High prevalence of olfactory disorders 18 months after contracting COVID-19

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Abstract

Reduced olfactory function is the symptom with the highest prevalence in COVID-19 with nearly 70% of individuals with COVID-19 experiencing partial or total loss of their sense of smell at some point during the disease. Recent reports suggest that more than 7 months after recovering from COVID-19, a large proportion of these individuals still have olfactory dysfunction of some form. To establish the prevalence of olfactory dysfunction 18 months and beyond, we tested 100 individuals with established COVID-19 in the first wave of the pandemic using psychophysical full-scale testing of smell and taste functions as well as assessments of parosmia. Participants were recruited from an ongoing study, comprising healthcare workers at a hospital in Stockholm, Sweden, that are regularly tested for SARS-CoV-2 IgG antibodies since the start of the pandemic in Sweden. To assess potential skewed recruitment of individuals with prior olfactory dysfunction and assess normal rate of dysfunctions in the used population, 44 SARS-CoV-2 IgG naïve individuals were also tested as a control group. One and a half year after COVID-19, more than one third of individuals recovered from COVID-19 demonstrated a clinical reduction in their sense of smell. Critically, nearly half of COVID-19-recovered individuals' complaint about parosmia. Prevalence of gustatory dysfunction was, however, low (3%). In summary, a full 65% of individuals recovered from COVID-19 experience olfactory dysfunction of some form 18 months later. Given the amount of time since initial insult to the olfactory system, it is likely that these olfactory problems are permanent.

Introduction

Olfactory dysfunction (OD) is a key symptom of COVID-19 with the prevalence of anosmia due to COVID-19 reported as 50% with an additional 10-20% reporting hyposmia[1]; a significant portion also report parosmia (olfactory distortion). Hence, at some point of the disease, nearly 70% experience either partial or total loss or distortion of their sense of smell[2]. Because OD is associated with a range of aversive health effects, such as depression and weight gain, the prevalence of COVID-19-related OD, and whether its transient or persistent, are vital public health questions. Early reports indicate that OD prevalence remains high beyond 7 months. However, many studies suffer from relaying on self-reports and either recruitment bias by recruiting individuals with pre-existing OD or not controlling for a potential self-selection of individuals with olfactory complaints, as well as lacking control group. To establish the prevalence of various ODs 1.5 year after COVID-19, we tested individuals confirmed as either COVID-positive or -negative using psychophysical testing of smell and taste functions and questionnaires.

Methods

Participants were recruited from the ongoing COMMUNITY study comprising healthcare workers at Danderyd Hospital, Stockholm. All participants are tested for SARS-CoV-2 IgG antibodies every four months since the start of the pandemic in Sweden[3]. From a total of 320 SARS-CoV-2 IgG positive healthcare workers (COVID+; average time since seroconversion 18 months), 100 volunteered, with two exclusions, leaving a final sample of 98 COVID+ participants (mean age 47; SD 12; all having had mild COVID-19). To assess potential recruitment bias towards individuals with OD, and to provide a prevalence of OD within the SARS-CoV-2 naïve sample population, an equal number of healthcare workers who were SARS-CoV-2 IgG negative at all sampling time points was invited (COVID-). Forty-four individuals (with 3 exclusions) were tested, giving a final COVID- sample of 41 (M=50 yo; SD=11). Olfactory function was assessed using the validated Sniffin' Sticks (Burghart, Germany) with its TDI score indicating normosmia (≥ 30.75), hyposmia (16.25-30.5), and anosmia (≤ 16.0). Gustatory evaluation was performed using a whole-mouth spray test of 5 taste qualities; score ≤3 labeled as hypogeusia. Prevalence of parosmia was assessed using a validated scale[4] and nasal problems/discomfort was assessed using the SNOT22 questionnaire[5]. Details on methods can be found in the eMethods. Informed consent was obtained, and all aspects approved by the Swedish Ethical Review Authority.

Results

One and a half year after COVID-19, the prevalence of olfactory loss in the COVID+ group was 37% (60% were unaware), with anosmia constituting 4% and hyposmia 33%. For COVID-, 20% were classified as hyposmic (clustered just below the hyposmia cut-off value; Figure 1A). SNOT222 confirmed that COVID+ experienced more nasal discomfort (M=45.9; SD=17.8) than COVID- (35.4; 11.7) (W=2482.5, p=0.0013; Figure 1B).

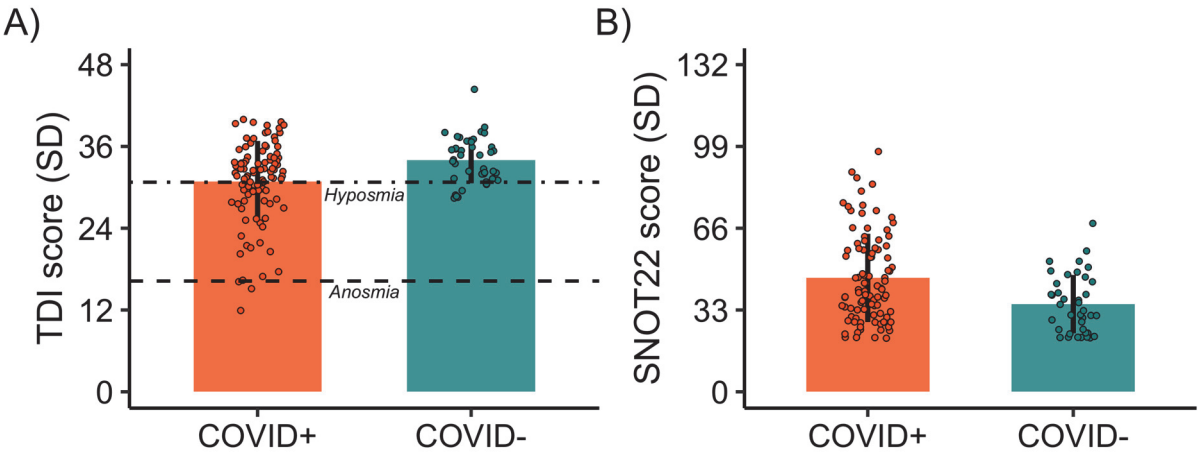

Figure 1. A) Mean and distribution of olfactory performance scores (TDI) in the COVID+ (orange) and COVID- (green) groups. Higher scores indicate better sense of smell. Dot-dashed line indicates cut-off for hyposmia (TDI < 30.7) and dashed line indicates cut-off for anosmia TDI < 16.0). **B**) Mean and distribution of SNOT22 scores. Higher scores indicate more nasal irritations/problems. In both panels, bars indicate group mean, circles indicate individual values, and error bars indicate standard deviation.

Gustatory testing showed that 3% of COVID+ suffered from hypogeusia compared to 0% in COVID-. Critically, 1.5 years after recovering from COVID-19, 49% of all COVID+ (excluding anosmia) experienced parosmia as compared to only 5% in COVID- (Figure 2A). Interestingly, the overlap between olfactory dysfunction and parosmia classification in the COVID+ group was small (20%; Figure 2B).

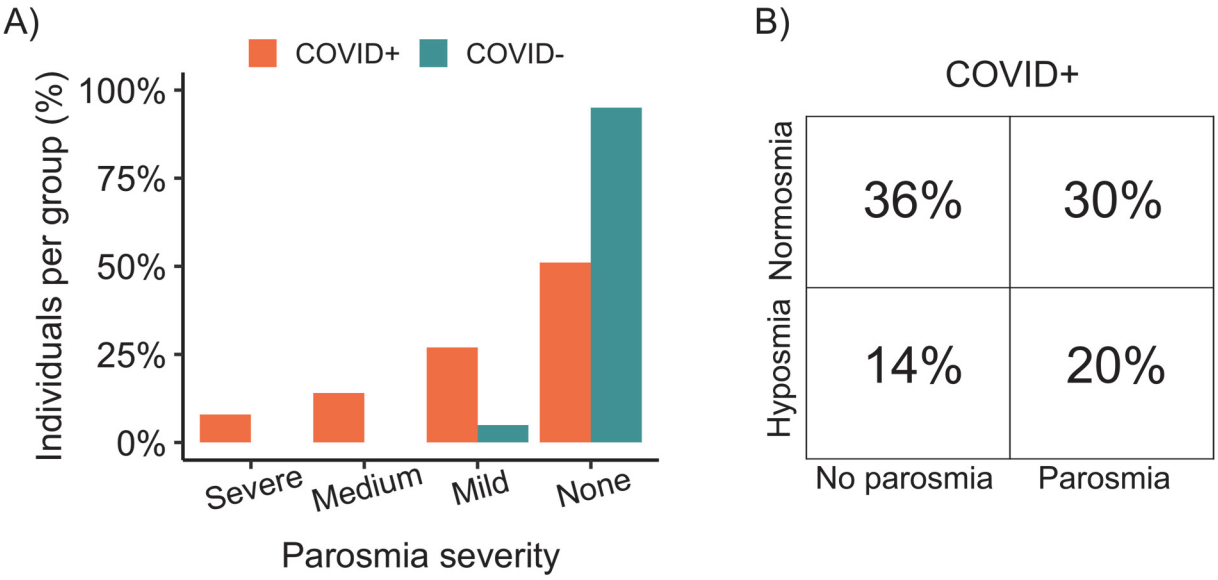

Figure 2. A) Percentage participants, per group, separated by their reported parosmia severity. **B**) Percentage of COVID+ participants with remaining olfactory functions (normosmia or hyposmia), grouped by classification of existing smell loss and existence of parosmia.

Discussion

A year and a half after recovering from COVID-19, more than a third of all SARS-CoV-2 IgG positive individuals still exhibit a clinically reduced sense of smell; very few display a loss of taste but a full 49% experience parosmia. Notable is that a fifth of individuals in the control group also displayed smell loss, a value often found in the general population[6], suggesting that the true COVID-19-related increase in prevalence is around 17%. In summary, a full 65% of individuals recovered from COVID-19 experience OD after 18 months, suggesting that these dysfunctions are permanent.

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eMethods

Participants

Two participants in the SARS-CoV-2 IgG positive (COVID+) group were excluded due to an inability to perform the tests and 3 participants in the SARS-CoV-2 IgG naïve (COVID-) group were excluded; reasons being a Parkinson's disease diagnose (a diagnose known to affect the sense of smell), excessive construction noise during testing, and refusal to perform some tests.

Psychometric odor assessment

Individual olfactory performance was assessed after the MRI data acquisition in both the pre- and the post-study. We measured odor detection threshold, olfactory quality discrimination, and cued olfactory identification, using the validated Sniffin' Sticks testing set which consists of felt-tipped pens filled with odorants; see details below. The sum of the threshold, discrimination, and identification (TDI) scores was used as an estimate of olfactory function.

Odor detection threshold: Absolute sensitivity was assessed for the odor n-Butanol using a three-alternative forced-choice staircase procedure with seven reversals in a 16-step binary dilution series.

Odor quality discrimination: Sixteen triplets of pens were presented to the participant. Each triplet consisted of two pens with identical odorants and one with an odorant of different quality.

Cued odor identification: Olfactory identification performance was assessed with a forced-choice cued identification task using 16 different odorants. Each odor was presented together with a cue card listing four alternative odor labels, and participant picked the label which best described the quality of the perceived odor.

The possible range for the threshold measure was 1-16, and for the discrimination and identification measures 0-16, with higher scores indicating better performance. Participants were blindfolded during the threshold and discrimination tests.

Psychometric taste assessment

The five taste qualities were delivered with a spray bottle to the whole mouth in the following concentrations: sweet, 1 g sucrose; sour, 0.5 g citric acid; salty, 0.75 g sodium chloride; Umami, 0.4 g monosodium glutamate; and bitter, 0.005 g quinine hydrochloride, each diluted in 10 g distilled water. After each stimulus, participants identified the taste qualities by pointing to the selected one on a card where all four qualities were listed. The participant rinsed their mouth twice with water between each taste quality.

Statistical analyses

To correct for the uneven sample size between the two groups, non-parametric statistical group comparisons was performed using a two-sided Wilcoxon rank sum test with continuity correction.

Bibliography