Olfactory Dysfunction in Recovered Coronavirus Disease 2019 (COVID-19) Patients

It has been reported that loss of smell could be an early sign of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, even before other typical symptoms such as cough, fever, and shortness of breath for patients with coronavirus disease 2019 (COVID-19).[1] Dysosmia was identified in 5.1% of the patients with COVID-19 in Wuhan, China.[2] Previous studies have shown that the olfactory dysfunction could be resolved within 2 to 4 weeks in the majority of patients with COVID-19.[1,3] It remains unclear with the duration of olfactory dysfunction and the long-term effects of persistent olfactory dysfunction in patients with COVID-19. The persistent dysosmia not only has a negative impact on patients' quality of life but also may indicate an early symptom of neurodegenerative disease such as Parkinson's disease.[4]

Here we present a multicenter, prospective cohort study for long-term follow-up of patients with COVID-19 with

TABLE 1 Olfactory characteristics of 145 recovered COVID-19 patients and 170 control subjects

Characteristic	COVID-19, n = 145	Control, n = 170	*P* Value
Age, average (range), y	49 (13–80)	37 (17–71)	**9.36E-19**
≦29 no. (%)	12 (8)	51 (30)	**1.55E-06**
30–39 no. (%)	20 (14)	56 (33)	**7.53E-05**
40–49 no. (%)	37 (26)	36 (21)	3.63E-01
50–59 no. (%)	39 (27)	23 (14)	**1.13E-09**
≧60 no. (%)	37 (26)	4 (2)	–
Sex no. (%)			
Women	88 (61)	73 (43)	**1.68E-03**
Men	57 (39)	97 (57)	**1.68E-03**
Smoking no. (%)	8 (6)	35 (21)	**1.03E-04**
Nose trauma or surgery no. (%)	1 (1)	1 (1)	9.10E-01
Rhinitis no. (%)	20 (14)	14 (8)	1.13E-01
Days from symptom onset, median (range)	62 (25–95)	–	–
Dysosmia no. (%)	16 (11)	2 (1)	**1.72E-04**
≦29	0 (0)	1 (2)	6.25E-01
30–39	2 (10)	0 (0)	**1.65E-02**
40–49	0 (0)	0 (0)	–
50–59	4 (10)	1 (4)	3.85E-01
≧60	10 (27)	0 (0)	2.32E-01
Women no. (%)	7 (8)	0 (0)	**1.37E-02**
Men no. (%)	9 (16)	2 (2)	**9.05E-03**
Smoking no. (%)	4 (50)	0 (0)	**1.12E-05**
Nose trauma or surgery no. (%)	0 (0)	0 (0)	–
Rhinitis no. (%)	2 (10)	0 (0)	2.23E-01
Odor			
Garlic no. (%)	7 (5)	1 (1)	**1.71E-02**
Pineapple no. (%)	13 (9)	1 (1)	**3.23E-04**
Mint no. (%)	11 (8)	1 (1)	**1.22E-03**
Ginger no. (%)	38 (26)	12 (7)	**3.56E-06**
Rose no. (%)	24 (16)	10 (6)	**2.35E-03**
T&T score, mean ± standard deviation	−0.53 ± 1.10	−0.74 ± 0.65	**3.42E-02**

P values comparing COVID-19 patients and control subjects were from χ^2 tests or Fisher's exact tests. $P < 0.05$ was considered statistically significant (in bold). COVID-19, coronavirus disease 2019; T&T, Toyota-Takagi olfactometry.

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Relevant conflicts of interests/financial disclosures: Nothing to report.

Funding agencies: This work was supported by Grants 2016YFC1306600 and 2018YFC1314700 from the National Key R&D Program of China and Grant 81873782 from the National Natural Science Foundation of China, all to N.X.

Received: 9 May 2020; **Revised:** 21 May 2020; **Accepted:** 26 May 2020

Published online 30 June 2020 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.28172

dysosmia. We compared 145 patients with COVID-19 with dysosmia with 170 healthy subjects to investigate the frequency and duration of dysosmia. All subjects completed the smell identification testing by using Toyota-Takagi (T&T) olfactometry scores system, with odors generally familiar to the Chinese population, as an auxiliary diagnosis of dysosmia.[5]

We find for the first time that dysosmia may last up to 95 days or longer (median duration 62 days) in patients with COVID-19. Among all these patients, 2-4 weeks after discharge, 11% of patients (16 of 145) still had dysosmia ($P = 1.72 \times 10^{-4}$). The duration of olfactory dysfunction is much longer compared with the European report.[1] Our results showed that 10 of 16 patients with COVID-19 with dysosmia were older than 60 years old, consistent with the fact that olfactory dysfunction is more common in the elderly population.

In these 2 groups, 8 (6%) of patients with COVID-19 and 35 (21%) of healthy subjects were smokers. Of the 8 patients with COVID-19 with smoking history, 4 (50%) had dysosmia. Patients with COVID-19 with a smoking history were more likely to have long-term dysosmia ($P = 5.67 \times 10^{-4}$; Table 1).

As for smell identification tests, the dysosmia of garlic was in 7 (5%) of 145 patients with COVID-19 versus one (1%) of 170 healthy subjects ($P = 1.72 \times 10^{-4}$); pineapple in 13 (9%) and 1 (1%), mint in 11 (8%) and 1 (1%), ginger in 38 (26%) and 12 (7%), and the rose in 24 (16%) and 10 (6%), respectively. Postdischarge T&T scores in the patient group were significantly lower than the healthy group ($P = 0.03$), implying a long-term smell dysfunction in the recovered cases of patients with COVID-19.

The sample size of this study was not large enough to show any statistical difference of olfactory dysfunction between age subgroups. Longitudinal studies and larger cohort follow-up would help better understand the prognosis. It is still unclear if the SARS-CoV-2 virus can use the olfactory nerve as a shortcut to enter the central nervous system similar to other coronaviruses.[7] As COVID-19 and neurodegenerative disorders (ie, Parkinson's disease) both have higher prevalence in the elderly population and olfactory dysfunction could be an early sign of both disorders, we will monitor patients with COVID-19 with dysosmia in a longer term to investigate possible predisposition to neurodegenerative diseases.

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