Danish Validation of a Retronasal Olfactory Powder Test and Development of a Novel Quick Retronasal Olfactory Test

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Abstract

Introduction Quality of life is closely linked to retronasal olfactory function. Familiarity with odors vary, so tests need validation. Testing can be time-consuming, so a quick test and a thorough test are needed for clinical and research settings.

Objectives The objectives of this study were to validate the original retronasal powder olfactory test in a Danish population and to develop a novel quick retronasal test for easy application.

Methods Ninety-seven participants were included in the study, 59 healthy controls and 38 patients with olfactory impairment. The retronasal test was modified by substituting unfamiliar odors and descriptors and validated with a criterion of correct identification rate of 50% in the original test and 90% in the quick test. Items with over 90% correct identification rate in the modified original test were included in the quick test, resulting in a 10-item test.

Results The modified retronasal olfactory test achieved good test characteristics, with a 10th percentile cut-off value of 13: sensitivity was 88.9%, specificity 83.0%, positive predictive value 78%, negative predictive value 91.7%, and the receiver operating characteristics area under the curve (ROC-AUC) was 0.86. The quick test achieved acceptable test characteristics, with a 10th percentile cut-off value of 8.2: sensitivity was 72.2%, specificity 90.6%, positive predictive value 83.9%, negative predictive value was 82.8%, and ROC-AUC 0.81.

Conclusion Validation of both tests demonstrated satisfactory accuracy. We recommend the quick test for screening purposes, and the modified original version for a thorough evaluation. The tests are easily implemented as they are easy to understand and very affordable.

Keywords
- smell
- olfaction disorders
- anosmia
- diagnosis
- validation study

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Introduction

The olfactory function can be divided into the orthonasal and the retronasal routes, based on the odor molecules reaching the olfactory epithelium by two distinctive pathways: the nostrils (orthonasal olfaction) and the oral cavity (retronasal olfaction).[1] The flavor from food and beverages provides us with pleasure and quality of life. Flavor is a multisensory experience that works as a combination of several sensory components—smell, taste, and mouthfeel. It is a common misconception that the sensation of flavor derives solely from the tongue's gustatory sensation—up to 80% of flavor perception stems from retronasal olfaction.[2,3] Olfactory disorders are common in up to 20% of the general population—15% with a reduced sense of smell (hyposmic) and 5% being unable to smell (functionally anosmic).[4–6] Impaired olfactory function is associated with reduced quality of life, and the development of depression has been reported in up to a third of affected individuals.[7] This tendency correlates to the many restrictions in everyday life caused by reduced olfactory function. One of the main problems for patients with reduced olfactory function is flavor perception while eating or drinking. Food is an essential source of enjoyment and pleasure, and reduced quality of life correlates more with retronasal olfactory function than with orthonasal olfactory function.[8] To specify the exact mechanisms of olfactory dysfunction, quantification of olfaction is essential. Quantification of both the orthonasal and retronasal olfactory function is crucial in the discrepancy between subjective orthonasal and retronasal olfactory function, for instance, in patients with a normal subjective sense of smell, but complaints of impaired flavor sensation, or in patients with a reduced sense of smell and normal flavor perception.

Three different types of retronasal olfactory tests exist: powder tests with odors in powdered form, candy tests with aromas in candy form, and odorant presentation containers with scents in air- or vapor-phase.[9] The powder tests are most commonly used. The powders are readily available grocery store products and are applied to assess the retronasal olfactory capacity. The powder test has been validated in several countries.[10–12] The original retronasal olfactory powder test consists of 20 various grocery condiments in powdered form.[10] Previous studies have evaluated the test's internal validity by its test-retest reliability, the test's correlation to orthonasal olfactory function, and correct identification rate $>50\%$ in a healthy population. Satisfactory external validity has been found in terms of applicability in different cultural settings in seven European countries, but modifications are essential.[10–12] Familiarity with odors differs a lot among various cultures[13]—consequently, the test's performance depends on familiarity with the odors and descriptors. Adaptation of the odors and descriptors taking cultural differences in familiarity into account has been suggested to improve the test's performance.[12] The test method is time-consuming, with 20 condiments included, and is often reserved for cases in which thorough investigation of retronasal olfactory function is needed. A quicker version of the test could be used more widely for screening of the retronasal olfactory function.

Therefore, the objective of the present study was to validate and modify the original retronasal olfactory powder test (MOROT) for the Danish population and, based on the MOROT, to develop a quick retronasal olfactory test (QROT) with a reduced number of retronasal odors for screening purposes.

Methods

Participants and Ethics

A total of 97 participants—59 healthy controls and 38 patients—were enrolled. A pilot study was conducted in which modifications of the odors and descriptors used in the original retronasal powder test were performed in combination with previous results from a Danish familiarity study.[14] The modified test was applied to 8 of the healthy participants. The pilot study was not repeated, and neither was the testing of patients, as they were offered treatment for the olfactory dysfunction.

Healthy participants were recruited through social media, advertisement in the local newspaper, and public places: universities, hospitals, and libraries. The inclusion criteria was participants aged between 18 and 80 years. For healthy participants, additional inclusion criteria were no history of sinonasal diseases, no previously diagnosed olfactory or gustatory dysfunction, and subjectively normal gustatory and olfactory function.

Healthy participants were tested with Taste Sprays and Sniffin' Sticks (Burghardt, Wedel, Germany) to ensure normal gustatory and olfactory function. They filled out a questionnaire with general information and a familiarity questionnaire. They rated their familiarity with each modified original retronasal test odors on a Likert scale from 1 to 5 ($1 =$ not familiar at all, and $5 =$ very familiar). Furthermore, on a Likert scale from 1 to 5, participants rated each odor's hedonics ($1 =$ not pleasant at all and $5 =$ very pleasant) and how intense they perceived the odor ($1 =$ not recognizable at all and $5 =$ very recognizable). After completing the tests, participants were also asked to rate their familiarity with the odors. A re-test of the modified original retronasal test (MOROT) was performed in 7 of the 59 healthy controls 6 to 8 months after the 1st test session to investigate re-test reliability.

All patients were enrolled at a specialized Smell and Taste Clinic (Flavour Clinic, The ENT Department, Regional Hospital West Jutland, Denmark).

Testing was performed in quiet, ventilated rooms the Department of Clinical Medicine, Aarhus University, Denmark. Participants were informed only to drink water and not eat, drink, smoke, or brush their teeth for 1 hour before participation.

The study was conducted in accordance with the Helsinki Declaration. Approval from the regional data committee for research projects (Central Denmark Region) was obtained with project number 1–16–02–47–18. Informed consent was obtained from all participants.

Tests

Retronasal Test

Twenty edible grocery condiments in powdered form were provided from grocery stores and internet webshops. The substances were applied one at a time to the midline of the tongue using a plastic spatula. The participants were free to sample each stimulus twice. They could spit out or swallow the test condiment. Afterward, they rinsed their mouth with tap water before applying the next condiment. An interval of minimum 30 seconds between each odor was used to avoid olfactory habituation. Participants rated the intensity of their flavor experiences on a scale from 1 to 5 (1 = not sensible, and 5 = highly sensible) along with the hedonic rating of the condiments on a scale from 1 to 5 (1 = not pleasant at all, and 5 = very pleasant).

The participants identified the condiment by choosing from a set of four written and visually presented descriptors using a forced-choice regimen. The duration of the modified original retronasal test was < 15 minutes. The duration of the quick test was < 7 minutes.

Sniffin' Sticks

The Sniffin' Sticks (Burghart Messtechnik) are pens containing odors. The test comprises three subtests: threshold, discrimination, and identification. The threshold (T) subtest consists of 16 triplets, one containing the odor (n-butanol) that must be identified, and the other two only solvent. A single staircase forced-choice method was used, giving a T-score of 1 to 16. In the discrimination (D) subtest, 16 triplets are presented, two pens contain the same odor, and the other a different smell, which must be identified, giving a D-score from 0 to 16. The identification (I) subtest includes 16 pens (SIT-16) containing 16 different odors, which must be identified by choosing from a set of four written descriptors using a forced-choice regimen, giving an I-score of 0 to 16. The participants started with reading the descriptors, smelling the pen, and then choosing one of four possibilities. The participants were free to smell the pen twice before making their decision. The subtest scores can be combined to an overall olfactory function score—the threshold-discrimination-identification (TDI)-score ranging from 1 to 48. The test has been extensively validated internationally, including in a Danish population.[13,15]

Healthy participants underwent testing for orthonasal olfactory function with the SIT-16 test to screen for intact olfactory function. Cut-off values for the SIT-16 were used to separate normosmia from hyposmia, with a score < 13 indicating hyposmia.[13] Patients were tested with the full Sniffin' Sticks TDI battery to specify the severity of olfactory impairment. The TDI-score cut-off values were used to separate olfactory function into groups of anosmia (≤ 16), hyposmia (≤ 29.8), and normosmia (> 29.8).[13]

Taste Sprays

To evaluate the participants' gustatory function, the Taste Sprays were used. The Taste Sprays comprise sweet, sour, salty, and bitter taste qualities in supra-threshold concentrations. The sprays contain sucrose (1 g in 10 ml water), citric acid (0.5 g in 10 ml water), sodium chloride (0.75 g in 10 ml water), and quinine hydrochloride (0.005 g in 10 ml water).[16,17] The sprays were applied in a pseudo-randomized order on the participant's tongue, and a forced-choice paradigm was used. Participants then had to answer if the applied spray tasted sweet, sour, salty, or bitter. Participants were free to sample each spray twice.

Modifications of the Original Test and Development of the Quick Test

Based on a Danish familiarity study, modifications to the chosen descriptors and odors were made.[14] In the present study, odors were either substituted or left out if they had a familiarity of less than 60% in a healthy adult population. Newly replaced odors had a familiarity of > 60% in a healthy population and were edible condiments in powdered form. After these modifications were made, eight adults were tested with the test kit in a pilot study. Odors that were correctly identified in 50% or less were substituted or removed. This was the case for banana (25%), blueberry (37.50%), and tomato (50%). These powders were exchanged for other powder brands. A decision was made to use peach as a descriptor in two odor items (orange and raspberry) – as this item was fitting the fruity themes and having roughly the same gustatory sensation of the odor items, however peach was removed as an individual odor based on low familiarity. The next step was to evaluate the modified original test in a healthy population of another 51 participants. In this step, items with < 50% correct identification rate were omitted—this was the case for two items: peach and mushroom. The process resulted in an 18-item test with all items having > 50% correct identification.

For the development of the QROT, items from the modified original test correctly identified by more than 90% of the healthy participants were included in the test, thus resulting in a 10-item test.

Statistics

An unpaired *t*-test was used to analyze normally distributed data. The test-re-test reliability coefficients (Pearson correlation) were calculated for the test, and Bland-Altman plots with limits of agreement were produced. Pearson correlations were also used to evaluate age's effect on retronasal scores and retronasal test consistency with the Sniffin' Sticks test. Test characteristics of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. The statistical analyses were conducted using STATA/IC 16.1 for Mac (StataCorp, College Station,TX, USA). The α level of significance was set at 0.05.

Results

Participants

The healthy participants and the patient population were similar in terms of age and gender distribution (see ►**Table 1**). There were more smokers in the healthy population. The SIT16 scores were significantly higher in the

Table 1 Descriptive data of the study population

	Normosmic participants ($n = 51$); mean (95% CI)	Patients with olfactory dysfunction ($n = 38$); mean (95% CI)
Age	42.18 (37; 47)	49.31 (44; 55)
Sex (male/female)	(15/36)	(13/25)
Smokers	5	1
SIT-16 score	14.5 (14.4; 15)	9.7 (8.5; 11)
Taste spray score	3.98	4

Abbreviation: SIT, Sniffin' Sticks identification test

healthy population than in the patient population ($t = 8.9$, $p < 0.0000$). The patients were tested with the complete TDI test, demonstrating a mean TDI score of 21.74 (95% CI: 19.5;24). The gustatory function tested with the Taste Sprays was similar in both groups.

Modifications of the Original Retronasal Test

First, odors and descriptors with low familiarity were substituted or removed if the familiarity was lower than 60% in the healthy population (see ►**Table 2**). This was the case in the following two odors and nine descriptors: asparagus (46%), almond (43%), hazelnut (37%),nutmeg (54%), grapefruit (54%), cloves (58%), celery (50%), broccoli (37%), cherry (51%), peach (54%), and mushroom (50%). Furthermore, we decided to remove the descriptor smoked food since this condiment's exact meaning was unclear. This resulted in an 18-item test with all odors correctly identified by more than 50% of the healthy participants (see ►**Fig. 1**). The final version of the MOROT can be seen in ►**Table 3**.

Items with > 90% correct identification rates were selected for inclusion in the QROT, resulting in a 10-item test (see ►**Table 4** for the final version of the QROT)

Table 2 Odors and descriptors from Croy et al.[10]

		Descriptors		
1	Apple (72/75)	Orange (88/99)	Pineapple (76/92)	Raspberry (60/61)
2	**Asparagus (26/46)**	**Almond (46/43)**	**Hazelnut (41/37)**	Parsley (61/71)
3	Banana (70/86)	**Hazelnut (41/37)**	Cacao (80/78)	Caramel (75/69)
4	Black pepper (81/82)	**Nutmeg (26/54)**	Paprika (73/56)	Onion (87/85)
5	Blueberry (N/A)	Strawberry (77/83)	Apple (72/75)	**Grapefruit (43/54)**
6	Caramel (75/69)	Vanilla (89/95)	Banana (70/86)	**Almond (43/46)**
7	Cinnamon (92/99)	Coffee (95/98)	Tomato (60/61)	Curry (93/92)
8	**Cloves (34/58)**	Curry (93/92)	Cinnamon (92/99)	Garlic (87/97)
9	Coconut (72/84)	Cacao (80/78)	Banana (70/86)	Cinnamon (92/99)
10	Coffee (95/98)	**Cloves (34/58)**	**Nutmeg (26/54)**	Black Pepper (81/82)
11	Curry (93/92)	**Celery (28/50)**	Coffee (95/98)	**Nutmeg (26/54)**
12	Garlic (87/97)	Ham (61/55)	Black Pepper (81/82)	**Smoked food (%)**
13	**Mushroom (46/50)**	Paprika (73/56)	Fish (92/94)	Onion (87/85)
14	**Nutmeg (26/54)**	**Celery (28/50)**	Coffee (95/98)	Mustard (66/72)
15	Onion (87/85)	**Broccoli (41/37)**	Curry (93/92)	Paprika (73/56)
16	Orange (88/99)	Raspberry (60/64)	Peach (45/54)	Pineapple (76/92)
17	**Peach (45/54)**	Peppermint (78/87)	Apple (72/75)	**Grapefruit (43/54)**
18	Raspberry (60/64)	Peach (45/54)	Lemon (79/92)	Orange (88/99)
19	Strawberry (77/83)	**Cherry (51/51)**	Orange (88/99)	Pineapple (76/92)
20	Tomato (60/61)	Onion (87/85)	**Asparagus (26/46)**	**Broccoli (41/37)**

Familiarities from 238 adults and 172 adolescents modified with permission from Fjaeldstad et al.[14]
%/% = Adolescent/adult familiarity.
The first column represents the correct odor.
Bold indicates the odors or descriptors that were substituted.
N/A = Not available

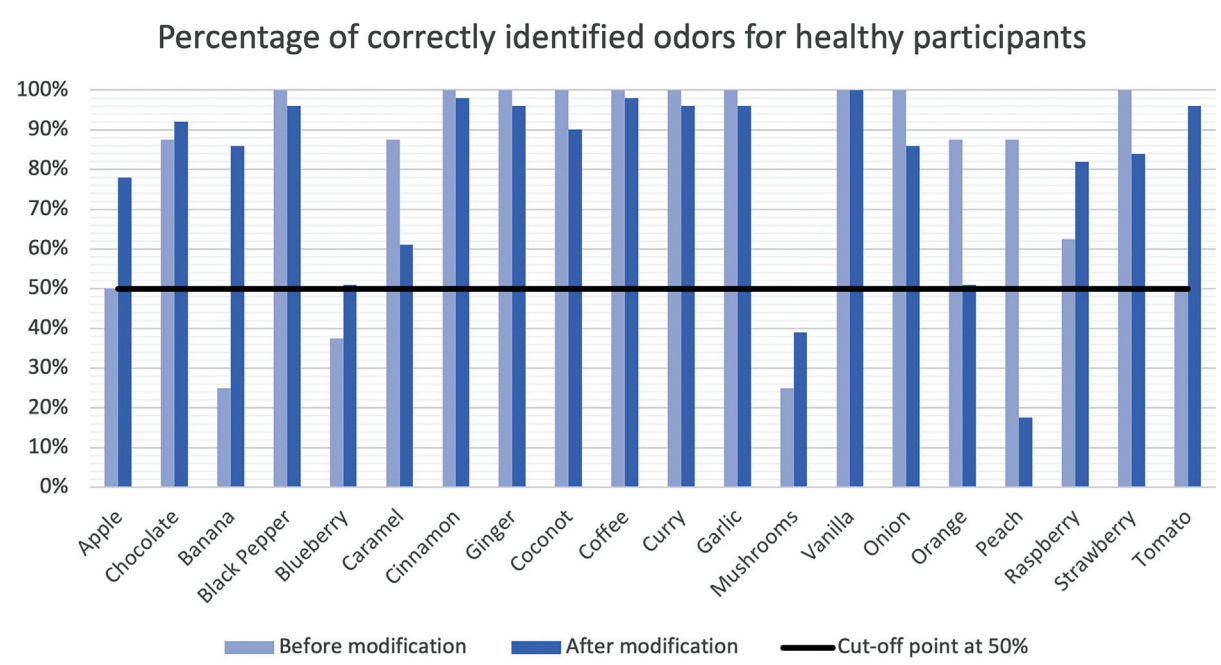

Fig. 1 : Percentage of odors correctly identified by healthy participants. The line marks the cut-off point at 50%, at which point odors that were correctly identified in 50% of cases or less were substituted or removed.

Table 3 The final odors and descriptors

	Correct odor	Distractor descriptors	Name and source of product
1	Apple	Orange, pineapple, raspberry	"Summer Apple," Nutramino
2	Chocolate	Burnt almonds, popcorn, parsley	"Kage Mousse med Chokolade smag," Dr. Oetker[Cake mousse with chocolate flavor]
3	Banana	Popcorn, cacao, caramel	"Banana," Bulkpowders.com
4	Black pepper	Vanilla, paprika, onion	"Sort Peber - stødt," Budget [Black pepper – ground]
5	Blueberry	Strawberry, apple, lemon	"Blueberry flavor," Bodylab
6	Caramel	Vanilla, banana, burnt almonds	"Budding – Karamel," Dr. Oetker [Pudding – caramel]
7	Cinnamon	Coffee, tomato, curry	"Kanel - stødt," Budget[Cinnamon – ground]
8	Ginger	Curry, cinnamon, garlic	"Stødt ingefær," Santa Maria[Ground ginger]
9	Coconut	Cacao, banana, cinnamon	"Kokosfibermel," Urtekram [Coconut flour]
10	Coffee	Ginger, vanilla, black pepper	"Gold Crema," Nescafe
11	Curry	Ketchup, coffee, mustard	"Karry," Budget[Curry]
12	Garlic	Ham, black pepper, smoke	"Hvidløgspulver" Santa Maria[Garlicpowder]
13	Vanilla	Ketchup, coffee, mustard	"Vanilie sukker," Tørleffs[Vanilla sugar]
14	Onion	Cheese, curry, paprika	"Løgpulver," Karlsens Krydderier[Onion powder]
15	Orange	Raspberry, peach, pineapple	"Frysetørret appelsinpulver," Specialkøbmanden [Freeze dried orange powder]
16	Raspberry	Peach, lemon, orange	"Freeze dried raspberry powder," HoneyBerry Ltd
17	Strawberry	Honey, orange, pineapple	"Freeze dried strawberry powder," HoneyBerry Ltd
18	Tomato	Onion, chocolate, cheese	"Tomato powder," Tongmaster Seasonings Ltd

Name and source of available grocery products.
English translation of danish product names is in squared brackets.

Table 4 The final odors and distractor descriptors for the quick test

	Correct odor	Distractor descriptors	Name and source of product
2	Chocolate	Burnt almonds, popcorn, parsley	"Kage Mousse med Chokolade smag," Dr. Oetker [Cake mousse with chocolate flavor]
4	Black pepper	Vanilla, paprika, onion	"Sort Peber - stødt," Budget [Black pepper – ground]
7	Cinnamon	Coffee, tomato, curry	"Kanel - stødt," Budget[Cinnamon – ground]
8	Ginger	Curry, cinnamon, garlic	"Stødt ingefær," Santa Maria [Ground ginger]
9	Coconut	Cacao, banana, cinnamon	"Kokosfibermel," Urtekram [Coconut flour]
10	Coffee	Ginger, vanilla, black pepper	"Gold Crema," Nescafe
11	Curry	Ketchup, coffee, mustard	"Karry," Budget [Curry]
12	Garlic	Ham, black pepper, smoke	"Hvidløgspulver" Santa Maria [Garlic powder]
14	Onion	Cheese, curry, paprika	"Løgpulver," Karlsens Krydderier [Onion powder]
18	Tomato	Onion, chocolate, cheese	"Tomato powder," Tongmaster Seasonings Ltd

Name and source of available grocery products.
English translation of danish product names is in squared brackets.

Retronasal Test Scores

The mean MOROT score in healthy participants was 15.39 (95% CI: 14.83; 15.95) (out of 18), with the 10th percentile being 13. The mean QROT score in healthy participants was 9.59 (95% CI: 9.35; 9.83) (out of 10), and the 10th percentile was 8.2. In the patient population, the mean MOROT score was 9.89 (95% CI: 8.9; 10.9), and the mean QROT was 7.03 (95% CI: 6.3; 7.58). There was a significant difference between mean scores of MOROT ($t = -10.3$, $p < 0.0001$) and QROT ($t = -7.5$, $p < 0.0001$) between patients and controls.

For the whole sample, a correlation between Sniffin' Sticks (orthonasal olfactory function) and retronasal test scores was observed ($r = 0.76$, $p < 0.000$). There was a significant difference in scores between controls and hyposmic patients ($t = -9.44$, $p < 0.000$) and between controls and anosmic patients ($t = -8.76$, $p < 0.000$). Furthermore, anosmic patients had significantly lower scores than hyposmic patients ($t = -3.27$, $p = 0.0024$).

Correlations between age and retronasal scores in all participants were investigated, and a slight significant decline was observed with age ($r = -0.28$, $p = 0.0075$). The mean retronasal scores in healthy women and men were 15.8 (95% CI: 15.29; 16.32) and 14.4 (95%CI: 12.94; 15.86), respectively. This difference was statistically significant ($t = -2.39$, $p = 0.02$).

Hedonics, Familiarity, and Intensity

All odors were familiar to the participants, with a mean familiarity of more than 4 for all odors (►**Table 5**). The hedonic rating was around 3 for most odors, except for vanilla, chocolate, and raspberry, with mean ratings above four and black pepper and caramel being below 3 (see ►**Table 5**). In general, the intensity for most odors was rated high with means above 4, except for chocolate, banana, and blueberry, which scored below 4, and caramel and coconut, which scored below 3 (see ►**Table 5**).

The Validity of the Tests

The 10th percentile in the healthy population (13 for MOROT and 8.2 for QROT) was used to calculate sensitivity and specificity using these percentiles as cut-off values for a normal retronasal olfactory function. The sensitivity of the MOROT was 88.9%, and the specificity was 83.0%, while the positive predictive value was 78%, the negative predictive value 91.7%, and the ROC curve area was 0.86 (►**Fig. 2A**). For the QROT, the sensitivity was 72.2%, and the specificity was 90.6%, while the positive predictive value was 83.9%, the negative predictive value was 82.8%, and the ROC curve area was 0.813 (►**Fig. 2B**). Re-testing of the MOROT was performed in 7 healthy participants (14%) to evaluate the test-retest reliability resulting in a strong association between the two test sessions (Pearson correlation = 0.704). A Bland-Altman plot showed a mean difference of -0.28 (between test and re-test) with 0% outside the limits of agreement (95% limits of agreement: -2.74; 2.17).

The Final Test

A picture of the test and a picture of a participant taking the test can be seen in ►**Fig. 3**.

Discussion

Key Findings

- Modification to the retronasal test resulted in 2 odors being removed and 10 descriptors changed to more familiar odors. This resulted in all odors being correctly identified by more than 50% of the healthy population.

Table 5 Familiarity, hedonic rating, and intensity scores for the healthy participants

Sampling nr.		After modification ($n = 51$)	Familiarity score mean (95%CI)	Hedonics score mean (95%CI)	Intensity score (95%CI)
1	Apple	**78%**	4.73 (4.57; 4.89)	3.86 (3.62; 4.10)	4.02 (3.78; 4.26)
2	chocolate	**92%**	4.98 (4.94; 5.02)	4.21 (4.02; 4.41)	3.94 (3.67; 4.21)
3	Banana	**86%**	4.94 (4.87; 5.01)	3.73 (3.49; 3.96)	3.61 (3.34; 3.87)
4	Black Pepper	**96%**	4.90 (4.82; 4.99)	2.53 (2.24; 2.82)	4.76 (4.64; 4.89)
5	Blueberry	**51%**	4.12 (3.87; 4.36)	3.92 (3.75; 4.10)	3.17 (2.95; 3.41)
6	Caramel	**61%**	4.65 (4.46; 4.83)	2.75 (2.50; 2.99)	2.37 (2.05; 2.69)
7	Cinnamon	**98%**	4.90 (4.80; 5.00)	3.96 (3.72; 4.21)	4.51 (4.34; 4.68)
8	Ginger	**96%**	4.74 (4.60; 4.88)	2.90 (2.59; 3.22)	4.47 (4.27; 4.67)
9	Coconut	**90%**	4.47 (4.24; 4.70)	3.31 (3.04; 3.58)	2.96 (2.66; 3.26)
10	Coffee	**98%**	4.92 (4.83; 5.02)	3.16 (2.78; 3.54)	4.69 (4.50; 4.87)
11	Curry	**96%**	4.73 (4.59; 4.86)	3.25 (2.99; 3.52)	4.73 (4.59; 4.86)
12	Garlic	**96%**	4.92 (4.84; 4.99)	3.43 (3.14; 3.73)	4.92 (4.84; 4.10)
13	Vanilla	**100%**	4.92 (4.83; 5.02)	4.69 (4.52; 4.85)	4.92 (4.83; 5.02)
14	Onion	**86%**	4.67 (4.50; 4.83)	2.98 (2.75; 3.22)	4.67 (4.50; 4.83)
15	Orange	**51%**	4.82 (4.70; 4.95)	3.86 (3.64; 4.08)	4.82 (4.70; 4.95)
16	Raspberry	**82%**	4.67 (4.45; 4.88)	4.12 (3.91; 4.33)	4.67 (4.45; 4.88)
17	Strawberry	**84%**	4.78 (4.63; 4.94)	3.82 (3.56; 4.09)	4.78 (4.63; 4.94)
18	Tomato	**96%**	4.76 (4.60; 4.93)	3.51 (3.26; 3.76)	4.76 (4.60; 4.93)

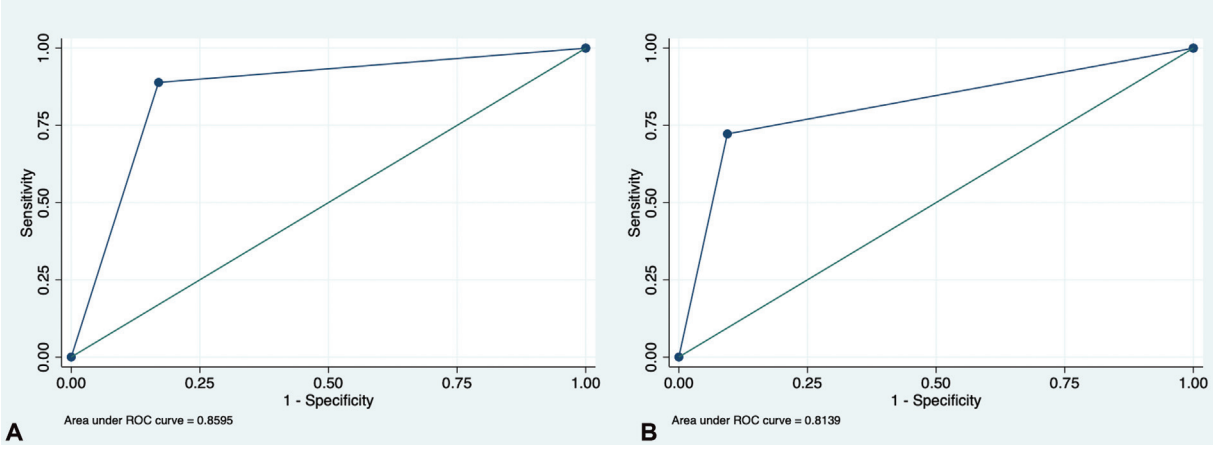

Fig. 2 : (**A**) Receiver operating characteristic curve for the modified retronasal olfactory test. (**B**) Receiver operating characteristic curve for the 10-item quick retronasal olfactory test.

- A quick 10-item test was developed with correct identification rates of more than 90% in the healthy population.
- Both tests are now validated with acceptable test-characteristics and cut-off values to separate a normal retronasal olfactory function from an impaired function.
- A significant correlation was found between orthonasal and retronasal olfactory function.
- Women had significantly higher retronasal olfactory scores than men.
- A slight but significant decline in retronasal olfactory scores with increasing age was observed.

Testing retronasal olfactory function is essential, as this is linked closely to quality of life.[8] Testing is vital for correct diagnostics when patients report olfactory impairment but normal enjoyment of food. This phenomenon is not seldom observed in clinical practice, and often after being tested with a retronasal olfactory test, the patients are dysosmic both orthonasally and retronasally. Liu et al.[18] suggested that subjective flavor perception in these patients might be

Fig. 3 (**A**) A picture of the test. **3B:** A picture of a participant taking the test.

centrally mediated through unconscious memory recall and not intact retronasal olfactory function. For correct diagnostics in situations like this, retronasal olfactory testing is essential.

Cultural differences have a significant impact on the familiarity of different odors in different countries. It is paramount to modify the odors and descriptors of an olfactory test in different cultural settings and populations, so the participants are familiar with the options in the test. The present study validated a retronasal olfactory powder test by removing unfamiliar odors and descriptors and adding familiar odors instead. This resulted in a validated test with 18 odors with good test-retest reliability and decent sensitivity and specificity. Furthermore, we introduced a validated quick retronasal olfactory test with 10 items, which can be performed in less than 7 minutes, making it practical for use in a clinical or research setting for screening of retronasal olfactory function. This test also had acceptable test characteristics in terms of sensitivity and specificity.

Previous studies have investigated the performance of the original retronasal powder test.[10,12] In the present study, two levels of modifications were done to the original test to increase the applicability of the test in a Danish population. The total number of participants in our study was 97, 59 healthy participants and 38 patients. This is a relatively small population compared with Croy et al.,[10] which provided data from 518 participants from 7 different countries, 292 healthy participants and 226 patients. However, 58 healthy participants are participants than than 6 out of the 7 countries from the study, with only Germany having more healthy participants ($N = 133$).[10] Thirty-eight patients are comparable to the patient population from the study by Croy et al.,[10] where the 7 countries had 0, 0, 10, 29, 42, 45, and 100 patients, respectively, which would have put the present study as the median, if it were included. Another study by Heillmann et al.[11] had 120 controls and 110 patients, and one by Salihoğlu et al.[12] had 330 healthy participants and no patients. Other studies testing retronasal olfactory function by Landis et al.[19] had 18 patients and no controls, Pfaar et al.[20] had 33 healthy controls and no patients, Rombaux et al. had 25 patients and no controls in one study,[21] and 11 healthy controls and 33 patients in another study.[22]

In agreement with Croy et al.[10] and Heilmann et al.,[11] a robust significant correlation was found between the Sniffin' Stick scores, representing orthonasal olfactory function, and retronasal test scores, representing the retronasal olfactory function. For correlation between age and retronasal olfactory test scores, a slight significant decline was observed. This was in agreement with the findings of Heilmann et al.[11] However, Croy et al.[10] found no age differences in relation to retronasal olfactory function. There seem to be some discrepancies concerning possible age decline, which might indicate that more research is needed on the effect of age on retronasal olfactory function. For women and men, the difference was statistically significant, as scores in women were higher than in men in the present study, in agreement with Croy et al.[10] and Heilmann et al.[11]

The odors used in the present study were not purely olfactory stimuli but also contained elements that would stimulate the gustatory and the trigeminal senses, which might provide information about the tested odor. This problem was also a concern in previous studies,[10] in which it was suggested to use descriptors with the somewhat same gustatory modality, as we have done in the present study. While this does not eliminate the issue, it is a way of decreasing it. Due to the stimulation of olfaction, trigeminal and gustatory sensation, the test is not purely testing retronasal olfaction, but it gives an indication of the functionality of a combined multisensory sensation, which should be kept in mind when interpreting the test. A limitation to the study was that the healthy population was only screened for intact orthonasal olfactory function with the SIT-16 and not tested with the full TDI test. Furthermore, a limitation of retronasal powder tests, including the present study, is the unknown concentration of

odors in the products; however, using high correct identification rates ensures they are at supra-threshold concentrations. Future studies could investigate retronasal threshold levels in healthy participants and patients and use this information to develop retronasal tests with known concentrations of odors to improve retronasal powder tests.

Conclusion

We present two versions of a retronasal olfactory test—a thorough and a quick test validated for use in clinical and research settings. These diagnostic tools can be used to assess the retronasal olfactory function in patients in depth and quickly, respectively. We recommend using the QROT for screening purposes and the MOROT when thorough evaluation of retronasal olfactory function is needed—mainly when the QROT shows possible impairment. Cut-off values to separate normal olfactory function from olfactory impairment are required in clinical and research settings. In this study, we suggest using the cut-off values of the 10th percentile in a healthy normosmic population, as this is the same principle used in the Sniffin' Sticks for orthonasal olfactory function.[15] In conclusion, the tests are now validated and are easily implemented in clinical settings as they are easy to understand, quick to perform, and very affordable.

Conflict of Interests
Dr. Therese Ovesen reports royalties from Danish textbooks.

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