The Journal of Laryngology & Otology

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Threshold and suprathreshold component analysis in olfactory dysfunction: a retrospective study

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Abstract

Objective. To analyse variations in the n-butanol threshold and odour identification scores of the Connecticut Chemosensory Clinical Research Centre test in various grades of olfactory dysfunction and in different nasal conditions leading to olfactory loss.

Method. Retrospective observational study.

Results. All grades of olfactory dysfunction were predominantly noted among males. In chronic rhinosinusitis, anosmia or severe hyposmia was seen in 87.5 per cent of patients without polyps in comparison with 68 per cent of patients with polyps. In addition, 90 per cent of patients with atrophic rhinitis and post-traumatic loss had anosmia, but only 30.7 per cent of patients with allergic rhinitis had anosmia. Pepper was the most affected smell for all the nasal diseases except atrophic rhinitis, in which asafoetida and baby powder smells were affected more.

Conclusion. In most inflammatory sinonasal conditions, odour identification is relatively preserved even when the threshold is maximally affected. In patients with comparable olfactory dysfunction based on the Connecticut Chemosensory Clinical Research Centre test score, a relatively preserved suprathreshold odour identification score may predict better prognosis.

Main Article

Lalee Varghese takes responsibility for the integrity of the content of the paper

Cite this article: Brabahar BS, Kurien R, Panicker R, Rebekah G, Varghese L. Threshold and suprathreshold component analysis in olfactory dysfunction: a retrospective study. *J Laryngol Otol* 2024;**138**:647–651. https://doi.org/10.1017/S0022215123002268

Received: 31 July 2023
Revised: 16 October 2023
Accepted: 2 November 2023
First published online: 7 December 2023

Keywords:
olfaction disorders; anosmia; olfaction; identification; threshold; nasal diseases

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Introduction

Olfaction, one of the cardinal special senses, is linked not only to detecting environmental chemicals, improving social interactions and cognitive functions, but also in combination with taste and somatosensory stimuli helps to enhance the pleasure of eating.[1] The optimum performance of this vital physiological function necessitates an intact and well-functioning olfactory epithelium situated in the olfactory cleft in the roof of the nose, enhancing the quality of life.[2]

The prevalence of olfactory dysfunction in the general population is around 22.2 per cent,[3] with multiple etiological factors, including conductive, sensorineural and mixed,[4] with a significant overlap among them. Although the majority of olfactory dysfunction is secondary to sinonasal causes, other aetiologies include post-traumatic and idiopathic. A variety of psychophysical olfactory tests have been developed to assess various aspects of olfaction, including testing at threshold (olfactory threshold) and suprathreshold (olfactory identification, discrimination) levels.[5] Olfactory threshold testing preferentially tests peripheral causes of olfactory dysfunction, whereas the suprathreshold tests of discrimination and identification assess central or cognitive causes.[6]

Although the literature shows reduced olfactory composite scores in a variety of olfactory disorders, there is a paucity of knowledge regarding how severely the individual components are affected. Whitcroft *et al.* showed that subjects with olfactory loss due to sinonasal disease were particularly impaired in their odour threshold scores, whereas patients with Parkinson's disease were preferentially impaired in suprathreshold olfactory tasks (odour discrimination and identification).[6] Patients with human immunodeficiency virus-induced dementia had preservation of odour threshold scores, with only the identification component being affected.[7]

This study aimed to assess how severely the different components of olfactory tests were affected in various grades of olfactory dysfunction and in different nasal conditions leading to olfactory loss. It also aimed to examine how different odours are affected in each of these situations.

Materials and methods

This retrospective observational cohort study used tertiary hospital-collected data from the institutional database for patients over 16 years of age who were diagnosed with olfactory dysfunction based on Connecticut Chemosensory Clinical Research Centre olfaction testing between January 2018 and March 2020. Patients with normal olfaction and

children were excluded. The details for each patient, including demography, presenting symptoms, duration of symptoms, clinical examination and olfaction testing, were recorded.

All the procedures in this study were performed in accordance with the ethical standards of the institutional research committee and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Institutional review board approval was obtained prior to the commencement of the study (IRB number: 13359).

Results

A total of 245 patients with olfactory dysfunction were recruited for this study. As each nasal cavity was assessed separately, the total sample size was 490. Based on the results of the two components of the Connecticut Chemosensory Clinical Research Centre test, the composite score was calculated and a diagnosis of anosmia, severe hyposmia, moderate hyposmia, mild hyposmia or normosmia was made. Nasal cavities with normosmia were excluded from the analysis.

The highest number of patients ($n = 231$, 47.14 per cent) had anosmia followed by severe hyposmia ($n = 102$, 20.82 per cent). Eighty-seven patients (17.76 per cent) had moderate hyposmia while 63 (12.86 per cent) had mild hyposmia.

Demographics

The age of patients ranged from 18 to 72 years, with a mean of 41 years across the entire cohort. The majority of patients across all four types of olfactory dysfunction fell into the 18–45 years age group. The study population consisted of 151 males (61.63 per cent) and 94 females (38.37 per cent). All four grades of olfactory dysfunction were seen predominantly in the male population.

Prevalence of nasal diseases

The most common nasal disease found among the study population was allergic rhinitis ($n = 212$, 44.4 per cent). Other nasal conditions encountered were chronic rhinosinusitis with nasal polyposis ($n = 96$, 20.1 per cent), chronic rhinosinusitis without nasal polyposis ($n = 32$, 6.7 per cent), post-traumatic loss of smell ($n = 26$, 5.4 per cent) and atrophic rhinitis ($n = 20$, 4.2 per cent). Ninety-two patients (25 per cent) had idiopathic olfactory loss without any identifiable underlying cause. Post-surgical patients were not included in the study.

Connecticut Chemosensory Clinical Research Centre test results

The two components of the Connecticut Chemosensory Clinical Research Centre test are the n-butanol threshold and odour identification. Both the n-butanol threshold and odour identification scores range from 0 to 7.

Olfactory threshold

Most of the patients with anosmia and severe hyposmia had a predominant olfactory threshold score of 0. Among patients with moderate hyposmia, the majority had a threshold score of 2 followed by a score of 1. In the mild hyposmia group, the dominant score was 3. The distribution of the olfactory threshold in all grades of olfactory loss is shown in Table 1.

Odour identification

The odour identification scoring was based on the ability of the patient to identify odours (cinnamon, asafoetida, coffee, tea, pepper, clove oil and baby powder). In the study cohort,

Table 1. Connecticut Chemosensory Clinical Research Centre test scores for types of olfactory dysfunction

	Anosmia ($n = 231$)		Severe hyposmia ($n = 102$)		Moderate hyposmia ($n = 87$)		Mild hyposmia ($n = 63$)	
Test score	*n*	%	*n*	%	*n*	%	*n*	%
Olfactory threshold								
0	217	93.94	69	67.65	0	0	0	0
1	11	4.76	15	14.71	18	20.69	0	0
2	1	0.43	14	13.73	52	59.77	0	0
3	2	0.87	4	3.92	9	10.34	53	84.13
4	0	0	0	0	7	8.05	6	9.52
5	0	0	0	0	0	0	4	6.35
6	0	0	0	0	1	1.15	0	0
Odour identification								
0	187	80.95	0	0	0	0	0	0
1	16	6.93	0	0	0	0	0	0
2	19	8.23	0	0	1	1.15	0	0
3	9	3.90	8	7.84	0	0	0	0
4	0	0	18	17.65	1	1.15	0	0
5	0	0	29	28.43	9	10.34	3	4.76
6	0	0	29	28.43	18	20.69	4	6.35
7	0	0	18	17.65	58	66.67	56	88.89

https://doi.org/10.1017/S0022215123002268 Published online by Cambridge University Press

Table 2. Prevalence of nasal diseases *vs* types of olfactory dysfunction

	Anosmia		Severe hyposmia		Moderate hyposmia		Mild hyposmia	
Type of nasal disease	*n*	%	*n*	%	*n*	%	*n*	%
Allergic rhinitis (*n* = 212)	65	30.66	49	23.11	57	26.89	40	18.87
CRSsNP (*n* = 32)	17	53.13	11	34.38	2	6.25	2	6.25
CRSwNP (*n* = 96)	56	58.33	9	9.38	13	13.54	15	15.63
Post-traumatic loss (*n* = 26)	24	92.31	0	0	2	7.69	0	0
Atrophic rhinitis (*n* = 20)	18	90	2	10	0	0	0	0
Idiopathic (*n* = 92)	43	46.74	31	33.70	11	11.96	4	4.35

CRSsNP = chronic rhinosinusitis without nasal polyposis; CRSwNP = chronic rhinosinusitis with nasal polyposis

the majority of patients with anosmia had an odour identification score of 0, whereas the severe hyposmia group most patients scored 6 followed by 5. In the moderate and mild hyposmia populations, 66.7 and 88.9 per cent of patients, respectively, could identify all seven odours and hence the most common score was 7 (Table 1).

Severity of olfactory dysfunction among various nasal diseases

All patients with atrophic rhinitis had either anosmia (90 per cent) or severe hyposmia (10 per cent), and 92 per cent of patients with post-traumatic loss had anosmia. Among patients with chronic rhinosinusitis, anosmia or severe hyposmia was seen in 87.5 per cent of those without polyps compared with 68 per cent of those with polyps. Patients with allergic rhinitis showed marginally higher anosmia (30.7 per cent) and moderate hyposmia (26.9 per cent) (Table 2).

Connecticut Chemosensory Clinical Research Centre test results

The patients in the study cohort had a predominant olfactory threshold score of 0 for all the nasal diseases. Patients with chronic rhinosinusitis with and without polyposis, post-traumatic olfactory loss, atrophic rhinitis or idiopathic loss of smell had a predominant odour identification score of 0, whereas this score was 7 for patients with allergic rhinitis (Table 3).

Most common odour affected

The four different types of olfactory dysfunction, namely, anosmia, severe hyposmia, moderate hyposmia and mild hyposmia, showed specific predilection in the loss of smell. More than 90 per cent of patients with anosmia failed to identify all the seven tested odours. Pepper was the least perceived smell among patients with anosmia, severe hyposmia and moderate hyposmia. The mild hyposmia group showed less perception of cinnamon compared with the other smells.

On analysing the specific smell loss in various nasal diseases, pepper was the least perceived smell among patients with allergic rhinitis, chronic rhinosinusitis without nasal polyposis, chronic rhinosinusitis with nasal polyposis and idiopathic loss. In patients with atrophic rhinitis, the asafoetida and baby powder smells were most affected (Table 4).

Discussion

The present study comprised 245 patients with a predominance of anosmia and severe hyposmia. Although the composite scores were low in these patients, subcomponent analysis of threshold and suprathreshold scores showed a relative preservation of olfactory identification, especially in those with moderate and severe hyposmia. Pepper was the least perceived smell among patients with anosmia, severe hyposmia and moderate hyposmia. Patients with allergic rhinitis, which was the most common sinonasal cause of olfactory dysfunction, showed a relative preservation of identification scores, unlike

Table 3. Connecticut Chemosensory Clinical Research Centre Olfactory test scores in nasal diseases

	Allergic rhinitis (*n* = 212)		CRSsNP (*n* = 32)		CRSwNP (*n* = 96)		Post-traumatic loss (*n* = 26)		Atrophic rhinitis (*n* = 20)		Idiopathic (*n* = 92)	
Test score	OT (%)	OI (%)	OT (%)	OI (%)	OT (%)	OI (%)	OT (%)	OI (%)	OT (%)	OI (%)	OT (%)	OI (%)
0	42.86	19.34	75	43.75	61.05	48.96	92.31	76.92	90	90	71.11	46.74
1	10	4.25	12.50	0	13.68	4.17	0	7.69	5	0	4.44	0
2	20.48	6.13	6.25	0	4.21	5.21	7.69	7.69	0	0	17.78	0
3	21.43	3.77	6.25	12.5	14.74	1.04	0	0	5	0	4.44	1.09
4	4.29	6.13	0	6.25	3.16	0	0	0	0	0	0	4.35
5	0.95	7.55	0	6.25	3.16	4.17	0	0	0	0	2.22	20.65
6	0	13.21	0	12.5	0	7.29	0	0	0	10	0	9.78
7	–	39.62	–	18.75	–	29.17	–	7.69	–	0	–	17.39

CRSsNP = chronic rhinosinusitis without nasal polyposis; CRSwNP = chronic rhinosinusitis with nasal polyposis; OT = olfactory threshold; OI = odour identification

https://doi.org/10.1017/S0022215123002268 Published online by Cambridge University Press

Table 4. Odour affected

Olfactory dysfunction	Cinnamon (%)	Asafoetida (%)	Coffee (%)	Tea (%)	Pepper (%)	Clove oil (%)	Baby powder (%)
Anosmia	91	90	95	97	99	95	97
Severe hyposmia	5	14	9	20	65	12	46
Moderate hyposmia	5	5	5	2	17	6	10
Mild hyposmia	5	3	0	3	3	2	0
Nasal diseases							
Allergic rhinitis	28.30	29.25	33.02	37.26	50.94	32.08	42.45
CRSsNP	46.88	53.13	43.75	62.50	71.88	56.25	65.63
CRSwNP	58.33	56.25	55.21	56.25	64.58	59.38	62.50
Post-traumatic loss	84.62	80.77	92.31	92.31	92.31	92.31	88.46
Atrophic rhinitis	90.00	95.00	90.00	90.00	90.00	90.00	95.00
Idiopathic	50.00	55.43	50.00	50.00	73.91	50.00	66.30

CRSsNP = chronic rhinosinusitis without nasal polyposis; CRSwNP = chronic rhinosinusitis with nasal polyposis

those with the other sinonasal diseases, who showed low threshold and identification scores. Similar to the findings in the cohort, pepper was the least perceived smell among patients with various sinonasal diseases.

Most patients with all four types of olfactory dysfunction were in the 18–45 years age group, with a male predominance. Because women are more involved in cooking and care giving, they are thought to appreciate smell disturbances more than men (38.3 *vs* 27.6 per cent).[8] The male predominance (61.63 per cent) in our cohort may arise because this is a hospital-based study and men seek medical help faster in Indian population.[9] The comparatively lower mean age (42 years) in our study population could indicate that people of prime working age seek medical help, whereas elderly people tend to live with the problem.

Unlike hearing or vision, olfactory losses can go unrecognised for a long time, especially when there is unilateral or less than complete loss. Less than 25 per cent of people with demonstrable smell loss are aware of their loss until they are tested quantitatively. In conditions with gradual deterioration in smell sensation, a certain threshold must be reached before the loss becomes noticeable and the person seeks medical help.[10] This could explain why almost 68 per cent of patients in the study cohort had anosmia or severe hyposmia. Sudden loss of smell may be recognised and reported more quickly.

The most commonly experienced associated condition was allergic rhinitis (44.4 per cent), followed by chronic rhinosinusitis with nasal polyposis (20.1 per cent) and chronic rhinosinusitis without nasal polyposis (6.7 per cent). A quarter of patients did not state an identifiable cause for the loss of smell.

Different aetiologies affect the olfactory pathway in different ways. Age-related smell decline can be attributed to olfactory cell damage due to repeated exposure to air pollutants, cigarette smoke, viruses, bacteria and other airborne xenobiotics along with reduced olfactory receptor cell regeneration from the basal cells. As age advances, the number and size of foramina in the cribriform plate reduces, resulting in fewer olfactory receptor cell axons from the nasal cavity reaching the brain and inducing olfactory receptor cell necrosis.[11]

Chronic rhinosinusitis, which accounts for 14–30 per cent of cases with olfactory dysfunction, produces a gradual loss of olfaction. While respiratory mucosal oedema and polyps impede the access of odorants to the olfactory cleft, alterations in the composition and transport of the mucus layer can impair access to or removal from the receptor sites.[12] A sensorineural component has also been implicated based on the olfactory neuroepithelial inflammation seen on histopathology and the clinical response to systemic corticosteroids.[13] Hence, in chronic rhinosinusitis the aetiology could be multifactorial.[14]

In post-infectious hyposmia and anosmia, the sensory deficit is probably due to a disproportionately high rate of olfactory neuronal apoptosis when compared with the compensatory increased rate of neurogenesis.[15] The lack of basal cells in some post-viral disorders explains the loss of regenerative capacity. However, in post-traumatic olfactory dysfunction the damage resulting from the external force is inflicted on the olfactory filament, and the basal cells with their regenerative capacity are retained in the olfactory epithelium.[16]

Olfactory abilities assessed by various psychophysical tests measure three main domains, namely, threshold (lowest detectable concentration of odours), discrimination (ability to differentiate between odours) and identification (ability to identify odours). The criteria for olfactory dysfunction based on the measurement of odour detection thresholds for one or more chemicals (e.g. butanol, pyridine, phenylethyl alcohol) and performance on a multiple-item odour identification task are superior to scaling measures or questionnaires because they are less prone to subjective biases and variability.

Compared with higher-order olfactory tasks, such as identification and discrimination, threshold tests place few demands on cognitive function and are independent of cultural adaptation.[17] It has been suggested that the olfactory threshold is strongly related to sensory capability because it is often impaired in peripheral sinonasal disorders, while olfactory discrimination and identification require higher cognitive functions, including working memory, judgment and decision making, and their dysfunction may represent generalised cognitive deterioration.

Soler *et al.* reported that olfactory dysfunction in patients with chronic rhinosinusitis showed the greatest loss for threshold levels, with only 60 per cent having a loss in the identification domain, and a much greater disparity between the chronic rhinosinusitis without nasal polyposis (38 per cent) and chronic rhinosinusitis with nasal polyposis (75 per cent) subgroups.[18] Furthermore, 20–40 per cent of patients with allergic rhinitis have olfactory dysfunction, with the severity

https://doi.org/10.1017/S0022215123002268 Published online by Cambridge University Press

of dysfunction increasing with the duration, type and severity of allergic rhinitis.

This study showed that patients with chronic rhinosinusitis without nasal polyposis had worse odour threshold scores and showed more anosmia and severe hyposmia than those with chronic rhinosinusitis with nasal polyposis. Although 75 per cent of patients with chronic rhinosinusitis without nasal polyposis and 61 per cent of patients with chronic rhinosinusitis with nasal polyposis had olfactory threshold values of 0, only 43.75 and 48.96 per cent, respectively, of chronic rhinosinusitis with nasal polyposis and chronic rhinosinusitis without nasal polyposis patients had an olfactory identification score of 0. Among allergic rhinitis patients, even though 42.86 per cent of patients had threshold values of 0, 39.62 per cent of patients had identification scores of 7.

Because most of the patients in our cohort had allergic rhinitis and chronic rhinosinusitis, which in turn affected the peripheral olfactory system, preferential involvement of the olfactory threshold with preservation of identification scores even in patients with anosmia and severe hyposmia seems plausible.[19] Apter *et al.* reported a higher incidence and severity of olfactory loss among allergic rhinitis patients than rhinosinusitis patients because allergic rhinitis patients are prone to respiratory infections, which can cause olfactory epithelial loss.[20]

When analysing the specific smell loss in various nasal diseases, pepper was found to be the least perceived smell among the allergic rhinitis, chronic rhinosinusitis without nasal polyposis, chronic rhinosinusitis with nasal polyposis and idiopathic anosmia patients. In patients with atrophic rhinitis, the asafoetida and baby powder smells were affected the most. Because this study examined a retrospective cohort, the onset and sequence of loss of different odours was not assessed.

The novel finding from our study is that in most inflammatory sinonasal conditions the odour identification component is relatively preserved, even when the threshold is maximally affected. In patients with comparable severity of olfactory dysfunction based on the composite score of Connecticut Chemosensory Clinical Research Centre testing, a relatively preserved suprathreshold odour identification score may predict better prognosis and recovery. Pepper was the least perceived and most probably the earliest odour to be lost in patients with olfactory dysfunction. Our study is the first to arrive at these conclusions and there are no similar studies with which it can be compared.

- There was a male predominance among patients presenting with olfactory dysfunction
- Allergic rhinitis was the most common sinonasal cause for olfactory dysfunction
- In patients with moderate and severe hyposmia, there was relative preservation of olfactory identification scores in comparison with threshold scores
- Pepper was the least perceived smell among patients with allergic rhinitis, chronic rhinosinusitis without nasal polyposis and chronic rhinosinusitis with nasal polyposis
- In patients with atrophic rhinitis, asafoetida and baby powder were the smells that were affected the most

The limitations of our study are that it was retrospective in nature and the study subjects were a self-selected group of individuals who had sought medical help. However, many individuals with sinonasal and neurological disorders may not be aware of their olfactory dysfunction unless specific olfactory tests are performed, therefore the conclusions of our study may not extrapolate to the distribution of general olfactory dysfunction in these conditions. A well-designed prospective study of various diseases causing olfactory loss will help to determine the pattern of olfactory dysfunction they cause and the sequence of loss of different odours. This may also help in the early diagnosis and prognostication of neurodegenerative diseases.

Competing interests. None declared

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