Applying a new version of the Brazilian-Portuguese UPSIT smell test in Brazil

Laura Silveira-Moriyama[1], Adriana M.S. Azevedo[2], Ronald Ranvaud[2], Egberto R. Barbosa[3], Richard L. Doty[4], Andrew J. Lees[1]

ABSTRACT

Standardized olfactory tests are now available to quantitatively assess disorders of olfaction. A Brazilian-Portuguese version of the University of Pennsylvania Smell Identification Test (UPSIT) is currently being developed specifically for the Brazilian population. The most recent Brazilian-Portuguese version of the UPSIT (UPSIT-Br2) was administered to 88 Brazilian subjects who had no history of neurological or otorhinolaryngological disease. UPSIT-Br2 scores decreased with age, were lower in men than in women, and were lower in subjects with lower income. The degree to which the poorer performance of subjects with lower socio-economic status reflects lack of familiarity with test items is not known. Although this version of the UPSIT provides a sensitive and useful test of smell function for the Brazilian population, a revision of some test items is needed to achieve comparable norms to those found using the North American UPSIT in the United States.

Key words: olfaction, odor, smell identification, olfactory test, smell test, UPSIT, Brazil, Portuguese, Brazilian, income.

Aplicando uma nova versão brasileira do UPSIT no Brasil

RESUMO

Testes padronizados já estão disponíveis para testagem do olfato e uma versão em Português esta sendo desenvolvida para o University of Pennsylvania Smell Identification Test (UPSIT), especificamente para a população brasileira. A versão mais recente deste teste (chamada UPSIT-Br2) foi aplicada a 88 sujeitos brasileiros que não tinham história de qualquer problema neurológico ou otorrinolaringológico. Compatível com dados prévios da literatura, a performance no UPSIT-Br2 decaiu com a idade e foi inferior no genero masculino. Os resultados foram mais baixos em participantes de menor nível sócio-econômico e a relação deste achado com a falta de familiaridade para com os itens do teste não é conhecida. Apesar desta versão do UPSIT poder ser útil para o teste da função olfativa da população brasileira, a revisão de alguns itens se faz necessária para alcançar valores comparáveis aos dados normativos norte-americanos.

Palavras-chave: olfato, olfação, teste de olfato, UPSIT, Brasil, Português, fatores socio-econômicos.

Correspondence
Andrew Lees
Reta Lila Weston Institute
of Neurological Studies
UCL Institute of Neurology
1 Wakefield St, London, WC1N 1PJ
United Kingdom
E-mail: a.lees@ion.ucl.ac.uk

Support / Conflicts of interest
Prof Richard L Doty is president and major shareholder of Sensonics, Inc., the manufacturer of the UPSIT. This research was funded by the Reta Lila Weston Trust for Medical Research and Dr Silveira-Moriyama is a beneficiary of a Reta Lila Weston fellowship.

Received 20 October 2009
Received in final form 4 March 2010
Accepted 11 March 2010

A normal sense of smell is critical for safety, nutritional status, and quality of life. While the importance of olfaction is understood by the food and cosmetic industry, it is often neglected by clinicians as an important cause of morbidity and is seldom assessed in clinical practice. This is due, in part, to the fact that self-reported olfaction is unreliable. A recent study[1] compared the prevalence of olfactory im-

[1]Reta Lila Weston Institute of Neurological Studies and Queen Square Brain Bank for Neurological Diseases, UCL Institute of Neurology, London, UK; [2]Department of Physiology and Biophysics, Institute of Biomedical Sciences, University of São Paulo, São Paulo SP, Brazil; [3]Neurology Department, São Paulo School of Medicine, São Paulo SP, Brazil; [4]Smell & Taste Center, University of Pennsylvania School of Medicine, Philadelphia, USA.

pairment in 2491 adults aged 53 to 97 by self-report and an 8-item smell test and found that less than half the hyposmic subjects reported smell difficulties. The accuracy of self-reported olfaction decreased with age and in subjects older than 80 less than a fifth of hyposmic subjects reported dysfunction. A similar phenomenon has been observed for patients with smell loss secondary to Alzheimer's disease[2] and sporadic Parkinson's disease (PD)[3]. Unfortunately, most validated smell identification tests are not cross-cultural, and those that are currently available commercially have been developed on study of populations from the United States of America, Europe and Asia.

The most widely used olfactory test is the 40 item University of Pennsylvania Smell Identification Test (UPSIT)[4]. This test is comprised of four "scratch-and-sniff" booklets that can be either self-administered or be applied by a care giver, nurse practitioner, or physician. The UPSIT has been used in research and clinical settings and has proven to be of value in diagnosing smell loss due to neurological disease as well as primary otorhinolaryngological conditions such as chronic sinusitis. It has also been used to aid the differential diagnosis of parkinsonism[5] and dementia[6]. A standardized translation of the UPSIT has been previously applied in Brazil, where it was proven to be able to differentiate PD and control subjects with specificity 83.5% and sensitivity 82.1%; nevertheless, some test items were not well identified by the Brazilian subjects with normal smell function[7].

A newer Brazilian-Portuguese version of the UPSIT, termed the UPSIT-Br2, has been developed in which items and response options thought to be unsuited to Brazilians were replaced with items and options believed to be more familiar to Brazilians. We administered this new version to 88 Brazilians without a previous history of head trauma or neurologic, psychiatric or otorhinolaryngological diseases in order to evaluate its efficacy, investigate demographic factors that influence test performance, and provide provisional normative data for its use in Brazil.

METHOD

Subjects

The subjects were recruited from the staff, visitors and patients attending general medical and surgical departments of the General Hospital of the University of São Paulo Medical School, São Paulo, Brazil. The primary inclusion criterion was that the subject must be between 20 and 90 years of age. Exclusion criteria included any history or evidence, upon a cursory physical examination, of neurological, psychiatric (except depression or anxiety), or otorhinolaryngological disease. Subjects were also excluded if they failed to score 26 or more on the Brazilian-Portuguese validated version of the Mini Mental State Examination[8]. Of the 100 subjects who were recruited, 12 failed to score more than 25 in the MMSE or to finish the test and were excluded. Informed consent was obtained from all subjects according to approved ethical protocols from the local research ethics committee.

The final study group was comprised of 88 subjects; 45 (51%) were women and 43 (49%) were men. Their mean age was 54.7 years (range 24-86 years, SD 17.1 years). Eleven subjects (12.5%) had a history of current smoking, whereas 16 (18.2%) had previously smoked but had stopped. The mean number of cigarette packs × years was 7.45 (range 0 to 108.0, SD 19.1). The mean number of years of schooling was 11.25 years (range 1 to 17 years, SD 5.6 years), and the mean MMSE score was 29.08 (range 26 to 30, SD 1.2). Regarding monthly income, 26 (29%) of subjects received R$ 410 (US$ 230) or less per month, 35 (40%) received between R$ 410 and R$ 1640 (US$ 230-920), 14 (16%) received between R$ 1640 and R$ 4100 (US$ 920-2300), and 13 (15%) received more than R$ 4100 per month. Only 4 subjects complained of difficulties smelling, and only one reported difficulties tasting. Twenty-five subjects reported an associated medical condition (15 had high blood pressure, 4 had diabetes, 3 thyroid problems, 3 osteoporosis, 3 osteoarthritis, 2 high cholesterol under treatment, 1 asthma, 1 chronic kidney disease, 1 hepatic steatosis, 1 chronic back pain) and 21 reported regularly using any type of prescription medication (mostly anti-hypertensive drugs).

Smell testing

The UPSIT-Br2 was administered with the help of an examiner who explained how the test worked. The examiner read a standard explanatory script and used an example card to demonstrate how to scratch, sniff and mark the correct option. The test was subsequently self-administered by the subject if he or she was deemed by the examiner as able to understand and fully cooperate. In other cases, the test was performed with the help of the examiner who scratched the test, read the options aloud, and marked the subject's responses on the answer page.

Statistical analysis

Descriptive statistics were initially obtained. To evaluate the factors that affected the UPSIT-Br2 test scores in this population, multiple linear regression was performed using the UPSIT-Br2 as the outcome variable and the covariates of age, gender, current history of smoking, previous history of smoking, cigarettes × years of smoking, MMSE score, years of schooling and personal income in an average month. Personal income in an average month was quantified as an ordinal variable with four different levels: ≤US$ 230, US$ 230-920, US$ 920-2300, >US$

2300. Assumptions for the regression analyses were confirmed by analysis of residuals. A significance level of 0.05 was used throughout, except where otherwise stated.

In light of evidence that personal income was associated with smell test scores, we performed additional multiple linear regression analyses to better defined the influence of income group. In these analyses, we used the UPSIT-Br2 as the dependent variable and the covariates of age, gender, and three dummy variables (to compare the four different income groups between themselves). In each regression we compared one of the groups against the other three groups. To compensate for multiple comparisons we used a more stringent significance level of 1% for these analyses.

We then lumped together the groups that did not differ significantly in their performance in the UPSIT-Br2 creating two major income groups, and performed Chi-square tests to compare the proportion of subjects in each of these two groups who correctly identified each of the UPSIT-Br2 items to see if particular items were more influenced by socio-economic differences than others. A modified UPSIT-Br2 score was calculated excluding the items which were more identifiable for higher income subjects than lower income subjects and a multiple linear regression analysis was performed with this score as the outcome variable and age, gender, current history of smoking, previous history of smoking, cigarettes × years of smoking, MMSE score, years of schooling and personal income in an average month as covariates.

Because in Brazil MMSE is known to be affected by schooling and schooling is known to be affected by income, we performed Pearson correlation coefficients among the variables of age, income, schooling, and MMSE scores. We also performed t-tests to compare schooling and MMSE between the two gender groups, and used χ^2-tests to compare the income between the genders.

RESULTS

The first multiple linear regression using the UPSIT-Br2 as the outcome variable showed that age (p=0.005, 95%CI for β= –0.14 to -0.02), gender (p=0.01, 95%CI for β= –3.27 to –0.40, female as reference group) and personal income (p=0.004, 95%CI for β=0.46 to 2.41) were independent predictors of the UPSIT scores, but not current or previous history of smoking (p=0.6 and 0.7), total number of cigarette packs × years (p>0.9), years of schooling (p=0.9) or the MMSE score (p=0.6). Figure displays the scatter plot of age against the UPSIT-Br2 score in males and females.

Subsequent analyses showed that when adjusting for age and gender, the UPSIT-Br2 scores of those who received more than US$ 2300 differed significantly from the UPSIT-Br2 scores of those who received less than

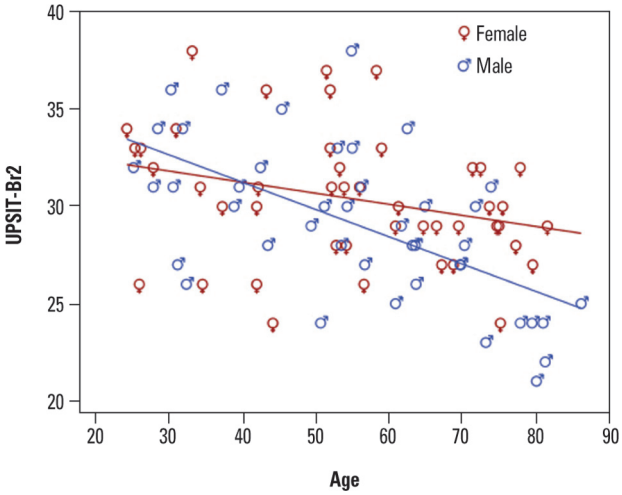

Figure. Scatter plot of UPSIT-Br2 scores according to age in males and females.

US$ 230 (p<0.001) and those who received between US$ 230 and US$ 920 (p=0.003), but not from those who received between US$ 920 and US$ 2300 (p=0.03). There was no significant difference between those who received between US$ 920 and 2300 and either of the other two groups (p>0.1 for both comparisons), or between those receiving less than US$ 230 and those who received between US$ 230 and 920 (p=0.1).

We combined the two higher and two lower income group and compared the proportion of subjects who correctly identified each item in the lower (less than US$ 920) and higher (US$ 920 or more) income groups (Table).

Twenty-seven of the 40 items were highly identifiable (more than 75% subjects identified them correctly) by subjects in the higher income group, while only 21 were highly identifiable in the lower income group. A modified score of the UPSIT-Br2, excluding the three items that were more identifiable to higher income subjects (items gasoline, ruber tire and walnut) was used as outcome variable in a multiple linear regression that showed again that age (p=0.001), gender (p=0.006) and personal income (p=0.004) were independent predictors of the UPSIT scores.

Some of the variables in the first multiple linear regression were intercorrelated. Age correlated negatively with schooling (r= –0.64, p<0.001) and with MMSE score (r= –0.55, p<0.001), but not with income (r= –0.20, p=0.057), while income correlated positively with schooling (r=0.66, p<0.001) and MMSE score (r=0.52, p<0.001). Mean number of years of schooling was higher in the higher income group (mean and standard error of difference=8.0 and 0.7, p<0.001) as well as mean MMSE score (mean and standard error of difference=1.2 and 0.2, p<0.001). A t-test revealed no difference in age between males and fe-

Table. Percentage of subjects who correctly identified each item in the different income groups.

Item	Less than US$ 920	US$ 920 or more	Difference between the two groups	χ^2 p–value
Pizza	73.8%	77.8%	4%	0.8
Bubble gum	90.2%	96.3%	6.1%	0.4
Menthol	85.2%	92.6%	7.3%	0.5
Cherry	60.7%	74.1%	13.4%	0.3
Motor oil	44.3%	63%	18.7%	0.2
Mint	98.4%	96.3%	–2.1%	0.5
Banana	83.6%	96.3%	12.7%	0.2
Clove	90.2%	100%	9.8%	0.2
Leather	90.2%	88.9%	–1.3%	>0.9
Coconut	41%	59.3%	18.3%	0.2
Onion	96.7%	96.3%	–0.4%	>0.9
Fruit punch	82%	81.5%	–0.5%	>0.9
Baby-powder	100%	100%	0%	>0.9
Jasmine	88.5%	88.9%	0.4%	>0.9
Cinnamon	88.5%	96.3%	7.8%	0.4
Gasoline	59%	88.9%	29.9%	0.006*
Strawberry	83.6%	77.8%	–5.8%	0.6
Coffee	67.2%	74.1%	6.9%	0.6
Chocolate	59%	40.7%	–18.3%	0.2
Apple	63.9%	70.4%	6.4%	0.6
Lilac (“Flower”)	50.8%	66.7%	15.8%	0.2
Popcorn	9.8%	11.1%	1.3%	>0.9
Peach	70.5%	85.2%	14.7%	0.2
Tire	49.2%	81.5%	32.3%	0.005*
Cucumber	26.2%	48.1%	21.9%	0.52
Pineapple	83.6%	81.5%	–2.1%	0.8
Raspberry	85.2%	96.3%	11.1%	0.2
Orange	90.2%	92.6%	2.4%	>0.9
Walnut	67.2%	92.6%	25.4%	0.015*
Watermelon	96.7%	96.3%	–0.4%	>0.9
Paint thinner	85.2%	100%	14.8%	0.052
Grass	57.4%	51.9%	–5.5%	0.6
Smoke	55.7%	59.3%	3.5%	0.8
Wood	65.6%	55.6%	–10%	0.5
Grape	98.4%	96.3%	–2.1%	0.5
Garlic	91.8%	92.6%	0.8%	>0.9
Soap	37.7%	37%	–0.7%	>0.9
Gas	70.5%	85.2%	14.7%	0.2
Perfume	80.3%	85.2%	4.9%	0.8
Peanut	77%	92.6%	15.5%	0.1

Difference is expressed as the subtraction of the percentage of subjects who correctly identified the item in the group with higher income minus that in the group with lower income. A star indicates significance at the 5% level.

males (p=0.90), and Chi-square tests showed a significant difference of proportion of subjects into different income groups between genders (p=0.004) with most women (46.7%) receiving less than US$ 230, and most men (51.1%) receiving between US$ 230 and 920. There were no differences in mean years of schooling (p=0.1) or MMSE score (p=0.09) between males and females.

DISCUSSION

The present study demonstrates that the UPSIT-Br2 is sensitive to age and sex differences in a diverse group of Brazilian subjects, in accord with findings of previous smell identification studies using the UPSIT and other olfactory tests in non-Brazilian populations. This work also suggests that socio-economic factors are important determinants of smell test scores in Brazil. This study provides preliminary normative data of value for assessing smell function of Brazilians using the UPSIT-Br2.

Our data are in agreement with studies within other populations demonstrating better performance of women than men in identifying odors[9]. The estimated β coefficient for gender was –1.8 (95%CI for β= –3.27 to –0.40), suggesting that, on average, females score higher than men by roughly a third of a point to 3 points. The basis for this sex difference is not known, although straight-forward associations between circulating levels of gonadal hormones and measures of smell function are rare[10]. For example, girls tend to outperform boys on identification tests long before puberty; indeed, in some instances, relatively soon after birth[11]. In general, olfactory measures in which semantic memory plays a role tend to exhibit greater sex differences than measures in which semantic memory does not play a role[12].

This study also demonstrates that the UPSIT-Br2 is sensitive to age. In our multiple regression analysis the estimated β coefficient for age was –0.082 (95%CI for β= –0.14 to –0.02). This suggests that a subject who is 10 years older would score almost one less point, assuming all other variables are constant and a linear relationship is present between age and UPSIT-Br scores. These findings are in agreement with numerous other studies demonstrating that age is the main risk factor for smell impairment. Thus, between 65 and 80 years of age about 50% of the population has demonstrable smell loss and over 80 years this increases to nearly 75%[4]. Age-related degeneration of the olfactory epithelium and olfactory bulb[13,14], occlusion of the olfactory foramina by ossification[15], cumulative damage to the olfactory epithelium as a result of repeated xenobiotic insults[16] and, in some cases, neurodegenerative disease pathology within the central olfactory system are some of the suggested causes[17].

The association of socio-economic level, as measured by personal income, with UPSIT-Br2 scores, is novel and of relevance. It is possible that lower income Brazilians are more likely to live or gain employment in farms or industries in which greater exposure to occupational dusts, fertilizers, and other pollutants are present. It is also well established that smell loss is more prevalent in highly polluted regions of cities and in some industrial environments associated with lower economic status[18,19]. An alternative, but not mutually exclusive, explanation for the poorer performance of individuals of lower socio economic status might be that they have had less or no exposure to some of the test items. Thus, the finding could be an artefact of education or experience. In accordance to Brazilian literature, income is correlated with schooling, which is correlated with performance in the MMSE[8].

Although we tried to select subjects to represent equally the different age groups and genders, we did not choose subjects based on income or occupation. Brazil is a very large and diverse country characterized by high levels of socio-economic disparities, as reflected in our sample. Even though education is compulsory in Brazil, up to 7% of the Brazilian population is illiterate, and more than 20% may not be fully able to understand written language despite having attended school for more than a year[20]. Despite the fact that our strict cut-off of MMSE scores of 25 probably excluded persons too demented to understand our test procedure (the recommended cut-off for dementia in Brazil is 25 for subjects with 1 or more years of schooling[8]), this cut off does not exclude persons with mild cognitive deficit or who may be illiterate or unfamiliar with a number of the test items. It is also noteworthy in this regard that the three items that differed significantly between the lower and higher income groups were gasoline, rubber tyres, and walnut. Although walnut is not native in Brazil, it was correctly identified by 67% of the low income subjects. However, it is better known among Brazilians of higher income (correctly identified by 93% of subjects in this group). Nonetheless, the higher income individuals, on average, tended to better identify most of the test items than the lower income individuals. Indeed, the overall difference in test scores between the two groups remained significant even after exclusion of these three test items, suggesting that they do not in isolation explain the observed differences.

The data from the 88 Brazilian subjects provides provisional normative data for the routine use of this test in subjects aged between 20 and 90 years. Our data also imply that additional refinements in the UPSIT-Br might be needed. Specifically, at least 10 items were not highly identifiable by subjects in either income group, and popcorn, dill pickle (mistakenly translated as "pepino", which means cucumber) and soap were not correctly identified by the majority of the subjects in our sample and should be modified in future versions of the test. These items

should be reconfigured or replaced to increase the level of test performance to be comparable to that observed in North American populations. Additional work with larger and more diverse samples are needed to determine to what degree the differences we observed in test scores among the socio-economic classes evaluated in this study reflect true sensory deficits, lack of familiarity with test items, or some combination of these variables.

REFERENCES

1. Murphy C, Schubert CR, Cruickshanks KJ, et al. Prevalence of olfactory impairment in older adults. JAMA 2002;288:2307-2312.
2. Doty RL, Reyes PF, Gregor T. Presence of both odor identification and detection deficits in Alzheimer's disease. Brain Res Bull 1987;18:597-600.
3. Doty RL, Deems DA, Stellar S. Olfactory dysfunction in parkinsonism: a general deficit unrelated to neurologic signs, disease stage, or disease duration. Neurology 1988;38:1237-1244.
4. Doty RL, Shaman P, Dann M. Development of the University of Pennsylvania Smell Identification Test: a standardized microencapsulated test of olfactory function. Physiol Behav 1984;32:489-502.
5. Silveira-Moriyama L, Petrie A, Williams DR, et al. The use of a color coded probability scale to interpret smell tests in suspected parkinsonism. Mov Disord 2009;24:1144-1153.
6. Doty RL. Odor perception in neurodegenerative diseases. In: Doty RL (Ed). Handbook of olfaction and gustation, 2nd Ed. Philadelphia: Marcel Dekker, 2003:479-501.
7. Silveira-Moriyama L, Carvalho MJ, Katzenschlager R, et al. The use of smell identification tests in the diagnosis of Parkinson's disease in Brazil. Mov Disord 2008;23:2328-2334.
8. Brucki SM, Nitrini R, Caramelli P, et al. [Suggestions for utilization of the mini-mental state examination in Brazil]. Arq Neuropsiquiatr 2003;61:777-781.
9. Doty RL, Applebaum S, Zusho H, et al. Sex differences in odor identification ability: a cross-cultural analysis. Neuropsychologia 1985;23:667-672.
10. Doty RL, Cameron EL. Sex differences and reproductive hormone influences on human odor perception. Physiol Behav 2009;97:213-228.
11. Doty RL. Gender and endocrine-related influences upon olfactory sensitivity. In: Meiselman HL, Rivlin RS (Eds). Clinical measurement of taste and smell. New York: MacMillan, 1986:377-413.
12. Larsson M, Lovden M, Nilsson LG. Sex differences in recollective experience for olfactory and verbal information. Acta Psychol (Amst) 2003;112:89-103.
13. Bhatnagar KP, Kennedy RC, Baron G, et al. Number of mitral cells and the bulb volume in the aging human olfactory bulb: a quantitative morphological study. Anat Rec 1987;218:73-87.
14. Duda JE, Shah U, Arnold SE, et al. The expression of alpha-, beta-, and gamma-synucleins in olfactory mucosa from patients with and without neurodegenerative diseases. Exp Neurol 1999;160:515-522.
15. Kalmey JK, Thewissen JG, Dluzen DE. Age-related size reduction of foramina in the cribriform plate. Anat Rec 1998;251:326-329.
16. Nakashima T, Kimmelman CP, Snow Jr JB. Structure of human fetal and adult olfactory neuroepithelium. Arch Otolaryngol 1984;110:641-646.
17. Hawkes CH, Doty RL. The neurology of olfaction. Cambridge: Cambridge University Press, 2009.
18. Hudson R, Arriola A, Martinez-Gomez M, et al. Effect of air pollution on olfactory function in residents of Mexico City. Chem Senses 2006;31:79-85.
19. Calderon-Garciduenas L, Franco-Lira M, Henriquez-Roldan C, et al. Urban air pollution: influences on olfactory function and pathology in exposed children and young adults. Exp Toxicol Pathol 2009;62:91-102.
20. Analfabetismo funcional é mais um desafio que o Brasil precisa enfrentar. Available at http://www.ibope.com.br/calandraWeb/servlet/CalandraRedirect?temp=6&proj=PortalIBOPE&pub=T&nome=home_materia&db=caldb&docid=7BA408FB9CC828DE832575B7005A487E . Accessed May ,15, 2009.