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# Development of Normative Data for the Brazilian Adaptation of the University of Pennsylvania Smell Identification Test

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## Abstract

It is well established that olfactory dysfunction has significant implications for safety, nutrition, and quality of life. The more reliable standardized tests of olfactory function, such as the University of Pennsylvania Smell Identification Test (UPSIT), assess odor identification ability. Unfortunately, cultural factors can influence such tests, as a number of odors are not universally recognized. In this study, a Portuguese language version of the UPSIT was administered to an age- and sex-stratified prospective sample of 1820 Brazilian subjects. Normative data were developed for a subset of 1578 subjects who reported having no difficulties smelling or tasting. Individuals with a history of head trauma or, in the case of those over the age of 64 years, Mini-Mental State Examination Scores <24, were excluded from analysis. As in other populations, the test scores were significantly influenced by age and sex. The median overall difference between the North American and Brazilian UPSIT scores was 2.2 points for men and 0.8 points for women, although subtle age-related differences were also apparent. This research represents that largest clinical study of olfaction ever performed in South America. Correction factors based upon age and sex are provided to allow for direct comparisons of Brazilian test scores to those based upon North American norms.

**Key words:** age, culture, humans, odors, odor identification, olfaction, olfaction disorders/diagnosis, psychophysics, sex, smell, smell physiology, UPSIT

## Introduction

Olfactory impairment is a public health problem. Estimates of prevalence range widely, being as low as 3.7% and as high as 75%, depending upon the age of the subjects, the tests employed, and the populations evaluated (Doty et al. 1984a; Murphy et al. 2002; Brämerson et al. 2004; Shu et al. 2009; Schubert et al. 2012). It is now well established that smell dysfunction accompanies a number of diseases and acquired disorders. For example, such dysfunction is well documented in head trauma, upper respiratory infections, nasal sinus disease, multiple sclerosis, myasthenia gravis, schizophrenia, Alzheimer's disease, Parkinson's disease, and Levy-body dementia, among others (Hawkes and Doty 2009). In some, such as Alzheimer's and Parkinson's disease, the smell loss can precede the classical clinical phenotype by years and is higher in relatives than nonrelatives (Doty et al. 1991; Serby et al. 1996; Doty et al. 1999; Burns 2000; Devanand et al. 2000; Kopala et al. 2001; Ross et al. 2008; Doty 2012). Whatever their cause, compromises in the ability to smell result in poor quality of life, decrements in the flavor of food, and exposure to dangers from fire, leaking natural gas, and spoiled food. In some cases, significant anxiety, depression, and even increased mortality have been reported (Deems et al. 1991; Toller 1999; Miwa et al. 2001; Santos et al. 2004; Hummel and Nordin 2005; Wilson et al. 2011). Despite such facts, physicians, including otolaryngologists, neurologists, psychiatrists, and geriatricians, rarely quantitatively assess this important sensory system, in contrast to the common evaluations made in hearing and vision.

Olfaction is most commonly measured in the clinic using odor identification tests (Fokkens et al. 2007). The majority of such tests employ odorants presented *via* microencapsulated odor strips, pen-like devices, squeeze bottles, or sniff bottles (Doty 2007). The patient is asked to identify the odor, usually by choosing an answer from a short list of written alternatives. A major limitation of such tests, however, is that a number of odors are not universal and, hence, are not familiar to persons in all cultures. Although it would be ideal to have a single universal test, at the present time only tests using a small number of odorants have proved to be universal. Hence, culture-specific adaptations must be applied to most existing tests to allow for the use of common normative data (Ogihara et al. 2011). Unfortunately, attempts at harmonization are often confounded by small and unrepresentative sample sizes that do not reflect the underlying structure of the populations to which their findings are to be generalized.

In this study we administered a recently developed Brazilian version of the University of Pennsylvania Smell Identification Test (UPSIT) to a large number of residents of São Paulo, Brazil. The test population was selected to reasonably represent a cross-section of the society and was conducted in a governmental institution attended by people of diverse races and economic, cultural, and educational backgrounds. Our main objective was to develop normative data useful in Brazil and to provide correction factors that will make it possible to compare test scores from Brazilians to those based upon published North American UPSIT norms. This study follows in the tradition of other studies in expanding accessibility of quantitative clinical olfactory testing outside of North American and Western European countries.

## Materials and methods

### Subjects

The initial study population was comprised of 1820 volunteers 20 years of age and older. Of these volunteers, 242 were excluded from analysis. Forty-four (2.4%) were excluded on the basis of self-reported loss of smell or taste, 57 (3.1%) on the basis of inability to complete the testing, 43 (2.4%) for having a current upper respiratory infection, 58 (3.2%) for having a history of head trauma, and 32 (1.7%) for having a history of a neurological or neuropsychiatric disorder or, in the case of those over the age of 64 years, Mini-Mental State Examination Scores <24. Data from those persons under the age of 55 years who failed to correctly identify at least half of the olfactory test items were also excluded (<1%). The mean (standard deviaton [SD]) years of education of the group was 10.9 years (5.1); 34.3% were of African descent and considered themselves black Brazilians (BB) and 65.7% were white Brazilians (WB). Family monthly incomes were respectively less than US$540 for slightly more than half of the subjects (58.6%). The study was approved by the Ethics Committee for Analysis of Research Projects of the Clinical Board of Clinics Hospital, Faculty of Medicine, University of São Paulo. All subjects provided informed written consent.

With the exception of a group of persons over the age of 64 who were members of churches and activity clubs for the elderly, all of the subjects were sampled from waiting rooms at a state-run matriculation center in Sao Paulo. Visitors to this unique facility represent a cross-section of the São Paulo community at large, since all residents of São Paulo must come to it to obtain national identity cards, driver's licenses, vehicle registration licenses, working permits, and other documents. This complex is visited by over 15 000 persons a day. According to the 20 trained test administrators, less than 1 in 10 persons approached for the study refused to participate, suggesting that the sample was a good reflection of the people of the community at large.

### Test procedures

A team of 20 trained research specialists administered a 37-item questionnaire detailing basic health and demographic information and a Brazilian version of the UPSIT to the subjects. The UPSIT, a 40-item odor-microencapsulated odor identification test described in detail elsewhere (Doty 1995; Mackay-Sim and Doty 2001), is widely used throughout the world and has been translated into more than a dozen languages. From the original English version, a total of 8 odorants were changed in the first phase of validation. For example, the smell of root beer was replaced by the scent of rubber tire. Our initial work showed a good applicability of this initial version for the Brazilian population; however, 11 odorants did not achieve an index of 75% of correct answers (Fornazieri et al. 2010). In an attempt to improve the score of some of the questions, in the second phase of validation we changed some of the foils to emphasize the correct odorant (Fornazieri et al. 2013). The Portuguese language version of the UPSIT employed in this study was essentially the one we previously developed and validated, with the exception that the popcorn odor item was changed to daffodil and several changes were made to the response alternatives for questions 15, 32, and 34 (Table 1). For example, in question 15, the alternative "cola" was changed to "motor oil," and the alternative "coconut" to "baby powder", a trained examiner explained the test procedure to each participant and obtained written informed consent. The examiner then sat individually with the subject to ensure that the odor was released properly and that an answer was clearly marked in the test's answer column. In a few instances where a subject had difficulty self-administering the test, the examiner released the microencapsulated odorant with a pencil tip, presented it to the examinee's nose, and read aloud the response alternatives.

### Statistical analysis

Normative data were developed depicting medians, interquartile ranges, and percentiles for the test scores for each sex and for each of 13 age groups containing 58 or more

**Table 1** Comparative table of the changes among the North American version and the 3 successive Brazilian versions

| Item number | Alternatives | North American version | Brazilian version (edition 1) | Brazilian version (edition 2) | Brazilian version (edition 3) |
|---|---|---|---|---|---|
| 2 | A | Dill pickle | Dill pickle | Dill pickle | Dill pickle |
| | **B** | **Bubble gum** | **Bubble gum** | **Bubble gum** | **Bubble gum** |
| | C | Wintergreen | Walnut | Walnut | Walnut |
| | D | Watermelon | Watermelon | Watermelon | Watermelon |
| 3 | A | Tomato | Tomato | Tomato | Tomato |
| | B | Licorice | Gasoline | Gasoline | Gasoline |
| | C | Strawberry | Strawberry | Strawberry | Strawberry |
| | **D** | **Menthol** | **Menthol** | **Menthol** | **Menthol** |
| 4 | A | Whiskey | Beer | Fish | Fish |
| | B | Honey | Honey | Lemon | Lemon |
| | C | Lime | Vanilla | Garlic | Garlic |
| | **D** | **Cherry** | **Cherry** | **Cherry** | **Cherry** |
| 6 | A | Skunk | Dog | Dog | Dog |
| | **B** | **Mint** | **Mint** | **Mint** | **Mint** |
| | C | Fruit punch | Fish | Fish | Fish |
| | D | Cola | Cola | Cola | Cola |
| 8 | A | Licorice | Baby powder | Baby powder | Baby powder |
| | **B** | **Clove** | **Clove** | **Clove** | **Clove** |
| | C | Chili | Spaghetti | Spaghetti | Spaghetti |
| | D | Banana | Banana | Banana | Banana |
| 10 | A | Skunk | Dog | Dog | Dog |
| | **B** | **Coconut** | **Coconut** | **Coconut** | **Coconut** |
| | C | Cedar | Tomato | Tomato | Tomato |
| | D | Honey | Honey | Honey | Honey |
| 12 | A | Soap | Soap | Soap | Soap |
| | **B** | **Fruit punch** | **Fruit punch** | **Fruit punch** | **Fruit punch** |
| | C | Menthol | Menthol | Menthol | Menthol |
| | D | Pumpkin pie | Garlic | Garlic | Garlic |
| 13 | **A** | **Licorice** | **Baby powder** | **Baby powder** | **Baby powder** |
| | B | Pineapple | Pineapple | Pineapple | Pineapple |
| | C | Cheddar cheese | Cheese | Cheese | Cheese |
| | D | Cherry | Cherry | Cherry | Cherry |
| 14 | A | Paint thinner | Paint thinner | Paint thinner | Paint thinner |
| | B | Cherry | Tire | Tire | Tire |
| | C | Coconut | Coconut | Coconut | Coconut |
| | **D** | **Cheddar cheese** | **Jasmine** | **Jasmine** | **Jasmine** |
| 15 | A | Cola | Cola | Cola | Cola |
| | **B** | **Cinnamon** | **Cinnamon** | **Cinnamon** | **Cinnamon** |
| | C | Pine | Pineapple | Pineapple | Pineapple |
| | D | Coconut | Coconut | Coconut | Baby powder |

**Table 1** *Continued*

| Item number | Alternatives | North American version | Brazilian version (edition 1) | Brazilian version (edition 2) | Brazilian version (edition 3) |
|---|---|---|---|---|---|
| 16 | A | Rose | Rose | Rose | Rose |
| | B | Lemon | Garlic | Garlic | Garlic |
| | C | Peach | Peach | Peach | Peach |
| | **D** | **Gasoline** | **Gasoline** | **Gasoline** | **Gasoline** |
| 17 | **A** | **Strawberry** | **Strawberry** | **Strawberry** | **Strawberry** |
| | B | Dill pickle | Dill pickle | Dill pickle | Dill pickle |
| | C | Chocolate | Chocolate | Chocolate | Chocolate |
| | D | Cedar | Gasoline | Gasoline | Gasoline |
| 18 | **A** | **Cedar** | **Coffee** | **Coffee** | **Coffee** |
| | B | Gasoline | Bubble gum | Bubble gum | Bubble gum |
| | C | Lemon | Garlic | Garlic | Garlic |
| | D | Root beer | Tire | Tire | Clove |
| 19 | A | Lemon | Garlic | Garlic | Garlic |
| | **B** | **Chocolate** | **Chocolate** | **Chocolate** | **Chocolate** |
| | C | Root beer | Tire | Tire | Tire |
| | D | Black pepper | Pepper | Pepper | Pepper |
| 20 | A | Menthol | Menthol | Menthol | Menthol |
| | B | Apple | Baby powder | Baby powder | Baby powder |
| | **C** | **Gingerbread** | **Apple** | **Apple** | **Apple** |
| | D | Cheddar cheese | Cheese | Cheese | Cheese |
| 21 | **A** | **Lilac** | **Flower** | **Perfume** | **Perfume** |
| | B | Chili | Chili | Chili | Chili |
| | C | Coconut | Coconut | Gasoline | Gasoline |
| | D | Whiskey | Beer | Smoke | Smoke |
| 22 | **A** | **Turpentine** | **Popcorn** | **Rubber** | **Flower** |
| | B | Soap | Soap | Pineapple | Gingerbread |
| | C | Skunk | Dog | Pizza | Apple |
| | D | Pepper | Spaghetti | Mint | Strawberry |
| 24 | **A** | **Root beer** | **Tire** | **Tire** | **Tire** |
| | B | Watermelon | Watermelon | Watermelon | Watermelon |
| | C | Banana | Banana | Banana | Banana |
| | D | Smoke | Smoke | Gingerbread | Gingerbread |
| 25 | A | Pineapple | Pineapple | Pineapple | Pineapple |
| | **B** | **Dill pickle** | **Dill pickle** | **Dill pickle** | **Dill pickle** |
| | C | Root beer | Tire | Watermelon | Watermelon |
| | D | Pepper | Pepper | Flower | Flower |
| 27 | A | Musk | Cola | Cola | Cola |
| | B | Garlic | Garlic | Garlic | Garlic |
| | C | Turpentine | Paint thinner | Paint thinner | Paint thinner |

**Table 1** *Continued*

| Item number | Alternatives | North American version | Brazilian version (edition 1) | Brazilian version (edition 2) | Brazilian version (edition 3) |
|---|---|---|---|---|---|
| | **D** | **Lime** | **Raspberry** | **Raspberry** | **Raspberry** |
| 28 | A | Cheddar cheese | Cheese | Cheese | Cheese |
| | **B** | **Orange** | **Orange** | **Orange** | **Orange** |
| | C | Bubble gum | Spaghetti | Spaghetti | Spaghetti |
| | D | Turpentine | Paint thinner | Paint thinner | Paint thinner |
| 29 | A | Lime | Raspberry | Raspberry | Raspberry |
| | **B** | **Mint** | **Walnut** | **Walnut** | **Walnut** |
| | C | Pumpkin pie | Fish | Fish | Fish |
| | D | Leather | Bubble gum | Bubble gum | Bubble gum |
| 30 | A | Pepper | Beer | Beer | Beer |
| | B | Menthol | Menthol | Menthol | Menthol |
| | C | Orange | Orange | Orange | Orange |
| | **D** | **Watermelon** | **Watermelon** | **Watermelon** | **Watermelon** |
| 32 | A | Mint | Mint | Gingerbread | Baby powder |
| | B | Gingerbread | Apple | Apple | Apple |
| | **C** | **Grass** | **Grass** | **Grass** | **Grass** |
| | D | Strawberry | Strawberry | Strawberry | Strawberry |
| 33 | A | Dill pickle | Dill pickle | Dill pickle | Dill pickle |
| | B | Grass | Grass | Grass | Grass |
| | **C** | **Smoke** | **Smoke** | **Smoke** | **Smoke** |
| | D | Peach | Peach | Peach | Peach |
| 34 | **A** | **Pine** | **Wood** | **Wood** | **Wood** |
| | B | Smoke | Smoke | Baby powder | Leather |
| | C | Lilac | Flower | Bubble gum | Cheese |
| | D | Orange | Orange | Grape | Tire |
| 36 | A | Motor oil | Motor oil | Motor oil | Motor oil |
| | B | Pumpkin pie | Vanilla | Vanilla | Vanilla |
| | C | Rose | Rose | Rose | Rose |
| | **D** | **Lemon** | **Garlic** | **Garlic** | **Garlic** |
| 37 | **A** | **Soap** | **Soap** | **Soap** | **Soap** |
| | B | Black pepper | Pepper | Pepper | Pepper |
| | C | Licorice | Baby powder | Orange | Orange |
| | D | Peanut | Peanut | Peanut | Peanut |
| 38 | A | Orange | Orange | Orange | Orange |
| | B | Musk | Perfume | Perfume | Perfume |
| | C | Cola | Cola | Cola | Cola |
| | **D** | **Natural gas** | **Natural gas** | **Natural gas** | **Natural gas** |
| 39 | A | Lime | Vanilla | Vanilla | Vanilla |
| | **B** | **Rose** | **Rose** | **Rose** | **Rose** |

**Table 1** *Continued*

| Item number | Alternatives | North American version | Brazilian version (edition 1) | Brazilian version (edition 2) | Brazilian version (edition 3) |
|---|---|---|---|---|---|
| | C | Mint | Mint | Mint | Mint |
| | D | Bubble gum | Bubble gum | Bubble gum | Bubble gum |
| 40 | **A** | **Peanut** | **Peanut** | **Peanut** | **Peanut** |
| | B | Lemon | Garlic | Garlic | Garlic |
| | C | Apple | Apple | Apple | Apple |
| | D | Root beer | Tire | Tire | Tire |

Alternatives in bold are the correct answers.

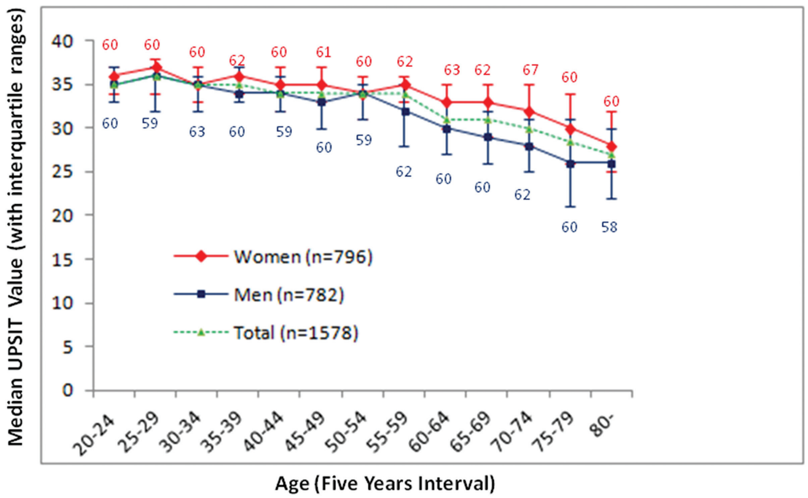


**Figure 1** Relation between UPSIT scores, age, and gender. Number by data points indicate sample sizes.

individuals: 20–24, 25–30, 31–34, 35–40, 41–44, 45–50, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, and ≥80 years. We then established a correction factor to equate the test scores to those of published North American norms. This was done, separately for each sex, by obtaining averages of the test scores for the Brazilian data within each age group and then calculating the difference between these scores and the corresponding scores of published UPSIT normative data (Doty 1995). As with the original development of the UPSIT (Doty et al. 1984b), we also evaluated the relative influences of age, sex, education, and ethnic background on the test scores. Correlations were done using Spearman test. The Wilcoxon-Mann-Whitney test was used to comparisons of UPSIT scores among races and income classes.

## Results

As in other populations, the test scores were significantly influenced by age and sex (Figure 1). The normative data for males and females are presented in Figures 2 and 3, respectively. The bold lines indicate the 25th, 50th, and 75th percentiles. The use of these figures are straightforward and the norms reflect the differences between men and women. For example, a 73-year-old man who scores 35 on the UPSIT falls at the 93rd percentile of men of his same age, that is, 93% of men score equal or below this value (Figure 2). In contrast, a 73-year-old woman who scores 35 falls at the 80th percentile for women of her age (Figure 3). This lower percentile reflects that fact that women in this age category outperform their male counterparts. To fall at the 93rd percentile of her peer group, a 73-year-old Brazilian woman would need to obtain an UPSIT score of ~37. Ethnicity and familial income were also related to the test scores, with those of the WB subjects being slightly higher than those of the BB subjects (respective mean [SD] scores = WB 32.3 [5.3] and 31.7 [5.3]; $P = 0.007$). Subjects whose family income was less than US$540 a month had lower test scores than those from families that made more than this amount (respective mean [SD] scores = 31.6 [5.3] and 33.0 [5.0]; $P < 0.0001$). A moderate positive correlation was found between years of schooling and the UPSIT scores ($r = 0.34$, $P < 0.0001$).

In general, the test scores of the Brazilians were slightly lower than those published for the North American norms (Doty 1995). This phenomenon was relatively

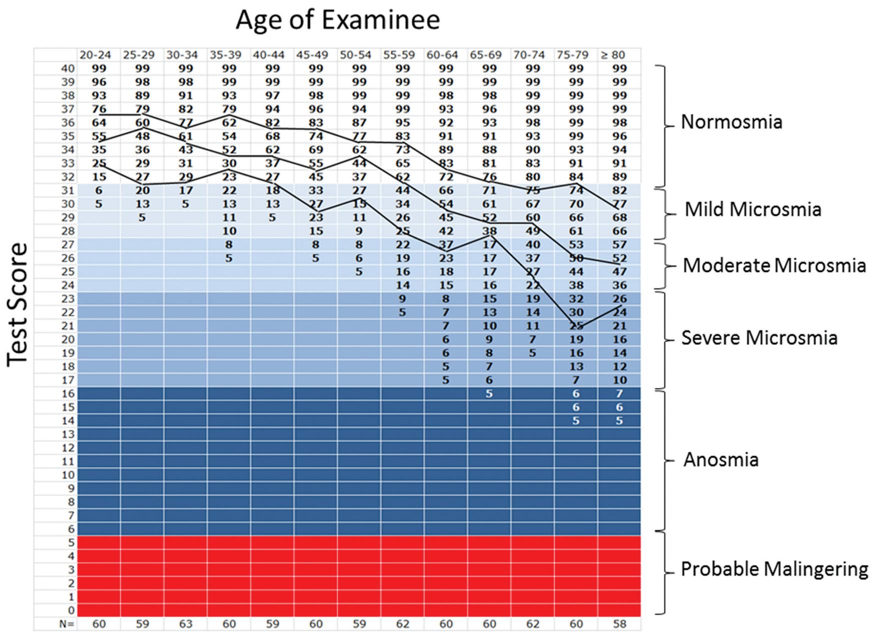


**Figure 2** Male norms: percentile values (bold lines: 25th, 50th, and 75th percentiles).

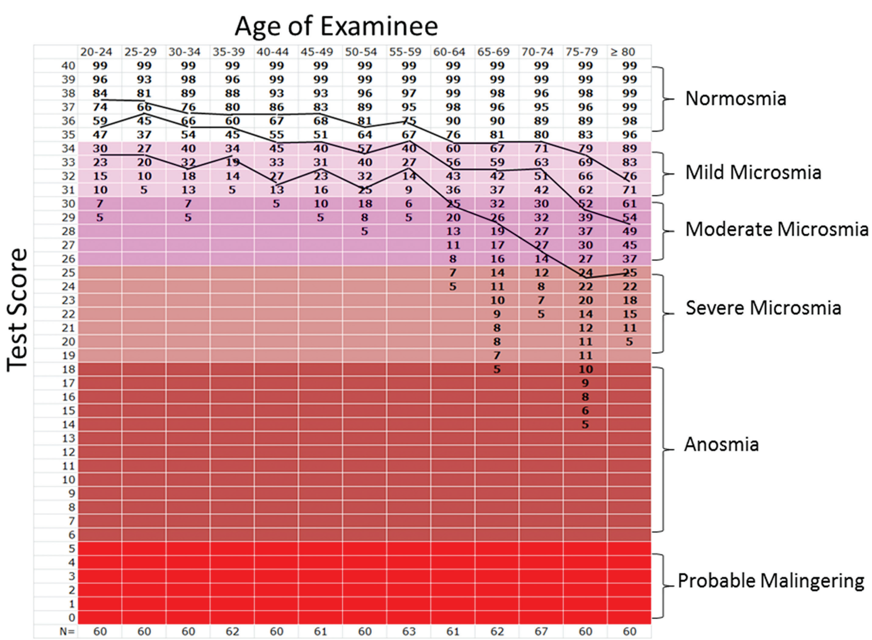


**Figure 3** Female norms: percentile values (bold lines: 25th, 50th, and 75th percentiles).

uniform across all age categories for each sex. Thus, the mean overall difference was 2.2 UPSIT points in men and 0.8 UPSIT points in women. To provide more refined adjustments for comparisons to data based upon North American norms, we calculated the sex-specific correction factors for 3 different age groups. That for men between 20 and 39 years was 1.5, that for men between 40 and 59 years was 2.2, and that for men older than 59 years was 2.6. The respective correction factors for women were 0.5, 1.5, and 0.4.

## Discussion

This study is the largest clinical study of olfaction performed outside of North America and Europe to date. Normative data were developed for an improved culture-specific version of the 40-item UPSIT for use in Brazil. The sampling algorithm was designed to ensure reasonable representation of a cross-section of the population of São Paulo. Although the obtained test scores were slightly below those of North American norms (Doty 1995), the pattern of change over the age categories was strikingly similar. Correction factors were computed to allow for a direct comparison of Brazilian test scores to test scores of other studies that are based upon North American norms. As with earlier work, our data clearly document the changes that occur across later stages of life in both men and women. As can be seen in Figures 2 and 3, smell function decreases significantly in later years, with the decrease occurring earlier in men than in women. As reviewed elsewhere (Doty and Kamath 2014), multiple factors contribute to the age-related loss in the general population, including altered nasal engorgement (Frye and Doty 1992), increased propensity for nasal disease (Settipane 1996; Cho et al. 2012), cumulative damage to the olfactory epithelium from viral and other environmental insults (Loo et al. 1996), decrements in mucosal metabolizing enzymes (Krishna et al. 1995), ossification of cribriform plate foramina (Kalmey et al. 1998), loss of selectivity of receptor cells to odorants (Rawson et al. 1998), changes in neurotransmitter and neuromodulator systems (Volkow et al. 2000), and neuronal expression of aberrant proteins associated with neurodegenerative disease (Attems et al. 2014). Although it is likely that the differences in test scores between the Brazilian and North American populations mainly reflect cultural factors, other factors cannot be ruled out, including the effects of airborne pollutants. São Paulo is a city of more than 12 million people and it has been shown that high levels of urban air pollution can adversely affect performance on the UPSIT (Calderón-Garcidueñas et al. 2010; Altman et al. 2011).

The present work confirms the findings of earlier studies that a large difference exists between men and women in their ability to identify odors (Cain 1982; Doty et al. 1985; Platek et al. 2001; Choudhury et al. 2003). Although this study examined only subjects 20 or more years of age, this phenomenon is known to occur at earlier ages, indeed even before puberty, conceivably reflecting prenatal organizational effects of hormones on the central nervous system (Doty and Cameron 2009).

Although the present study provides data that allow for direct assessment of the relative function of Brazilian subjects, it also provides information that makes it possible to compare test results from such subjects to those of North Americans. It is remarkable that the degree of correction needed across different age groups is relatively small and quite similar, ranging from 0.5 UPSIT points in younger women to 2.5 points for men 60 years of age or older. Similarly small correction factors have been employed in Taiwan and Australia to allow for the use of North American norms (Mackay-Sim and Doty 2001; Jiang et al. 2010). Such correction factors make it possible to compare the results among subjects from different cultures on a common normative metric. Although multiple factors may contribute to the differences in test results among different cultures, familiarity with test items appears to be a significant contributor. It should be noted that 8 of the test items included in the UPSIT employed in this study, namely, pizza, motor oil, apple, cucumber, walnut, paint thinner, grass, and rose (8 item) were identified by less than 75% of the study group.

### Conclusion

The present research provides normative data for assessing olfactory function of members of the Brazilian population. Although the subjects came from the city of São Paulo, it is quite likely that the findings based on this group can be generalized to larger populations, particularly in light of the similarities of the normative data to those obtained from North Americans. The sample we assessed represented a range of ages, varying degrees of education and income, and diverse racial populations. Interestingly, the sample included a number of persons who had moved to São Paulo from other states within Brazil; indeed, persons whose origins were from 22 of the 26 Brazilian states were represented in our sample.

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## Conflict of Interest statement

R.L.D. is president and major shareholder of Sensonics, Inc., the manufacturer of the commercial version of UPSIT.

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