

Odour identification and discrimination in Dutch adults over 45 years*

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SUMMARY

Objectives: The aim of the study was to establish normative values for the two culture dependent components (odour identification and odour discrimination) of the "Sniffin' Sticks" test battery in the Dutch population over 45 years of age, and to assess the influence of age and sex on olfactory function in this population.

Methods: This study was performed in 150 healthy Dutch subjects (87 male and 63 female, mean age 59.2 years, range 45-78 years). Olfactory performance was assessed using the odour identification and discrimination parts of the "Sniffin' Sticks" test battery.

Results: In women, odour discrimination scores declined significantly with age, whereas there was no effect of age on odour discrimination performance in men. For odour identification, there were no effects of age or sex in this population. A moderate correlation was found between identification and discrimination test scores.

Conclusion: Provisional population-specific normative data for olfactory testing using the identification and discrimination parts of the "Sniffin' Sticks" olfactory test battery have been established for the Dutch population over 45 years of age. The current data are applicable to the clinical evaluation of patients with olfactory disorders.

Key words: olfaction, identification, discrimination, normative values, "Sniffin' Sticks"

INTRODUCTION

The prevalence of olfactory dysfunction in the general population depends on how it is defined. Subjective impairments of the sense of smell are present in 1.4% of US adults⁽¹⁾. When using psychophysical tests of olfactory function, approximately 15% of the population can be classified as having mild to moderate hyposmia and around 5% as being anosmic^(2, 3). With increasing age, the prevalence of hyposmia increases⁽⁴⁻⁶⁾. However, it is important to realize that there may be a difference between physiological age-related loss ("presbyosmia") and excessive or unexplained loss of olfactory function in older age. A recent study⁽⁷⁾ suggests that true presbyosmia is only a minor component of age-related olfactory impairments. In this study, much of the commonly observed age-related decline in olfactory function appeared to be associated with other age-related factors such as use of medication.

Olfactory dysfunction can also be an early sign of a neurodegenerative disorder, in particular Parkinson's disease^(8, 9) or Alzheimer's disease⁽¹⁰⁾. In Parkinson's disease, hyposmia may even be a prodromal sign, preceding the development of the characteristic motor features such as tremor and slowness of

movement^(11, 12). Assessment of olfactory function in the elderly using validated tests is therefore bound to become an important element of early diagnostic strategies in neurodegenerative disorders⁽¹³⁾.

In order to reliably assess olfactory function, many psychophysical tests have been developed that provide a quantitative measure of olfactory function (for review see⁽¹⁴⁾). The University of Pennsylvania Smell Identification Test (UPSIT) and the "Sniffin' Sticks" are the most widely used. The UPSIT is a 40-item, forced-choice odour identification test, developed for the US population⁽¹⁵⁾. The "Sniffin' Sticks" is an olfactory test battery that can be used to assess three different aspects of olfactory function: odour identification, discrimination and detection⁽¹⁶⁾. Normative values for the "Sniffin' Sticks" have been established in various populations^(6, 17, 18). While odour threshold values are not culture dependent⁽¹⁹⁾, performance on odour identification (and discrimination) tests relies on prior exposure to and familiarity with the odours⁽²⁰⁾. This could severely limit the tests' validity in other cultures or populations. For instance, recently published normative values for the

“Sniffin’ Sticks” in a Greek population⁽¹⁸⁾ were clearly different from those in a previously published German study⁽⁶⁾.

The present study was initiated to establish normative values for the two culture dependent components (odour identification and odour discrimination) of the “Sniffin’ Sticks” in the Dutch population over 45 years of age, and to assess the influence of age and sex on olfactory function in this population.

MATERIALS AND METHODS

Subjects

This study was performed in 150 Dutch subjects (87 male and 63 female, mean age 59.2 years, range 45-78 years), who did not have a history of major olfactory or neurological disorders. The age range was chosen to enable evaluation of olfactory function in (mostly) elderly patients with (suspected) neurodegenerative disorders. All participants were volunteers recruited among employees and partners of patients from the outpatient clinics of the Departments of Neurology of the VU University Medical Center (VUMC; n = 70) and the Leiden University Medical Center (LUMC; n = 80). All subjects provided written informed consent. The study was approved by the Medical Ethics Committees of the VUMC and the LUMC.

Olfactory function testing

The “Sniffin’ Sticks” test battery (Burghart, Wedel, Germany) is an olfactory test battery comprising reusable felt-tip pens (‘sticks’) containing odorants dissolved in propylene glycol which the subject has to sniff. Olfactory tests were administered birhinally in a quiet, well-ventilated room to avoid any background smell interfering with the test odours.

Odour identification was measured by presenting 16 odorants in suprathreshold intensity, in a multiple (4)-forced choice format with verbal descriptions. Each stick was held approximately 2 cm in front of the nostrils for 2-3 seconds, with an interval of 20-30 seconds between each stick. In the odour discrimination test, subjects were blindfolded and presented with 16 odour-triplets, with an interval of 30 seconds between each triplet. Each triplet consisted of two identical and one aberrant odour. Subjects were asked to select the odd odour out of the three odorants presented, without the need to recognize or name the odours.

In both tests, olfactory scores were defined as the number of correct responses (0-16). The test odours and their response choices are listed in Table 1a and 1b.

Data analysis

To verify that there were no differences in olfactory test scores between the two sites of recruitment (VUMC, LUMC), data from the two centres were compared using the univariate general linear model UNIANOVA, with ‘recruitment centre’ as factor, and corrected for age (covariate) and sex (factor).

To explore the influence of sex and age on olfactory function, olfactory test scores were submitted to linear regression analysis by means of a GLM UNIANOVA with ‘sex’ as factor, ‘age’

Table 1a. Forced choice odour identification items.

	Target	Alternative response choices	% correct responses
Odour 1	Orange	Blueberry, Strawberry, Pineapple	85.3
Odour 2	Leather	Smoke, Glue, Grass	88.7
Odour 3	Cinnamon	Honey, Vanilla, Chocolate	71.3
Odour 4	Peppermint	Chives, Fir, Onion	96.0
Odour 5	Banana	Coconut, Walnut, Cherry	94.7
Odour 6	Lemon	Peach, Apple, Grapefruit	58.0
Odour 7	Liquorice	Caramel, Chewing gum, Biscuit	75.3
Odour 8	Turpentine	Mustard, Rubber, Menthol	38.7
Odour 9	Garlic	Onion, Sauerkraut, Carrot	83.3
Odour 10	Coffee	Cigarette, Wine, Candle smoke	84.7
Odour 11	Apple	Melon, Peach, Orange	48.7
Odour 12	Cloves	Pepper, Cinnamon, Mustard	91.3
Odour 13	Pineapple	Pear, Plum, Peach	70.7
Odour 14	Rose	Chamomile, Raspberry, Cherry	81.3
Odour 15	Aniseed	Rum, Honey, Fir	88.7
Odour 16	Fish	Bread, Cheese, Ham	99.3

Table 1b. Discrimination items.

	Target	Distracter	% correct responses
Odour 1	Octylacetate	Cinnamonaldehyde	81.3
Odour 2	<i>n</i> -Butanol	2-Phenylethanol	68.0
Odour 3	Isoamylacetate	Anethole	76.0
Odour 4	Anethole	Eugenol	78.7
Odour 5	Geraniol	Octylacetate	74.7
Odour 6	2-Phenylethanol	Isoamylacetate	87.3
Odour 7	(+)-Limonene	(+)-Fenchone	80.7
Odour 8	(-)-Carvone	(+)-Carvone	44.0
Odour 9	(-)-Limonene	Citronellal	62.7
Odour 10	2-Phenylethanol	(+)-Menthol	72.0
Odour 11	(+)-Carvone	Geraniol	70.0
Odour 12	<i>n</i> -Butanol	(-)-Limonene	85.3
Odour 13	Citronellal	Linalool	54.7
Odour 14	Pyridine	(-)-Limonene	68.7
Odour 15	Eugenol	Cinnamonaldehyde	70.7
Odour 16	Eucalyptol	α -Ionone	67.3

as covariate and the interaction ‘age*sex’. Analyses were performed for odour identification and odour discrimination separately.

Subsequently, the 95% lower bound of the individual prediction interval of the linear regression lines for each of the olfactory tests plotted against age was used to determine cut-off values for men and women separately in six age-groups (45-49 years, 50-54 years, 55-59 years, 60-64 years, 65-69 years, \geq 70 years). When the regression lines for men and women coincided, the combined regression line was used to calculate cut-off values. The 95% prediction interval used indicates that 95% of the population with a specific age will have a test score within the computed interval.

Pearson correlation coefficients were computed to determine the correlation between identification and discrimination scores, both overall and for men and women separately.

To determine which items were best identified, the percentage

Table 2. Descriptives and parameter estimates of the regression lines for identification and discrimination scores plotted against age (in years) of men and women. ns = non-significant.

	Identification			Discrimination		
	Male	Female	All	Male	Female	All
Mean	12.5	12.7	12.6	11.4	11.5	11.4
SD	2.3	2.2	2.3	2.2	2.5	2.3
Intercept	11.97	15.99	13.62	11.46	22.11	15.80
b coefficient	0.008	-0.056	-0.018	-0.001	-0.179	-0.074
R ²	< 0.001	0.033	0.003	< 0.001	0.273	0.055
p value	ns	ns	ns	ns	< 0.001	0.004

of subjects that had responded correctly was calculated for each item of the identification and discrimination tasks.

Data were analyzed using SPSS 15.0 for Windows.

RESULTS

Forced choice odour identification scores were not significantly different between centres (VUMC mean identification score = 12.5; LUMC = 12.6; $F [1,146] = .240$, $p = 0.625$). The same was true for the discrimination scores of subjects tested at the different centres (VUMC mean discrimination score = 11.2; LUMC = 11.7; $F [1,146] = 1.370$, $p = 0.244$). Furthermore, there was no significant age difference between men (mean age 59.3 years) and women (mean age 59.1 years; $t = 0.225$, $p = 0.822$).

Forced choice odour identification

The mean identification score (\pm SD) of men and women combined was 12.6 ± 2.3 ; for men only this was 12.5 ± 2.3 , and for women 12.7 ± 2.2 (Table 2). There was no significant interaction effect between age and sex ($F [1,146] = 1.590$, $p = 0.209$), nor was there a main effect of age ($F [1,147] = 0.501$, $p = 0.480$) or sex ($F [1,147] = 0.292$, $p = 0.590$).

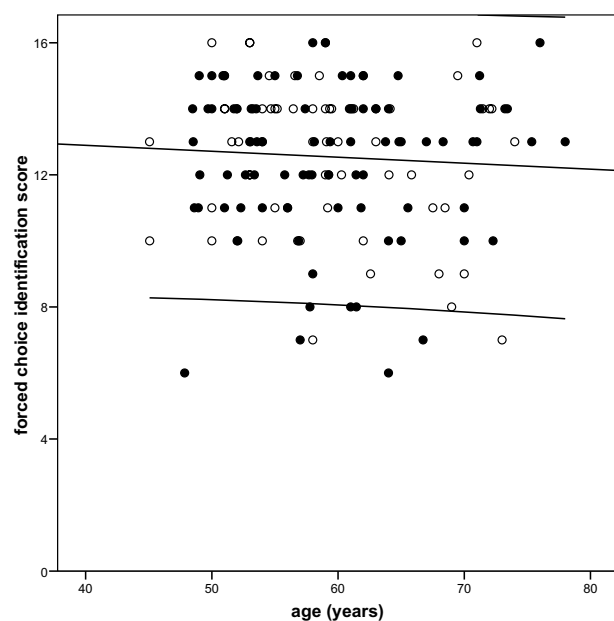


Figure 1. Forced choice identification scores plotted against age.

● Male subjects; ○ Female subjects; the solid lines are the combined regression line and 95% limits of the prediction interval for all subjects.

Regression analysis revealed no significant decline in identification scores with increasing age in men (regression coefficient $b = 0.008$, $p = 0.798$) or women ($b = -0.056$, $p = 0.157$) (Table 2). Furthermore, the regression lines for men and women were not significantly different from each other ($F [2,146] = 0.942$, $p = 0.392$). No age effects were found when data of all subjects were pooled ($b = -0.018$, $p = 0.473$), therefore a horizontal line through the overall mean identification score was used to determine the 95% lower bound of the individual prediction interval in order to calculate cut-off values for hyposmia. The 95% cut-off value for hyposmia based upon all subjects was 8.81 (see Table 3). Ten subjects (6.7%; three women, seven men) scored below the 95% lower bound of the individual prediction interval for identification scores (Figure 1).

Items that were best identified by the Dutch subjects were 'fish' (99.3% correct) and 'peppermint' (96.0% correct). 'Turpentine' was least often identified correctly (38.7% correct identification), followed by 'apple' (48.7% correct) (Table 1a).

Odour discrimination

The mean odour discrimination score of men and women combined was 11.4 ± 2.3 ; for men only this was 11.4 ± 2.2 , and for women 11.5 ± 2.5 (Table 2). There was a significant interaction effect between age and sex ($F [1,146] = 12.983$, $p < 0.001$): a decrease in discrimination scores with increasing age was found for women ($b = -0.179$, $p < 0.001$), but not for men ($b = -0.001$, $p = 0.962$) (Table 2). Furthermore, the regression lines for men and women were significantly different from each other ($F [2,146] = 6.563$, $p = 0.002$). For men, a horizontal line through their mean discrimination score was used to determine the 95% lower bound of the individual prediction interval in order to calculate cut-off values for hyposmia. The 95% cut-off value for hyposmia for men was 7.76 (Table 3). For women,

Table 3. Cut-off values for hyposmia based upon the 95% lower bound of the individual prediction interval of the linear regression lines for identification (ID) or discrimination (DIS) scores plotted against age, for both sexes.

	Cut-off value 95% ID male	Cut-off value 95% ID male	Cut-off value 95% ID male	Cut-off value 95% ID male
45-49 years	8.81	8.81	7.76	9.99
50-54 years	8.81	8.81	7.76	9.15
55-59 years	8.81	8.81	7.76	8.28
60-64 years	8.81	8.81	7.76	7.38
65-69 years	8.81	8.81	7.76	6.46
≥ 70 years	8.81	8.81	7.76	5.11

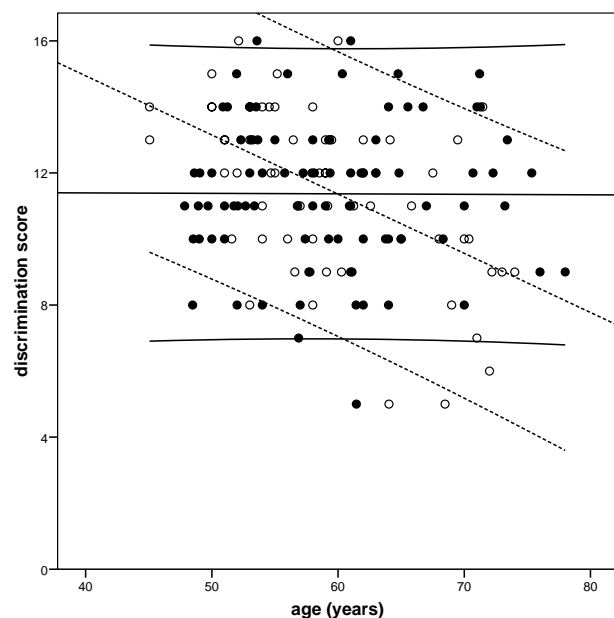


Figure 2. Discrimination scores plotted against age.

● Male subjects; ○ Female subjects; solid lines are the regression line and 95% limits of the prediction interval for male subjects; dotted lines are the regression line and 95% limits of the prediction interval for female subjects.

the 95% lower bound of the individual prediction interval of the regression line was used to calculate the cut-off values for hyposmia (Table 3).

A total of six subjects (4.0%; four women, two men) scored below the 95% lower bound of the individual prediction interval of the regression lines for discrimination scores (Figure 2). Odour combinations that were best discriminated by the Dutch subjects were 2-phenyl ethanol with distracter isoamyl acetate (87.3% correct), and n-butanol with distracter (-)-limonene (85.3% correct). The odour combination with target (-)-carvone and distracter (+)-carvone was least often discriminated correctly (44.0% correct), followed by citronellal with linalool as distracter (54.7% correct) (Table 1b).

Correlation between identification and discrimination scores

Identification and discrimination scores were only moderately correlated (Pearson correlation coefficient $r = 0.296$, $p < 0.001$). When analyzed separately for men and women, a moderate correlation was found in men ($r = 0.350$, $p = 0.001$) but not in women ($r = 0.229$, $p = 0.071$). At the individual level, two subjects (1.3%, one male: identification score = 8, discrimination score = 5; one female: identification score = 7, discrimination score = 8) had a deviant score on both tests.

DISCUSSION

The present study provides normative data for routine clinical use of the identification and discrimination parts of the “Sniffin’ Sticks” olfactory test battery in the Dutch population over 45 years of age. Effects of age and sex were observed for discrimination scores, but not for identification scores. Furthermore, only in men a moderate correlation between

identification and discrimination task performance was found.

The normative data and cut-off values established for the Dutch population in the present study are comparable to the German normative data for subjects over 55 years⁽⁶⁾, but lower than the values recently reported for the Greek population⁽¹⁸⁾. Although Katotomicelakis et al. suggested that climatological differences would be the most likely explanation for the differences between the Greek and German populations, there are no clear data to support their hypothesis⁽²¹⁾. Since performance on olfactory tasks is dependent on familiarity with the odours⁽²⁰⁾ and eating habits⁽²²⁾, the differences in odour discrimination and identification performance between the Greek population on the one hand and the German and Dutch populations on the other hand might alternatively be explained by a more important role of odours in the Greek cuisine. The odour discrimination and identification tasks of the “Sniffin’ Sticks” test battery mainly make use of odours related to food and spices, and could therefore give the Greek population an advantage over the Dutch and German populations.

In the present study, there was no influence of sex on odour identification scores in healthy controls aged between 45–78 years. Although women have previously been shown to outperform men on tests of olfactory function⁽⁴⁾, data from two recent studies using the “Sniffin’ Sticks”^(6, 23) indicate that the influence of sex on identification performance may not necessarily be a consistent finding. Hummel et al. found the sex difference to be age-related, and only present in subjects under 55 years of age⁽⁶⁾. The present data confirm that there is no sex-effect on odour identification scores in older adult subjects, at least when using the “Sniffin’ Sticks”.

In the present population of subjects over 45 years of age, we were unable to confirm the age-related decline in identification scores that has been reported previously^(4, 6). The current results are in agreement with the results of two recent studies in which there were no significant age-related differences between subgroups of older subjects^(23, 24). In the latter study, using “Sniffin’ Sticks”, an age-related difference in odour identification scores could only be demonstrated when comparing younger age groups (under 36 years) with older age groups (36 years and up)⁽²³⁾. Apparently, the age-related decline in identification scores measured using the “Sniffin’ Sticks” per decade is small, and can therefore only be demonstrated in samples with a broad representation of all ages^(4, 6, 18, 23, 25). Another factor that may explain the discrepancy with earlier studies, is the difference in sample size between the present study and some of the previous studies^(4, 6).

Odour discrimination performance in the present study was related to age in women, but not in men. In a very large sample, Hummel et al. found odour discrimination performance to decline more rapidly with increasing age than identification performance⁽⁶⁾. In addition, women’s discrimination scores tended to decline more than those of men in the age groups

36-55 years and > 55 years. In those over 55 years of age, there was no difference in mean odour discrimination score between men and women. The present data obtained in a smaller sample are largely in accordance with these findings.

Previously, Doty et al. found a correlation between identification and discrimination test scores of 0.59⁽²⁸⁾, and proposed that both olfactory modalities load on a primary component. In the present study, only in men a moderate correlation (0.35) between identification and discrimination scores was found, suggesting that the odour discrimination task assesses a different aspect of olfactory function than the identification task. The differences with respect to the effects of age and sex on the two olfactory test scores in the current study seem to strengthen this notion. Several imaging studies provide additional anatomical evidence for this concept, demonstrating that olfactory functions are mediated by common as well as task-specific regions in the brain⁽²⁶⁾. Specifically, a PET study showed distinct areas to be active during odour discrimination (hippocampus) and identification (Broca's area and left inferior frontal lobe)⁽²⁷⁾. Combining all of these data, we hypothesize that odour identification and odour discrimination tests involve at least partly differential components of olfactory information processing.

Cognitive status is an important factor in olfactory function; odour identification may be considered a semantic memory task, whereas odour discrimination draws more on working memory (for review see⁽²⁹⁾). Variations in cognitive function are inevitable in the general population and may therefore influence olfactory function. The aim of the present study was to establish normative values applicable to the general population. Therefore we did not correct for variations in cognitive function, but did exclude individuals suffering from a neurological disorder. It is therefore unlikely that the presence of disease-related cognitive dysfunction could have negatively influenced olfactory test scores.

Data obtained in a recent study⁽⁷⁾ suggest that the actual physiological age-related decline in olfactory function (presbyosmia) is probably smaller and more gradual than previously assumed. The authors argue that the commonly observed age-related decline in olfactory function results to a large degree from age-related factors, such as use of medication or (a history of) nasal disease, that each independently affect olfactory function⁽⁷⁾. Furthermore, smoking is generally reported to be adversely associated with olfactory function in a dose-related manner^(30, 31). Clearly, 'pure' normative values based upon selected healthy, non-smoking subjects are valuable in showing the true effect of aging on olfactory function. However, when olfactory testing is used in a clinical setting, e.g. to screen for neurodegenerative diseases, it is important to avoid unnecessarily high proportions of false positives (subjects with impaired olfactory ability from other causes). In this situation, normative values based upon a non-selected heterogeneous population as estab-

lished in this study are more appropriate.

In conclusion, provisional normative values for the identification and discrimination parts of the "Sniffin' Sticks", as well as cut-off scores for hyposmia, are now available for the Dutch population over 45 years of age. Although normative values for younger subjects are also recommended, the current results are applicable to the clinical evaluation of patients with olfactory disorders, including those with olfactory dysfunction after head trauma or (sino)nasal surgery. They can also be used to quantify olfactory function for medico-legal purposes. Future applications may include the incorporation of olfactory testing into screening strategies for incipient neurodegenerative disorders.

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