Psychophysical tests reveal impaired olfaction but preserved gustation in COVID-19 patients

To the Editor:

The current coronavirus disease 2019 (COVID-19) pandemic is challenging healthcare systems and societies worldwide in an unprecedented way. Nonspecific symptoms including fever and cough are frequently observed and serve as indicators for home quarantine and molecular testing by polymerase chain reaction (PCR).[1] Interestingly, sudden dysfunctions in smell and taste have been described, first anecdotally, and then in retrospective reports.[2,3] These pathognomonic symptoms have led to the consensus that olfactory and gustatory defects should equally be regarded as highly suspicious for severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection, even in the absence of other symptoms.[4] Because of home quarantine and the short duration of chemosensitive disorders, reports so far have mostly been retrospective. Psychophysical tests of olfactory and gustatory function have mainly been performed in hospitalized patients only.[5]

Here, we report on a controlled prospective trial enrolling COVID-19 patients from southeast Germany to objectively assess complaints of smell and taste loss using reliable and validated psychophysical tests. Respiratory samples of all subjects were tested positive for the presence of SARS-CoV-2 RNA by reverse-transcription quantitative real-time PCR (RT-qPCR) in the diagnostic unit of our tertiary care hospital. Patients under home quarantine were contacted directly after a positive result had been reported. Following informed consent, participants were sent both a 4-item smell test ("Pocket Smell Test"; Sensonics International, Haddon Heights, NJ) and a 4-item taste test ("Taste Strips"; taste qualities of sweet, sour, salty, and bitter; Burghart Messtechnik, Wedel, Germany). A combined online manual and questionnaire ensured correct self-administration and queried subjective smell and taste. In the case of a suspected pregnancy, the bitter strip was skipped to prevent possible adverse effects through quinine hydrochloride. Hyposmia and hypogeusia respectively were defined as $\geq$1 incorrect answer. Statistical analysis was done by Fisher's exact test (SPSS, version 26.0; IBM Corp. in Armonk, NY). Values of $p < 0.05$ were regarded as significant.

A total of 41 (median age 37 years, 68% female, 32% male) patients answered the online questionnaire and self-administered the olfactory and gustatory tests in median 5 days after the positive SARS-CoV-2 PCR result and 13 days after the first symptoms. As shown in Table 1, 25 (61%) and 18 (44%) patients described a current hyposmia and hypogeusia, respectively. This is in line with previous reports.[6] There was no case of isolated hypogeusia whereas 28% of patients reported isolated hyposmia. The control group consisted of 30 patients (median age 33 years, 73% female, 27% male) who tested negative for immunoglobulin G (IgG) antibodies against SARS-CoV-2. In comparison, the subjective loss in smell and taste occurred significantly more often in COVID-19 patients (61% vs 10%, $p < 0.0001$; 44% vs 10%, $p = 0.0003$; see Table 1). SARS-CoV-2 infection was significantly associated with a positive test for hyposmia but not hypogeusia (54% vs 27%, $p = 0.03$; 20% vs 10%, $p = 0.34$; see Table 1). In COVID-19 patients, the subjective loss in smell was confirmed by a hyposmic test result in 72%, whereas the subjective loss in taste was confirmed by a hypogeusic test in only 33%. Within the group of SARS-CoV-2–positive patients, there was a tight dependence between subjective ratings of smell dysfunction and hyposmia in the olfactory test (44%, $p = 0.005$; see Table 2); this was not the case for subjective ratings of taste function and gustatory testing (15%, $p = 0.11$; see Table 2).

In conclusion, these results show that a high proportion of COVID-19 patients describe a loss of taste. However, in contrast with prior publications, standardized functional testing of the gustatory modalities of sweet, sour, salty, and bitter did not reveal a bona fide hypogeusia. The subjectively altered taste is most likely caused by impaired retronasal olfaction.[4] To the best of our knowledge, this controlled prospective trial shows for the first time that COVID-19 is tightly associated with olfactory loss but not with gustatory dysfunction when tested psychophysically. Our results may be limited by the relatively small number of study participants. Nevertheless, Moein et al.[5] recently demonstrated that 98% of 60 hospitalized COVID-19 patients were hyposmic. It is therefore possible that hyposmia directly relates to SARS-CoV-2 infection severity. Further research is needed to confirm these findings in a larger cohort of COVID-19 patients and to better understand how SARS-CoV-2 impacts the olfactory pathway.

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TABLE 1. Self-reported chemosensitive function/results of psychophysical tests vs SARS-CoV-2 positive/negative*

Parameter	SARS-CoV-2 PCR positive n (%)	SARS-CoV-2 IgG antibodies negative n (%)	*p*
Self-reported olfactory function			
Decreased	25 (61%)	3 (10%)	<0.0001
Normal	16 (39%)	27 (90%)	
Self-reported gustatory function			
Decreased	18 (44%)	3 (10%)	0.003
Normal	23 (56%)	27 (90%)	
Smell test			
Hyposmia	22 (54%)	8 (27%)	0.03
Normosmia	19 (46%)	22 (73%)	
Taste test			
Hypogeusia	8 (20%)	3 (10%)	0.34
Normogeusia	33 (80%)	27 (90%)	

*Data shown are absolute values and relative values as column percentages, respectively.
IgG = immunoglobulin G; PCR = polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome-coronavirus-2.

TABLE 2. Self-reported chemosensitive function vs results of psychophysical tests*

Parameter	SARS-CoV-2 PCR positive n (%)		SARS-CoV-2 IgG antibodies negative n (%)	
	Decreased	Normal	Decreased	Normal
Self-reported olfactory function				
Smell test				
Hyposmia	18 (72)	4 (25)	2 (67)	6 (22)
Normosmia	7 (28)	12 (75)[a]	1 (33)	21 (78)
Self-reported gustatory function				
Taste test				
Hypogeusia	6 (33)	2 (9)	2 (67)	1 (4)
Normogeusia	12 (67)	21 (91)[b]	1 (33)	26 (96)

*Data shown are absolute values and relative values as column percentages, respectively.
[a]$p = 0.005$.
[b]$p = 0.11$.
IgG = immunoglobulin G; PCR = polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome-coronavirus-2.

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