Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Olfactory-related quality of life impacts psychological distress in people with COVID-19: The affective implications of olfactory dysfunctions

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) often causes chemosensory impairment, and olfactory dysfunctions may have negative consequences on psychological distress. This study aimed at assessing which dimension of perceived olfactory disfunctions (i.e., subjective olfactory capability, smell-related problems, or olfactory-related quality of life [QoL]) was most associated with psychological distress in people diagnosed with COVID-19.

Methods: 364 participants (65 men and 299 women) diagnosed with COVID-19 on average 7 months prior to the beginning of the study were recruited between June 5 and 21, 2021, to take part in an online cross-sectional survey. Participants answered questions on demographics, clinical factors, perceived olfactory functioning, and psychological distress. Hierarchical multiple linear regression analysis was conducted, assessing the role of demographics, clinical factors, and perceived olfactory functioning dimensions on psychological distress.

Results: More than half of the participants met the cut-off for all perceived olfactory dysfunctions scales and psychological distress. Being women, smoker, with comorbidities, and greater severity of COVID-19 symptoms were associated with higher scores on psychological distress. Among perceived olfactory functioning scales, only impairment in olfaction QoL was associated with psychological distress.

Limitations: Limitations concerned the cross-sectional nature of the study and the unbalanced sample in terms of gender.

Conclusions: The study confirmed the core intertwining between mood, perceived QoL, and olfactory functioning, showing how impairments in olfactory processing are strongly correlated with psychological distress through the impact they have on the perceived QoL.

1. Introduction

Coronavirus disease 2019 (COVID-19), which is caused by the Sars-Cov-2 virus, has spread across the world very quickly, representing a global health emergency due to the impressive rates of deaths and hospitalizations (Cantone and Gamerra, 2020; Cecchetto et al., 2021). COVID-19 is mainly characterized by symptoms of fever, cough, and shortness of breath, as well as by the onset of chemesthesis, smell and taste dysfunctions, particularly anosmia and hyposmia. In addition to being iatrogenic as to the overall individual's mental health (Xiong et al., 2020; Salari et al., 2020), COVID-19 is indeed associated with loss or impairment of the sense of smell (Cameron et al., 2021). Therefore, the outbreak of the COVID-19 witnessed a renewed interest in the research on olfactory dysfunctions and the effects they have on the individuals affected by the disease.

Even before the outbreak of the COVID-19 pandemic, it was well-known that olfactory dysfunctions have negative consequences on the quality of life (QoL; Frasnelli and Hummel, 2005; Shu et al., 2011), which can be defined as the individuals' conscious perception of their well-being. Food and eating habits, feelings of vulnerability, mood changes, and social life all appear to worsen in the face of smell loss or impairment (Hummel and Nordin, 2005). More specifically, olfactory dysfunctions are associated with decreased QoL and mental health problems (e.g., anxiety and depression) (Erskine and Philpott, 2020).

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Olfactory deficits have been also reported as markers for several neuropsychiatric disorders such as neurodegenerative pathologies (e.g., Parkinson's or Alzheimer's disease; Wilson et al., 2009) and mental illnesses (e.g., schizophrenia; Turetsky et al., 2009). The four processes in which olfaction is typically articulated, namely, perception, discrimination, identification, and valence, have been less studied in individuals suffering from bipolar disorder (Henry et al., 2020). However, identification of pleasant odors seems also to be altered in this population (Kazour et al., 2020). The volume of the olfactory bulb is significantly reduced in patients with acute major depression disorder (Negoias et al., 2010), and appears to be closely related to symptom severity (Wang et al., 2020). Depression has also been associated to olfactory dysfunctions (Siopi et al., 2016). Furthermore, by virtue of their power to elicit emotions, odors have been suggested to be useful in treating this condition (Kadohisa, 2013). In fact, patients suffering from depression have reduced olfactory ability compared to healthy controls; conversely, patients with olfactory dysfunction tend to suffer from depression that worsens with severity of smell loss (Kohli et al., 2016).

The association between olfactory dysfunctions and mood disorders can be better understood if we focus on the neurobiological processes entailed in the decorrelation of the olfactory stimulus. Primary olfactory areas, indeed, are directly linked with many brain regions involved in emotion and mood, even though these can be differently influenced by olfaction (Kontaris et al., 2020). Whether consciously perceived or not, odors can modulate mood and emotion, and are also associated with emotional memory (Kadohisa, 2013). Odors elicit dichotomic affective responses, which can be pleasant or unpleasant. In fact, olfactory processing is associated with brain regions that subserve emotional processing, namely, the orbitofrontal cortex, the amygdala, and the hippocampus (Gottfried, 2006). Olfactory impairments can indeed cause reduced emotional processing, which relies on several distributed networks in the brain, also depending on whether emotions are perceived as positive or negative (Han et al., 2019). Even though it is the phylogenetically oldest sensory mode, human beings and many other animals possess to appraise the world, olfaction has long been considered of minor importance in human action and perception (Bochicchio and Winsler, 2020; Calvi et al., 2020). The development of the neocortex in humans and some other primates determined the predominance of the visual sensory modality over olfaction. However, evidence exists as to the influence that chemosensory signals associated with body odors have on human and animal behavior (Hofer et al., 2020). As opposed to sight, where the intertwining between context and background is essential to determine visual perception, olfaction refers to a sensory mode that produces unified, one-dimensional, and all-saturating perceptions (Bochicchio et al., 2018, 2019; Bochicchio and Winsler, 2020).

Considering the role of olfactory disfunctions in COVID-19, Sedaghat et al. (2020) pointed out the relevance of hyposmia and anosmia as a tool for identifying infected patients, in particular, those that are asymptomatic carriers and therefore unaware of their disease. Dubé et al. (2018) had already shown that coronaviruses attack the central nervous system through the neuroepithelium and propagate from the olfactory bulb. Coronaviruses-related olfactory dysfunctions are caused by the destruction of the olfactory epithelium, whereby odors are impaired from binding to the corresponding receptors (Murphy et al., 2003). Besides the intensification or precipitation of negative mental health outcomes – namely, post-traumatic stress disorder, alcohol abuse, obsessive-compulsive behaviors, anxiety, depression, panic, and paranoia (Pedrosa et al., 2020) – COVID-19-related olfactory dysfunctions are also significantly correlated with psychological distress and affective disorders (Nettore et al., 2021). In addition, smell loss caused by COVID-19 has been shown to negatively impact the individual's QoL, significantly influencing the person's daily activities associated with olfactory functions (Elkholi et al., 2021). In this regard, Speth et al. (2020) found that decreased sense of smell due to COVID-19 is associated with depressed mood and anxiety, which in turn are not associated with other COVID-19 symptoms such as fever, cough, or shortness of breath. In other words, the severity of core, typical COVID-19 symptoms (i.e., fever, cough, and shortness of breath) is not associated with emotional problems, whereas olfactory dysfunctions are. Therefore, Speth et al. (2020) raised the hypothesis that emotional disturbances, psychological distress, and olfactory dysfunctions might be possible manifestations of a central nervous system mechanism related to COVID-19. However, no previous studies clarified which dimension of perceived olfactory disfunctions – that, according to Pusswald et al. (2012) are the subjective olfactory capability, the smell-related problems, and the olfactory-related QoL – is most associated with psychological distress and affective disorders in people diagnosed with COVID-19.

Thus, the current study had the objective to assess which domain of perceived olfactory disfunctions is stronger associated with psychological distress. Several confounding variables were considered, as follows: age, gender, educational level, smoking history, duration of the COVID-19 related symptoms, hospitalization, comorbidities (e.g., anxiety, depression, cancer, diabetes), drug consumption to treat the COVID-19 (yes vs. no), and severity of COVID-19 symptoms. Indeed, previous research has shown that certain socio-demographic and clinical factors can affect the olfactory functioning more than others; therefore, it is plausible to hypothesize that they may exacerbate the impact of olfactory dysfunctions on psychological distress. Specifically, Hasan et al. (2021) found that younger patients and smokers are more likely to experience olfactory dysfunctions than their counterparts. Meini et al. (2020) found that olfactory dysfunctions in women are less frequent than men, but longer lasting. Castillo-López et al. (2020) found that low educational level and medical comorbidities were associated with greater olfactory dysfunctions. Findings concerning the association between severity of the COVID-19 and olfactory dysfunctions are mixed (Lechien et al., 2021; Vaira et al., 2020), while the longer the duration of the disease, the stronger the olfactory dysfunctions (Vaira et al., 2020).

2. Methods

2.1. Procedures

A cross-sectional web-based Italian survey was administered via Qualtrics software between 5 and 21 June 2021. The participants were reached through advertisements published on Italian online social groups sharing their experiences about being infected by Sars-Cov-2. Additionally, participants were also involved through a snowball recruitment procedure, by asking people interested in the survey to share the study to other potential interested participants they personally knew. All participants took part in our survey on a voluntary basis and were not granted any economic incentive for their participation.

By clicking on the link provided, participants were directed to the first page of the survey, where informed consent of the study was uploaded. Thus, participants were informed about objectives, benefits, risks, information about researchers, and anonymity of the survey. After reading the informed consent, participants had to give their consent to participate in the study by clicking "I accept to participate in the study." To avoid missing data, all questions were mandatory, but participants were informed about their right to stop the survey in any moment they wanted.

The study was approved by the ethical committee of the University of *Blinded for Review* (protocol number *Blinded for Review*), developed in accordance with the EU General Data Protection Regulation, and designed in accordance with the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects.

2.2. Participants

Participants could take part in the survey if they satisfied the following inclusion criteria: (1) being at least 18 years old (the Italian age of consent); (2) being or having been positive for COVID-19 not >1 year ago; and (3) having received a certified diagnosis (e.g., by swab or

serological test). A total of 383 participants took part in the survey. Among these, 19 did not satisfy one of the inclusion criteria. Thus, the final sample was composed of 364 Italian participants.

2.3. Measures

2.3.1. Demographics and clinical information

Sociodemographic and clinic variables included age, gender (men, women, and other with specification), smoking history (never smoker, past smoker, and current smoker), time of the diagnosis for COVID-19 (from "less than one month ago" to "1 year ago"), duration of the COVID-19 related symptoms, hospitalization (yes vs. no), comorbidities (e.g., anxiety, depression, cancer, diabetes; yes vs. no), drug consumption to treat the COVID-19 (yes vs. no), and severity of COVID-19 symptoms. This latter dimension was measured by asking participants to rate the typical COVID-19 related symptoms (i.e., fever, myalgia, cough, shortness of breath, chest pain, hearth palpitations, gastrointestinal disturbances, conjunctivitis, sore throat-rhinorrhea, and headache; olfactory and taste disorders were excluded as assessed through a specific scale) reported by Adorni et al. (2020) on a 10-Likert scale, from 1 ("absent") to 10 ("maximum"). A composite scale of "severity of COVID-19 symptoms" was created by summing the scores obtained at each symptom.

2.3.2. Perceived olfactory functioning

Subjective perceptions of one's own olfactory functioning were measured through the 12-item questionnaire for the Assessment of Self-Reported Olfactory Functioning and Olfaction-Related Quality of Life (ASOF; Pusswald et al., 2012). ASOF consisted of three domains, as follows: (1) Subjective Olfactory Capability scale (SOC), that assesses perceived olfactory performance through 1 item (i.e., "How would you rate your sense of smell over the past four weeks?") on a Likert scale ranging from 0 ("unable to smell") to 10 ("best possible smell"); (2) Smell-Related Problems scale (SRP), that measures subjective capability of perceiving specific odors scale (e.g., "During the past four weeks, how often have you had problems smelling the odor of spoiled food?") through 5 items on a Likert scale ranging from 1 ("very often") to 5 ("never"); and (3) Olfactory-Related Quality of Life scale (ORQ), that assesses perceived QoL concerning olfactory functioning in different domains (i.e., cooking, sexual life, eating food, drinking beverages, using perfumes, and perceiving the scent of flowers) through 6 items on a Likert scale ranging from 1 ("Very much impaired") to 5 ("not at all impaired"). SOC $\leq$ 3, SRP $\leq$ 2.9, and ORQ $\leq$ 3.7 have been individuated as cut-off scores indicating, respectively, abnormal olfactory capabilities, problems in smelling odors, and smell-related problems in QoL. Thus, lower scores on all ASOF subscales indicate greater perceived impairment in olfactory functioning. The α coefficient for the current sample was 0.97 for SRP scale and 0.92 for ORQ.

2.3.3. Psychological distress

Psychological distress was assessed through the Kessler Psychological Distress Scale (K10; Kessler et al., 2002), a 10-item questionnaire detecting psychological distress based on questions about anxiety and depressive symptoms experienced during the last 30 days. The response options ranged from 1 ("none of the time") to 5 ("all of the time"). An example item is "During the last 30 days, about how often did you feel tired out for no good reason?". Higher scores indicate greater psychological distress. Consistently with Andrews and Slade (2001), the cut-off score of 24 was adopted to detect the likelihood of presence of moderate-to-severe psychological distress. The α coefficient for the current sample was 0.93.

2.4. Preliminary and statistical analyses

Preliminary analyses concerned the translation and reliability assessment of the ASOF, a scale that was not previously validated in Italy. For this reason, ASOF has been translated into Italian following all the phases of the back-translation method suggested by Behling and Law (2000). Then, a Confirmatory Factor Analysis (CFA) with the Maximum Likelihood estimation with Robust Standard Errors was performed to assess the goodness of fit of the ASOF using R-Studio, and the following indices were used (Kline, 2011): Chi-Square/degrees of freedom (χ^2/df), Root Mean Square Error of Approximation (RMSEA), Standardized Root Mean Square Residual (SRMR), Comparative Fit Index (CFI), and Tucker–Lewis Index (TLI). The fit indices of the ASOF were: χ^2/df = 1.92, p = 0.058; RMSEA = 0.050; SRMR = 0.021; CFI = 0.992; TLI = 0.988. Based on the suggestions by Hooper et al. (2009), the goodness of fit indices of the Italian version of the ASOF can be considered more than acceptable. In addition, although K-10 is a scale widely used in Italy both before (e.g., Barbero et al., 2015; Bartoli et al., 2018; Carrà et al., 2011) and during the Covid-19 outbreak (e.g., De Micco et al., 2020; Janiri et al., 2021; Moccia et al., 2020), there is no specific Italian study on its validation. Therefore, we performed another CFA with the same method used for ASOF. The CFA showed very good fit indices for the Italian version of K10, as follows: χ^2/df = 1.89, p = 0.061; RMSEA = 0.049; SRMR = 0.022; CFI = 0.992; TLI = 0.984.

All other statistical analyses were performed with SPSS version 27, setting the level of significance at 0.05.

First, participants characteristics, descriptive statistics (means, standard deviation, and cut-off scores of the scales), and bivariate correlations between the main study's variables (perceived olfactory functioning and psychological distress) were calculated.

Then, the associations between perceived olfactory functioning and psychological distress were assessed through a hierarchical multiple linear regression analysis, with psychological distress as the outcome variable and perceived olfactory functioning dimensions as independent variables. This analysis was controlled for age, gender (1 = male; 2 = female), smoking history (0 = smoker; 1 = no-smoker), duration of the COVID-19 related symptoms, hospitalization (0 = no; 1 = yes), comorbidities (0 = no; 1 = yes), drug consumption to treat the COVID-19 (0 = no; 1 = yes), and severity of COVID-19 symptoms. As an indicator of the effect size, Cohen's f^2 method was used, according to which $f^2 \geq 0.02$, $f^2 \geq 0.15$, and $f^2 \geq 0.35$ represent small, medium, and large effect sizes (Cohen, 1988). To ascertain the absence of multicollinearity, we assessed the variance inflation factor (VIF). Conventionally, VIFs near or above 5 may be considered acceptable values (Akinwande et al., 2015).

3. Results

3.1. Socio-demographic and clinical characteristics of participants

Sixty-five (17.9 %) participants were males and 299 (82.1 %) females. Participants ranged in age from 18 to 79 years old (M = 42.46, SD = 13.53). Most of the sample had an educational level $\leq$ high school (n = 231; 63.5 %).

Participants were diagnosed with COVID-19 on average 7 months prior to the start of the study (SD = 3.10), only 8 (2.2 %) were asymptomatic, 32 (8.8 %) were hospitalized, and 180 (49.5 %) took drugs to treat the Sars-Cov-2. About a quarter of the participants (n = 94; 25.8 %) declared to have some type of comorbidities, as follows: anxiety (n = 39; 10.7 %), depression (n = 12; 3.3 %), cancer (n = 1; 0.3 %), or diabetes (n = 3; 0.8 %). Finally, 61 participants (16.8 %) were smokers.

3.2. Descriptive statistics and bivariate correlations

Means, standard deviations, and bivariate correlations between the main variables analyzed (perceived olfactory functioning and psychological distress) are reported in Table 1. Percentages of participants who were above the cut-off of dimensions analyzed are also reported.

Results of the Pearson correlation indicated that all healthy olfactory functioning variables correlated positively with each other and negatively with psychological distress.

Table 1
Descriptive statistics and bivariate correlations between perceived olfactory functioning and psychological distress.

	1	2	3	4	*M* ± *SD*	> *cut-off n (%)*
SOC	–				3.65 ± 3.59	238 (65.4)
SRP	0.50***	–			2.25 ± 1.37	226 (62.1)
ORQ	0.54***	0.70***	–		2.78 ± 1.36	238 (65.4)
K10	−0.12*	−0.20***	−0.33***	–	29.39 ± 10.09	247 (67.9)

Notes. *SOC* = Subjective Olfactory Capability; *SRP* = Smell-Related Problems; ORQ = Olfactory-Related Quality of Life; K10 = Kessler Psychological Distress Scale; *M* = Mean; *SD* = Standard Deviation. *$p < 0.05$; ***$p < 0.001$.

Furthermore, more than half of the sample met the cut-off for all the perceived olfactory dysfunctions scales and psychological distress.

3.3. Associations between perceived olfactory functioning and psychological distress

Results for hierarchical multiple linear regression analysis are reported in Table 2. All VIFs were acceptable, ranging from 1.03 to 2.34.

Demographics and clinical characteristics in step 1 explained 23.9 % of variation in psychological distress, with a medium effect size (f^2 = 0.31). Specifically, being women, smoker, with comorbidities, and greater severity of COVID-19 symptoms were associated with higher scores on psychological distress.

Adding perceived olfactory functioning scales in step 2 of the regression model explained a significant additional 5.1 % of the variation in psychological distress. Specifically, among perceived olfactory functioning scales, only impairment in olfaction QoL was associated with higher levels of psychological distress.

The final statistical model for all dimensions accounted for 29.1 % of the variance in psychological distress, with a large effect size ($f^2 = 0.41$).

Table 2
Hierarchical multiple linear regression of psychological distress on perceived olfactory functioning dimensions.

	Psychological distress		
	B (SE)	*β*	*95 % CI*
Step 1 – Control variables			
Age	−0.05 (0.04)	−0.07	−0.12, 0.22
Gender (male)	5.74 (1.26)	0.22***	3.25, 8.23
Smoker (no)	2.63 (1.28)	0.10*	0.12, 5.14
Duration of symptoms	0.27 (0.21)	0.06	−0.14, 0.67
Hospitalization (no)	−0.56 (1.76)	−0.02	−4.01, 2.90
Drugs for COVID-19 (no)	−0.56 (0.96)	−0.03	−2.44, 1.32
Comorbidities (no)	3.42 (1.10)	0.15**	1.25, 5.59
Severity of symptoms	1.80 (0.27)	0.33***	1.27, 2.33
	R^2 = 0.239; F = 13.97***		
Step 2 – Olfactory functioning			
Age	−0.05 (0.04)	−0.07	−0.12, 0.02
Gender (male)	5.28 (1.23)	0.20***	2.85, 7.70
Smoker (no)	2.77 (1.24)	0.10*	0.32, 5.22
Duration of symptoms	0.29 (0.20)	0.07	−0.10, 0.68
Hospitalization (no)	0.29 (1.72)	0.01	−3.09, 3.67
Drugs for COVID-19 (no)	−0.08 (0.93)	−0.01	−1.92, 1.75
Comorbidities (no)	3.79 (1.07)	0.16***	1.67, 5.90
Severity of symptoms	1.36 (0.28)	0.25***	0.81, 1.91
SOC	0.09 (0.15)	0.03	−0.22, 0.39
SRP	0.16 (0.48)	0.02	−0.78, 1.10
ORQ	−2.02 (0.51)	−0.27***	−3.02, −1.02
	R^2 = 0.291; ΔR^2 = 0.051***; F = 13.11***		

Notes. *B* = Unstandardized regression coefficient; *SE* = Standard error; *CI* = Confidence interval; *β* = Unstandardized regression coefficient; R^2 = R-square; ΔR^2 = Change in R^2; *SOC* = Subjective Olfactory Capability; *SRP* = Smell-Related Problems; ORQ = Olfactory-Related Quality of Life. ***$p < 0.001$; **$p < 0.01$; *$p < 0.05$.

Finally, to assess the weight of specific ORQ dimensions on psychological distress we run another hierarchical multiple linear regression, with psychological distress as the outcome variable and the six items of the ORQ as independent variables. This analysis was controlled for covariates resulted significant in the previous regression model (i.e., gender, smoker status, comorbidities, and severity of symptoms). Among all items, only item 8 (i.e., sexual life) and item 11 (i.e., using perfumes) resulted statistically significant (F (10, 353) = 15.59, $p < 0.001$), explaining 28.7 % of the variance in psychological distress, with a large effect size ($f^2 = 0.40$). Specifically, impairment in sexual life ($b = -0.17$, $p = 0.003$) and in using perfumes ($b = -0.20$, $p = 0.023$) were associated with higher scores on psychological distress.

4. Discussion

The current study was aimed at assessing the association between domains and effects of olfactory dysfunctions and psychological distress. Results mainly indicated that, among the domains of perceived olfactory functioning, the impairment in olfaction QoL was the only domain associated with psychological distress.

First, it is noteworthy that more than half of the participants of our study met the cut-off for all perceived olfactory dysfunctions scales and psychological distress. This result confirmed a finding already present in the literature, namely, the fact that olfactory dysfunctions are strongly correlated with psychological distress. Houghton et al. (2019), for instance, found that individuals who consider themselves "odor sensitive" show increased symptoms of anxiety, depression, and psychological distress. In fact, reduced olfactory sensitivity tends to accompany depressive symptoms, and this correlation has been suggested to be mediated by modifications in brain regions that subserve primary olfactory processing, such as the amygdala and piriform cortex (Pollatos et al., 2007). Conversely, depressive symptomatology negatively impacts olfactory functioning (Pabel et al., 2018), which might thus be taken as a marker for depression (Croy et al., 2014). Also, the severity of major depressive disorders has been shown to be associated with impairments in odor identification (Khil et al., 2016). Lower thresholds in odor detection, greater olfactory awareness, and enhanced reactivity to odors have been found in individuals with panic disorder as well (Burón et al., 2015). When compared to non-infected persons, COVID-19 patients can maintain a similar capacity to recognize odors, but the intensity of the perceived odors appears as significantly diminished (Nettore et al., 2021). That is, COVID-19 seems to be associated with impairment of the *quantitative* features of odor recognition, but not with its *qualitative* aspects. Impairment in the sense of olfaction, which is the phylogenetically oldest sensory mode human beings are endowed with, significantly impacts mental health and psychological well-being. Therefore, mental health seems to be strongly influenced by how functional our senses are in determining the features of our surroundings. Ultimately, COVID-19-related anosmia can have serious consequences for the person's sense of mental health and well-being (Gerkin et al., 2021).

As to the significance of covariate variables, we found that being women, being a smoker, having comorbidities, and manifesting greater severity of COVID-19 symptoms was associated with higher scores on psychological distress. It is well-known that, even when they present similar physical or psychiatric problems, women tend to seek medical care more than men (Koopmans and Lamers, 2007). Barsky et al. (2001) also found that gender differences exist as to the referred psychosomatic problems by men and women, whereby the latter report more intense, frequent, and numerous symptoms than the former. Smoking habits seem also to be intrinsically related to psychological distress. There is indeed a significant relationship between tobacco smoking and mental conditions such as depression (Wiesbeck et al., 2008) and anxiety (Morissette et al., 2007). In this regard, Fischer et al. (2012) demonstrated the interconnectedness between the use of tobacco and psychopathology. Instead, results concerning the associations of comorbidities

and greater severity of COVID-19 symptoms with psychological distress confirmed previous studies reporting that, among others, these variables are significant predictors of negative mental health outcomes in people diagnosed with COVID-19 (e.g., Liu et al., 2020).

However, the main result of our study consists in the fact that, among the measures obtained through the ASOF (Pusswald et al., 2012), only impairment in olfactory-related QoL was associated with higher levels of psychological distress. This finding may be explained by taking into account that the impact of olfaction on QoL seems to be mediated by the immediacy that characterizes the pathway of the sense of olfaction when the odor is processed in the olfactory areas of the brain, and by the subsequent recording of the smell as a pre-reflective perception, as it can be registered also by non-concept-using individuals (Roberts, 2015). Conscious awareness is often bypassed by the unconscious triggering of memories upon odor perception, which can be influenced by stimulus-related emotions, and by the individual's actual emotional state as well (Chen and Dalton, 2005). Yet olfaction first and foremost impacts the "here and now," as it is associated with the degree to which we can sense the external world immediately and pre-reflectively, in a way that points to the relevance of our core bodily self-awareness (Colombetti, 2011). Olfaction appears to shed light on the realm of pre-reflective experience because smell is often not (yet) explicitly thematized as an "object" for one's self-awareness (Picolas and Soueltzis, 2019). Therefore, olfactory perception may strongly impact the QoL as a pre-reflective appraisal of the external world and may be associated with the immediacy of our perception of the surroundings and our modalities of non-verbal communication as well (Andersen and Andersen, 2005). Ultimately, the results of our study point to the fact that it is not the olfactory dysfunction per se that causes the person's psychological distress, but rather the impact that olfactory dysfunctions have on the perceived QoL. Therefore, it seems that is the *relationship* between olfactory dysfunctions and the *impact* they have on the QoL that determines the severity of the person's perceived psychological distress.

Finally, among the ASOF measures, the ORQ assessed the perceived QoL associated with olfactory functioning in different domains (i.e., cooking, sexual life, eating, drinking, using perfumes, and perceiving the scent of flowers). The results of our study showed that only impairments in sexual life and in using perfumes were associated with higher levels of psychological distress. As opposed to the other activities (cooking, eating, drinking, and perceiving the scent of flowers), which, although being also interactive actions, do not necessarily involve significant relationships with others, sexual life and the perception of a person's scent imply our core interconnectedness with other persons. From a speculative point of view, this seems a very relevant finding, which would point to the significance of olfaction of relevant relationships in human life. Our existence, indeed, takes shape according to the value that interpersonal interchanges have in the very constitution of our *Self*. From the beginning of life, we are embedded in our caring environment, whose features massively influence our (more or less successful) growth trajectories. Every developmental stage of human existence is shaped through relational figures, which in turn significantly contribute to determine one's well-being. The results of our study can therefore be interpreted within the relational framework that encompasses the individual's physical and psychological health and well-being. The interpersonal dimension of human existence is grounded in all the features that characterize the significant others. Not only we become able to grasp the others' thoughts through the meaning we bestow on their intentional life (as described in the theories of mind), but we are also able to "sense" them through our sensory modes of perception (e.g., when we smell their scent). Sexual life is essentially intertwined with the capacity to understand the other person's intentions, whereas the person's perfume deeply influences the emotional value of the interpersonal situation. In fact, among the ORQ domains, these appear to be the only activities that are directly related to the intersubjectively constituted world, which confirms that the possibility to find a common framework of perception and interaction is rooted in the very nature of us *as* human beings.

Although this study was intended to fill a gap in the explanation of the impact that COVID-19-related olfactory dysfunctions have on psychological distress, its limitations should be considered when interpreting the results. First, the study was cross-sectional in nature, and allowed for a picture of the sample only, taken as representative of a larger population. Future research should pay attention to this aspect, by expanding the sample size and exploring hypothesized relationships between variables in a longitudinal manner (e.g., by assessing the impairment of the perceived olfactory functioning domains throughout the course of the disease). Second, there is a clear gender disparity in the sample, as 299 participants (82.1 %) were female, and only 65 (17.9 %) were male. Future research should consider whether including a more gender-balanced sample might offer the opportunity to improve these results. Third, this study was conducted online, which prevented us from recruiting participants who do not have access to the Internet. Contemporary society is widely provided with access to the Internet, however, especially the elderly might not have the same chances that younger individuals have to be reached by the researchers. Lastly, the study utilized self-report measures as opposed, for instance, to olfactory sniffin' sticks, which would have been more accurate as to the measurement of the individual's olfactory functioning. Therefore, future studies could use this type of measure instead of basing the interpretation of the results on self-reported information, thus improving the accuracy levels of the measurement.

Despite limitations, the findings of the current study may inform clinical practice related to emotional disorders. Indeed, it is important to stress that clinicians (psychologists and/or psychiatrists) must be aware that anosmia – and olfactory impairment in general – can be a triggering factor for psychic distress such as depression and anxiety, which must be taken seriously into account. Anosmia involves a worsening of the individual's psychic condition, and has significant affective implications. Therefore, the presence of anosmia and olfactory impairment, along with other possible Covid-19-related symptoms, seem crucial in their potential to impact the patient's mood. This is the reason why it is important that clinicians take into account the possibility of psychological support for individuals exhibiting signs of olfactory dysfunctions.

5. Conclusions

Sensory modes of perception, such as olfaction (the phylogenetically oldest sensory mode human beings are endowed with) strongly influence how the world and the surroundings are perceived in relation to others. In particular, olfactory impairments can significantly impact the person's feeling of psychological well-being. Our study showed that COVID-19 olfactory dysfunctions strongly impact the person's reported psychological distress, and that COVID-19-related anosmia can have serious consequences as to the person's perception of his or her QoL. More specifically, among the perceived olfactory functioning scales, only impairment in olfactory-related QoL was associated with higher levels of psychological distress. This result points to the fact that it is the impact that olfactory dysfunctions have on the perceived QoL that mediate the perceived psychological distress, rather than olfactory dysfunctions being per se the causes of such distress. In other words, it is the very relationship between olfactory functioning and the impact it has on the perceived QoL that appears to correlate with the person's feeling of being psychologically distressed. Ultimately, this study confirmed the core intertwining between mood, perceived QoL, and olfactory functioning, showing how impairments in olfactory processing are strongly correlated with psychological distress through the impact they have on the perceived QoL.

CRediT authorship contribution statement

Vincenzo Bochicchio (VB), Selene Mezzalira (SM), and Cristiano Scandurra (CS) designed the study. VB, SM, Nelson Mauro Maldonato

(NMM), Elena Cantone (EC), and CS contributed to the acquisition of data. VB and CS analyzed the data. VB, SM, NMM, EC, and CS interpreted the data. VB, and SM, drafted the manuscript. EC, NMM, and CS critically revised the manuscript. VB and CS had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analyses. All authors have read the manuscript and have agreed with its submission.

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Consent to participate and for publication

By clicking on the link provided, participants were directed to the first page of the survey containing the informed consent of the study, its objectives, benefits, and risks, information about researchers, and their emails and telephone numbers. Furthermore, in the informed consent was clearly reported that the data would have been published in scientific journals and that the data would have been analyzed in aggregate ways. After reading all information, participants gave their consent to participate in the survey by clicking "I accept to take part in the survey."

Declaration of competing interest

The authors declare that they have no conflict of interest.

Data availability

The data and materials that support the findings of this study are available from the corresponding author upon reasonable request.

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