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Olfative and taste perception in Parkinson's disease

Percepção olfativa e gustativa na doença de Parkinson

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Keywords

Parkinson's Disease
Smell
Taste
Perception
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ABSTRACT

Purpose: To analyze the olfactory and gustatory perception and discrimination and self-perception of smell and taste in people with Parkinson's disease, comparing them with healthy nodes. **Methods:** Observational, analytical, cross-sectional, and quantitative study. Olfactory and gustatory perception and discrimination were verified following Parkinson's disease, compared to a control group, matched by sex and age, using the Olfactory Perception and Taste Strips Tests, respectively, after nasal cleaning and oral brushing. Self-perception was assessed by the Visual Analogue Scale before and after specific tests of perception and discrimination. **Results:** We included individuals of both sexes, 35 with Parkinson's Disease and 20 assigned to the control group, matched for mean age. The olfactory self-perception of the group with Parkinson's disease improved after the olfactory test. There was no difference in taste self-perception in the Parkinson's disease group before and after the taste test. In the olfactory perception assessment test, the Parkinson's disease group discriminated fewer essences than the control group. Both groups have similar generation and taste discrimination. **Conclusion:** The olfactory perception of people with Parkinson's disease was lower, compared to the group of healthy desires, and the self-perception of olfactory efficacy improved after the test, in both groups. As for taste, there was no difference in perception and discrimination between groups, the sour taste was the most identified and there was an improvement in self-perception of taste efficiency in the group without Parkinson's disease after the test.

Descritores

Doença de Parkinson
Olfato
Paladar
Percepção
Autopercepção

RESUMO

Objetivo: Analisar a percepção e discriminação olfativa e gustativa e a autopercepção do olfato e paladar em pessoas com Doença de Parkinson, comparando-as com indivíduos hígidos. **Método:** Estudo observacional, analítico, transversal e quantitativo. Verificou-se a percepção e a discriminação olfativa e gustativa em indivíduos com Doença de Parkinson, comparados a um grupo controle, pareado por sexo e idade, por meio dos Testes de Percepção Olfativa e de Tiras Gustativas, respectivamente, após limpeza nasal e escovação oral. A autopercepção foi avaliada pela Escala Visual Analógica antes e após os testes específicos de percepção e discriminação. **Resultados:** Foram incluídos indivíduos de ambos os sexos, sendo 35 com Doença de Parkinson e 20 designados ao grupo controle, pareados pela média de idade. A autopercepção olfativa do grupo com Doença de Parkinson melhorou após o teste olfativo. Não houve diferença na autopercepção gustativa no grupo Doença de Parkinson antes e após o teste gustativo. No teste de avaliação da percepção olfativa, o grupo Doença de Parkinson discriminou menos essências que o grupo controle. Ambos os grupos apresentaram semelhante percepção e discriminação gustativa. **Conclusão:** A percepção olfativa das pessoas com Doença de Parkinson foi menor, comparativamente ao grupo de indivíduos hígidos e a autopercepção da eficácia olfativa melhorou após o teste, em ambos os grupos. Quanto ao paladar, não houve diferença na percepção e discriminação entre os grupos, o sabor azedo foi o mais identificado e houve melhora na autopercepção da eficácia gustativa somente no grupo sem a doença de Parkinson, após o teste.

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INTRODUCTION

Parkinson's disease (PD) corresponds to a neurodegenerative disease caused by the reduction of dopamine in the synaptic cleft in the midbrain, causing motor symptoms and other alterations[1-4] including the sensory ones, of which the reduction or absence of olfactory sensitivity, called hyposmia and anosmia, are the most evident[5-9].

The olfactory sensitivity in PD changes concerning perception and has been used as one of the criteria for the early diagnosis of PD, since it can occur about less than seven years before the onset of motor symptoms, due to impairment of the olfactory bulb, which occurs even before the loss of neural cells from the midbrain black substance, where neurons with dopamine are found[5].

Olfactory dysfunction in PD may also be more pronounced in individuals at risk of the onset of dementia and changes in odor identification may be related to hippocampal dysfunction secondary to cholinergic and dopaminergic denervations[10]. Given the direct relationship between smell and taste, taste sensitivity in PD can also undergo significant changes[8].

Taste sensitivity (palate) occurs through the perception of different flavors recognized through the papillae, located diffusely throughout the language[11]. The study of changes in taste sensitivity in PD is still little explored; however, this change has been suggested as a component of non-motor changes in PD[7,8].

Since smell and taste are important chemical sensitivities for the perception of taste, which are generally activated together[12,13], changes in smell, both concerning the identification of odors and the discrimination of their concentration, can directly interfere with the effectiveness of taste, compromising food intake and, consequently, the individual's nutrition, serving as a trigger for other consequences, such as lack of appetite and social confinement.

For this reason, the use of diagnostic tests for these functions can be a complementary clinical and investigative tool in the population with PD[7-9]. Also, considering the possible dietary difficulties[14] of these individuals, the early detection of their changes, through specific tests, could assist in the prevention of disease aggravations.

It is worth mentioning that the studies of olfactory and gustatory functions in people with PD did not consider the patient's self-perception regarding their difficulties[7,8,10], which is relevant data for the treatment, as this perception can interfere both in the search and in the treatment adherence. In addition, the methods used to assess these functions are still discussed[3,8-10,13] and must be adapted to different regional and cultural realities.

Thus, the guiding question that motivated this study was: "Is there a change in the self-perception of the efficiency of olfactory and gustatory functions and the perception of smell and taste in people with PD?". The hypothesis raised was that both olfactory and gustatory functions, as well as the self-perception of the efficiency of these functions, are impaired in individuals with such a disease.

Therefore, the present study aims to analyze the perception and discrimination of smell and taste and the self-perception of smell and taste in people with Parkinson's disease, comparing them with healthy individuals.

METHODS

This is an observational analytical cross-sectional study and quantitative analysis with individuals of both sexes. We included individuals with a clinical diagnosis of idiopathic PD in stages HY1, HY2 and HY3 classified according to the original version of the Hoehn and Yahr[15] stage scale and subjects without PD, assigned to the Control Group (CG), who were paired with the PD group, by the average age.

This research was approved by the Ethics Committee on Research with Human Beings, under protocol number 2.938.051. After inviting the subjects to participate in the research, the volunteers signed the Informed Consent form. A semi-structured interview was carried out to check the eligibility criteria and characterize the sample among the eligible subjects.

We excluded patients with cognitive decline assessed using the Mini-Mental State Examination (MMSE)[16], whose cutoff point considers the education level (illiterate: 18 points; individuals with 1 to 3 years of schooling: 21 points; individuals with 4 to 7 years of schooling: 24 points, and individuals with more than 7 years of schooling: 26 points)[17].

Individuals who were alcoholics or current smokers, with symptoms of flu, fever, nasal constipation, during collection, or who underwent surgery to control PD symptoms (deep brain stimulation or ablative surgeries) were not included in the study.

Data collection

Data collection was performed according to the flowchart illustrated in Figure 1.

Self-perception of the effectiveness of smell and taste

Two key questions were asked to participants about their sense of smell and taste: "What score do you give to your sense of smell" and "What score do you give to your taste?". Each question was asked separately, before and after the olfactory and gustatory perception tests. The patient marked his response on a Visual Analogue Scale (VAS), consisting of a line of 100 mm (millimeters). The left extreme was totally dissatisfied and the right extreme was totally satisfied.

As a reference, we assumed the following intervals: 1st interval (0 to 2.5): self-perception of severe problems in smell/taste; 2nd interval (2.6 to 5.0): self-perception of moderate problems in smell/taste; 3rd interval (5.1 to 7.5): self-perception of slight problems in smell/taste; 4th interval (7.6 to 10): self-perception of very slight problems in smell/taste[18].

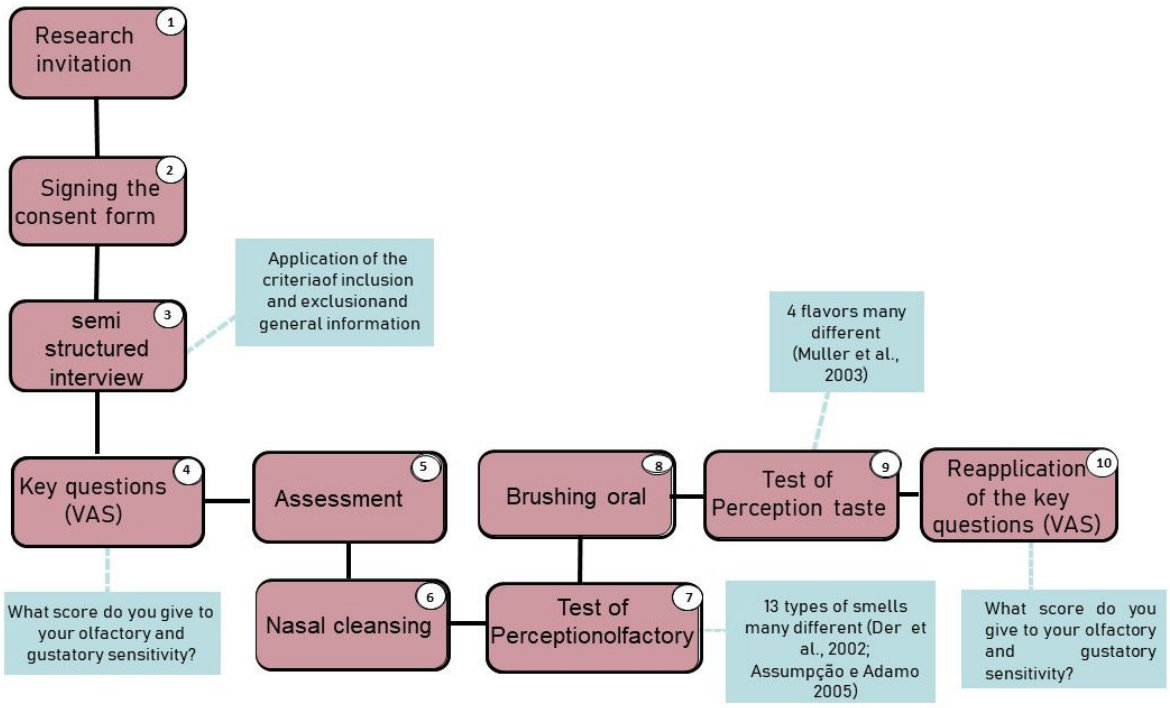

Figure 1. Flow chart of data collection. *Wilcoxon test aP = 0.0011; bP <0.0001; PD = group with Parkinson's disease; CG = control group

Nasal cleansing

After applying the VAS, we performed the nasal cleaning procedure, before applying the Olfactory Perception Test, to remove possible secretions present in the nasal cavity that could influence the assessment, changing the probable results of the research. For this purpose, 0.9% sodium chloride solution flasks with 10 ml, of the Isofarma® brand, were used at room temperature, with 5 ml for each nostril[11]. The saline was inserted into the volunteer's nostril, using a disposable 5 ml syringe from the Descarpack® brand, and then he was asked to blow his nose. This process was performed in each nostril, separately.

Assessment of olfactory perception

To evaluate smell, we applied two tests: 1) identification of different odors; 2) discrimination of odor concentration.

For the identification of different odors, the adapted aqueous solution test was used[11,19,20]. We chose 13 aqueous solutions of essences (vanilla, fennel, roses, eucalyptus, cloves, strawberry, vinegar, garlic, lemon, cinnamon, onions, ginger, coffee) according to the criteria of probable exposure to the study population and easy making, in a standardized way, by the manipulation pharmacy of a public university.

Each essence was presented after placing a drop of the solution on a strip of filter paper, formed by two parts: a rod 8 cm long and a tip of 0.2 cm^2 for the placement of the different aqueous solutions[11]. Also, strips of filter paper soaked in distilled water were also presented every four or five odors exposed to the individual, to neutralize the stimulus.

The filter paper strip was spaced approximately 5 cm horizontally and vertically from the nostrils. Concomitantly with the presentation of each odor, the individual was exposed to three cards, simultaneously, containing the thirteen representative figures of the thirteen essences, available as follows: two cards with four figures and a card with five figures, so that one of the figures was always representative (target) and the others, distracting.

The individual was asked to smell the odor indefinitely until he felt safe in pointing out the figure that he believed corresponded to the odor to which he was exposed[11]. The figures, which portray reality, were used as an aid to olfactory memory[11]. An interval of 15 seconds was given between the presentation of the essences to avoid contamination and odor confusion.

The result of the smell test was based on a percentage classification[21]. Thus, the results were classified as follows: 0-50% (between 0 and 8 correct answers); 51% - 100% (between 9 and 16 correct answers). For classificatory level and not of diagnosis, normosmia was considered from 51% of correct answers and hyposmia below 50% of correct answers.

After testing the identification of the 13 odors, discrimination tests were carried out on the different concentrations (one stronger and one weaker) of seven odors: fennel, roses, eucalyptus, cloves, garlic, onions, and coffee. The same procedure described above was carried out concerning the placement of the solutions on the strips, positioning, and time of presentation to the patient;

however, the individual was asked to identify which strip of filter paper had the strongest and weakest smell, among the pairs of the same odor presented, in different concentrations[11].

Mouth brushing

Oral brushing with water was performed before all the proposed evaluations, to eliminate possible changes in the perception of flavors[11]. For this, we used a disposable toothbrush with Colgate® toothpaste, and water at room temperature. The volunteer brushed his teeth by himself. All participants used the same toothpaste to avoid bias in the research.

Assessment of taste perception

To taste, we used the taste test, based on a validated test[21]. Strips of filter paper made up of two parts were used: a rod of 8 cm in length and an end of 0.2 cm^2 for the placement of four basic flavors: salty, sweet, bitter, and sour, with four different concentrations and two solutions containing distilled water (without flavor), totaling 18 strips. The concentrations used are described in Chart 1.

The strips were positioned in the middle of the volunteer's tongue, at a distance of approximately 1.5 cm from the apex of the tongue, and the test started with the lowest concentration. After the administration of each strip, the volunteer was instructed to close his mouth and choose between five possible answers (salty, sweet, bitter, sour, and without flavor), pointing to the figure that he believed to represent the flavor to which he was exposed[21].

These figures are representative, showing the reality by association, and was an aid in the identification of flavors[11]. During the evaluation of each strip, the volunteer rinsed his mouth with water to remove the flavor to which he was previously exposed. In the end, a score from 0 to 16 was assigned, considering that the two strips with water were not counted. Notes less than or equal to 08 characterize hypogeusia and note 00 (zero) means ageusia[21].

Statistical analysis

The data obtained were organized in a Microsoft Excel® spreadsheet. To verify normality, we performed the Shapiro-Wilk test. The descriptive analysis of the sample was expressed through the number of cases (n) and percentage (%), mean and standard deviation. The Mann-Whitney test and Chi-Square test were used to characterize the sample. The Wilcoxon test compared VAS between groups. The Mann-Whitney compared the variables of the gustatory perceptual and olfactory perceptual tests, between the PD and CG groups. For the gustatory identification of the four basic flavors, the Chi-Square or Fisher's Exact Test was used. The analyzes were performed using the SPSS program, version 21, with a significance level of 5% ($p < 0.05$) for all tests used.

Chart 1. Concentration of substances related to the flavors to be discriminated[21]

Flavors	Sour	Bitter	Sweet	Salty
	(Citric acid)	(quinine hydrochloride)	(sucrose)	(sodium chloride)
Concentrations (g/ml)	0.3000	0.0060	0.4000	0.2500
	0.1650	0.0024	0.2000	0.1000
	0.0900	0.0009	0.1000	0.0400
	0.0500	0.0004	0.0500	0.0160

RESULTS

The sample consisted of 55 subjects, 35 with PD (25 men and 10 women) and 20 in the CG (16 men and 4 women). The mean age in the PD group was 66.0 (8.0) years old and in the CG, 60.4 (8.0) years old. Among subjects with PD, the average duration of the disease was 7.6 (5.1) years, with 10 subjects in the HY1 stage, 12 in the HY2, and 13 in the HY3 stage of the disease. In the PD group, 21 subjects never smoked and 14 did not report alcohol consumption. Table 1 shows the characteristics of the sample about smoking, consumption of alcoholic beverages, use of dental prosthesis, perception of smell, taste, dry mouth, and sialorrhea (Table 1).

The comorbidities reported in the sample were hypertension, diabetes, cardiovascular diseases, hypertension associated with diabetes, and others. However, 11 subjects (31%) with PD and 6 controls (30%) did not report the presence of comorbidities. Table 2 shows the comorbidities observed in the groups.

The result of self-perception of olfactory efficiency assessed using VAS demonstrated that there was an improvement for both groups, after the application of the specific smell test (Figure 2), while the self-perception of taste improved only in the CG, after the application of the Taste test (Figure 3). Such results were considered to improve self-perception, as the subjects identified their difficulty in perception, after applying perception tests, indicating less satisfaction about the efficiency of their sense of smell and taste.

Regarding the Perceptual Olfactory Test, on average, the PD group identified 1.6 (1.4) essences while the control group identified 3.3 (1.6) essences. In the PD group, the most identified essences were vinegar and garlic, followed by cloves and onions. In the CG, the most identified essences were cloves and vinegar, followed by garlic and coffee. The vinegar essence was the most identified in both groups. The olfactory perception of the essence was lower in the PD group. In the Taste Perceptual Test, there was no difference between the groups (Table 3).

Regarding the olfactory discrimination of concentration (strong/weak), the PD group had a lower result but did not reach statistical significance (Mann-Whitney, P=0.426). It is important to note that in this test the volunteer was already aware of the essence he was inhaling, and it was only necessary to discriminate which concentration was strong or weak of the same essence.

On average, the PD group discriminated the concentration (strong/weak) in 4.8 (1.4) essences and the CG discriminated the concentration in 5.1 (1.1) essences (69% vs. 72%, respectively). In the PD group, the essence most discriminated in concentration was onion (80.0%), followed by the essence of eucalyptus (74.29%). In the CG, the most discriminated

Table 1. Characteristics of the sample about smoking, consumption of alcoholic beverages, use of dental prosthesis, perception of smell, taste, dry mouth, and sialorrhea

	CG (n=20)	PD (n=35)	P-value
[m]Ex-smoker (time in years) x (±)	17 (18)	12 (18)	0.297
[m]Ex-alcoholic (time in years) x (±)	19 (16)	10 (14)	***0.038***
[x]Dental prosthesis use - n (%)	14 (70)	27 (77)	0.559
[x]Perceives loss of smell - n (%)	7 (35)	21 (60)	0.074
[x]Perceives taste loss - n (%)	5 (25)	12 (34)	0.473
[x]Perceives dry mouth - n (%)	7 (35)	14 (40)	0.714
[x]Sialorrhea - n (%)	2 (10)	15 (43)	***0.011***

[m]Mann-Whitney test; [x]Chi-Square Test
Caption: CG = Control group; PD = Parkinson's disease group

Table 2. Comorbidities observed in the groups. Values expressed in n (%)

Comorbidities	CG (n=20)	PD (n=35)
Hypertension	5 (25)	9 (26)
Diabetes	4 (20)	3 (9)
Cardiovascular diseases	0 (0)	1 (3)
Hypertension associated with diabetes	4 (20)	2 (6)
Other	1 (5)	9 (26)
Total comorbidities	14 (70)	24 (69)
No comorbidities	6 (30)	11 (31)
Total	20 (100)	35 (100)

Caption: CG = Control group; PD = Parkinson's disease group

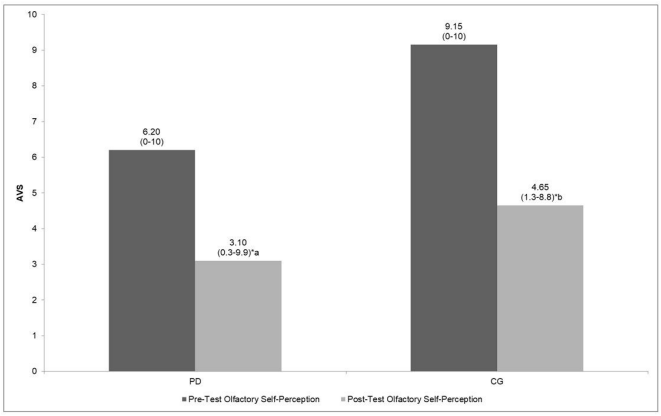

Figure 2. Comparison of pre-test versus post-test olfactory discrimination self-perception in groups PD and CG. *Wilcoxon test. P = 0.004; PD = group with Parkinson's disease; CG = control group

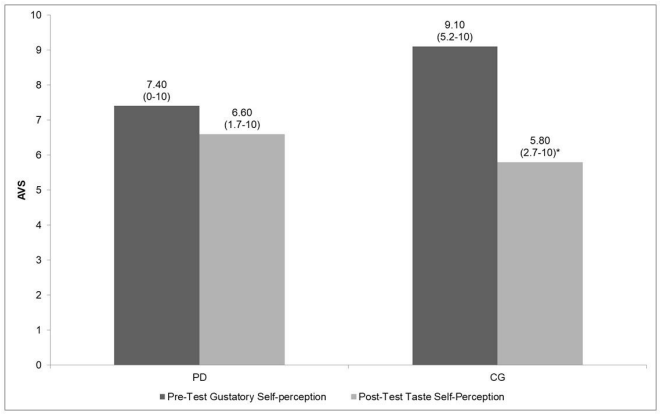

Figure 3. Comparison of pre-test versus post-test taste discrimination self-perception in the PD and CG groups

Table 3. Comparison of the variables of the olfactory perceptual and gustatory perceptual tests between the groups (PD - n = 35 and CG - n = 20)

Tests	Group	Average (±)	P-Value*
OPT	PD	1.6 (1.4)	***0.0001****
	CG	3.3 (1.6)	
TPT	PD	9.5 (2.6)	0.248
	CG	8.8 (2.2)	

*Mann-Whitney test
Caption: OPT = olfactory perception test; TPT = taste perception test

Table 4. Taste identification of the four basic flavors. Values are expressed by the percentage of discrimination.

Groups	Sweet	Salty	Sour	Bitter	Total	*P-Value
PD	69%	54%	80%	36%	60%	
CG	66%	38%	81%	34%	55%	0.553
[x]P-value	0.529	0.347	1.000	0.740	1.000	

[x]Chi-Square or Fisher's Exact Test

essence in concentration was carnation (95.0%), followed by fennel (90.0%) and roses (90.0%).

In the taste discrimination related to the concentration, both groups showed similar discrimination, with no difference in any of the flavors presented. (Table 4).

DISCUSSION

Self-perception, measured by VAS, about the smell and taste of individuals with PD, seems to be lower than in individuals in the CG before the perceptual olfactory and gustatory tests. This data demonstrates that in PD, the self-perception of the effectiveness of smell and taste may be impaired, and with the self-perception of smell and taste being compromised, food can be affected, with the ingestion of foods not suitable for consumption, less food intake, among other consequences[7].

On the other hand, both the PD group and the CG group showed better self-perception after the results of the tests of olfactory and gustatory perception, considering that they perceived more their difficulties in these parameters, after the application of the test, demonstrating that just asking is not enough in the investigation of a function. It is important to use a specific test that directs the patient to the diagnosis. However, it is valid to apply instruments such as the Visual Analogue Scale (VAS) [22,23] that can assist in self-assessment and perception of both PD and healthy individuals.

The olfactory perception in participants with PD was lower than in the CG. This result corroborates the statement that there is a decrease in olfactory sensitivity in PD, with the identification of odors being the most impaired olfactory function in this population[8,24,25]. Bearing in mind that the loss of smell is a pre-existing sign of PD, which can manifest itself in less than seven years before the motor symptoms of the disease, it is important to pay more attention to this symptom, especially in the elderly population, since that one of the multifactorial causes for the loss of olfactory sensitivity is aging[3,5]. Also, hippocampal neurodegeneration also favors the olfactory deficit in the population with PD, especially those more cognitively impaired, with impaired olfactory memory[10].

Also, the olfactory deficit can directly interfere in the quality of life of individuals, with repercussions in food, when inappetence may be present, generating less food consumption, with consequent weight loss, which may lead the individual to malnutrition, muscular atrophy, seclusion among other consequences[7,26].

The essences used were chosen to favor the identification by the participants, being essences from day to day. This care in choosing the essences for the test facilitated the identification of the most common smells, such as vinegar, garlic, cloves, and onions for the PD group, demonstrating that the olfactory memory directly interferes in the identification of the essences, especially in older age[10]. However, the participants often reported that they were smelling the essence, but did not remember what it corresponded to. Thus, the lower olfactory perception of participants with PD may have suffered interference from olfactory memory, considering the dysfunctions of the hippocampus harmful to the identification of odors[10].

Therefore, the visual cues (images) used in the present study are a support for the participants' olfactory memory[20], being a differential from other research. The use of images was based on the assumption that these would favor the studied group that could present changes in olfactory memory, differently from what occurs in childhood, when the capacity for olfactory discrimination is very sharp, even in the presence of allergic conditions, such as rhinitis, for example, when cognition, perception, and neurotransmission are preserved, favoring the evocation of olfactory memory[11].

Regarding the olfactory discrimination of concentration (strong/weak), the participants with PD presented a result very close to the CG. Onions and eucalyptus were the essences most discriminated in concentration by the PD group, while fennel, roses, cloves, garlic, and coffee were the essences less discriminated in concentration. This result can be explained by the fact that, in this test, the volunteers were already aware of which essence they were inhaling, making it easier to discriminate concentration, as they did not need to remember what the essence corresponded to.

On the other hand, fennel and roses are normally milder essences; therefore, difficult to differentiate the concentration, since even the strongest concentration ends up being also mild in comparison to the other essences. On the other hand, cloves, garlic, and coffee are essences that have more striking characteristics, where even the weakest concentration is very noticeable, which could explain the greater difficulty in differentiating the concentration.

Thus, knowing that cholinergic and dopaminergic denervation/ can alter the function of the hippocampus[10], it is assumed that the evocation of olfactory memory, and not the perception of odors, may be compromised in PD.

Regarding gustatory perception, participants with PD did not differ from the CG, both in taste discrimination and in the concentration experienced, presenting very similar results. The CG had a higher number of individuals with diabetes and hypertension associated with diabetes than the group with PD. This characteristic is one of the limitations of the study that may have contributed to a lower taste perception of the individuals in the CG, as diabetes can directly interfere with taste, changing the perception of flavors[27].

As for the possible relationship between changes in smell and taste in individuals with PD, deficits in taste perception were found in women with PD compared to a control group[7], opposing a recent study that found no taste alteration, but only olfactory deficit in individuals with PD[28], as well as in the present study. Despite different results, the authors agree that there are few studies on taste perception in PD and that different variables such as sex, age, medication, type of instruments used, can interfere with the results.

Therefore, despite the direct relationship between smell and taste[12,13], the results of the present study corroborate the hypothesis that people with PD have less olfactory perception than individuals without PD, but the same does not happen with perception gustatory[28,29] although this alteration was found in another study[8]. Therefore, this result should be further investigated in later studies, in a larger population, and with a CG without comorbidities that interfere with taste.

One of the possible causes of different results in olfactory and gustatory perception is the fact that the four tastes presented were repeated in four different concentrations, that is, the taste of the participants had access to information on taste three times more than that of smell. This difference may also have facilitated the identification of flavors more than essences since the repetition of information helps to evoke the memory that may be altered in PD[30].

The differences between the results of the studies can be justified by several factors, such as the number of participants, the method, instruments used, eligibility criteria, among others. This study differs by using nasal cleaning and oral brushing before the olfactory and gustatory tests, respectively, minimizing bias in the results, in addition to not including smokers or alcoholics. On the other hand, the number of participants in the present study decreased, which is a limiting factor, since many individuals with PD used alcohol or tobacco, and were not eligible for data collection.

The test used in this study to assess olfactory perception has volatile material and is also admitted as a limitation of the study. However, the results proved its effectiveness, comparing it to other studies of the population with PD[8,25,28].

Finally, individuals with PD may have dysfunction of the olfactory memory input and not of the essence presented since they recognized the strong/weak concentration of the essences similarly to the control group and did not present any interference in the gustatory perception, even though the strong relationship between smell and taste. Thus, we suggest new studies that investigate not only the olfactory perception but also their memory, separately, and as for the taste, in addition to the gustatory perception, to analyze the sensation that each taste evokes to the evaluated subject, to each solution presented.

CONCLUSION

In this study, the olfactory perception of people with Parkinson's disease was lower than the group of healthy individuals, and the self-perception of olfactory efficacy improved after the

test in both groups. As for taste, there was no difference in perception and discrimination between the groups, the sour taste was the most identified and there was an improvement in the self-perception of gustatory efficacy only in the group without Parkinson's disease, after the test.

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WRPLA study design, data collection, analysis and interpretation, writing of the article; AOCG and LRB analysis and interpretation of data, writing, and review of the article; LBL making the test material; MGWSC conception, study design, data interpretation, writing, and review of the article.