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Original articles

Is there auditory impairment in Parkinson's disease?

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ABSTRACT

Objective: to describe the audiological profile of a group of patients with Parkinson's disease and to investigate the association between hearing loss and the disease.

Methods: 50 individuals with and 46 without Parkinson's disease underwent Pure Tone Audiometry, Otoacoustic Emissions by Distortion Product, and auditory processing tests. The results of the patients were compared to those obtained in individuals without the disease, according to clinical and biological variables.

Results: in individuals with Parkinson's disease, 82% presented hearing loss, 53.5% alterations in Otoacoustic Emissions by Distortion Product, 78%, alterations in temporal processing , and 12%, changes in binaural integration. Individuals with the disease had a greater impairment in the recognition of duration patterns when compared to those without the disease, with a worse performance in men and in individuals aged between 42 and 65 years old and Hoehn and Yahr I and II stages.

Conclusions: the profile found corresponds to descending sensorineural hearing loss and alteration in otoacoustic emissions, temporal ordering and noise gaps detection. Only losses in temporal order are associated with the disease, especially in men, individuals under the age of 65 and in the initial stage.

Keywords: Parkinson's disease; Aging; Auditory Perception; Hearing Loss

INTRODUCTION

Hearing loss affects approximately 1/3 of people over 65 years of age, being the second largest disability among the various functional impairments in this part of the population[1].In a recent Editorial[2], the hearing loss was pointed out as a worrisome world health problem, being in the fifth position in the ranking of the conditions that increase years lived with incapacity.

With the increasing life expectancy and, consequently, the increase of populations over 60 years old, the health problems related to aging[1], such as hearing loss and chronic-degenerative diseases, deserve greater attention.Among these, Parkinson's disease (PD) is present in 1% to 2% of the elderly over 60 years of age, whose incidence varies between 8-18 per 100,000 person-years[3].

PD is characterized by motor-related signs and symptoms, such as bradykinesia, tremor, muscle stiffness and postural instability.However, it is currently recognized by a broad spectrum of non-motor manifestations due to neuronal damage in regions that extrapolate nigrostriatal pathways[4] and influence its prognosis and evolution[5].These manifestations are characterized by cognitive, autonomic and sensory impairments[6] related to the neurobiological processes common to aging and the neurodegenerative process of the disease[4].

Among the sensitive alterations, more recent studies have suggested the inclusion of hearing loss in the list of sensorial manifestations of the clinical phase of the disease[6-9], as well as its correlation with the increased risk for PD in the elderly[7].These studies described a worse sensitivity to pure tones and a higher frequency of hearing loss in PD patients when compared to controls[6,8,9], however, it has not been clearly established if hearing loss in this population is related to changes in cochlear mechanics.

It is known that the decline in the auditory sensitivity for pure tones is related to the decrease in the ability to understand speech, but the reduction of this sensitivity does not accurately predict the difficulties reported by the individuals, and there are other damages that may be involved in this process[10].In addition, the temporal processing abilities of speech sounds have been impaired in the elderly without significant sensory hearing losses, as well as in situations where the effects of this loss are minimized by testing strategies, reinforcing the idea that the losses in temporal processing reflect a mechanism independent of auditory acuity[11].

Thus, the investigation of the frequency of impairment in temporal auditory processing skills is relevant to indicate the extent of auditory impairment, which needs to be better described in PD.Furthermore, it remains controversial whether patients perform poorly in these skills when compared to individuals without the disease[12,13].Thus, the objective of the present study is to describe the audiological profile of individuals with Parkinson's disease and to investigate the association between hearing disorders and the disease.

METHODS

The protocol of this study was approved by the Research in Ethics Committee of the University Hospital Prof. Edgard Santos - UFBA (number 843.890 / 2014) and all individuals signed a free and informed consent term.

A cross-sectional study was conducted between March 2015 and June 2016, with individuals diagnosed with idiopathic PD (Group PD) who were followed at an outpatient clinic for involuntary movements of a University Hospital.The diagnosis of idiopathic PD was established from the clinical criteria proposed by the Brain Bank of the United Kingdom and all individuals were evaluated in the period "on" of the antiparkinsonian medication.The comparison group (Non-PD group) was composed of users from other outpatient clinics at this hospital, spouses and caregivers of individuals with PD, following the same ratio of gender and age of the PD group.

For both groups, individuals with a history of trauma or stroke, history of severe psychiatric disorders and otological diseases, other neurodegenerative diseases, chronic renal dialysis and congenital or diagnosed hearing loss before age 40 were considered ineligible. All individuals with scores suggestive of cognitive impairment in the Mini Mental State Examination were excluded, characterized by a performance below 13 points for illiterate, 18 points for low and medium schooling and 26 points for high schooling[14].

Data were collected regarding the time of diagnosis of PD, the time elapsed since the onset of symptoms, current drug treatment, current otoneurological history and progression (otological and vestibular signs and symptoms), data on noise exposure, diagnosis of diabetes mellitus and hypertension and stage of DP according to Hoehn and Yahr.

All participants were submitted to a battery of auditive tests performed by a qualified professional in an acoustic booth.The Interacoustics audiometer of two

channels AC 40, coupled to supra aural headphones TDH39, immitaciometer Interacoustics AZ7 and portable equipment Madsen AccuScreen for research of the Otoacoustic Emissions were used.

The Pure Tone Audiometry (PTA) was performed according to the ASHA recommendation (2005)[15] and the hearing loss was characterized regarding the level according to Russo, Pereira, Carvallo et al.[16].In the immittanciometry, the differential between the tonal threshold and the contralateral acoustic-stapedian reflex threshold (RAEC) was analyzed. Differentials lower than 60 dB were classified as Metz Objective Recruitment and differentials greater than 100 dB as suggestive of impairment between the VIII nerve and the brainstem.

In the Otoacoustic Emissions by Distortion Product (DPOAE), the responses to the 2, 3, 4 and 5 kHz frequencies were analyzed. The DPOAE was identified as present when the signal measurement was above -5 dB and also higher than the background noise by at least 3 dB[17]. The absence of DPOAE at three or more frequencies was considered as indicative of cochlear impairment.

In the evaluation of auditory (central) processing, temporal auditory processing and dichotic listening skills were investigated using Duration Pattern Sequence (DPS), Gaps in Noise (GIN) and Dichotic Digits Test (DDT):

DPS: The test was performed with the presentation of a pure tone recording at the frequency of 440 Hz, configured for periods of long (2000 milliseconds) and short (500 milliseconds) duration, organized into ten sequences of three.After each sequence, the subject was instructed to name the perceived presentation order (example: long-short-long).The percentage of correctly recognized sentences was computed and classified as altered when less than 83%[18].

GIN: Were presented white noise tracks with six milliseconds (ms) in duration, interrupted by zero to three intervals of two to 20 milliseconds.The stimulus was emitted by headphones, simultaneously to both ears, in the intensity of 40 dBNS. Along the list of 29 noise tracks, there were six intervals of duration of 2 ms, six of 3 ms, six of 4 ms, and so on.The participant was instructed to signal every time he noticed the interval. The interval detection threshold was established by the shortest interval correctly identified in four of the six presentations, with thresholds greater than 5 ms being considered altered[19].

DDT: A recording of 20 four-digit sequences, pronounced in pairs (combinations of numbers between four and nine) was presented, each pair of digits being an output on one of the headphones with a difference of a few milliseconds in each ear.The participant was instructed to repeat orally the four numbers presented, regardless of the order.It was calculated the percentage of correctly recognized numbers per ear and consideredas altered a percentage of less than 78% (individuals without hearing loss) or 60% (individuals with hearing loss)[20].

For the analyzes, in all the monoaural tests, the results obtained in the worst ear were considered. The frequency of changes in each of the tests was characterized and described according to the non-PD and PD groups.

In order to verify the association between auditory changes and socio-demographic and clinical variables, the measures obtained in the tests were compared between the non-PD and the PD groups, according to gender, age group (42 ⊢⊣ 64 and 65 ⊢⊣ 86 years), age at the time of onset of PD symptoms (greater or less than 55 years) and disease staging (H & Y I and II x H & Y III and IV).

Statistical Analysis

The comparison between the groups, through inferential statistical measures, for the analysis of dichotomous or ordinal variables, was performed with the chi-square test, Fisher's exact test and Equality of proportions test. For the numerical variables, the T-student and Mann-Whitney tests were used, according to the normality of the distributions.The Shapiro-Wilk test was used for the normality tests of the variables and the F-test was applied to compare the variances between the distributions of the variables.

RESULTS

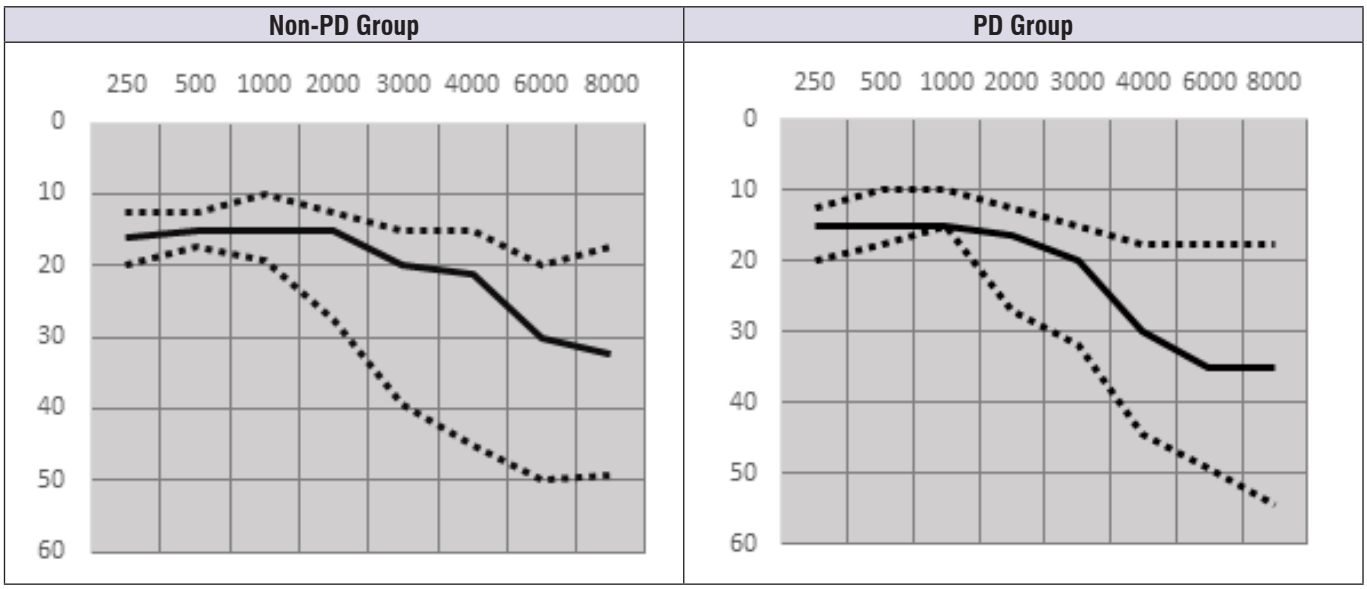
Table 1 shows the demographic and general health characteristics of the 46 non-PD and the 50 PD subjects. Participants in the PD group had an average disease time of 9.2 years (SD 6.5), with a minimum of 6 months and a maximum of 36 years. The onset of motor manifestations occurred on average at 54.2 years old (SD 11.3), with a minimum age of 27 and a maximum of 78. As for the severity of the motor signals, classified according to the H & Y stages, individuals predominated in the initial stages of the disease (68%), with 13 and 21 participants in stages I and II, respectively, and in the more advanced stages 11 individuals with H & Y III and five with H & Y IV.

Table 1. Biological characteristics, comorbidities and exposure to noise of the individuals, according to the groups without (Non-DP) and with Parkinson's disease (PD)

Variables	Groups				p-value*
	Non-PD (46)	%	PD (50)	%	
Gender					
Females	18	39,1	15	30.0	0.347
Males	28	60,9	35	70.0	
Age group (yrs)					
42 ⊢⊣ 64	26	56,5	31	62.0	0.585
65 ⊢⊣ 86	20	43,5	19	38.0	
Diabetes mellitus					
Yes	8	17,4	9	18.0	0.938
SAH					
Yes	12	26,1	10	20.0	0.478
Noise exposure					
Yes	10	21,7	14	28.0	0.479

Subtitle: SAH = Systemic Arterial Hypertension
*chi square of Pearson

The PTA results for each pure tone investigated are shown in Figure 1. Hearing loss in at least one of the pure tones surveyed was observed in 40 subjects from the non-PD group (86.9%) and 41 from the PD group (82%), with no difference between groups (p = 0.377). All patients presented hearing loss of the sensorineural type, and it was possible to classify the degree in only 17 individuals from the non-PD group (34%) and 18 from the PD group (39.1%), as shown in Table 2. No differences were observed between the groups in the audiometric results considering gender, age, age at the onset and staging of PD (p> 0.05). The changes observed in RAEC, in both groups, indicate the presence of the Metz target recruitment.



Subtitle: Continuous-Median line of the audiometric threshold distribution; upper dotted line - Percentile 25; bottom dotted line - Percentile 75
Note: p-value> 0.05 for all pure tones compared

Figure 1. Representation of the audiometric thresholds identified in the groups without (Non-PD Group) and with Parkinson's disease (PD Group)

Two and three individuals from the non-PD and PD groups, respectively, were excluded from the DPOAE survey, due to probe-checking conditions not suitable for testing, even after several repositioning attempts. Thus, the results presented correspond to the responses obtained in 44 individuals from the non-PD group and 47 from the PD group. The percentage of changes in this study did not show differences between groups (Table 2).

Table 2. Frequency of changes in audiological procedures, according to the groups without (Non-PD group) and with Parkinson's disease (PD group)

Procedures	Groups				p-value*
	Non-PD		PD		
	N	%	N	%	
PTA					
Degree (0,5 a 4 kHz)					
Mild	14 (n=18)	77,8	13 (n=17)	76.5	0.798
Moderate	4 (n=18)	22,2	4 (n=17)	23.5	1.000
DPOAE	25 (n=44)	56,8	25 (n=47)	53.2	0.728
DPS	26 (n=46)	56,5	39 (n=50)	78.0	0.025
GIN	37 (n=46)	80,4	39 (n=50)	78.0	0.769
DDT	1 (n=46)	2,2	6 (n=50)	12.0	0.145

Subtitle: PTA = Pure Tone Audiometry; DPOAE= Otoacoustic Emissions by Distortion Product; DPS = Duration Pattern Sequence; GIN = Gaps in Noise; DDT = Dichotic Digits Test.
* chi square of Pearson

Regarding performance in auditory processing tests, it was observed that the percentage of correct answers in DPS was on average 73.9% (SD 24.2) in the non-PD group and 61.0% (SD 25.2) in the PD group. Regarding GIN, the average threshold obtained in the non-PD group was 8.1 ms (SD 2.7ms) and in the PD group it was 8.2 ms (SD 3.1ms). In the DDT test, the percentage of correct answers was 90.9% (SD 9.8) and 86.4% (SD 18.8) for the non-PD and PD groups, respectively. Only in the DPS test there was a difference between the groups (p = 0.012).

Table 3 shows the results of the groups in the auditory processing tests, according to gender, current age, age at the time of the onset of symptoms and severity of disease.

Table 3. Means and standard deviations of the results in the auditory processing tests obtained in the groups without (Non-PD group) and with Parkinson's disease (PD group) according to the demographic and clinical variables

Variáveis	DPS				GIN				DDT			
	Non PD n=46	PD n=50		p-value**	Non PD n=46	PD n=50		p-value**	Non PD n=46	PD n=50		p-value**
Gender												
Female	68.3 (24.3)	64.0 (29.2)		0.645	8.6 (3.4)	8.7 (3.6)		0.922	91.7 (6.8)	83.8 (21.3)		0.132
Male	77.5 (23.8)	59.7 (23.7)		**0.004**	7.8 (2.2)	8.0 (2.9)		0.788	90.2 (11.4)	87.5 (17.8)		0.487
Age Group												
42 ⊢⊣ 64	79.6 (20.7)	63.2 (24.1)		**0.008**	7.5 (2.8)	7.7 (3.0)		0.869	94.0 (7.2)	92.3 (9.7)		0.824
65 ⊢⊣ 86	66.5 (26.8)	57.4 (27.2)		0.298	8.9 (2.5)	9.0 (3.2)		0.868	86.6 (11.3)	76.6 (25.4)		0.108
PD Age Onset		*DP< 55	*DP≥ 55			*DP< 55	*DP≥ 55			*DP< 55	*DP≥ 55	
42 ⊢⊣ 64	79.6(20.7)	63.8(25.6)	60.0(15.8)	[a]**0.018**	7.5 (2.8)	7.7(3.1)	7.8(2.7)	a0.851	94.0(7.2)	92.5(10.3)	91.6(6.3)	[a]0.546
				[b]**0.047**				b0.849				[b]0.476
65 ⊢⊣ 86	66.5(26.8)	66.7(32.1)	55.6(27.1)	[a]0.993	8.9(2.5)	8.7(1.1)	9.1(3.5)	a0.798	86.6(11.3)	77.0(28.2)	76.5(25.8)	[a]0.607
				[b]0.237				b0.829				[b]0.152
PD Stage		H&Y I-II	H&Y III-IV			H&Y I-II	H&Y III-IV			H&Y I-II	H&Y III-IV	
42 ⊢⊣ 64	79.6(20.7)	63.6(21.9)	62.2(30.3)	[c]**0.013**	7.5 (2.8)	6.9(2.15)	9.6(4.1)	c0.414	94.0(7.2)	94.0(6.1)	88.2(15.1)	[c]0.981
				[d]0.139				d0.197				[d]0.297
65 ⊢⊣ 86	66.5(26.8)	63.3(26.7)	47.1(26.9)	[c]0.748	8.9(2.5)	8.2(1.9)	10.6(4.4)	c0.361	86.6(11.3)	84.8(20.5)	62.4(28.2)	[c]0.758
				[d]0.130				d0.373				[d]**0.062**

Note: DPS = Duration Pattern Sequence; GIN = Gaps in Noise; DDT = Dichotic Digits Test; * Age of onset of PD before and after 55 years of age; [a] Non PD x PD age at onset <55 years; [b] Non PD x PD age at onset ≥ 55 years; [c] Non PD x PD H & Y I-II; [d] Non PD x PD H & Y III-IV;
**T-student / Mann-Whitney test

DISCUSSION

The majority of subjects with PD assessed had a reduction in the sensitivity to pure tones, characterized as sensorineural hearing loss more pronounced in high frequencies, as well as alteration in the DPOAE research. This finding evidences alterations in the micromechanics of the outer hair cells of the cochlea and, together with the findings of the RAEC research, contributes to the understanding that the reduction of the sensitivity to pure tones in PD is related to losses in the cochlear dynamics[21,22].

Although the frequency of hearing loss in the PD group was high, as reported in previous studies[8,9], our results contradict investigations in which hearing loss was more frequent and severe in individuals with PD when compared to controls[6,8,9]. Thus, the identification of similar results between the non-PD and PD groups in the PTA in our study suggests that the identified hearing loss may be related to the aging process of the peripheral auditory system and not specifically to some pathophysiological process of PD. The process of degeneration of the auditory system related to aging involves lesions in the peripheral structures, initially affecting the perception of high tones, evolving to also hinder low and medium sounds[23].

The temporal auditory processing tests revealed a high frequency of alterations in temporal ordering (DPS) and temporal resolution (GIN) in the PD group, which may potentiate the losses due to the reduction of auditory sensitivity in speech perception[10]. It is known that the perception of temporal order contributes to the individual discriminating words with subtle differences in the position of the phonemes[24] and it has been related to sound processing in the region of the temporal cortex[25]. The temporal resolution, however, translates the ability of the auditory system to process fast stimulus fluctuations[19]. The degradation of temporal aspects has a significant impact on the intelligibility of speech[11], since temporal processing seems to contribute to the identification of the speed of the neural oscillations that will respond by processes of analysis and decoding of the signal, both in terms of its temporal constitution itself, as well as in their spectral patterns[26].

A possible explanation for the difficulties of temporal perception among patients would be the existence of the slowness of the "internal clock"[12]. The internal clock theory is cited as one of the mechanisms of time perception and, in general, is expressed by the idea that the structures of the central nervous system would function as an "accumulating pacemaker". The perception of time would then be derived from the number of nerve impulses received during a period, classifying the duration of the event in long or short from the quantification of a greater or lesser number of

accumulated impulses[27]. The role of the base nucleus and its dopaminergic pathways, in connection with prefrontal, parietal and cerebellar structures, is essential throughout this mechanism and, thus, the pathophysiology of PD will compromise all the gearing involved in the perception of time[27].

The DDT is a widely used test to evaluate binaural integration and is recommended as screening with high sensitivity and specificity to detect auditory processing disorders in individuals with brain lesions[20]. In our study, we observed a reduced frequency of individuals in the PD group with change in DDT, demonstrating that the impairment of inter-hemispheric communication is not relevant in the disease. Thus, it is believed that other disorders may be related to the temporal auditory processing alterations found in the majority of individuals evaluated in the PD group. However, the observation of a worse performance in DDT in individuals older than 65 years of age and in the advanced stage of PD suggests that aging and PD act together, affecting in a more diffused way the brain functionality of these individuals.

While the audiometric findings of this study suggest that hearing loss in individuals with PD is related to age-related alterations. The auditory processing assessment results show that impairment in temporal ordering ability is worse and more frequent in the disease. In DPS, the task used involves, in addition to the differentiation of sound duration patterns, the identification of the order of presentation of three stimuli, thus implying greater complexity and proximity to the necessary abilities to discriminate speech sounds. These characteristics may justify the divergent findings obtained in previous research in individuals with PD[13], in which the method used involved discrimination of subtle differences of the duration of two syllables, not requiring the memorization and naming of the stimuli. Thus, it is important to consider in our results the influence of difficulties regarding executive functions and attention present in PD[28].

In our study, we found a worse performance in temporal ordering ability among men with PD. This finding is consistent with the greater expression of motor and non-motor damage related to sex in the disease[29]. Considering that men without the disease have better performance in temporal order tasks[30], our data reinforce the premise that there is a synergy between the pathophysiological process in the PD with biological conditions related to sex. Therefore, experimental studies have revealed an association between the action of circulating androgen hormones with more expressive neuronal damage in dopaminergic pathways, especially in those that support activities with a greater contribution of the working memory[31,32]. Thus, it is believed that the effects of PD in working memory are responsible for the worse performance in PDS among men.

Regarding age, the worst performance in PDS in younger individuals leads us to assume that the losses in the ability of temporal ordering are anticipated by PD. Considering that the degenerative process involved in PD has a pathophysiological basis common to aging[4,33,34], it is believed that the clinical and pathological manifestations of PD result from the breakdown of the compensatory mechanism of substantia nigra pars compacta dopaminergic cells recovery [35], leading to an early impairment in cognitive processes related to temporal ordering ability. Therefore, if the worst performance of younger individuals and in early stages of the disease was due to the effects of PD in the auditory system, the same behavior would be expected in GIN and DDT.

However, the most pronounced temporal auditory impairment in PD remains controversial. The results of the GIN test in our study revealed no difference between the non-PD and the PD groups, as it was observed in previous investigations that evaluated temporal perception[12,13]. On the other hand, worse detection, discrimination and naming of gaps have already been identified in individuals with PD[12,13]. It is believed that these findings are a reflection of tasks used that recruited greater cognitive expression, since they approached the indication of intervals by means of the comparison between listening conditions at different moments, also involving memorization, besides the perception of the interval itself. In the GIN, the simplest task was considered, since the subject indicates the perception of the interval immediately after the presentation of the same, thus requiring less contribution of the working memory in the execution of the test. Although the methods applied in the evaluation procedures use the temporality of sound perception as a common axis, it is possible that the differential between the procedures is the implication, to a greater or a lesser degree, of attention, memory and executive functions.

The present study contributes with relevant data to the understanding about the audiological profile of the individuals with PD, however some aspects impose limitations on the interpretation of the results found. It

is possible that the sample size of our study may have contributed to non-statistically significant differences in the stratified analyzes. It is also necessary to consider a possible selection bias of the participants, both by a greater inclusion of individuals without PD with auditory complaints, and by the lower inclusion of individuals with PD in later stages of the disease, profiles found more frequently in specialized outpatient centers.

In addition, a possible association between PD and changes in temporal perception should be interpreted with caution, since the evaluation of this ability seems to be influenced by the complexity of the task required by the testing method and higher cognitive conditions, such as executive functions and attention. In the quest to reduce the interference of cognitive issues in the testing procedures, our methodological choice was to use the MMSE to exclude potentially cognitively affected individuals. However, although the MMSE is a simple, fast and widely used cognitive screening tool in elderly populations, its limitations should be considered in the application in individuals with PD, whose cognitive impairments are more expressive in executive functions superficially evaluated by the MMSE.

Therefore, we recommend, in future investigations, choices of methods that are not involved in this bias or that can correlate the auditory data with assessments of memory and attention abilities should be considered.

CONCLUSION

The results of the present study allow us to conclude that auditory changes are frequent in individuals with PD and affect both the peripheral and central auditory systems. The most frequently found audiological profile is individuals with sensorineural hearing loss, with descending configuration, alteration of otoacoustic emissions by distortion product, as well as impairment in temporal ordering abilities and detection of noise gaps. However, although these changes are frequent among individuals with PD, only impairments in temporal ordering ability are associated with the disease, especially in men, in individuals under the age of 65 and at an early stage.

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