45, p=0.002), daily life (r=0.41, p=0.004) scores and mean daily levodopa dose (r=0.37, p=0.011) (Table 4). HAM-A score significantly correlated with HAM-D score in the male group (r=0.84, p<0.001), however in the female

**Table 3: Correlations of Arizona Sexual Experiences Scale Scores in the Whole Group**

| | Arizona Sexual Experiences Scale (ASEX) | | | | | |
|---|---|---|---|---|---|---|
| | **Total Score** | **Desire** | **Stimulation** | **Erection/ Lubrication** | **Orgasm** | **Orgasm Satisfaction** |
| **Age** | 0.31** | 0.27* | 0.2 | 0.32** | 0.27* | 0.32** |
| **Age at disease onset** | 0.25* | 0.23* | 0.15 | 0.21 | 0.26* | 0.25* |
| **Duration of the disease** | 0.09 | 0.05 | 0.07 | 0.18 | 0.01 | 0.1 |
| **HAM-D** | 0.05 | 0.04 | 0.03 | 0.04 | 0.05 | 0.1 |
| **HAM-A** | 0.36** | 0.31** | 0.33** | 0.23* | 0.34** | 0.32** |
| **MMSE** | -0.22 | -0.14 | -0.21 | -0.14 | -0.23* | -0.29** |
| **UPDRS** | | | | | | |
| Total score | 0.06 | -0.01 | 0.09 | 0.07 | 0.07 | 0.11 |
| Motor | 0.08 | 0.01 | 0.13 | 0.09 | 0.07 | 0.13 |
| Daily life | -0.01 | -0.05 | 0.01 | 0.01 | 0.01 | 0.02 |
| Cognition | 0.07 | 0.05 | 0.01 | 0.05 | 0.12 | 0.12 |
| Complication | -0.05 | -0.01 | -0.05 | -0.02 | -0.06 | -0.08 |
| **Levodopa dose** | 0.18 | 0.17 | 0.19 | 0.13 | 0.18 | 0.15 |

Spearman's Correlation test. r values. *p<0.05, **p<0.01; HAM-D: Hamilton Depression Scale; HAM-A: Hamilton Anxiety Scale; MMSE: Minimental State Examination; UPDRS: Unified Parkinson's Disease Rating Scale

**Table 4. Predictors of sexual dysfunction in groups**

| | Unstandardized Coefficients | | Standardized Coefficients | | |
|---|---|---|---|---|---|
| | **B** | **Standard Error** | **Beta** | **t** | **p** |
| **Whole Group** | | | | | |
| Age | 0.29 | 0.1 | 0.31 | 3.02 | 0.003 |
| HAM-A Score | 0.5 | 0.15 | 0.35 | 3.43 | <0.001 |
| **Female Group** | | | | | |
| Age at Disease Onset | 0.34 | 0.13 | 0.39 | 2.66 | 0.012 |
| HAM-A Score | 0.62 | 0.23 | 0.4 | 2.72 | 0.011 |
| **Male Group** | | | | | |
| Age | 0.29 | 0.1 | 0.37 | 3.05 | 0.004 |
| UPDRS Total Score | 0.2 | 0.06 | 0.42 | 3.47 | <0.001 |

Linear regression analysis. Dependent Variable: Arizona Sexual Experiences Scale Total Score; Independent Variables: Age, age at disease onset, duration of the disease, Hamilton Anxiety Rating Scale (HAM-A) score, Hamilton Depression Rating Scale (HAM-D) score, Minimental State Examination score, total, motor, daily life, cognition and complication subscores of Unified Parkinson's Disease Rating Scale (UPDRS), Levodopa dose. In the whole group: F= 10.702; df: 2.76; Adjusted $R^2$: 0.199. In the female group: F= 9.424; df: 2.30; Adjusted $R^2$: 0.345. In the male group: F= 13.338; df: 2.43; Adjusted $R^2$: 0.354

group HAM-A and HAM-D scores did not show any correlation (r=0.26, p=0.122). Only cognition subscore of UPDRS showed significant correlation with HAM-A (r=0.58, p<0.001) and HAM-D (r=0.69, p<0.001) scores in the male group. No other subscores of UPDRS showed any correlation in the male group. In the female group, HAM-D score correlated to UPDRS cognition (r=0.43, p=0.014) and treatment complication (r=0.49, p=0.004), but HAM-A score did not show any correlation with UPDRS scores. Duration of the disease correlated to HAM-D scores (r= -0.24, p=0.035) but not HAM-A scores. No significant correlation was detected between HAM-A and HAM-D scores and age and age at disease onset.

Determinants of SD (ASEX total score) in the whole group were age (p=0.003) and anxiety (p=0.001) in linear regression analysis (F=10.702; df: 2.76; Adjusted $R^2$: 0.199) (Table 4). In the female group, determinants of SD were age at disease onset (p=0.012) and anxiety (p=0.011) (F=9.424; df: 2.30; Adjusted $R^2$: 0.345). In the male group, determinants of SD were age (p=0.004) and severity of motor symptoms (p<0.001) (F=13.338; df: 2.43; Adjusted $R^2$: 0.354).

## DISCUSSION

Both in males and females, gonadal steroids decline with advancing age may cause SD. In a study with a large healthy sample (n=1455) most common reported problems in males were: lack of interest (65%), erectile dysfunction (90%), anxiety about performance (75%) and inability to climax (73%) (30). Levels of sex hormones and decrease with age of sex hormones may vary among different ethnic groups. SD may also be due to dopamine loss in PD. Dopamine has roles in desire, erection, reward-seeking behavior and sexuality. Dopamine replacement may improve these symptoms and this treatment may also cause the hypersexuality seen in some patients with PD (31).

Clinical and pathological differences between males and females in PD have been shown in many studies. Estrogen has several effects on dopamine neurotransmission (32). The amount of synaptic contacts is changed by the estrous cycle according to the estrogen levels. In addition, estrogen increases dopamine synthesis and release with many complex mechanisms, and inhibits dopamine reuptake. Also, estrogen has an effect on the expression of dopamine receptors in the basal ganglia. In addition, estrogen has been found to protect nigrostriatal neurons from toxins.

Patients with PD present anxiety symptoms with a frequency rate of 67% (33). Anxiety is shown to deteriorate quality of life in PD (34). Autonomic symptoms of anxiety, fatigue, tension in muscles, insomnia, vigilance and attention deficiency and agitation are some features of anxiety that may resemble some symptoms of PD such as akathisia or dyskinesia. Hamilton Anxiety Scale is an instrument to assess anxiety, however somatic symptoms are weighted heavily and that makes it difficult to distinguish symptoms of anxiety and symptoms of PD. Nevertheless, Krummer and colleagues (35) showed that HAM-A is a valid and reliable measure of anxiety in PD.

In contrast to previous studies reporting no correlation between SD and depression or anxiety in PD (3,5-7,19,36), anxiety levels (in the whole group and in the female group) predicted SD in this study. Cultural diversities may be influential on perception of sexuality. Women are reported to be more preoccupied with and influenced by the body image in PD (5). Furthermore with similar levels of disease severity, women perceive greater disability than men with PD (32). Higher disability perception and impaired body image may be the reason of higher rate of anxiety in female patients with PD in comparison to male patients, consistent with some previous studies (37,38).

Contradictory results have been reported whether anxiety is associated to motor symptoms in PD or not. It has been suggested in two studies that anxiety may cause worsening in motor symptoms in PD (33,39), while three studies found no relation between severity of motor symptoms and anxiety in PD (40-42). High levels of anxiety have also been reported to be associated to treatment complications such as dyskinesia or on/off fluctuations (39,43). In this study, we found a correlation between depression and treatment complications in the whole group and in female group; however, no significant correlation was detected between severity of motor symptoms and anxiety or depression.

Consistent with previous studies (4-6), motor functions predicted SD in male patients. Studies comparing subjects with physical disability and patients with PD in terms of SDs reported that there were no difference between groups (7,8), that may mean physical disability of the patients with PD is the reason of SD. Dopamine depletion may cause SD with its dual effects, including erectile dysfunction as well as motor disturbances in PD (1). Besides, with increasing severity of disabling physical illness, autonomic, limbic and neocortical association areas, such as frontal and temporal cortex may be compounded with functional deficits (30). Sexual functions correlated with severity of the illness and mean daily levodopa dose in male patients indicating a dopaminergic involvement in this study. However, SD may not necessarily arise solely from the neurodegenerative processes of PD. Several other disease-related factors, such as the psychosocial stress, burden of chronic illness, changed appearance, fatigue, relative immobility in bed, difficulty in fine finger movements, and lowered self-esteem associated with increasing loss of independence, may contribute substantially to SD (4).

Relatively small sample size is a limitation of this study. Cross-sectional design did not let to establish medication effects evidently. More detailed urologic/gynecologic anamnesis and examination would let to control other causes of SD. Longitudinal studies may provide more detailed data in different phases of the disease.

Central and peripheral physiology of sexual response has been clarified to some extent, but information about neuronal circuits implicated in sexual functions remains fragmentary. PD is a complex disease and has physical, psychological, neurobiological and pharmacological features. Multidisciplinary future researches including neurology, psychiatry, gynecology and endocrinology are required for SD in female patients with PD. Dopaminergic medication effects are needed to be further investigated with follow up researches particularly in male patients. In evaluation of SD, functional roles of dopamine on sexual physiology are of particular importance in PD. External dopaminergic agents may be imperfect sources of dopamine to supply the deficits in certain circuits employed for sexual functions in PD.

## REFERENCES

1. Fearnley JM, Lees AJ. Ageing and Parkinson's disease: substantia nigra regional selectivity. Brain 1991; 114:2283–2301.

2. Mulligan T, Retchin SM, Chinchilli VM, Bettinger CB. The role of aging and chronic disease in sexual dysfunction. J Am Geriatr Soc 1988; 36:520-524.

3. Koller WC, Vetere-Overfield B, Williamson A, Busenbark K, Nash J, Parrish D. Sexual dysfunction in Parkinson's disease. Clin Neuropharmacol 1990; 13:461-463.

4. Basson R. Sexuality and Parkinson's disease. Parkinsonism Relat Disord 1996; 2:177-185.

5. Welsh M, Hung L, Waters CH. Sexuality in women with Parkinson's disease. Mov Disord 1997; 12:923-927.

6. Wermuth L, Stenager E. Sexual problems in young patients with Parkinson's disease. Acta Neurol Scand 1995; 91:453-455.

7. Lipe H, Longstreth WT Jr, Bird TD, Linde M. Sexual function in married men with Parkinson's disease compared to married men with arthritis. Neurology 1990; 40:1347-1349.

8. Jacobs H, Vieregge A, Vieregge P. Sexuality in young patients with Parkinson's disease: a population based comparison with healthy controls. J Neurol Neurosurg Psychiatry 2000; 69:550-552.

9. Drench ME, Losee RH. Sexuality and sexual capacities of elderly people. Rehabil Nurs 1996; 21:118-123.

10. Brann DW, Dhandapani K, Wakade C, Mahesh VB, Khan MM. Neurotrophic and neuroprotective actions of estrogen: basic mechanisms and clinical implications. Steroids 2007; 72:381-405.

11. Craig MC, Murphy DG. Estrogen: effects on normal brain function and neuropsychiatric disorders. Climacteric 2007; 10 (Suppl.2):97-104.

12. Lynch WJ, Roth ME, Carroll ME. Biological basis of sex differences in drug abuse: preclinical and clinical studies. Psychopharmacology (Berl) 2002; 164:121-137.

13. McEwen BS, Alves SE. Estrogen actions in the central nervous system. Endocr Rev 1999; 20:279-307.

14. Toran-Allerand CD. Estrogen and the brain: beyond ER-alpha, ER-beta and 17 beta-estradiol. Ann N Y Acad Sci 2005; 1052:136-144.

15. Rajput AH, Offord KP, Beard CM, Kurland LT. Epidemiology of parkinsonism: incidence, classification, and mortality. Ann Neurol 1984; 16:278-282.

16. Celikel E, Ozel-Kizil ET, Akbostancı MC, Cevik A. Assessment of sexual dysfunction in patients with Parkinson's disease: a case-control study. Eur J Neurol 2008; 15:1168-1172.

17. Sakakibara R, Shinotoh H, Uchiyama T, Sakuma M, Kashiwado M, Yoshiyama M, et al. Questionnaire-based assessment of pelvic organ dysfunction in Parkinson's disease. Auton Neurosci 2001; 92:76-85.

18. Lucon M, Pinto AS, Simm RF, Haddad MS, Arap S, Lucon AM, et al. Assessment of erectile dysfunction in patients with Parkinson's disease. Arq Neuropsiquiatr 2001; 59:559-562.

19. Brown RG, Jahanshahi M, Quinn N, Quarrington B. Sexual function in patients with Parkinson's disease and their partners. J Neurol Neurosurg Psychiatry 1990; 53:480-486.

20. Singer C, Sanchez-Ramos J, Weiner WJ, Ackerman M. Sexual dysfunction in parkinsonian males. Neurology 1989; 3:145.

21. Macht M, Schwarz R, Ellgring H. Patterns of psychological problems in Parkinson's disease. Acta Neurol Scand 2005; 111:95-101.

22. Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. Neurology 1967; 17:427-442.

23. Fahn S, Elton R. Unified Parkinson's disease rating scale: In Fahn S, Marsoen CD, Calne D, Goldstein M (editors). Recent developments in Parkinson's disease. New Jersey: MacMillian Healthcare Information, 1987, 153-163.

24. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960; 23:56-62.

25. Hamilton M. The assessment of anxiety states by rating. Br J Med Psychol 1959; 32:50-55.

26. Folstein MF, Folstein S, Mc Hugh PR. 'Mini mental state: a practical method for grading the cognitive state of patient for the clinician. J Psych Res 1975; 12:189-198.

27. Güngen C, Ertan T, Eker E, Yaşar R, Engin F. Reliability and validity of the standardized mini mental state examination in the diagnosis of mild dementia in Turkish population. Turk Psikiyatri Derg 2002; 13:273-181.

28. McGahuey CA, Gelenberg AJ, Laukes CA, Moreno FA, Delgado PL. The Arizona Sexual Experience Scale (ASEX): Reliability and validity. J Sex Marital Ther 2000; 26:25-40.

29. Soykan A. The reliability and validity of Arizona sexual experiences scale in Turkish ESRD patients undergoing hemodialysis. Int J Impot Res 2004; 16:531-534.

30. Lindau S, Schumm P, Laumann EO, Levinson W, O'Muircheartaigh CA, Waite LJ. A study of sexuality and health among older adults in the United States. New Engl J Med 2007; 357:762-774.

31. Atagün İ, Mutlu A, Özer F, Atmaca B, Çetin S. Relationship between dopaminergic treatment and sexual behavior in Parkinson's disease. Journal of Parkinson's Disease and Movement Disorders 2010; 13:29-35.

32. Shulman LM. Gender differences in Parkinson's disease. Gend Med 2007; 4:8-18.

33. Chagas MHN, Tumas V, Loureiro SR, Correa ACR, Nakabayashi TIK, Crippa JAS. Does the association between anxiety and Parkinson's disease really exist? A literature review. Curr Psychiatry Rev 2009; 5:29-36.

34. Rahman S, Griffin HJ, Quinn NP, Jahanshahi M. Quality of life in Parkinson's disease: the relative importance of the symptoms. Mov Disord 2008; 23:1428-1434.

35. Krummer A, Cardoso F, Teixeria AL. Generalized anxiety disorder and the Hamilton Anxiety Rating Scale in Parkinson's disease. Arq Neuropsiquiatr 2010; 68:495-501.

36. Yu M, Roane DM, Miner CR, Fleming M, Rogers, JD. Dimensions of sexual dysfunction in Parkinson's disease. Am J Geriatr Psychiatry 2004; 12:221-226.

37. Jenkins RB, Groh RH. Mental symptoms in Parkinsonian patients treated with L-dopa. Lancet 1970; 2:177-179.

38. Tandberg E, Larsen JP, Aarsland D, Cummings JL. The occurrence of depression in Parkinson's disease. A community-based study. Arch Neurol 1996; 53:175-179.

39. Siemers ER, Shekhar A, Quaid K, Dickson H. Anxiety and motor performance in Parkinson's disease. Mov Disord 1993; 8:501-506.

40. Stein MB, Heuser IJ, Juncos JL, Uhde TW. Anxiety disorders in patients with Parkinson's disease. Am J Psychiatry 1990; 147:217-220.

41. Menza MA, Robertson-Hoffman DE, Bonapace AS. Parkinson's disease and anxiety: comorbidity with depression. Biol Psychiatry 1993; 34:465-470.

42. Hughes TA, Ross HF, Mindham RH, Spokes EG. Mortality in Parkinson's disease and its association with dementia and depression. Acta Neurol Scand 2004; 110:118-123.

43. Tumas V, Rodrigues GG, Farias TL, Crippa JA. The accuracy of diagnosis of major depression in patients with Parkinson's disease: a comparative study among the UPDRS, the geriatric depression scale and the Beck depression inventory. Arq Neuropsiquiatr 2008; 66:152-156.

44. Braak H, Bohl JR, Müller CM, Rüb U, de Vos RA, Del Tredici K. Stanley Fahn Lecture 2005: The staging procedure for the inclusion body pathology associated with sporadic Parkinson's disease reconsidered. Mov Disord 2006; 21:2042-2051.

45. Simpson ER. Genetic mutations resulting in estrogen insufficiency in the male. Mol Cell Endocrinol 1998; 145:55-59.