Attia and Hamdan *The Egyptian Journal of Otolaryngology* (2021) 37:18
https://doi.org/10.1186/s43163-021-00070-4

The Egyptian Journal
of Otolaryngology

ORIGINAL ARTICLE

Open Access

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

Tamer M. Attia[1,2] and Ahmad M. Hamdan[1*]

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

---

* Correspondence: Ahmed.Hamdan@med.menofia.edu.eg
[1]Otolaryngology Head & Neck Surgery Department, Faculty of Medicine, Menoufia University, Shebin El-kom, Egypt
Full list of author information is available at the end of the article

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

Table 1 Ranking of the odorants of the Arabic version of UPSIT regarding pleasantness according to the preliminary pilot study

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

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

Table 2 Demographic and clinical data of the main study group

Variable	Value	
Age, mean ± SD	35.92 ± 8.49	
	No.	**%**
Gender		
Male	18	36
Female	32	64
Degree of hyposmia		
Mild	20	40
Moderate	18	36
Severe	12	24

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,” and “decayed,” and large and structurally complex molecules were perceived to be more pleasant. Kerman et al. [10] assessed the relationship between molecular complexity based on bond connectivity, diversity of non-hydrogen atoms and symmetry at one axis, and odor pleasantness at the other axis. They found that larger compounds exhibit greater complexity than smaller ones, but large symmetrical compounds and large compounds with low diversity of atom kinds were downgraded. They found that low complexity odorants were rated as more unpleasant than medium (p = 0.016) or high (p = 0.010) complexity odorants. Keller [11] organized a crowd-sourced DREAM Olfaction Prediction Challenge. Using a large olfactory psychophysical data set, teams developed machine-learning algorithms to predict sensory attributes of molecules based on their chemoinformatic features. The resulting models accurately predicted odor intensity and pleasantness and also successfully predicted eight among 19 rated semantic 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 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 odorants with less response to unpleasant stimuli compared with other locations responding maximally to unpleasant odorants 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

Acknowledgements

Not applicable for this article.

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

Funding

No funding for this research.

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.

Author details

[1]Otolaryngology Head & Neck Surgery Department, Faculty of Medicine, Menoufia University, Shebin El-kom, Egypt. [2]Otolaryngology, Head & Neck Surgery Department, Zulekha Hospital LLC, Sharjah, United Arab Emirates.

Received: 26 October 2020 Accepted: 6 January 2021

References

1. Hoffman HJ, Rawal S, Li CM, Duffy VB (2016) New chemosensory component in the US National Health and Nutrition Examination Survey (NHANES): first-year results for measured olfactory dysfunction. Rev Endocr Metab Disord 17:221–240
2. Kern DW, Wroblewski KE, Schumm LP, Pinto JM, Chen RC, McClintock MK (2014) Olfactory function in wave 2 of the national social life, health, and aging project. J Gerontol B Psychol Sci Soc Sci 69:S134–S143
3. Croy I, Nordin S, Hummel T (2014) Olfactory disorders and quality of life – an updated review. Chem Senses 39:185–194
4. Malnic B, Hirono J, Sato T, Buck LB (1999) Combinatorial receptor codes for odors. Cell 96:713–723
5. Hallem EA, Carlson JR (2006) Coding of odors by a receptor repertoire. Cell 125:143–160
6. Mori K, Takahashi YK, Igarashi KM, Yamaguchi M (2006) Maps of odorant molecular features in the Mammalian olfactory bulb. Physiol Rev 86:409–433
7. Johnson BA, Leon M (2007) Chemotopic odorant coding in a mammalian olfactory system. J Comp Neurol 503(1):1–34
8. Khan RM, Luk CH, Flinker A, Aggarwal A, Lapid H, Haddad R, Sobel N (2007) Predicting odor pleasantness from odorant structure: pleasantness as a reflection of the physical world. J Neurosci 27(37):10015–10023
9. Keller A, Vosshall LB (2016) Olfactory perception of chemically diverse molecules. BMC Neurosci 17(1):55
10. Kermen F, Chakirian A, Sezille C, Joussain P, Le Goff G, Ziessel A, Chastrette M, Mandairon N, Didier A, Rouby C, Bensafi M (2011) Molecular complexity determines the number of olfactory notes and the pleasantness of smells. Sci Rep 1:206
11. Keller A, Gerkin RC, Guan Y, Dhurandhar A, Turu G, Szalai B, Mainland JD, Ihara Y, Yu CW, Wolfinger R, Vens C, Schietgat L, De Grave K, Norel R, DREAM Olfaction Prediction Consortium, Stolovitzky G, Cecchi GA, Vosshall LB,

Meyer P (2017) Predicting human olfactory perception from chemical features of odor molecules. Science 355(6327):820–826
12. Ohloff G, Pickenhagen WD, Kraft P (2012) Scent and chemistry: the molecular world of odors, 1st edn. Wiley VCH, Weinheim
13. Djordjevic J, Boyle JA, Jones-Gotman M (2012) Pleasant or unpleasant: attentional modulation of odor perception. Chemosens Percept 5:11–21
14. Lapid H, Shushan S, Plotkin A, Voet H, Roth Y, Hummel T, Schneidman E, Sobel N (2011) Neural activity at the human olfactory epithelium reflects olfactory perception. Nat Neurosci 14(11):1455–1461

Publisher's Note