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Original Article

Longitudinal follow-up of taste function and trigeminal perception in COVID-19 patients with olfactory dysfunction – The COVORTS study

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SUMMARY

Background & Aims: Chemosensory dysfunction is one of the hallmarks of a COVID-19 infection. While most patients recover within a few weeks after infection, in 5–10% of the patients chemosensory dysfunction turns into a long-term problem. While olfactory loss has been extensively investigated, information regarding taste and trigeminal function has remained scarce. The COVORTS study was set up to assess the natural progression of olfactory, taste and trigeminal alterations in a prospective cohort of COVID-19 patients.

Methods: We included 76 patients aged between 18-60 years old with olfactory dysfunction (>1 month) after a recent (<3 months) confirmed COVID-19 infection, and followed them for a period of 6 months. At time of inclusion (T1), 3 months (T4) and 6 months (T7) later, psychophysical testing of gustatory function was conducted (Taste Strips). Questionnaires on taste and trigeminal ability, as well as at-home self-testing of taste and trigeminal perception were performed every month.

Results: We found that, subjectively, there was a large decline in taste and trigeminal functioning at baseline compared to before COVID-19 infection. Apart from salty taste, an improvement in taste and trigeminal functioning was seen over time, though not towards full recovery. The majority of patients had scores within

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the normative range on the Taste Strips at baseline; nonetheless, almost half of patients showed clinical improvement over time.
Conclusions: Although taste and trigeminal dysfunction appear less prominent than olfactory dysfunction after COVID-19 infection, patients can and do suffer from this over a prolonged period of time. Understanding the trajectory of symptom burden and recovery from post-COVID-19 condition is essential for policy making, therapeutic interventions, and providing appropriate care and (nutritional) advice to patients.

Introduction

In 2020, the world was startled by an unprecedented pandemic, in which olfactory loss turned out an early and specific predictive symptom of COVID-19 infection [1]. Additionally, it became clear that COVID-19-associated chemosensory impairment was not just limited to smell, but also affected taste perception [2,3]. Nevertheless, the initial wave of research heavily leaned upon subjective accounts provided by patients. It is however well established that individuals often confuse their sense of smell with their sense of taste due to the retronasal component of olfaction and its oral referral, leading to overlap in the perception of flavor [4–6]. For olfaction, studies have consistently observed that self-evaluation tends to underestimate the true prevalence of dysfunction when gauged against psychophysical assessments [7–10]. In contrast, a recent review suggests that the prevalence of COVID-19 induced taste impairment is similar across self-report and 'direct' measurement paradigms [11], though only few studies have used 'objective' psychophysical tests, currently considered the golden standard for assessing gustatory function [12]. Consequently, it remains unclear to what extent COVID-19 patients develop persistent taste dysfunction, as most studies that do include psychophysical measures are cross-sectional in design.

Correspondingly, although changes in sense of smell and taste have been extensively studied for diagnostic value, longitudinal investigations are scarce and little is known about the clinical course of such symptoms post-COVID-19, with limited evidence on the duration of recovery. It is evident however that this detrimental effect of COVID-19 transcends the acute phase of infection [13–15].

Beyond smell and taste loss, COVID-19 induced chemosensory dysfunction is also reported to include loss of trigeminal perception, or chemesthesis [2]. Trigeminal sensations encompass an array of tingling, spicy, prickling, cooling experiences, that are mediated via the trigeminal nerve. Given the diverse spectrum of these sensations, both oral and nasal, no comprehensive validated objective or psychophysical tests including normative benchmarks exist to properly assess this ability. Nonetheless, several papers unveiled high rates of severe reduction in trigeminal sensitivity in COVID-19 patients based on self-report appraisals [16,17], while psychophysical and electrophysiological measurements report only limited alterations of the trigeminal system [13,17–20].

Beyond the immediate realm of chemosensory alteration, the sustained loss of smell and taste is associated with a significant reduction in patients' quality of life, including increased depressive symptoms and nutritional challenges [21,22]. Understanding the trajectory of symptom burden and recovery from post-COVID-19 condition holds pivotal implications for policy making, therapeutic interventions, and the coordination of patient care [23]. Given the current limited empirical evidence, longitudinal and objective standardized monitoring is thus imperative to provide a coherent picture on the progression and trajectory of chemosensory disorders associated with COVID-19. In this study, we describe the progression of taste (dis)ability and trigeminal function, and its recovery over the course of 6 months, within a cohort of COVID-19 patients enduring olfactory dysfunction.

Methods

Study population

Patients in this study were part of the COVORTS study (COVid cohORT on Smell loss). For this cohort, patients aged between 18-60 years old with smell loss (>1 month) were recruited within 3 months after COVID-19 infection, confirmed with a positive PCR-test, or a positive SARS-CoV-2-antigen self-test. Patients were excluded if they had a pre-existing smell and/or taste disorder or were pregnant/intended to become pregnant. This study was approved by a regional medical research ethics committee (28-09-2021, file NL77954.091.21) and carried out in compliance with relevant laws and institutional guidelines and in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

For the cohort, patients were recruited via traditional and social media, the Dutch association for patients with smell or taste loss (Reuksmaakstoornis.nl), the patient organization PostCovid NL, and the Dutch National Institute for Public Health and the Environment. Interested patients were contacted by phone call, during which verbal informed consent was obtained. After this, patients filled out a screening questionnaire. When patients were eligible for inclusion in the study, the first test session was scheduled. At the start of this first test session, written consent was provided by the patients. Patients received financial compensation for their contribution.

In total, 85 patients underwent a first test session. Eight patients were excluded because they did not have a smell disorder according to the outcomes of a standardized psychophysical smell test (score > 30.5 points on the Sniffin' Sticks [24] or did not self-report parosmia complaints. One patient was excluded due to pregnancy at baseline, leaving 76 patients to be included.

Study design

All patients were followed longitudinally for one year. In this manuscript results are reported up until 6 months (Figure 1). Every 3 months, patients were visited at home by the researchers and underwent an extensive testing protocol, including psychophysical testing for smell and taste. Time points for these measurements were T1 (performed within 3 months after infection, 'baseline'), T4 (3 months after baseline), and T7 (6 months after baseline), and were scheduled based on the patients' availability. In addition, every month, patients performed a home-use test for smell and taste and trigeminal sensations (see [3]), and filled in a set of online questionnaires.

Measurements

For the home visits, patients were instructed not to eat or drink anything (except water or tea) at least one hour before the start of the test session. A home visit consisted of the following measurements (in order of performance): the SCENTinel olfactory test (not included in this manuscript), the SSParoT (not included in this manuscript),the Taste Strips test, and the Sniffin' Sticks test battery.

The set of online questionnaires included: a demographics questionnaire; questions on self-reported smell and taste function and trigeminal perception, eating behavior (not included in the manuscript), and olfactory-related quality of life (not included in this manuscript). Patients could self-assess their sense of smell, taste and trigeminal ability by means of a home-use test.

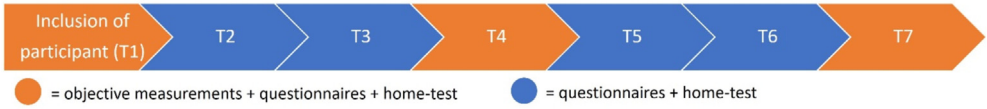

Figure 1. Time line of measurements for patients during the study.

Demographics questionnaire

Patients were asked to report their birth date, gender (male, female, other), height (cm), weight (kg), severity of COVID-19 symptoms during the acute phase (No complaints or mild complaints; Moderate complaints; Severe complaints; Critical complaints), COVID-19 vaccination status (yes/on), whether they performed any smell training or received any treatment for their chemosensory loss (yes/no), and whether they were reinfected with COVID-19 in the past period.

Self-reported smell and taste function and trigeminal perception

Similar to [2], patients were asked to quantify their former (i.e., before COVID-19 infection) and current ability to smell, taste, and perceive cooling, tingling, and burning sensations (trigeminal sensations) on a 100 unit visual analogue scale (VAS), anchored 'no sense at all' to 'excellent sense'. In addition, patients were asked whether they experienced any of the following changes in smell (I cannot smell at all, Odors smell less strong than they did before, Odors smell different than they did before (the quality of the odor has changed), I can smell things that are not there (for example, I smell fire when nothing is on fire) Sense of smell fluctuates (comes and goes), None of the above; check-all-that-apply) and whether they experienced changes to specific tastes (sweet, salty, sour, bitter, umami/savory, no specific changes; check-all-that-apply).

Home-use test

A home-use test for direct self-assessment of the chemical senses was developed during the initial pandemic phase of COVID-19, in which lockdowns were frequent, and no close contact with COVID-19 patients was allowed. It was aimed for patients worldwide to quickly assess their own sense of smell, taste and trigeminal sensation, using household items. During the test, patients had to gather five household items and five food items, of which the intensity of the smell, taste and nasal and oral trigeminal sensations (when appropriate) had to be rated on a 100 unit VAS, anchored from 'not strong at all', to 'very strong'. For more details, see [3].

Sniffin' Sticks

Olfactory function was measured using the Sniffin' Sticks test battery (Burghart, Wedel, Germany), an olfactory test battery that includes an odor threshold detection test (T), using butanol, an odor discrimination test (D), and an odor identification test (I). For the threshold detection test, scores could range between 1 and 16, for the odor discrimination and identification test, scores were defined as the number of correct responses (0–16), with higher scores indicating better olfactory function. A composite "TDI score" (range 1–48) was calculated as the sum of the results obtained for threshold, discrimination, and identification measures [24].

Taste Strips

Taste function was assessed using the Taste Strips (Burghart, Wedel, Germany). This validated test uses filter-paper taste strips impregnated with different concentrations of the basic tastes sweet, salty, bitter and sour 21, 22. The filter papers are impregnated with four concentrations of sweet (0.05, 0.1, 0.2 or 0.4 g/ml sucrose), salty (0.016, 0.04, 0.1 or 0.25 g/ml sodium chloride), sour (0.05, 0.09, 0.165 or 0.3 g/ml citric acid) or bitter (0.0004, 0.0009, 0.0024, 0.006 g/ml quinine hydrochloride) taste. After placing a paper on the tongue, patients were asked to identify the taste stimulus with five possible answers (sweet, sour, salty, bitter or no taste). Taste strips were presented in a semi-randomized forced choice procedure. Patients rinsed their mouth with water before each taste strip. Scores for each taste range from 0 to 4, and total taste scores range from 0-16, which is the sum of the four basic taste scores. Higher scores indicate a better taste function. Patients who scored lower than 9 were considered hypogeusic (reduced taste ability) and patients with a score of 9 or higher were considered normogeusic (normal taste) [25].

Analysis

Self-reported data that we considered as highly unlikely due to misinterpreting of the questions or response scale (e.g. self-reported smell or taste ability before COVID-19 < 40) were excluded (n=21

data points). Not all patients filled out all questionnaires or performed the home-use test at all time points; these are treated as missing values (ranging from 0-12 per time point).

Descriptive statistics are given as means and standard deviations or standard errors for continuous variables, and as frequencies for categorical variables. Recovery of self-reported taste and trigeminal ability was computed as an improvement of at least 80% of pre-illness function rating, in line with [3,15]. Clinical improvement on the Taste Strips was evaluated as $\geq$ 2 points increase, see [26]).

To evaluate differences over time, linear mixed model analyses were performed using IBM SPSS statistics (version 28) with the Taste Strips and VAS scores (from the self-report and the home-use test) as dependent variables, time points as fixed factor and patient as random factor, with the intercept included and a variable covariance structure. Post-hoc analyses were performed when the main analysis yielded significant results, as determined by a *P*-value < 0.05.

Results

Baseline patient characteristics

In total, 76 patients were included between September 2021 and March 2023. Date of infection was between July 2021 and December 2022, and baseline (T1) measurements were performed around 80 days after COVID-19 infection had been diagnosed.

The average age of patients was 46 years, most patients were female and vaccinated against COVID-19 at time of inclusion. For an overview of demographic characteristics of the patients, see Table 1.

Self-reported taste and trigeminal ability

Patients report significant lower taste ability (34.9 ± 27.4) and trigeminal sensations (41.0 ± 29.0) at time of inclusion compared to before their COVID-19 infection (92.5 ± 10.8 and 83.0 ± 18.5, respectively, both $P < 0.001$; see Figure 2). Only one patient rated their pre-COVID-19 taste ability as (marginally) lower than at inclusion, while four patients rated their pre-COVID-19 trigeminal ability as lower than at T1.

Both taste ability and trigeminal sensations increased over the course of 6 months ($P < 0.001$; see Figure 2). However, barely up to 30% of patients indicated recovery of their taste ability, computed as an improvement of at least 80% of pre-illness function rating (see Table 2). For trigeminal ability, up to 55% of patients reported to recover to at least 80% of their pre-illness ratings.

Table 1
Patient characteristics (N=76) at T1 (<12 weeks after infection).

Age (years, mean ± SD, range)	46.7 ± 10.5 (18–60)
Gender (female/male)	63/13
BMI (kg/m^2, mean ± SD, range)	25.7 ± 4.3 (19.3–37.9)
Vaccination status (yes/no)[b]	65/11
Severity of COVID-19 complaints during infection (N)	
- No complaints or mild complaints	11
- Moderate complaints	53
- Severe complaints	12
- Critical complaints	0
Sniffin' Sticks score (TDI, mean ± SD, range)	24.1 ± 6.4 (6.00–37.25)
Self-reported smell (0–100 unit VAS, mean ± SD, range)	
- Former sense of smell (before COVID-19 infection)	94.4 ± 7.9 (60.6–100.0)
- Current sense of smell	20.3 ± 16.9 (0.2–82.8)
Self-reported smell complaints (N)[a]	
- I cannot smell at all	24
- Odors smell less strong than they did before	52
- Odors smell different than they did before	40
- I can smell things that are not there	33
- Sense of smell fluctuates (comes and goes)	36

[a] Patients could report multiple complaints.
[b] Only one of the unvaccinated patients did get their first vaccination during the study.

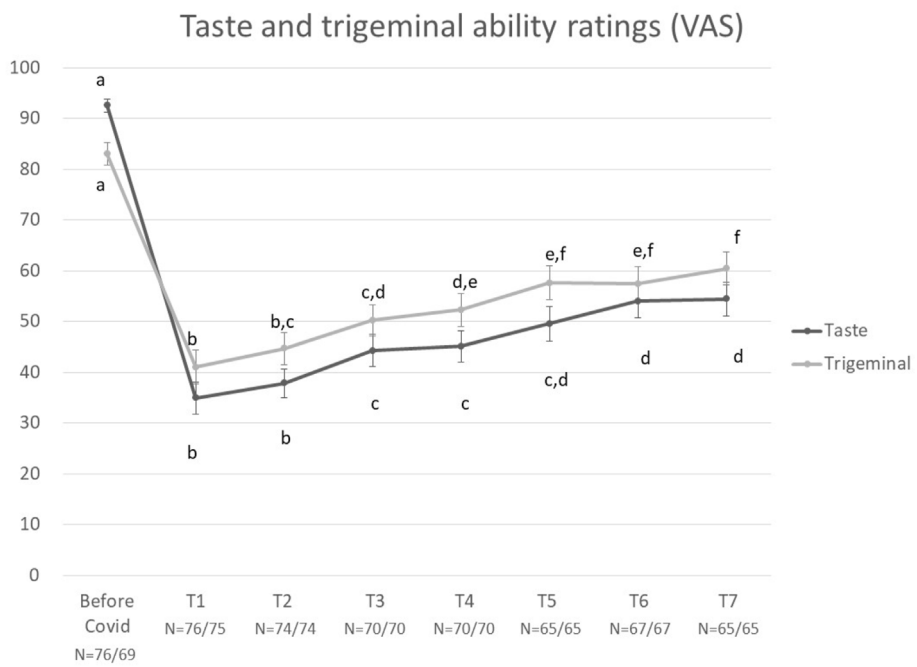

Figure 2. Means and standard errors for self-reported taste and trigeminal ability at all time points measured on a VAS, 0–100. Different letters indicate significant different means according to post-hoc testing of linear mixed models. N indicates number of included data points for taste/trigeminal ability at each time point.

Table 2
Percentage of patients recovered for taste and trigeminal ability per time point. Recovery is considered an improvement of at least 80% of pre-illness function rating on a VAS, 0–100. In between brackets is the total number of data points per time point.

Recovery rate (%)	T1	T2	T3	T4	T5	T6	T7
Taste ability	10.5 (76)	9.9 (71)	17.1 (70)	24.3 (70)	26.2 (65)	29.2 (65)	29.2 (65)
Trigeminal ability	30.4 (69)	36.5 (74)	41.4 (70)	44.3 (70)	55.4 (65)	49.3 (67)	53.8 (65)

Patients could also indicate whether they experienced changes to specific tastes. Most patients initially reported changes in salt and sweet taste perception. Over time, fewer patients tended to report changes in taste qualities, while more patients reported no changes in taste qualities (see Table 3).

Table 3
Frequencies (n) of patients self-reporting changes in each taste quality. In between brackets is the total number of data points per time point. Patients could indicate multiple taste qualities to have changed (or no changes).

	T1 (76)	T2 (74)	T3 (70)	T4 (70)	T5 (65)	T6 (67)	T7 (65)
Sweet	36	27	27	31	21	17	17
Salty	39	30	24	25	20	21	23
Sour	33	30	29	28	22	18	21
Bitter	31	31	27	28	25	29	22
Umami	31	31	24	28	21	26	21
No taste changes	21	26	27	23	30	29	33

Taste and trigeminal intensity ratings by an at-home self-test

Patients used an at-home test to self-assess their taste, nasal and oral trigeminal sensitivity, using various household items. For results, see Figure 3. For sweet, sour and bitter taste and nasal and oral irritation, patients' intensity ratings increased over time (all $P < 0.05$). Surprisingly, salty taste intensity ratings decreased over time, though not significant ($P = 0.09$).

Psychophysical taste function and clinical improvement

The mean (±SD) total score on the Taste Strips was 9.5 ± 3.4 at T0, 10.7 ± 2.8 at T3, and 10.9 ± 3.1 at T6, demonstrating a significant increase over time ($F [2, 138]$, $P < 0.001$). For an overview of the overall scores on the Taste strips, as well as the scores per basic taste, see Figure 4. Mean scores for the individual taste qualities also increased significantly over time (all $P < 0.05$), except for salty taste.

Most patients (71%) had scores within the normative range on the Taste Strips at time of inclusion. The number of patients who were normogeusic increased slightly across time points, while the number of patients with hypogeusia declined over time (see Figure 5). Six months after baseline, 18% (n = 12, out of 68) of patients were still hypogeusic.

From T1 to T4, 30 patients showed clinical improvement on the Taste Strips (≥2 points increase, see [26]); from T4 to T7, 16 patients showed clinical improvement, and from T1 to T7, 32 patients showed clinical improvement on the Taste Strips.

Discussion and conclusion

In this paper, we investigated the natural course of taste ability and trigeminal self-reported and psychophysically assessed ability, and its recovery over time, in COVID-19 patients with initial olfactory dysfunction. We found that, by retrospective self-report, there was a large decline in taste and trigeminal functioning at time of inclusion (<3 months since infection) compared to before COVID-19 infection. Apart from salty taste, an improvement in taste and trigeminal functioning was seen over time, though not towards full recovery. Based on psychophysical testing, the majority of patients had a normal sense of taste at time of inclusion. Nonetheless, almost half of patients showed clinical improvement on their sense of taste.

In line with previous reports [2,3,11,27], we here demonstrate that self-reported taste loss is present after COVID-19 infection. Besides self-report ratings, we also included at-home direct self-assessments of the chemical senses using household items, as well as objective, standardized psychophysical measurements. Nguyen et al. [3] already demonstrated the validity of the home-use self-assessment test, by showing that COVID-19-positive individuals report taste dysfunction when self-tested with stimuli that have little to none olfactory components. They concluded that assessing the smell and taste intensity of household items is a promising, cost-effective screening tool that complements self-reports and may help to disentangle taste loss from smell loss. Indeed, the self-report ratings from the current cohort are in line with the results from the home-use test, showing a gradual improvement over time.

However, self-report or direct self-assessment does not replace standardized validated psychophysical tests. As recently critically reviewed by both Hintschich et al. and Hannum et al. [11,12], during the last years, only few studies have assessed gustatory function in COVID-19 using psychophysical tests. Those studies confirmed hypogeusia in 10–53% of patients [28–32], which is less frequent compared to self-report or direct self-assessment. Those results approximate ours, confirming hypogeusia in up to 30% of COVID-19 patients within 3 months after infection and almost 20% six months later based on psychophysical assessment, while self-report ratings show much higher prevalence of taste loss with only up to 30% recovery six months after inclusion (Table 2). These higher numbers of self-reported taste loss may in fact reflect more pronounced smell loss, as individuals often confuse smell and taste perception. Other studies relying on self-report demonstrated that approximately 10% of individuals who report initial changes to their sense of smell or taste after COVID-19 recover their pre-illness ability to taste six months later [15]. Moreover, in a longitudinal case-control study, Boscolo-Rizzo et al. identified that 27% of mild COVID-19 patients suffered persistent gustatory impairments one year post-infection [13]. Overall, both self-report, direct assessment and psychophysical

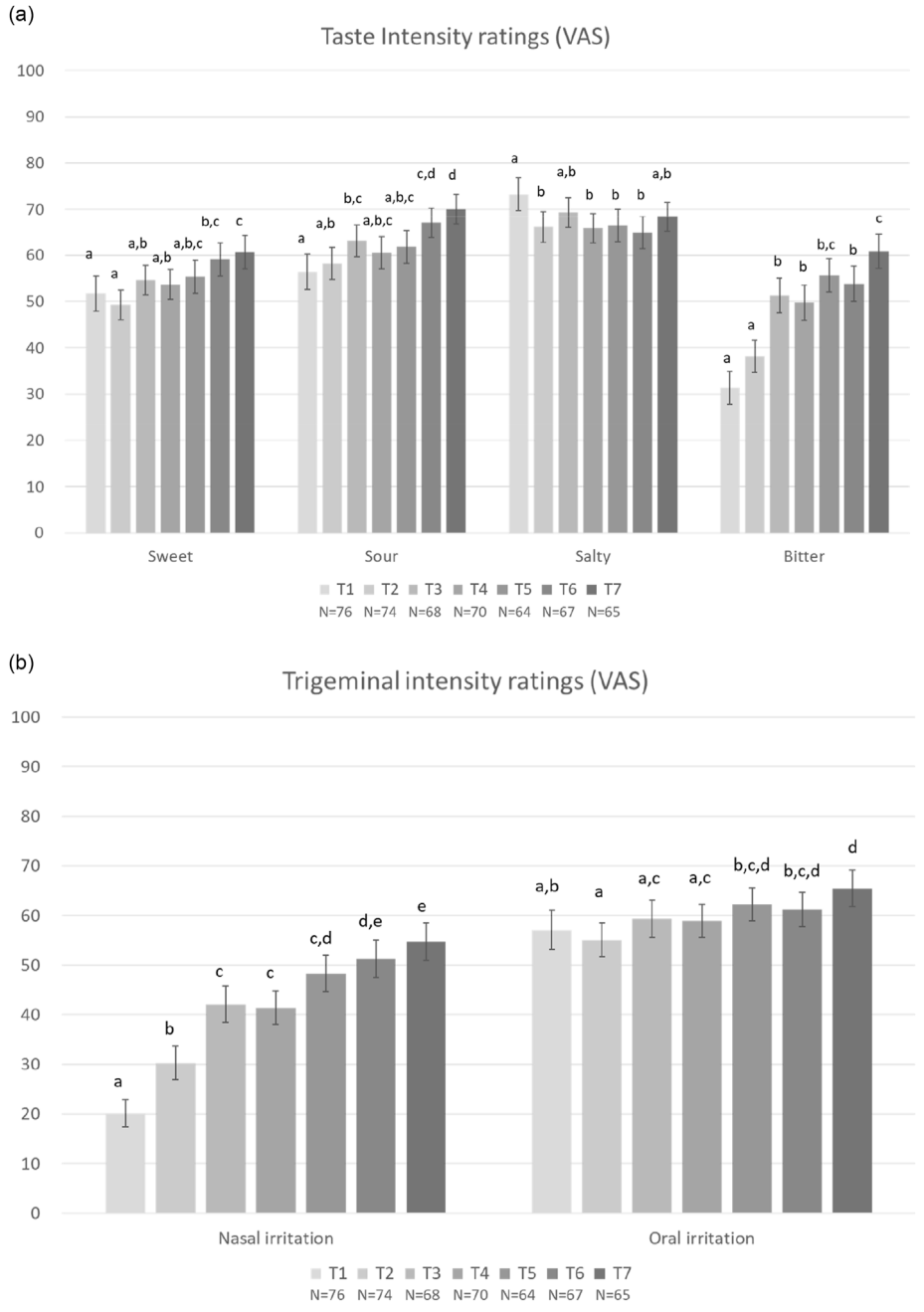

Figure 3. a) Mean taste intensity ratings with standard errors obtained from an at-home self-test at all time points measured on a VAS, 0–100. **b)** Mean nasal and oral irritation ratings with standard errors obtained from an at-home self-test at all time points measured on a VAS, 0–100. Different letters indicate significant different means according to post-hoc testing of linear mixed models. N indicates number of included data points at each time point.

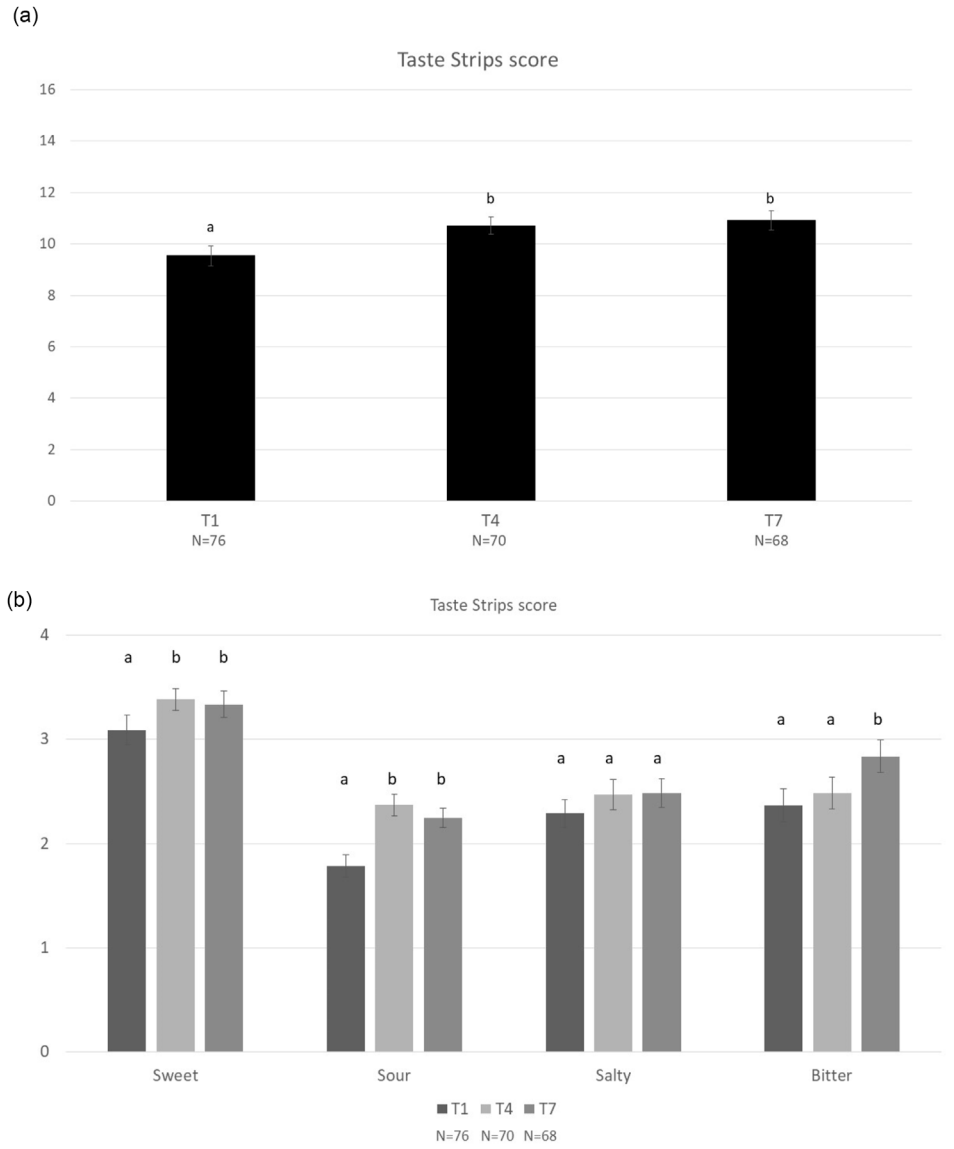

Figure 4. Mean scores with standard errors on Taste Strips over time; **a)** total score, **b)** scores per taste quality. Different letters indicate significant different means according to post-hoc testing of linear mixed models. N indicates number of included data points at each time point.

testing confirm that there is significant improvement in taste functioning over the course of six months, though not to the extent of full recovery.

A closer look at our data also reveals that the number of normogeusic patients remains more or less stable over time, while the frequency of hypogeusia declines. Given that normogeusic patients are more likely to be lost at follow-up (n=7 vs n=1 for hypogeusia, see Figure 5), this may indicate that 20% hypogeusia six months after inclusion is in fact an overestimation and more patients may have recovered.

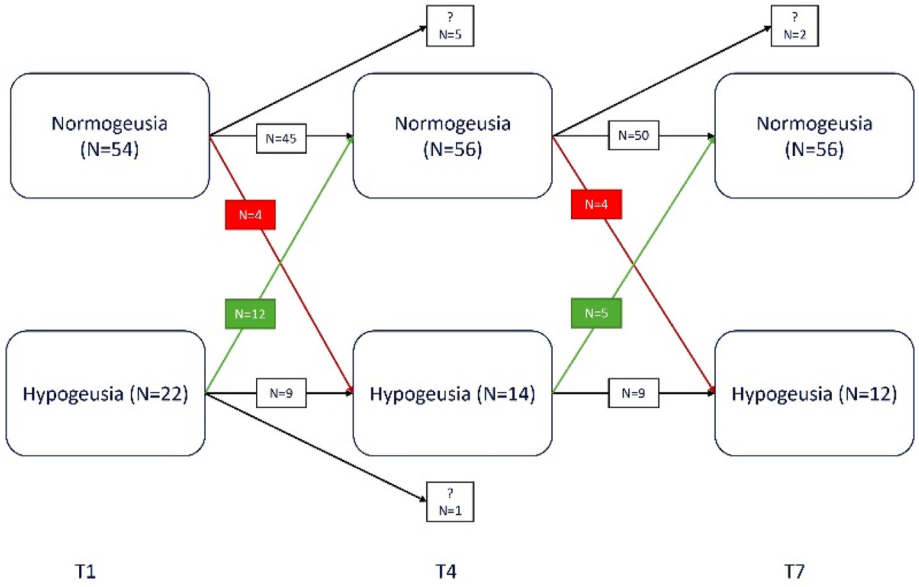

Figure 5. Number of patients with normogeusia (a score of 9 or higher on the Taste Strips) and hypogeusia (a score > 9 on the Taste Strips). 76 patients were included at T1, 70 patients at T4, 68 patients at T7.

Moreover, it is striking that taste functioning fluctuates over time, and patients may shift from normogeusia to hypogeusia, or may recover taste function only to lose it again. Although reinfection did take place during the time of study (for 6 patients), this resulted in a decrease in taste functioning (shifting from normogeusia to hypogeusia) in only one patient. This further highlights the need for extensive longitudinal monitoring, encapsulating subjective and objective, standardized assessments over multiple time points, to provide patients with a perspective regarding the trajectory of their recovery.

Perhaps surprisingly, when assessing the basic taste qualities individually, both the psychophysical test and the home-use test show similar findings, that salty taste did not improve over time, while the other taste qualities did. However, while sweet taste was least affected according to the Taste Strips and sour taste most, this did not align with direct self-assessment results where bitter appeared as least intense. This confirms that individuals are not always capable of correctly assessing their own sense of taste, or could reflect that patients used low bitter household items for the home-use test (e.g. green tea instead of coffee). Alternatively, it may also suggest that there might be complaints that can only be retrieved through self-report. This was for example shown in cancer patients undergoing chemotherapy: while psychophysical testing might show no changes in taste ability during treatment, patients often report complaints such as a metal taste [33]. As each type of gustatory receptor utilizes a distinctive transduction mechanism, it has been hypothesized that COVID-19 might specifically impair the ion channel transduced qualities sour and salty [31], but also that G protein-coupled receptors might be the target of SARS-CoV-2 leading to a specific dysfunction of sweet and bitter taste [34]. Though our results seem to hint towards a specific salt dysfunction, we can neither confirm nor reject these hypotheses. For a more detailed overview of the pathogenesis of COVID-19-related taste dysfunction, see [27,35].

In addition to taste, we also assessed trigeminal perception in the COVORTS study. As no validated objective or psychophysical tests including normative values currently exists for evaluating trigeminal function, we opted to include self-report ratings and direct self-assessment methods, similar to our employed taste measurements. Our results indicate that there is a severe loss of trigeminal sensations at time of inclusion, which gradually improves over time. up to 55% of patients reported to recover to at

least 80% of their pre-illness ratings after six months. This aligns with previous self-reports of severe reduction in trigeminal sensitivity in COVID-19 patients [2,16,17], which recovered in the majority of patients within nine months [16,17]. Additionally, the current study shows distinct differences between nasal and oral irritation ratings, with a greater loss of nasal irritation. This could be analogous to the in general greater severity and frequency of smell loss compared to taste loss after COVID-19, and potentially indicates patients' misperception when self-assessing their chemosensory ability. Although literature is scarce, psychophysical and electrophysiological measurements report only limited or subclinical alterations of the trigeminal system in COVID-19 patients, both during the acute phase and at 1 and 2-year follow-up assessment [17], [19], [20], [21], [22].

Beyond the immediate realm of chemosensory alteration, the sustained loss of smell and taste is associated with a significant reduction in patients' quality of life, including increased depressive symptoms and nutritional challenges [21,22,36,37]. Moreover, long-lasting chemosensory changes align with a broader constellation of persistent symptoms categorized as Post-Acute Sequelae of COVID-19 (PACS, post-COVID) [15,38], with subsequent repercussions on both physical and mental health. Understanding the trajectory of symptom burden and recovery from post-COVID-19 infection holds pivotal implications for policy making, therapeutic interventions, and the coordination of patient care [23]. With this study, we aimed to gather more insights in the course of taste and trigeminal dysfunction and recovery among COVID-19 patients. We show that six months after inclusion, almost 1 in 5 patients with initial smell loss still have decreased taste function, underlining the importance of medical attention for these problems. While corticosteroid treatment seemed promising at first to alleviate smell dysfunction, our recent randomized clinical trial has conclusively demonstrated no beneficial effect [39]. Another recent clinical trial highlighted that early administration of oral ensitrelvir has potential as treatment for smell and taste disorder in patients with COVID-19 [40]. Thus far, the most promising treatment for COVID-19-related olfactory dysfunction is smell training [39,41,42], but for taste or trigeminal dysfunction, no treatments have been investigated so far in COVID-19 patients. Only one pilot study [26] investigated the effect of taste training in a small sample of cancer patients undergoing chemotherapy, and found a clinically relevant improvement on taste functioning. As long-term chemosensory dysfunction can lead to nutritional challenges, also in COVID-19 patients [36,37], it is imperative that post-COVID-19 studies also include nutritional parameters, such as appetite, energy intake and food enjoyment.

Participants for this cohort were included with an infection date between July 2021 and December 2022, a time period in which the alpha variant was declining in presence, while delta and, later, omicron variants of SARS-CoV-2 became dominant in the Netherlands [43]. Studies have shown that the prevalence of chemosensory alterations differs between variants, with a higher frequency in the earlier (alpha and delta) variants, and lower prevalence for omicron [44]. Although our participants were included based on a positive PCR-test, or a positive SARS-CoV-2-antigen self-test, this did not provide information regarding the variant of SARS-CoV-2 infection and we can thus not draw any conclusions related to this.

The COVORTS cohort was not specifically designed to investigate natural course of taste and trigeminal alterations after COVID-19, as patients were included based on having initial smell loss. This means that our findings cannot be generalized to COVID-19 patients in general. However, our results are in line with most other studies describing taste and trigeminal dysfunction after COVID-19 infection.

In addition, in our cohort, significantly more women than men were included. This is in line with several studies and meta-analyses showing that women were significantly more affected by chemosensory dysfunction after a COVID-19 infection [45] and experience higher rates of taste loss than men [11,46]. In addition, it has been shown that COVID-19-associated taste loss peaks in middle age, which corresponds to the mean age of our cohort [11,46].

Conclusion

Our results show that sustained taste and trigeminal loss can be present in a cohort of COVID-19 patients with initial olfactory loss. Although on average there is clinical and subjective improvement over time, taste and trigeminal dysfunction persists in a subset of patients for at least 6 months.

Surprisingly, recovery is fragile, and patients may easily backslide, highlighting the need for longer term follow-up studies. Moreover, as persistent chemosensory changes align with broader post-COVID-19 complaints with subsequent repercussions on nutrition, physical and mental health, understanding the trajectory of this symptom burden and recovery is essential for therapeutic interventions, and providing appropriate care and (nutritional) advice to patients.

Statement of authorship

Conceptualization: SB, EP, DK, WB. Data curation: EP, BvD. Formal analysis: SB. Funding acquisition: SB, DK, WB. Methodology: SB, EP, DK, WB. Project administration: EP, BvD. Supervision: SB. Visualization: SB. Roles/Writing - original draft: SB. Writing - review & editing: EP, BvD, DK, WB.

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Data statement

Once the entire COVORTS study is finished, data will be made publicly available in a repository in line with the FAIR data principles.

Declaration of competing interest

The authors report no conflict of interest.

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