SHORT COMMUNICATION



Assessment of postviral qualitative olfactory dysfunction using the short SSParoT in patients with and without parosmia

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Abstract

Purpose To examine if the short formed Sniffin Sticks Parosmia Test (SSParoT), a test for parosmia can distinguish cases with parosmia from cases without parosmia.

Methods In this study, 63 patients with postviral olfactory dysfunction were investigated including both COVID and non-COVID cases. The age, symptom duration, degree of parosmia/phantosmia was collected. For olfactory function, the Sniffin Sticks olfactory score was obtained including scores for odor threshold, discrimination and identification. For assessment of parosmic changes, the short SSParoT was adopted and both hedonic range (HedRang) and direction (HedDir) was calculated. **Results** The mean HedRang of patients with parosmia (2.35, standard deviation, SD=1.40) and without parosmia (2.78, SD=1.09) was smaller than that in controls (4.5, SD=2.15). However, the mean HedDir of both parosmia (-0.32, SD=0.98) and non-parosmia patients (0.04, SD=1.07) was similar to controls (-0.1, SD=1.55). When considering that the 10th percentile of the distribution of SSParoT score should distinguish between patients with and without parosmia, the sensitivity of the HedRang was 29% and specificity was 67%. For HedDir, the sensitivity was 6% and specificity was 100%. Only the odor identification score (r=0.34, p=0.01) discriminated parosmia and non-parosmia while other measures including HedRang and HedDir did not.

Conclusion The present study showed that the short SSParoT score could not distinguish patients with parosmia from patients without parosmia. Although the SSParoT represents an innovative approach to assess parosmia, and could be useful in the tracking of parosmic changes, the development of measures to diagnose parosmia in an objective way remains a challenge.

Keywords Chemosensory perception · Hedonic · Olfaction · Parosmia

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Introduction

Qualitative olfactory dysfunction of parosmia has been reported since more than 100 years [1]. Due to the SARS-CoV2 pandemic olfactory dysfunction has received a different level of attention, because the life-threatening COVID-19 is associated with quantitative and, importantly, also qualitative olfactory dysfunction. Hence, parosmia cases are in the spotlight since 2020. Until to date the presence of parosmia is diagnosed only on the basis of the patient's medical history or structured questionnaires [2]. In an effort to provide more quantitative measures of parosmia recently the "Sniffin Stick Parosmia Test" (SSParoT) was introduced [3]. The SSParoT was tested in healthy subjects and 3 patients with qualitative olfactory dysfunctions. Hence, the present retrospective study aimed to investigate whether, in routine clinical application, the SSParoT score can help to distinguish not only healthy people and patients with parosmia, but also to distinguish patients with and without parosmia.

Materials and methods

Data for this retrospective study were part of the routine clinical examination at the Smell & Taste Clinic of the Department of Otorhinolaryngology of the Technical University of Dresden. The study design was approved by the Ethics Committee at the University Clinic of the Technical University Dresden (application number BO-EK-254062022).

Participants

We gathered the data from 63 postviral olfactory dysfunction patients including both COVID-19 and non-COVID-19 cases (18 men, 45 women). Patients with signs of chronic rhinosinusitis or neurodegenerative disease (e.g., Parkinson's disease) were excluded from participation. Forty-four patients had history of COVID-19 infection and also positive result of either PCR or antigen test, 4 had negative result and 15 failed to do the test.

Although there were a few missing data, no one was excluded from whole study but was excluded on a case-bycase basis from analyses for each individual variable.

We asked patient if they have either parosmia or phantosmia and we explained each symptom in great detail, for example, "Parosmia typically presents itself as a uniform, unpleasant odor. Odors are perceived different from what they used to smell, e.g., coffee smells like smoke", "Patients with phantosmia are those who affected smell a pleasant or unpleasant odor even though no odor is present".

Forty-eight patients had parosmia, 15 did not report parosmia. The median age was 41 years (interquartile range, IQR = 21.5, 18–80 years). The median duration of olfactory dysfunction was 11 months (IQR = 2, 1–18 months). The degree of parosmia and phantosmia (0–3) [4] was also collected as a clinical estimate of qualitative olfactory dysfunction. To define if the patient has either parosmia or phantosmia, we explained concrete symptom and asked directly to the participants. All patients received a full ENT general examination including nasal endoscopy. Computed Tomography was done only if deemed necessary for the diagnosis.

Sensory testing

Sniffin stick parosmia test (SSParoT)

For assessment of parosmic changes we used the short version of the SSParoT [3]. SSParoT comprises 2 main scores called hedonic range (HedRang) and hedonic direction (HedDir). They are based on the patients' ratings of the pleasantness of pairs of two oppositely valanced odors. Four pairs of odors from the original Sniffin Sticks odor identification test are presented. HedRang indicates the hedonic distance between two odors (difference between ratings of the two odors on a 9-point rating scale from -4 to +4). HedDir is the average of the mean hedonic ratings of the pairwise presented odors. The patients' SSParoT scores were interpreted in comparison to the results of Liu et al. [3] with a mean HedRang of 4.5 (standard deviation, SD=2.15), and a mean HedDir of -0.1 (SD=1.55). Patients with parosmia should score below the 10th percentile of the normal distribution of the SSParoT scores obtained in healthy subjects. The 10th percentile of the distribution of HedRang score was -1.5 and that for HedDir was -2.0. For the control data, we averaged results for men and women.

Sniffin sticks, TDI score

The Sniffin' Sticks test battery (Burghart, Wedel, Germany) was administered to evaluate olfactory function. Odor Threshold (T), Odor Discrimination (D), and Odor Identification (I) was examined as described previously [5]. According to the previous data we defined as normosmia, hyposmia and anosmia as Table 1.

Statistical analysis

The program jamovi (The jamovi project (2021). Jamovi (version 1.6) [Computer Software]. Retrieved from https:// www.jamovi.org, Sydney, Australia) was used for statistical analysis. Spearman statistics were used for correlational analysis (ρ, p) . A Spearman's rank correlation was examined between age, duration, T score, D score, I score, TDI score, degree of Parosmia and Phantosmia, HedRang and HedDir. We also performed *t*-tests for independent samples on differences in D score, HedRang and HedDir between groups of olfactory dysfunctions with parosmia and without parosmia. An independent samples t-test was done to examine possible differences in T score, D score, I score, TDI score on between groups of parosmia patient and nonparosmia patient. A t-test was done to examine differences between mean of HedRang, HedDir in control from parosmia patient to non-parosmia patient. For non-normal distribution, Mann-Whitney U test was used and the results

 Table 1
 Definition of normosmia, hyposmia and anosmia in each age group based on TDI score

	18-20	21–40	41–50	50<
Normosmia	>29	> 31	>29	>28
Hyposmia	16–29	16–31	16–29	16–28
Anosmia	<16	<16	<16	<16

are expressed as median, IQR. For normal distribution, Student's *t*-test was used and the results are expressed as mean, SD or 95% confidence intervals (95% CI) are shown. A *p* values < 0.05 were considered significant. The program GraphPad Prism (version 9.3.1(350), GraphPad Software, San Diego, U.S) was used to create figures.

Result

For parosmia patients, mean of HedRang was 2.35 (SD=1.40) and HedDir was -0.32 (SD=0.98). For nonparosmia patients, mean of HedRang was 2.78 (SD=1.09) and HedDir was 0.04 (SD=1.07). The HedRang of both parosmia patient and non-parosmia patient was smaller (Parosmia and non-parosmia, p < 0.001) than the mean HedRang of controls (4.5), but HedDir was similar (parosmia, p=0.13 and non-parosmia, p=0.62) in controls (-0.1) and patients. For HedRang, 19 patients scored below the 10th percentile (1.5) and 14 of them (74%) actually had parosmia. For HedDir, 3 patients scored below the 10th percentile (-2.0) and all of them actually had parosmia. The sensitivity of HedRang was 29% and specificity was 67%. For HedDir, the sensitivity was 6% and specificity was 100%.

There was a correlation of HedRang with the odor identification I score (r=0.34, p=0.01) and the composite TDI score (r=0.28, p=0.03), but not with age (r=-0.18, p=0.16), duration of symptoms (r=0.01, p=0.95), threshold T score (r=0.14, p=0.26), discrimination D score (r=0.24, p=0.06), degree of parosmia (r=-0.01, p=0.92) or phantosmia (r=0.26, p=0.74). HedDir did not correlate significantly with any of the variables (Table 2).

According to the TDI score and with respect to the agerelated normative data [5], there were 2 patients with anosmia, 38 with hyposmia and 22 with normosmia. Independent samples *t*-test showed a significant difference between parosmia patient and non-parosmia patient with I score (p=0.02). By contrast, no significant difference was found in other variable including T score (p=0.52), D score (p=0.49), TDI score (p=0.14), HedRang (p=0.28) and HedDir (p=0.23) (Fig. 1a, b).

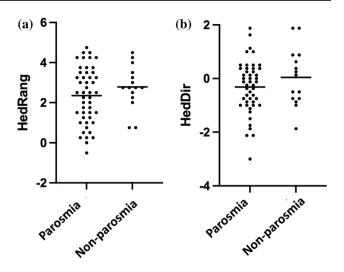


Fig. 1 a Comparison between patients with and without parosmia for HedRang. b Comparison between patients with and without parosmia for HedDir. Error bar indicates standard deviation of uncertainly

Discussion

The aim of the study was to investigate whether the SSParoT can distinguish (1) healthy subjects from patient with parosmia and (2) distinguish patient with parosmia from without parosmia. We adopted short version of SSParoT to our study instead of extended version because no extra odorant preparation is needed and it is easier to adjust to routine examination. Our results suggest that HedRang could distinguish healthy subjects from patient with parosmia but not from without parosmia. The I score was the only variable that could distinguish patient with parosmia from without parosmia. Since the state of parosmia implies the distortion of odor perceptions, this difference is easily explained.

Until to date, the diagnosis of parosmia relies only on the patients' responses, or on the directed interview with the patient [4]. Sensory testing is often better to combine with both subjective and objective ways and expected to be invented to know more deeper about parosmia.

The SSParoT is unique in the way to focus on the hedonic dimension of olfactory perception rather than

Table 2Correlation betweenHedRang, HedDir and Age,Duration of Symptom, T score,D score, I score and TDI score

Variables		Age	Duration	Т	D	Ι	TDI
HedRang	Spearman's rho	- 0.18	0.01	0.14	0.24	0.34	0.28
	<i>p</i> -value	0.16	0.95	0.62	0.06	0.01*	0.03*
HedDir	Spearman's rho	0.12	-0.04	0.03	0.21	0.10	0.13
	<i>p</i> -value	0.35	0.76	0.83	0.11	0.45	0.33

All factors are analyzed with the ρ -value and p-value using Spearman's test. An asterisk indicates significance of *p*-value <0.05

on odor identification. Although the SSParoT did not discriminate between patient with parosmia from without parosmia it may be that the discrimination between the two groups could be improved if the test focuses on pleasant odors only. Although parosmia is associated with the distortion of pleasant and unpleasant odors the separation between patient with parosmia and without parosmia, patients appear to be less clear when only unpleasant are looked at. More effective results might be found when focusing on pleasant odors which only become unpleasant in parosmia patients [6].

In order to assess parosmia future scales should not only focus more on the hedonic perception of generally pleasant odors, but should also involve odor identification which, as indicated in the present study, appears to be effective to distinguish patient with parosmia and without parosmia. In addition, a "parosmia score" could also include the simple rating of patients in response to a range of pleasant odors whether they are pleasant, unpleasant or neutral. Such scores could then be used in future studies to follow up on the patients' recovery from parosmia.

Limitation

Because of the retrospective design we did not perform separate measurements in healthy controls. Instead of recruiting healthy subject, we adopted data from Liu et al.'s study [3]. In addition, apart from the short SSParoT we did not estimate the degree of parosmia with an independent questionnaire, e.g., Landis's study [2]. The number of subjects without qualitative OD was less compared to controls and to parosmia cases, largely due to the many COVID-19 cases involved. Due to the gender-related imbalance of postviral olfactory loss the presently investigated group comprised more women than men which was different from the gender ratio in controls [3]. There was also an age-related difference between patients and controls. Although patients with COVID-19 related OD are younger than patients with OD due to infections with other viruses, still postviral OD patients were older than participants from Liu's study [3]. Another limitation of this retrospective research was the lack of information on comorbidities which should be remedied in future studies.

Conclusion

Although the short SSParoT is a unique approach to the assessment of parosmia, the score did not distinguish olfactory dysfunction patients with and without parosmia. While the short SSParoT may be useful in the follow-up of patients with and without parosmia, it still remains a challenge to develop objective measures for the diagnosis of parosmias. Acknowledgements Not applicable.

Author contributions All authors contributed to the study conception and design. Rumi Sekine performed data collection, conceptualization, data analysis, writing of the original draft, editing of the final manuscript. Susanne Menzel performed data collection and data analysis. Antje Hähner performed data collection and total project administration and supervision. Thomas Hummel performed conceptualization, data collection and analysis, methodology, resources, project administration, supervision. The first draft of the manuscript was written by Rumi Sekine and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials Not applicable.

Code availability Not applicable.

Declarations

Conflict of interest All authors declare no conflict of interest.

Ethical approval This retrospective study was performed in accordance with the guidelines of the Declaration of Helsinki on Research Involving Human Subjects. The study design was approved by the Ethics Committee at the University Clinic of the Technical University Dresden (application number BO-EK-254062022).

Consent to participate Not applicable.

Consent for publication Not applicable.

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