



Commentary

Affected olfaction in COVID-19: Re-defining “asymptomatic”

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It has been reported that olfactory dysfunction (OD) is a premonitory symptom of COVID-19 in various populations [1–3], and may persist even in recovered patients [4]. These data suggest that OD may be a reliable symptom of COVID-19. Therefore, the rapid and accurate identification of olfactory impairment is positioned to enhance early COVID-19 diagnosis for timely and preventive intervention.

In their article entitled “Quantitative assessment of olfactory dysfunction accurately detects asymptomatic COVID-19 carriers” published in *EClinicalMedicine*, Anindya Bhattacharjee et al. introduced a novel tool to quantify olfactory deficits in asymptomatic COVID-19 patients [5]. Their quantitative assessment of olfactory dysfunction as described is novel, economical, convenient, and has a high sensitivity. Furthermore, it can be applied for large-scale COVID-19 screening, especially among asymptomatic carriers.

COVID-19 asymptomatic carriers are patients with a positive nucleic acid result but without common clinical symptoms such as fever and chest imaging manifestations. Asymptomatic carriers are currently diagnosed by using nucleic acid testing kits, which are regarded as the gold standard for the diagnosis. However, laboratory detection may be time-consuming and requires rigorous laboratory specifications. Furthermore, due to the limited sensitivity of the molecular testing kits, false-negative results cannot be avoided, increasing the difficulty to contain this disease. However, as reported by Anindya Bhattacharjee et al., the current diagnosis can be further assisted by this novel approach, allowing earlier health management and minimizing further transmission.

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E-mail address: nianxiong@hust.edu.cn (N. Xiong).¹ These authors contributed equally to this work.² Joint last author.<https://doi.org/10.1016/j.eclinm.2020.100628>2589–5370/© 2020 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Few tests of olfactory function have been previously described, including the University of Pennsylvania Smell identification Test [6], the T & T Olfactometer test [7], and the Sniff Sticks test [8]. However, these methods are subjective and have limitations, highlighting the need for a more objective tool to identify OD. The tool described by Anindya Bhattacharjee et al. has its unique advantages. The test is rapid, taking 20 min or less, and uses a custom-built ten-channel olfactory-action meter, which can deliver odors with high temporal precision for a precise readout of olfactory fitness. Its evaluation system indicators include the odor matching performance index and the olfactory function score (OFS), which are accurate and comprehensive. There are two important aspects of an olfactory test that the subjects should pay attention to. One aspect is trying to detect but not to identify the odors delivered. Another is that all subjects performing the olfactory function test must wear a face mask. In addition, the method combines olfactory detection abilities at threshold levels and olfactory matching skills reflecting cognitive functioning, which mirrors deficits in olfactory perception caused by malfunction of sensory periphery and higher brain centers. According to Anindya Bhattacharjee et al., this objective tool identified 82% of the asymptomatic SARS-CoV-2 carriers with olfactory deficits while on subjective evaluation, only 15% of the patients noticed a compromised ability to smell.

Based on its high sensibility and feasibility, the novel method may be incorporated into routine examinations such as blood tests, nucleic acid testing and chest computerized tomography (CT). The combination of these tools is expected to reduce the rate of missed diagnosis and maximize the sensitivity of diagnosis. However, this new method still has some limitations. Firstly, participants should be tested with 10 odors and each odor has three different degrees, which may lead to olfactory fatigue for inaccurate results. Secondly, in addition to age and gender, education level and life experience could be confounding factors.

As a mechanistic insight, COVID-19-related OD is supported by the finding that human olfactory epithelium expresses high levels of angiotensin-converting enzyme 2 (ACE2), the receptor for SARS-CoV-2 [9] that causes COVID-19. In fact, olfactory epithelium has a shorter route to the airway than the lung which is currently the diagnostic epicenter of airborne infection. Such information may suggest that it is indeed the olfactory epithelium that bears the brunt of the coronavirus infection.

In a broader spectrum, OD is commonly observed in several other diseases, including neurodegenerative diseases such as Parkinson's

disease [10]. Therefore, the tool described by Anindya Bhattacharjee et al. may find wide applications. Further studies are needed to verify such broader applications.

Critically, in the diagnosis of COVID-19, OD should be considered as one of the symptoms in infected patients, re-defining “asymptomatic” for increased screening sensitivity and enhancing public health during the pandemic.

Declaration of Competing Interest

The authors have nothing to declare.

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