

Taste and Smell Impairment in SARS-CoV-2 Recovers Early and Spontaneously: Experimental Data Strongly Linked to Clinical Data

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Cite This: <https://dx.doi.org/10.1021/acschemneuro.0c00296>

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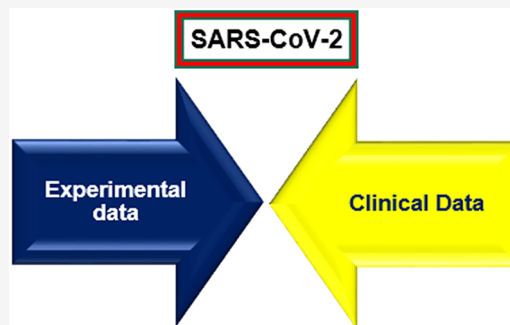
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ABSTRACT: A growing body of literature indicates that smell and taste impairment has frequently occurred during the Severe Acute Respiratory Syndrome (SARS)-like Coronavirus (SARS-CoV-2) outbreak. Experimental studies have mostly found that non-neural-type cells are responsible for SARS-CoV-2-related taste and smell impairment. If this is the case, smell/taste impairment needs to recover early. Literature data from clinical studies indicated a strong correlation between experimental and clinical findings. This article presents clinical studies related to SARS-CoV-2-induced smell/taste impairment that reported recovery rates. Experimental researchers may use these data to observe the dynamics of smell impairment and implement these findings in their research (e.g., correct timing of sampling) to perform further studies.

KEYWORDS: COVID-19, chemosensory, smell, gustatory, olfactory, anosmia



Two articles recently appeared in *ACS Chemical Neuroscience* that need attention.^{1,2} The article published by Bilinska et al. indicated that sustentacular cells are responsible for Severe Acute Respiratory Syndrome (SARS)-like Coronavirus (SARS-CoV-2) entry and related smell impairment.¹ Bilinska et al. also reported that non-neuronal cells of the olfactory epithelium (OE) are more likely to be the entry point of SARS-CoV-2 virus rather than olfactory receptor neurons (ORNs).¹ In the second report, Butowt and Bilinska highlighted the need for OE-oriented experimental studies to clarify various points related to SARS-CoV-2 virus and the continuous need for clinical data related to SARS-CoV-2 and related smell loss.²

Brann et al. reported that direct involvement of olfactory sensory neurons (OSNs) may not occur in SARS-CoV-2 infection since OSNs did not express ACE2. Non-neural cell types (e.g., stem cells, TMPRSS2 support cells, and perivascular cells) express ACE2, and they are responsible for related smell impairment.³ Brann et al. hypothesized that inflammation, deteriorated signaling, and diffuse architectural damage of the OE may be the mechanisms for smell impairment.

On the basis of these experimental studies, in the clinical setting smell impairment needs to be resolved early and spontaneously because in the majority of the cases direct involvement of OSNs did not widely occur. In order to evaluate the consistency between experimental and clinical findings, we systematically reviewed clinical studies that reported resolution rates in SARS-CoV-2-related smell impairment.^{4–14}

The results are presented in Table 1. Published studies indicated that smell impairment in SARS-CoV-2 recovered early. At present, no treatment for SARS-CoV-2-related smell impairment exists. In two studies, some treatments, including nasal saline irrigation, intranasal corticosteroids, systemic corticosteroids, dietary supplements, vitamin A, and olfactory training, on limited number of the subjects were reported.^{7,11} However, no definite conclusion could be made concerning the effect of treatment on recovery rates. Smell loss mostly recovered in a few weeks after the infection and seemed to reduce with time.

The present report has some limitations. This report's knowledge was limited to published data to date. The reviewed articles were mostly observational and questionnaire-based. Among the reviewed articles for this report; only one study used objective testing methods and reported outcomes.¹⁴ Literature data point out that there will be an inconsistency between patient-reported and objective-testing-determined smell/taste impairment. However, nasal procedures, detailed examinations, and close contact with subjects were avoided during the pandemic, which resulted in a limited number of studies that reported objective outcomes. Besides, the studies

Received: May 17, 2020

Accepted: June 15, 2020

Published: June 15, 2020

Table 1. Summary of Studies of SARS-COV-2-Related Smell/Taste Impairment That Reported Recovery Dynamics^a

authors	design	number of subjects	test method	smell/taste impairment rate	recovery characteristics
Sayin et al. ⁴	comparative between COVID-19 (+) and COVID-19 (-) subjects	64 COVID-19 (+) subjects compared with 64 COVID-19 (-) subjects	RT-PCR	71.9% for the COVID-19 (+) group vs 26.6% for the COVID-19 (-) group	45.7% for COVID-19 (+) subjects and 64.7% for COVID-19 (-) subjects at the time of the study
Lee et al. ⁵	single-arm descriptive	3191 COVID-19 subjects	NS	15.3% (<i>n</i> = 488)	the median time to recovery from anosmia and ageusia was 7 days, ^b and most of the subjects recovered in 3 weeks
Paderno et al. ⁶	comparative between COVID-19 (+) hospitalized and COVID-19 (+) home-quarantined subjects	508 subjects (295 hospitalized and 213 home-quarantined)	RT-PCR	overall OD and GD were present in 56% and 63% of the subjects	complete resolution of OD and GD was 52% and 55% at the time of the questionnaire; mean RT was 9 ± 5 days
Hopkins et al. ⁷	single-arm descriptive	382 subjects underwent an initial survey and a follow-up survey 1 week after the first survey	NS ^c	overall 97.9% smell impairment rate	80.1% of subjects reported improvement in smell impairment in 1 week (recovery appearing to plateau after 3 weeks)
Kaye et al. ⁸	single-arm descriptive	237 subjects	NS	100% ^d	some improvement on 27% of the subjects (mean improvement time 7.2 days)
Beltrán-Corbellini et al. ⁹	comparative between COVID-19 (+) and influenza (+) subjects	70 COVID-19 (+) and 40 influenza (+) subjects	RT-PCR	39.2% for COVID-19 (+) and 12.5% for influenza (+) subjects	40% complete recovery after 7.4 ± 2.3 days and 16.7% partial recovery after 9.1 ± 3.6 days. For influenza (+) subjects, 100% recovered
Yan et al. ¹⁰	comparative between COVID-19 (+) and COVID-19 (-) subjects	59 COVID-19 (+) subjects compared with 203 COVID-19 (-) subjects	RT-PCR	smell and taste loss were reported in 68% and 71% of COVID-19 (+) subjects and 16% and 17% of COVID-19 (-) subjects	74% reported resolution of anosmia with clinical resolution of illness; RT was noted as less than 2 weeks; GD: NS
Lechien et al. ¹¹	single-arm descriptive	417 subjects	RT-PCR	85.6% reported OD and 88.0% GD	early olfactory RT was 44.0%; GD: NS
Klopfenstein et al. ¹²	single-arm descriptive	114 subjects	RT-PCR	47.3% OD and 40.3% GD	98% subjects with anosmia improved in 28 days; GD: NS
Dell'Era et al. ¹³	single-arm descriptive	355 subjects	RT-PCR	66% for OD and 65.4% for GD	62.9% of subjects with OD fully recovered at the time of the survey (median RT 10 days, range 1–25 days), and 63.8% of subjects with GD fully recovered at the time of the survey (median RT 10 days, range 2–25 days)
Vaira et al. ¹⁴	single-arm descriptive	345 subjects underwent objective chemosensitive evaluation	RT-PCR	65% for OD and 67.8% for GD	complete resolution for OD and GD were 31.3% and 50.4%, respectively, at the time of the study; improvement was evident in the first and second weeks of disease

^aAbbreviations: RT-PCR, real-time polymerase chain reaction; NS, not specified; OD, olfactory dysfunction; GD, gustatory dysfunction; RT, recovery time. ^bPercentage not specified in the manuscript. ^cSome subjects were tested, but there was a lack of confirmed COVID-19 status. ^dThe American Academy of Otolaryngology—Head and Neck Surgery Anosmia Reporting Tool was used, and only subjects with anosmia completed the tool.

regarding smell/taste impairment were mostly cross-sectional single-arm studies. Comparative studies with SARS-CoV-2 (−) subjects and comparative studies with other upper respiratory tract infection causes were limited in number. Even for the studies that presented followup, the followup period was limited to weeks. Larger studies with objective testing methods and longer followup periods will deepen our knowledge about SARS-CoV-2-related taste/smell impairment.

These findings represent a well-linked relation between experimental studies and clinical studies. Experimental researchers may use these data to observe the dynamics of smell impairment and implement these findings in their researches (e.g., correct timing of sampling) to perform further studies.

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<https://pubs.acs.org/10.1021/acschemneuro.0c00296>

Author Contributions

I.S. made the conceptual design of the paper. I.S. and Z.M.Y. performed the literature search. Z.M.Y. had a role in acquisition of the data, and I.S. analyzed and interpreted the data. I.S. and Z.M.Y. wrote the manuscript. Z.M.Y. made the literature search for revision, and I.S. revised the manuscript for intellectual content. I.S. and Z.M.Y. gave final approval of the manuscript.

Notes

The authors declare no competing financial interest.

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