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Original Article

Randomized testing of taste discrimination in a case of congenital aglossia

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ABSTRACT

Aims: Isolated Congenital Aglossia (ICA) is a rare syndrome where an individual is born without a tongue. A few anecdotal reports have identified taste as a sensation experienced by the person with congenital aglossia (PWCA). To date no systematic investigations have been reported. This study aimed to systematically determine gustatory function in a PWCA.

Methods: The current study utilized a randomized, double-blinded, controlled trial that tested the five basic tastes: sweet (sucrose), sour (acetic acid), salty (sodium chloride), bitter (caffeine), and umami (monosodium glutamate, MSG) in a 44 year old female PWCA. Five concentration levels (three for salty) were tested in triplicate for each stimulus. A nose clip was used to exclude contribution by olfactory detection. Contingency tables were constructed to determine relationships between identification accuracy and stimulus or concentration level.

Results: The sweet (17.1 g/L), salty (0.58 g/L), and bitter (0.02 g/L) stimuli were detected at comparable concentrations to those reported in non-randomized trials, while sour (0.02 g/L) was detected at a lower concentration. The most common substitution was salty for umami ($n = 7$). Identification accuracy was significantly associated with taste stimuli $\chi^2 = 12.634$, $p = 0.013$. Concentration level was significantly associated with identification accuracy only for salty, $\chi^2 = 9.000$, $p = 0.011$.

Conclusion: This study has demonstrated the perception of different tastes in a PWCA. This is the first known report of umami being identified as a unique taste in a PWCA. Variations in threshold taste concentrations compared to normal individuals indicate certain gustatory dysfunction.

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The aim of this current study was to extend previous research by scientifically examining gustatory function in a case of isolated congenital aglossia (ICA). This rare syndrome, in which an individual is born without a tongue, was first reported by de Jussieu in 1718. Since then, eleven reports of congenital aglossia (CA) have appeared in the literature without the presence of other syndromes or symptoms.[1–13] Co-anatomical morbidities that have been associated with ICA are generally limited to micrognathia (abnormally small lower jaw), which is a common finding among hypoglossia and aglossia, as it is unlikely that normal mandibular formation would occur without the development of the tongue.

It is well known that the tongue's primary biological functions are in the areas of taste, mastication and deglutition. In the normal population, the tongue plays a major role in the sensory discrimination of taste, through receptors which are located on the tongue surface.[14] This sensation would logically be disrupted without the structure, yet there are reports in the literature[2,4–9,12,13,15–18] mentioning or describing taste awareness in persons with congenital aglossia (PWCA). These reports describe the ability to taste but do not go into any particular detail with the exception of three authors. Eskew and Shepherd indicated taste could be distinguished only on the surface of the soft palate following application by small brush in various regions of the oral cavity at threshold levels of 3% cane sugar, 1% sodium chloride, 0.1% sulfuric acid, and 0.01% quinine.[2] Goto reported testing of taste with resulting thresholds of 5% cane sugar, 10% sodium chloride, 0.1% quinine, and 1% acetic acid.[4] The solutions were applied with a brush to various areas of mucus membrane in the oral cavity. Results indicated taste was distinguished in the sublingual area and anterior faucial pillers. In 2008, Salles et al included a description of taste testing in a 14 year old female PWCA who was reported to eat her family's regular diet without difficulty.[13] Results indicated recognition of acid taste from the lowest concentration (sulfuric acid, 0.015 g/L), bitter was reported as a new taste at the third concentration (quinine, 0.012 g/L) and was perceived as sweet upto the last concentration; sweet was perceived as a new taste at the fifth concentration (sucrose, 8 g/L) and perceived as bitter at the last concentration (16 g/L); salty was perceived as a new taste at the forth concentration (sodium chloride, 0.75 g/L) and identified as salty from the fifth concentration on (1.5 g/L). Salles' results suggested inverted sweet and bitter tastes could be considered a difficulty in perception; however, there appeared to be a greater sensitivity to salty and acid substances. Salles and Costa-Bezerra tested the taste sensitivity of the 44 year old PWCA from the current study at the University of Brasilia in 2013[19] (personal unpublished report to Dr. McMicken). The identical flavors from Salles et al,[19] as in 2008,[13] were presented in random order with doses of increasing concentrations. Water was given between each presentation. Each flavor had 5 concentrations. When the PWCA identified a flavor, no further same substance concentrations were offered. A nose clip was not used. Threshold results were: acid (citric), 0.015 g/L lowest concentration; bitter (caffeine) 0.003 g/L, lowest concentration; salt (sodium chloride) 0.09 g/L, lowest concentration and sweet (sucrose), 0.2.0 g/L, 3rd concentration. These researchers conclude the PWCA appeared to have greater sensitivity than their normal control group.

Limitations of these four previous reports include: no details of the experimental methodology, the number of trials, the total substance dilution amounts, complete taste substitution details, and in most cases, whether a nose clip was used to lessen the chance of a possible olfactory component.

1. Background on taste in the normal population

In the normal population, taste buds are in groups of upto 100 neuroepithelial cells embedded in the epithelium of the oral cavity. In humans, there are approximately 5000 taste buds in the oral cavity. They are located on the surface of the tongue, the palate, and the epiglottis.[20,21] It is the taste buds or sensory receptors on the surface of the tongue, activated by saliva, which are responsible for perception and taste discrimination of sweet, sour, salty, bitter, and umami (the taste of glutamate and other L-amino acids).[22] According to Kinnamon, taste buds on the anterior two thirds of the tongue, located within papillae, are innervated by the cranial nerve VII, the facial nerve. Taste buds on the posterior tongue are housed in a different group of papillae, and are innervated primarily by cranial nerve IX, the glossopharyngeal nerve.[20] Taste buds on the soft palate are innervated by a branch of the lingual nerve, while the epiglottis and larynx by the superior laryngeal nerve, which is a branch of the cranial nerve X (vagus nerve). Despite the various locations of taste buds in different sections of the oral cavity, and supposed differences in regional sensitivity on the tongue, the concept of a tongue map with zones for sweet, bitter, salty, and sour has been proven to not be a valid or reliable concept.[23] Gustatory function and cell specificity is reportedly maintained regardless of location. Kinnamon stated that despite the often-related tongue diagram of taste, it is well known that there is no credible map of taste sensitivity on the tongue, although variations in thresholds are present in the many different oral cavity locations.[20]

The olfactory and gustatory senses are closely linked in their chemo-sensitivity.[24] Testing for taste with or without the presence of a tongue must be accomplished without olfactory influence. As noted by Steele et al, an additional complication when testing for taste is the olfactory receptors possibly being responsive to the odor.[25] To avoid this possibility, it is recommended an odorless stimulus be used in research as well as the implementation of a nose clip.

The present research explores the gustatory threshold levels in the PWCA described in prior research.[9–11] The following questions guided the current research:

1) What is the taste sensitivity response of the PWCA in a randomized, multi sample, double-blind controlled study using sweet, sour, salty, bitter, and umami substances as taste stimuli.
2) How do the thresholds from current study in 2014 compare with previous reported thresholds obtained on this PWCA at the University of Brasilia[19]?
3) What are the confusion substitutions in taste testing with this PWCA?

2. Materials and methods

2.1. Subject

A PWCA female, 44 years old, who reported never having feeding issues other than being fed with a long-nippled baby bottle due to the aglossia. She described the normal change of dietary consistency (from liquid to soft and then to normal) without presenting difficulty. Currently she denies any major limiting issues with eating or swallowing. She does report some difficulty in chewing substances such as apples, which she cannot bite into due to a severe class II malocclusion. Her reported preference is for softer fruits and meats in small bites. She denied perceiving any change in smell or taste of food and has maintained a diet of normal consistency, with consumption of all food groups.

She reported one instance of loss of taste that occurred over a year prior to the initiation of the current study, when the PWCA experienced a loss of taste sensation after oral anesthetic injection for dental work. In July of 2012, the patient in the current study underwent a dental procedure for molar fillings and teeth cleaning. Attempts at administrating local anesthesia to block the third division of the trigeminal (Vth Cranial) nerve was difficult due to oral cavity limited access and micrognathia of mandible; usual landmarks were absent. She was given an inferior alveolar injection with 1 ampoule (1.7 ml) of 2% Xylocaine® with 1:100,000 Epinephrine using a 27 gauge long (yellow) disposable needle and followed by a 10-min delay before starting procedure. The PWCA continued to experience discomfort during removal of copious decay, so an infiltration injection was performed in the buccal and lingual vestibule of tooth #18 using 2/3 ampoule (1.1 ml) of Septocaine®. After 5 min more of waiting, profound anesthesia was achieved. The PWCA reported the next day that she was experiencing some loss of feeling and with complete loss of taste in the oral cavity. This lasted for two weeks, with eventual full restoration of taste. This prolonged parasthesia, resulting from a reversible anesthesia related lesion of the lingual nerve branch lying between the emergence of the third division of the fifth cranial nerve and cheek, appears to have impaired the functional ability of the subjects taste buds from transmitting flavors.

2.2. Stimuli

Sucrose (C&H Sugar), sodium chloride (Mortons Salt), acetic acid 5% (generic), monosodium glutamate (Ajinomoto), and anhydrous caffeine (Sigma Aldrich) were used as stimuli solutes. To eliminate taste contribution from the solvent, distilled water was purchased from the local grocer and used for all taste testing solutions. Approximately 100 mL of each taste stimuli were prepared at various concentrations by serial dilution (Table 1). These concentration ranges span threshold levels as reported in both those with and without isolated congenital aglossia.[2,4,13,26] Solutions were stored in Erlenmeyer flasks at 4 °C overnight. The morning of the experiment, approximately 30 mL of each stimuli and concentration level were transferred to 60 mL polystyrene soufflé cups and allowed to warm to ambient temperature (~19 °C) for 1 h. Cups were labeled with a randomized number between 1 and 78. Both the researchers and subject were blinded to sample identities.

2.3. Procedure

All procedures were initiated following the protocol approved by the Institutional Review Board at California State University, Long Beach. Informed consent was obtained prior to the beginning of experimentation. The subject was instructed to use a nose clip during the experiment to prevent olfactory contribution to taste sensation. Sample stimuli were presented to the subject in numerical (randomized) order in batches of fifteen samples with 10 min of rest between batches. The subject was instructed to transfer the stimuli solution to her mouth and manipulate the fluid so as to coat the inside of the oral cavity. The subject was instructed to dispose of the solution into a waste container and identify the unknown stimuli as sweet, salty, sour, bitter, umami, or not identifiable. The subject was allowed to repeat the solution manipulation if there was any remaining in the sample cup. There was no time restriction for identification of samples. After identification was made, the subject was instructed to rinse with distilled water atleast once and dispose of the solution into the waste container. This process was repeated for all samples. Threshold values were set at $\geq$66.6% accurate identification (two of three). Significance was set at $p < 0.05$.

2.4. Data analysis

Data analysis was performed using SPSS 21. Descriptive statistics were run to determine the percentage of trials that accurately identified stimuli solutions and the frequency and types of taste substitutions. A series of taste matrices were constructed in order to perform qualitative analysis. Frequencies of taste substitutions were plotted on a heat map of

Table 1 – Stimuli solution concentrations.

	Sweet (sucrose)		Salty (NaCl)		Sour (Acetic acid)		Bitter (Caffeine)		Umami (MSG)	
	M	g/L	M	g/L	M	g/L	M	g/L	M	g/L
a	0.5	171	0.1	5.8	0.1	6.6	0.001	0.2	0.01	1.7
b	0.05	17.1	0.01	0.58	0.01	0.66	0.005	0.1	0.005	0.85
c	0.005	1.7	0.001	0.058	0.001	0.066	0.0001	0.02	0.001	0.17
d	0.001	0.34	–	–	0.0005	0.033	0.00005	0.010	0.0005	0.085
e	0.0005	0.17	–	–	0.0001	0.0066	0.00001	0.002	0.0001	0.017

Table 2 – Frequency of taste substitutions.

			Perceived Taste							
		n	Sweet	Salty	Sour	Bitter	Umami	Salty or Umami	Salty, Umami, or Bitter	Not Sure
Actual Taste	Sweet	15	8	2	0	2	0	0	1	2
	Salty	9	2	3	1	0	1	1	0	1
	Sour	15	0	1	11	0	1	0	0	2
	Bitter	15	2	1	1	5	2	0	1	3
	Umami	15	1	7	0	1	2	1	0	3

perceived versus actual taste (Table 2). Lighter cell shading indicates lower substitution frequency while darker indicates higher frequencies. Hashed cells indicate accurate identification. A substitution panel was also constructed for each actual taste and showed the perceived tastes at varying concentration levels. Cross-tabulations of actual taste vs. taste realization and the effect of presentation order on identification accuracy were constructed and chi-square statistics performed to determine if there was any association.

3. Results

Due to difficulties in preparation of salt solutions at higher concentrations at the time of the experiment, only three concentration levels of sodium chloride were used. Additionally, three water blanks were not utilized, resulting in a total of 69 samples being tested. The subject was allowed multiple sips for each stimuli sample if unable to identify on the first attempt. Only five samples required more than one attempt (two sips). Four, 10-min, breaks were taken during the course of experimentation. Of the 69 total samples, only 29 were correctly identified. The participant was most accurate at discerning, in order, sour and sweet followed by bitter, salty, and umami (Table 2). Out of a possible 15 attempts (nine for salty), the subject correctly identified sour eleven times, sweet eight times, bitter five times, salty three times, and umami twice. In total, the participant could not discern any taste eleven times during the experiment, could narrow it down to salty or umami twice, or narrow it down to salty, umami, or bitter twice.

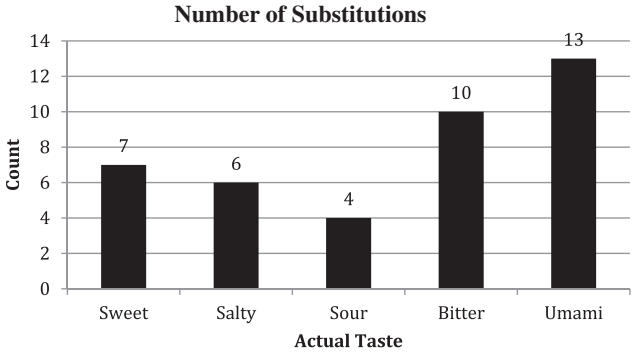

Fig. 1 – The frequency of misidentification for each stimulus.

The most common taste substitution was mistaking salty for umami ($n = 7$) (Fig. 1). There was a signification association between identification accuracy and particular taste, $\chi^2(4) = 12.634$, $p = 0.013$. Sour was accurately identified 73.3% of the time, sweet 53.3%, both salty and bitter both 33.3% of the time, and umami 13.3% (Table 3).

There was a significant association between identification accuracy and concentration level for salty stimuli, $\chi^2(2) = 9.000$, $p = 0.011$, but not for the other four tastes. The subject had 100% identification of sweet samples at concentrations of 171 g/L, 66.6% at 17.1 g/L and only 33.3% at all lower concentrations. Salty solutions were accurately identified 100% of the time at a concentration of 5.8 g/L and 0% at lower concentrations (0.58 and 0.058 g/L). The subject had 66.6% accurate identification or sour stimuli at a concentration of 6.6 g/L, 100% at 0.66 g/L and 0.066 g/L, 66.6% at 0.033 g/L, and 33.3% at 0.0066 g/L. Bitter was accurately identified 0% of the time at a concentration of 0.2 g/L, 66.6% at 0.1 g/L and 0.02 g/L, 0% at 0.01 g/L, and 33.3% at 0.002 g/L. The subject had 0% accurate identification of umami stimuli at a concentration of 1.7 g/L, 33.3% identification at 0.85 g/L, 0% at 0.17 g/L, 33.3% at 0.085 g/L, and 0% at 0.017 g/L. There was no apparent temporal trend in accuracy (data not shown). Presentation order had no significant effect on identification accuracy, $\chi^2(5) = 2.297$, $p = 0.807$ (Table 5).

4. Discussion

Due to the rare nature of isolated congenital aglossia, little if any systematic, randomized controlled experimental data is available. In addition, prior reports have been limited to investigation of the original four tastes (sweet, salty, sour, and bitter) with, to our knowledge, no discussion of umami.

Table 3 – Percent of trials accurately identified.

Actual taste	% Realized
Sweet	53.3%
Salty	33.3%
Sour	73.3%
Bitter	33.3%
Umami	13.3%

Table 4 – Comparison of threshold concentrations between subject and normal individuals.

Taste	Compound	Current[a]		Brasilia[19,b]		Normal[26]	
		M	g/L	M	g/L	M	g/L
Sweet	Sucrose	0.05	17.1	0.006	2	0.00065	0.22
Salty	NaCl	0.1	0.58	0.002	0.09[c]	0.00102	0.06
Sour	Acetic acid	0.0005	0.033	0.00007	0.015	~0.00011[d]	0.007
Bitter	Caffeine	0.0001	0.02	0.00001	0.003	0.0004	0.097
Umami	MSG	0.0005[f]	0.085[f]	–[e]	–[e]	0.0005	0.085

[a] Randomized, double-blinded.
[b] Not randomized, only researcher aware of compound.
[c] Citric acid, 0.015 g/L threshold in normal individuals.
[d] Average of range.
[e] Not measured.
[f] Only 33.3% accurate identification.

Therefore, this study aimed to investigate both the ability of a PWCA to discern among all five tastes in a controlled and double-blinded experimental setting and the threshold values at which positive identification occurs.

4.1. *Stimuli response*

Sour stimuli (acetic acid) had the highest rate of positive identification at a lower concentration (0.033 g/L) than had previously been reported in a PWCA (10 g/L),[4] but higher than normal reports (0.007 g/L)[26] (Table 4 & Fig. 2). Response to sweet stimuli (sucrose), with a threshold level of 17.1 g/L, was comparable to prior reports in a PWCA by Goto et al[4] of 50 g/L and 30.1 g/L by Eskew & Shepherd,[2] but higher than the 7.9 g/L by Salles et al[13] in a PWCA and considerably higher than the threshold in normal individuals (0.22 g/L).[26] Salty and bitter stimuli had the same rates of positive identification, with the former being detected at a lower concentration than the 10 g/L reported in a PWCA by Eskew & Shepherd[2] but higher than the 0.76–1.52 g/L found by Salles et al[13] in a PWCA and the 0.06 g/L in the normal population.[26] The high variability in accurate identification for bitter stimuli mirrors the taste dysfunction reported by Salles et al[13] Threshold was achieved at 0.02 g/L, which is greater than experienced in Brasilia (0.003 g/L) but lower than those in normal individuals (0.097), indicating a possible sensitivity to bitter stimuli. The lower accuracy in identifying umami may indicate a dysfunction in the ability to discern umami as a distinct taste in a PWCA. Concentrations for umami solutions were chosen based on thresholds for those in the normal population and span several orders of magnitude. Since there have been no prior reports of umami gustation in a PWCA, the concentrations used in the current experiment may be outside of the sensation range. There is also a possibility that the subject was unfamiliar with the umami taste or associates it with salty foods. In addition, the stimuli for salty and umami were both sodium solutions, sodium chloride and monosodium glutamate (MSG), respectively. Having the same cation (Na^+) in solutions for the two stimuli might also have contributed the confusion between umami and salty tastes. There was also concern that presentation order may have affected the accuracy of subsequent presentations. However, these concerns were unfounded, as no relationship was found.

Table 5 – Effect of order presentation on stimuli identification.

Prior stimuli	Substitution *n* (%)	Match *n* (%)	χ^2	*p*
Sweet	9 (64.3)	5 (35.7)	2.297	0.807
Salty	6 (66.7)	3 (33.3)		
Sour	7 (53.8)	6 (46.2)		
Bitter	9 (69.2)	4 (30.8)		
Umami	7 (50.0)	7 (50.0)		
First/break	2 (40.0)	3 (50.0)		

In the current study, the subject accurately identified all stimuli at a higher concentration when compared to the results by Salles et al from Brasilia[19] of the same subject. The randomized, double-blinded nature of this study may have affected the results when compared to the non-randomized conditions used in Brasilia. During the evaluation in Brasilia, the PWCA was informed that she would receive solutions containing the four basic tastes. She was not informed, however, about which flavor she would be receiving. The patient also was not informed that the concentrations of the solutions would gradually increase. The PWCA identified some of the flavors in their first concentration level. The correct identification of a flavor at any level of concentration was the criterion for stopping the supply of that flavor. In the current study, use of a nose clip to prevent olfaction limited the duration of the solution in the oral cavity due to the necessity to resume breathing, and may have reduced the subject's sensitivity.

4.2. *Study limitations*

The current study was only able to prepare three concentration levels for the salt stimuli solutions. Prior literature reported a salt solution concentration of 99.9 g/L,[4] but there was difficulty in completely dissolving the solute for the current study. Since the subject had a strong response to salty solutions at the highest concentration, this did not appear to have affected threshold results. Unfortunately, the number of trials for each stimuli and concentration level were limited by subject availability for testing. Future studies may benefit from testing each taste stimuli on a different day and

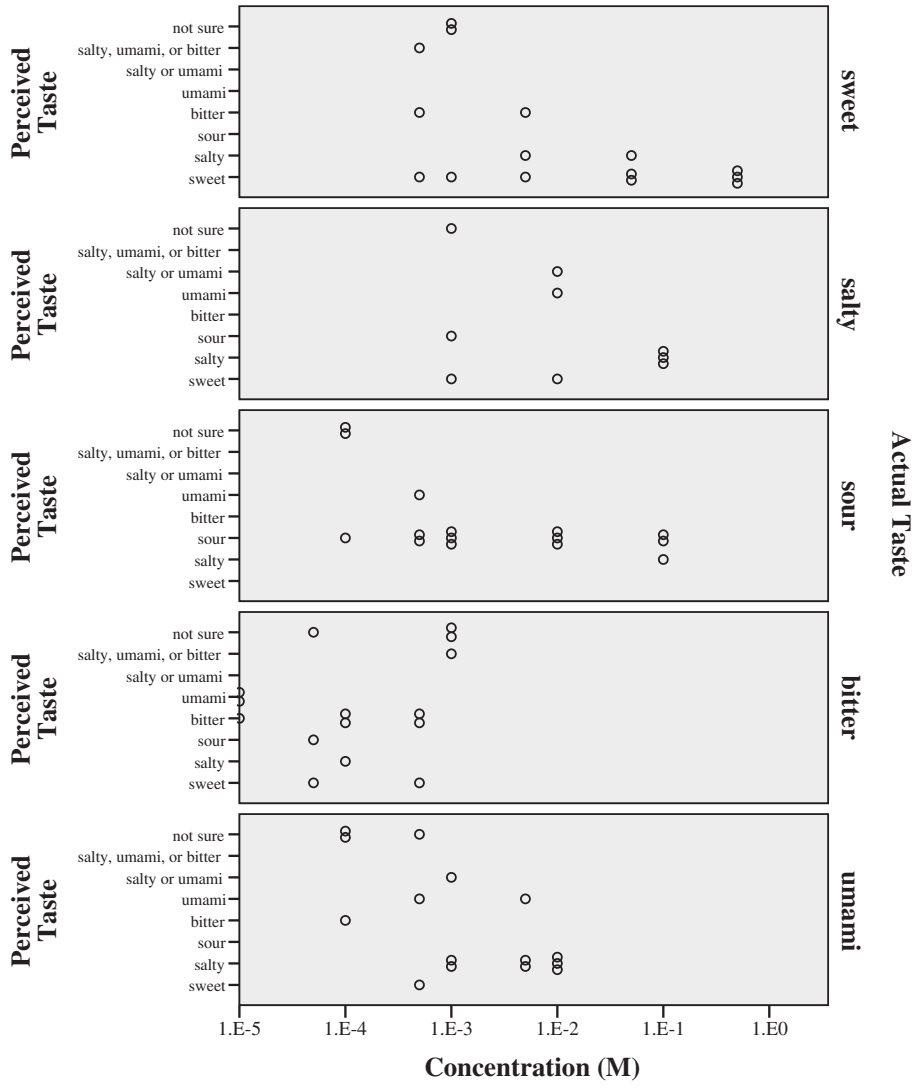

Fig. 2 – Comparison of perceived vs actual taste for varying concentration levels of each stimulus.

including more trials and concentration levels to allow for more accurate measurements and additional statistical power. In addition, the subject reported discomfort while wearing the nose clip and felt that she did could not keep the stimuli solutions in contact with her oral cavity for an adequate duration due to the urge to breathe. Due to the volatile nature of the acetic acid, the nose clip was necessary to isolate the gustation to the oral cavity without interference from olfaction.

5. Conclusions

The anecdotal reports in the literature, since 1718, point to taste as a sensation that is experienced by the PWCA. Our randomized controlled trial (RCT) confirms that assumption, although the current threshold values differ from the few previously reported non-randomized reports. The question of course remains as to where exactly in the oral cavity does the PWCA experience the sensation of taste. It was confirmed inadvertently prior to our research that oral anesthesia for dental work aimed at the mandibular branch of the trigeminal nerve did for a period of 2 weeks remove the oral sensation of taste for this PWCA.

Future research is planned for a follow-up study in which there will be a greater number of trials, salt will have the full five levels, and umami will be explored to a greater degree in both samples and strengths. Future studies may also benefit from the use of citric acid as the sour stimulus, therefore eliminating the need for occlusion of the nasal passage. The RCT nature of the study will be maintained.

Conflicts of interest

All authors have none to declare.

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