

## Barcelona Olfactory Test – 8: validation of a new test on Spanish population during COVID-19 pandemic

Rojas-Lechuga MJ<sup>1,2,3</sup>, Ceballos JC<sup>1,2</sup>, Valls-Mateus M<sup>4</sup>, Mackers P<sup>5</sup>, Izquierdo-Domínguez A<sup>2,6,7</sup>, López-Chacón M<sup>1,2,3</sup>, Langdon C<sup>1,2,3</sup>, Mariño-Sánchez F<sup>8</sup>, Valero J<sup>9</sup>, Mullol J<sup>1,2,3\*</sup>, Alobid I<sup>1,2,3,7\*</sup>

<sup>1</sup>Rhinology Unit & Smell Clinic, Department of Otorhinolaryngology, Hospital Clinic, Universitat de Barcelona, Spain

<sup>2</sup>Clinical and Experimental Respiratory Immunoallergy, IDIBAPS, Barcelona, Spain

<sup>3</sup>CIBER of Respiratory Diseases (CIBERES), Spain

<sup>4</sup>Department of Otorhinolaryngology, Hospital Universitari Son Espases, Mallorca, Spain

<sup>5</sup>Department of Otorhinolaryngology, Hospital del Mar, Barcelona, Spain

<sup>6</sup>Department of Allergology, Consorci Sanitari de Terrassa, Barcelona, Spain

<sup>7</sup>Unidad Alergo Rino, Centro Médico Teknon, Barcelona, Spain

<sup>8</sup>Rhinology and Skull Base Surgery Unit. Otorhinolaryngology Department, Hospital Ramón y Cajal, Madrid, Spain

<sup>9</sup>Departament de Físicoquímica. Facultat de Farmàcia. Universitat de Barcelona, Spain.

\*These authors equally contribute as senior and corresponding authors

### Corresponding Authors:

Isam Alobid

Rhinology and Skull Base Unit  
ENT Department, Hospital Clinic  
C/ Villarroel 170, 08035 Barcelona  
Barcelona, Spain

E-mail: [jmullol@clinic.cat](mailto:jmullol@clinic.cat)

Joaquim Mullol

Rhinology and Skull Base Unit  
ENT Department, Hospital Clinic  
C/ Villarroel 170, 08035 Barcelona  
Barcelona, Spain

E-mail: [jmullol@clinic.cat](mailto:jmullol@clinic.cat)

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## Abstract

*Background:* In daily clinical practice, most smell tests are difficult to implement due to their long duration. The aim of the present study was to develop and validate a short, easy to perform, and reusable smell test to be implemented during COVID-19 pandemic.

*Methods:* 120 healthy adults and 195 patients with self-reported olfactory dysfunction (OD) were included. Barcelona Olfactory Test (BOT-8) was used for detection, memory/recognition, and forced-choice identification. In addition, rose threshold test and VAS was performed. The Smell Diskettes Olfaction test (SDOT) was used for correlation in healthy volunteers, and UPSITTM for patients with OD to establish an anosmia and hyposmia cut-off point. Considering COVID-19 pandemic disposable cotton swabs with odorants were compared with the original test.

*Results:* In healthy population, BOT-8 mean scores for detection was 100%, memory/recognition was 94.5% (SD=1.07), and identification was 89.6% (SD=0.86). In OD patients was 86% (SD=32.8), 73.2% (SD=37.9) and 77.1% (SD=34.2), respectively. BOT-8 demonstrated good test–retest reliability with a 96.7% of observed agreement and a quadratic kappa of 0.84 ( $p<0.001$ ). Strong correlation was observed for BOT-8 with SDOT ( $r=0.67$ ,  $p<0.001$ ) and UPSITTM ( $r=0.86$ ,  $p<0.001$ ). Disposable cotton swabs showed an excellent agreement with a kappa of 0.79 compared to the original test. The cut-off point for anosmia was  $\leq 3$  (AUC=0.83, Se= 0.673, Sp=0.993).

*Conclusions:* BOT-8 offers an efficient and fast method to be used in clinical routine to assess the smell threshold, detection, memory, and identification. Disposable cotton swabs with odorants are a useful and safe method during the COVID-19 pandemic.

**Key words:** Olfaction. Smell test. Smell loss. Anosmia. COVID-19.

## Resumen

*Introducción:* Las olfatometrías son difíciles de implementar en la práctica clínica diaria por su larga duración. El objetivo del presente estudio fue desarrollar y validar una prueba simple, fácil y reutilizable para ser utilizada durante la pandemia de COVID-19.

*Material y Métodos:* Se incluyeron 120 voluntarios sanos  $\geq 18$  años y 195 pacientes con disfunción olfatoria (DO) autoreportada. Se utilizó el Barcelona Olfactory Test (BOT-8) con 8 odorantes para la detección, memoria / reconocimiento e identificación. Además, se hizo una prueba de umbral de rosa (alcohol feniletílico) de 6 diluciones, escala visual analógica (EVA). Se compararon los resultados con una prueba validada Smell Diskettes Olfaction test (SDOT), para definir puntos de corte de hiposmia y anosmia se comparó en pacientes con DO con UPSIT™. Considerando la pandemia de COVID-19, se compararon hisopos de algodón desechables con los odorantes respecto a la prueba original.

*Resultados:* BOT-8 se tarda entre 3 y 7 minutos en realizar. En población sana, la media de detección fue del 100%, memoria 94,5% (DE = 1,07) e identificación 89,6% (DE = 0,86). En pacientes con DO fue de 86% (DE=32.8), 73.2% (DE=37.9) y 77.1% (DE=34.2), respectivamente. BOT-8 demostró buena fiabilidad test-retest con 96,7% de concordancia observada y una kappa cuadrática de 0,84 ( $p < 0,001$ ). Presentó una fuerte correlación con SDOT ( $r=0.673$ ,  $p < 0,001$ ) en población sana y con UPSIT™ en pacientes con DO ( $r=0.86$ ,  $p < 0.001$ ). Los hisopos de algodón desechables mostraron una excelente concordancia (kappa de 0,79) en comparación con la prueba original. El punto de corte para anosmia fue  $\leq 3$  (AUC=0.83, Se= 0.673, Sp=0.993) y de hiposmia  $\leq 6$  (AUC=0.451, Se= 0.088, Sp= 0.814).

*Conclusiones:* BOT-8 ofrece un método eficiente y rápido para ser utilizado en la práctica clínica diaria para evaluar el sentido del olfato mediante la detección, memoria, identificación y umbral. Los hisopos de algodón desechables con odorantes son un método útil y seguro de aplicación durante la pandemia de COVID-19.

**Palabras claves:** Olfato. Olfatometría. Pérdida de olfato. Anosmia. COVID-19.

## Introduction

Olfaction is described as the earliest and most primal sense [1, 2]. Smell identification and discrimination reflect the health of the sinonasal cavity, the cognitive state and the higher cortical centers [3].

Olfactory dysfunction (OD) is common in many disease states. These include sinonasal diseases [4], post-infectious disorders [2], traumatic brain injuries [5,6], and neurodegenerative disorders [7], among others [8,9]. Olfactory function also plays an important role in daily living such as the enjoyment of food, ability to detect spoilage, detection of safety hazards, socialization and overall quality of life [10].

Methods for subjective measuring of OD are an important component of diagnosis as well as monitoring treatment success. Nowadays, one of the most common problems in olfactory tests is the time they take and the difficult applicability in daily practice [11].

Currently, the COVID-19 pandemic has brought to the scientific literature the importance of OD in these patients [12], which is why the need to adapt the current olfactory tests to be safely used for medical personnel and patients, either with single-use and/or self-administered tests [13]. This situation raises considerably the cost of explorations creating the need to seek alternatives more cost-effective such as disposable cotton swabs.

## Aims and objectives

The aim of the present study was to develop and validate a simple, easy-to-perform, and reusable smell test to be implemented in a short period of time (5 to 10 minutes), adaptable and enforceable with the necessary safety measures during the COVID-19 pandemic.

## Subjects and Methods

### *Participants*

Two groups were recruited at Hospital Clínic of Barcelona. The first included healthy adult volunteers aged  $\geq 18$ -years-old with symmetric distribution by sex and in age groups of 10 in 10 years without subjective loss of smell. Patients with upper

respiratory tract infection in the last two weeks, known psychiatric or neurocognitive impairment, pregnancy, sinonasal inflammatory disorders, head trauma, nasal surgery, or any other disease linked to olfactory dysfunction were excluded.

A second group of participants with self-reported OD, aged  $\geq 18$ -years-old was assessed. Inclusion criteria was smell loss visual analogue scale (VAS)  $\geq 30$  millimeters (mm).

All patients provided signed informed consent for the use of their data for scientific purposes. The study was approved by the Ethics Committee of our institution (HCB-2015-0076).

### *Testing procedure*

All the volunteers were tested individually in a noise isolated, well-ventilated room with controlled humidity and temperature (21-23°C). They were tested simultaneously at both nostrils, first for the Barcelona Olfactory Test (BOT-8): smell detection, recognition/memory forced choice identification, and smell threshold with rose (*phenyl-ethyl alcohol*) while measuring the total time of the test (Figure 1A). To compare the results of our smell test with a smell identification test, already validated and standardized, all healthy volunteers were also tested using the Smell Diskettes Olfaction test (SDOT) [14] and all cases with self-reported OD were compared with the Smell Identification Test™ (UPSIT) in order to define hyposmia and anosmia cut-off points.

Along with these two tests, the study population underwent a smell VAS (being 0mm no smell loss and 100mm maximum smell loss), a nasal endoscopy evaluating septal deviation, turbinates hypertrophy, and ruling out the presence of nasal polyps in healthy controls.

A sub-group of 30 healthy adults were tested in two separate sessions with a two-weeks interval to evaluate the BOT-8 test-retest reliability.

Considering the current situation of the SARS-CoV-2 outbreak and the safety limitation to perform multiuse smell tests, a sub-group of 20 healthy adults were tested with disposable cotton swabs with odorants to evaluate the agreement between the swab and the routine smell test (BOT-8), in order to favor single-use

material during the COVID-19 pandemic as the guides recommend [15] (Figure 1 B/C).

#### *Barcelona Olfactory Test (BOT-8)*

BOT-8 is a *supraliminal orthonasal subjective olfactometry*. The different odors were presented in random order using semi-solid-state odorants contained in glass jars and placed about 3 cm below the nostrils for 3-5 seconds, with a latency of 30 seconds between every smell. Eight odorants were selected: Banana, Chocolate, Lemon, Rose, Coffee, Onion, Mint and Vinegar (Table 1). The selection of the odors was made by an expert consultant analysis based on international guidelines and previous validated BAST-24 smell test.

Participants were asked to answer Yes or No to the following questions: 1) do you smell something? (smell detection) 2) do you remember having smelt it before? (smell memory/recognition), and finally 3) which of these four odorants is correct? (smell forced-choice identification).

The score was calculated independently for detection, memory and identification, in absolute value and percentage, being 8/8 (100%) the maximum score.

Detection, identification and threshold are different tools to assess smell. In this test, as in the BAST-24, the recognition/memory item has been added, since we consider that smell has a cultural component and requires prior exposure to the odorant, so when asking if you have ever smelled it, we first know if you have been previously exposed to that odorant. It also tells us about the patient's olfactory memory.

#### *Rose (phenyl-ethyl alcohol) threshold test*

Six geometric dilutions were presented in glass jars placed 3 cm below the nostrils. The lowest dilution was showed first (1/1000) and progressively increased (1/500, 1/100, 1/50, 1/10, and 1/1 corresponding the 15% from the pure essence) until the patient could detect the smell. Inversion of the ladder to lower concentrations was used when the odor was correctly identified in 2 successive

tests, or towards higher concentrations when the odor was not recognized in an assay. The threshold was defined as the mean of the last 2 scale reversals [16].

### *Smell Diskettes Olfaction Test (SDOT)*

Our objective was to validate our test in a healthy population against a screening test capable of identifying normality from abnormality. For this, the SDOT test was used.

SDOT is composed of 8 odorants: coffee, vanilla, peach, smoke, orange, rose, chocolate and vinegar using reusable diskettes as odor applicators. These floppy disks are made of polyester and measure 5 x 6 cm, can be opened to release odors and closed after testing.

The test has a three-forced multiple-choice test, resulting in a score from 0 to 8 correct answers. A score of 6.2 (SD 1.0) for the age group 18-50 years, and a score 6.0 (SD 0.9) for the age group 51-50 is defined as normal.

### The Smell Identification Test™ (UPSIT)

In order to be able to determine our cut-off points for hyposmia and anosmia in the pathological population, the UPSIT™ test was used.

UPSIT™ is an olfactory Identification test of comprehensive 40-item in spanish version for self application. It provides an absolute indication of loss of smell (anosmia; mild, moderate, or severe hyposmia), as well as a relative indication based on percentiles related to age and gender, with a test-retest  $r=0.94$ .

In order to compare it with our test that has 8 odorants, we have reduced the UPSIT™ classification to 3 categories: anosmia, hyposmia (including mild, moderate, and severe categories), and normosmia.

### *Statistical Analyses*

Frequencies, means and standard deviations (SD) were calculated for the demographic and clinical characteristics of the participants. We performed an independent-sample *t*-test to compare means between sexes, and a pearson's correlation was used to analyze smell outcomes correlation to age.

Agreement between BOT-8 and cotton swab was determined using the weighted  $\kappa$  statistic, as described by Cohen [17]. The maximum  $\kappa$  statistic is 1.00, when agreement is perfect, and zero indicates no agreement. We assessed the weighted  $\kappa$  statistic for strength of agreement using guidelines by Fleiss et al [18]. Poor agreement is  $< 0.40$ , good agreement is  $0.40$  to  $0.75$ , and excellent agreement is  $\geq 0.76$ ).

Pearson's correlation was calculated between the BOT-8 items and VAS, UPSIT™, and SDOT scores. ("poor" is less than  $0.3$ , "fair" is  $0.3$  to  $0.5$ , "moderately strong" is  $0.6$  to  $0.8$ , and "very strong" is  $> 0.8$ ) [19].

The Cronbach's  $\alpha$  coefficient was calculated to determine BOT-8's reliability (the Cronbach's  $\alpha$  coefficient should have a minimum value of  $0.7$  for preliminary research) [20]. The *test-retest* reliability was performed using Cohen's weighted  $\kappa$  coefficient for ordinal scales.

The BOT-8 performance was assessed with sensitivity, specificity, positive and negative predictive values. Cut-off point for anosmia was settled in  $\leq 18$  for UPSIT™. A receiver operating characteristic (ROC) curve was calculated for the BOT-8 cut of point.

Data management and statistical analysis were performed by means of SPSS vs. 21 (SPSS Inc., Chicago, IL, USA) with the alpha level set at  $0.05$ .

## Results

### *Demographics*

A total of 120 volunteers whose age mean was 47.7 years (SD=18.3, range=18-89). From them, 57 (47.5%) were women (mean age=47.1, SD=18.1, range=21-89) and 63 (52.5%) were men (mean age=48.2, SD=18.6, range=18-87).

A total of 195 cases with self-reported OD were recruited. The age mean was 51.0 years (SD = 16.8). From them, 107 (54.9%) were women (mean age=49.2, SD=16.6, range= 23-86), and 88 (45.1%) were men (mean age=53.5, SD=16.8, range=18-86).

The demographics and clinical characteristics of the cohort are presented in Table 2.

### *BOT-8*

Among healthy volunteers, the detection score was 100%, memory/recognition score was between 37.5% and 100% (mean= 94.5%, SD=13.4), and the identification score was between 62.5% and 100% (mean= 89.6%, SD=10.8). Women outperformed men for memory/recognition and identification scores. The most identified smell was lemon (n=119, 99.2%), followed by mint (n=118, 98.3%), and the least frequently identified was coffee (n=96, 80%). Rose (*phenyl-ethyl alcohol*) threshold test (TT) score was between 2 (1/10 dilution) and 6 (1/1000 dilution) (mean=4.14, SD=0.80). The BOT-8 examination time was between 3 to 18 minutes (mean= 6.6, SD=2.8). Olfactory test scores in healthy volunteers are summarized in Table 3.

Pearson's correlation between smell identification and age, together with the same analysis by memory scores showed no significant differences ( $r=-0.17$ ,  $p=0.062$  and  $r=-0.10$ ,  $p=0.26$ , respectively) (Figure 2).

In patients with OD, the BOT-8 detection score was 86.0% (SD=32.8), memory/recognition was 73.2% (SD=37.9), and identification score was 77.1% (SD=34.2). Examination mean time was 3.6 minutes (SD=2.4). No differences between sexes in detection, memory or identification was found. Rose TT mean score was 3.1 (SD=1.9). Olfactory test scores in OD patients are summarized in Table 4.

Pearson's correlation between smell detection and age was significant for memory/recognition and identification,  $r= -0.18$  (95%CI -0.31—0.04,  $p=0.013$ ), and  $r= -0.19$  (95%CI= -0.32 - -0.05,  $p=0.008$ ), respectively. No significant correlation was found for detection  $r=-0.07$  (95%CI= -0.22-0.06),  $p=0.28$ .

### *Reliability (test-retest)*

The Cronbach's  $\alpha$  coefficient was 0.837. BOT-8 test-retest reliability demonstrated excellent agreement with a weighted  $\kappa$  statistic of 0.84 and a 96.7% of observed agreement (CI=0.67-0.99,  $P < 0.001$ ) (Figure 3).

### *Agreement between BOT-8 and single-use cotton swabs*

A quadratic kappa correlation between disposable swabs and BOT-8 identification was assessed with a 98.75% of observed agreement and a kappa of 0.79 (95%CI= 0.78 - 0.81).

### *VAS score*

In healthy volunteers, the mean for VAS for smell loss in women was 11.4 (SD=13.6), and 17.4 (SD=15.5) in men. Pearson's correlation was calculated between the BOT-8 total score for identification and memory/recognition and VAS scale with a poor correlation ( $r=-0.086$ ,  $p=0.352$  and  $r=-0.115$ ,  $p=0.210$ , respectively).

In patients with OD, significant Pearson's correlation was found between VAS and BOT-8 detection, identification and memory score. For detection  $r=-0.73$  (95%CI=-0.79- -0.655),  $p<0.001$ , for memory/recognition was  $-0.79$  (95%CI= -0.84- -0.73),  $p<0.001$ , and identification was  $-0.86$  (95%CI= -0.89 - -0.82),  $p<0.001$ .

### *BOT-8 and Olfactory tests' correlation*

In healthy volunteers, SDOT mean was 7.0 (SD=0.1) and BOT-8 identification was 7.17 (SD=0.9) (Table 3). A Pearson's correlation between BOT-8 identification score and SDOT was assessed with a strong correlation,  $r=0.673$ ,  $p<0.001$ .

In patients with OD, UPSIT™ mean was 22.8 (SD=9.3) and BOT-8 identification score was 6.2 (2.7) (Table 4). Pearson's correlation between BOT-8 identification and UPSIT™ was 0.86 (95%CI= 0.82 – 0.89),  $p<0.001$ .

### *Contingency table for anosmia and receiver operator characteristic (ROC) curve*

In OD patients, the UPSIT™ score was categorized as normal or abnormal following the  $\leq 18$  cut-of point for anosmia. Using this cutoff value, a ROC curve was plotted (Figure 4). The area under de curve (AUC) was 0.833 (95%CI= 0.762-0.904). The result with an acceptable sensitivity and excellent specificity for anosmia was  $\leq 3$  for BOT-8 with a sensitivity of 0.673 (95%CI=0.546-0.801), and specificity of

0.993 (95%CI= 0.979-1.000). The positive likelihood ratio and the negative likelihood ratio were 0.972 (95%CI= 0.919-1.000) and 0.893 (95%CI=0.845-0.941), respectively. Contingency table is presented in Table 5.

Same analysis underwent for hyposmia cut of point, with an AUC of 0.451 (95%CI 0.377-0.524). Sensitivity was 0.088 (95%CI= 0.041-0.136) and specificity of 0.814 (95%CI=0.714 – 0.913). The positive likelihood ratio and the negative likelihood ratio were 0.522 (95%CI= 0.318-0.726) and 0.279 (95%CI=0.212-0.346), respectively.

## Discussion

In the present study, we developed and validated an orthonasal supraliminal olfactory test for adults. The advantages of the BOT-8 Smell test are the short time needed for testing (around 3 to 6 minutes), and that is easy-to perform and reuseable. Recently, the paediatric Barcelona Olfactory Test-6 (pBOT-6), including an identification and threshold test, was validated for Spanish children population demonstrating high sensitivity and specificity to detect children with hyposmia [21].

Our results indicate BOT-8 smell test has a 0.837 Cronbach's  $\alpha$  coefficient, demonstrating good internal consistency and an excellent agreement in the test-retest reliability. Also, when compared with the SDOT test, BOT-8 proved a strong correlation, with a correlation coefficient  $r$  of 0.67, and a very strong correlation coefficient  $r$  of 0.86 when compares with UPSIT in patients with OD. BOT-8 identification score  $\leq 3$  for anosmia demonstrated an acceptable sensitivity and an excellent specificity for anosmia (0.673 and 0.993 respectively).

Considering the current pandemic situation produced by SARS-CoV-2, we consider that it is important to validate the use of the test in a safe way for the patient and health professionals. Consequently, the application of cotton swabs with the odorant has shown an excellent agreement, maintaining the safety of the olfactory test in these times of pandemic. We encouraged to use disposable swabs or single-use test as the guides recommend [8]. This modality of cotton swabs is an alternative to evaluate our patients with a lower cost than the single-use tests as well as safer for viral pandemic situations.

According to literature, a recent meta-analysis of Wang et al. concluded that females outperformed males in young adult groups between 18 to 50 years [22, 23] as well as in all the span life in the OLFACAT survey performed in the Catalan population [15]. In our cohort, healthy females scored slightly better, showing better olfactory outcomes when compared with males. No differences were found by sexes in the case of patients with OD.

We found higher identification scores in younger participants compared with the older ones. However, this tendency did not reach statistical significance in healthy volunteers ( $p=0.06$ ), we believed that in a bigger sample size it would be significant. In the cases, we found higher identification and memory/recognition scores in younger patients ( $p=0.013$  and  $p=0.008$ , respectively).

We found a poor correlation between VAS scale and BOT-8 test in healthy volunteers. Similar results were obtained by Zou et al. who interpreted these results on the base that subjective ratings of olfactory function are overshadowed by a multitude of different aspects, such as motivation to seek counseling for olfactory loss or coping with this situation [24]. In contrast, in patients with OD, VAS score had a strong correlation with BOT-8 detection, identification and memory/recognition scores.

The low reliability of self-reported olfactory function such as VAS scale, and the numerous difficulties associated with the actual tests in our daily practice: time-consuming, expensive, and most of them not reusable, reveals the need of developing more cost-effective olfactory dysfunction tests. Some examples, Barcelona smell test 24 (BAST-24) is a validated Spanish cross-cultural smell test [25] which its main disadvantage is the long completion time (20-40 min), University of Pennsylvania Smell Identification Test (UPSIT™) [26] is a worldwide validated single-use test with the great advantage that can be self-administered, but has a high cost per test, Sniffin' sticks [27] another worldwide spread test is reusable, affordable cost; however, it is not disposable or single-use. Although, the transmission of COVID-19 by fomites is currently in controversy [28].

The cost associated with the commercially available test of OD precludes their common use in clinical practice [29]. The need for more cost-effective tools related

to olfaction makes BOT-8 a good option to be considered due to its fast application, reasonable cost per kit, and its reusable with or without disposable cotton swabs one-year lifetime.

This study has some potential limitations. We applied the test exclusively in Spanish population and did not compare the test performance on patients from other cultures, we advise the validation of the test in case to applied in other cultures. Also, the test we chosed for validation in healthy population is not among the most widely used in the current literature and discriminates only between abnormality and normality. Therefore, in order to define cut-off points for hyposmia and anosmia, we have used UPSIT™, which does have cut-off points for hyposmia and anosmia and has been validated in the Spanish population [26].

## **Conclusions**

BOT-8 offers an efficient, fast, and easy-to-perform method which is useful in daily clinical practice to assess the smell threshold, detection, recognition/memory and identification in adults. The test has a strong correlation with validated smell tests, and a high agreement in test-retest reliability. Considering COVID-19 pandemic, disposable cotton swabs showed a high agreement with the original test, being a safe and economic alternative to self-administered single-use smell tests. Therefore, we propose our test as a useful screening tool for olfactory dysfunction in Spanish population and to be used not only by ENT specialists but also by allergists, chest physicians, internists, or general practitioners.

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**Conflicts of Interest**

- Isam Alobid: Consultant for Roche, Novartis, GlaxoSmithKline, Viatrix, Menarini, MSD, Salvat
- Joaquim Mullol: member of national or international advisory boards, received speaker fees, or funding for clinical trials and research projects from ALK, AstraZeneca, Genentech, GlaxoSmithKline, Glenmark, Menarini, Mitsubishi-Tanabe, MSD, Mylan-MEDA Pharma, Novartis, Regeneron Pharmaceuticals, SANOFI-Genzyme, UCB Pharma, and Uriach Group.

The other authors declare that they have no conflicts of interest.

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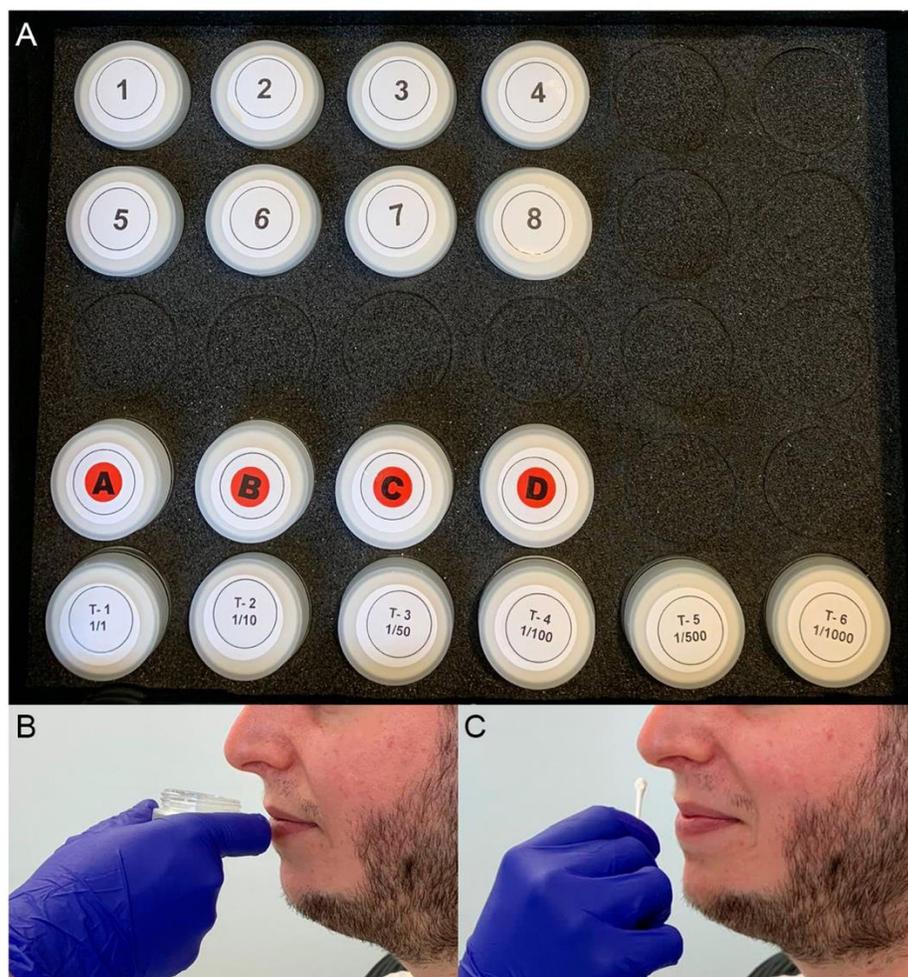
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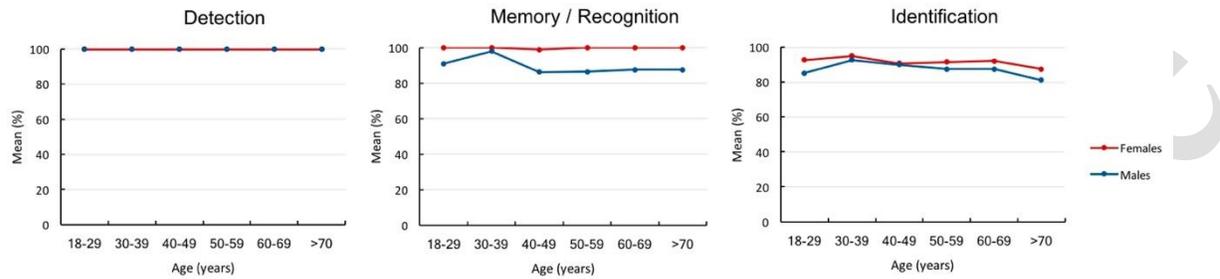
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**FIGURES**

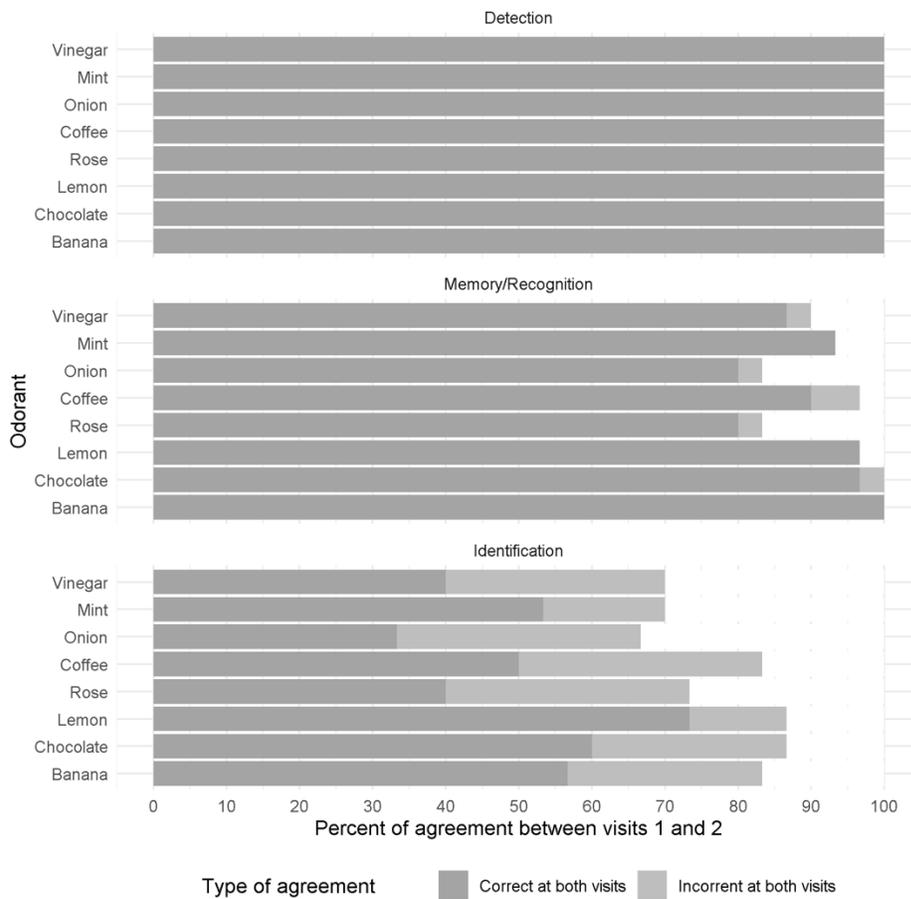
**Figure 1.** Barcelona Olfactory Test (BOT-8). Upper photo (A): the kit includes 8 odorants (1, Banana; 2, Chocolate; 3, Lemon; 4, Rose; 5, Coffee; 6, Onion; 7, Mint; 8, Vinegar), and 6 rose threshold odor concentrations (T1-T6). Lower photo: application of the Barcelona Olfactory Test (BOT-8) with the original glass jar (B) or with disposable cotton swab (C).



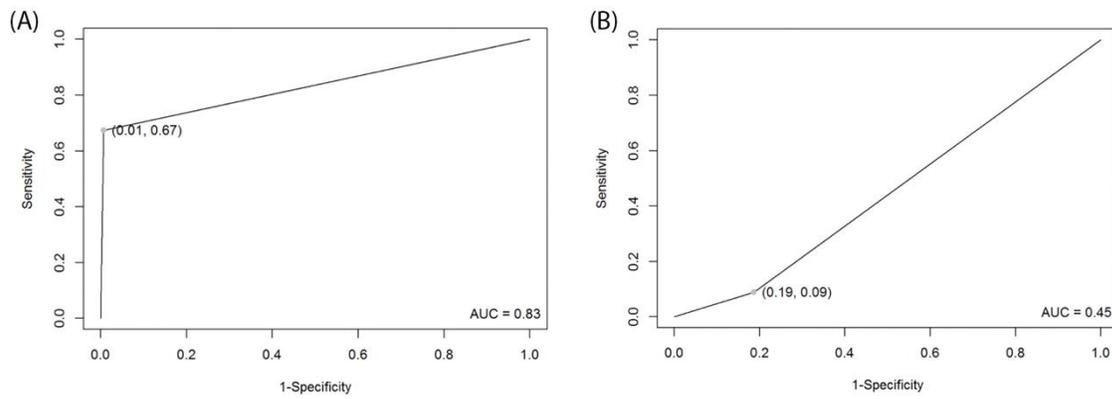
**Figure 2.** Barcelona Olfactory Test-8 (BOT-8). Smell detection, memory/recognition, and identification by gender (females vs. males) and over the life span by age.



**Figure 3.** Percent agreement in test -retest for correct identification of each odorant included in the BOT-8 for detection, memory/recognition, and identification. Shading indicates types of agreement present (correct determination at both visits vs. incorrect determination at both visits)



**Figure 4.** Receiver operator characteristic (ROC) curve for anosmia (A) and hyposmia (B)



## TABLES

**Table 1.** Odorants selected for BOT-8 identification test with their chemical compounds and descriptors used for the forced choice task.

<b>N</b>	<b>Odorant</b>	<b>Chemical compound</b>	<b>% from pure essence</b>	<b>Descriptors</b>
1	Banana	Isoamyl acetate	15	vanilla, sausage, chicken
2	Chocolate	Pyrazines	5	tangerine, pineapple, soap
3	Lemon	Citral	15	cheese, popcorn, fish
4	Rose	Phenethyl alcohol	15	apple, honey, cookies
5	Coffee	furans, pyrazines	5	coconut, mustard, cherry
6	Onion	dipropyl disulfide	10	cinnamon, strawberry, ham
7	Mint	Menthol	15	tomato, peach, gasoline
8	Vinegar	Acetic acid	5	smoke, ammonia, orange

**Table 2.** Demographics and clinical characteristics of the controls (healthy volunteers) and cases (self-reported olfactory dysfunction).

<b>Characteristics</b>	<b>Controls (N=120)</b>	<b>Cases (N=195)</b>
Age, years, mean (SD)	47.7 (18.3)	51.0 (16.8)
Sex, female, N (%)	57 (47.5)	107 (54.9)
Smoking history, N (%)		
. Current/Past	41 (34.2)	32 (16.6)
. Never	79 (65.8)	161 (83.4)
Septal deviation, N (%)	83 (69.2)	64 (34.0)
Inferior turbinate hypertrophy, N (%)	21 (17.5)	47 (25.0)

Abbreviations: SD, standard deviation

**Table 3.** Olfactory test scores in healthy volunteers by gender.

<b>Characteristics</b>	<b>Total (N=120)</b>	<b>Men (N=63)</b>	<b>Women (N=57)</b>	<b><i>p</i>-value</b>
<b>BOT-8</b>				
• Detection, mean (SD)	8.0 (0)	8.0 (0)	8.0 (0)	
• Memory, mean (SD)	7.6 (1.1)	7.2 (1.4)	8.0 (0.1)	<0.001
• Identification, mean (SD)	7.2 (0.9)	7.0 (0.9)	7.4 (0.8)	0.032
Rose threshold test, mean (SD)	4.1 (0.8)	4.2 (0.9)	4.1 (0.7)	0.481
BOT-8 time (min), mean (SD)	6.6 (2.9)	7.1 (3.2)	6.1 (2.3)	0.050
SDOT (Identification), mean (SD)	7.0 (0.1)	7.0 (0.1)	7.1 (0.1)	0.337
VAS 0-100mm for smell loss, mean (SD)	14.5 (14.9)	17.4 (15.5)	11.4 (13.6)	0.043

Abbreviations: SD, standard deviation; min, minutes; mm, millimeters.

\**p*-value for mean difference (men - women).

**Table 4.** Olfactory test scores in patients with self-reported olfactory dysfunction by gender.

<b>Characteristics</b>	<b>Total (N= 195)</b>	<b>Men (N= 88)</b>	<b>Women (N= 107)</b>	<b><i>p</i>-value</b>
<b>BOT-8</b>				
• Detection, mean (SD)	6.9 (2.6)	6.9 (2.6)	6.9 (2.7)	0.920
• Memory, mean (SD)	5.9 (3.0)	6.0 (3.0)	5.8 (3.1)	0.649
• Identification, mean (SD)	6.2 (2.7)	6.0 (2.8)	6.3 (2.7)	0.399
Rose threshold test, mean (SD)	3.1 (1.9)	3.1 (1.8)	3.2 (2.0)	0.774
BOT-8 time (min), mean (SD)	3.6 (2.4)	3.2 (1.4)	3.9 (3.0)	0.061
UPSIT, mean (SD)	22.7 (9.3)	21.5 (9.1)	23.7 (9.3)	0.108
VAS 0-100mm for smell loss, mean (SD)	77.0 (3.1)	76.4 (4.3)	77.6 (4.7)	0.852

Abbreviations: SD, standard deviation; min, minutes; mm, millimeters.

\**p*-value for mean difference (men - women)

**Table 5.** Contingency table in olfactory dysfunction patients

BOT-8	UPSIT		Total (N)	
	Normal	Abnormal		
Unimpaired	142	17	159	NPV= 0.893 [0.845-0.941]
Impaired	1	35	36	PPV= 0.972 [0.919-1.000]
Total (N)	143	52	195	
	Sp = 0.993 [0.979 – 1.000]]	Se = 0.673 [0.546 – 0.801]		

Abbreviations: Se, Sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value; [ ], 95% confidence interval.  
 UPSIT abnormal  $\leq 18$ , BOT-8 Impaired  $\leq 3$