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ORIGINAL RESEARCH

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The effects of comorbidities on the change of taste and smell in COVID-19 patients

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Abstract

Background: Sudden chemosensory changes were considered an early predictor of COVID-19. Here, the effects of comorbidities on changes in taste and smell in COVID-19 patients were investigated based on a worldwide study.

Methods: Data analyzed here were collected from the Global Consortium for Chemosensory Research (GCCR) core questionnaire, including questions regarding preexisting disease conditions. Overall, the final sample of 12,438 participants who were diagnosed with COVID-19 included patients with preexisting conditions. Mixed linear regression models were used to test our hypothesis, and the *p*-value of interaction was examined.

Results: A total of 61,067 participants completed the GCCR questionnaire, including 16,016 participants had preexisting diseases. The multivariate regression analysis showed that individuals with high blood pressure, lung disease, or sinus problems, or neurological diseases exhibited worse self-reported smell loss ($p < .05$), but no apparent significant differences in the smell or taste recovery. COVID-19 patients with seasonal allergy/hay fever lost their olfactory ability more than patients who did not have it (with 11.90 [9.67, 14.13] vs. without 6.97 [6.04, 7.91], $p < .0001$). The taste ability, smell loss and taste loss after COVID-19 recovery also decreased in the COVID-19 patients with seasonal allergy/hay fever ($p < .001$). Preexisting condition of diabetes did not worsen to chemosensory disorder but also had no obvious impact on the chemosensory recovery after acute infection. Preexisting diseases also affected the type of smell change in the COVID-19 patients with seasonal allergy/hay fever or sinus problems ($p < .05$).

Conclusions: COVID-19 patients with high blood pressure, lung disease, or sinus problems, or neurological diseases exhibited worse self-reported smell loss, but no

differences in the smell or taste recovery. COVID-19 patients with seasonal allergy/hay fever had greater loss of smell and taste, poorer smell and taste recovery.

Level of Evidence: 4

KEYWORDS
comorbidity, COVID-19, smell, taste

1 | INTRODUCTION

Globally, the total number of disease cases caused by contracting SARS-CoV-2, that is, COVID-19, has topped over 624 million. The number of deaths has reached over 6.57 million so far, as of October 15, 2022, according to the Johns Hopkins University coronavirus resource center (coronavirus.jhu.edu/map.html).[1] Among fatal cases, an estimated 84.1% had one or more comorbidities. COVID-19 patients with preexisting diseases had poor outcomes that extra precautions had to be taken in treating such patients.[2,3] COVID-19 patients with some specific preexisting comorbidities, such as heart disease, high blood pressure, chronic obstructive pulmonary disease, asthma, allergic rhinitis, and so on, were especially vulnerable.[4,5]

Chronic rhinosinusitis (CRS), asthma, seasonal allergy, and allergic rhinitis can induce inflammation in the olfactory mucosa and cause olfactory dysfunction.[6] SARS-CoV-2 and preexisting comorbidities interact with the immune system and the comorbidities-related target organs (e.g., olfactory mucosa), which induce dysfunctional immune responses along with the progress of the disease.[7] Studies have shown a correlation between olfactory function and immune function.[8]

Numerous studies indicated that respiratory inflammation affects the perception of smell, and poor olfactory function is common in patients with respiratory inflammatory diseases, such as CRS.[9] Olfactory dysfunction occurs in approximately 10%–88% of the patients with allergic rhinitis.[10]

The influence of chronic diseases on chemosensory function seems to be significant. If COVID-19 patients also suffered from one of those comorbidities, their olfactory function and/or gustatory function might have been already affected by the comorbidities before they were infected with SARS-CoV-2. Therefore, they may not be able to effectively detect chemosensory dysfunction due to COVID-19. It is worth exploring the influences of comorbidities on the perceived changes in the taste and smell in the COVID-19 patients. Few studies have reported the influences of COVID-19 on patients with preexisting diseases,[11,12] let alone the influences of preexisting conditions on the changes of their chemosensory function.

Exploring the effects of preexisting disease on the changes of taste and smell in the COVID-19 patients may help us reduce the global spread of COVID-19 by detecting it as early as possible. We hypothesize that COVID-19 patients with respiratory inflammatory-related preexisting disease are susceptible to smell or taste disorder and require longer to recover the olfactory function. In contrast, the COVID-19 patients without respiratory-related preexisting conditions are less vulnerable to smell or taste disorders and recover faster. In this study, we propose to mine the Global Consortium for Chemosensory Research (GCCR) database to capture the influences of preexisting diseases on the changes of taste and smell due to COVID-19. This database was analyzed and used so far to determine the occurrence of COVID-19 induced chemosensory dysfunction,[13,14] but it was not used to determine the influence of preexisting conditions on chemosensory dysfunction.

2 | METHODS

Data from a preregistered, online survey study, which was created under the guidance of the Global Consortium for Chemosensory Research (GCCR), was used. GCCR was founded by a diverse group of chemosensory scientists, clinicians, patient advocates, and community partners in March 2020 following the outbreak of COVID-19, which caused chemosensory dysfunction (https://gcchemosensr.org).[14]

The present study is registered as one of the OSF (Open Science Framework) of GCCR, and the information and the research plan in detail are available on the website of OSF (https://osf.io/ax3p5/). The Office of Research Protections at The Pennsylvania State University

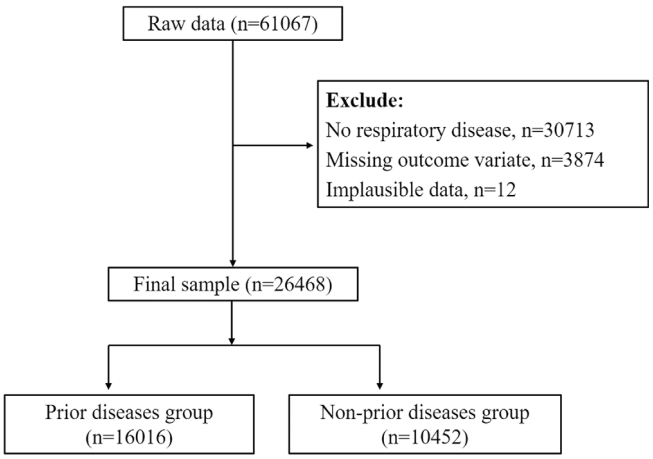

FIGURE 1 Flow diagram showing the data collection process. Missing outcome variates refers to the absence of any listed prior conditions in the questionnaire including the choice of "None," and parts of the survey respondents did not state their chemosensory ability before, during, and after COVID-19. Implausible data means all the self-reported ratings for smell, taste, chemesthesis ability, and nasal obstruction before and during illness are 0 or 100

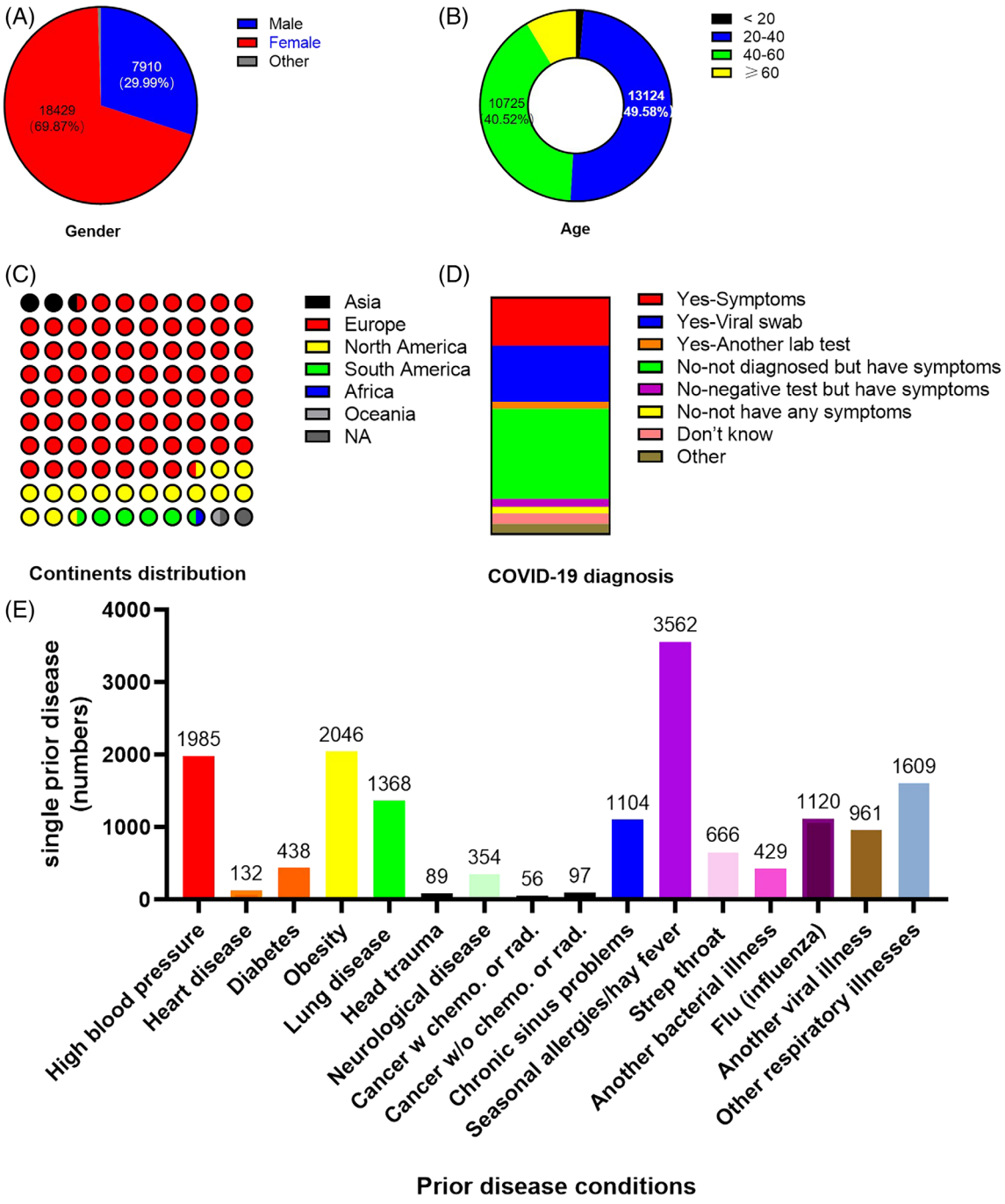

FIGURE 2 The characteristics of Global Consortium for Chemosensory Research core questionnaire participants ($n = 26{,}468$). Gender (A), age (B), continents distribution(C), COVID-19 diagnosis (D), prior disease conditions (E). "Cancer w chemo. or rad." means "cancer that required chemotherapy or radial therapy", "Cancer w/o chemo. or rad." means "cancer that did not require chemotherapy or radial therapy"

in the United States and The Ethics Committee from Second affiliated hospital at Xi'an Jiaotong University both approved this study, the approval numbers were STUDY 00014904 and 2,020,075 from United States and China, respectively. All the protocol complies with the revised Declaration of Helsinki. Data reported here are part of the data collected in the GCCR001 survey's core questionnaire (https://gcchemosensr.org).[14]

All the participants signed the informed consent form before entering the formal survey. The participants self-evaluated their ability of taste, smell, and chemesthesis before and during COVID-19 and their preexisting disease conditions during the 6 months before they got infected with COVID-19. This crowdsourced online survey listed the following choices of preexisting disease conditions: high blood pressure, heart disease, diabetes, obesity, lung disease (asthma or chronic obstructive pulmonary disease), neurological disease, cancer that required chemotherapy or radial therapy, cancer that did not require chemotherapy or radial therapy, chronic sinus problems, and seasonal allergies/hay fever, and so on. All languages were extracted.

Baseline characteristics of participants and the change of smell and taste were presented as means with SDs for continuous variables and frequencies with percentages for categorical variables. Stratified mixed linear regression models were used to test our hypothesis, and the stratified factors were prior diseases (high blood pressure, seasonal allergy/hay fever, lung disease, sinus, diabetes, neurological disease). The regression coefficient of each layer and the *p*-value of interaction were examined. All the potential covariates, such as age (year), gender (male and female), the continents, smoking status, and the conditions of comorbidities except for the stratified factor in that model, were adjusted in the stratified mixed linear regression models.

3 | RESULTS

3.1 | The characteristics of GCCR core questionnaire participants

A total of 61,067 participants completed the GCCR questionnaire. There were, however, invalid data that were excluded for the following reasons: "no respiratory disease ($n = 30{,}713$)," "missing outcome variable ($n = 3874$)," and "the content does not meet the requirements ($n = 12$)." The final data used in this study reached at 26468. Of those included in the final sample, 16,016 participants had preexisting diseases, and 10,452 did not have any preexisting illness (Figure 1). Of the 26,468 samples, 18,429 (69.87%) were women (Figure 2), and other demographic data are summarized in Table 1. In the group of 16,016 participants who had preexisting diseases (Figure 2E). Due to the low numbers of a patient with other preexisting diseases, the following conditions were not analyzed in this study: heart disease (heart attack or stroke), head trauma, cancer that required chemotherapy or radiation, cancer that did not need chemotherapy or radiation, strep throat, and another bacterial illness. The median timepoint following infection was 27 days.

3.2 | COVID-19 patients with prior diseases had greater smell and taste loss

The degrees of smell/taste loss and the degrees of smell/taste recovery were compared (Table 2), which indicated that COVID-19 patients with high blood pressure, diabetes, lung diabetes, neurological disease, or chronic sinus problems, who had lower smell/taste impairment (all *p* value <.05). Except for the changes in the smell sense, which had no significant differences between COVID-19 patients with seasonal allergies/hay fever and the COVID-19 patients without seasonal allergies/hay fever (80.23 ± 27.73 vs. 79.81 ± 29.28, $p > .05$). The analysis results did not accord with our hypothesis that the degree of smell loss (during) would be more in the COVID-19 group with preexisting diseases.

Regarding the multiple factors that may affect the chemosensory functions in patients, we performed a multivariate regression analysis by adjusting age, gender, and continent, in addition to with/without preexisting diseases. As Table 3 listed that olfactory sense was lost more in the group of COVID-19 patients with high blood pressure (12.66 [9.69, 15.63] vs. 7.25[6.34, 8.15], $p = .001$), same taste loss

TABLE 1 Baseline characteristics of participants ($n = 26{,}468$)

Variable	*n*	%
Gender		
Female	18,429	69.87
Male	7910	29.99
Age, year		
<20	350	1.32
20–40	13,124	49.58
40–60	10,725	40.52
≥60	2269	8.57
Continent		
Asia	724	2.83
Europe	19,820	77.41
North America	3942	13.64
South America	1330	5.19
Africa	171	0.67
Oceania	66	0.26
COVID diagnosis		
Yes—symptoms	5346	20.20
Yes—viral swab	6288	23.76
Yes—another lab test	804	3.04
No—not diagnosed but have symptoms	10,098	38.15
No—negative test but have symptoms	917	3.46
No—not have any symptoms	738	2.79
Do not know	1191	4.50
Other	1086	4.10
Prior condition		
High blood pressure	1985	8.66
Heart disease (heart attack or stroke)	132	0.58
Diabetes (high blood sugar)	438	1.91
Obesity	2046	8.93
Lung disease (asthma/COPD)	1368	5.97
Head trauma	89	0.39
Neurological disease	354	1.54
Cancer that required chemotherapy or radiation	56	0.24
Cancer that NOT required chemotherapy or radiation	97	0.42
Chronic sinus problems	1104	4.82
Seasonal allergies/hay fever	3562	15.55
Strep throat (Streptococcal bacteria)	666	2.52
Another bacterial illness	429	1.62
Flu (influenza)	1120	4.23
Another viral illness	961	3.63
Other respiratory illnesses	1609	6.08

TABLE 2 The change degree of smell and taste between prior disease and nonprior disease in COVID-19 patients

Prior disease	The change degree of loss/recovery	Nonprior disease patients	Prior disease patients	*t*	*p*-value
High blood pressure	Smell loss	80.36 ± 28.51	73.80 ± 34.62	6.01	<.001
	Smell recovery	47.90 ± 38.41	47.38 ± 39.39	2.19	.029
	Taste loss	68.98 ± 31.95	66.23 ± 34.78	3.10	.002
	Taste recovery	40.63 ± 39.83	37.74 ± 34.85	1.92	.055
Diabetes	Smell loss	80.10 ± 28.83	67.34 ± 37.59	5.90	<.001
	Smell recovery	47.90 ± 38.41	33.17 ± 37.89	4.64	<.001
	Taste loss	69.76 ± 32.12	66.41 ± 35.20	1.40	.162
	Taste recovery	40.53 ± 36.35	34.17 ± 33.77	2.13	.033
Lung disease	Smell loss	80.22 ± 28.76	73.84 ± 33.21	4.42	<.001
	Smell recovery	47.89 ± 38.41	43.14 ± 39.76	2.54	.011
	Taste loss	69.88 ± 32.06	66.46 ± 34.16	2.45	.015
	Taste recovery	40.51 ± 36.24	38.64 ± 37.64	1.08	.282
Neurological disease	Smell loss	79.98 ± 28.93	71.55 ± 36.85	2.64	.009
	Smell recovery	47.67 ± 38.45	45.06 ± 42.15	0.70	.481
	Taste loss	69.80 ± 32.08	61.78 ± 38.40	2.42	.017
	Taste recovery	40.43 ± 36.22	38.55 ± 42.65	0.46	.643
Chronic sinus problems	Smell loss	80.22 ± 28.76	71.57 ± 34.37	5.05	<.001
	Smell recovery	47.88 ± 38.44	41.90 ± 39.38	2.80	.005
	Taste loss	69.93 ± 32.05	64.06 ± 34.69	3.37	<.001
	Taste recovery	40.55 ± 36.35	36.97 ± 35.24	1.77	.077
Seasonal allergies	Smell loss	79.81 ± 29.28	80.23 ± 27.73	0.54	.591
	Smell recovery	46.25 ± 38.50	56.32 ± 37.33	8.30	<.001
	Taste loss	69.52 ± 32.39	70.79 ± 30.93	1.47	.142
	Taste recovery	39.14 ± 36.22	48.41 ± 35.83	8.14	<.001

results could be seen in the COVID-19 patients with high blood pressure (9.52 [6.38, 12.66], $p = .026$), and taste loss in the COVID-19 patients without high blood pressure were lower than whom (5.80 [4.85, 6.76]). The results indicated that COVID-19 patients without high blood pressure had negative effects on the chemosensory function.

Meanwhile, the recovery of smell and taste also were investigated and showed no apparent statistically significant differences in the smell or taste recovery between the COVID-19 patients with and without high blood pressure. Same smell loss and taste loss were seen in COVID-19 patients with lung disease, sinus problems, or neurological diseases during the infection of SARS-CoV-2 (Table 3), whereas which did not have any influence on the smell or taste recovery after COVID-19 recovery ($p > .05$).

As we know, olfactory dysfunction is frequently experienced by patients with allergic rhinitis, and decreases quality of life. In this study, it can be observed same results from Table 3, the COVID-19 patients with seasonal allergy/hay fever lost their olfactory ability more than patients who did not have it (smell: with seasonal allergy/hay fever, 11.90 [9.67, 14.13]; without seasonal allergy/hay fever 6.97 [6.04, 7.91], $p < .0001$). It is worth noting that the taste ability also decreased in the COVID-19 patients with seasonal allergy/hay fever (with: 13.66 [10.66, 16.66] vs. without: 7.67 [6.46, 8.88], $p < .0001$). Meanwhile, the smell loss and taste loss after COVID-19 recovery were dramatically decreased in the patients with seasonal allergy/hay fever (all the *p*-values of interaction <.001). Interestingly, preexisting condition of diabetes did not worsen to chemosensory disorder but also had no obvious impact on the chemosensory recovery after acute infection of SARS-CoV-2. For a clear display of the prior diseases on the change of chemosensory function in COVID-19 patients, all the impacts of prior diseases were summarized in Table 4.

3.3 | The effect of preexisting diseases on the type of smell change in the COVID-19 patients

Participants were asked to indicate the type(s) of smell dysfunction they experienced, which are "can't smell/less sensitive than before," "changes in quality," "smell something that doesn't exist," "sometimes good but sometimes bad (fluctuates)." We analyzed the odds ratio of smell change type between COVID-19 patients with/without the preexisting disease. The results indicated no significant differences in the type of smell changes in COVID-19 patients with high blood pressure, diabetes, or neurological illness ($p > .05$; Table 5). However, preexisting seasonal allergies significantly affected COVID-19-induced smell dysfunction. The dysfunction type of "can't smell/less sensitive than before" had an odds ratio of 2.94 in the COVID-19 patients with seasonal allergies, and the

TABLE 3 Regression coefficient (β) for degree of chemosensory disorder and recovery by COVID-19 participants with or without six prior diseases

		β (95% CI)			
Prior diseases[a]	***n***	**Smell loss**	**Smell loss after recovery**	**Taste loss**	**Taste loss after recovery**
High blood pressure	1985	12.66 (9.69, 15.63)	10.89 (7.00, 14.78)	9.52 (6.38, 12.66)	6.34 (2.76, 9.92)
Nonhigh blood pressure	20,934	7.25 (6.34, 8.15)	8.27 (7.10, 9.45)	5.80 (4.85, 6.76)	7.06 (5.97, 8.14)
p-value of interaction		.001	.204	.026	.704
Seasonal allergy/hay fever	3562	11.90 (9.67, 14.13)	13.66 (10.66, 16.66)	10.60 (8.24, 12.96)	11.93 (9.16, 14.69)
Nonseasonal allergy/hay fever	19,343	6.97 (6.04, 7.91)	7.67 (6.46, 8.88)	5.34 (4.35, 6.33)	6.23 (5.11, 7.35)
p-value of interaction		<.001	<.001	<.001	<.001
Lung disease	1368	11.81 (8.25, 15.37)	11.41 (6.74, 16.07)	10.00 (6.25, 13.75)	8.71 (4.42, 12.99)
Nonlung disease	21,551	7.48 (6.58, 8.37)	8.34 (7.18, 9.50)	5.90 (4.96, 6.85)	6.93 (5.86, 8.00)
p-value of interaction		.020	.209	.037	.428
Sinus	1104	13.35 (9.31, 17.40)	7.64 (2.34, 12.95)	11.79 (7.49, 16.09)	6.95 (2.03, 11.86)
Nonsinus	21,804	7.46 (6.57, 8.35)	8.54 (7.39, 9.70)	5.88 (4.94, 6.82)	7.03 (5.97, 8.09)
p-value of interaction		.005	.745	.008	.975
Diabetes	438	9.25 (3.00, 15.50)	1.58 (−6.59, 9.75)	10.47 (3.84, 17.10)	3.10 (−4.45, 10.66)
Nondiabetes	22,481	7.65 (6.78, 8.53)	8.60 (7.47, 9.74)	6.03 (5.10, 6.95)	7.07 (6.02, 8.12)
p-value of interaction		.619	.095	.192	.307
Neurological disease	354	17.46 (10.42, 24.50)	16.87 (7.52, 26.22)	14.68 (7.27, 22.10)	10.06 (1.47, 1 8.64)
Nonneurological disease	22,561	7.57 (6.70, 8.45)	8.39 (7.25, 9.53)	6.00 (5.08, 6.93)	6.98 (5.93, 8.03)
p-value of interaction		.006	.078	.023	.486

Note: CI, confidence interval.
[a]The model was adjusted for age, gender, continents, smoking, and other prior diseases.

TABLE 4 Summary of the prior diseases on the chemosensory change in COVID-19 patients

	Smell		**Taste**	
Type of preexisting conditions	**During infection**	**Recovery from COVID-19**	**During infection**	**Recovery from COVID-19**
High blood pressure	X	O	X	O
Seasonal allergy/hay fever	X	X	X	X
Lung disease	X	O	X	O
Sinus problems	X	O	X	O
Diabetes	O	O	O	O
Neurological diseases	X	O	X	O

Abbreviations: O, no influences; X, worsens.

confidence interval was 2.47–3.51. In contrast, the odds ratio in COVID-19 patients without seasonal allergies was 1.86, and the confidence interval was 1.73–2.01 ($p < .001$, Table 5). COVID-19 patients with chronic sinus problems were also at higher risk for COVID-19 than the COVID-19 patients without chronic sinus problems (with a chronic sinus problem, odds ratio [OR]: 2.77 [2.08, 3.68], without chronic sinus problem, OR: 1.95 [1.82, 2.10], $p = .020$).

4 | DISCUSSION

The present analyses revealed the underlying effects of preexisting diseases on the change of chemosensory function in the COVID-19 patients. The patients had worse taste and smell if they had high blood pressure, lung disease (asthma/COPD), neurological disease, chronic sinus problems, or seasonal allergies/hay fever when SARS-CoV-2 infected them. However, diabetes did not have an influence on COVID-19 induced chemosensory dysfunction.

Studies have found many risks factors that affect the severity of the symptoms of COVID-19, such as high blood pressure, diabetes, chronic lung disease, and so on.[15] High blood pressure was more frequently found in COVID-19 patients with severe symptoms than patients with mild to moderate levels of symptoms.[16] COVID-19 patients with diabetes had a higher risk of hospitalization, critical illness, death, and a higher rate of ICU admissions.[17,18] Lung disease, such as COPD, is not a predisposing factor for SARS-CoV-2 infection.

TABLE 5 Odds ratio (OR) of smell change between prior and nonprior disease in the COVID-19 patients

		OR (nonprior disease)	OR (prior disease)	Common OR	*p* value
High blood pressure	Cannot smell/less sensitive than before	1.94 (1.80, 2.09)	2.41 (1.95, 2.97)	1.99 (1.86, 2.13)	.059
	Change in quality	0.82 (0.75, 0.89)	0.88 (0.68, 1.16)	0.82 (0.76, 0.89)	.571
	Smell sth dosen't exist	0.82 (0.75, 0.89)	0.86 (0.64, 1.15)	0.90 (0.82, 0.98)	.736
	Sometimes good sometimes bad	0.81 (0.75, 0.88)	0.74 (0.58, 0.95)	0.81 (0.75, 0.87)	.490
Seasonal allergies	Cannot smell/less sensitive than before	1.86 (1.73, 2.01)	2.94 (2.47, 3.51)	2.01 (1.87, 2.15)	<.0001
	Change in quality	0.83 (0.76, 0.91)	0.79 (0.65, 0.95)	0.82 (0.76, 0.89)	.588
	Smell sth dosen't exist	0.95 (0.86, 1.05)	0.68 (0.55, 0.85)	0.90 (0.82, 0.98)	.007
	Sometimes good sometimes bad	0.84 (0.77, 0.91)	0.67 (0.56, 0.80)	0.81 (0.75, 0.87)	.023
Lung disease	Cannot smell/less sensitive than before	1.98 (1.84, 2.12)	2.39 (1.87, 3.05)	2.01 (1.87, 2.15)	.148
	Change in quality	0.82 (0.76, 0.90)	0.80 (0.60, 1.07)	0.82 (0.76, 0.89)	.868
	Smell sth dosen't exist	0.91 (0.83, 1.00)	0.78 (0.57, 1.07)	0.90 (0.82, 0.98)	.350
	Sometimes good sometimes bad	0.83 (0.76, 0.89)	0.61 (0.46, 0.80)	0.81 (0.75, 0.87)	.039
Chronic sinus problems	Cannot smell/less sensitive than before	1.95 (1.82, 2.10)	2.77 (2.08, 3.68)	2.00 (1.86, 2.14)	.020
	Change in quality	0.82 (0.75, 0.89)	0.92 (0.65, 1.31)	0.82 (0.76, 0.89)	.504
	Smell sth dosen't exist	0.90 (0.82, 0.99)	0.90 (0.62, 1.29)	0.90 (0.83, 0.99)	.974
	Sometimes good sometimes bad	0.82 (0.76, 0.88)	0.71 (0.52, 0.96)	0.81 (0.75, 0.87)	.359
Diabetes	Cannot smell/less sensitive than before	2.01 (1.87, 2.16)	2.15 (1.42, 3.24)	2.01 (1.88, 2.16)	.758
	Change in quality	0.82 (0.75, 0.89)	0.93 (0.57, 1.54)	0.82 (0.75, 0.89)	.600
	Smell sth dosen't exist	0.90 (0.82, 0.98)	0.77 (0.43, 1.38)	0.90 (0.82, 0.98)	.609
	Sometimes good sometimes bad	0.81 (0.75, 0.87)	0.73 (0.46, 1.17)	0.80 (0.75, 0.87)	.690
Neurological disease	Cannot smell/less sensitive than before	2.00 (1.86, 2.14)	2.60 (1.61, 4.19)	2.01 (1.87, 2.15)	.282
	Change in quality	0.81 (0.75, 0.88)	1.20 (0.71, 2.02)	0.82 (0.76, 0.89)	.148
	Smell sth dosen't exist	0.81 (0.75, 0.88)	1.03 (0.58, 1.84)	0.90 (0.82, 0.98)	.627
	Sometimes good sometimes bad	0.81 (0.75, 0.87)	0.62 (0.36, 1.06)	0.80 (0.75, 0.87)	.328

Once the patient was infected with SARS-CoV-2, the risk of hospitalization, ICU admission, or receiving invasive mechanical ventilation would be higher significantly elevated. Suppose we can identify the SARS-CoV-2 infected patients with comorbidities early. In that case, the patients can get treatments early, which may reduce the possibility that their conditions will turn into serious situations, reducing hospitalization and ICU admissions, thus reducing the number of deaths. It is crucial to identify the COVID-19 patients at an early stage after the infection to the virus so that it is possible to treat them early.

Sudden changes in smell and taste were found as the initial signs of COVID-19.[19,20] Quickly identifying the patients with sudden olfactory or gustatory dysfunction could be a more optimal protection strategy to reduce the spread of the COVID-19 pandemic. The dramatic increase of incidences of sudden smell and taste changes in the general population may be used as a valuable and minimally invasive indicator of the spread of SARS-CoV-2.[13,20–22] Since many patients with COVID-19 have underlying diseases, using changes in smell and taste as an early indicator of COVID-19 infection may be affected by the presence of underlying conditions. This may affect early screening of COVID-19 patients. To reduce severe cases and mortality, we need to pay more attention to changes in smell and taste in COVID-19 patients with underlying diseases. Considering that there were no notable differences in the recovery of smell or taste between the COVID-19 patients with or without sinus problems, it could be either that the ability of smell/taste recovered to the level of premorbid or could not be recovered to the same level in both.

Here, we confirmed that COVID-19 patients with high blood pressure had even more significant smell loss (16.44) than patients without high blood pressure (9.11), which was shown in Table 3. Similar results were found in the patients with seasonal allergy/hay fever, lung diseases, chronic sinus problems, and neurological disorders. In COVID-19 patients with these diseases, sudden smell and taste change may be perceived in an earlier stage than those of patients with diabetes because there was no difference in the ability of smell or taste in COVID-19 patients with or without diabetes (Table 3). Diabetes is a common preexisting disease in COVID-19 patients[23] and is considered to be a risk factor of fetal and severe COVID-19 cases.[24] Therefore, it is crucial for diabetes patients to pay attention to early and subtle chemosensory changes.

It is worth noting that some literature suggests that some prior diseases, such as CRS, may even be protective against COVID-19.[25,26] However, those papers were related to susceptibility of SARS-CoV-2 and did not explore the degree of smell and taste disorder and recovery by COVID-19 in sinus and nonsinus participants. In our paper, we aimed to explore the effects of comorbidities on the change of taste and smell in COVID-19 patients.

A strength of our study is that the data was collected worldwide. All the data were compiled by the global study translated into more than 30 languages by the members of the Global Consortium for Chemosensory Research (GCCR) (see Section 2). The results published by GCCR showed that the onset of changes in smell and taste could be used as an early indicator for local COVID-19 outbreaks.[13,14,20] This is the first study to show the effects of most common comorbidities on the change of taste and smell in the COVID-19 patients worldwide except the obesity reported on *Rhinology*,[27] which may raise the awareness of chemosensory fluctuation from COVID-19 patients with comorbidities and health care providers. Although surveys using self-report are not as precise as objective olfactory or gustatory testing in laboratory circumstances, it is safe, efficient, and effective in confirming early, new disease indicators for an emerging public health event with a global context.[28]

From another perspective, a limitation of our study is that the chemosensory dysfunction was not well-documented with olfactory/gustatory validation. Self-reported smell and taste evaluation by questionnaires are considered less reliable than objective tests.[29] Meanwhile, published paper indicated that self-report smell evaluation consistently underestimate true smell loss in COVID-19 patients.[30] Subjective methodologies were easy and costless the expedient for chemosensory evaluation in COVID-19 pandemic. Base on those reasons, we speculated that COVID-19 patients with prior diseases may have much more serious degree of smell and taste loss than what we reported in this paper. If possible, we strongly recommend that the possibly infected patients go to medical institutions for smell and taste tests.

5 | CONCLUSIONS

COVID-19 patients with high blood pressure, lung disease, or sinus problems, or neurological diseases exhibited worse self-reported smell loss, but no differences in the smell or taste recovery. COVID-19 patients with seasonal allergy/hay fever had greater loss of smell and taste, poorer smell and taste recovery. Exploring the effects of preexisting conditions on the change of taste and smell in COVID-19 patients may help us understand a possible involvement of comorbidities in COVID-19 patients who lost the sense of smell and/or taste. This raises the concern of chemosensory dysfunction and commodity with COVID-19.

AUTHOR CONTRIBUTIONS

Conception and design: Jingguo Chen and Baibing Mi. Acquisition of data Jingguo Chen, Miaojia Yan and Yutong Wang. Analysis and interpretation of data: Jingguo Chen, Kang Zhu, Yanni Zhang, Chao Yu and Baibing Mi. Drafting of the manuscript: Jingguo Chen, Yanni Zhang and Sachiko Koyama. Critical revision of the manuscript: Jingguo Chen, Baibing Mi, Miaojia Yan, Yutong Wang, Kang Zhu, Sachiko Koyama and Xiaoyong Ren. All authors approved the final version of the manuscript.

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CONFLICT OF INTEREST

The authors declare no competing financial interests concerning the work described.

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