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ORIGINAL ARTICLE

Assessment of patient recognition of coronavirus disease 2019 (COVID-19)-associated olfactory loss and recovery: a longitudinal study

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Abstract

Background: The clinical course of coronavirus disease 2019 (COVID-19) olfactory dysfunction remains poorly characterized, often limited by self-reported measures. Given the logistical challenges of psychophysical testing, understanding the longitudinal relationship between self-reported and quantitative measures can help accurately identify patients with persistent olfactory dysfunction. This study aimed to longitudinally correlate measured and subjective olfactory function in COVID-19 subjects.

Methods: A prospective, longitudinal study evaluating subjective and measured olfaction was conducted on ambulatory COVID-19 subjects. Olfaction scores were obtained using a visual analogue scale (VAS) (0 = anosmia, 10 = normosmia) and the validated 12-item Brief Smell Identification Test (BSIT). Weekly testing was performed until recovery (BSIT \geq 9/12 and/or VAS = 10/10) or study completion.

Results: Eighty-six polymerase chain reaction (PCR)-positive COVID-19 subjects were recruited \leq 3 days from diagnosis and 52 completed longitudinal testing. Among those with self-reported smell loss at recruitment, similar levels (75.8%) of objective (BSIT \geq 9/12) and subjective recovery were obtained using a VAS cutoff \geq 8, yet only 30.3% reported complete subjective recovery (VAS = 10). Median times to objective and complete subjective olfactory recovery were 12 ± 2.3 and 24 ± 3.5 days, respectively. Although both measures showed chemosensory improvement, the distributions of objective and full subjective olfactory recovery differed significantly (log rank test $\chi^2 = 6.46$, degrees of freedom [df] = 1, $p = 0.011$). Overall correlation between BSIT and VAS scores was moderate to strong across longitudinal follow-up ($r_s = 0.41$ – 0.65).

Conclusion: Self-reported and psychophysically measured COVID-19 olfactory dysfunction improve at similar levels and are moderately correlated longitudinally, yet there is a significant delay in complete subjective recovery. Psychophysical testing in conjunction with qualitative assessments may be considered for counseling and follow-up of patients with COVID-19 smell loss.

KEYWORDS

BSIT, COVID-19, disease screening, psychophysical testing, smell loss

INTRODUCTION

Olfactory and gustatory dysfunction have been identified as unique symptoms of coronavirus disease 2019 (COVID-19) infection.¹⁻⁴ Sudden loss of smell has been identified as an early and often isolated symptom of COVID-19, prompting many institutions to use patient-reported olfaction as a screening tool for COVID-19 infection.⁵⁻⁷ Several prospective longitudinal studies have used either self-reported data or psychophysical testing to demonstrate that a majority of ambulatory COVID-19 patients spontaneously recover olfactory function while a subset develop persistent smell loss.⁸⁻¹⁰ However, there has not been a direct analysis of the longitudinal relationship between self-reported and psychophysical measures in COVID-19-associated olfactory loss. Such an understanding could help guide us in efficiently and accurately identifying and following patients with persistent olfactory dysfunction due to COVID-19.

The relationship between self-reported and psychophysical olfactory measures has been previously studied in the context of smell loss due to aging, trauma, cognitive disorders, and upper respiratory tract infections.¹¹⁻¹⁵ Overall, individuals tend to underreport olfactory dysfunction compared to objective measures.¹¹ In the context of COVID-19, it has been previously demonstrated that self-reported and psychophysically tested olfaction measures are well-correlated in ambulatory COVID-19 patients at the onset of smell loss.¹⁶ There remains concern, however, that self-reported measures may poorly assess persistent COVID-19-related olfactory dysfunction,¹⁷ suggesting that perhaps psychophysical testing is a necessary component for long-term follow-up of COVID-19 patients. Few studies have used both self-reported and objective olfactory measurements and none have compared these measurements longitudinally as the primary study aim.

The present study is a prospective longitudinal study that captured ambulatory subjects immediately post-COVID-19 diagnosis and concurrently obtained self-reported and psychophysical olfactory measurements until objective recovery of olfactory function. The aim was to understand how patients longitudinally assess their olfactory function as it correlates with their recovery. We hypothesized that based on the acuity and severity of virally induced olfactory dysfunction, subjects with COVID-19-related smell loss can determine their olfactory function with high accuracy, and that self-reported and

psychophysically tested measures are strongly correlated longitudinally.

PATIENTS AND METHODS

A prospective, longitudinal study evaluating subjective and measured olfactory function was conducted on ambulatory COVID-19 subjects. Patient-reported olfaction scores were obtained using visual analog scales (VAS, 0 = no smell, 10 = normal smell) and validated psychophysical testing was achieved using the 12-item Brief Smell Identification Test (BSIT®; Sensonics International, Haddon Heights, NJ). Repeated testing was performed weekly until smell recovery, defined as a BSIT \geq 9/12 or VAS = 10/10.

Study design and population

Adults presenting to the UC San Diego Health System with confirmed polymerase chain reaction (PCR)-positive severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) viral nucleic acid from nasopharyngeal/nasal cavity swabs were eligible for inclusion. Between May 8, 2020 and October 4, 2020, subjects were recruited within 3 days of COVID-19 test confirmation through an initial phone call to complete an online survey (Qualtrics, Provo, UT) that included an initial self-reported olfactory assessment at the time of enrollment as well as a recalled self-assessment of olfactory function prior to COVID-19 infection. Subjects were mailed a BSIT to quantitatively assess olfactory function with a subjective olfactory assessment contemporary to the BSIT testing. Repeated BSIT testing and subjective olfactory assessments were performed weekly until smell recovery was achieved, defined as BSIT \geq 9/12 and VAS = 10/10. Inclusion criteria included: adult subjects \geq 18 years old, confirmed COVID-19 positive testing by PCR, and completion of initial survey \leq 3 days post-COVID-19 diagnosis. Patients were excluded if they were non-English speaking or admitted for COVID-19 at any point during their disease course.

Olfactory and clinical assessments

During initial recruitment, subjective olfactory assessment included a binary yes/no smell loss question as well as a

continuous 10-point slide visual analog scale (VAS, with 0: no sense of smell, 10: normal sense of smell),¹⁸ with progressively lower scores indicating worsening severity of hyposmia. At initial enrollment, two self-reported VAS scores were obtained, (1) baseline VAS capturing the pre-COVID-19 olfactory rating, and (2) VAS at the time of enrollment within 3 days of COVID-19 confirmation by PCR. Longitudinal VAS assessments were obtained at the same time as BSIT test scores. We evaluated subjective measures of olfactory recovery using two VAS cutoffs, ≥ 8 as well as 10 out of 10. The BSIT (previously known as the cross-cultural smell identification test) is a 12-item well-validated and reliable olfactory test that utilizes microencapsulated “scratch and sniff” odorants (Sensoics International). A BSIT score of ≤ 8 was considered abnormal.¹⁹ Concurrent BSIT and VAS scores were obtained weekly until subjects achieved two consecutive normal BSIT ($\geq 9/12$) or VAS (= 10/10) scores or four time points of data were collected. The study end-point was chosen after four time points (median 33 days postdiagnosis) given prior data suggesting that the majority of COVID-19 subjects recover chemosensory function within 1 month of symptoms.^{1,20,21}

Patient demographic data, clinical characteristics, and additional presenting disease symptoms were collected using a combination of patient survey responses and the electronic health record system (Epic, Verona, WI). This study was approved by the Institutional Review Board (IRB) of University of California San Diego (IRB #200485).

Statistical analysis

Statistical analysis was performed using RStudio 1.3.1056 (RStudio PBC, Boston, MA). Wilcoxon signed-rank tests were performed to compare paired VAS and BSIT scores at each time point. Spearman correlation coefficients were calculated for the distribution of VAS and BSIT scores at each time point. An alpha value of 0.05 was considered statistically significant.

RESULTS

A total of 86 outpatient COVID-19 subjects confirmed by PCR were prospectively enrolled in the study (Figure 1). Of these, 67 (78%) completed at least one time point of BSIT testing and 52 (61%) completed at least two time points of testing. The mean duration between COVID-19 diagnosis and initial BSIT testing was 7.5 ± 2.4 days, accounting for time for mail delivery and test completion. The initial dropout of 19 subjects (22%) was due to disease progression requiring admission or an inability to receive or complete a BSIT. This study included those who reported either the

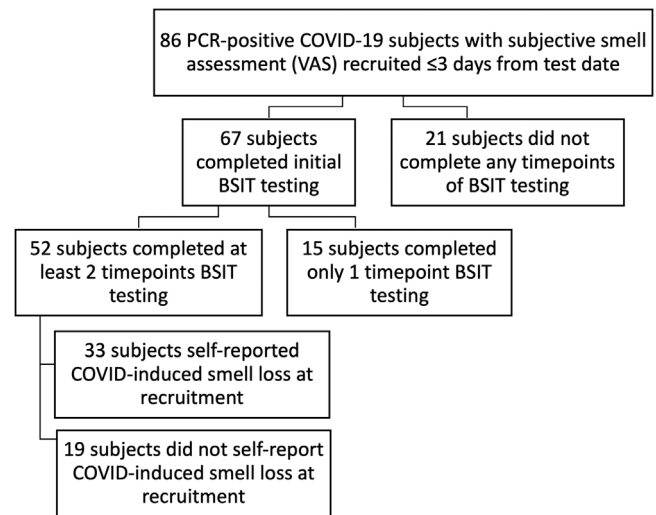


FIGURE 1 Flowchart of study recruitment. Abbreviations: BSIT, Brief Smell Identification Test; VAS, visual analogue scale

presence or the absence of olfactory dysfunction to establish the longitudinal correlation between subjective and objective olfactory measurements as related to COVID-19. While all subjects had to partake in at least two assessments, the study was complete once they demonstrated either subjective or objective normality of smell across two time points.

During initial recruitment (within 3 days of COVID-19 diagnosis), 33 subjects reported COVID-19–induced smell loss (33/52, 63%) in response to a binary yes/no question, whereas 19 reported no smell loss (19/52, 37%). The mean baseline (pre-COVID-19) VAS for olfactory function was 9.60 ± 1.11 . The demographic, clinical, and COVID-19 symptom characteristics of these 52 subjects are summarized in Table 1. Subjects had a mean age of 40.1 ± 16.1 years and 53.8% (28/52) identified as male. Only 5.8% (3/52) of subjects had a history of prior smell loss and none sought treatment for COVID-19–induced smell loss prior to completing BSIT testing.

Among the 33 subjects with a binary self-reported smell loss during recruitment, 32 (97.0%) continued to report subjective loss at the time of first BSIT, whereas only 16 (48.5%) had measurable olfactory dysfunction on BSIT testing (Table 2). Although 75.8% achieved normalization on BSIT testing, only 30.3% (10/33) of those with subjective COVID-19–related smell loss reported full recovery (VAS = 10/10) at the completion of all study time points, suggesting either a delayed subjective recovery or the presence of olfactory deficits undetectable on BSIT testing. However, when a VAS cutoff ≥ 8 was used, a 75.8% subjective olfactory improvement rate was noted.

Of the 19 subjects who reported no initial subjective smell loss, 21.1% (4/19) and 26.3% (5/19) had abnormal initial and subsequent BSIT and VAS scores, respectively,

TABLE 1 Demographic and clinical characteristics of study subjects ($N = 52$ subjects)

Characteristic	Value
Age (years), mean \pm SD	40.1 \pm 16.1
Gender, n (%)	
Male	28 (53.8)
Female	23 (44.2)
Gender diverse	1 (1.9)
Clinical characteristics, n (%)	
History of smell loss	3 (5.8)
Treated for COVID-19 smell loss	0 (0)
History of tobacco use	7 (13.5)
Diabetes mellitus	4 (7.7)
Cardiac disease	2 (3.8)
Hypertension	6 (11.5)
Lung disease	3 (5.8)
Cancer	4 (7.7)
Sinus disease	5 (9.6)
Allergies	3 (5.8)
Immunosuppression	3 (5.8)
Head trauma	2 (3.8)
Neurological disease	0 (0)
Depression or anxiety	9 (17.3)
COVID-19 symptoms, n (%)	
Cough	31 (59.6)
Fever	28 (53.8)
Fatigue	30 (57.7)
Shortness of breath	8 (15.4)
Diarrhea	13 (25)
Headaches	27 (51.9)
Nasal congestion	29 (55.8)
Runny nose	20 (38.5)
Sore throat	17 (32.7)
Muscle or joint pain	28 (53.8)
Dizziness	13 (25)
Nausea/vomiting	13 (25)
Loss of taste	26 (50)
Eye pain	10 (19.2)
No symptoms (asymptomatic)	7 (13.5)
Days between COVID-19 diagnosis and initial BSIT, mean \pm SD	7.5 \pm 2.4

Abbreviations: BSIT, Brief Smell Identification Test; COVID-19, coronavirus disease 2019; SD, standard deviation.

suggestive of late or unperceived presentations of olfactory loss (Table 2). Overall, of the 52 subjects longitudinally evaluated, 12/52 (23%) had an objectively abnormal BSIT scores at final time points of testing. A univariable regression analysis of demographic and clinical characteristics associated with discordant self-reported and

psychophysical measures of olfactory dysfunction at final time points of testing was also performed but did not yield any significant associations.

A time-to-event analysis was conducted on the durations between COVID-19 diagnosis and objective olfactory recovery (BSIT \geq 9/12) and complete subjective olfactory recovery (VAS = 10/10) (Figure 2A). The median time to objective olfactory recovery was 12 \pm 2.3 days while the median time to subjective olfactory recovery was 24 \pm 3.5 days. Based on the log rank test, there was a significant difference between distributions of objective and subjective olfactory recovery ($\chi^2 = 6.46$, $df = 1$, $p = 0.011$), indicating delayed recognition of recovered olfaction. A time-to-event analysis was also conducted utilizing BSIT \geq 9/12 and VAS \geq 8/10 as thresholds for olfactory recovery (Figure 2B). The median times to objective and subjective recovery were 12 \pm 2.3 and 13 \pm 3.1 days, respectively. Using a VAS cutoff of 8/10 as subjective recovery, there was no significant difference between these distributions of olfactory recovery ($\chi^2 = 0.138$, $df = 1$, $p = 0.710$).

Longitudinal BSIT and VAS assessment were conducted weekly until subjects demonstrated recovery of olfaction (either subjective or objective) at two time points. Subjects who continued to exhibit olfactory dysfunction underwent repeated testing for a maximum of four time points. Four time points of data were collected at a median of 7, 12, 21, and 33 days after COVID-19 diagnosis from a total of 52, 52, 27, and 14 subjects, respectively. Figure 3 demonstrates longitudinal concurrent BSIT and VAS scores for subject cohorts which each completed two ($n = 52$; red), three ($n = 27$; green), and four ($n = 14$; blue) time points. Across all 52 subjects, VAS scores increased significantly ($p < 0.001$) between VAS1 and VAS2, while BSIT scores did not increase significantly between BSIT1 and BSIT2 (Figure 3A,B). For the 27 subjects who required at least three time points of testing, VAS scores increased significantly across all time points ($p < .001$), whereas BSIT scores only increased significantly between BSIT1 and BSIT3 ($p = 0.001$). The final median BSIT scores for data obtained at either 2 weeks, 3 weeks, or 4 weeks reached \geq 9 (BSIT scores of 9, 9, and 9.5, respectively), suggesting that all subjects tended to reach objective smell recovery by 1 month after onset of symptoms. In the 14 subjects who required all four time points of testing, their last BSIT score ranged from 6 to 11 with a median score of 9.5. However, the final median VAS score for these 14 subjects obtained at last time point remained lower than those who demonstrated recovery prior to 1 month with a median of 8 compared to a median of 9 in cohorts with 27 and 52 subjects each.

To compare self-reported olfactory function with objectively measured olfactory testing, the correlation between BSIT and VAS scores at each of the four time points was determined as demonstrated in Figure 4. At every time

TABLE 2 Psychophysical (BSIT) and subjective (VAS) scores at first and final time points for subjects with and without self-reported COVID-19 associated smell loss

Parameter	Subjects reporting smell loss (n = 33)			Subjects Reporting No smell loss (n = 19)		
	Normal first BSIT	Abnormal first BSIT	Total	Normal first BSIT	Abnormal first BSIT	Total
Normal final BSIT	16 (49%)	9 (27%)	25	15 (79%)	0 (0%)	15
Abnormal final BSIT	1 (3%)	7 (21%)	8	2 (10.5%)	2 (10.5%)	4
Total	17	16	33	17	2	19
Parameter	Subjects reporting smell loss (n = 33)			Subjects Reporting No smell loss (n = 19)		
	Normal first VAS	Abnormal first VAS	Total	Normal first VAS	Abnormal first VAS	Total
Normal final VAS	1 (3%)	9 (27%)	10	14 (74%)	2 (10.5%)	16
Abnormal final VAS	0 (0%)	23 (70%)	23	1 (5%)	2 (10.5%)	3
Total	1	32	33	15	4	19

Notes: First time point was defined by first concurrent BSIT and VAS scores available (median 7 days after COVID-19 diagnosis). Final time point was defined by final concurrent BSIT and VAS scores available. Normal scores were defined by VAS = 10/10 and BSIT ≥ 9/12.

Abbreviations: BSIT, Brief Smell Identification Test; COVID-19, coronavirus disease 2019; VAS, visual analogue scale.

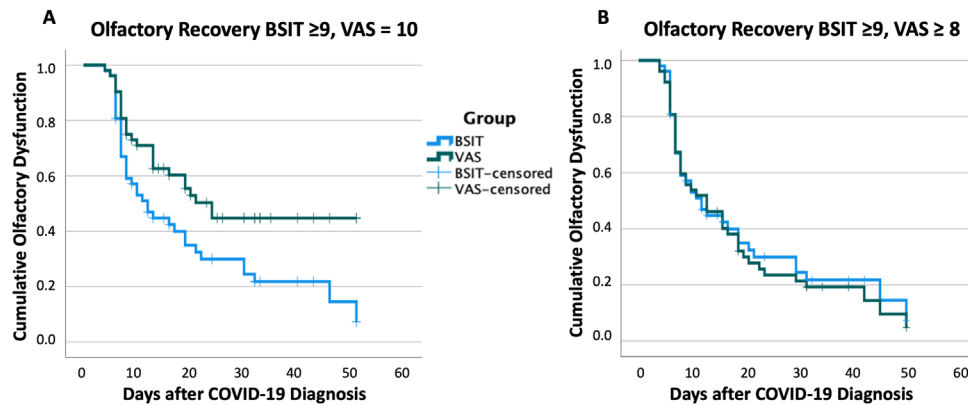


FIGURE 2 Time-to-event analysis of olfactory recovery. Time of olfactory recovery measured as number of days after COVID-19 diagnosis. (A) Olfactory recovery defined as BSIT ≥ 9/12 (objective) and VAS = 10/10 (subjective). Median time to olfactory recovery was 12 ± 2.3 days for BSIT scores and 24 ± 3.5 days for VAS scores. Log rank test indicated significant difference between distributions ($\chi^2 = 6.46$, $df = 1$, $p = 0.011$). (B) Olfactory recovery defined as BSIT ≥ 9/12 (objective) and VAS ≥ 8/10 (subjective). Median time to olfactory recovery was 12 ± 2.3 days for BSIT scores and 13 ± 3.1 days for VAS scores. Log rank test indicated no significant difference between distributions ($\chi^2 = 0.138$, $df = 1$, $p = 0.710$). Abbreviations: BSIT, Brief Smell Identification Test; df , degrees of freedom; VAS, visual analogue scale

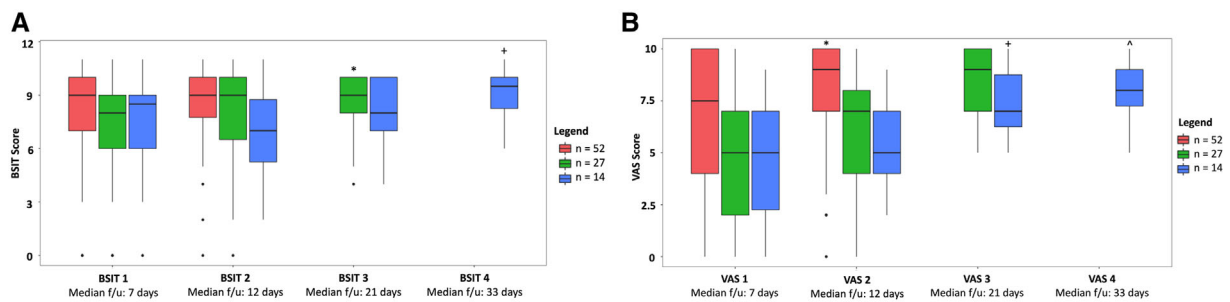


FIGURE 3 Box-and-whisker plots of BSIT and VAS scores across four longitudinal time points. Subjects were divided into cohorts based on number of time points of follow-up: two ($n = 52$; red), three ($n = 27$; green), four ($n = 14$; blue). Outlying data points (located beyond $Q1 - 1.5[IQR]$ or $Q3 + 1.5[IQR]$) are represented as dots outside the box-and-whisker plots. Wilcoxon signed rank test analysis was performed to compare paired BSIT and VAS scores between time points for each cohort. (A) In BSIT score plots, statistically significant changes are indicated as follows: * indicates $p = 0.001$ when comparing BSIT3 to BSIT1 in green ($n = 27$) cohort, + indicates $p < 0.05$ when comparing BSIT4 to BSIT1, BSIT2, and BSIT3 in blue ($n = 14$) cohort. (B) In VAS score plots, statistically significant changes are indicated as follows: * indicates $p < 0.001$ when comparing VAS2 to VAS1 in red ($n = 52$) cohort, + indicates $p < 0.001$ when comparing VAS3 to VAS1 and VAS2 in green ($n = 27$) cohort, and ^ indicates $p < 0.01$ when comparing VAS4 to VAS1 and VAS2 in blue ($n = 14$) cohort. Abbreviations: BSIT, Brief Smell Identification Test; IQR, interquartile range; Q1, first quartile; Q3, third quartile; VAS, visual analogue scale

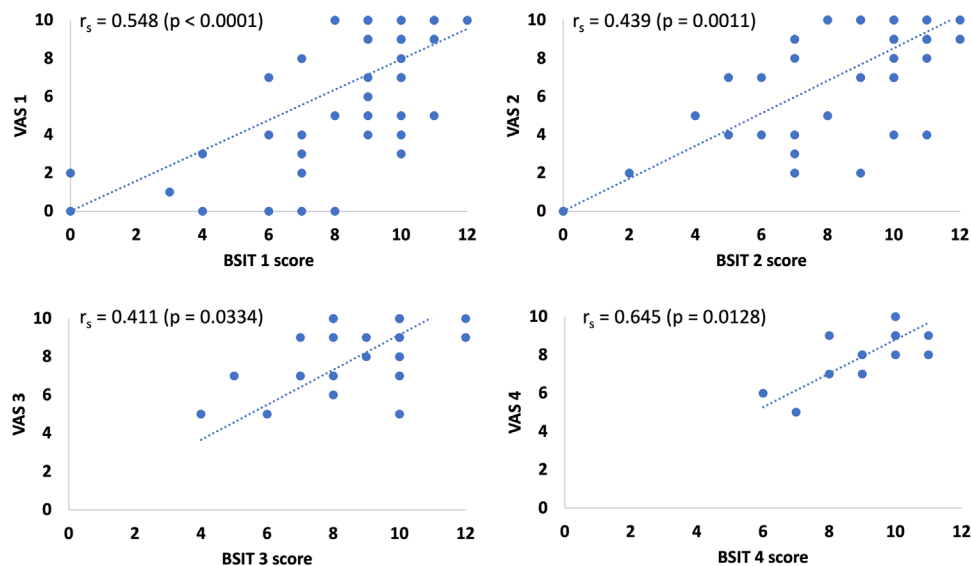


FIGURE 4 Scatterplot of correlation between BSIT and VAS scores with calculated Spearman correlation coefficients. Correlation coefficients for time points one through four are as follows: $r_{s1} = 0.55$ ($p < 0.0001$), $r_{s2} = 0.44$ ($p = 0.001$), $r_{s3} = 0.41$ ($p = 0.03$), and $r_{s4} = 0.65$ ($p = 0.01$). Abbreviations: BSIT, Brief Smell Identification Test; VAS, visual analogue scale

point, there is a moderate correlation between objective and subjective olfactory assessment with r_s value of 0.55 ($p < 0.0001$), 0.44 ($p = 0.001$), and 0.41 ($p = 0.03$) at a median of 7, 12, and 21 days after COVID-19 testing, respectively. At a median of 33 days after COVID-19 testing, the correlation is the strongest with an $r_s = 0.65$ ($p = 0.01$).

DISCUSSION

This study longitudinally compared self-reported olfactory function and validated 12-item odor identification testing in ambulatory COVID-19 patients who were prospectively enrolled within 3 days following their diagnosis of COVID-19 and followed weekly until recovery of olfactory function.

Our data suggest that objective BSIT and subjective VAS scores are moderately correlated longitudinally, with both measures of olfactory dysfunction improving at similar levels. However, when assessing for complete subjective recovery using the highest possible VAS score of 10, there is a perceived significant delay in olfactory recovery with a potential ceiling effect for some. A proportion of subjects will continue report persistent olfactory dysfunction despite normal olfaction on psychophysical testing.

The delay in subjective recovery or continued perception of olfactory dysfunction may be explained by several possibilities including: (1) a limitation in granularity of the BSITs and the use of only odorant identification; (2) a subject's interpretation of olfactory "loss" that may include qualitative disturbances such as parosmias; or (3) a subjects' poor recognition of olfactory function recovery.

First, the 12-item BSIT may fail to detect hyposmias with the same sensitivity as its parent olfactory battery, the 40-item University of Pennsylvania Smell Identification Test (UPSIT), or other batteries such as the Sniffin' Sticks that evaluate threshold and discrimination in addition to identification.²² Although one may note that a normal BSIT was classified as a score of $\geq 9/12$ and a normal VAS as 10/10 and thus subjects may sense a mild loss while still obtaining objective scores in the normal limits, the objective improvements via BSIT scores outpaced the subjective improvements via VAS longitudinally. Second, although VAS assessments were intended to query degree of olfactory loss, participants may have also interpreted this to include disturbances in olfactory quality such as parosmia or phantosmias, known to occur following COVID-19-associated smell loss.²³ Qualitative changes in olfaction or deficits in odor threshold and discrimination may have contributed to delayed subjective recovery. Finally, the speed of olfactory loss has been proposed as an important variable in one's ability to predict olfactory impairment.²⁴ Those with slow-onset olfactory dysfunction tend to underestimate their loss, while those with acute-onset olfactory dysfunction, as in COVID-19 infection, tend to overestimate their loss.¹⁴ Similarly, in a longitudinal analysis of postinfectious smell loss in non-COVID-19 patients, concordance between subjective and objective occurred after several months of follow-up, even as olfactory function significantly improved at earlier time points.²⁵ Thus, patients with COVID-19-related olfactory loss may take several weeks beyond our 1-month follow-up period to recognize their olfactory recovery. In support of this

theory is the stronger correlation noted between VAS and BSIT ($r_{S4} = 0.65$) at the final time point, in comparison to earlier time points, suggesting that with time subjects will be able to more accurately recognize their chemosensory recovery. We suspect that repeated olfactory assessments may also contribute to strengthened recognition.

Our findings are based on subjective recovery defined as VAS = 10/10, which was selected based off the mean baseline VAS score of 9.6 ± 1.11 . We also sought to identify subjects with absolute recovery of olfactory function and account for interrater variability inherent to the VAS assessment. Interestingly, using a subjective olfactory recovery defined as VAS $\geq 8/10$ removed the measurable delay in subjective recovery compared to objective recovery, suggesting that patients acknowledge improvements in their smell, but the extent of improvement may not be adequate. Maintaining a higher threshold for subjective recovery may be better suited for identifying qualitative changes in olfactory function which cannot be easily assessed using psychophysical measurements, as well as determining the impact of subjective impairment on patient quality of life.

Several studies on ambulatory COVID-19 patients have demonstrated that subjective olfactory dysfunction may present without concurrent findings on psychophysical testing when patients are queried 2 to 3 weeks after onset of symptoms.^{26,27} Few studies, however, have longitudinally compared self-reported and psychophysically tested olfactory function in ambulatory COVID-19 patients. Our results are consistent with findings from Otte et al.²⁸ and Lechien et al.,²⁹ who report that 25% to 33% of patients self-reported persistent olfactory dysfunction at 2 months of follow-up despite 85% to 100% of these patients demonstrating normal olfactory function on concurrent Sniffin Sticks' psychophysical testing. In comparison to these studies, our study obtained concurrent BSIT and VAS data shortly after COVID-19 diagnosis, rather than 2 months after diagnosis, and was therefore able to capture weekly improvements in both subjective and objective olfactory dysfunction. Furthermore, rather than using a binary yes/no question to assess subjective olfactory dysfunction, use of the VAS allowed us to capture nuances in subjective olfaction and demonstrate that BSIT and VAS scores are moderately correlated with increasing correlation upon subsequent testing.

Altogether, our findings support the use of repeated objective assessments, in conjunction with subjective evaluations, in helping providers assess disease course and facilitate treatment options and outcomes for patients with persistent COVID-19 smell loss. Current data for treatment of COVID-19-induced olfactory dysfunction is limited. Olfactory training and oral steroids have both demonstrated efficacy in preliminary studies in patients

with COVID-19 olfactory dysfunction.^{30,31} Given the well-known side effects of systemic steroids and high frequency of spontaneous olfactory recovery, however, repeated objective testing can help determine treatment necessity and efficacy. Psychophysical testing such as the BSIT or UPSIT, which can be self-administered at home in accordance with COVID-19 quarantine and social distancing guidelines, offer reasonable means of longitudinally assessing olfactory dysfunction. Qualitative olfactory assessments can be conducted with psychophysical testing in order to capture patients with persistent subjective olfactory dysfunction which may impair quality of life.

Given the limited sample size and length of follow-up period, this study does not accurately represent the prevalence rates of initial or longitudinal olfactory dysfunction in COVID-19 patients. Thirteen of 52 (25%) subjects in this study had persistent smell loss on psychophysical testing at last available follow-up. This value is lower than 37% to 45% with hyposmia reported at 6 to 8 weeks after onset of smell loss in other studies,^{21,28} although more recently Lechien et al.²⁹ demonstrated that long-term olfactory loss may be as low as 5%.

This study was limited by sampling at a single institution, as well as a notable dropout of initially recruited subjects due to a lack of completion of longitudinal BSIT assessments to assess return of olfactory function (subsequent assessments until normalization of BSIT or subjective recovery was required as per inclusion criteria) or disease progression. In surveying home-quarantined subjects after COVID-19 diagnosis, there was a risk of post hoc interpretations of smell loss, and potential recall bias in the context of extensive media coverage of COVID-19 anosmia. In addition, unsupervised home BSIT testing on a weekly basis may have led to several immeasurable confounders, including a possible form of olfactory training with repeated use of an identical set of 12 odorants and questionnaire answer choices. Although not previously studied for the BSIT, the test-retest reliability for the parent UPSIT is strong ($r = 0.95$).³² Additional limitations include the limited granularity of the 12-item BSIT, which may fail to detect hyposmia with the same sensitivity as its parent olfactory battery, the 40-item UPSIT, or those evaluating threshold and discrimination in addition to identification.

CONCLUSION

In this longitudinal study of ambulatory COVID-19 patients, self-reported and psychophysically measured olfactory dysfunction were moderately correlated and show similar improvement rates. Yet achievement of complete subjective recovery of olfactory function remains difficult with a measurable delay compared to objective

testing. Future investigations using both self-reported and psychophysical testing over an extended follow-up period may help us understand the prognosis of persistent subjective olfactory dysfunction, as well as the potential etiology of latency in subjective recovery. Self-reported olfactory function in the ambulatory setting therefore demonstrates utility in initial patient screenings for olfactory function, while psychophysical testing in conjunction with subjective assessments may be useful for counseling and following COVID-19 patients with persistent olfactory dysfunction.

CONFLICTS OF INTEREST

Adam S. DeConde is a consultant for Stryker endoscopy, Olympus, IntersectENT, Sanofi, and Optinose. The other authors have no financial disclosures.

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