Assessment of the difference in detection of pleasant and unpleasant odors in different grades of hyposmia

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Abstract

Background: Olfaction is a complex process involving different neurological mechanisms with a correlation between the chemical structure and quality of odors regarding pleasantness. This study aimed to compare the detection of pleasant and unpleasant odors in different grades of hyposmia. A descriptive cross-sectional study was conducted preceded by a preliminary pilot study, including 20 normal subjects without a history of hyposmia. The pilot study was carried out using the University of Pennsylvania Smell Identification Test (UPSIT) with the assessment of pleasantness of odors using a visual analog scale (VAS). Fifty patients diagnosed with organic hyposmia/anosmia were included in the main study and assessed for the degree of hyposmia/anosmia using UPSIT. The number of detected odors out of the five odors with highest VAS for pleasantness and five odors with lowest VAS for pleasantness, as detected by the pilot study, for every patient was assessed and compared.

Results: There was a significant difference between the detection of pleasant and unpleasant odors in mild, moderate, and severe hyposmia (p value = 0.02, 0.005, and 0.03 respectively) with a highly significant difference in the whole study group (p < 0.00001) with more loss of ability to detect unpleasant odors compared with pleasant odors.

Conclusion: The current study showed significantly less ability to detect unpleasant odors compared with pleasant odors in different grades of hyposmia. This finding suggests that the pattern of degeneration of the olfactory sense organ is not uniform with the topographic nature of the olfactory membrane.

Keywords: Hyposmia, Odorants, Odor detection, Olfaction disorders, Pleasant odors, Quality of odors, Unpleasant odors

Background

Anosmia or hyposmia, the inability or decreased ability to smell, is estimated to affect 3–20% of the population [1]. Several etiologies exist for anosmia, including bilateral nasal obstruction, post-viral neuritis, head trauma, brain tumors, uncinate fits, or neurodegenerative diseases with increasing risk in old age [2]. Hyposmia has a considerable impact on different aspects of quality of life, including the flavor of food, warning odors in the environment, and social relations. This provides a rationale for the exhaustive research regarding the pathophysiology of anosmia [3].

Previous literature has provided four principles for the physiology of olfaction. First, a large number of genes reaching up to 1000 genes in mammals encode olfactory receptors (ORs). Second, each olfactory sensory neuron expresses only a single receptor responding to a distinct odor profile. Third, several olfactory sensory neurons can encode the same receptor, but their axons converge on the same glomerulus in the olfactory bulb. Fourth, each odor is encoded in a combinatorial manner: one odor can activate multiple ORs, and each OR can
respond to multiple odors [4, 5]. As a result, odor information is spatially encoded in the first relay station of the brain [6]. Responses to hundreds of pure odorants are arranged systematically in space across the olfactory bulb according to odorant chemical structure and to the bilateral projections of homologous olfactory sensory neurons [7]. This study aimed to compare the detection of pleasant and unpleasant odors in cases with different grades of hyposmia.

Methods
This study was a descriptive cross-sectional study conducted during the period from October 2018 to May 2020. Patients were recruited from the outpatient otorhinolaryngology clinics. All procedures performed were following the ethical standards of the institutional research committee and the 1964 Helsinki Declaration and its later amendments. Informed consent was obtained from all individual participants included in the study to participate in the research.

A pilot study, including 20 normal subjects without a history of any degree of hyposmia was carried out before proceeding to the main study. These 20 patients were subjected to the University of Pennsylvania Smell Identification Test (UPSIT). The UPSIT score should be higher than 33, indicating normosmia for all the subjects of the pilot study. The patients were instructed to give every odor in the test a score out of 10 with 10 being an extremely pleasant odor and 1 being an extremely unpleasant odor. The results of this pilot study showed that jasmine flower, rose, peppermint oil, apple, and fruit drink had the highest five average scores. In contrast, natural gas, onion, garlic, motor oil, and cheese had the lowest five average scores (Table 1).

Our main study included fifty adult patients diagnosed with organic hyposmia with either idiopathic etiology or following upper respiratory tract infection. Adult patients with an age range from 18 to 60 years were selected to allow a broader experience for odors identification and better cooperation. Patients with a history of post-traumatic anosmia, or having other neurological disorders or manifestations were excluded from the study as every case among them has its specific patchy affection of the olfactory apparatus.

Patients of the study were assessed by history taking and complete otorhinolaryngology examination, including endoscopic nasal examination to exclude any intranasal pathology which may be a cause for the hyposmia. Computed tomography of the nose and paranasal sinuses was done for some patients to confirm any nasal pathology. The degree of hyposmia was assessed using the UPSIT with hyposmia graded as mild (scores of 30 to 33), moderate (scores of 26 to 29), and severe (scores of 19 to 25). The number of detected odors out of the five odors with highest VAS for pleasantness and five odors with lowest VAS for pleasantness, as detected by the preliminary pilot study, for every patient was assessed and compared. All fifty patients of the study completed the test with no missed answers or double answers. The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Statistical analysis
Data were collected, tabulated, and statistically analyzed using an IBM personal computer with IBM Statistical Package of Social Science (SPSS) version 23, Armonk, NY, USA. Qualitative data were presented as numbers and percentages, while quantitative data were presented as mean and standard deviation. Data turned up to be non-normally distributed according to the Kolmogorov-Smirnov test. Wilcoxon signed-rank test was used to compare the paired data of the number of lost pleasant and unpleasant odors for every patient. A two-sided p value of (< 0.05) was considered statistically significant, while a p value of (< 0.001) was considered highly significant.

Results
The current study included 50 patients, including 32 (64%) females and 18 (36%) males with a mean age of 35.92 ± 8.49 SD years. The results of UPSIT showed that 20 (40%) patients had mild hyposmia, 18 patients (36%) patients had moderate hyposmia, and 12 (24%) patients had severe hyposmia (Table 2).

In the current study, there was a significant difference between detection of pleasant and unpleasant odors in mild, moderate, and severe hyposmia (p value = 0.02, 0.005, and 0.03, respectively) with a highly significant difference in the whole study group (p < 0.00001) with more loss of ability to detect unpleasant odors compared with pleasant odors (Table 3).

Discussion
The current study aimed to assess the difference between the loss of perception of pleasant and unpleasant odors in cases of hyposmia. We found that the incidence of loss of unpleasant odors was more than pleasant odors in cases of hyposmia. This finding puts two questions into consideration: does each of pleasant and unpleasant odors share a similar physicochemical profile, which will be reflected in the perception of odor quality? Is there a difference regarding the perception of pleasant odors and unpleasant odors at a central or peripheral level?

Regarding the first question, the relationship between the physicochemical structure of odorant molecules and their quality regarding pleasantness has been described...
by several studies. Khan et al. [8] applied a statistical method to correlate between odor percepts and physicochemical descriptors for a large set of molecules. They found that the primary axis of physicochemical properties reflected the primary axis of olfactory perception. This finding allowed them to predict the pleasantness of novel molecules by their physicochemical properties alone. Their findings suggested that olfactory

| Odor rank | Smell                  | VAS for smell pleasantness, mean ± SD |
|-----------|------------------------|---------------------------------------|
| 1.        | Jasmine flower         | 9.85 ± 0.37                           |
| 2.        | Rose                   | 9.8 ± 0.41                            |
| 3.        | Peppermint oil        | 9.75 ± 0.44                           |
| 4.        | Apple                  | 9.7 ± 0.47                            |
| 5.        | Fruit drink            | 9.7 ± 0.47                            |
| 6.        | Orange                 | 9.5 ± 0.51                            |
| 7.        | Chocolate              | 9.15 ± 0.59                           |
| 8.        | Soap                   | 8.95 ± 0.51                           |
| 9.        | Peach                  | 8.9 ± 0.79                            |
| 10.       | Mint                   | 8.7 ± 0.47                            |
| 11.       | Children powder        | 8.4 ± 0.50                            |
| 12.       | Strawberry             | 7.9 ± 0.55                            |
| 13.       | Lemon                  | 7.75 ± 0.44                           |
| 14.       | Banana                 | 7.7 ± 0.47                            |
| 15.       | Pineapple              | 7.55 ± 0.51                           |
| 16.       | Gum                    | 7.2 ± 0.52                            |
| 17.       | Clove                  | 7.1 ± 0.55                            |
| 18.       | Coconut                | 6.95 ± 0.39                           |
| 19.       | Coffee                 | 6.8 ± 0.52                            |
| 20.       | Watermelon             | 6.7 ± 0.47                            |
| 21.       | Grapefruit              | 6.3 ± 0.57                            |
| 22.       | Pine                   | 6.3 ± 0.47                            |
| 23.       | Grape                  | 5.85 ± 0.59                           |
| 24.       | Walnut                 | 5.45 ± 0.51                           |
| 25.       | Peanut                 | 5.45 ± 0.60                           |
| 26.       | Grass                  | 4.9 ± 0.45                            |
| 27.       | Pizza                  | 4.7 ± 0.47                            |
| 28.       | Cumin                  | 4.6 ± 0.50                            |
| 29.       | Cardamom               | 4.3 ± 0.47                            |
| 30.       | Fish                   | 3.95 ± 0.51                           |
| 31.       | Benzene                | 3.7 ± 0.57                            |
| 32.       | Rubber framework       | 3.35 ± 0.49                           |
| 33.       | Leather                | 3.1 ± 0.31                            |
| 34.       | Dill pickle            | 2.75 ± 0.64                           |
| 35.       | Smoke                  | 2.2 ± 0.41                            |
| 36.       | Cheese                 | 1.95 ± 0.83                           |
| 37.       | Motor oil              | 1.4 ± 0.50                            |
| 38.       | Garlic                 | 1.3 ± 0.47                            |
| 39.       | Onion                  | 1.2 ± 0.41                            |
| 40.       | Natural gas            | 1.2 ± 0.41                            |
pleasantness is also partially innate, corresponding to a natural axis of maximal discriminability among biologically relevant molecules. Keller and Vosshall [9] tested the olfactory perception of 480 structurally and perceptually diverse molecules at two concentrations using a panel of 55 healthy human subjects. They found that the number of sulfur atoms in a molecule was correlated with the odor quality descriptors “garlic,” “fish,” “sweet,” “fruit,” “burnt,” “spices,” “flower,” and “sour”). These models helped to predict the perceptual qualities of virtually any molecule with high accuracy.

All the previous studies clarified the close association between the chemical structure of odorants and their perceptual quality regarding pleasantness. In the current study, we found that the five pleasant odors selected by the subjects in the preliminary pilot study, namely, jasmine flower, rose, peppermint oil, apple, and fruit drink, share a plant origin being flowers and fruits. Esters are main ingredients of fruits and flowers, with their structure containing a carbonyl group with a second oxygen atom bonded to the carbon atom in the carbonyl group by a single bond, and this second oxygen atom bonds to another carbon atom. Esters have very pleasant odors and flavors and contribute to the odor of flowers and the taste of fruits. Other esters are synthesized industrially and are added to food products to improve their smell or taste [12]. On the other hand, the five unpleasant odors selected by the subjects in the preliminary pilot study, namely, smoke, natural gas, onion, cheese, and motor oil share a sulfur component in their structure. Sulfur, in its different chemical combinations, including hydrogen sulfide, is known to be associated with a characteristically unpleasant smell [12].

Regarding the second question at the beginning of this discussion, at the central level, several studies have investigated the difference between the central processing of pleasant and unpleasant stimuli. Djordjevic et al. [13] used positron emission tomography to investigate whether regional brain activations differ as a function of exposure to pleasant versus unpleasant components of odors. They found that several brain regions were involved in both types of exposure, and these included ventral striatum, right orbitofrontal cortex, and anterior cingulate cortex. Subtle differences were also revealed: Attending to pleasantness was associated preferentially with a sensory/perceptual network (piriform cortex and

| Table 2 | Demographic and clinical data of the main study group |
|---------|-----------------------------------------------|
| Variable | Value                                         |
| Age, mean ± SD | 35.92 ± 8.49                                  |
| Gender | No. | % |
| Male | 18 | 36 |
| Female | 32 | 64 |
| Degree of hyposmia | Value |
| Mild | 20 | 40 |
| Moderate | 18 | 36 |
| Severe | 12 | 24 |

| Table 3 | Comparison between the loss of perception of pleasant and unpleasant odors in different grades and allover cases of hyposmia |
|---------|---------------------------------------------------------------------------------------------------------------|
| Degree of hyposmia | Number of pleasant smells detected | Number of unpleasant smells detected | Statistical test, Wilcoxon signed-rank test | p value |
| Mild hyposmia (20 patients) | 3.85 ± 0.37 | 3.4 ± 0.5 | z = −2.4006 | 0.02* |
| Moderate hyposmia (18 patients) | 3.22 ± 0.55 | 2.56 ± 0.62 | z = −2.8249 | 0.005* |
| Severe hyposmia (12 patients) | 2.08 ± 0.67 | 1.42 ± 0.51 | z = −2.2424 | 0.03* |
| All over group | 3.2 ± 0.88 | 2.66 ± 0.89 | z = −4.039 | < 0.00001** |

*Significant
**Highly significant
amygdala), whereas attending to unpleasantness engaged a component of the attentional (right parietal) network. However, in the current study, we tried to neutralize the central element in olfactory perception in cases of anosmia by excluding post-traumatic cases and cases with neurological disorders. We aimed to investigate the difference in perception loss between pleasant and unpleasant odors at the peripheral level, i.e. at the level of the olfactory membrane.

Regarding the peripheral level of perception, organization of receptive surfaces of the retina and cochlea reflects primary axes of perception of visual and auditory stimuli. However, the organization of the olfactory receptive surface is still under investigation. Lapid et al. [14] found a patchy variation in odor-evoked electrical activity in the human olfactory epithelium to be correlated with stimulus pleasantness. They conducted their study by inserting an electrode into the human olfactory epithelium to measure odorant-induced evoked responses (electro-olfactogram) directly. They found that variation in odorant pleasantness resulted in variation of response magnitude. Also, certain locations of the olfactory epithelium responded maximally to pleasant odors with less response to unpleasant stimuli compared with other locations responding maximally to unpleasant odors with less response to pleasant stimuli. This finding suggested a similarity of the olfactory receptive surface to receptive surfaces for vision and audition in the correlation between the organization of the receptor surface and the key axes of perception, including quality.

The findings of our study, in the light of the answers to these two questions, support the spatial coding of olfactory stimuli in the olfactory membrane with a patchy distribution having specific locations for pleasant odors and other locations for unpleasant odors. Locations for pleasant stimuli which are known to have a more complex structure are more resistant to degeneration compared with locations for unpleasant stimuli in cases with different grades of hyposmia. Our study has a limitation of being based only on clinical assessment. Confirmation of the findings with electro-olfactogram should be planned in future studies for a more precise correlation between the clinical presentation of hyposmia and pattern of degeneration of the olfactory membrane.

**Conclusion**

The current study showed significantly less ability to detect unpleasant odors compared with pleasant ones in different grades of hyposmia. This finding suggested that the pattern of degeneration of the olfactory sense organ is not uniform with the topographic nature of the olfactory membrane, with locations for unpleasant odor perception more prone to degeneration than locations for pleasant odor perception.

**Abbreviations**

NY: New York; ORs: Olfactory receptors; SD: Standard deviation; UPSIT: University of Pennsylvania Smell Identification Test; USA: United States of America; VAS: Visual analog scale

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**Authors’ contributions**

TA provided the concept, design with the definition of the intellectual content, clinical studies, data collection, manuscript editing. AH conducted literature research, clinical studies, data collection, data analysis, and manuscript preparation. All authors have read and approved the manuscript.

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**Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Ethics approval and consent to participate**

This study was approved by the institutional review board of Menoufia Faculty of Medicine with approval number 7-2020 ENT. The participants of the study provided written consent before participation in the study.

**Consent for publication**

Not applicable.

**Competing interests**

No potential competing interests relevant to this article were reported for any of the authors.

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