Assessing parosmia patients: a study on the evaluation method using a self-administered odor questionnaire for parosmia
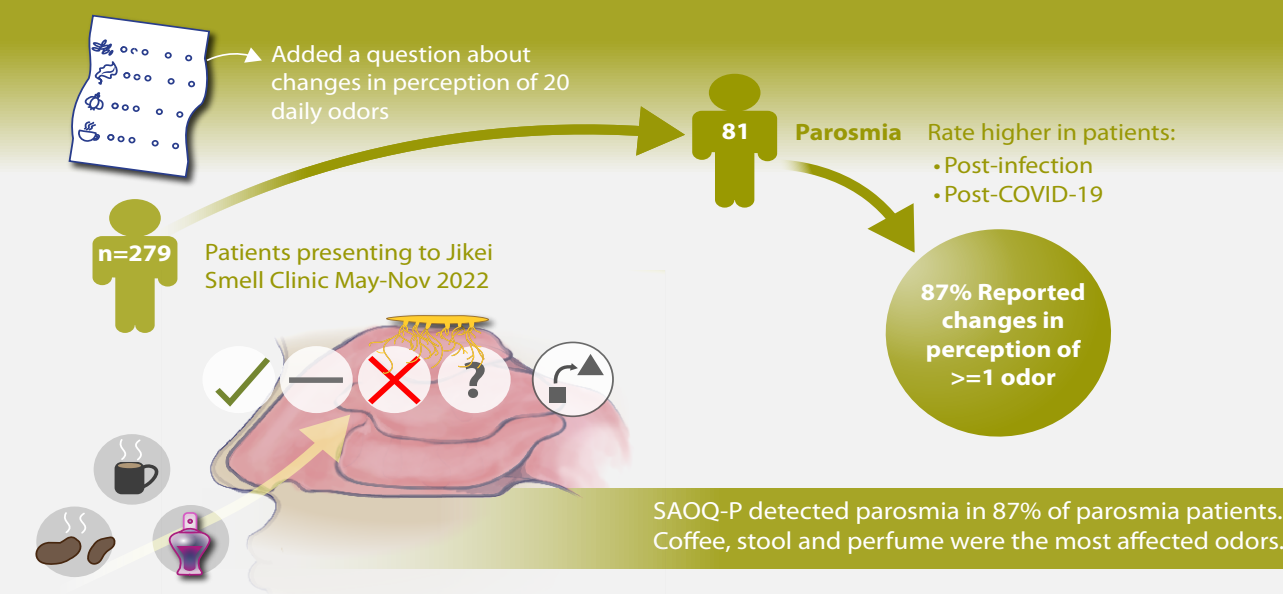
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SAOQ-P: Self-Administered Odor Questionnaire for Parosmia

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Abstract

Background: Parosmia symptoms are difficult to quantify due to their heterogeneity among patients, and thus a clinical challenge. This study aimed to assess parosmia with Self-Administered Odor Questionnaire for Parosmia (SAOQ-P), a modification of the widely used SAOQ in Japan. The primary objective was to assess the effectiveness of SAOQ-P in identifying parosmia symptoms and its potential integration into the clinical assessment process. The study also explored traditional olfactory test differences between patients with and without parosmia. **Methods**: Patients at Jikei Smell Clinic that presented between May 2022 and November 2022 were recruited and administered the SAOQ-P, which had an added question about changes in the perception of 20 daily odors compared to the original SAOQ. Traditional olfactory tests utilized T&T olfactometry and Open Essence. **Results**: Of 279 patients, 81 had parosmia, while 198 did not exhibit parosmic symptoms. Parosmia prevalence was influenced by the cause of olfactory dysfunction, with post-infectious and post-COVID-19 patients showing higher parosmia rates. Among parosmia patients, 87% reported changes in their perception of at least one odor assessed by SAOQ-P, with coffee, stool, and perfume most commonly affected. Traditional olfactory tests showed no significant differences between parosmia and non-parosmia groups. The number of odors causing parosmia was negatively correlated with age. **Conclusion**: SAOQ-P offers a promising approach to assess and quantify parosmia symptoms, seamlessly integrating into clinical assessments. SAOQ-P identified parosmia in 87% of patients and revealed insights into triggering factors. Traditional olfactory tests' limitations underscore the need for more accurate, patient-centric diagnostic approaches for parosmia.

Key words: diagnostic techniques and procedures, olfaction disorders, surveys and questionnaires, symptom assessment

Introduction

Olfactory dysfunction can be categorized into two types: quantitative and qualitative [1]. Quantitative olfactory dysfunction is typically evaluated through olfactory threshold measurements, focusing on assessing the severity of the dysfunction. In contrast, qualitative olfactory dysfunction is more challenging to assess, as it involves distortions in the perception of odors and cannot be measured using thresholds alone. Often, it is evaluated through medical interviews and questionnaires, making it less emphasized by healthcare professionals compared to quantitative olfactory dysfunction.

Parosmia is a prevalent manifestation of qualitative olfactory dysfunction that is characterized by distorted odor perception. It frequently occurs after infections or head trauma, with a reported prevalence rate of 13-59% [2-5] and an even higher rate of up to 60-70% [6-8] in coronavirus disease 2019 (COVID-19) cases. Despite its prevalence, our understanding of its symptoms and its relationship with quantitative olfactory dysfunction remains limited.

Parosmia symptoms are challenging to quantify due to their qualitative nature and the variability among patients. A systematic review on qualitative olfactory dysfunction assessment [9] described that assessment methods for qualitative olfactory dysfunction predominantly rely on questionnaires, with only a few incorporating objective measures. Many of these questionnaires are not specifically designed for parosmia symptoms, and even those that focus on parosmia often lack a clear scoring system or statistical evaluation. Therefore, we aimed to help quantify and understand the symptoms of parosmia by adapting the Self-Administered Odor Questionnaire (SAOQ) [10, 11]. A widely used tool in Japan for assessing olfactory dysfunction, SAOQ primarily addresses quantitative changes associated with 20 daily odors that are familiar to the Japanese population. Recognizing the potential for the same 20 odors to address qualitative changes, we adapted the questionnaire for this purpose and added a question to the original SAOQ. In this study, we present our findings on the clinical utility of this adapted SAOQ for parosmia that we named SAOQ-P, along with the results of quantitative olfactory tests for parosmic patients compared to non-parosmic patients.

Materials and methods

We recruited patients who visited Jikei University hospital smell clinic between May 2022 and November 2022. All patients who visited during this period provided consent for participation, and no patient was excluded from the study. Diagnosis of parosmia was primarily based on patient interviews and SAOQ-P questionnaires that asked if the patients had symptoms of odors smelling different from before. Interviews were conducted by board-certified otorhinolaryngologists, and the diagnosis of parosmia was confirmed through consensus among 2-3 board-certified otorhinolaryngologists in daily meetings. A total of 279 patients (430 in total count, including multiple visits) were categorized into parosmia and non-parosmia groups based on their diagnosis.

SAOQ-P was administered to all patients by olfactory technicians, and responses were collected and validated by both technicians and board-certified otorhinolaryngologists. SAOQ includes a series of questions about changes in the perception of 20 daily odors, including steamed rice, miso, seaweed, soy sauce, baked bread, butter, curry, garlic, orange, strawberry, green tea, coffee, chocolate, household gas, garbage, timber, sweat, stool, flower, and perfume [10, 11]. Patients could choose from four response options: "Always smelled," "Sometimes smelled," "Never smelled," or "Unknown or no recent experience." SAOQ-P added an additional question regarding whether the smell differed from their previous experiences for each odor. Additionally, visual analogue scale (VAS) questions gauged the sense of smell, nasal obstruction, taste, and binary questions evaluated parosmia, phantosmia, hyperosmia, and dysgeusia. Supplementary Data 1 includes the SAOQ-P, VAS, and binary questionnaires used in this study. The questionnaire and medical interview were predominantly conducted in Japanese, reflecting the nationality of most patients.

Olfactory measurement was carried out using T&T olfactometry [12] and Open Essence [13] (OE). T&T olfactometry is a standard olfactory test in Japan that uses five odors at 7 to 8 different concentrations, with results presented as average detection and recognition thresholds. The average recognition threshold is used for olfactory evaluation, with values between -2.0 and 1.0 for normosmia, values between 1.1 and 2.5 for mild olfactory dysfunction, values between 2.6 and 4.0 for moderate olfactory dysfunction, values between 4.1 and 5.5 for severe olfactory dysfunction and values between 5.6 and 5.8 for anosmia. OE is an olfactory identification test used in Japan with 12 cards, each printed with odor-containing microcapsules. Odors are released upon opening each card and the participants are asked to write an answer from six given choices: one correct smell, three wrong smells, one choice stating the smell is indistinguishable and one choice stating there is no smell. Each of the 12 OE cards contains a distinct odor: calligraphy ink, condensed milk, curry, cypress, household gas, timber, menthol, orange, perfume, rose, garlic, or sweaty socks/body odor.

Epidemiological and statistical differences were compared between the parosmia and non-parosmia groups. Analysis of gender, age, and causative factors used the number of patients, while SAOQ-P responses and olfactory test results, such as T&T thresholds and OE responses, employed the total counts, including multiple visits.

Ethics

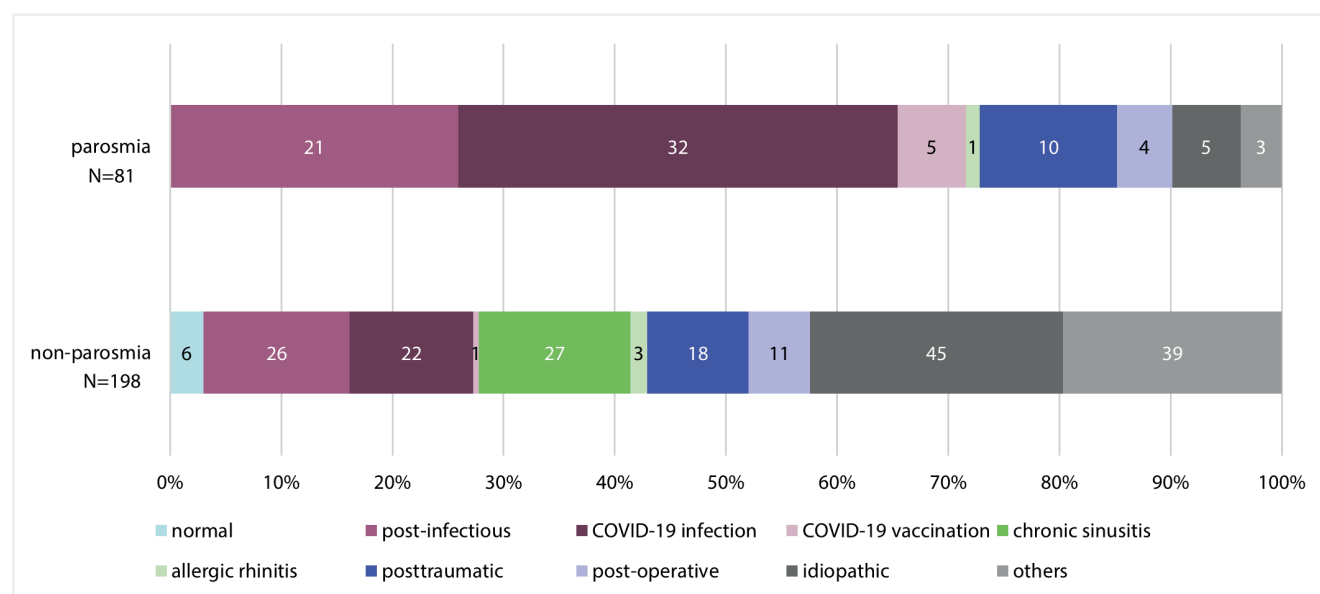The study received ethical approval from the ethics committee

Figure 1. The numbers on the graph represent the patient number for each cause. Patient numbers only include the first visits. Parosmia cases are primarily associated with viral infections and vaccination, whereas non-parosmia cases exhibit a broader spectrum of causal factors.

of Jikei University School of Medicine, with approval number 33-248(10866).

Statistical analysis

Statistical analyses were performed using JMP Pro 16 and EZR. The Wilcoxon rank sum test, chi-square test, and Fisher's exact test compared differences between two groups such as parosmia and non-parosmia groups, while analysis of variance and linear regression analysis assessed relationships between variables. A p-value below 0.05 (two-sided) was considered statistically significant, and missing data were addressed as missing completely at random.

Results

Supplementary Table 1 presents patient statistics, with a total of 279 patients (430 in total count, including multiple visits) visiting the clinic during the study period. Among them, 81 patients (29%) had parosmia (111 in total count, including multiple visits) and were categorized as the parosmia group, while the remaining 198 patients (319 in total count, including multiple visits) without parosmia formed the non-parosmia group. The parosmia group had significantly more female patients (p=0.0012, chi-square) and younger patients (p<0.0001, Wilcoxon rank sum).

The cause of olfactory dysfunction is depicted in Figure 1. Over 70% of the cases in the parosmia group were attributed to post-infectious causes, post-COVID-19 infection, or post-COVID-19 vaccination. In contrast, the non-parosmia group exhibited a more diverse range of causative factors. Notably, the prevalence of parosmia was 47% among post-infectious patients (21 out of

47 patients) and even higher at 59% in cases of COVID-19 infection (32 out of 55 patients), while patients with chronic sinusitis did not present with parosmia symptoms (0 out of 27 patients). Figure 2A illustrates the number of odors that patients reported as contributing to their parosmia symptoms. The patient numbers depicted in Figures 2 to 5 represent the total counts, which include multiple visits. Of 111 parosmia patients in total count, 98 questionnaires were collected, 85 (87%) reported that one or more of the 20 daily odors smelled different from their previous experiences. The remaining 13 patients did not fill out the questionnaire. The majority reported a change in a single odor, followed by zero or two odors. Figure 2B displays the percentage of patients reporting a change for each of the odors, with coffee, stool, and perfume being the most affected, at 48%, 46%, and 38%, respectively.

Figures 3A and 3B present the average T&T detection and recognition thresholds, along with the number of patients in parosmia and non-parosmia groups. Each graph exhibits bimodal distribution, with distinct peaks in the lower and higher threshold ranges. In the non-parosmia group, the most frequent value in the higher threshold range was 5.8 for both detection and recognition thresholds, indicating anosmia patients. In the lower threshold range, the most frequent value was 0.6 for both parosmia and non-parosmia groups in the detection thresholds, while in the recognition threshold, it was 2.8 for the parosmia group and 1.0 and 3.2 (equal frequency) for the non-parosmia group. Figure 3C demonstrates the gap between T&T detection and recognition thresholds, with the parosmia group having a mean value of 1.2, while the non-parosmia group had a mean
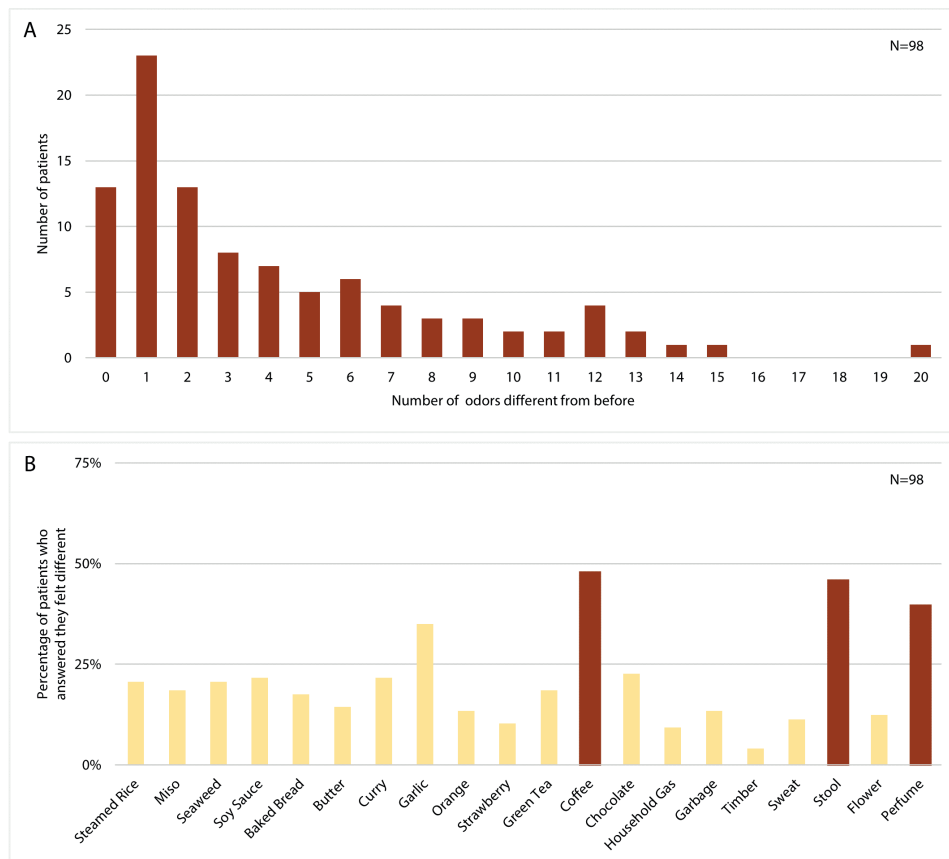
Figure 2. Patient numbers include multiple visits. Figure 2A displays the patient count and the number of odors they perceived differently compared than before. Notably, 87% of the patients reported changes in at least one odor. Figure 2B illustrates the percentage of patients reporting alterations for each specific odor. Coffee, stool, and perfume exhibited a higher frequency of changes compared to other odors. Out of a total count of 111 parosmia patients, 98 provided valid responses.

value of 0.8. The Wilcoxon rank sum test revealed a significant difference between the two groups (p=0.0047), suggesting that the parosmia group had weaker olfactory recognition ability. Further multivariable linear regression analysis that investigated potential confounders such as age and gender revealed significant associations between the gap in detection and recognition thresholds and parosmia status, age, and gender, with parosmia status demonstrating the largest F ratio (F=7.46) and smallest p-value (p=0.0066) (Figure 3D).

Figure 4A illustrates the distribution of the number of correct answers on the OE test. The parosmia group exhibited a peak at 8, while the non-parosmia group had a peak at 0. Figure 4B displays the total number of OE answers, which were categorized as "correct smell," "wrong smell," "indistinguishable," and "no smell." The chi-square test indicated a significant difference between the two groups, although no significant difference was observed when excluding the "no smell" responses, as shown in Figure 4C. Individual chi-square tests for each of the 12 cards in OE, with "no smell" excluded, revealed no significant differences

across all 12 cards.

Five odor items were present in both the SAOQ-P and OE: curry, garlic, household gas, orange, and perfume. A comparative analysis of SAOQ-P and OE results for these shared odor items exposed similarities and disparities in odor identification between olfactory threshold testing and self-assessment. Figure 4D presents the total numbers of OE answers without "no smell," and categorized the answers into "changed" for patients who reported perceiving each odor differently from before and "unchanged" for those who did not in SAOQ-P. Among these shared odors, only household gas exhibited a statistically significant difference (p=0.037) as revealed by the Fisher's exact test.

Relationships between the number of odors perceived differently and various factors, including gender, age, T&T detection threshold, T&T recognition threshold, the gap between T&T detection and recognition thresholds, the number of correct answers on the OE test, smell VAS, and taste VAS were analyzed. As shown in Figure 5A, an analysis of variance for age yielded a significant p-value of 0.006, with an R2 value of 0.07.
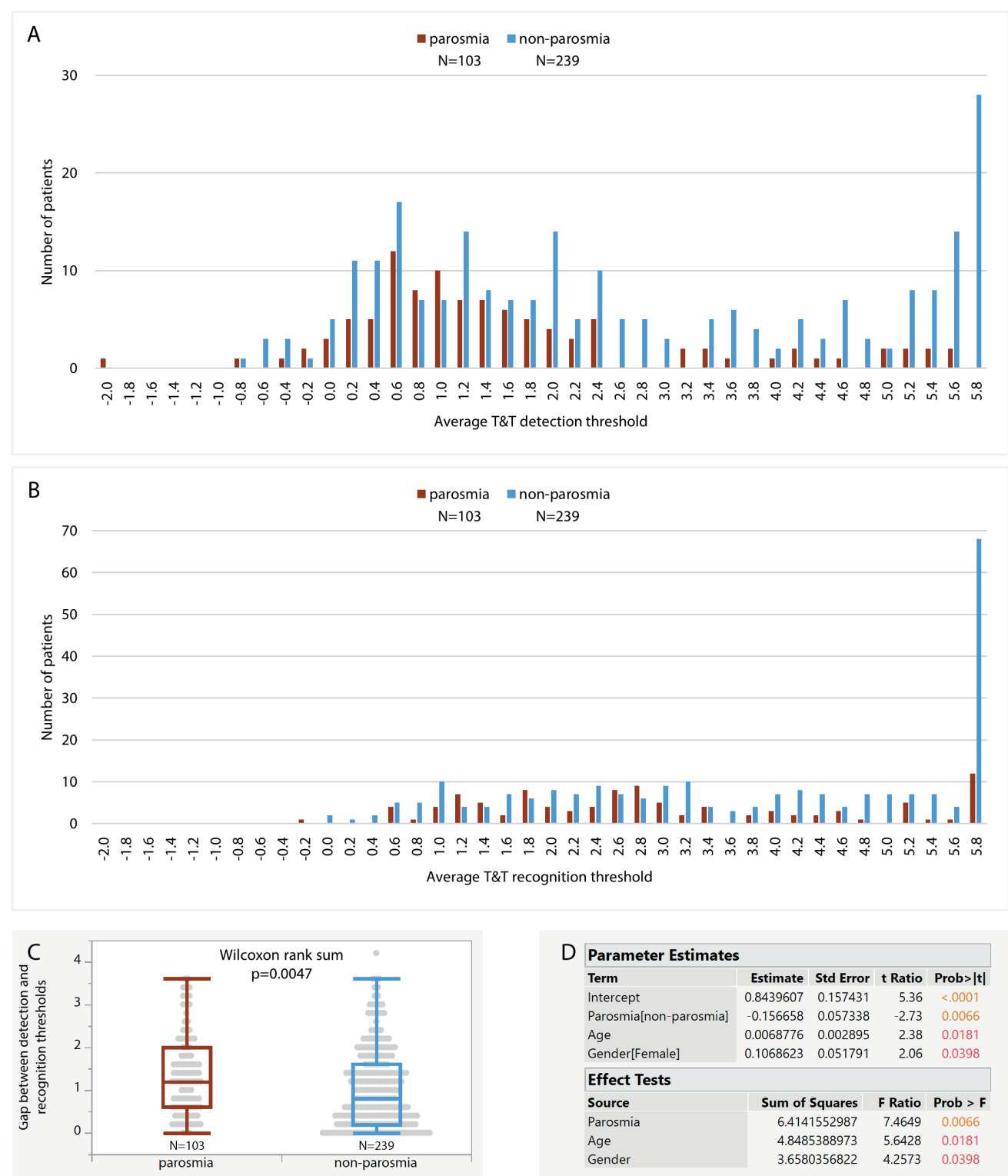
Figure 3. Patient numbers include multiple visits. Figure 3A displays the average T&T detection thresholds, and Figure 3B displays the average T&T recognition thresholds along with patient counts. Both graphs exhibit bimodal distribution, with distinct peaks in the lower and higher threshold ranges. A prominent bulge is evident at 5.8 for anosmia patients. Figure 3C illustrates the gap between detection and recognition thresholds, with parosmia patients showing a higher mean value compared to non-parosmia patients. The Wilcoxon rank sum test revealed a significant difference (p=0.0047). Out of a total count of 111 parosmia patients and 319 non-parosmia patients, 103 parosmia patients and 239 non-parosmia patients provided valid responses. Figure 3D shows multiple linear regression parameter estimates and effect tests result by least square method with the gap between detection and recognition thresholds as the dependent variable and parosmia status, age, and gender as explanatory variables. Parosmia status had the largest F Ratio and least p value.
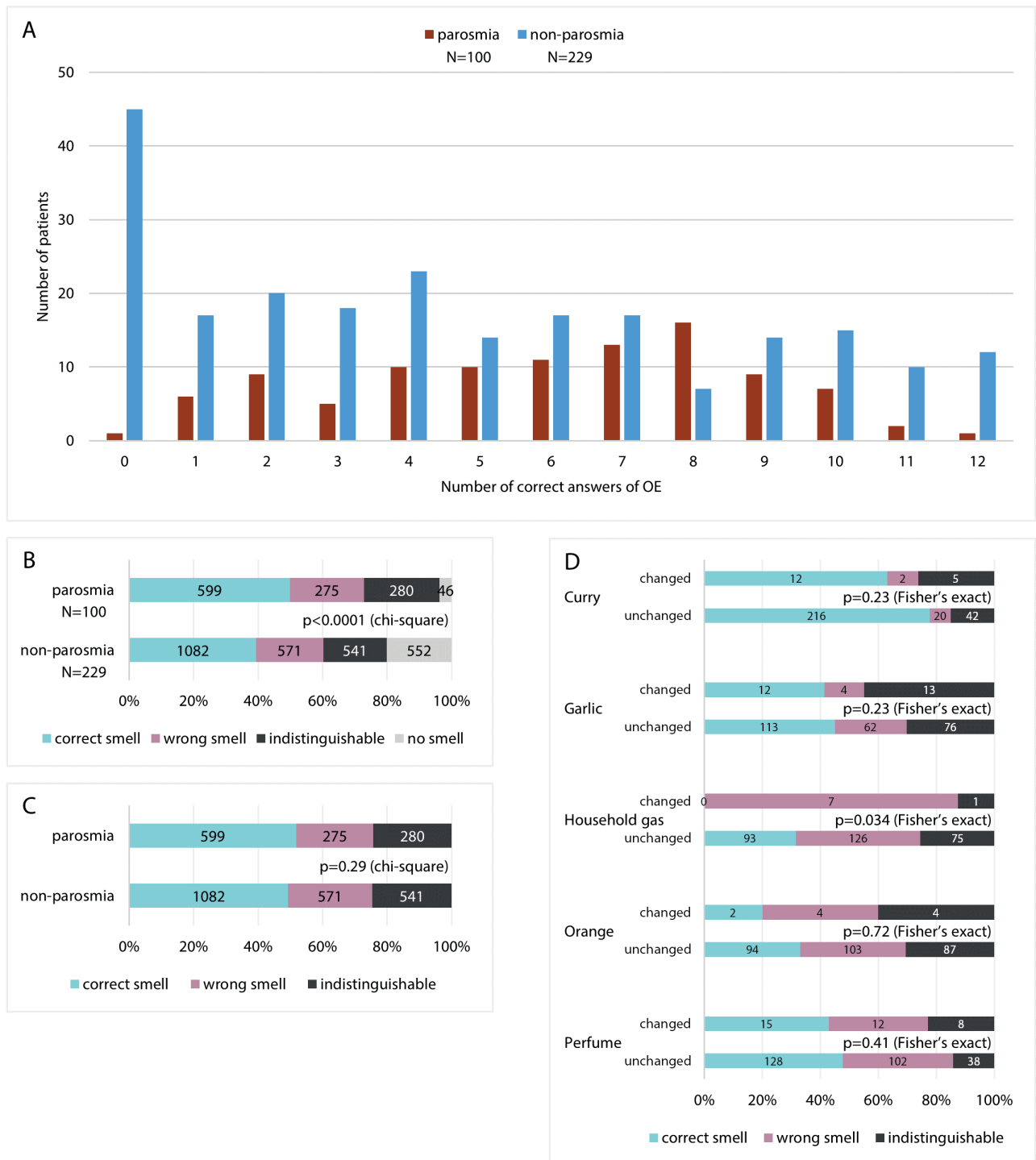
Figure 4. Patient numbers include multiple visits. Figure 4A displays the distribution of the number of correct answers on the OE test. The parosmia group exhibited a peak at 8, while the non-parosmia group showed a peak at 0. Figure 4B presents the total number of OE test responses, and Figure 4C illustrates the total number of OE test responses, excluding "no smell." While a significant difference was observed in Figure 4B, it was not evident in Figure 4C. Figure 4D presents the total number of OE answers without "no smell," categorized into "changed" for patients who reported perceiving each odor differently from before and "unchanged" for those who did not, as indicated in SAOQ-P. A significant difference was observed for house-hold gas. Out of a total count of 111 parosmia patients and 319 non-parosmia patients, 100 parosmia patients and 229 non-parosmia patients provided valid responses. OE: Open Essence, SAOQ-P: Self-Administered Odor Questionnaire for Parosmia.
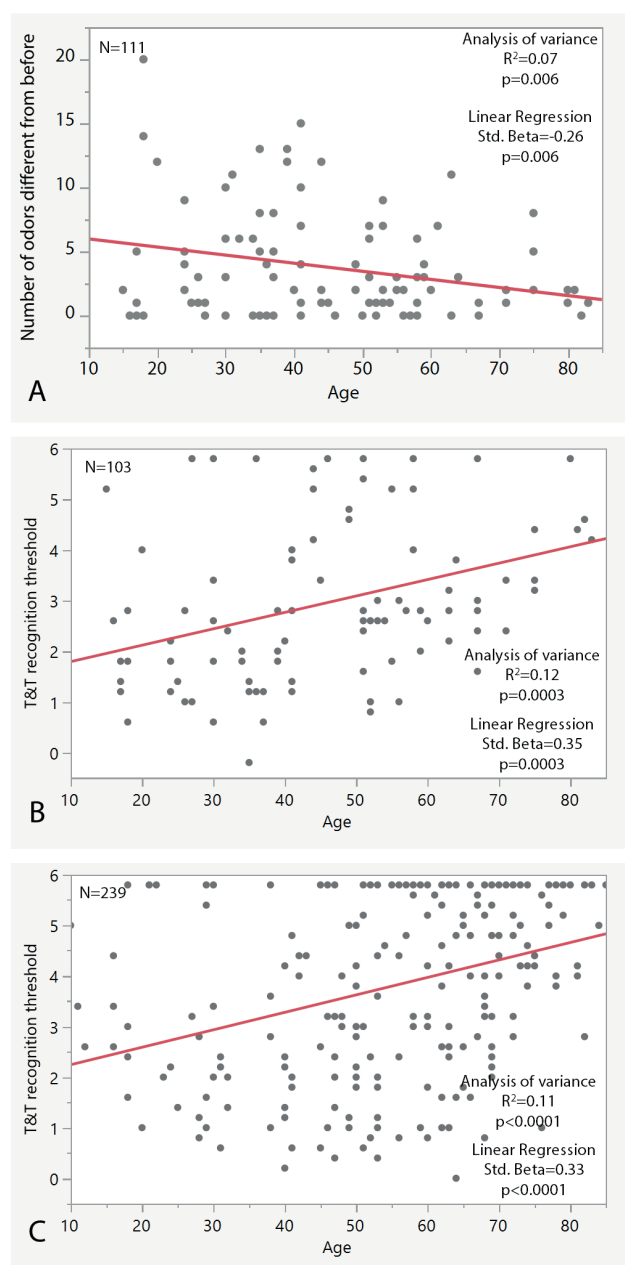
Figure 5. Patient numbers include multiple visits. Figure 5A illustrates the relationship between the number of odors perceived differently and age, which showed a statistically significant negative correlation. Figures 5B and 5C illustrate the relationships between T&T recognition threshold and age in the parosmia group and non-parosmia group, respectively. Both groups showed statistically significant correlations. The sample size (N) is indicated in each graph.

Linear regression analysis showed a standardized beta value of -0.26 and p=0.006, indicating that for every 16-year increase in patient age, there was a decrease of one in the number of odors perceived differently, with age accounting for only 7% of the variability observed. The other seven factors did not show significant differences.

Figures 5B and 5C present the relationship between T&T recognition threshold and age in the parosmia group and non-parosmia group, respectively. Both parosmia and non-parosmia groups showed statistically significant correlations, with p-values of 0.0003 and <0.0001, R2 values of 0.12 and 0.11, respectively, strongly indicating olfactory decline with aging.

Discussion

Prevalence of parosmia

The prevalence of parosmia among olfactory dysfunction patients in this study was 29% (81 out of 279 patients). However, this rate varied depending on the cause of olfactory dysfunction. Our study showed a parosmia prevalence of 47% in post-infectious patients, 59% in COVID-19 patients, and 0% in chronic sinusitis patients. Past articles [4, 14] have reported similar tendencies regarding the prevalence of parosmia among different causes. This heterogeneity in parosmia prevalence could be attributed to the underlying cause of olfactory dysfunction. Conductive olfactory dysfunction typically does not lead to parosmia, whereas sensorineural olfactory dysfunction, particularly one associated with COVID-19 infection, is more likely to result in parosmia.

Quantifying parosmia

Parosmia symptoms remain challenging to quantify due to their heterogeneity and the lack of correlation between their severity and quantitative olfactory dysfunction. While some studies [14] aimed to score parosmia, the majority of questionnaires relied on dichotomous questions [9] and very few have tried questionnaires on specific odors [15] or objective methods [16, 17]. In this study, SAOQ-P effectively quantified parosmia by assessing changes in the perception of 20 daily odors. Remarkably, 87% of parosmia patients reported alterations in at least one odor. However, the number of odors perceived differently did not correlate with the patients' self-assessed smell or taste on the VAS scale. This suggests that the quantity of odors perceived differently does not necessarily reflect the severity of parosmia or its impact on the patients' quality of life. Nevertheless, this metric can serve as a useful indicator during follow-up visits and may help identify which odors are most affected.

Age and parosmia

The negative correlation between the number of odors perceived differently and age could be due to the natural decline in the quantitative and qualitative aspects of olfactory ability. This phenomenon can be also seen from Figure 3D, which indicated age as a factor for a greater gap between T&T detection and recognition thresholds. As individuals age, their capacity to sense and identify smells diminishes, affecting their ability to experience parosmia. Furthermore, Figures 5B and 5C illustrate a clear decline in olfactory function with aging in both the parosmia
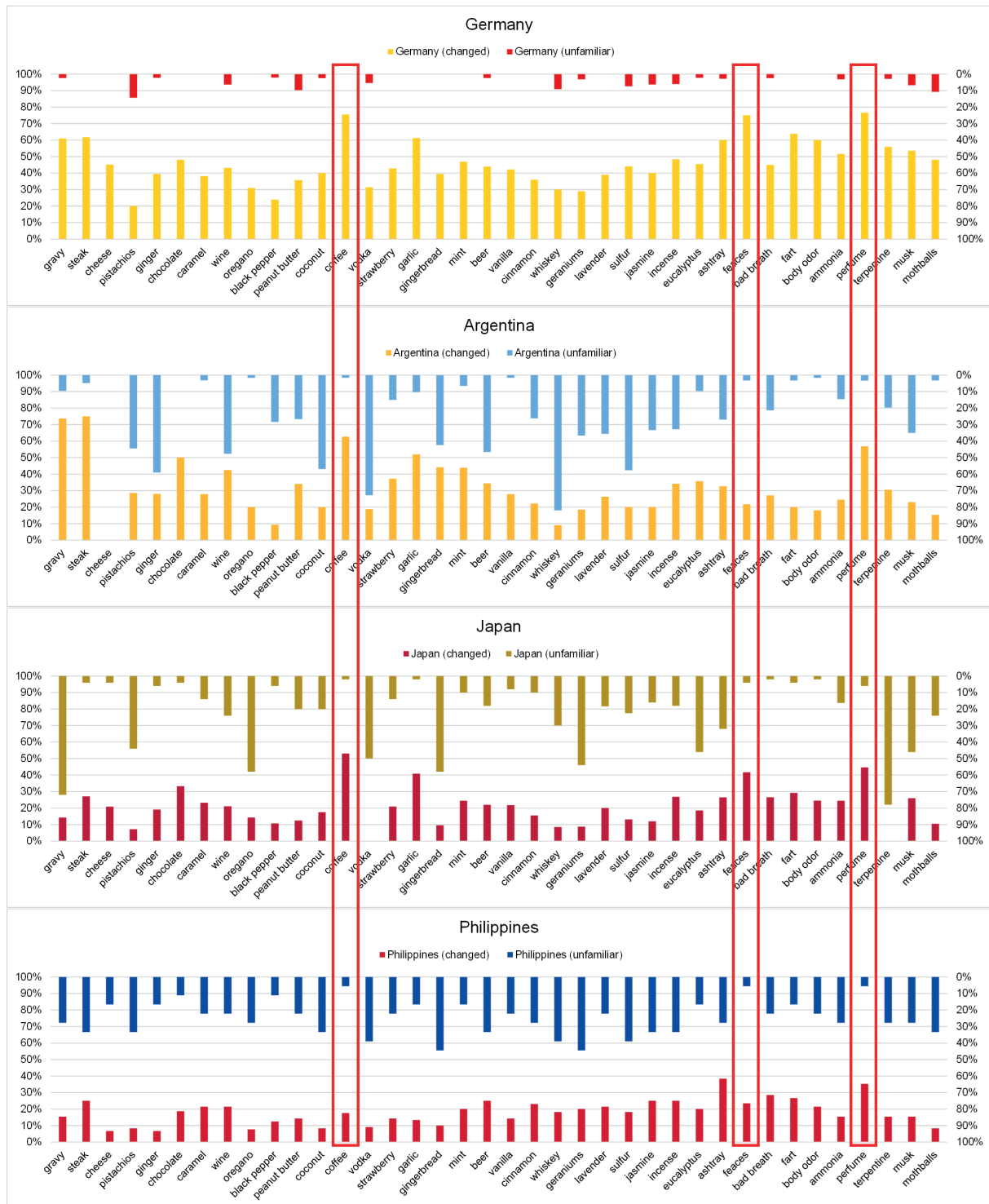
Figure 6. The upper bars show the percentages of odors unfamiliar, and the lower bars show the percentages of odors changed.

and non-parosmia groups.

Commonly affected odors

Coffee, stool, and perfume were identified as the odors most commonly affected by parosmia, with nearly half of parosmia patients reporting changes in these odors. A previous study [15]

by the authors, involving a different patient cohort and study period, also highlighted these odors as common triggers for parosmia, as shown in Figure 6. This consistency across studies and cultural contexts suggests that these odors may serve as potential benchmarks for parosmia detection. The familiarity of individuals with these odors could make them more likely to

notice slight differences and develop parosmia. These findings could provide valuable insights for future research on parosmia triggers.

Olfactory tests and parosmia

The results of olfactory tests in this study did not reveal significant differences between the parosmia and non-parosmia groups. While there was a statistically significant but small difference in the gap between T&T detection and recognition thresholds, indicating weaker olfactory recognition ability in the parosmia group, this difference was not substantial enough to establish a clear cutoff value. The results from OE also failed to demonstrate a significant difference when "no smell" answers were excluded from the analysis. These findings emphasize that traditional olfactory tests, designed primarily for quantifying olfactory dysfunction, are ill-suited for detecting or measuring quantitative olfactory dysfunction. Considering that parosmia patients performed better in T&T olfactometry and had fewer "no smell" answers in OE compared to non-parosmia patients, patients with qualitative olfactory symptoms, such as parosmia, may be underdiagnosed if solely evaluated using these tests. It is essential to exercise caution and accuracy in diagnosing and evaluating patients with qualitative olfactory symptoms, given their higher vulnerability to depressive tendencies and weight losses, as noted in previous studies [18, 19].

Analysis of common odors between SAOQ-P and OE

The presence of five common odors between SAOQ-P and OE provided a unique opportunity for deeper analysis. Overall, patients who experienced parosmia for a specific odor tended to have a lower percentage of "correct smell" and a higher percentage of "indistinguishable" responses in the OE test. Notably, among these five shared odors, household gas stood out as the only odor exhibiting a significant difference between the two patient groups. This aligns with findings from other studies [20, 21], which have similarly reported that household gas is more affected in terms of identifiability compared to other odors. One plausible explanation for this phenomenon could be that while everyday odors are typically composed of complex combinations of odor molecules, the scent of household gas is primarily generated by a single type of artificially added molecule, such as tert-Butylthiol. Fewer molecular components might activate fewer olfactory receptors, making the olfactory system more susceptible to distortion and the development of parosmia when exposed to such singular, chemically distinct odors.

Limitations and future perspectives

A potential issue with studies on parosmia is the definition of "parosmia." In some past articles, this term has been used to describe both quantitative and qualitative olfactory dysfunction, and in some articles, terms such as "dysosmia," "cacosmia," and "troposmia" have been used to describe parosmic symptoms [1]. In Japanese, the term "ikyu-syo" is commonly used, which can mean both parosmia and phantosmia. The accurate term for parosmia in Japanese is "shigekisei ikyu-syo" as defined in the Japanese guideline for olfactory dysfunction [12]. This ambiguity in term usage and definition results in the seemingly wide range of parosmia prevalence. In this study, the authors ensured that parosmia diagnosis was based on the definition stated in the position paper [1] to mitigate selection bias and report accurate data and results.

In the future, SAOQ-P can be easily implemented in olfactory clinics in Japan since it only adds one question column to the original form, SAOQ, which is widely used and included in the Japanese guideline. By maintaining its original questions, SAOQ-P is backward compatible with the original SAOQ and allows for comparative studies using existing data. The utility of SAOQ-P can be further validated with future studies, including longitudinal assessments of SAOQ-P responses among the same patients and analysis of changes in answers and symptoms over time.

This study provided valuable insights into the assessment of parosmia using a questionnaire-based approach. The SAOQ-P, an adapted version of the SAOQ, is a concise and backward-compatible tool that can be seamlessly integrated into the existing assessment process. While the ultimate diagnosis should be made by medical professionals, the 20-odor questionnaire itself was effective in detecting parosmia in 87% of patients. The relatively high percentages of patients reporting changes in the odors of coffee, stool, and perfume suggest that these odors could serve as useful benchmarks or screening targets for parosmia. Future research could explore changes in parosmic symptoms over time by repeatedly administering SAOQ-P to the same patients.

Conclusion

This study aimed to assess and quantify parosmia symptoms by modifying the SAOQ with the addition of one more question and incorporating the new questionnaire (SAOQ-P) into patient assessments. Notably, SAOQ-P successfully identified parosmia in 87% of parosmia patients. It also provided interesting insights, such as coffee, stool, and perfume being common triggers for parosmia symptoms.

Traditional olfactory tests like T&T olfactometry and OE were found to be less suitable for evaluating qualitative olfactory dysfunction. These tests, if used alone, may potentially lead to the underdiagnosis of qualitative olfactory dysfunction, particularly in parosmia cases.

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Authorship contribution

Conflict of interest

Funding

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