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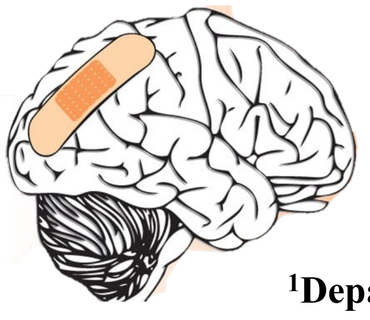

# Long COVID-19 effects on the olfactory, gustatory, and cognitive functions

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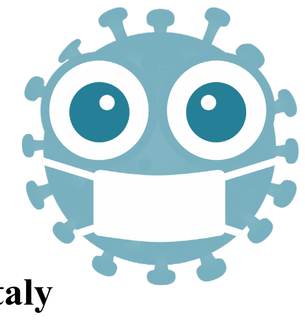


## INTRODUCTION & AIM

COVID-19, caused by the SARS-CoV-2 virus, emerged in late 2019 in Wuhan, China, giving rise to a global pandemic with severe health, social, and economic consequences [1]. Beyond the acute phase of infection, Long COVID-19 has been identified as a clinical condition characterized by the persistence of symptoms for weeks or months following the initial infection [2,3]. The most frequently reported symptoms include chronic fatigue, cognitive impairment, myalgia, respiratory difficulties, and memory deficits [4,5]. SARS-CoV-2 infection has further highlighted the crucial role of olfaction and taste in daily life, which are often impaired during both the acute phase and Long COVID-19 [6]. Chemosensory dysfunctions are associated with damage in the olfactory and gustatory functions and represent a clinically relevant manifestation of the disease [7,8].

**This study aimed** to analyze the frequency of the most common symptoms of Long COVID-19. Long COVID-19 symptoms were evaluated, with particular emphasis on olfactory and gustatory impairments, as well as potential cognitive dysfunctions. Additionally, the willingness of participants residing in Sardinia to undergo objective testing was assessed, to integrate self-reported data with clinical experimental measures.

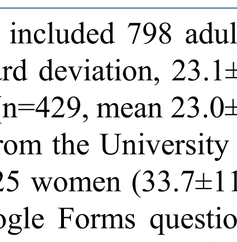
## MATERIAL & METHODS

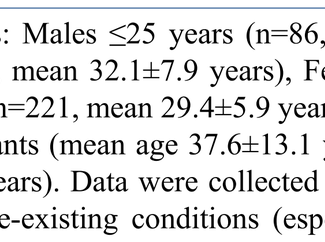
This study included 798 adults, stratified by sex and age groups: Males ≤25 years (n=86, mean age±standard deviation, 23.1±1.5 years), Males >25 years (n=62, mean 32.1±7.9 years), Females ≤25 years (n=429, mean 23.0±1.6 years), and Females >25 years (n=221, mean 29.4±5.9 years).
A subset from the University of Cagliari consisted of 48 participants (mean age 37.6±13.1 years), including 25 women (33.7±11.0 years) and 23 men (41.7±14.1 years). Data were collected via an online Google Forms questionnaire, capturing demographics, pre-existing conditions (especially neurological disorders), olfactory disturbances, symptoms during acute COVID-19 and Long COVID phases (with emphasis on fatigue and cognitive impairments). Responses used a binary Yes/No scale (coded as 1/0). **Olfactory function** was evaluated with the Sniffin' Sticks test (Burghart Messtechnik, Wedel, Germany), measuring odor threshold (**OT**), discrimination (**OD**), and identification (**OI**); the total **TDI** score classified outcomes as anosmia (≤16), hyposmia (16.25–30.5), normosmia (30.75–41.25), or hyperosmia (>41.5) [9,10]. **Gustatory function** was assessed using Taste Strips (Burghart Messtechnik, Wedel, Germany) for sweet (**SW**), sour (**SO**), salty (**SA**), bitter (**BI**) tastes (total score 0–16; normogeusia ≥9, hypogeusia <9), with different concentrations [11].

## RESULTS

**Table 1**. Prevalence (%) of gustatory and olfactory dysfunction, asthenia, myalgia, and dyspnea among participants divided by gender (M = male, W = female) and age (<25 years, >25 years). Data are reported in COVID-19 (C) and Long COVID-19 (LC) subjects. Differences between COVID-19 and Long COVID-19 groups (C/LC) are shown for each subgroup. Significant differences are indicated in bold with p-values ($p < 0.05$).

| | Percentages | | | | Significance | | | |
|---|---|---|---|---|---|---|---|---|
| | M<25 years | M>25 years | W<25 years | W>25 years | M<25 years C/LC | M>25 years C/LC | W<25 years C/LC | W>25 years C/LC |
| Olfactory dysfunction | | | | | | | | |
| C | 10.5% | 24.2% | 20.5% | 20.8% | p>0.05 | **p<0.001** | **p<0.0001** | **p<0.0001** |
| LC | 4.7% | 3.2% | 3.7% | 3.2% | | | | |
| Gustatory dysfunction | | | | | | | | |
| C | 11.6% | 22.6% | 21.2% | 19.5% | p>0.05 | p>0.05 | **p<0.0001** | **p<0.01** |
| LC | 10.5% | 9.7% | 7.9% | 9.0% | | | | |
| Asthenia | | | | | | | | |
| C | 65.1% | 64.5% | 82.8% | 81.0% | **p<0.0001** | **p<0.02** | **p<0.0001** | **p<0.0001** |
| LC | 30.2% | 43.5% | 55.7% | 60.6% | | | | |
| Myalgia | | | | | | | | |
| C | 52.3% | 56.5% | 59.7% | 66.1% | **p<0.0001** | **p<0.0001** | **p<0.0001** | **p<0.0001** |
| LC | 7.0% | 11.3% | 13.8% | 18.6% | | | | |
| Dyspnoea | | | | | | | | |
| C | 23.3 % | 24.2% | 40.6% | 41.6% | p>0.05 | p>0.05 | p>0.05 | p>0.05 |
| LC | 18.6% | 27.4% | 38.2% | 40.7% | | | | |



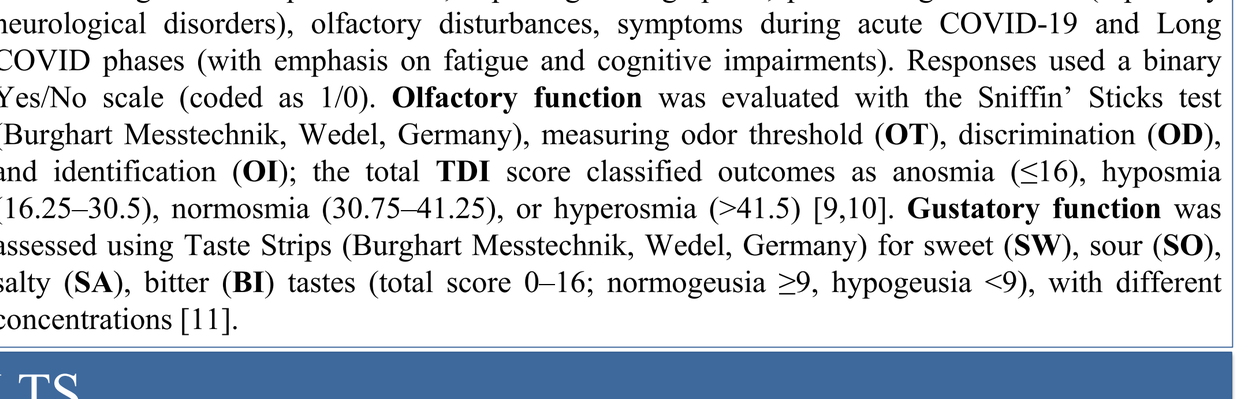




**Figure 1**. **A)** Mean olfactory test scores (mean ± SD) for Sardinian control subjects (red bars) versus patients (purple bars) in the OT, OD, OI, TDI. **B)** Mean gustatory test scores for SW, SA, SO, BI and TOT measures. Group differences were assessed using independent-samples t tests; asterisks indicate statistically significant differences between controls and patients.
*p < 0.05, **p < 0.01

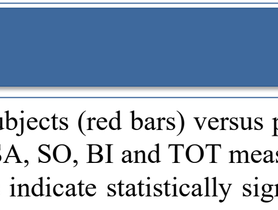



**Table 2**. Heatmap of the Pearson Correlation (r) between cognitive and neuropsychiatric symptoms by sex and age (*p < 0.05, **p < 0.01)

1 / 0,5 / 0,25 / 0 / -0,05

**M<25 years**

| | *Insomnia* | *Brain fog* | *Anxiety* | *Difficulty concentrating* | *Memory disorders* | *Cognitive slowing* |
|---|---|---|---|---|---|---|
| *Insomnia* | 1,0 | | | | | |
| *Brain fog* | 0,152 | 1,0 | | | | |
| *Anxiety* | -0,035 | 0,195 | 1,0 | | | |
| *Difficulty concentrating* | 0,144 | 0,899** | 0,260* | 1,0 | | |
| *Memory disorders* | -0,048 | 0,618** | 0,184 | 0,522** | 1,0 | |
| *Cognitive slowing* | -0,032 | 0,417** | 0,051 | 0,308** | 0,214* | 1,0 |

**M>25 years**

| | *Insomnia* | *Brain fog* | *Anxiety* | *Difficulty concentrating* | *Memory disorders* | *Cognitive slowing* |
|---|---|---|---|---|---|---|
| *Insomnia* | 1,0 | | | | | |
| *Brain fog* | 0,382** | 1,0 | | | | |
| *Anxiety* | 0,435** | 0,306* | 1,0 | | | |
| *Difficulty concentrating* | 0,058 | 0,828** | 0,215 | 1,0 | | |
| *Memory disorders* | 0,334** | 0,699** | 0,330** | 0,544** | 1,0 | |
| *Cognitive slowing* | 0,180 | 0,555** | 0,077 | 0,476** | 0,175 | 1,0 |

**F<25 years**

| | *Insomnia* | *Brain fog* | *Anxiety* | *Difficulty concentrating* | *Memory disorders* | *Cognitive slowing* |
|---|---|---|---|---|---|---|
| *Insomnia* | 1,0 | | | | | |
| *Brain fog* | 0,301** | 1,0 | | | | |
| *Anxiety* | 0,399** | 0,320** | 1,0 | | | |
| *Difficulty concentrating* | 0,314** | 0,897** | 0,332** | 1,0 | | |
| *Memory disorders* | 0,244** | 0,599** | 0,356** | 0,550** | 1,0 | |
| *Cognitive slowing* | 0,187** | 0,396** | 0,202** | 0,306** | 0,360** | 1,0 |

**F>25 years**

| | *Insomnia* | *Brain fog* | *Anxiety* | *Difficulty concentrating* | *Memory disorders* | *Cognitive slowing* |
|---|---|---|---|---|---|---|
| *Insomnia* | 1,0 | | | | | |
| *Brain fog* | 0,277** | 1,0 | | | | |
| *Anxiety* | 0,368** | 0,381** | 1,0 | | | |
| *Difficulty concentrating* | 0,265** | 0,911** | 0,370** | 1,0 | | |
| *Memory disorders* | 0,262** | 0,603** | 0,307** | 0,606** | 1,0 | |
| *Cognitive slowing* | 0,124** | 0,460** | 0,215** | 0,370** | 0,417** | 1,0 |

## CONCLUSION

This study enphasizes the importance of ongoing follow-up of patients beyond the acute phase of SARS-CoV-2 infection, with a particular focus on persistent neurological, cognitive, and sensory symptoms. Objective assessments supported patients' subjective reports of olfactory and gustatory dysfunction, indicating that these tests should be incorporated into routine clinical evaluation.
Future research should identify predictors of Long COVID, clarify its pathophysiological mechanisms, and guide the development of targeted rehabilitation strategies.

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