



Gustatory Function in Acute COVID-19 - Results From Home-Based Psychophysical Testing

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Objective: Gustatory function during COVID-19 is self-reported by around 50% of patients. However, only a few studies assessed gustation using psychophysical testing during acute infection. The objective of this study is to test gustatory function on threshold tests in the very first days of COVID-19.

Methods: Psychophysical testing consisted of validated and blinded tests for olfaction (NHANES Pocket Smell Test) and gustation (Taste Strips Test). These test kits were sent to home-quarantined patients and self-administered using a detailed instruction sheet.

Results: A total of 51 patients were included in this study. Testing was performed 6.5 ± 2.7 days after sampling of respiratory swabs. At this time 37% of patients stated to currently experience a gustatory impairment. The mean Taste Strips score was 10.0 ± 3.4 with 28% scoring in the range of hypogeusia. Interestingly, no significant difference in the results of gustatory testing could be observed between the group with subjectively preserved gustation and the group with self-rated taste impairment.

Conclusion: During the very first days of COVID-19, psychophysical gustatory testing revealed hypogeusia in 28%. This is far lower than patients' self-reports. Different from previous studies, we did not find clear evidence for an impairment of only certain taste qualities.

Key Words: COVID-19, gustation, olfaction, psychophysical tests, smell, taste.

Level of Evidence: 3

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INTRODUCTION

Olfactory and gustatory dysfunctions are distinct symptoms of the Corona Virus Disease 19 (COVID-19) and are self-reported by around 50% of patients.¹ Although, various studies confirmed a high prevalence of impaired olfaction through psychophysical testing,^{2,3} for gustation such evidence is yet rather limited. This might be caused by the challenges of chemosensitive testing during acute COVID-19: Mostly these disorders last only a few days before chemosensors recover.^{4,5} Moreover, after a positive test result patients are normally home-quarantined and

cannot visit outpatient clinics to undergo psychophysical testing. Thus, many previous studies used improvised homemade tests, which have been firstly prepared and then self-administered by the patient. However, those gustatory tests were suprathreshold and poorly validated, hence possibly leading to false high prevalences of hypogeusia.⁶ Up to now blinded and validated tests of the gustatory threshold have been performed in only three studies and showed prevalences of hypogeusia between 12% and 53% (Table I).^{7–9} Two of these studies examined taste sensation only on average 13 days after the onset of COVID-19. So, these studies might have not captured gustatory function during the acute phase of COVID-19, as chemosensitive disorders often recover quickly. This prompted us to investigate gustatory function during the very first days after the diagnosis of COVID-19. Therefore, test kits for blinded self-administration were sent to home-quarantined patients.

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MATERIAL AND METHODS

The prospective study was conducted between February and April 2021 at the Department of Otorhinolaryngology of Regensburg University Hospital in collaboration with the Institute of Clinical Microbiology and Hygiene of Regensburg University Hospital. It was supported by a grant for COVID-19 related research of the Bavarian State Ministry for Science and Art and conducted after approval by the ethics committee of the University Regensburg (approval number 20-1766_6–101).

TABLE I.
Studies on Validated Psychologically Tested Gustation in COVID-19.

	<i>n</i>	Mean duration between first symptoms and gustatory test (days)	Prevalence of psychophysically tested hypogeusia (%)	Prevalence of subjective taste impairment (%)	Gustatory test
Le Bon et al., 2021	93	13.0 ± 2.7	12	48	16 item threshold Taste Strips Test
Niklassen et al., 2021	15	*	53	-	16 item threshold Taste Strips Test
Singer-Cornelius et al., 2021	39	12.6 ± 6.6	26	100	16 item threshold Taste Strips Test

*Maximum 3 days After Diagnosis.

The study was performed in accordance with the ethical standards of the Declaration of Helsinki and its later amendments. Detailed information was provided to the patient in written form and their consent was obtained in written form, too.

Patients

The aim of this study was to psychophysically assess gustation during the very acute stage of infection with SARS-CoV-2. To assure early psychophysical testing patients were invited just after being tested positive for SARS-CoV-2 by reverse transcription-polymerase chain reaction (RT-PCR) at the Institute of Clinical Microbiology and Hygiene of Regensburg University Hospital between February 4, 2021, and April 30, 2021.

To ensure participation early after the positive diagnosis study material was sent to quarantined patients without prior invitation. The information contained information material, an informed consent, a questionnaire, and psychophysical tests for smell and taste. An instruction manual ensured correct, home-based, and self-administered testing. Of 175 contacted patients, 62 responded and 47 could be included in the study. Exclusion criteria were an age below 18 years and delayed chemosensitive testing (>15 days after the swab of the positive PCR test has been taken).

Patients' Questionnaire

The questionnaire contained questions on medical preconditions and the individual course of the SARS-CoV-2 infection. Additionally, patients were asked to self-rate their subjective olfactory and gustatory function using a visual analog score (VAS) from 1 to 10 (1 having no smell/taste and 10 having no impairment in smell/taste).

Psychophysical Testing

Psychophysical testing consisted of validated and blinded tests for olfaction (NHANES Pocket Smell Test, Sensonics, Haddon Heights, NJ, USA) and gustation (Taste Strips Test, Burghart Messtechnik, Holm, Germany). Both tests can be self-administered using a detailed instruction sheet.²

The assessment of olfactory function was conducted with the NHANES Pocket Smell Test. This scratch-and-

sniff suprathreshold olfactory test consists of eight familiar smells: chocolate, strawberry, smoke, leather, soap, grape, onion, and natural gas. Six or more correct answers indicate normosmia, five and less correct answers indicate hyposmia/anosmia.¹⁰

The gustatory function was tested with the Taste Strips Test.¹¹ It contains 16 impregnated filter paper strips to test four different concentrations of the taste qualities sweet, sour, salty, and bitter (0.4, 0.2, 0.1, 0.05 g/ml sucrose; 0.3, 0.165, 0.09, 0.05 g/ml citric acid; 0.25, 0.1, 0.04, 0.016 g/ml sodium chloride; 0.006, 0.0024, 0.0009, 0.0004 g/ml quinine hydrochloride). These and two blank strips without any taste were packed in pseudo-randomly numbered paper bags to allow a blinded self-administration. Patients were instructed to rinse their mouths with tap water and to have a break of 1 min between two strips. To ensure correct self-administration the test was conducted as a non-forced choice task: In addition to the answers "sweet", "sour", "salty" and "bitter" they were offered "no answer." This non-forced choice paradigm has been previously validated for both operator- and self-administration previously^{12,13} and successfully used in multiple studies.¹⁴⁻¹⁷ Correctly identified taste strips sum up to the Taste Strips score. Nine or more correctly identified strips were defined as normogeusia, eight or less correctly identified strips as hypogeusia.¹⁸

Statistics

Data were analyzed using SPSS Statistics software (version 26, IBM, Armonk, NY, USA). Graphs were illustrated using Prism software (version 9, GraphPad Software, San Diego, CA, USA). Values are expressed as mean ± standard deviation (SD), and *p* < 0.05 was considered statistically significant. Continuous data were tested for statistical significance using unpaired two-tailed Student's t-tests or one-way ANOVA. Z-test was used to compare proportions and Pearson's correlation for correlations.

RESULTS

51 patients (mean age 42 ± 15 years), who were tested positive for SARS-CoV-2 between February 4, 2021, and April 30, 2021, were included in this study. 25 patients (49%) were female, and 26 patients (51%) were male. Patients conducted psychophysical testing 6.5 ± 2.7 days after sampling of respiratory swabs.

TABLE II.
Statistical Analysis Results of This Study.

	Olfaction		<i>p</i>	Gustation		<i>p</i>
	Subjectively impaired	Subjectively normal		Subjectively impaired	Subjectively normal	
Number of subjects	21 (41%)	30 (59%)		19 (37%)	32 (63%)	
Age (years)	37 ± 14	45 ± 16	n.s.	40 ± 14	43 ± 16	n.s.
Female	14 (67%)	11 (37%)	<0.05	14 (74%)	11 (34%)	<0.01
Duration between swab sampling and chemosensitive testing (days)	6.9 ± 2.4	6.2 ± 2.9	n.s.	6.5 ± 2.1	6.4 ± 3.0	n.s.
VAS	3.3 ± 2.4	8.7 ± 1.6	<0.0001	3.4 ± 1.4	9.1 ± 1.1	<0.0001
NHANES score	5.0 ± 2.4	5.8 ± 1.9	n.s.	-	-	-
Taste Strips score	-	-	-	9.2 ± 4.1	10.4 ± 2.9	n.s.
Psychophysically confirmed hyposmia	11 (52%)	14 (67%)	n.s.	-	-	-
Psychophysically confirmed hypogeusia	-	-	-	7 (37%)	7 (22%)	n.s.

n.s = not significant.

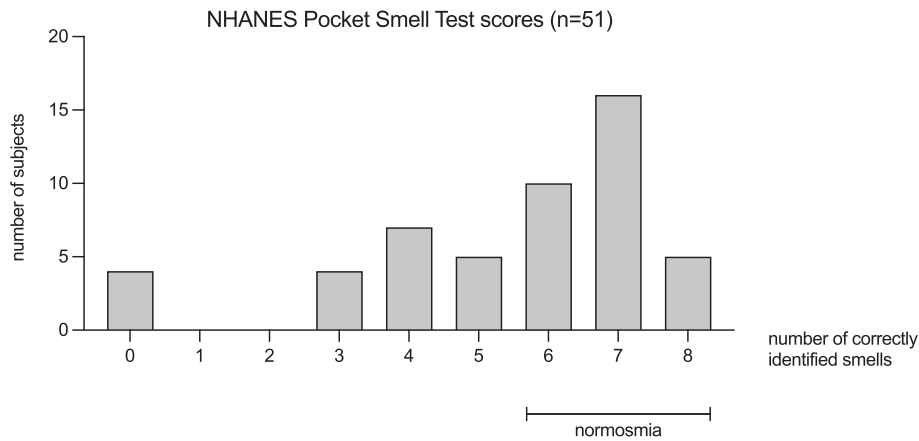


Fig. 1. NHANES pocket smell test score as number of correctly identified smells, and percentage of the total study population

At the time of the assessment 21 (41%) and 19 (37%) patients stated to currently experience an olfactory and a gustatory impairment, respectively. They self-rated olfactory function as 6.5 ± 3.3 and gustatory function as 6.9 ± 3.0 on the visual analog score (VAS). However, those who subjectively reported suffering from impaired smell or taste had a significantly lower VAS for both olfactions (3.3 ± 2.4 vs. 8.7 ± 1.6 ; $p < 0.0001$; effect size 5.4; 95% CI 4.2–6.6) and gustation (3.4 ± 1.4 vs. 9.1 ± 1.1 ; $p < 0.0001$; effect size 5.7; 95% CI 4.9–6.5) compared to those who reported a preserved taste or smell (see Table II).

In the NHANES Pocket Smell Test, the entire cohort scored 5.4 ± 2.2 . 20 patients (39%) scored 5 or less, which is defined as hyposmia, 31 patients (61%) scored 6 or more, which is defined as normosmia (Fig. 1). When considering all patients VAS of subjective olfactory function correlated positively with the score of the NHANES Pocket Smell Test ($r = 0.42$, $p = 0.002$; Fig. 2).

The mean Taste Strips score was 10.0 ± 3.4 with 14 patients (28%) scoring in the range of hypogeusia and the other 37 patients (72%) in the normogeusic range. The distribution of the Taste Strips test results is shown in Figure 3.

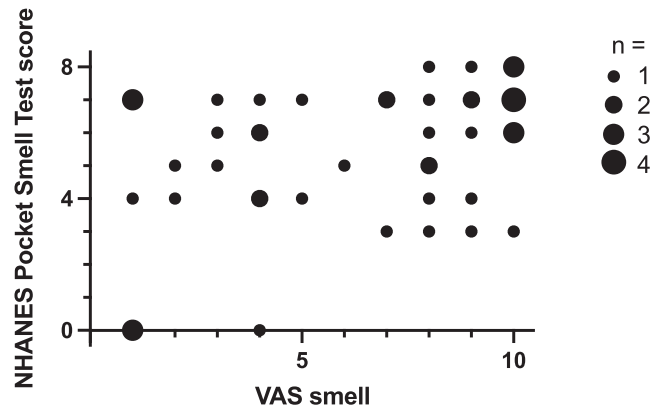


Fig. 2. Bubble plot for VAS smell versus NHANES pocket smell test score ($r = 0.42$, $p = 0.002$)

Interestingly and contrary to olfaction, no correlation could be observed between VAS of taste and Taste Strips score ($r = 0.04$, $p = 0.80$; Fig. 4).

Figure 5 shows the results of the single taste qualities sweet, sour, salty, and bitter. There was a difference

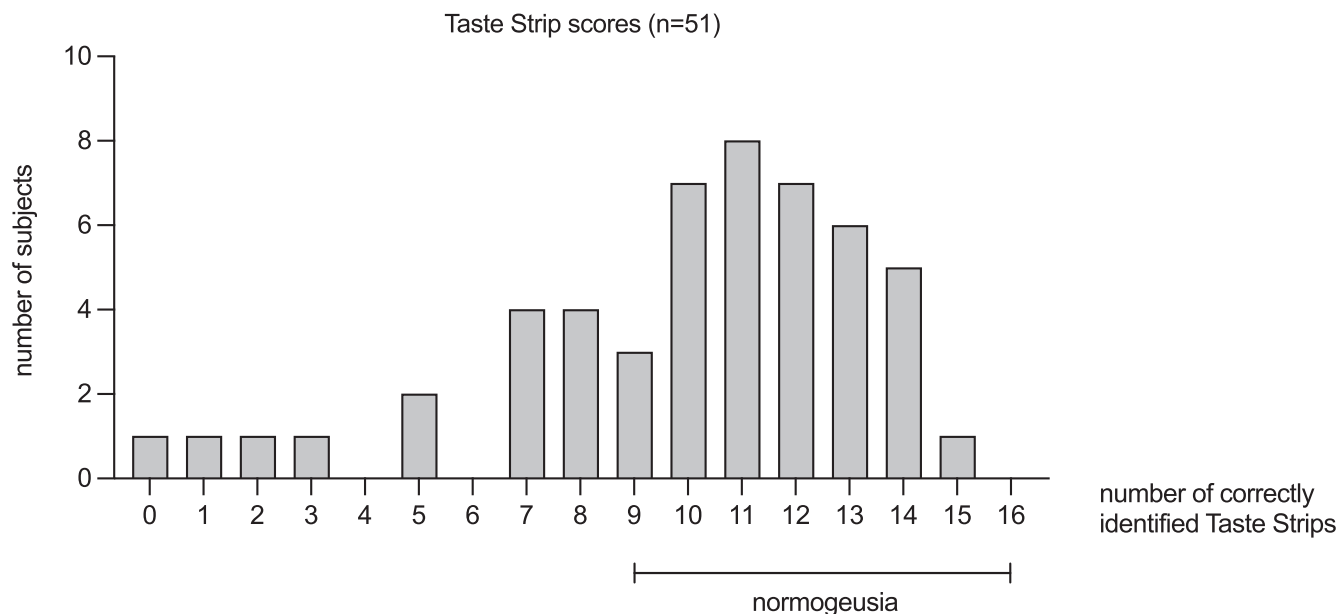


Fig. 3. Taste strips score as number of correctly identified strips, and percentage of the total study population

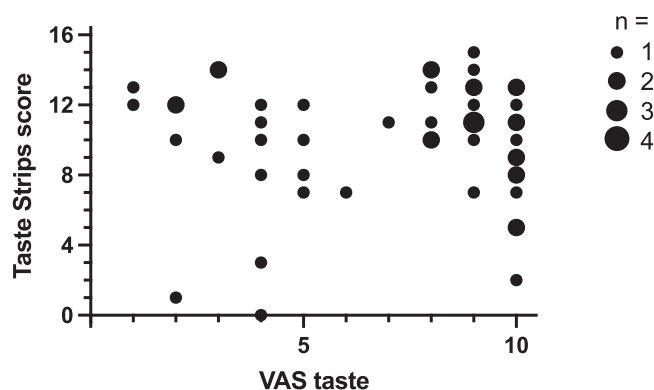


Fig. 4. Bubble plot for VAS taste versus taste strips score ($r = 0.04$, $p = 0.80$)

between the taste qualities with the mean score of sour being significantly lower compared to the other three taste qualities ($p < 0.05$).

Overall patients no correlation could be seen between the duration between swab sampling and gustatory testing and the Taste Strips score ($r = 0.10$, $p = 0.49$). Also, for the subgroup of patients who subjectively experience a taste impairment no such correlation was found ($r = 0.21$, $p = 0.39$).

DISCUSSION

Even almost two years after the beginning of the pandemic, data on psychophysically assessed gustatory function during acute COVID-19 is still rare. This is presumably due to the challenges of testing in COVID-19. Here, we report on a study using home-based and self-administered psychophysical testing during the very first days after the onset of symptoms.

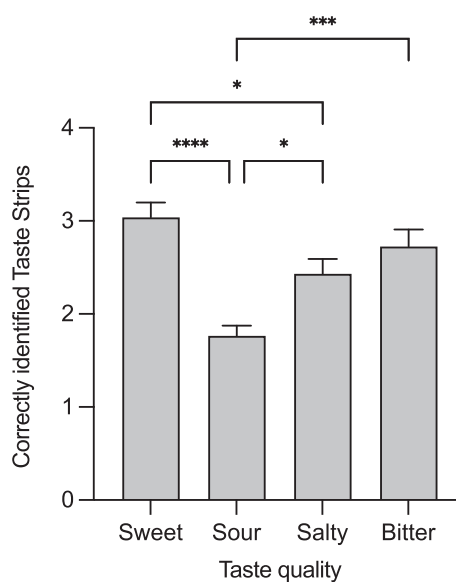


Fig. 5. Taste strips score for the single taste qualities (mean \pm SEM; one-way ANOVA; * $p < 0.05$, *** $p < 0.001$, **** $p < 0.0001$)

Importantly, chemosensitive testing was performed 6.5 ± 2.7 days after sampling of respiratory swabs, which is substantially earlier than in most previous studies (Table I). Different from many previous studies, we performed gustatory testing using validated and blinded testing for the thresholds of sweet, sour, salty, and bitter.

In our study, we could show that around 30% of our cohort is hyposgeusic in a very acute stage of COVID-19. This is lower than the subjective ratings of this cohort and various publications on self-reported gustatory dysfunction.¹ The prevalence is also lower than in various studies using patient-prepared suprathreshold testing

which were poorly validated and presumably overestimated hypogeusia.⁶ On the other hand, hypogeusia is substantially more frequent than in healthy subjects, for which a prevalence of only 5% has been established in a large pre-COVID-19 cohort.¹⁴

Our data is in good accordance with the results of Le Bon et al. and Singer-Cornelius et al.^{7,9}: Using the same 16-item Taste Strip Test they found hypogeusia/ageusia in 12% and 26%, respectively. However, they performed the testing later than in the current study, in a mean 13.0 ± 2.7 and 12.6 ± 6.6 days after the onset of the first symptoms of COVID-19. A third study by Niklassen et al. identified gustatory dysfunction in as much as 53% when performing an operator-performed threshold test. However, the study cohort was limited to only 15 patients.⁸

Psychophysically testing revealed a significantly lower Taste Strips score for sour compared to sweet, salty, and bitter (Fig. 5). Similar data have been shown before by Singer-Cornelius et al.⁹ As each type of gustatory receptors utilizes a distinctive transduction mechanism,¹⁹ Singer-Cornelius and others hypothesized that COVID-19 might impair the transduction of single taste qualities: In COVID-19 a potentially secondary upregulation of angiotensin II could impair the ion channel transduced qualities sour and salty.⁹ In contrast, another study suggested that G protein-coupled receptors of gustatory receptors might be the target of SARS-CoV-2 leading to a specific hypogeusia of sweet and bitter.²⁰

However, our data challenge the previous hypothesis of COVID-19 related dysfunction of individual taste qualities: First, in a large pre-pandemic study the cumulative Taste Strips scores differed between the taste qualities, too, with mean scores for sour being lower than those for sweet, salty, and bitter (sour 2.5; sweet 3.7; salty: 3.4; bitter: 3.3).¹⁴ Hence a divergent test sensibility between the single taste qualities could have led to a bias of the results of both Singer-Cornelius et al. and the current study. Second, in our study gustatory impairment was not limited to single taste qualities. When comparing the current study to the normative values of Welge-Lüssen et al. all taste quality specific Taste Strips scores highly impaired (Δ_{sweet} : 0.7; Δ_{sour} : 0.7; Δ_{salty} : 1.0; Δ_{bitter} : 0.6).

Different from the study of Singer-Cornelius et al., in which only COVID-19 patients with a subjectively reported taste impairment were included, our cohort consisted of patients with and without subjective taste disorders. Hence, we explored a potential correlation between subjectively assessed gustatory function and results of psychophysical gustatory testing. Contrary to olfaction, there was no correlation between VAS and Taste Stripe score.

This is in line with previous reports, that not only for pre-COVID-19 conditions²¹ but also in COVID-19^{2,9} the self-evaluation of taste does not match with psychophysical results. Hence, the gustatory function can hardly be self-evaluated correctly by the patient, which is likely due to the patients' confusion between gustation and retro-nasal olfaction.^{22,23} Therefore, the gustatory function should not only be self-evaluated but also assessed using validated psychophysical testing.

There are some limitations to our study. First, the study is limited by the relatively small cohort of

51 patients. Furthermore, only patients with a mild course of COVID-19 were included. Additionally, as shown in Figure 3, some patients scored in the Taste Strips Test between 7 and 10. This is close to the threshold between 8 and 9 which defines normogeusia and hypogeusia. As the self-administered testing, the non-forced choice paradigm, and a potential subconscious patient's bias could potentially have influenced these results, the prevalence of hypogeusia in acute COVID-19 could be overestimated. On the other hand, although we performed psychophysical testing earlier than most previous studies, it was still one week after the onset of the first symptoms. As chemosensitive dysfunctions improve in many COVID-19 cases quickly, our data might have missed out on some cases of early temporary hypogeusia.

CONCLUSION

During acute COVID-19, psychophysical gustatory testing revealed hypogeusia in around 30%, which is substantially lower than patients' self-reports. Importantly and different from previous studies, we did not find clear evidence for an impairment of only certain taste qualities. Furthermore, our data suggest that self-reporting of taste function does not correlate with the results of psychophysical gustatory testing. This emphasized the importance of psychophysical tests over the exclusive use of patients' subjective ratings for future studies.

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