

Furthering the understanding of olfaction, prevalence of loss of smell and risk factors: a population-based survey (OLFACAT study)

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ABSTRACT

Objectives: To investigate olfaction in general population, prevalence of olfactory dysfunction and related risk factors.

Design: Cross-sectional population-based survey, distributing four microencapsulated odorants (rose, banana, musk and gas) and two self-administered questionnaires (odour description; epidemiology/health status).

Setting: The survey was distributed to general population through a bilingual (Catalan, Spanish) newspaper in Catalonia (Spain), on December 2003.

Participants: Newspaper readers of all ages and gender; 9348 surveys were analysed from the 10 783 returned.

Main outcome measures: Characteristics of surveyed population, olfaction by age and gender, smell self-perception and smell impairment risk factors. Terms normosmia, hyposmia and anosmia were used when participants detected, recognised or identified all four, one to three or none of the odours, respectively.

Results: Survey profile was a 43-year-old woman with medium–high educational level, living in a city. Olfaction was considered normal in 80.6% (detection), 56% (recognition/memory) and 50.7% (identification). Prevalence of smell dysfunction was 19.4% for detection (0.3% anosmia, 19.1% hyposmia), 43.5% for recognition (0.2% anosmia, 43.3% hyposmia) and 48.8% for identification (0.8% anosmia, 48% hyposmia). Olfaction was worse ($p < 0.0001$) in men than in women through all ages. There was a significant age-related smell detection decline however smell recognition and identification increased up to fourth decade and declined after the sixth decade of life. Risk factors for anosmia were: male gender, loss of smell history and poor olfactory self-perception for detection; low educational level, poor self-perception and pregnancy for recognition; and older age, poor self-perception and history of head trauma and loss of smell for identification. Smoking and exposure to noxious substances were mild protective factors for smell recognition.

Conclusions: Sense of smell in women is better than in men suggesting a learning process during life with

ARTICLE SUMMARY

Article focus

- Population-based smell survey in 2003.
- Partial and total smell impairment by age and gender.
- Risk factors for olfactory disorders.

Key messages

- Olfaction is better in women than in men.
- Smell improves with a learning process and deteriorates in older ages.
- Poor olfactory self-perception, history of smell loss for over 1 week, head trauma and pregnancy are potential risk factors for olfactory disorders.

Strengths and limitations of this study

- The largest European population-based study providing data on partial/total loss of smell and their absolute risk factors.
- Self-administered survey (no control on how it was performed); the study was done in a middle-high sociocultural population (newspaper readers).

deterioration in older ages. Poor self-perception, history of smell loss, head trauma and pregnancy are potential risk factors for olfactory disorders.

INTRODUCTION

The sense of smell provides information on the surrounding environment, warns us about chemical dangers and putrid food and may even help people to mate. Smell disorders may affect the ability to enjoy food and aromas while interfering with the ability to notice potentially harmful chemicals and gases.¹

In 1987, the National Geographic Smell Survey (NGSS) studied a large US sample population (1.2 million) whereby 1% of

participants could not smell three or more of six odourants using a 'scratch and sniff' test.² Age was an important factor in smell deterioration and smell was rated better in women than in men. In 1994, the National Health Interview Survey³ reported data from 42 000 USA households with 1.4% prevalence of self-reported olfactory dysfunction, exponentially increasing with age. This study, however, did not include any testing of smell function.

The prevalence and associated risk factors of olfactory impairment in the European population has been investigated to a limited extent. In the Swedish version of the NGSS,⁴ done in 532 individuals older than 45 years, increasing age was associated with impaired ability to detect/identify odourants, with no effect of gender on smell perception. Education has also been shown to account for a significant portion of the age-related variance in identification.⁵ Another European population-based study identified a significant relationship between impaired olfaction and aging, male gender and nasal polyps, but not with diabetes or smoking, reporting an olfactory dysfunction prevalence of 19.1%.⁶

Approximately two-thirds of smell dysfunction cases are likely due to prior upper respiratory infections, head trauma or sinonasal diseases.⁷ Toxic chemical exposure, epilepsy, pollution, drugs, nutritional disturbances and neurodegenerative diseases may also cause olfactory disorders.^{8,9} Smoking may cause a reversible reduction in the ability to smell^{10,11} while chronic rhinosinuitis/nasal polyps may result in a partial or total loss of smell.¹²

The aims of this study were to investigate the status of olfaction in the general population while determining the prevalence of olfactory dysfunction and its related risk factors.

METHODS

Study design

The OLFACAT (Olfaction in Catalonia) survey was carried out in the general population of Catalonia in Spain. Two questionnaires, olfaction and demography-health status and a set of four microencapsulated odourants were distributed in the 250 000 daily issues of the newspaper *El Periódico de Catalunya* on 23 December 2003. The survey was presented in both Catalan and Spanish languages to facilitate the choice of the preferred language. The present manuscript has followed the STROBE checklist guidelines.

The study was approved by the Institutional Ethics and Clinical Research Committee of Hospital Clínic de Barcelona (reference 1295).

Measurements

Survey odourants

Four common odourants were included in the survey: rose (2% of Bulgarian rose in 98% of phenyl-ethyl alcohol) as a floral odour; banana (amyl-isobutirate at 50% in diethyl-phtalate) as a food odour; musk (1:1 mixture of

galaxolide and diethyl-phtalate exaltolide) as a perfume odour; and gas (mixture of 30% mercaptan and 70% tetrahydrothiophene) as an industrial odour. Each compound was prepared following established formulas and the solution magnetically homogenised. Rose, banana and musk odourants were elaborated by Antonio Puig SA (Barcelona, Catalonia, Spain) and gas odourant by ENAGAS (Saragossa, Spain). Stability test protocols were performed by accelerating the olfactory aging of products at 40°C for 2 months, following their smell evolution after 1–8 weeks. The microencapsulation process was done by ARCADE Europe (Paris, France) as follows: essential oil component was contained and delivered from highly durable synthetic microcapsules manufactured using a proprietary polycondensated polymerisation method. The microcapsules were blended with a water-based polymer adhesive to form printable slurry. Odourants were adhered to a smell-less paper and dispatched using a folded-form design so as to prevent direct contact between odour samples.

Smell questionnaire

Participants were asked to scratch and sniff each odour and then answer three questions: first, odour detection: did you smell any scent? (yes, no); second, odour recognition/memory: have you ever smelt this scent? (yes, no) and third, forced-choice odour identification: which name defines the scent you have smelt?, whereby only one of the four given options was correct. The term 'normosmia' was used when a participant was able to detect, recognise (memory) or correctly identify all four tested odours; the term 'hyposmia' was used when a participant was not able to detect, recognise (memory) or correctly identify one, two or three tested odours and the term 'anosmia' was used when a participant was unable to detect, recognise (memory) or correctly identify any of the four tested odours.

Epidemiological and health-status questionnaire

From the 12-question questionnaire, four questions were on demography: first, gender (men and women); second, age (years); third, current educational level (primary school, secondary school, high school, University or College) and fourth, residential area (city and postcode). Two questions described smell self-perception: fifth, how do you consider your current sense of smell? (very good, good, poor and very poor) and sixth, have you ever lost the sense of smell? (never, up to 1 week and over 1 week). Two questions were on exposure to toxic or noxious substances: seventh, have you ever been exposed to dust, gases, fumes, vapours or/and volatile toxics at home and/or at work? (yes, no) and eighth, do you smoke? (no, exsmoker and smoker). Two questions were on health-status: ninth, have you ever had a severe face and/or head trauma? (yes, no) and 10th, have you ever been diagnosed with chronic rhinosinuitis? (yes, no). Finally, two questions were on women's

health: 11th, are you currently pregnant? (yes, no); and 12th, are you currently menstruating? (yes, no).

Data management and statistical analysis

The returned surveys were read using an optical system (BV Scan system, Voxpublica), the data were transferred to an electronic database, and then statistically analysed using Stata V.8 (Stata Statistical Software: Release 8.0 College Station, Texas, USA: *Stata Corporation* 2003).¹³ The data-cleaning process was based on programmed queries to identify records containing inconsistent or uncertain data. The corrupt or inaccurate values identified by these queries were subsequently recorded as missing values in the data set.

Only those surveys fully and consistently answered were considered for statistical analysis. Differences between gender in epidemiological and health-status characteristics were evaluated by χ^2 test (table 4). Adjusted (multivariate) logistic regression models for anosmia and hyposmia were estimated (tables 1–3). To estimate the multivariate models for anosmia, the covariates that do not have any events (anosmia cases) in any of its categories were not included. Results from estimated models were expressed as adjusted OR and 95% CI. The reference category used to calculate the OR for each level of variables measured on an ordinal scale was the immediately previous category, starting with the second. Results from estimated models were expressed as OR and 95% CI. All tests were performed using a two-tailed significance level of 0.05.

RESULTS

Characteristics of the surveyed population

Following the data cleaning process, 5.6% of answers from the 10 783 received surveys were identified as inconsistent. After the exclusion of both these inconsistent questionnaire returns and the incomplete epidemiological and health-status questionnaires (7.7%), the sample size for analysis was 9348 questionnaires (figure 1).

Age and gender

The mean age of the surveyed population was 43.3 years, ranging from 5 to 91 years. The analysis was performed in seven age groups to ensure a reasonable sample size for each age and gender group. Almost two-thirds of participants were women (65.7%), of which 2.1% were pregnant and 12.7% were menstruating (table 4).

Education and residential zone

Most participants (83.8%) had a high educational level (high school or University/College) and were living (93.9%) in an urban area, with no differences between genders (table 4).

Exposure to tobacco and noxious substances

More than one-fifth (21.4%) of participants were smokers, 28.3% were exsmokers, while almost a third

(29.9%) reported to be regularly exposed to toxic or noxious substances, either at home or at work. Men reported a higher exposure to both tobacco smoke (24.8%, $p<0.0001$) and noxious substances (33.9%, $p<0.0001$) than women (19.7% and 27.7%, respectively) (table 4).

Health status

In total, 4.4% of participants had received a diagnosis of chronic rhinosinusitis, with similar prevalence in women and men, while 5% reported a history of face/head trauma, this prevalence being higher in men than in women (6.2% vs 4.3%, $p<0.0001$) (table 4).

Sense of smell

All four odours (normosmia) were detected by 80.6%, recognised by 56%, and identified by 50.7% of the surveyed population. One to three odours (hyposmia) were detected by 19.1%, recognised by 43.3% and identified by 48%. None of the four odours (anosmia) were detected by 0.3%, recognised by 0.2% and identified by 0.8%. Individual odours were more highly detected (rose 99.4%, banana 98.9%, gas 96.9% and musk 84.4%) than recognised (rose 94.8%, banana 96.2%, gas 94.9% and musk 66.2%) or correctly identified (rose 91.8%, banana 89.8%, gas 92.1% and musk 65.4%). Moreover, individual odours were always better detected, recognised and identified by women than by men, except for rose and banana recognition.

Smell by gender and age

Within the population experiencing normosmia, there was a significant and progressive age-related decline of smell detection while smell recognition and identification increased up to the fourth decade of life, continued to plateau throughout the fifth and sixth decades, and declined thereafter. Significant but opposite findings were found for hyposmia and anosmia.

Normosmia was higher in women than in men ($p<0.0001$) either in smell detection (82.8% vs 76.5%), recognition/memory (58% vs 51.9%) or identification (54.1% vs 44.3%; figure 2). Hyposmia was higher in men than in women ($p<0.0001$) either in smell detection (22.8% vs 17.1%), recognition/memory (47.1% vs 41.4%) and identification (54% vs 44.9%; figure 3). Finally, anosmia was higher in men than in women in both smell detection (0.9% vs 0.1%; $p<0.0001$) and identification (1.2% vs 0.6%; $p=0.0057$), but not in smell recognition/memory (0.2% vs 0.2%, $p=0.9569$; figure 4). In the oldest group (over 70 years), the prevalence for anosmia of detection (4.4%) and identification (6.6%) was especially higher in men than in women (0% and 1.4%, respectively; figure 4).

Smell self-perception

Subjective description of smell

Regardless of gender and age, 93.1% of participants subjectively rated their sense of smell as good or very good,

Table 1 Distribution and relative risk for hyposmia (smell of one to three odours) or anosmia (smell of none of the four odours) in the case of smell detection using a multivariate logistic analysis of demographic and health problems

| Covariable | Hyposmia (detection) | | | | | Anosmia (detection) | | | | |
|---|---|--------------|-------------|----------------|---------|---------------------------------------|------------|-------------|-------------------|---------|
| | 8601 Subjects, 1639 with hyposmia (19%) | | | | | 9251 Subjects, 25 with anosmia (0.3%) | | | | |
| | No | Yes | Adjusted OR | (95% CI) | p Value | No | Yes | Adjusted OR | (95% CI) | p Value |
| Female | 4686 (67.3%) | 967 (59.0%) | 0.78 | (0.69 to 0.88) | <0.0001 | 6077 (65.9%) | 7 (28.0%) | 0.22 | (0.07 to 0.71) | 0.0111 |
| Educational level* | | | | | | | | | | |
| Elementary school | 23 (0.3%) | 7 (0.4%) | – | – | 0.0352 | 32 (0.3%) | 0 (0.0%) | – | – | – |
| Middle school | 1061 (15.2%) | 247 (15.1%) | 0.76 | (0.32 to 1.81) | | 1436 (15.6%) | 8 (32.0%) | – | – | |
| High school | 3053 (43.9%) | 683 (41.7%) | 1.02 | (0.86 to 1.21) | | 4020 (43.6%) | 11 (44.0%) | – | – | |
| University | 2825 (40.6%) | 702 (42.8%) | 1.18 | (1.05 to 1.34) | | 3738 (40.5%) | 6 (24.0%) | – | – | |
| Subjective description of sense of smell* | | | | | | | | | | |
| Very good | 1563 (22.5%) | 275 (16.8%) | – | – | <0.0001 | 1968 (21.3%) | 2 (8.0%) | – | – | <0.0001 |
| Good | 4990 (71.7%) | 1167 (71.2%) | 1.24 | (1.08 to 1.44) | | 6636 (71.9%) | 2 (8.0%) | 0.20 | (0.03 to 1.48) | |
| Poor | 388 (5.6%) | 188 (11.5%) | 1.94 | (1.58 to 2.37) | | 608 (6.6%) | 5 (20.0%) | 9.69 | (1.58 to 59.30) | |
| Very poor | 21 (0.3%) | 9 (0.5%) | 0.75 | (0.33 to 1.70) | | 14 (0.2%) | 16 (64.0%) | 109.54 | (30.51 to 393.35) | |
| Loss of smell history* | | | | | | | | | | |
| Never | 4829 (69.4%) | 1130 (68.9%) | – | – | 0.0935 | 6429 (69.7%) | 5 (20.0%) | – | – | 0.0172 |
| ≤1 week | 1796 (25.8%) | 384 (23.4%) | 0.88 | (0.78 to 1.01) | | 2324 (25.2%) | 1 (4.0%) | 0.71 | (0.08 to 6.35) | |
| >1 week | 337 (4.8%) | 125 (7.6%) | 1.25 | (0.97 to 1.62) | | 473 (5.1%) | 19 (76.0%) | 9.26 | (0.98 to 87.07) | |
| Exposure to noxious substances | 2023 (29.1%) | 491 (30.0%) | 1.02 | (0.91 to 1.16) | 0.7025 | 2749 (29.8%) | 9 (36.0%) | 2.00 | (0.67 to 5.92) | 0.2117 |
| Chronic rhinosinusitis | 296 (4.3%) | 75 (4.6%) | 0.99 | (0.76 to 1.30) | 0.9662 | 410 (4.4%) | 3 (12.0%) | 0.59 | (0.09 to 3.96) | 0.5887 |
| Menstruation | 616 (8.8%) | 116 (7.1%) | 0.97 | (0.78 to 1.20) | 0.7655 | 777 (8.4%) | 0 (0.0%) | – | – | – |
| Age (years)* | | | | | | | | | | |
| <20 | 374 (5.4%) | 54 (3.3%) | – | – | <0.0001 | 441 (4.8%) | 1 (4.0%) | – | – | – |
| 20–29 | 914 (13.1%) | 163 (9.9%) | 1.12 | (0.80 to 1.57) | | 1118 (12.1%) | 1 (4.0%) | – | – | |
| 30–39 | 1667 (23.9%) | 356 (21.7%) | 1.17 | (0.95 to 1.44) | | 2150 (23.3%) | 0 (0.0%) | – | – | |
| 40–49 | 1893 (27.2%) | 456 (27.8%) | 1.14 | (0.97 to 1.33) | | 2514 (27.2%) | 2 (8.0%) | – | – | |
| 50–59 | 1360 (19.5%) | 386 (23.6%) | 1.17 | (1.00 to 1.37) | | 1909 (20.7%) | 7 (28.0%) | – | – | |
| 60–69 | 528 (7.6%) | 162 (9.9%) | 1.08 | (0.88 to 1.34) | | 779 (8.4%) | 6 (24.0%) | – | – | |
| >70 | 226 (3.2%) | 62 (3.8%) | 0.85 | (0.61 to 1.19) | | 315 (3.4%) | 8 (32.0%) | – | – | |
| Residential zone† | | | | | | | | | | |
| Rural (reference) | 121 (1.7%) | 31 (1.9%) | 1 | – | 0.0821 | 165 (1.8%) | 0 (0.0%) | – | – | – |
| Semirural | 294 (4.2%) | 85 (5.2%) | 1.15 | (0.72 to 1.83) | | 403 (4.4%) | 1 (4.0%) | – | – | |
| Urban | 6547 (94.0%) | 1523 (92.9%) | 0.87 | (0.58 to 1.30) | | 8658 (93.8%) | 24 (96.0%) | – | – | |
| Smoking‡ | | | | | | | | | | |
| Non-smoker (reference) | 3535 (50.8%) | 789 (48.1%) | 1 | – | 0.9331 | 4646 (50.4%) | 10 (40.0%) | 1 | – | 0.9608 |

Continued

Table 1 Continued

| Covariate | Hyposmia (detection) 8601 Subjects, 1639 with hyposmia (19%) | | | | Anosmia (detection) 9251 Subjects, 25 with anosmia (0.3%) | | | |
|------------------------|---|-------------|-------------|----------------|--|------------|-------------|----------------|
| | No | Yes | Adjusted OR | p Value | No | Yes | Adjusted OR | p Value |
| Exsmoker | 1939 (27.9%) | 498 (30.4%) | 1.00 | (0.88 to 1.14) | 2603 (28.2%) | 11 (44.0%) | 1.10 | (0.34 to 3.57) |
| Smoker | 1488 (21.4%) | 352 (21.5%) | 1.03 | (0.89 to 1.19) | 1977 (21.4%) | 4 (16.0%) | 0.88 | (0.19 to 4.12) |
| History of head trauma | 343 (4.9%) | 75 (4.6%) | 0.85 | (0.66 to 1.11) | 456 (4.9%) | 1 (4.0%) | 0.33 | (0.03 to 3.98) |
| Pregnancy | 99 (1.2%) | 19 (1.2%) | 1.00 | (0.60 to 1.65) | 128 (1.4%) | 0 (0.0%) | - | - |

Data presented as adjusted OR, 95% CI.

*OR relative to the previous category.

†OR relative to the reference category.

while 6.9% of them reported their smell as poor or very poor, the smell score being better in women than in men ($p<0.0001$) (table 4).

Loss of smell history

A history of loss of smell was reported by almost one-third (30.4%) of participants, predominantly for less than 1 week (25.1%). The smell loss for over 1 week was more frequent in men (6.4% vs 4.8%, $p=0.0042$) (table 4).

Risk factors for smell impairment

Smell detection

Women detected odours more frequently than men (82.8% vs 76.5%, $p<0.0001$). The risk for anosmia of detection was lower in women (OR=0.22) and higher in subjects reporting a loss of smell history for over 1 week (OR=9.26); and anosmia was also associated with a worse smell self-perception (table 1). The risk for hyposmia of detection was lower in women (OR=0.78) and associated with older age (>50-year-old), a lower educational level and a worse smell self-perception (table 1).

Smell recognition/memory

Women showed a better capability to recognise odours than men (58% vs 51.9%; $p<0.0001$). The risk for anosmia of recognition was higher in pregnant women (OR=6.94) and associated with a lower educational level and a worse smell self-perception (table 2). The risk for hyposmia of recognition was lower in women (OR=0.79) and higher in subjects reporting a loss of smell history for over 1 week (OR=1.23); and it was associated with older age (>70 years old), a lower educational level, and a worse smell self-perception. Smoking (both exsmokers and smokers; OR=0.80 and 0.68, respectively) and frequent contact with noxious substances (OR=0.83) were found to have a mild but significant protective effect on odour recognition/memory (table 2).

Forced-choice smell identification

Women performed better than men on odour identification (54.1% vs 44.3%, $p<0.0001$). The risk for anosmia of identification was higher in subjects reporting a history of head trauma (OR=3.38) and a loss of smell for over 1 week (OR=2.79), and it was associated with older age (>60 years old) and a worse smell self-perception (table 3). The risk for hyposmia of identification was lower in women (OR=0.76) and higher in subjects reporting a loss of smell history for over 1 week (OR=1.28), and it was associated with older age (>60-year-old), a lower educational level and a smell worse self-perception (table 3).

DISCUSSION

The most important findings of the OLFACAT survey were: first, the overall prevalence of olfactory dysfunction in the case of detection was 19.4%, with a total loss of smell (anosmia) of 0.3%. Despite this high prevalence of

Table 2 Relative risk for hyposmia (smell of one to three odours) or anosmia (smell of none of the four odours) in the case of smell recognition/memory using a multivariate logistic analysis of demographic characteristics and health problems

| Covariable | Hyposmia (recognition/memory) | | | | | Anosmia (recognition/memory) | | | | |
|---|---|--------------|-------------|----------------|---------|---------------------------------------|------------|-------------|------------------|---------|
| | 6778 Subjects, 2936 with hyposmia (43%) | | | | | 9079 Subjects, 18 with anosmia (0.2%) | | | | |
| | No | Yes | Adjusted OR | (95% CI) | p Value | No | Yes | Adjusted OR | (95% CI) | p Value |
| Female | 2663 (69.3%) | 1885 (64.2%) | 0.79 | (0.71 to 0.88) | <0.0001 | 5986 (66.1%) | 12 (66.7%) | 1.26 | (0.41 to 3.81) | 0.6879 |
| Educational level* | | | | | | | | | | |
| Elementary school | 14 (0.4%) | 14 (0.5%) | – | – | 0.0200 | 31 (0.3%) | 2 (11.1%) | – | – | 0.0005 |
| Middle school | 536 (14.0%) | 505 (17.2%) | 1.20 | (0.56 to 2.60) | | 1387 (15.3%) | 4 (22.2%) | 0.05 | (0.01 to 0.29) | |
| High school | 1671 (43.5%) | 1272 (43.3%) | 0.84 | (0.72 to 0.97) | | 3942 (43.5%) | 11 (61.1%) | 1.18 | (0.34 to 4.08) | |
| University | 1621 (42.2%) | 1145 (39.0%) | 0.93 | (0.83 to 1.04) | | 3701 (40.8%) | 1 (5.6%) | 0.09 | (0.01 to 0.73) | |
| Subjective description of sense of smell* | | | | | | | | | | |
| Very good | 961 (25.0%) | 532 (18.1%) | – | – | <0.0001 | 1939 (21.4%) | 3 (16.7%) | – | – | 0.0039 |
| Good | 2690 (70.0%) | 2164 (73.7%) | 1.45 | (1.28 to 1.64) | | 6510 (71.8%) | 12 (66.7%) | 1.13 | (0.31 to 4.10) | |
| Poor | 187 (4.9%) | 234 (8.0%) | 1.62 | (1.30 to 2.01) | | 600 (6.6%) | 1 (5.6%) | 0.75 | (0.08 to 7.40) | |
| Very poor | 4 (0.1%) | 6 (0.2%) | 0.98 | (0.26 to 3.66) | | 12 (0.1%) | 2 (11.1%) | 65.35 | (4.60 to 927.55) | |
| Loss of smell history* | | | | | | | | | | |
| Never | 2620 (68.2%) | 2087 (71.1%) | – | – | 0.0020 | 6303 (69.6%) | 11 (61.1%) | – | – | 0.7159 |
| ≤1 week | 1050 (27.3%) | 685 (23.3%) | 0.81 | (0.73 to 0.91) | | 2299 (25.4%) | 4 (22.2%) | 1.22 | (0.38 to 3.91) | |
| >1 week | 172 (4.5%) | 164 (5.6%) | 1.23 | (0.95 to 1.59) | | 459 (5.1%) | 3 (16.7%) | 1.76 | (0.23 to 13.60) | |
| Exposure to noxious substances | 1201 (31.3%) | 803 (27.4%) | 0.83 | (0.74 to 0.93) | 0.0010 | 2694 (29.7%) | 4 (22.2%) | 0.58 | (0.18 to 1.82) | 0.3497 |
| Chronic rhinosinusitis | 168 (4.4%) | 127 (4.3%) | 1.02 | (0.80 to 1.30) | 0.8574 | 404 (4.5%) | 1 (5.6%) | 0.72 | (0.08 to 6.40) | 0.7720 |
| Menstruation | 347 (9.0%) | 249 (8.5%) | 1.08 | (0.90 to 1.29) | 0.4244 | 774 (8.5%) | 1 (5.6%) | 1.14 | (0.13 to 9.87) | 0.9070 |
| Age (years)* | | | | | | | | | | |
| <20 | 175 (4.6%) | 214 (7.3%) | – | – | <0.0001 | 437 (4.8%) | 1 (5.6%) | – | – | 0.7500 |
| 20–29 | 494 (12.9%) | 405 (13.8%) | 0.80 | (0.62 to 1.03) | | 1108 (12.2%) | 1 (5.6%) | 1.06 | (0.06 to 18.62) | |
| 30–39 | 956 (24.9%) | 663 (22.6%) | 0.81 | (0.68 to 0.96) | | 2115 (23.3%) | 4 (22.2%) | 1.29 | (0.14 to 11.82) | |
| 40–49 | 1088 (28.3%) | 689 (23.5%) | 0.91 | (0.79 to 1.04) | | 2475 (27.3%) | 2 (11.1%) | 0.46 | (0.08 to 2.66) | |
| 50–59 | 775 (20.2%) | 564 (19.2%) | 1.06 | (0.92 to 1.24) | | 1881 (20.8%) | 3 (16.7%) | 1.74 | (0.28 to 10.81) | |
| 60–69 | 268 (7.0%) | 257 (8.8%) | 1.22 | (0.99 to 1.50) | | 755 (8.3%) | 4 (22.2%) | 1.84 | (0.37 to 9.12) | |
| >70 | 86 (2.2%) | 144 (4.9%) | 1.64 | (1.19 to 2.26) | | 290 (3.2%) | 3 (16.7%) | 1.73 | (0.35 to 8.63) | |
| Residential zone† | | | | | | | | | | |
| Rural (reference) | 73 (1.9%) | 49 (1.7%) | 1 | – | 0.4187 | 164 (1.8%) | 0 (0.0%) | – | – | – |
| Semi-rural | 157 (4.1%) | 139 (4.7%) | 1.27 | (0.82 to 1.96) | | 390 (4.3%) | 2 (11.1%) | – | – | |
| Urban | 3612 (94.0%) | 2748 (93.6%) | 1.10 | (0.76 to 1.59) | | 8507 (93.9%) | 16 (88.9%) | – | – | |
| Smoking‡ | | | | | | | | | | |
| Non-smoker (reference) | 1857 (48.3%) | 1648 (56.1%) | 1 | – | <0.0001 | 4567 (50.4%) | 12 (66.7%) | – | – | – |
| Exsmoker | 1081 (28.1%) | 766 (26.1%) | 0.80 | (0.71 to 0.91) | | 2537 (28.0%) | 6 (33.3%) | – | – | |
| Smoker | 904 (23.5%) | 522 (17.8%) | 0.68 | (0.60 to 0.78) | | 1957 (21.6%) | 0 (0.0%) | – | – | |
| History of head trauma | 201 (5.2%) | 134 (4.6%) | 0.86 | (0.68 to 1.08) | 0.1917 | 446 (4.9%) | 0 (0.0%) | – | – | – |
| Pregnancy | 60 (1.6%) | 35 (1.2%) | 0.84 | (0.55 to 1.29) | 0.4243 | 125 (1.4%) | 1 (5.6%) | 6.94 | (0.74 to 65.52) | 0.0907 |

Data presented as adjusted OR, 95% CI.

*OR relative to the previous category.

†OR relative to the reference category.

Table 3 Relative risk for hyposmia (smell of one to three odours) or anosmia (smell of none of the four odours) in the case of forced-choice smell identification using a multivariate logistic analysis of demographic characteristics and health problems

| Covariable | Hyposmia (identification) | | | | | Anosmia (identification) | | | | |
|---|---|--------------|-------------|----------------|---------|-------------------------------------|------------|-------------|------------------|---------|
| | 8107 Subjects, 3894 with hyposmia (48%) | | | | | 9195 Subjects, 75 with anosmia (1%) | | | | |
| | No | Yes | Adjusted OR | (95% CI) | p Value | No | Yes | Adjusted OR | (95% CI) | p Value |
| Female | 2911 (69.1%) | 2368 (60.8%) | 0.76 | (0.69 to 0.84) | <0.0001 | 6008 (65.9%) | 38 (50.7%) | 0.96 | (0.55 to 1.67) | 0.8850 |
| Educational level* | | | | | | | | | | |
| Elementary school | 8 (0.2%) | 18 (0.5%) | – | – | 0.0007 | 31 (0.3%) | 0 (0.0%) | – | – | – |
| Middle school | 654 (15.5%) | 608 (15.6%) | 0.49 | (0.21 to 1.16) | | 1419 (15.6%) | 24 (32.0%) | – | – | |
| High school | 1881 (44.6%) | 1636 (42.0%) | 1.01 | (0.88 to 1.15) | | 3970 (43.5%) | 28 (37.3%) | – | – | |
| University | 1670 (39.6%) | 1632 (41.9%) | 1.21 | (1.09 to 1.34) | | 3700 (40.6%) | 23 (30.7%) | – | – | |
| Subjective description of sense of smell* | | | | | | | | | | |
| Very good | 1034 (24.5%) | 667 (17.1%) | – | – | <0.0001 | 1948 (21.4%) | 8 (10.7%) | – | – | <0.0001 |
| Good | 2979 (70.7%) | 2841 (73.0%) | 1.42 | (1.27 to 1.58) | | 6567 (72.0%) | 38 (50.7%) | 1.27 | (0.59 to 2.76) | |
| Poor | 183 (4.3%) | 374 (9.6%) | 2.06 | (1.69 to 2.51) | | 592 (6.5%) | 13 (17.3%) | 2.16 | (1.00 to 4.66) | |
| Very poor | 17 (0.4%) | 12 (0.3%) | 0.26 | (0.12 to 0.56) | | 13 (0.1%) | 16 (21.3%) | 36.06 | (13.12 to 99.13) | |
| Loss of smell history* | | | | | | | | | | |
| Never | 2895 (68.7%) | 2741 (70.4%) | – | – | 0.0005 | 6361 (69.7%) | 38 (50.7%) | – | – | 0.0415 |
| ≤1 week | 1130 (26.8%) | 901 (23.1%) | 0.82 | (0.74 to 0.91) | | 2301 (25.2%) | 12 (16.0%) | 0.93 | (0.48 to 1.81) | |
| >1 week | 188 (4.5%) | 252 (6.5%) | 1.28 | (1.02 to 1.62) | | 458 (5.0%) | 25 (33.3%) | 2.79 | (1.14 to 6.88) | |
| Exposure to noxious substances | 1255 (29.8%) | 1132 (29.1%) | 0.98 | (0.89 to 1.08) | 0.6930 | 2716 (29.8%) | 23 (30.7%) | 1.03 | (0.60 to 1.77) | 0.9111 |
| Chronic rhinosinusitis | 187 (4.4%) | 170 (4.4%) | 0.96 | (0.77 to 1.20) | 0.7290 | 403 (4.4%) | 5 (6.7%) | 0.80 | (0.28 to 2.29) | 0.6824 |
| Menstruation | 390 (9.3%) | 304 (7.8%) | 1.03 | (0.87 to 1.22) | 0.7157 | 772 (8.5%) | 2 (2.7%) | 0.49 | (0.11 to 2.14) | 0.3421 |
| Age (years)* | | | | | | | | | | |
| <20 | 203 (4.8%) | 194 (5.0%) | – | – | <0.0001 | 438 (4.8%) | 3 (4.0%) | – | – | 0.0006 |
| 20–29 | 551 (13.1%) | 466 (12.0%) | 0.82 | (0.64 to 1.04) | | 1106 (12.1%) | 8 (10.7%) | 0.76 | (0.19 to 2.96) | |
| 30–39 | 1032 (24.5%) | 839 (21.5%) | 0.94 | (0.80 to 1.10) | | 2131 (23.4%) | 11 (14.7%) | 0.65 | (0.25 to 1.68) | |
| 40–49 | 1198 (28.4%) | 1004 (25.8%) | 1.05 | (0.93 to 1.19) | | 2490 (27.3%) | 10 (13.3%) | 0.68 | (0.28 to 1.65) | |
| 50–59 | 822 (19.5%) | 831 (21.3%) | 1.20 | (1.05 to 1.37) | | 1886 (20.7%) | 12 (16.0%) | 1.40 | (0.58 to 3.38) | |
| 60–69 | 302 (7.2%) | 371 (9.5%) | 1.19 | (0.99 to 1.43) | | 763 (8.4%) | 17 (22.7%) | 3.38 | (1.51 to 7.55) | |
| >70 | 105 (2.5%) | 189 (4.9%) | 1.43 | (1.07 to 1.91) | | 306 (3.4%) | 14 (18.7%) | 1.24 | (0.51 to 3.01) | |
| Residential zone† | | | | | | | | | | |
| Rural (reference) | 76 (1.8%) | 71 (1.8%) | 1 | – | 0.3585 | 162 (1.8%) | 1 (1.3%) | 1 | – | 0.9858 |
| Semi-rural | 176 (4.2%) | 181 (4.6%) | 1.11 | (0.75 to 1.65) | | 400 (4.4%) | 3 (4.0%) | 0.87 | (0.08 to 8.95) | |
| Urban | 3961 (94.0%) | 3642 (93.5%) | 0.95 | (0.68 to 1.33) | | 8558 (93.8%) | 71 (94.7%) | 0.85 | (0.12 to 6.21) | |
| Smoking† | | | | | | | | | | |
| Non-smoker (reference) | 2118 (50.3%) | 1968 (50.5%) | 1 | – | 0.5326 | 4594 (50.4%) | 30 (40.0%) | 1 | – | 0.2814 |
| Exsmoker | 1169 (27.7%) | 1131 (29.0%) | 0.96 | (0.86 to 1.07) | | 2567 (28.1%) | 30 (40.0%) | 1.61 | (0.88 to 2.93) | |
| Smoker | 926 (22.0%) | 795 (20.4%) | 0.94 | (0.83 to 1.06) | | 1959 (21.5%) | 15 (20.0%) | 1.41 | (0.70 to 2.82) | |
| History of head trauma | 204 (4.8%) | 193 (5.0%) | 0.97 | (0.79 to 1.20) | 0.7963 | 442 (4.8%) | 12 (16.0%) | 3.38 | (1.69 to 6.74) | 0.0006 |
| Pregnancy | 62 (1.5%) | 48 (1.2%) | 1.02 | (0.69 to 1.51) | 0.9157 | 126 (1.4%) | 1 (1.3%) | 1.72 | (0.22 to 13.33) | 0.6017 |

Data presented as adjusted OR, 95% CI.

*OR relative to the previous category.

†OR relative to the reference category.

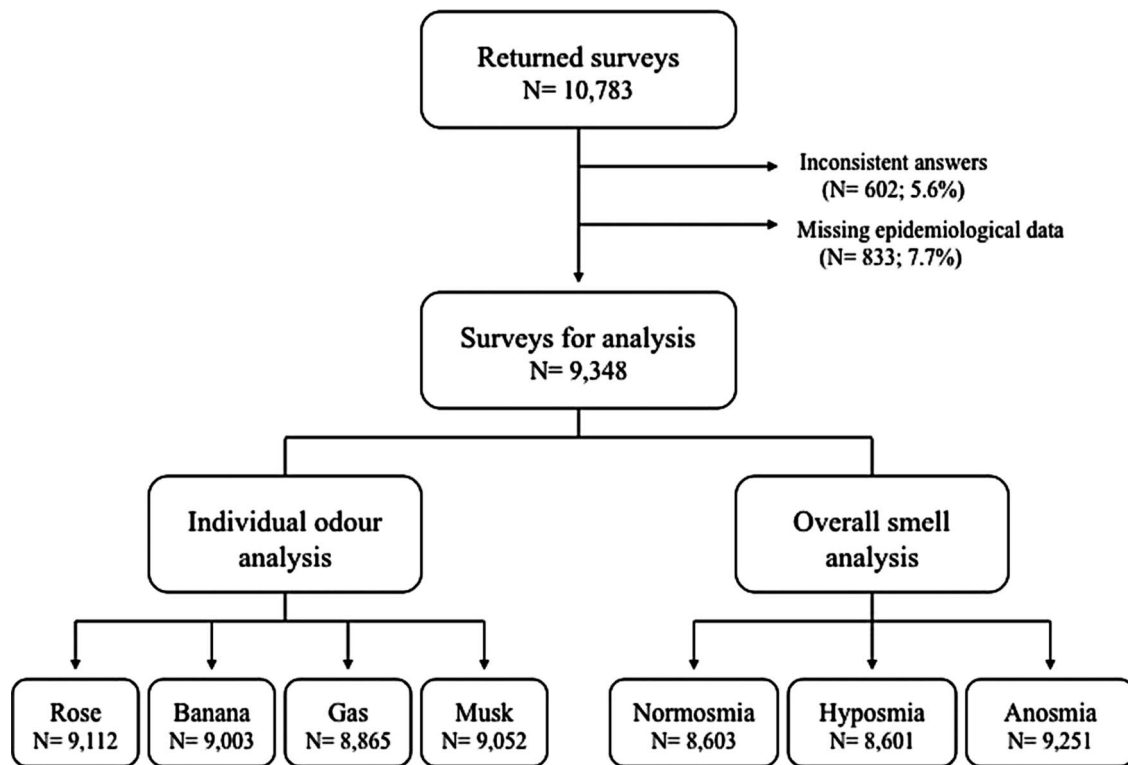


Figure 1 Flow-chart of participants in the OLFACAT (Olfaction in Catalonia) survey.

smell impairment, only 6.9% of the subjects considered having a poor or very poor sense of smell. Second, there was a significant age-related decline in smell detection for both genders. However, cognitive smell (recognition and identification) was increased and/or was maintained up to the sixth decade of life, declining thereafter. Third, besides women having a better self-perception of smell capabilities than men, women also scored better than men in smell detection, recognition and identification, and did so throughout their lifetime. Fourth, pregnancy, but not menstruation was associated with a partial loss (hyposmia) of smell recognition. Fifth, male gender, poor smell self-perception, low educational level and ageing, but not chronic rhinosinusitis, were risk factors related to smell impairment whether in terms of detection, recognition or identification. Subjects with a history of persistent olfactory loss or head trauma were also at higher risk of smell impairment. Sixth, finally and surprisingly, persistent exposure to noxious substances and smoking showed to be protective factors for cognitive smell impairment in either recognition or identification.

Approximately 6.4 million Catalans, 39.5 million Spaniards and 425 million European Union (EU) citizens are aged 15 years or older, according to Catalan, Spanish and European Statistic Institutes. Our survey therefore estimates that 1.2 million adult Catalans, 7.7 million Spaniards and over 82 million EU citizens suffering from olfactory dysfunction, of which 20 000 Catalans, 120 000 Spaniards and 1.5 million EU citizens have a total loss of sense of smell.

Brämerson *et al*⁶ reported an overall prevalence of olfactory impairment of 19.1% in a Swedish population which was very similar to our 19.4%. This prevalence is considerably higher than self-reported loss of smell in the NGSS² (1.4%) and in our own survey where 6.9% of participants were considered to have a poor or very poor sense of smell, suggesting a low sensitivity for the subjective assessment of smell loss. The fact that many people may be unaware of their smell dysfunction, especially the elderly and/or those living alone, implies an increased risk for both nutritional problems¹⁴ and safety in the face of a potential domestic fire or gas leak.¹⁵

In accordance with the OLFACAT survey data, previous studies have indicated that sense of smell detection is impaired with ageing, even in healthy individuals¹⁶ and from the second to the eighth decade of life.¹⁷ Our data also align with the NGSS and other studies in that the age decline in odour perception is universal across subjects regardless of gender odourants, outcome measures, or cultural diversity.²⁻⁶ Smell changes observed across the survey's age span are similar to a previous study reporting a progressive decline in odour.¹⁸ Concerning cognitive smell (memory and identification), we observed an increase in performance in the first decades of life, reaching a plateau during the third through to fifth decades of life and declining thereafter. Larsson *et al*⁴ reported that age was associated with an increased ability to identify banana odour (amylacetate). Our survey, in agreement with the NGSS findings, found not only an increased ability to recognise and identify

Table 4 OLFACAT (Olfaction in Catalonia) epidemiological characteristics and gender comparison: age, women's health, education level, smoking and toxic exposure, subjective description of smell, residential zone, history of head trauma, chronic rhinosinusitis and loss of smell history

| | Male, N (%) | Female, N (%) | Total, N (%) | p Value |
|---|-------------|---------------|--------------|----------|
| Population characteristics* | 3211 (34.3) | 6137 (65.7) | 9348 (100) | |
| Age (years)* | | | | |
| <20 | 127 (3.9) | 315 (5.1) | 442 (4.7) | <0.0001† |
| 20–29 | 241 (7.5) | 878 (14.3) | 1119 (12.0) | |
| 30–39 | 668 (20.8) | 1487 (24.2) | 2155 (23.1) | |
| 40–49 | 861 (26.8) | 1673 (27.3) | 2534 (27.1) | |
| 50–59 | 766 (23.9) | 1181 (19.3) | 1947 (20.8) | |
| 60–69 | 355 (11.1) | 454 (7.4) | 809 (8.6) | |
| >70 | 193 (6.0) | 149 (2.4) | 342 (3.7) | |
| Menstruation* | | 781 (12.7) | | |
| Pregnancy* | | 128 (2.1) | | |
| Educational level* | | | | |
| Elementary school | 7 (0.2) | 26 (0.4) | 33 (0.3) | <0.0001† |
| Secondary school | 508 (15.8) | 978 (15.9) | 1486 (15.9) | |
| High school | 1505 (46.9) | 2568 (41.9) | 4073 (43.6) | |
| University/college | 1191 (37.1) | 2565 (41.8) | 3756 (40.2) | |
| Smoking* | | | | |
| Non-smokers | 1185 (36.9) | 3513 (57.2) | 4698 (50.3) | <0.0001† |
| Ex-smokers | 1231 (38.3) | 1418 (23.1) | 2649 (28.3) | |
| Smoker | 795 (24.8) | 1206 (19.7) | 2001 (21.4) | |
| Subjective description of sense of smell* | | | | |
| Very good | 407 (12.7) | 1576 (25.7) | 1983 (21.2) | <0.0001† |
| Good | 2472 (77.0) | 4243 (69.1) | 6715 (71.9) | |
| Poor | 315 (9.8) | 305 (5.0) | 620 (6.6) | |
| Very poor | 17 (0.5) | 13 (0.2) | 30 (0.3) | |
| Residential zone* | | | | |
| Rural | 57 (1.8) | 109 (1.8) | 166 (1.8) | 0.9535† |
| Semirural | 142 (4.4) | 263 (4.3) | 405 (4.3) | |
| Urban | 3012 (93.8) | 5765 (93.9) | 8777 (93.9) | |
| History of head trauma* | 200 (6.2) | 264 (4.3) | 464 (5.0) | <0.0001† |
| Exposure to noxious substances* | 1090 (33.9) | 1703 (27.7) | 2793 (29.9) | <0.0001† |
| Chronic rhinosinusitis* | 137 (4.3) | 277 (4.5) | 414 (4.4) | 0.5814† |
| Loss of smell history* | | | | |
| Never | 2217 (69.0) | 4289 (69.9) | 6506 (69.6) | 0.0042† |
| ≤1 week | 789 (24.6) | 1555 (25.3) | 2344 (25.1) | |
| >1 week | 205 (6.4) | 293 (4.8) | 498 (5.3) | |

*Number of subjects (percentage).

† χ^2 test.

banana, but rose and gas also, with increase indicated up to the fifth decade of life but decreasing thereafter. Due to the fact that repeated exposure to odorants and olfactory training may increase olfactory identification skills without modifying odour detection,¹⁸ these age-increased abilities for smell identification but not for detection, could be explained by the acquisition of cognitive smell skills through learnt experience.

Among the potential mechanisms proposed for age-related olfactory loss are the replacement of olfactory mucosa with respiratory epithelium caused by disease or pollutant exposure,¹⁹ cribiform plate calcification,²⁰ olfactory bulb atrophy,²¹ decreased number of glomeruli/mitral cells in the olfactory tract²² and/or volume loss in temporal lobe areas.²³

In accordance with other studies,^{2 6 8} our survey found that women performed better in olfactory tasks compared with men of the same age group as well as self-reporting a better perception of smell sense. This gender difference was maintained across the lifespan, and increased considerably after the seventh decade of life. However, other studies have not found gender differences in olfactory sensitivity and identification, although women were slightly better.⁴ We have to note that the rates of correctly identified odours (54.1% by women, 44.3% by men) are lower than those found in the Barcelona Smell Test (BAST)-24 validation,²⁴ in which the present survey is based, and a potential explanation could be that the OLFACAT study was done in the general population, with both healthy and

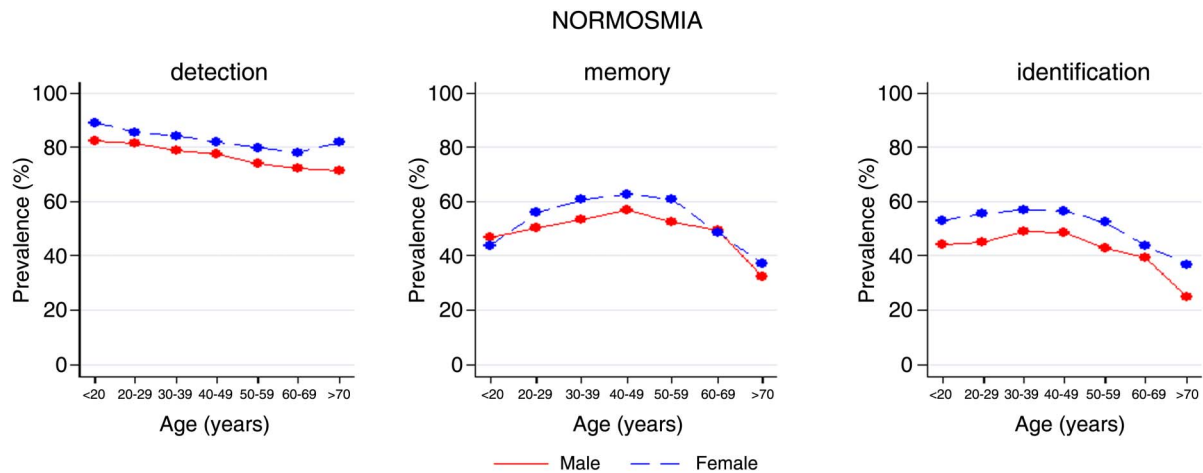


Figure 2 Evolution of normosmia (smell of all four odours) during lifetime. Smell detection showed a progressive decrease during the lifespan, while smell recognition/memory and identification increased up to the fourth decade of life, continued to plateau throughout the fifth and sixth decades, and declined thereafter. For detection, recognition/memory or identification, normosmia was significantly higher ($p < 0.0001$) in women (blue line) than in men (red line).

diseased participants, when in the BAST-24 validation all participants were healthy.

Interestingly, our survey found that pregnancy but not menstruation was associated with a lack of odour recognition/memory. Changes in odour perception during pregnancy have been investigated in small studies and with controversial findings,²⁵ with olfactory dysfunction being more linked to changes in nasal sensitivity than in real smell perception.²⁶ Clearly but not significantly, our survey showed that women had an increased risk for anosmia of smell recognition/memory during pregnancy ($n=125$, $OR=6.94$).

In addition to male gender and ageing, we found that a history of transient olfactory loss for more than 1 week was associated to impairment in odour detection, recognition and identification. Postviral olfactory dysfunction

has been found among the common causes of olfactory disorders of which spontaneous recovery might occur within 2 years.^{21 27}

Moreover, survey participants with a history of head trauma had a higher risk of anosmia in the forced-choice identification task. One of the major causes of smell dysfunction, affecting all ages, is traumatic brain injury, secondary to a partial or total damage of olfactory bulbs and tracts. This can involve frontal and temporal brain poles, as anosmia usually correlated with trauma severity.²⁸

Although severe chronic rhinosinusitis with nasal polyps usually has a negative impact on smell function,¹² our data did not identify chronic rhinosinusitis as being a risk factor for the loss of smell. This controversial finding, also described in other surveys,²⁶ may be due

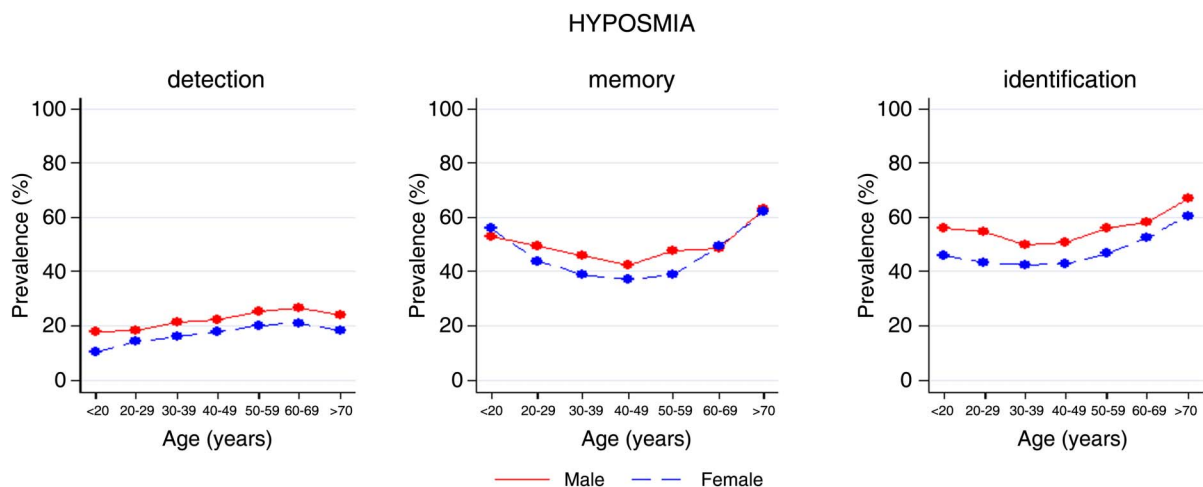


Figure 3 Evolution of hyposmia (smell of one to three odours) during lifetime. For detection, hyposmia showed a progressive increase during the life span, while for recognition/memory and identification hyposmia decreased up to the fourth decade of life, continued to plateau throughout the fifth and sixth decades and increased thereafter. For detection, recognition/memory or identification, hyposmia was significantly lower ($p < 0.0001$) in women (blue line) than in men (red line).

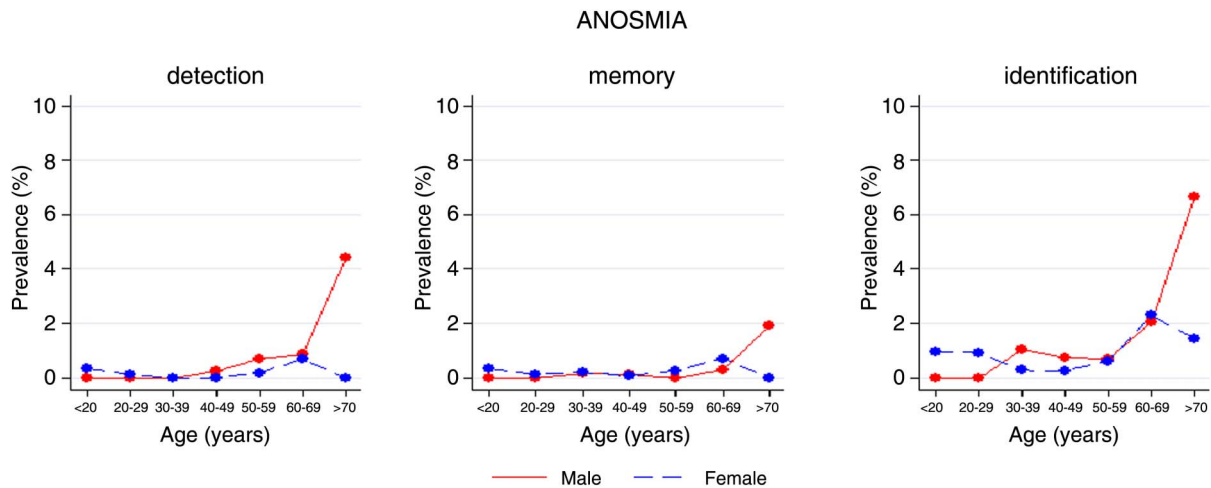


Figure 4 Evolution of anosmia (smell of none of the four odours) during lifetime. Anosmia showed a progressive mild increase during the life span but being more significant after the sixth decade of life. For detection, recognition/memory or identification, anosmia was significantly lower ($p < 0.0001$) in women (blue line) than in men (red line), with a maximal difference after the seventh decade of life.

either to possible mild levels of severity or self-misdiagnosis of the disease among survey participants.

Studies on the impact of smoking on the sense of smell are not conclusive, specially when different smell qualities are considered. Some studies have shown adverse effects on smell detection, identification and intensity for some odours^{8 10 11} whereas others have found no effect on smell detection and discrimination for other odorants.^{9 26 29} In our survey, data showed that smoking might be a mild but significant protective factor for cognitive smell. An explanation for this contradictory finding could be the activation of subtype-selective nicotinic receptors in the olfactory bulb. For instance, in neurodegenerative disorders such as Parkinson Disease (PD) olfactory loss is being considered as a significant early symptom that correlates with the progression of disease.³⁰ In addition to the current evidence for the protective effect of smoking in PD,³¹ recent studies suggest that therapy with nicotine receptor agonists mediate enhancement of olfactory working memory in rats³² and could delay the progress of neurodegeneration in PD.³³ However, further epidemiologic and mechanistic studies need to be done taking into account the different smell qualities (detection, memory and identification) to bring definitive light to the impact of smoking in the sense of smell.

Another interesting finding showed that odour performance was positively related to a level of education superior to primary school. It is known that odour identification and semantic memory proficiency tap the same domain,³⁴ and that educational background is one of the most important predictors of cognitive decline with age, with cognitive deficits occurring earlier and more extensively in people with a low educational level.³⁵ From an olfactory perspective, education and training may help to develop a wider repertoire of cognitive strategies to assist

performance in verbal memory tasks, such as odour identification.³⁶

As with all epidemiological studies, the OLFACAT survey may have some weaknesses. (1) The survey population cannot be considered a random sample since there was no control over who and how the survey was performed or whether participants were preferentially motivated to answer the survey. (2) The survey's data may not be fully representative of the general population since the readership survey (2003) shows that the newspaper's readers belong to a higher socio-cultural class (85.1% middle class) and have a higher educational level (31.1% finished secondary school) than the general Catalan population (65.0% and 25.6%, respectively, 2002 census). (3) Although other studies have not found smell differences among different ethnic groups, the lack of ethnic diversity in our sample (mainly Caucasians) could limit the generalisation to other ethnic groups. (4) Cognitive disturbances in elderly individuals are characterised by impaired smell function but also potentially accounting for unwillingness to participate in the survey. (5) Subjects with smell impairment could have been more/less interested in participating in the survey leading to an over/underestimation of the prevalence of dysfunction. (6) Observations were based on cross-sectional data, making it impossible to disentangle true ageing effects from cohort membership. (7) The survey could have a positive female response bias since almost two-thirds of participants who returned the surveys were women (65.7%).

In agreement with earlier findings in other cultures, the present survey on the general population indicates an age-related deterioration in odour detection, recognition and identification, with a higher prevalence and a more manifest age decline in men than in women. Pregnancy, head trauma and a transient olfactory loss

history are absolute risk factors for olfactory dysfunction while having a higher educational level and smoking may be protective factors for smell. In order to understand the role of smell in human behaviour and determine the potential influence of cognitive, sensorial and environmental factors, there is however an obvious need for well-designed longitudinal population-based studies, which deploy validated smell tests and consider the characteristics of the populations studied.

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Contributors JM is the guarantor of the study, and has contributed with the conception and design of the study, literature search, acquisition of data, analysis and interpretation of data and writing the manuscript. IA and FM have contributed through literature research, interpretation of data and by drafting the manuscript; they approved the final version. LQ has contributed with the study design, acquisition of data, statistical analysis and interpretation of data and drafting the manuscript and approved the final version. JH has contributed with the conception and design of the study, acquisition and interpretation of data and a critical reading of the manuscript and approved the final version. CP, AV and MB have contributed with the study design, interpretation of data, a critical reading of the manuscript and approved the final version. CM has contributed with the conception and design of the study, acquisition of data, analysis and interpretation of data and a critical reading of the manuscript; and approved the final version. All authors had full access to all of the data of the study including statistical reports and tables.

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