Taste sensitivity in healthy adults: gustatory test validation and observational study

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Gustatory sensitivity has important biological functions and taste disorders are generally difficult to diagnose and treat. The aim of this study was to investigate taste sensitivity on a sample of adult healthy patients through the validation and administration of a gustatory test, to describe a possible baseline of reference. A gustatory test was performed following a standardized protocol, using primary flavors solutions at 4 known increasing concentrations for a total of 16 sapid solutions. Taste sensitivity was investigated considering (a) the threshold of the flavor identification and (b) the intensity of stimulus perception. Seventy-one healthy patients were included in the study. Reliability measures were evaluated, supporting the validity of the test itself. Sweet, bitter, and salty flavors could be identified within the first concentration, sour flavor was detected within the second concentration in the majority of cases ($p<0.05$). Sour flavor showed the lowest value of perceived intensity for the less concentrated solution, sweet flavor showed the highest value. Regarding the most concentrated solution, bitter flavor showed the highest intensity value, while sour remained the lowest one. Both gender-based and age-based differences regarding threshold and intensity of perception were not statistically significant. However mean threshold averagely increased along with age. Within its limitations, this study validates a useful, easy-to-use tool for assessing taste function and it provides a possible baseline for perception of primary flavors in a healthy adult population, which can be used as a reference for future studies considering specific cohorts of patients.

Measuring human taste perception has both medical care and biomedical research implications, yet taste has received minor attention compared to other sensory functions. Taste sensitivity has important relations with nutrition and liquid intake: taste of foods and beverages is in fact fundamental in determining their edibility and palatability. In addition to this, primary flavors seem to be associated to different functions: sweet flavor is related to energy reserves, salty flavor helps maintain the electrolytic homeostasis, sour and bitter are involved in pH control; bitter flavor also often prevents the accidental intake of toxic substances (1, 2). However, the degree of pleasantness of a taste is subjective and can be influenced by experience and nutritional needs. Gustatory sensitivity provides information about chemical characteristics of substances that encounter the mucous membranes of the oropharynx. Gustatory receptors or primary taste cells interact with the dissolved molecules in saliva and transduce the chemical stimulus into nervous signals (3). The several hundred perceivable flavors derive from the combination of some primary flavors: sweet, salty, bitter, sour (4). Primary flavors differ in the chemical

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nature of the compounds capable of evoking them and in the mechanisms of capture and transduction. Taste and olfactory information guide the choice between different foods towards the ones that provide the most appropriate nutritional contribution. Taste information has also an important role in the control of digestive processes being the secretion of several glands (e.g. salivary, pancreatic, gastric) activated and modulated through connections between gustatory centers and nuclei involved in the control of vegetative efferences (1).

Most cases of taste alteration reported by patients are actually secondary to smell disorders. Primary taste distortion (dysgeusia), however, is quite common and frequently arises from secondary effects of medications, local and systemic diseases, or peripheral nerve injuries. The most important clinical factors able to induce taste disorders are impairment of the turnover of taste receptors, such as stomatitis and mucositis, drugs or radiations (5–7).

The oral cavity is often affected by local and systemic diseases and by side effects of drug therapies. Taste disorders may cause anxiety, depression and severe nutritional deficiencies that are extremely important, especially in patients undergoing cancer treatments such as chemotherapy, immune-therapy and radiation therapy. Dysgeusia can strongly reduce quality of life of patients and can lead to worsening of their general conditions, thus requiring the interruption or modification of medical protocols (8). Taste disorders are generally difficult to diagnose and treat. A known baseline of taste sensitivity features in healthy adult population is therefore of primary importance in order to intercept and characterize any taste dysfunction. Being the available literature on this topic scarce, the aim of this study was to investigate taste sensitivity on a sample of adult healthy patients through the validation and administration of a gustatory test, in order to describe a possible baseline of reference.

MATERIALS AND METHODS

Sample selection

Seventy-three consecutive volunteer patients were selected among the adult population attending the Dental Clinic of the University of Brescia (Brescia – Italy) from October 2018 to January 2020. Inclusion criteria were: (a) patients of both genders over 18 years of age. Exclusion criteria were: (a) patients with systemic diseases that can affect gustatory function (e.g., gastroenteric, neurological, oncohaematological, disorders), (b) patients with oral mucosa lesions, (c) patients who underwent antibiotic treatment in the last 6 months, (d) patients undergoing chronic pharmacological treatment, (e) patients who underwent anti-cancer therapies, (f) smoking patients. Data regarding age, sex and general medical history were collected. All patients were informed about the research and signed an informed consent. The study was approved by the Ethical Committee of ASST-Spedali Civili of Brescia (NP 3221-2018) and it was performed according to the Declaration of Helsinki.

Study design and gustatory test

The gustatory test was performed following a standardized protocol, repeated at two different timepoints: at baseline (T0) and after 2 weeks from baseline (T1) (4). At baseline, the test was performed by two trained and calibrated examiners on the same patient twice in the same day. Clinical examination of the oral cavity was carried out by a trained clinician each time before performing the gustatory test. The test was performed in a quiet room and the patients were asked to be 2 hours away from meals, in order to standardize subject's conditions. Taste sensitivity was investigated with regard to (a) the threshold of the flavor identification and (b) the intensity of stimulus perception. The gustatory test was carried out using solutions of 4 sapid substances (sucrose, sodium chloride, citric acid and quinine hydrochloride) corresponding to respective primary flavors (sweet, salty, sour and bitter). Four known increasing concentrations (shown in Table I) were set up for each flavor, for a total of 16 sapid solutions, as reported by other studies (4, 9). Samples were provided to the subjects as 4 ml of sterile solution at 24°C (namely room temperature) contained in test tubes. The participants were instructed to taste each solution for at least 10 seconds and between one solution and another they were invited to rinse for at least 10 second with water. Each flavor series started from the less concentrated solution, gradually increasing to determine the threshold of perception, defined as the lowest concentration at which the patient detects and correctly identifies the flavor. The patients were asked to rate the intensity of the flavor perception for each solution according to a 0-10 scale, being 10 the maximum intensity

perceivable and 0 the neutral stimulus (i.e. tap water). Flavor sequence was switched for each different patient and at different timepoints in order to avoid sequence biases. The patients were blinded to each flavor and to the increasing concentration setting.

Data analysis and statistical methods

All data were recorded in Microsoft Excel datasheets and statistical analysis was performed using IBM SPSS Statistics (v25, IBM, Armonk, NY, USA). Each series of solutions were numbered from 1 to 4, from the less concentrated to the most concentrated, as a reference in order to record the perception threshold. Reliability tests were carried out in order to ensure reproducibility and consistency of the measure. Inter-rater reliability was assessed by calculating Cronbach's α on the two sets of measures from baseline (T0). Test-retest reliability was evaluated by assessing the intraclass correlation coefficient (ICC) based on the two repeated measurements (T0-T1). Mean values obtained from T0 (mean values of datasets reported by the two raters) and T1 datasets were considered for the analysis. Mean values ± standard deviations (SD) of both threshold and intensity perception were then evaluated. After assessing data distribution through Kolmogorov-Smirnov test, Student's T test for independent samples was used to compare data between gender-based groups and Analysis of Variance (ANOVA) was used to compare data between age-based groups. ANOVA for paired samples along with post-hoc Tukey's test were used to compare intensity perception values between the same concentration of different flavors and threshold values. A p-value <0.05 was considered statistically significant.

RESULTS

Seventy-three consecutive patients were recruited for the study according to the eligibility criteria. Two of them were lost to T1 scheduled repeated measure and were excluded from the study. Therefore, a total of 71 subjects (49 females and 22 males) were included. The mean age of the patients was 40.58 (range 20-71).

The taste sensitivity test allowed the evaluation of the validity of the test itself, along with the assessment of the threshold and the intensity of the gustatory stimulus perception regarding the four examined flavors. In addition, this study allowed to investigate gender and age as a possible factor influencing these aspects of taste function. Cronbach's α (inter-rater reliability) evaluated on the two sets of measures from baseline (T0) was 0.84 and ICC (test-retest reliability) based on the two repeated measurements (T0-T1) was 0.89, thus supporting the validity and the reliability of the test itself.

Data regarding threshold are shown in Fig. 1. Mean threshold for sweet flavor (sucrose) was 1.33±0.64,

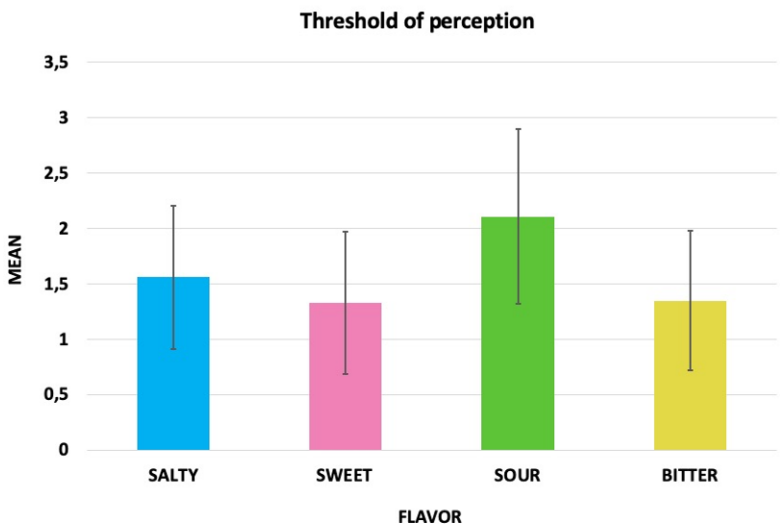

Fig. 1. *Mean threshold for each flavor evaluated through the gustatory test.*

meaning that sweet flavor could be detected within the first concentration, along with bitter (quinine hydrochloride) and salty (sodium chloride) flavors, which were 1.35±0.63 and 1.56±0.65 respectively. On the contrary, mean threshold for sour flavor (citric acid) was 2.11±0.79, which indicates that sour was detected within the second concentration in the majority of cases. Sour thresholds mean values were significantly higher than salty, sweet and bitter values (data not shown; ANOVA paired samples, $p<0.05$).

Data distribution regarding intensity of perception are shown in Table II and Fig. 2; level of significance of differences between flavors are shown in Table III. Sour flavor showed the lowest value of perceived

Table I. *Flavors and concentrations used for the gustatory test.*

A: Salty flavor (NaCl)	A1) 0.032 M	A2) 0.1 M	A3) 0.32 M	A4) 1 M
B: Sweet taste (Sucrose)	B1) 0.032 M	B2) 0.1 M	B3) 0.32 M	B4) 1 M
C: Sour taste (Citric acid)	C1) 0.001 M	C2) 0.0032 M	C3) 0.01 M	C4) 0.032 M
D: Bitter taste (Quinine hydrochloride)	D1) 3.2×10^{-5} M	D2) 1×10^{-4} M;	D3) 3.2×10^{-4} M	D4) 1×10^{-3} M

Table II. *Mean intensity perceived ± standard deviation (SD) for each flavor, recorded at 4 increasing concentrations.*

	SALTY	SWEET	SOUR	BITTER
CONC 1	1,09±0.92	2,21±1.33	0,65±0.63	2,04±1.68
CONC 2	3,72±1.55	4,46±1.59	2,46±1.85	4,73±2.09
CONC 3	6,99±1.39	6,74±1.93	6,93±1.09	7,75±1.08
CONC 4	9,17±0.75	9,03±1.18	8,95±0.92	9,31±0.74

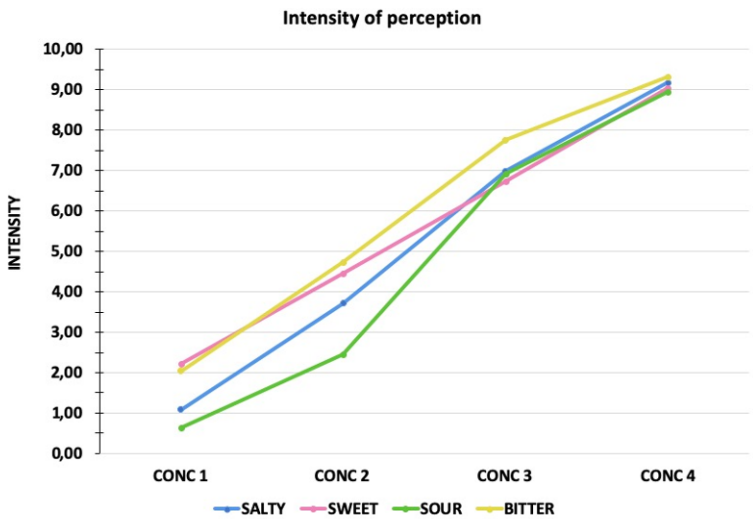

Fig. 2. *Mean intensity perceived for each flavor, recorded at 4 increasing concentrations.*

intensity for the less concentrated solution, whereas sweet flavor showed the highest value. Regarding the most concentrated solution, bitter flavor showed the highest intensity value, while sour remained the lowest one.

No statistically significant difference was found between males and females neither in the threshold perception nor in the intensity of perceived flavors (data not shown; Student's T test, $p>0.05$). The age-related distribution of mean thresholds is shown in Fig. 3. Differences regarding both threshold and intensity perception between age groups were not statistically significant (data not shown; ANOVA, $p>0.05$). However, except from bitter flavor, mean threshold averagely increased along with age.

Table III. *Difference of intensity perception between same concentration of different flavors.*

		SALTY	SWEET	SOUR	BITTER
		Sign. (*p*)			
CONC 1	SALTY		0.000*	0.266	0.001*
	SWEET			0.000*	0.903
	SOUR				0.000*
	BITTER				
CONC 2	SALTY		0.103	0.001*	0.01*
	SWEET			0.000*	0.825
	SOUR				0.000*
	BITTER				
CONC 3	SALTY		0.71	0.994	0.009*
	SWEET			0.850	0.000*
	SOUR				0.004*
	BITTER				
CONC 4	SALTY		0.795	0.476	0.778
	SWEET			0.954	0.245
	SOUR				0.082
	BITTER				

*level of significance $p<0.05$; ANOVA paired samples

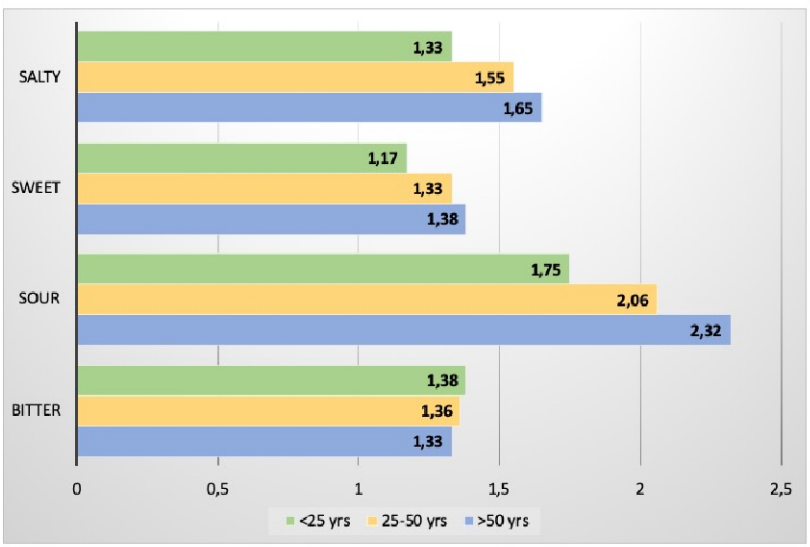

Fig. 3. *Mean threshold for each flavor in relation to age classes.*

DISCUSSION

Taste sensitivity significantly affects quality of life and well-being. Assessing standard gustatory function in adult healthy population is, therefore, fundamental to intercept both obvious and submerged chemosensory disorders in order to educate the public about potentially associated problems, to identify factors that may worsen or mitigate these disturbances and to improve the clinical management of chemosensory dysfunctions. This is especially important regarding taste dysfunctions induced by anti-cancer treatments, that are likely to lead to nutritional issues, thus compromising the overall outcome of the disease (4).

As for our findings, the test procedure itself seems to be adequate as a screening tool for taste function, being inexpensive, easy to set up and to administer. In addition, validity and reliability measures have proven to be solid. Other authors have proposed different tools, such as self-administered tests through taste strips, with promising results (10–12). However, we preferred the use of liquid solutions over taste strips, as rinses allow to reach taste buds more extensively throughout the oral cavity, thus providing more sensitive measures. Moreover, we chose a hetero-administered test to overcome potential mistakes and biases related to the sequence of administration.

Generally, the participants were able to identify well the flavor and to sense the increasing different concentrations, as indicated by the large ceiling effect (i.e., scores reach a maximum extreme). Consistently with other authors, we found no significant difference between genders in taste sensitivity, suggesting that mechanisms of taste perception for all primary flavors are common to both sexes (4, 13, 14).

A similar test has been successfully validated and used on children 5 to 12 years old by Majorana et al. (4). The trend of thresholds perception was similar, except from salty flavor which was detected earlier in adult population than in children. Salty taste, produced by sodium chloride, requires the diffusion of the Na ions through specialized membrane channels, such as the amiloride-sensitive Na channel (15). Accordingly, other authors have found a lower salt detection threshold in young adults than in children (16). This is thought to be related to children preferring foods with higher salt concentration, which can lead to habituation to this flavor, thus raising the perception threshold (17). However, none of the studies reviewed by Liem et al. could confirm any associations between salt taste detection threshold and salt intake (18, 19).

Sour was the least intense perceived flavors for adults as well as for children. Sour taste perception is a complex event from both chemical and physiological standpoints, which appears to be mediated via the PKD2L1 receptor, a member of the transient receptor potential protein family (15, 20). Acids are most commonly associated with sour taste, but it is well known that they are also able to elicit other non-sour characteristics such as bitterness, saltiness, and astringency (21, 22). This might be a reason for specific sensitivity to sour intensity being altered and resulting averagely lower than other flavors.

On the other hand, bitter showed the maximum perceived intensity among other flavors. Bitter taste perception involves not only multiple transduction mechanisms, but also a large number of receptors (23). This may partially explain the overall higher intensity perceived for bitter in comparison to other flavors.

Regarding age-related distribution, the overall threshold perception averagely increased along with age, thus confirming the findings of other authors, as the gustatory function seems to be more sensitive within the younger age categories (24). Multiple factors can cause changes in taste sensitivity with age, such as malnutrition, diabetes, and xerostomia. Physiologic neurologic and oral epithelial changes are also involved and a decline in taste bud numbers with age is prevalent in some regions of the tongue (25, 26). Also, poor dental hygiene can impact taste function in the elderly (19). However, in our data, bitter flavor showed an opposite trend, with a perceived threshold being lower in older adults. This finding was in contrast with other reports and it probably reflects once again the complexity of the mechanisms of bitter taste perception in comparison to other flavors (23, 24). In fact, while sweet taste sensation, for example, is mediated via G-protein-coupled receptor proteins located on receptor cell within the buds, encoded by three genes (TAS1R1-

TAS1R3), bitter receptors are encoded at least by 60 genes (TAS2R1-TAS2R60) (15). Therefore, bitter taste may exhibit extreme genetic variability and, consequently, widely variable taste sensitivity.

The main objective of this study was to investigate taste sensitivity in healthy adult population. However, some limitations should be pointed out. The study sample was on a voluntary base, therefore a non-homogeneous population regarding sex and age was enrolled. Patients with common factors that can influence taste sensitivity, such as cigarette smoke, drugs assumption and systemic diseases were excluded from the study. Further studies should consider these patients, in order to investigate the real standard gustatory sensitivity through multivariate analysis, as these subjects represent the large majority of adult population.

Nonetheless, within these limitations, this study served as a starting point, allowing the validation and the application of a solid gustatory test, through which a baseline of reference on taste sensitivity in healthy adults was provided. Starting from this baseline, future studies will investigate taste sensitivity alterations in patients affected by specific diseases and undergoing specific treatments, such as anti-cancer therapies, to provide worthwhile and rapid tools to diagnose and manage chemosensory disorders, to preserve patients' quality of life and to improve clinical outcome of the underlying diseases.

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