Sleep and Breathing (2019) 23:543–550
https://doi.org/10.1007/s11325-018-1729-0

SLEEP BREATHING PHYSIOLOGY AND DISORDERS • ORIGINAL ARTICLE

Laryngopharyngeal motor dysfunction and obstructive sleep apnea in Parkinson's disease

Christianne Martins Corrêa Silva Bahia[1] · João Santos Pereira[1] · Agnaldo José Lopes[2]

Received: 27 May 2018 / Revised: 18 September 2018 / Accepted: 21 September 2018 / Published online: 6 October 2018

Abstract

Purpose Obstructive sleep apnea (OSA) is a common sleep disorder in Parkinson's disease (PD), but the relationship between these two conditions remains uncertain. Upper airway (UA) dysfunction in PD is well documented in some patients and is believed to be a reflex of the motor involvement of laryngopharyngeal muscles. The aim of this study is to determine whether UA dysfunction and laryngopharyngeal motor dysfunction (LMD) are involved in the obstructive phenomenon of OSA in PD.

Methods Forty-eight PD patients underwent polysomnography for OSA diagnosis, functional evaluation of the UA by spirometry and a clinical protocol for analysis of laryngopharyngeal muscles and physical examination.

Results Thirty-one participants (64.6%) fulfilled the criteria for OSA according to the International Classification of Sleep Disorders- third edition (at least respiratory disturbance index of five or higher per hour of sleep plus specific symptoms). UA obstruction was observed in 25% of participants and LMD in 60.4%. Among the clinical indicators of LMD, hypophonia was the most common (58.3%). Participants with LMD had a threefold greater chance of presenting with OSA than those without LMD did (OR = 3.49; 95% CI, 1.01–12.1; $p = 0.044$). Individuals with LMD had more UA dysfunction (37.9 vs 10.5%, $p = 0.037$), higher scores on UPDRS III (20 vs 15, $p = 0.0005$) and the Hoehn-Yahr scale (2.5 vs 2.0, $p = 0.008$), and higher frequencies of postural changes (51.7 vs 21.1%, $p = 0.033$) and motor phenomena (65.5 vs 31.6%, $p = 0.021$). Obesity, snoring, neck circumference, and the Mallampati score did not correlate with OSA in PD.

Conclusion LMD should be considered a factor that is involved in the obstructive phenomenon of UA in patients with OSA and PD.

Keywords Parkinson's disease · Laryngopharyngeal motor dysfunction · Upper airway · Obstructive sleep apnea · Spirometry · Mallampati score

Introduction

Sleep disorders are part of the nonmotor symptom complex in Parkinson's disease (PD) [1]. Unlike other sleep disorders, such as insomnia, excessive daytime sleepiness (EDS), and rapid eye movement (REM) sleep behavior disorder, which have mechanisms linked to the neurodegenerative process itself and/or side effects of drugs used in the treatment of PD [2, 3], the relationship between PD and obstructive sleep apnea (OSA) remains uncertain. OSA is potentially just a comorbidity of PD as both conditions are more prevalent in older populations [4, 5]. However, there are reasons why the obstructive phenomenon of OSA in PD may include the participation of particular mechanisms that differ from the classical risk factors described in the general population. Commonly, parkinsonian apneics do not suffer from obesity [6], which is considered a major risk factor for OSA [7]. Moreover, parkinsonians have a high prevalence of upper airway (UA) obstruction and dysfunction, as shown by spirometry (24 to 65%) [8–10], which is potentially modifiable by the use of antiparkinsonian drugs [11].

The pathophysiology of UA obstruction in PD is not yet fully understood. UA patency is maintained by laryngopharyngeal muscles such as the palatal muscles, extrinsic muscles of the tongue, and hyoid muscles. These dilator muscles are assisted by the pharyngeal constrictors and postural muscles of the head and neck, which help in

✉ Christianne Martins Corrêa Silva Bahia
christianne.silva@uerj.br

[1] Movement Disorder Sector, Neurology Unit, Pedro Ernesto University Hospital, State University of Rio de Janeiro, Av. 28 de setembro, 77, Vila Isabel, Rio de Janeiro 20550-031, Brazil

[2] Rehabilitation Sciences Post-Graduation Program, Augusto Motta University Center, Rio de Janeiro, Brazil

sustaining the UA wall and preventing its collapse [12]. Therefore, proper functioning of the laryngopharyngeal musculature is fundamental in maintaining UA patency. Motor changes caused by PD may involve the laryngopharyngeal musculature [8–11] and cause UA obstruction. Peripheral neuropathy caused by alpha-synuclein accumulation in the vagus nerve and its pharyngeal branches [13], which is important in motor innervation of the laryngeal, pharyngeal, and some palatal muscles, may be another possible mechanism.

Laryngopharyngeal musculature motor dysfunction (LMD) may be evidenced clinically by the presence of hypophonia, which occurs due to a defect in movement of the vocal cords by the thyroarytenoid and cricoarytenoid muscles [12, 14]. Some methods for the clinical evaluation of this musculature include tongue protrusion (genioglossus muscle), elevation of the palate (palate elevator and soft palate tensor muscles), and complex actions, such as coughing, clearing one's throat, and swallowing, which require adequate coordination between the various muscles that control the opening and closing of the glottis [12].

In PD, the presence of OSA has been related to the degree of motor impairment in some studies [15, 16], while others have found no such association [17, 18]. Therefore, establishing whether LMD is involved in the pathophysiology of OSA in PD could open new horizons for the diagnosis and treatment of OSA in PD. Given the controversy surrounding the subject in the literature, the objective of this study is to evaluate whether changes that affect the laryngopharyngeal musculature and UA during the course of PD are important in regard to an increased risk of OSA.

Methods

The study included 48 participants with PD. The sample was selected by convenience after applying the inclusion and exclusion criteria. All volunteers were referred to neurology clinics in the state of Rio de Janeiro specializing in movement disorders. The main clinic was the Pedro Ernesto University Hospital where the study was conducted. The study was approved by the institutional research ethics committee. The inclusion criterion was a clinical diagnosis of PD, according to the UK Parkinson's Disease Society's Brain Bank Clinical Diagnostic Criteria for Idiopathic PD [19]. The exclusion criteria were as follows: chronic obstructive pulmonary disease or asthma requiring medication, current pneumonia, history of lobectomy surgery, chronic kidney failure undergoing dialysis, decompensated congestive heart failure, stroke history with sequelae, history of brain surgery, dementia, hallucinations and severe psychomotor agitation, current use of benzodiazepines, micrognathia and retrognathia, diagnosis of OSA prior to diagnosis of PD, and any condition that would prevent the tests necessary for conducting the study. After participant selection, evaluations were performed in the following stages: clinical evaluation, polysomnography, and spirometry.

Clinical evaluation

Data collection was performed, which included sex, age, skin color [20], PD duration, medication used, levodopa equivalent dose [21], presence of motor fluctuations ("on-off," "delayed-on," "wearing-off," dyskinesias or "freezing"), the presence of EDS, snoring, nocturia, hypertension, and diabetes. EDS was considered if there were complaints or a score greater than 10 on the Epworth Sleepiness Scale [22]; snoring was established according to the partner's account or technical recording during polysomnography; nocturia was considered when the participant urinated twice or more per night; hypertension and diabetes were considered when the participant used specific drugs to treat these conditions.

The Hoehn-Yahr scale (H-Y) and Unified Parkinson's Disease Rating Scale Part III (UPDRSIII) were then applied. Physical examination comprised inspection of the oral cavity and recording of the Mallampati index, measurement of the body mass index (BMI), neck circumference, and postural evaluation of the trunk and neck. A protocol for the clinical evaluation of laryngopharyngeal musculature motor function was developed and applied based on existing neurophysiological knowledge [12, 14]. Participants with at least one of the following symptoms were considered to have LMD: (a) hypophonia in spontaneous speech or in increasing tone of voice when asked, (b) difficulty in protruding at least one third of the tongue, (c) difficulty in coughing voluntarily, (d) difficulty in clearing the throat voluntarily, and (e) difficulty in elevating the palate during open-mouth inspection and vocalization of the /ah/ phoneme.

Polysomnography

After clinical evaluation, all participants underwent type 1 polysomnography for the diagnosis of OSA. On the day of the test, all patients took the last dose of antiparkinsonian medication before 7 pm. Patients who take bedtime medication were recommended to anticipate their medication instead of skipping it; thus, the total dosage of daily antiparkinsonian medication was unchanged on the day of exam. The test was started between 10 pm and 11 pm as this is considered the period in which the medication's effect is lowest. The minimum recording duration was 6 h, and the test was performed and interpreted according to standards set in the American Academy of Sleep Medicine's manual [23]. The diagnosis of OSA and its classification followed the criteria recommended by the latest version of the International Classification of Sleep Disorders (ICSD-3) [24].

Spirometry

After polysomnography was complete, at approximately 7 am, the participants underwent spirometry without taking their usual morning dosage of antiparkinsonian drugs. This period of approximately 12 h without the use of antiparkinsonian medication ("off") aimed to minimize the effect of these drugs on the pulmonary function test (PFT). A Collins Plus PFTs System® (Warren E. Collins, Inc., Braintree, MA, USA) apparatus was used. All PFTs met the American Thoracic Society (ATS) criteria [25]. The spirometry results were expressed as percentages of the value predicted for the Brazilian population [26].

The following parameters were obtained: forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), FEV_1/FVC ratio, FEV_1/forced expiratory volume in the first 30 s ($FEV_{0.5}$) ratio, peak inspiratory flow (PIF), peak expiratory flow (PEF), FEV_1/PEF ratio, forced expiratory flow during the middle half of the FVC ($FEF_{25–75\%}$), forced expiratory flow at 50% of FVC ($FEF_{50\%}$), forced inspiratory flow at 50% of FVC ($FIF_{50\%}$), and $FEF_{50\%}/FIF_{50\%}$ ratio, along with an analysis of the presence of flow oscillations in the inspiratory loop of the flow-volume curve. Oscillations were considered to occur if there were regular consecutive accelerations and decelerations in the inspiratory loop superimposed onto the flow-volume curve (flutter-type respiratory pattern) or abrupt and irregular changes in the inspiratory loop flow, often reaching zero and indicating intermittent closure of the UA [8].

For the definition of UA obstruction, the same criteria as those in Herer et al.'s [11] study were used, which defined obstruction as the presence of four of the six following criteria: (a) abnormal aspect of the flow-volume curve (flow oscillations), (b) PIF < 3 L/s, (c) FEV_1/PEF ratio > 8.5 ml/L/min, (d) $FEV_1/FEV_{0.5}$ ratio > 1.5, (e) $FEF_{50\%}/FIF_{50\%}$ ratio > 1, and (f) $PEF/FEF_{50\%}$ ratio < 2. In addition to the obstruction criteria, the presence of UA dysfunction was evaluated by spirometry using the following most characteristic parameters: presence of altered flow-volume curve and $FEF_{50\%}/FIF_{50\%} > 1$.

Statistical analysis

Descriptive statistics were performed on the sample demographics. The following were calculated: mean and standard deviation; median and interquartile range (Q1–Q3); odds ratio (OR); 95% confidence interval (95% CI); and p value to evaluate the associations between clinical, spirometric, and polysomnographic variables and the presence of OSA and LMD. The χ^2 test was used for categorical data, and the Mann-Whitney test was used for numeric data. Fisher's exact test was used instead of the χ^2 test when the subgroup sample size was small. The level of statistical significance adopted was 5%. Statistical analysis was performed using SAS® System statistical software, version 6.11 (SAS Institute, Inc., Cary, NC, USA).

Results

The sample comprised 48 participants, predominantly male (85.4%), with a mean age of 63 ± 10.3 years, a mean PD duration of 7.7 ± 4.2 years, and a mean UPDRS III score of 21 ± 11.6. The OSA criteria were met by 31 patients (64.6%), and most had the mild form (43.8%). The spirometric UA obstruction criteria were observed in 25% of participants ($n = 12$). According to the established clinical criteria, LMD was found in 29 patients (60.4%), and the main change was hypophonia (58.3%). Table 1 shows the main clinical, spirometric, and polysomnographic characteristics of participants included in the study.

The "OSA" and "without OSA" groups showed no significant differences in PD-related characteristics (PD duration, UPDRS III score, H-Y staging, levodopa equivalent dose, the presence of motor phenomena, or postural neck or trunk changes). Moreover, no significant differences were found in pulmonary function and the presence of UA obstruction and dysfunction parameters between the groups. The groups showed no significant differences in the clinical variables classically associated with OSA (age, male sex, obesity, snoring, EDS, nocturia, diabetes, neck circumference > 40 cm, and Mallampati indices III and IV). However, in the "OSA" group, 71% ($n = 22$) of participants had LMD, while in the "without OSA" group, 41.2% had LMD ($n = 7$). The presence of LMD determined a threefold increased chance of a diagnosis of OSA (OR: 3.49, 95% CI 1.01–12.1, $p = 0.044$; see Table 2).

The most prevalent LMD-defining clinical change in both groups was hypophonia, followed by impaired tongue protrusion. Figure 1 shows the frequency of LMD symptoms in the groups with and without OSA.

Participants with LMD had more UA dysfunction (37.9 vs 10.5%, $p = 0.037$) according to spirometry, higher UPDRS III scores (20 vs 15, $p = 0.0005$), higher H-Y scale scores (2.5 vs 2.0, $p = 0.008$), longer disease duration (8.7 vs 6.2 years, $p = 0.044$), and greater frequencies of postural trunk and neck changes (51.7 vs 21.1%, $p = 0.033$) and motor phenomena (65.5 vs 31.6%, $p = 0.021$) than those without LMD did (Table 3).

Discussion

OSA is common in PD, with a frequency ranging between 27 and 60% [15, 16, 18]. The frequency found in this study was slightly higher, likely due to the sample composition, which included a predominance of males with a mean age of approximately 60. These characteristics are associated with a higher

Table 1 Main clinical, spirometric, and polysomnographic features of all participants

Variable	*n*	%
Clinical		
Sex		
Male	41	85.4
Female	7	14.6
Skin color (IBGE)		
White	18	37.5
Brown	25	52.1
Black	5	10.4
Obesity (BMI > 30 kg/m^2)	8	16.7
Neck circumference > 40 cm	18	37.5
Mallampati III/IV	26	54.2
Hoehn and Yahr scale		
1.5–2.0	24	50.0
2.5–3.0	22	45.8
4.0	2	4.2
Laryngopharyngeal motor dysfunction	29	60.4
Hypophonia	28	58.3
Impaired tongue protrusion	12	25.0
Difficulty coughing	5	10.4
Difficulty clearing the throat	4	8.3
Impaired palate lift	4	8.3
Neck and trunk postural changes	19	39.6
Motor phenomena	25	52.1
Hypertension	23	47.9
Diabetes	8	16.7
Nocturia	31	64.6
Snoring	24	50
Excessive daytime sleepiness	43	89.6
ESS > 10	21	43.8
Obstructive sleep apnea (RDI ≥ 5)	31	64.6
Mild (RDI ≥ 5 and < 15)	21	43.8
Moderate (RDI ≥15 and < 30)	6	12.5
Severe (RDI ≥ 30)	4	8.3
REM without atony	3	6.2
High PLM index (> 15/h)	1	2.1
Extrasystoles	2	4.2
Spirometric		
Altered flow-volume curve	17	35.4
Upper airway dysfunction	13	27.1
Upper airway obstruction	12	25.0
Restrictive lung disease	4	8.3
Obstructive lung disease	5	10.41

IBGE, Brazilian institute of geography and statistics; *BMI*, body mass index; *ESS*, Epworth sleep scale; *REM*, rapid eye movement; *PLM*, periodic limb movement

frequency of OSA [5]. In addition, changes to the OSA diagnostic criteria [24] (use of the respiratory disturbance index instead of the apnea and hypopnea index) have increased the method's sensitivity. If we had used the old criteria, the frequency of OSA would have been 60.4%. Moreover, mild OSA was more prevalent than moderate or severe OSA, and this trend has also been observed in other studies [18, 27].

The frequency of UA obstruction, evaluated by spirometry, was similar to that described by Herer et al. [11] using a similar protocol (12 h without the use of levodopa and the same spirometric criteria for UA obstruction). Other studies using spirometry with parkinsonians have found higher [8, 9] or lower [27] UA obstruction frequency values but used different criteria, which makes comparison difficult. The frequency of restrictive damage in our study was low compared with the findings in the literature [9, 28]. This difference may be associated with the low frequency of patients with severe motor impairment, which is indicated by the low mean UPDRS III value. Restrictive damage in PD is related to a decrease in thoracic cage expansion due to more severe stiffness [10]. The use of an improper technique for performing the spirometry test may overestimate the frequency of restrictive damage as little or no patient compliance may lead to false-positive results. In this study, the test was conducted according to ATS standardization rules, which minimizes this type of bias [25].

The laryngopharyngeal musculature is responsible for maintaining UA patency and regulating the resistance of those airways [12]. This study proposes a clinical evaluation of this musculature that can be performed at the bedside. The main identified change was hypophonia, followed by impaired tongue protrusion. Hypophonia is a common manifestation in PD and affects approximately 70% of patients [10]. Hypophonia is believed to result from stiffness as much as from fatigability of thyroarytenoid muscles during vocalization [14]. Impaired tongue protrusion reflects compromise of the genioglossus, which is one of the main pharyngeal dilators [12].

The main finding of this study was a significant association between LMD and OSA. Patients with LMD had more than a threefold greater chance of having OSA than those without LMD did. These data support the hypothesis that dysfunction of this musculature can contribute to the obstructive phenomenon of OSA in PD. However, importantly, higher UPDRS III scores were not associated with OSA. Therefore, a specific evaluation of the laryngopharyngeal muscle group should be considered to establish the relationship between motor dysfunction and OSA in PD rather than UPDRS III alone, which has only one of 13 items dedicated to the evaluation of these muscles (item 18-speech). Moreover, UPDRS III is not specifically designed to detect functional changes in the laryngopharyngeal musculature, which might perhaps explain the very divergent results in the literature in regard to the relationship between OSA and motor performance in PD when only UPDRS III is taken into account [15–17, 27].

Table 2 Comparison between groups with OSA and without OSA

	With OSA				Without OSA				
Numerical variables	Average	SD	Median	IQR	Average	SD	Median	IQR	*p* value
Parkinson's disease									
Disease time (years)	8.4	4.1	8	5–10	6.5	4.3	6	2.5–10.5	0.096
Hoehn-Yahr scale	2.39	0.48	2.5	2–2.5	2.24	0.64	2	2–2.5	0.16
UPDRS III	22.3	11.9	19	14–24	17.8	10.8	17	8.5–25.5	0.17
Levodopa equivalent dose (mg)	738.9	321.5	682	475–950	658.1	453.7	500	338–904	0.27
Clinical									
Age (years)	62.8	10.1	65	53–70	63.3	11	65	53–72.5	0.98
BMI (kg/m^2)	26.2	4.1	25.7	22.7–28.7	25.5	3.1	25.7	23.3–27.4	0.67
Neck circumference (cm)	39	3.6	38.5	36.5–41.5	37.7	4.1	38.8	36.5–40.5	0.76
Abdominal circumference (cm)	95.2	14	97	81–105	94.8	9.9	97	87.5–102	0.85
Epworth sleep scale	10.7	4.4	10	8–14	9.5	4	8	6–12	0.28
Spirometric									
FVC (% predict)	98.8	13.7	99	91.8–107	94.3	20.4	97	89.3–107	0.53
FEV_1 (% predict)	97.9	15.7	97	85.8–110	93.2	22.4	96	89.3–108	0.72
FEV_1/FVC (%)	79.6	10.3	80.9	74.1–84.2	78.4	7.5	80.9	72.5–83.8	0.73
FEF maximal (L/S)	6.41	2.36	6.91	4.8–8	6.72	2.47	6.9	5.2–8.7	0.7
PIF (L/S)	3.74	1.67	3.79	2.5–4.6	3.57	1.65	3.01	2.1–5.1	0.78
FEV_1/PEF (ml/L/min)	7.16	2.3	6.92	5.6–8.3	6.55	1.79	6.63	6–7.6	0.62
$FEV_1/FEV_{0.5}$	1.3	0.15	1.25	1.2–1.4	1.3	0.7	1.23	1.2–1.3	0.35
FEF_{50}/FIF_{50}	1.4	0.75	1.16	0.9–1.8	1.48	0.72	1.45	0.9–2	0.54
PEF/FEF_{50}	1.74	0.66	1.58	1.2–2.3	1.79	0.77	1.52	1.2–2.2	0.96
Categorical variables			*n*	%	*n*	%	OR	CI 95%	*p* value
Parkinson's disease									
Motor phenomena			18	58.1	7	41.2	1.98	0.6–6.6	0.26
Neck and trunk postural changes			13	41.9	6	35.3	1.32	0.39–4.5	0.65
Clinical									
Male			26	83.9	15	88.2	0.69	0.12–4.03	0.52
Obesity (BMI > 30 kg/m^2)			5	16.1	3	17.6	0.9	0.19–4.3	0.6
Neck circumference > 40 cm			12	38.7	6	35.3	1.16	0.34–4	0.82
Mallampati III/IV			17	54.8	9	52.9	1.08	0.33–3.5	0.9
LMD dysfunction			22	71	7	41.2	3.49	1.01–12.1	*0.044**
Snore			14	45.2	10	58.8	0.58	0.17–1.9	0.37
Excessive daytime sleepiness			27	87.1	16	94.1	0.42	0.04–4.1	0.41

Table 2 (continued)

	With OSA		Without OSA			
Hypertension	15	48.4	8	47.1	1.06	0.32–3.4	0.93
Diabetes	7	22.6	1	5.9	4.67	0.52–41.6	0.14
Nocturia	21	67.7	10	58.8	1.47	0.43–5	0.54
Spirometric							
Altered flow-volume curve	11	35.5	6	35.3	1.01	0.29–3.5	0.99
Upper airway dysfunction	8	25.8	5	29.4	0.84	0.22–3.1	0.52
Upper airway obstruction	8	25.8	4	23.5	1.13	0.29–4.5	0.58
Restrictive lung disease	3	9.7	1	5.9	1.71	0.16–17.9	0.55

SD, standard deviation; *IQR*, interquartile range (Q1–Q3); *OR*, odds ratio; *CI*, confidence interval; *OSA*, obstructive sleep apnea; *UPDRS III*, unified Parkinson's disease rate scale part III; *FVC*, forced vital capacity; FEV_1, forced expiratory volume in 1 s; $FEV_{0.5}$, expiratory volume in the first 30 s; *PIF*, peak inspiratory flow; *PEF*, peak expiratory flow; $FEF_{25–75\%}$, forced expiratory flow during the middle half of the FVC; $FEF_{50\%}$, forced expiratory flow at 50% of FVC; $FIF_{50\%}$, forced inspiratory flow at 50% of FVC; *BMI*, body mass index; *LMD*, laryngopharyngeal motor dysfunction

*$p<0,05$

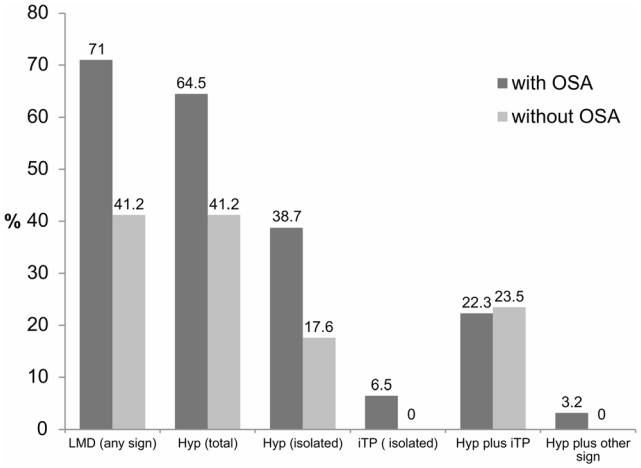

Fig. 1 Frequency of LMD signs in groups with OSA and without OSA. The graphic shows a greater frequency of the different LMD signs in the OSA group. LMD, laryngopharyngeal motor dysfunction; Hyp, hypophonia; iTP, impaired tongue protrusion; OSA, obstructive sleep apnea

In the parkinsonian population, the suspected diagnosis of OSA is a challenge as many of the characteristics normally associated with OSA in the general population [5, 7] do not have the same associations in individuals with PD. This study analyzed the correlation between the presence of OSA and the following findings: obesity (BMI > 30), increased neck circumference (> 40 cm), snoring, EDS, hypertension, diabetes, nocturia, Mallampati III/IV, and male sex. None of these characteristics were associated with a greater chance of having OSA in this population. Trotti et al. [18] also found no relationships between OSA and EDS, snoring, or obesity but did find an association between OSA and male sex. Cochen De Cock et al. [15] found no associations between OSA and male sex, EDS, depression, nocturia, snoring, or cardiovascular events. There was also no difference in mean age between the groups with and without OSA, which could have been a confounder, given that being over 60 years of age is a risk factor for OSA [5]. Notably, to the best of our knowledge, no previous study has evaluated the relationship between OSA and the Mallampati index in PD.

There was no difference in spirometric parameters between parkinsonians with and without OSA. One of the limitations of this study is that spirometry has a low sensitivity for the detection of UA obstruction, approximately 69.4% [29]. Potentially, some patients have received a false-negative result for spirometric UA dysfunction, which may weaken the power to show an association between spirometric UA dysfunction and OSA. In the literature, there are some comparisons of spirometric parameters between parkinsonians and controls without PD [16] and between nonparkinsonians with and without OSA [30]. The specific comparison of spirometric parameters in parkinsonian patients with and without

Table 3 Differences in participants with LMD compared with those without LMD

	LMD				Without LMD				*p* value
Numerical variables	Average	SD	Median	IQR	Average	SD	Median	IQR	
Parkinson's disease									
Disease time (years)	8.7	4.3	7.0	6.0–11.0	6.2	3.6	6.0	3.0–9.0	0.044*
Hoehn-Yahr scale	2.5	0.58	2.5	2.0–3.0	2.08	0.34	2.0	2.0–2.5	0.008*
UPDRS III	25.2	12.3	20.0	16.5–32.5	13.8	5.8	15.0	9.0–19.0	0.0005*
Categorical variables			*n*	%	*n*	%			
Parkinson's disease									
Motor phenomena			19	65.5	6	31.6			0.021*
Neck and trunk postural changes			15	51.7	4	21.1			0.033*
Spirometric									
Altered flow-volume curve			14	48.3	3	15.8			0.021*
Upper airway dysfunction			11	37.9	2	10.5			0.037*

SD, standard deviation; *IQR*, interquartile range (Q1–Q3); *UPDRS III*, unified Parkinson's disease rate scale part III

*$p<0,05$

OSA, as performed in this study, has not been previously described in the literature.

Finally, participants with LMD, irrespective of whether they had OSA, had PD for a longer period, higher frequencies of motor phenomena and postural trunk and neck changes, higher H-Y and UPDRS III scores, and lung function changes indicative of UA dysfunction. Although the lack of adjustment for multiple comparisons is a limitation for interpretation of these results, they associate LMD with parameters linked to the severity of PD. The association between LMD and spirometric UA dysfunction supports the hypothesis that LMD in PD patients impairs the function of UA and appears to increase the risk for OSA. Motor impairment in PD and its correlation with spirometric UA changes was reported by Sabaté et al. [9] who demonstrated a positive association between bradykinesia and the presence of UA obstruction ($t = 3.12$, $p = 0.003$).

Understanding the relationship between PD and OSA is critical to improve and develop new diagnostic and treatment methods. If PD-related mechanisms are involved in the genesis of obstructive phenomena as proposed in this study, treatment with antiparkinsonian drugs can potentially improve OSA in patients with PD [31, 32]. In addition, growing evidence indicates that OSA can lead to neurotoxin accumulation and neuronal death due to intermittent hypoxia and sleep fragmentation [33], thereby contributing to an acceleration of the neurodegenerative process. In a recent study [34] of an administrative database of over 20,000 subjects, the authors suggested that incident PD could be related to preexisting OSA, although the diagnosis of OSA used in that study was not defined by a physiologic measurement. This finding at least raises the possibility that the association with OSA might be bidirectional.

Conclusions

The results of this study indicate that LMD may be a factor involved in the occurrence of UA obstructive phenomena in OSA in patients with PD. However, more studies are needed to confirm this association. Nonetheless, LMD can help identify which PD patients should be monitored in regard to the development of OSA as most of the characteristics commonly associated with OSA in the general population do not apply to parkinsonians.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Research involving human participants and/or animals All procedures performed in the studies involving human participants were in accordance with the ethical standards of the Rio de Janeiro State University Research Committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

Ethical approval The study was approved by the institutional research ethics committee under number 500184.

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