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Impact of post-COVID-19 olfactory disorders on quality of life, hedonic experiences and psychiatric dimensions in general population

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Abstract

Background and objective Olfactory disorders in COVID-19 impact quality of life and may lead to psychological impairments. Prevalence ranges from 8 to 85%, persisting in about 30% of cases. This study aimed to evaluate the 6-month post-COVID-19 impact on quality of life, hedonic experiences, anxiety and depression due to olfactory disorders. Additionally, it sought to compare psychophysical tests and self-perceived olfactory evaluations.

Methods A prospective, longitudinal study was conducted over baseline (T0) and 6 months (T1) on individuals with persistent olfactory disorders post-COVID-19 for more than 6 weeks. Psychophysical tests employed the Sniffin' Sticks Test® (TDI score), and self-perceived olfactory evaluation used a Visual Analogue Scale. Quality of life was assessed with an Olfactive Disorder Questionnaire and the French version of the Quality of Life and Diet Questionnaire. Hedonic experiences were gauged using the Snaith-Hamilton Pleasure Scale, while anxiety and depression dimensions were measured by The State-Trait Anxiety Inventory, The Post Traumatic Stress Checklist Scale, and Hamilton Rating Scale for Depression. Participants were classified into the "normosmic group" (NG) and the "olfactory disorders group" (ODG) at T0 and T1 based on the TDI score.

Results Were included 56 participants (58.93% women, 41.07% men) with a mean age of 39.04 years and a mean duration of post-COVID-19 olfactory disorders of 5.32 months. At T1, ODG had a significantly lower quality of life and hedonic experiences than NG. No significant differences in anxiety and depression dimensions were observed between groups. At T0, psychophysical tests and self-perceived olfactory evaluations were significantly correlated with quality of life and hedonic experiences in both groups. At T1, self-perceived olfactory evaluation in NG correlated significantly with quality of life, hedonic experiences, anxiety and depression dimensions, whereas ODG only correlated with hedonic experiences.

Conclusion Individuals with persistent post-COVID-19 olfactory disorders after six months demonstrated compromised quality of life and hedonic experiences. Self-perceived olfactory evaluation played a more

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significant role in influencing quality of life and the dimension of anxiety and depression than the psychophysical presence of olfactory disorders. These findings emphasize the importance of considering patients' perceptions to comprehensively assess the impact of olfactory disorders on their well-being.

Trial registration ClinicalTrials.gov number (ID: NCT04799977).

Keywords Olfactory disorders, Odor perception, Covid-19, Psychiatric, Psychopathology, Emotion, Cognition, Hedonic experiences (8 words)

Introduction

The SARS-CoV-2 coronavirus, responsible for COVID-19, has had a global impact on the population, resulting in various acute and chronic symptoms [1]. Among these symptoms, olfactory disorders have been reported, with a highly variable prevalence ranging from 8 to 85%. This variability can be attributed to factors such as age, race, gender, vaccination status, smoking habits, genetic factors, time since the onset of infection, comorbidities, and specific COVID-19 variants [2–4]. Moein et al. discovered that, while 61% of the 82 study participants had recovered their sense of smell within 7–8 weeks after the onset of COVID-19, the remaining 39% continued to experience olfactory disorders [5]. Additional data from the literature also reveals that olfactory disturbances persist in 25–30% of COVID-19 cases [6] and remain stable for 1–6 months [7]. In a study involving 268 COVID-19 patients, 21.9% reported that their olfactory function had not returned to normal even one year after the initial diagnosis [8].

Olfactory disorders (OD), defined as the reduced or distorted ability to smell during sniffing (orthonasal olfaction) or eating (retronasal olfaction) [9], are associated with various adverse effects on the quality of life. Regardless of their underlying cause, olfactory disorders result in diminished food enjoyment, compromised safety and hazard awareness, challenges in maintaining personal hygiene, occupational limitations, and social isolation. Additionally, they can lead to psychological issues such as insomnia, anxiety, and depression, as well as cognitive impairments affecting frontoparietal cognitive functions and increasing the risk of neurodegenerative diseases [10–13].

Research has consistently shown higher levels of depression and anxiety among individuals with olfactory impairment, often resulting in social withdrawal [10, 14]. Furthermore, studies have established a correlation between the severity of olfactory disorders and the intensity of depressive symptoms [15]. The literature also reports that olfactory disorders during the acute phase of COVID-19 infection are linked to cognitive deficits and psychiatric disturbances [16].

In our study, we initiated the assessment of patients during the COVID-19 pandemic in 2020. Early on, we formulated a hypothesis that individuals experiencing post-COVID-19 olfactory complaints might be linked to a decline in their quality of life and exhibit psychiatric symptoms. Our observations align with the experiences shared by patients and have been subsequently described in the literature. Patients have reported experiencing a general sense of mental fatigue, a loss of enjoyment in the taste of food and in social interactions during mealtimes, a lack of comforting scents, and, in some cases, aversion to unpleasant and distorted odors [6, 17–21]. Based on our findings and the existing literature, we propose that olfactory disorders may contribute to the development of psychiatric symptoms.

The main objective of this study is to evaluate the impact at 6 months of the post COVID-19 olfactory disorders on several criteria: quality of life, hedonic experiences and dimensions of anxiety and depression dimensions in the general population. The second objective is to compare psychophysical tests and self-perceived olfactory evaluation of olfactory disorders using these same criteria.

Materials and methods

Study design/setting

This prospective longitudinal open-label cohort study, spanning a duration of six months, was conducted by a scientific consortium consisting of a multidisciplinary team of researchers and healthcare professionals, including psychiatrists, ENT specialists, infectious disease specialists, and speech therapists, among others. The study took place at the Nice University Hospital, running from October 2020 to October 2021.

Participants

The study included adult participants who had previously contracted COVID-19 and were experiencing persistent olfactory disorders for a duration exceeding six weeks. Most of the patients either referred themselves or were referred by general practitioners. The initial confirmation of COVID-19 infection was obtained through RT-PCR testing, followed by secondary confirmation through serology. Patients were included in the study when they reported ongoing olfactory disorders six weeks after the resolution of COVID-19 symptoms. Exclusion criteria for the study were: pre-existing hyposmia or anosmia prior

to contracting COVID-19, a history of sinus or cranial neoplasia, prior sinus or cranial radiotherapy, a neurodegenerative disease diagnosis, or a history of post-viral hyposmia or anosmia that had subsequently recovered.

Assessment

Olfactory disorder assessment

Studies concerning post-COVID-19 olfactory disorders list the different methods of measuring olfactory disorders [22, 23]. In this study, the aim is to compare the methods of psychophysical tests and self-perceived olfactory evaluation. The psychophysical tests of olfactory dysfunctions of the study participants were assessed using the "Sniffin' Sticks Test®" [24]. This psychophysical olfactory tests determines: the olfactory threshold level (T), olfactory discrimination abilities (D) and olfactory identification (I) in the form of an overall TDI score [25, 26]. The diagnosis of olfactory disorders is retained at a score ≤ 30.5 and thus includes anosmic and hyposmic disorders.

A visual analogue scale (VAS) was used to assess self-perceived olfactory evaluation of olfactory disorders. Patients indicated a score measuring the intensity of olfactory disturbances since COVID-19 infection: 0% when they smelled nothing and 100% when they smelled like before COVID-19. The literature reports that the VAS in post-COVID-19 olfactory disorders is a reliable diagnostic tool, simple and quick to apply [27, 28] as well as strong statistical power [29].

Quality of life assessment

The Olfactive Disorder Questionnaire (QOD) is a validated quality of life questionnaire centered on the consequences of a loss of smell and taste, in particular in a post-viral situation, such as the pleasure of sharing a meal, of creating social interactions or of forming intimate ties with others [30]. A short version (QODC) was proposed in 7 most relevant questions concerning the social aspect, diet, anxiety as well as boredom following olfactory loss [31]. It was validated in French [32, 33]. The responses are rated from 0 to 3 according to their importance for a total score ranging from 0 to 21 (21 reflecting no alteration in the quality of life related to olfaction).

The French quality of life and diet questionnaire (QV-AF) is validated in French and enables to assess the quality of life in adults, in particular the relationship to food [34]. The QV-AF questionnaire contains four subscales measuring quality of life in relation to food: pleasure, relationship, psychology, physical condition. The maximum total score is 100 per subscale and the maximum score on the questionnaire is 400, corresponding to the best possible quality of life.

Hedonic experiences

The Snaith-Hamilton Pleasure Scale (Shaps) is the most commonly used in the measurement of anhedonia [35]. This is a 14-item self-administered questionnaire designed to assess the patient's hedonic capacity in different circumstances of daily life. It is validated and translated into French [36] and covers four domains of hedonic experience: interests/hobbies, social interaction, sensory experience, and food/drink. A score of 3 or more indicates a significant reduction in hedonic capacity and appears to have discriminant value between controls and clinically depressed patients.

Psychiatric assessments

The State-Trait Anxiety Inventory (STAI) is a psychological inventory consisting of 40 self-report items on a 4-point Likert scale [37], translated and validated in French [38]. The STAI measures two types of anxiety: state anxiety and trait anxiety. Higher scores are positively correlated with higher levels of anxiety. Each score can therefore vary from 20 to 80 with an anxiety standard: "very high" when the threshold is >65; "high" between 56 and 65; "average" between 46 and 55; "weak" between 36 and 45 and "very low" for a score < or = 35.

The Post Traumatic Stress Checklist Scale (PCL-5) is a self-report measuring the 20 symptoms of post-traumatic stress disorder (PTSD) from the DSM-5 [39, 40]. The objectives of the PCL-5 are multiple: to screen people with PTSD or to monitor the evolution of symptoms during and after treatment. The PCL-5 scale is validated and translated into French [41, 42]. The questionnaire includes 20 items on a 5-point Likert scale and a threshold of 33 is proposed for screening for post-traumatic stress disorder (PTSD).

Hamilton Rating Scale for Depression (HDRS) [43], translated into French [44], is used to assess the severity and evolution of a patient's depressive state during a structured interview. This is a hetero-questionnaire consisting of 17 items completed by the examiner during the interview. The higher the score, the more severe the depression: from 10 to 13: depressive symptoms are mild; from 14 to 17: depressive symptoms are mild to moderate; above 18: depressive symptoms are moderate to severe.

Study procedures

Patients meeting the inclusion criteria underwent two separate and consecutive consultations with an ENT specialist and a psychiatrist. During the ENT specialist's consultation at T0, the assessment of olfactory disorder was conducted using the "Sniffin' Sticks Test®" (TDI), the Visual Analog Scale (VAS), and the evaluation of quality of life using the QODC questionnaire. In addition to these assessments, patients received information about

their health status and were provided with recommendations for olfactory disorder rehabilitation.

The psychiatrist's consultation at T0 focused on evaluating quality of life using the QV-AF questionnaire and assessing psychiatric dimensions using the STAI (State-Trait Anxiety Inventory), PCL-5 (Posttraumatic Stress Disorder Checklist-5), SHAPS (Snaith-Hamilton Pleasure Scale), and HDRS (Hamilton Depression Rating Scale). During this consultation, psychiatric disorders could be diagnosed, initially through the results of the scales and subsequently through clinical judgment. Patients diagnosed with psychiatric disorders were informed and referred to a therapist for treatment.

Six months later at T1, all participants in the study were contacted for a follow-up assessment, which was conducted by the ENT specialist and psychiatrist using the same assessment methods as in the initial T0 evaluation. At both T0 and T1, participants were categorized into the "normosmic" group (NG) if their TDI score > 30.5, or into the "olfactory disorder" group (ODG) if their TDI score ≤ 30.5.

Statistical analysis

The ENT specialist and psychiatrist directly enter the data into the database during the evaluations. The hypothesis is that post-COVID-19 olfactory disorders impair quality of life and hedonic experiences and lead to symptoms of anxiety and depression dimensions. Statistical analyses were performed using R software.

Differences in NG and ODG were assessed at T0 and T1 in independent samples. Given that the data did not follow a normal distribution, Wilcoxon's test was used to compare the means of the NG and ODG.We retained a significant difference between the two populations with $p<0.05$. Correlation test (rho) (with spearman method) measured correlation between psychophysical tests (TDI) and self-perceived olfactory evaluation (VAS) of olfactory disorder and quality of life, hedonic experiences, anxiety and depression dimensions in each group (NG and ODG).

Results

At T0, 56 patients were recruited, a majority of them being women, i.e. 33 (58.93%) vs. 23 men (41.07%). At T1, 36 patients were reassessed, 21 women (58.33%) and 15 men (41.66%). The average age of participants was 39.04 years (+/- 13.33). They presented post-COVID-19 olfactory disorders for an average of 5.32 (+/- 3.03) months. At T0, there were 14 patients in NG (TDI > 30.5) and 42 patients in ODG. At T1, there were 23 patients in NG and 13 patients in ODG. We lost to follow-up 20 patients between T0 and T1 (36% included at T0) (Fig. 1).

Difference between the normosmic and olfactory disorder groups (Table 1)

At T0, there was no significant difference between two groups for quality of life, hedonic experiences, anxiety and depression dimensions. At T1, ODG had a significantly lower quality of life with QODC ($p<0.05$) and QV-AF ($p=0.023$) and more particularly in subscales "Food/pleasure" ($p=0.011$) and "Food/psychology" ($p=0.012$). ODG had also a significantly lower hedonic experience with Shaps than NG ($p<0.05$). But there was no significant difference between the two groups regarding anxiety and depression dimensions.

Correlations between psychophysical tests and self-perceived olfactory evaluation of olfactory disorder (Table 2)

At T0, the psychophysical tests (TDI) and self-perceived olfactory evaluation (VAS) of ODG were significantly correlated with: quality of life (QODC) (rho = 0.367, $p=0.016$ for TDI and rho = 0.369, $p=0.016$ for VAS) and hedonic experiences (Shaps) (rho=-0.354, $p=0.021$ for TDI and rho=-0.416, $p=0.006$ for VAS).

At T1, the psychophysical tests was not significantly correlated with quality of life, hedonic experiences, anxiety and depression dimensions in the two groups of patients. The self-perceived olfactory evaluation of NG patient was significantly correlated with quality of life (QODC: rho = 0.520, $p=0.01$ and QV-AF: rho = 0.546, $p=0.006$), hedonic experience (Shaps: rho=-0.713, $p=0.0001$), PTSD (PCL-5: rho=-0.534, $p=0.008$) and depression (HDRS: rho=-0.544, $p=0.007$). The self-perceived olfactory evaluation of ODG was only significantly correlated with the hedonic experience (Shaps: rho=-0.608, $p=0.027$).

Discussion

This study aimed to assess the impact of post-COVID-19 olfactory disorders on the general population six months after infection. The findings revealed a significant difference between the group with olfactory disorders (ODG) and the normosmic group (NG) in terms of quality of life and hedonic experiences. However, no significant differences were observed in anxiety and depression dimensions.

In the NG, self-perceived olfactory evaluations were correlated with quality of life, hedonic experiences, and anxio-depressive dimensions. In the ODG, self-perceived olfactory evaluations were only correlated with hedonic experiences.

At both T0 and T1, there were significant differences between the NG and ODG in the TDI score ($p<0.05$) and the VAS score ($p=0.04$), affirming the appropriateness of the chosen tools for measuring olfactory disorders.

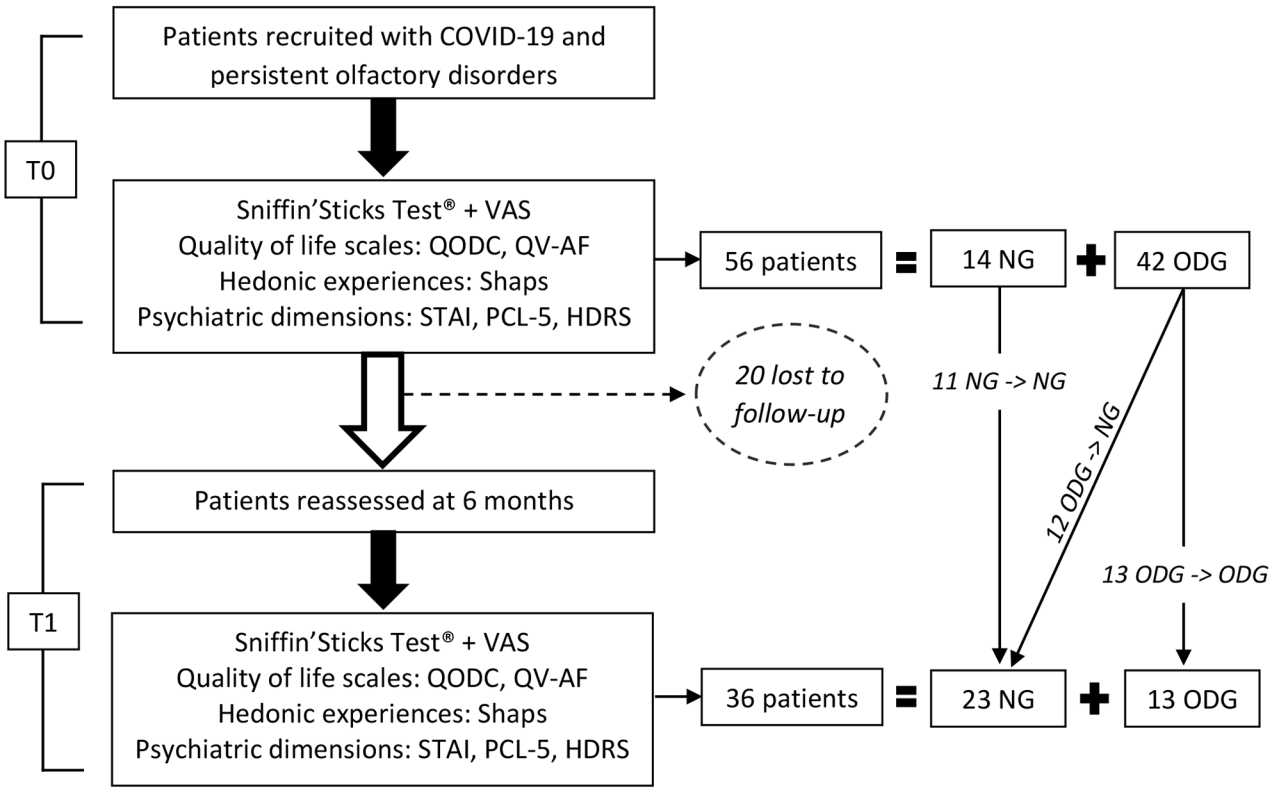

Fig. 1 Flow chart

The significant differences observed between NG and ODG at 6 months in terms of quality of life and hedonic experiences align with findings in the literature [45, 46]. For instance, an online survey involving 322 COVID-19 positive individuals who had experienced a loss of smell or taste reported 87% reduced enjoyment of food, 56% decreased enjoyment of life in general, and 55% loss of appetite [18].

However, the study did not yield significant results regarding anxiety and depressive dimensions, which were not consistent with the initial hypothesis and the existing literature. This discrepancy could potentially be attributed to methodological factors. Schou et al. conducted a systematic review that included 66 studies (selected from a total of 1725 studies) and reported a higher prevalence of anxiety and/or depression (61%), fatigue (48%), cognitive deficits (41%), sleep disturbances (35%), and symptoms of post-traumatic stress disorder (30%) [17]. This systematic review also highlighted the methodological variability across these studies, including variations in study instruments and the timing of follow-up examinations [17]. In our study, it is possible to hypothesize that a reassessment of the patients after 6 months might have revealed significant results for the anxious and depressive dimensions, aligning with the literature [5, 6, 17, 18]. Although our results did not reach statistical significance, there was a notable trend towards worsening scores at 6 months in both groups, suggesting potential emerging issues in these dimensions.

The statistical comparison of the groups was carried out between the NG and ODG groups at T0 and T1. But it was difficult to compare the same group (NG or ODG) between T0 and T1, because between T0 and T1, the number of patients in each of these groups are different (from 14 patients at T0 to 23 patients at T1 in NG; from 42 patients at T0 in ODG to 13 patients at T1 in ODG). However, we can only observe a trend in the evolution of the results between T0 and T1 for the same group.In the ODG, all indicators have a statistical tendency to decreased at T1 except the T score (olfactory perception) and the VAS. The link between the T score and the EVA is consistent since it is the measurement of olfactory perception by psychophysical tests (TDI score) or by self-perceived olfactory evaluation (EVA). But the worsening of the TDI total score and scores D (olfactory discrimination) and I (olfactory identification) seems to follow the decrease in quality of life indicators. We can discuss idea that a lack of olfactory recovery (TDI score)

Table 1 Descriptive analyses of the study populations with normosmic and with olfactory disorders

	T0				T1			
Variables	**Mean (SD) *N* = 56**	**Normosmic (SD) *N* = 14**	**Olfactory disorder (SD) *N* = 42**	***p***	**Mean (SD) *N* = 36**	**Normosmic (SD) *N* = 23**	**Olfactory disorder (SD) *N* = 13**	***p***
Age (years)	39.07 (13.33)	35.14 (11.35)	40.38 (13.80)	0.225				
Duration of olfactory disorder (month)	5.32 (3.03)	5.43 (2.77)	5.28 (3.15)	0.724				
TDI	24.73 (8.96)	36.11 (2.33)	20.93 (6.85)	< 0.05*	31.20 (10.49)	38.13 (3.51)	18.94 (6.59)	< 0.05*
Threshold (T)	4.83 (4.09)	10.32 (3.38)	3.01 (2.27)	< 0.05*	9.15 (5.24)	12.22 (3.57)	3.71 (2.57)	< 0.05*
Discrimination (D)	10.32 (3.05)	12.79 (1.31)	9.5 (3.02)	< 0.05*	11.39 (3.44)	13.22 (1.54)	8.15 (3.53)	< 0.05*
Identification (I)	9.57 (3.98)	13.00 (1.84)	8.42 (3.84)	< 0.05*	10.67 (3.52)	12.70 (1.96)	7.07 (2.69)	< 0.05*
VAS	35.39 (26.44)	47.86 (25.85)	31.24 (25.59)	0.031*	59.97 (32.02)	71.87 (22.94)	38.92 (35.68)	< 0.05*
QODC	11.21 (5.74)	12.71 (6.26)	10.71 (5.54)	0.267	13.14 (6.44)	15.96 (5.42)	8.15 (4.98)	< 0.05*
QVAF	253.60 (98.48)	281.21 (105.04)	244.40 (95.73)	0.194	271.94 (116.46)	301.50 (108.93)	219.62 (114.72)	0.023*
Food/pleasure	75.49 (23.13)	77.90 (18.81)	74.68 (24.55)	0.797	78.40 (21.87)	86.43 (13.73)	64.19 (26.59)	0.011*
Food/relational	60.43 (35.72)	68.94 (33.69)	57.59 (36.31)	0.327	62.96 (40.16)	70.30 (39.02)	49.97 (40.32)	0.121
Food/psychology	50.97 (32.58)	63.41 (34.23)	46.81 (31.33)	0.086	60.47 (39.68)	71.39 (36.82)	41.15 (38.39)	0.012*
Food/physical conditions	66.25 (34.49)	70.96 (31.66)	64.68 (35.60)	0.541	70.74 (36.59)	74.64 (34.58)	63.83 (40.40)	0.601
SHAPS	2.68 (2.23)	2.14 (2.35)	2.86 (2.19)	0.222	2.89 (2.60)	1.35 (1.75)	4.23 (2.89)	< 0.05*
STAI-AE	38.43 (12.84)	35.07 (14.41)	39.55 (12.25)	0.175	37.17 (14.12)	34.70 (13.67)	41.53 (14.36)	0.102
STAI-AT	42.20 (10.98)	38.71 (12.62)	43.36 (10.29)	0.127	42.42 (14.80)	40.26 (14.20)	46.23 (15.63)	0.269
PCL 5	15.36 (19.85)	13.36 (21.82)	16.02 (19.38)	0.509	13.64 (17.00)	10.57 (15.63)	19.07 (19.32)	0.171
HDRS	9.41 (7.41)	6.50 (5.00)	10.38 (7.87)	0.129	10.47 (7.05)	9.17 (6.92)	12.77 (6.94)	0.141

promotes a deterioration in quality of life over time. We could add that the appreciation of olfactory quality seems to have more impact on quality of life than perception alone. In the NG, the hedonic experience (Shaps) and anxious dimension (STAI-AE) scores would have a tendency to decrease, possibly due to the long-Covid impact on psychological health of individuals, regardless of any involvement dealing with sensory impairments.

The results of our study highlight the impact of self-perceived olfactory (by VAS) on quality of life, hedonic experience, anxious and depressive dimensions, in subjects without psychophysical impairment (by TDI score).

These results suggest the influence of the subjectivity of a sensory perception that is even more important than the perceptual disorder itself. Lechien and al. also found difference between psychophysical and self-perceived olfactory impairment in their study: among the patients who had an olfactory complaint, only a third had an psychophysical disorder in olfactory evaluation [47]. The literature proposed some explanation of this results by compared specificities in post-COVID 19 olfactory disorder to a cold [6]. During a cold, the loss of smell appears during or immediately after having contracted it, it is easily attributed to the nasal congestion felt and is reversible when this congestion disappears [48]. In the case of COVID-19, the olfactory loss is not attributed to a perceived nasal blockage [47] but considered as a novel perception [6]. This sensory loss without causal attribution is so unusual that several patients in our study have precise memories of when they became aware of the loss

Table 2 Correlations of psychophysical tests (TDI) and self-perceived olfactory (VAS) olfactory evaluations

	T0							
	TDI Normosmic (*N* = 14)		**TDI Olfactory disorder (*N* = 42)**		**VAS Normosmic (*N* = 14)**		**VAS Olfactory disorder (*N* = 42)**	
	rho	p	rho	*p*	rho	*p*	rho	*p*
QODC	0.278	0.334	0.367	0.016*	0.467	0.091	0.369	0.016*
QVAF	0.219	0.451	0.122	0.439	0.253	0.381	0.178	0.258
Food/pleasure	−0.031	0.915	0.250	0.109	0.121	0.677	0.215	0.170
Food/relational	0.244	0.399	0.097	0.537	0.264	0.360	0.165	0.296
Food/psychology	0.174	0.546	0.162	0.303	0.205	0.481	0.238	0.128
Food/physical conditions	0.412	0.142	-0.022	0.887	0.112	0.701	-0.028	0.855
SHAPS	0.029	0.92	-0.354	0.021*	−0.068	0.817	-0.416	0.006*
STAI-AE	−0.121	0.678	-0.084	0.594	−0.090	0.758	-0.291	0.061
STAI-AT	0.019	0.946	-0.085	0.588	0.294	0.307	-0.020	0.898
PCL 5	0.141	0.628	0.251	0.107	−0.157	0.589	0.147	0.35
HDRS	0.022	0.939	-0.013	0.931	0.026	0.927	-0.157	0.318
	T1							
	TDI Normosmic (*N* = 23)		TDI Olfactory disorder (*N* = 13)		VAS Normosmic (*N* = 23)		VAS Olfactory disorder (*N* = 13)	
	rho	*p*	rho	*p*	rho			
QODC	−0.160	0.464	0.289	0.337	0.520	0.010*	0.163	0.593
QVAF	−0.371	0.080	0.123	0.687	0.546	0.006*	0.082	0.788
Food/pleasure	−0.076	0.730	-0.198	0.516	0.573	0.004*	-0.101	0.740
Food/relational	−0.366	0.085	0.105	0.732	0.433	0.038*	0.162	0.595
Food/psychology	−0.303	0.159	0.168	0.581	0.491	0.017*	-0.025	0.935
Food/physical conditions	−0.293	0.174	0.018	0.951	0.338	0.114	-0.017	0.955
SHAPS	−0.042	0.847	-0.318	0.289	−0.713	0.0001*	-0.608	0.027*
STAI-AE	0.216	0.320	-0.046	0.879	−0.329	0.124	0.132	0.667
STAI-AT	0.403	0.056	0.132	0.666	−0.394	0.062	0.044	0.886
PCL 5	0.253	0.243	0.185	0.544	−0.534	0.008*	0.185	0.544
HDRS	0.332	0.121	-0.187	0.539	−0.544	0.007*	-0.377	0.202

of their sense of smell. Since this sudden olfactory loss is not attributable to a physical mechanism felt by the patient, its duration cannot be predicted between a few weeks to several months [7, 8]. These uncertainties could cause an emotional impact that contributes to olfactory subjectivity.

The emotional impact of self-perceived sensory impairment in the NG contributes to the risk of progression towards anxiety and depressive disorders [49]. The systematic review by Schou et al. reported that COVID-19 was a risk factor for PTSD [17]. Studies investigating olfactory impairment in populations with PTSD (veterans) [50] report increased sensitivity to odors reminiscent of trauma [51] and a disparity between self-perceived and psychophysical "sensitivity" to odors [50]. The literature supports too that reduced olfactory sensitivity accompanies depressive symptoms [52] and conversely, depressive symptomatology negatively impacts olfactory functioning [53], which could thus be taken as a marker of depression [54]. Thus the emotional impact would maintain the self-perceived olfactory impairment even if there is no longer any psychophysical olfactory disorder [55].

Limitations

This study had several limitations that may have influenced the results. First of all, we note the small number of patients included in the study. This may have led to low statistical power of our results and explained some non-significant trends. We also retain a significant number of people lost to follow-up (36%) in this study. We can wonder about the reasons for leaving the study of patients who were not seen again at 6 months: was it a patient who had regained their sense of smell? Or on the contrary patients whose olfactory disorders would have worsened and/or too discouraged to continue the protocol? In any case, this may have had an impact on the results of the study. In addition, a significant number (*N* = 12) of ODG individuals at T0 became NG at T1: this may represent a selection bias and have an impact in the analysis of the results.

This study may also have confounding bias in unaccounted data. The medical and psychiatric histories of the patients included in the study were not taken into account in the protocol. We choose not to collected this data through the speech of the patients because we didn't use a systematic way starting from a medical file standardized for the study. In the context of Post-COVID Condition Study, as defined by WHO, study participants could benefit from multidisciplinary care adapted to their symptoms. We selected patients in ENT specialist consultations with an olfactory complaint, which is a particularly significant symptom of Post-COVID condition and disruptive to patients' quality of life. Other COVID-19-related symptoms that patients might have exhibited were not included in the data collection also due to the small sample size of the study. This may lead to a selection bias resulting in the difference between the two groups not being specifically linked to olfactory disorders.The data collected for the study made it possible to differentiate hyposmia, anosmia but also distorted olfaction. But due to the small size of the study sample and to keep group sizes statistically comparable, we grouped these symptoms in the ODG. This protocol is an ancillary study to research work focused on olfactory rehabilitation in post-COVID-19 olfactory disorders. During the evaluation period, the patients included in the study benefited from olfactory rehabilitation which they carried out alone at home, following the recommendations of the ENT specialist. The random observance of this rehabilitation on a small number of patients included and a large number of patients lost to follow-up did not make it possible to retain this variable as relevant. No correlation were found with quality of life, hedonic experience and anxious and depressive dimensions. Further studies with a larger number of patients are needed.

Conclusion

This study has revealed a significant difference between the group with post-COVID-19 olfactory disorders and the normosmic group in terms of quality of life and hedonic experiences at 6 months. Moreover, the findings of this study suggest that the subjectivity of sensory perception plays a crucial role, which may be even more significant than the perceptual disorder itself. In line with existing literature, these results underscore the importance of a multidisciplinary clinical reassessment and psychological support as part of targeted sensory therapies.

It would be valuable to continue this research and explore the hypothesis that self-perceived olfactory evaluation, the subjective assessment of olfactory disorders, could act as a trigger for traumatic sensory experiences that may contribute to anxiety and depressive disorders. This avenue of investigation may lead to a deeper understanding of the psychological and sensory aspects of post-COVID-19 olfactory disorders and inform the development of more effective interventions and therapies.

Abbreviations

ENT specialist	Ear, nose and throat specialist
HDRS	Hamilton Rating Scale for Depression
NG	Normosmic group
ODG	Olfactory disorders group
PCL-5	Post Traumatic Stress Checklist Scale
PTSD	Post-Traumatic Stress Disorder
QOD	Questionnaire of Olfactory Disorders
QODC	Questionnaire of Olfactory Disorders– Short version
QV-AF	French quality of life and diet questionnaire
Shaps	Snaith-Hamilton Pleasure Scale
STAI	State-Trait Anxiety Inventory
TDI score	Threshold-Discrimination-Identification score
VAS	Visual Analog Scale
WHO	World Health Organization

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Author contributions

LED, CV and AG conducted and supervised data collection. VMF participated to the recruitment of patients. LED performed data analysis. PA and FA supervised the PhD. The author(s) read and approved the final manuscript.

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Data availability

The reported data is part of an ongoing recording program. Anonymized participant data is not available for legal and ethical reasons. Anonymized data will be made available for research purposes upon reasonable request. Dr Louise-Emilie Dumas can be contacted in the event of a request for access to study data.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of the Nice University Hospital (CNIL number: 412). It is part of a large work registered under a ClinicalTrials.gov number (ID: NCT04799977). This study was carried out as part of routine care. Patients have been informed of their inclusion in this study and have given their informed consent to participate. Patients' non-objection to study participation was requested orally and recorded in the patient's medical record. Patients were informed that they could refuse to participate or withdraw their consent at any time during the study. Data were anonymized before the analyses.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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