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ORIGINAL COMMUNICATION

Taste impairment in patients with Parkinsonism

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Abstract

Background Taste impairment is a prevalent issue among individuals with idiopathic Parkinson's disease (iPD). However, understanding taste disorders among different Parkinsonism remains incomplete. Our objective was to assess the incidence and severity of taste responses to sweet, salty, sour, bitter, and umami substances in patients with iPD, progressive supranuclear palsy (PSP), and multiple system atrophy (MSA).

Methods Taste function was evaluated by assessing the intensity ratings of four concentrations of sweet, salty, sour, bitter, and umami in 221 healthy controls (HCs), 251 iPD patients, 156 PSP patients, and 60 MSA patients. The Kruskal–Wallis one-way analysis was employed to discern differences in taste function among groups. Logistic regression models were utilized to analyze the association between disease severity and taste function.

Results Participants with iPD, PSP, and MSA exhibited lower total taste scores (TTS) compared to HCs ($P<0.0001$, $P<0.0001$, and $P=0.0002$, respectively). The TTS was significantly lower in iPD patients compared to PSP and MSA patients ($P=0.0024$ and $P=0.0464$, respectively), with no discernible difference between PSP and MSA patients ($P=0.9998$). Furthermore, in patients with iPD, both disease severity and gastrointestinal function exhibited a significant negative correlation with the TTS. However, the taste test lacked the potency to reliably distinguish iPD from PSP and MSA.

Conclusions These research findings suggest that taste impairment emerges as a phenotype of Parkinsonism, serving as a basis for differential diagnosis and guiding dietary adjustments for patients.

Keywords Taste impairment · iPD · PSP · MSA

Introduction

Idiopathic Parkinson's disease (iPD) is a progressive neurodegenerative disorder characterized by motor and nonmotor manifestations [1]. It is also important to note that sensory symptoms may occur prior to or concurrently with the development of parkinsonism and are considered integral to the neurodegenerative process associated with iPD [2]. The olfactory dysfunction has been identified as one of the most frequently evaluated sensory symptoms of iPD [3]. Moreover, taste plays an important role in our interaction with the environment, combined with the olfactory system, influencing our behavior and memory processes [4].

Gastrointestinal dysfunction has emerged as a prominent nonmotor symptom of iPD, often preceding the onset of motor symptoms and affecting approximately 90% of patients [5]. Notably, an international multi-center survey identified taste complaints and constipation as some of the most frequently reported symptoms in patients with iPD [6, 7]. However, the deficits of taste and constipation may also occur in healthy controls (HCs), progressive supranuclear palsy (PSP), and multiple system atrophy (MSA) [8, 9]. Among the various digestive dysfunctions in patients with iPD, constipation has been extensively studied, while taste disorders have received relatively little attention in

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iPD and parkinsonism [10, 11]. Understanding the potential importance of taste impairment akin to constipation in iPD could pave the way for the development of novel diagnostic approaches.

In this study, we investigated 688 participants using varying concentrations of the five basic tastes (sweet, salty, sour, umami, and bitter). Notably, umami, which has seldom been evaluated in large populations, was specifically included. Additionally, we assessed the characteristics of taste function and explored its potential association with disease severity and gastrointestinal function in the patient cohort.

Materials and methods

Approval and patient informed consent

This study was performed in line with the principles of the Declaration of Helsinki. Participants were consecutively recruited from the First Affiliated Hospital of Zhengzhou University from January 2021 to December 2023. All participants were enrolled according to the human experimentation, and approved by the Ethics Committees of The First Affiliated Hospital of Zhengzhou University (Approve Code: 2021-KY-372). Informed consent was diligently obtained from each participant or, in the case of patients lacking decision-making capacity, from their duly authorized surrogates.

Participants

Patients were consecutively recruited from the department of neurology at the First Affiliated Hospital of Zhengzhou University. Following the consensus criteria for iPD [12], PSP [13, 14], and MSA [15], all patients underwent detailed interviews and examinations conducted by two board-certified neurologists, each possessing more than a decade of experience in diagnosing movement disorders. HCs were recruited from the Physical Examination Center of the First Affiliated Hospital of Zhengzhou University. All control participants underwent thorough health assessments, including screening laboratory tests, electrocardiograms, medical history reviews, and physical examinations. They were confirmed to be in good health and were assessed as devoid of neurological disorders by two attending neurologists. Exclusion criteria encompassed conditions such as upper respiratory tract infection, Bell's palsy, otorhinolaryngological disorders, chronic alcoholism, postoperative status, a history of severe traumatic brain injury, a history of malignancy, chronic kidney disease, or other diseases that might affect taste perception. The selection process of participants, including different patient's categories and the reasons for exclusion, is illustrated in the accompanying flow diagram (Fig. 1).

Clinical assessments

All patients were treated with L-dopa or other dopaminergic agents and were evaluated in the ON state, ensuring they were capable of performing the required tasks. Disease severity was assessed using the Unified Parkinson's Disease Rating Scale (UPDRS) for patients with iPD [16], the Unified Multiple System Atrophy Rating Scale (UMSARS) for patients with MSA [17], and the Progressive Supranuclear Palsy Rating Scale (PSPRS) for patients with PSP [18]. Clinical stages of Parkinsonism were determined according to the Hoehn and Yahr (H&Y) scale [19]. Cognitive performance was evaluated using the Mini-Mental State Examination (MMSE) [20] and the Montreal Cognitive Assessment (MoCA) [20]. Non-motor symptoms were assessed using the Non-Motor Symptoms Scale (NMSS) [21], while autonomic dysfunction was measured by the Scales for Outcomes in Parkinson's disease—Autonomic (SCOPA-AUT) [22]. Additionally, gastrointestinal symptoms were surveyed using the Gastrointestinal Symptom Rating Scale (GSRS) [23].

Taste assessment

The "Taste Strips" method [24] was modified by using 1 mL syringes to deliver the tastants, replacing the use of filter paper strips. In the original "Taste Strips" method, the filter paper strips are applied to the tongue using spoon-shaped paper, with the examiner ensuring that the strips are placed directly on the tongue and not displaced. Patients with Parkinsonism experience rigidity and might have difficulty opening their mouths for a long time. In addition, the filter paper strips were easy to evaporate and cannot be quantified accurately. 1 mL syringe with the 0.05 ml tastants via 26-G needle as filter paper strips were used to ensure that the same amount of tastants was transferred to overcome this problem.

Solutions were prepared to test sweet, salty, sour, umami, and bitter tastes. A sucrose solution was used for sweet, sodium chloride for salty, citric acid for sour, monosodium glutamate for umami tastes, and quinine hydrochloride for bitter. The concentrations of the solutions for sweet, salty sour, and bitter were prepared at 4 levels based on the "Taste Strips" method [16]. For the umami taste, 4 concentrations of monosodium glutamate solutions were prepared using the method developed by Christian et al. [17] (Supplementary Table 1). Distilled water was used to prepare the test solutions for taste evaluation. Freshly taste solutions were prepared every month.

Participants had to refrain from drinking and smoking 2 h before the test and refrain from eating, brushing their

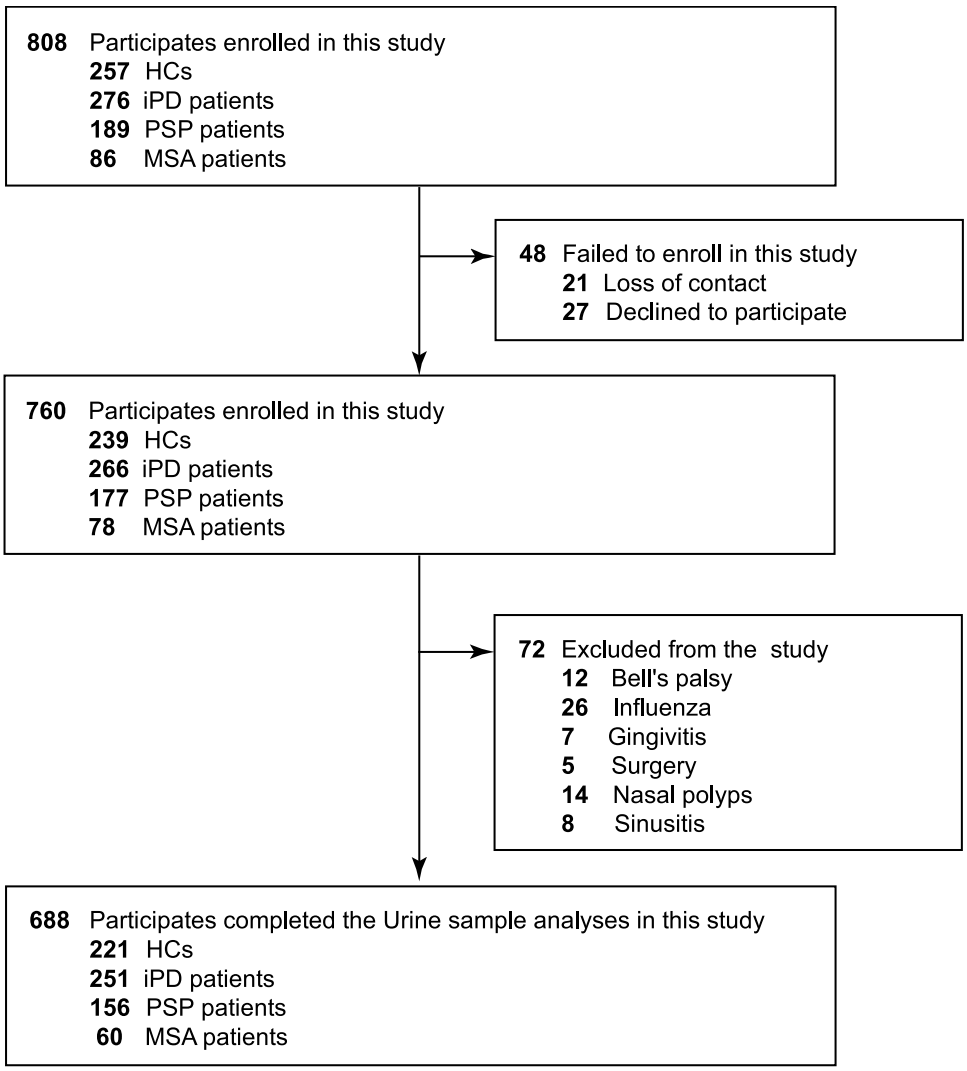

Fig. 1 CONSORT diagram. consolidated standards of reporting trials flow diagram showing study participants screening, eligibility and inclusion

teeth, and chewing gum at least 1 h prior. The participants were exposed to all the tastes in a randomized order at each of the four increasing levels of concentration. First, a solution with the lowest concentration (level 1) of a randomly selected taste was applied to them. 1 mL Syringe with the 0.05 ml solution was dipped onto the corresponding position of the taste buds carefully to avoid touching the tongue (Supplementary Fig. 1). Then, the syringe was removed, and the participants responded to whether they perceived a taste and identified its type in 3 s. If the taste was correctly identified it was defined as one point; if not, defined as 0. Before the next taste solution, the syringe was used a new one, and participants were asked to rinse their mouth several times with water to avoid interference between tastes. To obtain an impression of overall taste function, the number of correctly identified tastes was added up to a "total taste score (TTS)". Raw taste scores were calculated as the number of correct identifications, ranging from 0 to 20, with 20 representing perfect taste function, 11–19 representing hypogeusia, and ≤ 10 representing ageusia. The whole testing procedure typically required approximately 20 min for the 5 tastants.

Statistical analysis

Statistical analysis was performed using GraphPad Prism version 8.4.3 (GraphPad Software). Continuous clinical and demographic data are presented as means ± standard deviation (SD), while categorical data are reported as medians, frequencies, or percentages. Comparisons of quantitative variables between groups were made using the Kruskal–Wallis one-way analysis of variance, followed by post hoc testing with the Wilcoxon signed-rank test. Categorical variables were compared using Fisher's exact test, with Bonferroni adjustments for multiple comparisons. The association between two continuous variables was assessed using Pearson correlation and linear regression models. Logistic regression models were employed to examine

the impact of clinical factors on TTS and GSRS scores in patients with iPD. Diagnostic accuracy of the taste scores was evaluated via receiver operating characteristic (ROC) curve analysis. Clinical covariates, including sex, age, body mass index (BMI), and disease duration, were included in the regression models to adjust for potential confounders. A p-value of < 0.05 was considered statistically significant.

Results

Demographic and clinical features

In our study, a total of 808 new participants were initially recruited, including 257 HCs, 276 patients with iPD, 189 with PSP, and 86 with MSA. Among these, 48 participants (5.94%) who declined participation or could not be contacted due to incomplete or outdated contact information were excluded. Additionally, 72 participants (8.91%) who reported taste loss due to non-idiopathic causes (such as Bell's palsy, influenza, gingivitis, surgery, nasal polyps, or sinusitis) were also excluded from the study. Ultimately, 688 participants (85.15%) successfully completed clinical and taste assessments as per the Consolidated Standards of Reporting Trials (CONSORT) flow diagram (Fig. 1).

The demographic characteristics of the participants are detailed in Table 1. There were no significant differences observed in gender, age, or BMI across the four groups ($P = 0.9878$, $P = 0.4182$, and $P = 0.3354$, respectively). Similarly, there were no significant variations in H&Y, UPDRS, and GSRS scores among iPD, PSP, and MSA patients ($P = 0.4510$, $P = 0.9772$, and $P = 0.9606$, respectively). However, iPD patients exhibited significantly longer disease durations compared to PSP ($P = 0.0014$) and MSA patients ($P = 0.0298$). Notably, there was no significant difference in disease duration between PSP and MSA patients ($P = 0.9988$). Cognitive assessments, including MMSE and MoCA, indicated lower scores in PSP patients compared to iPD ($P < 0.0001$ and $P < 0.0001$, respectively) and MSA ($P = 0.0001$ and $P < 0.0001$, respectively) patients. However, MMSE and MoCA scores did not significantly differ between iPD and MSA patients ($P = 0.9761$ and $P = 0.1885$, respectively).

Taste impairment

The distribution of taste scores among study participants is depicted in Fig. 2. Our taste assessment indicated that HCs achieved significantly higher scores for correctly identifying tastes compared to patients with iPD, PSP, and MSA (Fig. 2, and Supplementary Fig. 2). Specifically, in the sweet taste test, mean scores were 3.41 for HCs, 3.10 for iPD, 3.13 for PSP, and 3.17 for MSA ($P = 0.0117$). Notably, iPD patients showed significantly lower scores compared to HCs ($P = 0.0098$), while no significant differences were observed among HCs, PSP, and MSA patients ($P = 0.0741$, $P = 0.4153$, and $P = 0.9975$, respectively) (Table 1, Fig. 2A). In detail, mean scores were 3.41 for HCs, 2.69 for iPD, 3.17 for PSP, and 2.90 for MSA ($P < 0.0001$) in the salty taste test. Here, iPD and MSA patients had significantly lower scores compared to HCs ($P < 0.0001$ and $P = 0.0105$, respectively), while no significant difference was found between HCs and PSP patients ($P = 0.1630$). Additionally, iPD patients exhibited lower scores than PSP patients ($P = 0.0002$) (Table 1, Fig. 2B). For the sour taste test, mean scores were 3.19 for HCs, 2.71 for iPD, 2.76 for PSP, and 3.15 for MSA ($P < 0.0001$). Scores were significantly lower in iPD and PSP patients compared to HCs ($P < 0.0001$ and $P = 0.0029$, respectively), with no significant difference observed between HCs and MSA patients ($P = 0.9967$). Furthermore, iPD patients showed lower scores compared to MSA patients ($P = 0.0029$) (Table 1, Fig. 2C). In the umami taste test, mean scores were 3.27 for HCs, 2.65 for iPD, 2.75 for PSP, and 2.63 for MSA ($P = 0.0001$). Scores were significantly lower in iPD, PSP, and MSA patients compared to HCs ($P = 0.0001$, $P = 0.0182$, and $P = 0.0342$, respectively), with no significant differences among iPD, PSP, and MSA patients ($P = 0.8214$, $P > 0.9999$, and $P = 0.9371$, respectively) (Table 1, Fig. 2D). In the bitter taste test, mean scores were 3.87 for HCs, 3.23 for iPD, 3.58 for PSP, and 3.58 for MSA ($P < 0.0001$). Scores were significantly lower in iPD, PSP, and MSA patients compared to HCs ($P < 0.0001$, $P = 0.0057$, and $P = 0.0041$, respectively), with no significant differences observed between iPD and MSA patients ($P = 0.8374$), or between PSP and MSA patients ($P = 0.7599$). Notably, iPD patients had lower scores than PSP patients ($P = 0.0029$) (Table 1, Fig. 2E). Figure 2F illustrates the distribution of total TTS across the four study groups. Statistical analysis revealed significantly lower TTS in iPD, PSP, and MSA patients compared to HCs ($P < 0.0001$, $P < 0.0001$, and $P = 0.0002$, respectively). Moreover, TTS was significantly lower in iPD patients compared to PSP and MSA patients ($P = 0.0024$ and $P = 0.0464$, respectively), with no significant difference between PSP and MSA patients ($P = 0.9988$) (Table 1, Fig. 2F). In the MSA group, there were no significant differences in the taste test results for sweet, salty, sour, umami, and bitter flavors, as well as in TTS, between MSA-parkinsonian and MSA-cerebellar subtypes. (Supplementary Fig. 3).

To further explore the impact of parkinsonism on TTS, we stratified TTS into three categories: Class I (perfect taste function), Class II (hypogeusia), and Class III (ageusia). Among HCs, 42 (19.00%) demonstrated perfect taste function, while 117 (80.09%) had hypogeusia, and 2 (0.90%) had ageusia (Supplementary Fig. 2F). In contrast, among iPD patients, 11 (4.38%) had perfect taste function, 204 (81.27%)

Table 1 Demographics and clinical characteristics of the subjects in the study

	HCs (n = 221)	iPD (n = 251)	PSP (n = 156)	MSA (n = 60)	Overall P-value	Pairwise comparisons					
						iPD vs. HCs	PSP vs. HCs	MSA vs. HCs	iPD vs. PSP	iPD vs. MSA	PSP vs. MSA
Male, n (%)	112 (50.68%)	125 (49.80%)	79 (50.64%)	29 (48.33%)	0.9878	0.9458	0.9942	0.7473	0.8691	0.8382	0.7613
Age, y	64.81 (6.43)	65.00 (6.09)	64.29 (6.14)	65.80 (5.65)	0.4182	0.9855	0.8595	0.6872	0.6479	0.8074	0.3787
BMI	22.04 (2.56)	22.17 (2.08)	22.04 (1.99)	21.62 (2.13)	0.3354	0.9084	> 0.9999	0.5062	0.9355	0.2565	0.5356
Taste Strip Test, Total score (0–16)	17.15 (2.36)	14.37 (3.42)	15.40 (2.55)	15.43 (2.33)	< 0.0001	< 0.0001	< 0.0001	0.0002	0.0024	0.0464	0.9998
Sweet	3.41 (0.92)	3.10 (1.25)	3.13 (1.05)	3.17 (1.08)	0.0117	0.0098	0.0741	0.4153	0.9853	0.9693	0.9977
Salty	3.41 (1.86)	2.69 (1.36)	3.17 (1.00)	2.90 (1.23)	< 0.0001	< 0.0001	0.1630	0.0105	0.0002	0.5650	0.4067
Sour	3.19 (1.07)	2.71 (1.24)	2.76 (1.20)	3.15 (1.02)	< 0.0001	< 0.0001	0.0029	0.9967	0.9617	0.0385	0.1240
Umami	3.27 (0.94)	2.65 (1.48)	2.75 (1.32)	2.63 (1.28)	0.0001	0.0001	0.0182	0.0342	0.8214	> 0.9999	0.9371
Bitter	3.87(0.60)	3.23 (1.25)	3.58 (0.68)	3.58 (0.79)	< 0.0001	< 0.0001	0.0057	0.0041	0.0420	0.8374	0.7599
Disease duration, y	NA	3.56 (2.05)	2.78 (2.35)	2.77 (2.26)	0.0006	/	/	/	0.0014	0.0298	0.9988
H&Y score	NA	2.60 (0.79)	2.48 (1.06)	2.52 (0.98)	0.4510	/	/	/	0.4346	0.8196	0.9638
UPDRS score	NA	63.98 (21.97)	63.94 (34.82)	63.12 (35.08)	0.9772	/	/	/	> 0.9999	0.9761	0.9804
PSPRS score	NA	NA	46.97 (11.62)	NA	/	/	/	/	/	/	/
UMSARS	NA	NA	NA	43.98 (8.76)	/	/	/	/	/	/	/
MMSE	NA	25.60 (4.86)	21.10 (5.45)	24.32 (5.25)	< 0.0001	/	/	/	< 0.0001	0.1885	0.0001
MoCA	NA	24.67 (6.27)	19.85 (7.16)	25.97 (4.48)	0.0113	/	/	/	< 0.0001	0.3356	< 0.0001
SCOPA	NA	36.41 (12.77)	36.42 (11.68)	36.07 (10.74)	0.9787	/	/	/	> 0.9999	0.9787	0.9797
Olfactory dysfunction	NA	169 (76.47%)	56 (35.90%)	17 (28.33)	/	/	/	/	0.0109	0.4990	0.3371
GSRS	NA	23.51 (10.60)	23.17 (16.36)	23.45 (13.94)	0.9606	/	/	/	0.9574	0.9992	0.9874

Results are presented as mean (S.D.) unless otherwise stated. *P*-values evaluated with Kruskal–Wallis one-way analysis of variance with post hoc testing. Olfactory dysfunction was accessed by Non-Motor Symptoms Scale (NMSS) scale

iPD idiopathic Parkinson's disease, *PSP* progressive supranuclear palsy, *MSA* multiple system atrophy, *BMI* body mass index, *UPDRS* unified Parkinson's disease rating scale, *PSPRS* Progressive Supranuclear Palsy Rating Scale, *UMSARS* Unified Multiple System Atrophy Rating Scale, *MoCA* Montreal Cognitive Assessment, *MMSE* mini-mental state examination, *SCOPA* Scales for Outcomes in Parkinson's Disease, *GSRS* gastrointestinal symptom rating scale, *NA* not applicable

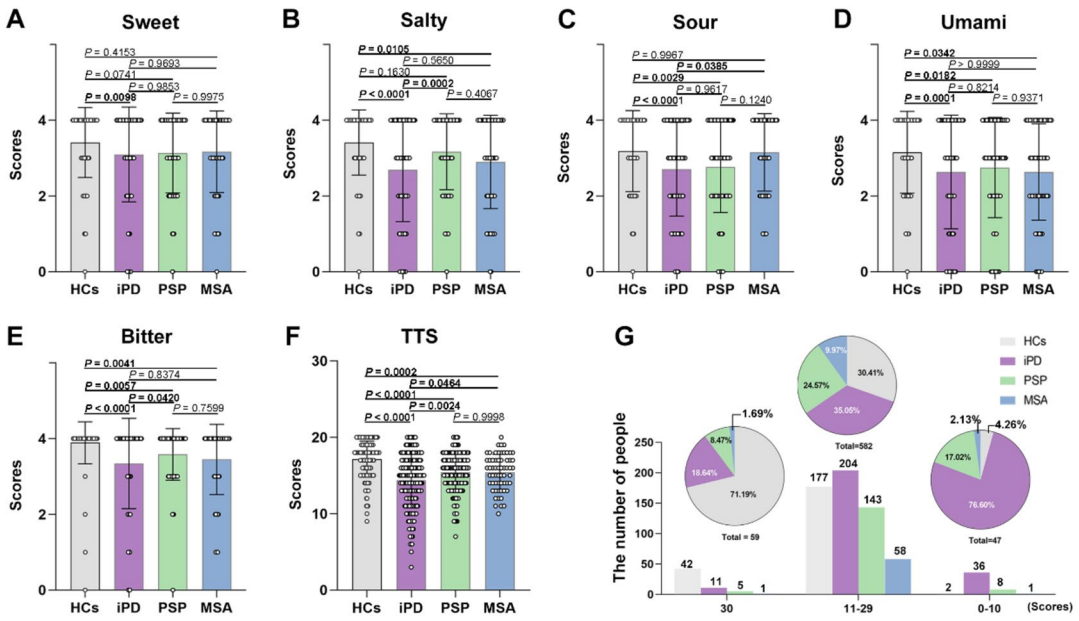

Fig. 2 The distribution and comparison of taste scores. The comparison of taste scores in sweet (**A**), salty (**B**), sour (**C**), umami (**D**), bitter (**E**) test, and TTS (**F**) among the HCs, iPD, PSP and MSA groups. All box-and-whisker plots depict the median, quartiles and range. **G** The distributions of HCs, iPD, PSP and MSA in absolute numbers and relative percentage among perfect taste function, hypogeusia, and ageusia. Statistical significance was determined by Kruskal–Wallis one-way analysis of variance with post hoc testing

had hypogeusia, and 36 (14.34%) had ageusia (Supplementary Fig. 2G). Similarly, among PSP patients, 5 (3.21%) had perfect taste function, 143 (91.67%) had hypogeusia, and 8 (5.13%) had ageusia (Supplementary Fig. 2H). Lastly, among MSA patients, 1 (1.67%) had perfect taste function, 58 (96.67%) had hypogeusia, and 1 (1.67%) had ageusia (Supplementary Fig. 2I). The distribution of taste function classes revealed a significantly higher prevalence of hypogeusia and ageusia among iPD patients compared to other groups, indicating more pronounced gustatory dysfunction in iPD (Fig. 2G).

Correlation between taste impairment and clinical characteristics

The association between taste scores and clinical characteristics was assessed in the study participants. Pearson's correlation analysis revealed no correlation between age and taste scores among HCs or patients with iPD, PSP, or MSA (Supplementary Table 2). In iPD patients, significant correlation was observed between sweet taste scores and GSRS scores ($P = 0.013$, $r = -0.156$), and a similar correlation was noted between salty taste scores and MDS-UPDRS score ($P = 0.048$, $r = -0.156$). Additionally, sour taste scores showed mild negative correlations with MDS-UPDRS ($P = 0.007$, $r = -0.168$) and GSRS scores ($P = 0.038$, $r = -0.131$) in iPD patients. Umami taste scores were negatively correlated with MDS-UPDRS score ($P = 0.012$, $r = -0.159$), while bitter taste scores exhibited negative correlations with H&Y, MDS-UPDRS, SCOPA-AUT, and GSRS scores in iPD patients ($P = 0.002$, $r = -0.197$; $P = 0.001$, $r = -0.202$; $P = 0.038$, $r = -0.131$; and $P = 0.005$, $r = -0.178$, respectively). Moreover, TTS showed negative correlations with H&Y, MDS-UPDRS, and GSRS scores in iPD patients ($P = 0.013$, $r = -0.157$; $P < 0.001$, $r = -0.283$; and $P < 0.001$, $r = -0.247$, respectively) (Fig. 3A, Supplementary Table 2). Among PSP patients, salty taste scores exhibited small but significant correlations with MMSE and MoCA scores ($P = 0.025$, $r = 0.180$; and $P = 0.026$, $r = 0.178$, respectively), and TTS showed a correlation with H&Y score ($P = 0.049$, $r = 0.256$) (Fig. 3C, Supplementary Table 2). These findings suggest that taste scores are significantly associated with disease severity in iPD patients. Further validation was conducted through logistic regression analysis, which confirmed a negative correlation between TTS and disease severity assessed by H&Y staging scale and UPDRS in iPD patients ($r = -0.1574$, $P = 0.0126$; $r = -0.2834$, $P < 0.0001$, respectively) (Fig. 3D and E). Additionally, gastrointestinal function assessed by GSRS scores was significantly negatively correlated with TTS in iPD patients ($r = -0.2466$, $P < 0.0001$) (Fig. 3F).

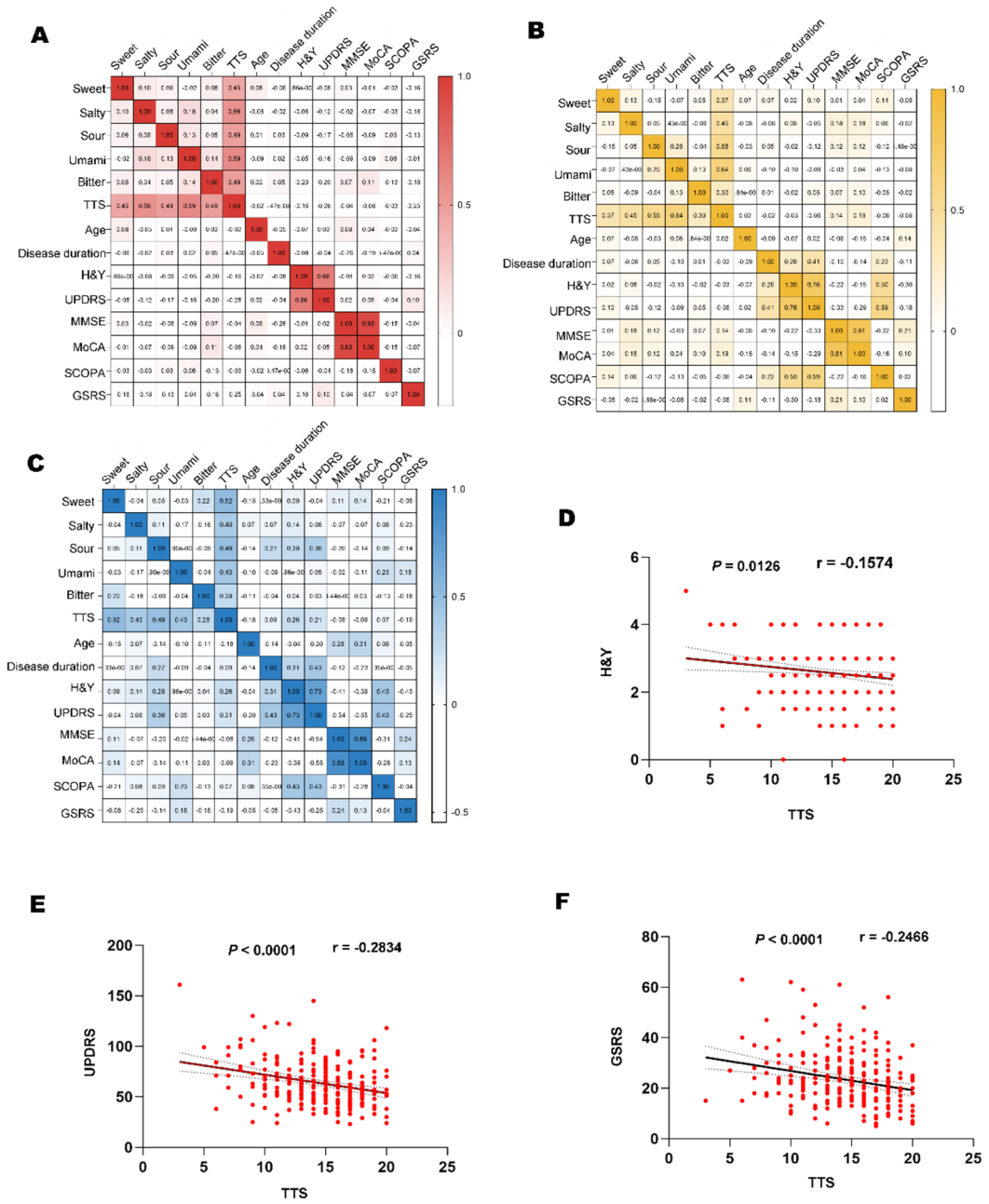

Fig. 3 Association between the taste function and clinical characteristics in patients. **A-C,** Association between the taste function and clinical characteristics in patients with iPD **(A)**, PSP **(B)** and MSA **(C)**, respectively. **D-F,** Scatterplots showing the correlation analysis in patients with iPD between the TTS and H&Y **(D)**, UPDRS **(E)** and GSRS **(F)**, respectively. Associations were assessed using Spearman correlation **(A-C)**. Solid line indicates regression line, and dotted lines border the 95% confidence interval using linear correlation analysis **(D-F)**

Predictive value of taste impairments for iPD

We performed ROC curve analyses of taste scores, as shown in Supplementary Table 3, to identify effective markers for stratifying Parkinsonism. In the sweet test, the ROC analysis distinguished HCs from iPD patients with an AUC (Area Under Curve) of 0.5585, specificity of 45.42%, and sensitivity of 63.80%. It also differentiated HCs from PSP patients with an AUC of 0.5757, specificity of 50.00%, and sensitivity of 63.80%. For the salty test, the analysis differentiated HCs from iPD patients with an AUC of 0.6456, specificity of 60.16%, and sensitivity of 60.63%. It also separated HCs

from PSP patients (AUC = 0.5644, specificity = 49.36%, sensitivity = 60.63%), HCs from MSA patients (AUC = 0.6100, specificity = 55.00%, sensitivity = 60.63%), and iPD from PSP patients (AUC = 0.5891, specificity = 50.64%, sensitivity = 60.16%). In the sour test, the ROC analysis distinguished HCs from iPD patients (AUC = 0.6127, specificity = 64.14%, sensitivity = 54.75%), HCs from PSP patients (AUC = 0.6049, specificity = 64.74%, sensitivity = 54.75%), iPD from MSA patients (AUC = 0.5994, specificity = 51.67%, sensitivity = 64.14%), and MSA from PSP patients (AUC = 0.5896, specificity = 51.67%, sensitivity = 64.74%). For the umami test, the analysis identified differences between HCs and iPD patients (AUC = 0.5868, specificity = 57.77%, sensitivity = 53.39%), HCs and PSP patients (AUC = 0.5868, specificity = 63.46%, sensitivity = 53.39%), and HCs and MSA patients (AUC = 0.6189, specificity = 66.67%, sensitivity = 53.39%). In the bitter test, the analysis differentiated HCs from iPD patients (AUC = 0.6256, specificity = 29.48%, sensitivity = 95.93%), HCs from PSP patients (AUC = 0.6379, specificity = 32.69%, sensitivity = 95.93%), and HCs from MSA patients (AUC = 0.6344, specificity = 31.67%, sensitivity = 95.93%). These results suggest that individual taste tests are not highly effective for distinguishing between different forms of Parkinsonism. However, the TTS might be a more reliable marker, capable of differentiating iPD, PSP, and MSA patients from HCs with AUC values of 0.7448, 0.7014, and 0.7066, respectively. Moreover, the TTS differentiated iPD patients from PSP (AUC = 0.5827, specificity = 66.67%, sensitivity = 47.01%) or MSA patients (AUC = 0.5823, specificity = 65.00%, sensitivity = 47.01%) (Supplementary Table 3, Supplementary Fig. 4).

Discussion

Although an increasing number of studies suggest that taste impairment is associated with iPD, research on this topic remains limited, with heterogeneous and contradictory findings reported. [10]. In this study, we assessed taste function at four different concentrations in HCs, patients with iPD, PSP, and MSA. Our data indicated that taste impairment was significantly more severe in patients with iPD than other groups. Previous cross-sectional studies using various measurement techniques have consistently found that patients with iPD more frequently exhibit impaired taste compared with controls [18–21]. Our findings corroborate this conclusion. Notably, responsiveness to different taste qualities varied among patients. Specifically, PSP patients exhibited significant impairment in salty taste compared to iPD and MSA patients. Furthermore, iPD patients had the lowest scores for sour and bitter tastes among the four groups. These results highlight the diverse nature of taste impairment across different types of Parkinsonism, which could aid in managing expectations and improve dietary compliance.

The pathogenesis of taste impairment in Parkinsonism may be related to the distinct neurodegeneration associated with each condition. In iPD, the primary pathological feature is the loss of dopaminergic neurons in the substantia nigra, which may contribute to broader sensory processing deficits. This could explain the lower scores for sour and bitter tastes, likely reflecting a general decline in sensory integration rather than impairment of specific taste modalities. [22]. In PSP, the accumulation of tau protein primarily affects the basal ganglia and frontal regions, potentially disrupting the neural circuits involved in taste processing, especially for salty taste [14]. In contrast, MSA presents a more varied pathology, often involving oligodendrocytic degeneration, resulting in a less pronounced effect on taste compared to PSP and iPD. This may account for the milder taste impairment observed in this group of patients [23].

The mechanism of taste impairment in iPD has not been identified. According to the Braak's staging theory of iPD, there are no defects in first-order taste neurons (cranial nerves VII, IX, and X) or second-order taste neurons (nucleus of the solitary tract) [4, 24]. This has led some researchers to propose that taste impairment in advanced iPD may be associated with cortical involvement of the primary gustatory cortices[3, 11]. A recent neuropathological study, contrary to previous reports, demonstrated α-synuclein deposition in both the nucleus of the solitary tract and cranial nerve nuclei in some patients with iPD [25]. In our study, taste impairment was also observed in early-stage iPD, and we confirmed a correlation between the severity of iPD and the degree of taste loss. Although an increasing number of studies have reported taste and gastrointestinal dysfunction in patients, data specifically addressing these changes in iPD patients remain limited [26, 27].

Both MSA and PSP are neurodegenerative disorders that affect various brain regions involved in taste perception, particularly through damage to the brainstem and other areas disrupting neural pathways responsible for taste processing [4, 28, 29]. Additionally, both diseases can lead to dysphagia, or swallowing difficulties [30, 31], which may further affect the overall eating experience and alter taste perception. The presence of α-synuclein aggregates in peripheral biopsies, including the gastrointestinal tract, skin, and salivary glands, may also damage taste bud function [32, 33]. Furthermore, medications such as dopaminergic treatments or anticholinergics can affect taste perception, leading to alterations in taste perception [34].

In this study, we observed no correlation between taste impairment and gastrointestinal dysfunction, age, disease duration, or cognitive dysfunction in the HC, PSP, or MSA groups. Given the established functional and

neuroanatomical links between taste perception and the gastrointestinal tract, we further explored gastrointestinal symptoms using the GSRS [23]. Our findings revealed a significant negative correlation between gastrointestinal dysfunction and the TTS in patients with iPD. The primary nucleus of the trigeminal nerve in the brainstem, the nucleus of the solitary tract in the medulla [4], is implicated in taste perception. Moreover, the presence of α-synuclein deposits in both the nucleus of the solitary tract and cranial nerve nuclei likely contributes to the heightened sensitivity to taste dysfunction observed in early Parkinson' s disease [33]. These observations suggest that taste dysfunction may be associated with the early stages of iPD and could serve as a potential marker of initial pathological changes.

Several limitations of this study should be considered when interpreting our findings. Although we utilized the NMSS to assess taste and olfactory functions, only the degree of olfactory changes was recorded. The biological relationship between taste and olfactory impairments in Parkinsonism remains unclear and warrants further investigation. Future studies employing more rigorous experimental designs and early follow-up cohorts are necessary to better understand the nature of taste and olfactory dysfunction in Parkinson's disease. Additionally, we were unable to assess the impact of other clinical and demographic factors, such as smoking history, emotional status, and medication use. These variables should be addressed in future research.

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Author contributions Q.Z. and H.L. contributed equally to this work. X.D. and Q.Z. conceived and designed this study; X.D. and H.L. coordinated the whole project; Q.Z. and X.D. were responsible for the initial assessment and diagnosing of patients; Q.Z. and X.W. were responsible for assessing and documenting patients' information. H.L. and J.W. were responsible for taste assessment. R.F. was responsible for taste analysis; Q.Z. and M.M. participated in final data analysis and interpretation; X.D., Q.Z., and H.L. carried out most of the writing with input from other authors. All authors discussed the results and commented on the manuscript.

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Data availability The authors confirm that the data supporting the findings of this study are available within the article.

Declarations

Conflicts of interest All the authors disclose no conflicts of interest.

References

1. Homayoun H (2018) Parkinson disease. Annals Intern Med 169:ITC33–ITC48. https://doi.org/10.7326/aitc201809040
2. Leite Silva ABR, Gonçalves de Oliveira RW, Diógenes GP, de Castro Aguiar MF, Sallem CC, Lima MPP, de Albuquerque Filho LB, Peixoto de Medeiros SD, Penido de Mendonça LL, de Santiago Filho PC, Nones DP, da Silva Cardoso PMM, Ribas MZ, Galvão SL, Gomes GF, Bezerra de Menezes AR, Dos Santos NL, Mororó VM, Duarte FS, Dos Santos JCC (2023) Premotor, nonmotor and motor symptoms of Parkinson's disease: a new clinical state of the art. Ageing Res Rev 84:101834. https://doi.org/10.1016/j.arr.2022.101834
3. Oppo V, Melis M, Melis M, Tomassini Barbarossa I, Cossu G (2020) "Smelling and tasting" Parkinson's disease: using senses to improve the knowledge of the disease. Front Aging Neurosci 12:43. https://doi.org/10.3389/fnagi.2020.00043
4. Rolls ET (2019) Taste and smell processing in the brain. Handb Clin Neurol 164:97–118. https://doi.org/10.1016/B978-0-444-63855-7.00007-1
5. Fasano A, Visanji NP, Liu LWC, Lang AE, Pfeiffer RF (2015) Gastrointestinal dysfunction in Parkinson's disease. Lancet Neurol 14:625–639. https://doi.org/10.1016/S1474-4422(15)00007-1
6. Pont-Sunyer C, Hotter A, Gaig C, Seppi K, Compta Y, Katzenschlager R, Mas N, Hofeneder D, Brücke T, Bayés A, Wenzel K, Infante J, Zach H, Pirker W, Posada IJ, Álvarez R, Ispierto L, De Fàbregues O, Callén A, Palasí A, Aguilar M, Martí MJ, Valldeoriola F, Salamero M, Poewe W, Tolosa E (2015) The onset of nonmotor symptoms in Parkinson's disease (the ONSET PD study). Mov Disord 30:229–237. https://doi.org/10.1002/mds.26077
7. Breen KC, Drutyte G (2013) Non-motor symptoms of Parkinson's disease: the patient's perspective. J Neural Transm (Vienna) 120:531–535. https://doi.org/10.1007/s00702-012-0928-2
8. Ansoleaga B, Garcia-Esparcia P, Llorens F, Moreno J, Aso E, Ferrer I (2013) Dysregulation of brain olfactory and taste receptors in AD, PSP and CJD, and AD-related model. Neuroscience 248:369–382. https://doi.org/10.1016/j.neuroscience.2013.06.034
9. Chaithra SP, Prasad S, Holla VV, Stezin A, Kamble N, Yadav R, Pal PK (2020) The non-motor symptom profile of progressive supranuclear palsy. J Mov Disord 13:118–126. https://doi.org/10.14802/jmd.19066
10. Kwak I-Y, Kim KS, Min HJ (2023) Gustatory dysfunction is related to Parkinson's disease: a systematic review and meta-analysis. Int Forum Allergy Rhinol 13:1949–1957. https://doi.org/10.1002/alr.23158
11. Cecchini MP, Fasano A, Boschi F, Osculati F, Tinazzi M (2015) Taste in Parkinson's disease. J Neurol 262:806–813. https://doi.org/10.1007/s00415-014-7518-1

12. Postuma RB, Berg D, Stern M, Poewe W, Olanow CW, Oertel W, Obeso J, Marek K, Litvan I, Lang AE, Halliday G, Goetz CG, Gasser T, Dubois B, Chan P, Bloem BR, Adler CH, Deuschl G (2015) MDS clinical diagnostic criteria for Parkinson's disease. Mov Disord 30:1591–1601. https://doi.org/10.1002/mds.26424
13. Höglinger GU, Respondek G, Stamelou M, Kurz C, Josephs KA, Lang AE, Mollenhauer B, Müller U, Nilsson C, Whitwell JL, Arzberger T, Englund E, Gelpi E, Giese A, Irwin DJ, Meissner WG, Pantelyat A, Rajput A, van Swieten JC, Troakes C, Antonini A, Bhatia KP, Bordelon Y, Compta Y, Corvol J-C, Colosimo C, Dickson DW, Dodel R, Ferguson L, Grossman M, Kassubek J, Krismer F, Levin J, Lorenzl S, Morris HR, Nestor P, Oertel WH, Poewe W, Rabinovici G, Rowe JB, Schellenberg GD, Seppi K, van Eimeren T, Wenning GK, Boxer AL, Golbe LI, Litvan I (2017) Clinical diagnosis of progressive supranuclear palsy: the movement disorder society criteria. Mov Disord 32:853–864. https://doi.org/10.1002/mds.26987
14. Boxer AL, Yu J-T, Golbe LI, Litvan I, Lang AE, Höglinger GU (2017) Advances in progressive supranuclear palsy: new diagnostic criteria, biomarkers, and therapeutic approaches. Lancet Neurol 16:552–563. https://doi.org/10.1016/S1474-4422(17)30157-6
15. Wenning GK, Stankovic I, Vignatelli L, Fanciulli A, Calandra-Buonaura G, Seppi K, Palma J-A, Meissner WG, Krismer F, Berg D, Cortelli P, Freeman R, Halliday G, Höglinger G, Lang A, Ling H, Litvan I, Low P, Miki Y, Panicker J, Pellecchia MT, Quinn N, Sakakibara R, Stamelou M, Tolosa E, Tsuji S, Warner T, Poewe W, Kaufmann H (2022) The movement disorder society criteria for the diagnosis of multiple system atrophy. Mov Disord 37:1131–1148. https://doi.org/10.1002/mds.29005
16. Landis BN, Welge-Luessen A, Brämerson A, Bende M, Mueller CA, Nordin S, Hummel T (2009) "Taste Strips" - a rapid, lateralized, gustatory bedside identification test based on impregnated filter papers. J Neurol 256:242–248. https://doi.org/10.1007/s00415-009-0088-y
17. Mueller CA, Pintscher K, Renner B (2011) Clinical test of gustatory function including umami taste. Ann Otol Rhinol Laryngol 120:358–362
18. Lang CJG, Leuschner T, Ulrich K, Stössel C, Heckmann JG, Hummel T (2006) Taste in dementing diseases and parkinsonism. J Neurol Sci 248:177–184
19. Shah M, Deeb J, Fernando M, Noyce A, Visentin E, Findley LJ, Hawkes CH (2009) Abnormality of taste and smell in Parkinson's disease. Parkinsonism Relat Disord 15:232–237. https://doi.org/10.1016/j.parkreldis.2008.05.008
20. Deeb J, Shah M, Muhammed N, Gunasekera R, Gannon K, Findley LJ, Hawkes CH (2010) A basic smell test is as sensitive as a dopamine transporter scan: comparison of olfaction, taste and DaTSCAN in the diagnosis of Parkinson's disease. QJM 103:941–952. https://doi.org/10.1093/qjmed/hcq142
21. Kim H-J, Jeon BS, Lee J-Y, Cho Y-J, Hong K-S, Cho J-Y (2011) Taste function in patients with Parkinson disease. J Neurol 258:1076–1079. https://doi.org/10.1007/s00415-010-5884-x
22. Kalia LV, Lang AE (2015) Parkinson's disease. Lancet 386:896–912. https://doi.org/10.1016/S0140-6736(14)61393-3
23. Stefanova N, Bücke P, Duerr S, Wenning GK (2009) Multiple system atrophy: an update. Lancet Neurol 8:1172–1178. https://doi.org/10.1016/S1474-4422(09)70288-1
24. Braak H, Del Tredici K, Rüb U, de Vos RAI, Jansen Steur ENH, Braak E (2003) Staging of brain pathology related to sporadic Parkinson's disease. Neurobiol Aging 24:197–211
25. Seidel K, Mahlke J, Siswanto S, Krüger R, Heinsen H, Auburger G, Bouzrou M, Grinberg LT, Wicht H, Korf H-W, den Dunnen W, Rüb U (2015) The brainstem pathologies of Parkinson's disease and dementia with lewy bodies. Brain Pathol 25:121–135. https://doi.org/10.1111/bpa.12168
26. Nolden A, Joseph PV, Kober KM, Cooper BA, Paul SM, Hammer MJ, Dunn LB, Conley YP, Levine JD, Miaskowski C (2019) Co-occurring gastrointestinal symptoms are associated with taste changes in oncology patients receiving chemotherapy. J Pain Symptom Manage 58:756–765. https://doi.org/10.1016/j.jpainsymman.2019.07.016
27. van Elst JM, Ijzerman NS, Mathijssen RHJ, Steeghs N, Reyners AKL, de Haan JJ (2022) Taste, smell and mouthfeel disturbances in patients with gastrointestinal stromal tumors treated with tyrosine-kinase inhibitors. Support Care Cancer 30:2307–2315. https://doi.org/10.1007/s00520-021-06658-z
28. Poewe W, Stankovic I, Halliday G, Meissner WG, Wenning GK, Pellecchia MT, Seppi K, Palma J-A, Kaufmann H (2022) Multiple system atrophy. Nat Rev Dis Primers 8:56. https://doi.org/10.1038/s41572-022-00382-6
29. Williams DR, Holton JL, Strand C, Pittman A, de Silva R, Lees AJ, Revesz T (2007) Pathological tau burden and distribution distinguishes progressive supranuclear palsy-parkinsonism from Richardson's syndrome. Brain 130:1566–1576
30. Clark HM, Stierwalt JAG, Tosakulwong N, Botha H, Ali F, Whitwell JL, Josephs KA (2020) Dysphagia in progressive supranuclear palsy. Dysphagia 35:667–676. https://doi.org/10.1007/s00455-019-10073-2
31. Vogel A, Claus I, Ahring S, Gruber D, Haghikia A, Frank U, Dziewas R, Ebersbach G, Gandor F, Warnecke T (2022) Endoscopic characteristics of dysphagia in multiple system atrophy compared to parkinson's disease. Mov Disord 37:535–544. https://doi.org/10.1002/mds.28854
32. Zheng Y, Yu Z, Cai H, Kou W, Yang C, Li S, Zhang N, Feng T (2024) Detection of α-Synuclein in oral mucosa by seed amplification assay in synucleinopathies and isolated REM sleep behavior disorder. Mov Disord 39:1300–1309. https://doi.org/10.1002/mds.29828
33. Zheng Y, Cai H, Zhao J, Yu Z, Feng T (2022) Alpha-Synuclein species in oral mucosa as potential biomarkers for multiple system atrophy. Front Aging Neurosci 14:1010064
34. Henkin RI (1994) Drug-induced taste and smell disorders. Incidence, mechanisms and management related primarily to treatment of sensory receptor dysfunction. Drug Saf 11:318–377