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Comparing the accuracy of different smell identification tests in Parkinson's disease: Relevance of cultural aspects

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ABSTRACT

Objective: The aim of this study is to determine the usefulness of the University of Pennsylvania smell identification test (UPSIT), sniffin sticks (SS-16) and brief smell identification test (B-SIT) to assess smell identification in the Mexican population and its accuracy in discriminating subjects with Parkinson's disease (PD).
Methods: We included 199 nondemented PD subjects and 199 control subjects matched by gender. Smell identification was tested using the UPSIT and SS-16. Our group obtained B-SIT data from a previous report.
Results: The mean number of UPSIT items correctly identified by controls was 27.3 ± 6; the PD group had a mean score of 19.4 ± 6. UPSIT had a sensitivity of 82% with a specificity of 66% for a cut-off score of ≤ 25 for detection of PD. The mean number of SS-16 items correctly identified by controls was 10.3 ± 2.2, while the PD group had 7.4 ± 2.8 correct answers. For SS-16, sensitivity was 77.8% and specificity of 71.2% when using a cut-off value of ≤ 9. Lemon, turpentine and rose had an identification rate below the 25th percentile for all three tests. Odors with an identification rate above the 75th percentile include banana for all three tests, and gasoline, onion and chocolate for UPSIT and B-SIT.
Conclusion: The sensitivity and specificity of the smell tests that were evaluated were lower in comparison to other published reports. Cultural biases and smell familiarity may influence the test results. The development of a true cross-culturally adapted smell identification test is warranted may improve test accuracy.

1. Introduction

Olfactory dysfunction is associated with several neurodegenerative diseases, including Parkinson's disease (PD) [1]. In PD, smell loss may present as an early sign even years before the onset of motor symptoms [2–4]. As a consequence, smell testing has been proposed as a biomarker for PD diagnosis.

Cultural differences may prevent odor identification tests from being used in different countries. Because of this, cultural specific tests have been developed. These tests include the Barcelona smell test-24 (BAST-24) for Spain [5], the odor stick identification test for Japanese (OSIT-J) for Japan [6] and the Italian olfactory identification test (IOIT) [7]. Nevertheless, their high cultural specificity impedes comparison between populations.

The University of Pennsylvania smell identification test (UPSIT) [8], is a widely used standardized test of olfaction. It consists of four booklets, each containing ten scratch and sniff microencapsulated odorant strips (40 items). The UPSIT is most commonly used in the United States; nevertheless it has proved to be suitable to assess olfactory function in other populations [9,10] and is commercially available in multiple languages including Spanish. Test-retest reliability has been reported to be greater than $r = 0.90$ [11].

The brief smell identification test (B-SIT) is a shorter 12-item version of the UPSIT. Several versions of the B-SIT exist but only version A is currently available in Spanish. The empiric test-retest

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reliability is acceptable ($r = 0.71$). Additionally; a modified B-SIT is available that allows the subject to rate each odor's strength, pleasantness and familiarity.

The sniffin sticks is a test based on pen-like dispensing devices [12]. The screening 12 test is an identification test with 12 different smells while the sniffin sticks 16 (SS-16) is used to further evaluate odor identification. Finally, an "extended test" which evaluates smell threshold, discrimination and identification is commercially available. A high test-retest reliability ($r = 0.88$) for odor identification has been reported [2]. The SS-16 is mainly used in European countries, but it has also been validated in the Asian region [13,14].

In Latin America, results of smell identification tests have been reported mainly in Brazilian, Chilean and Mexican populations. In Brazil, the UPSIT applicability was tested, with a mean score below of what is considered normal for US citizens. Culturally adapted translations of the UPSIT and the SS-16 for the Brazilian population were developed. Both have proved to be reliable measures and potentially useful for improving the accuracy of diagnosis of PD. The SS-16 specificity was 89% and sensitivity was 82.1%. The UPSIT specificity was 83.5% with a sensitivity of 82.1% [15]. In Chile, the SS-16 was used to provide age and gender-specific values for normal olfaction, hyposmia and anosmia in healthy subjects [16]. A small study in Chilean PD patients and controls, with 40 subjects in each group, reported a sensitivity of 100% and a specificity of 95% when using a cut-off value of 10 correct answers on the SS-12 [17].

Currently, there are no smell tests tailored for the Mexican population. Our group translated and adapted the B-SIT for use in Mexico. A 71.4% sensitivity and 85.7% specificity were found [18]. Sensitivity and specificity for other smell tests in Mexican subjects with Parkinson's disease have not been yet reported.

Changes either in odorant items or response alternatives for foreign-language versions of UPSIT, B-SIT and SS-16 have been necessary in order to improve their accuracy. A pilot study in Taiwan markedly improved test scores by changing several odors and response alternatives. Nevertheless, some items still caused the total test score to be lower than that observed in the U.S. population [19]. In Australia, researchers suggested adding a correction factor of two points to total scores [20]. In Brazil, a cultural adaptation of the UPSIT Portuguese translation was effective in increasing average scores. Nevertheless, whether this scores fall within normative values obtained in the United States has not been determined [21]. The B-SIT was created as a cross-cultural smell identification test. Nonetheless, several items have been poorly identified in Mexican population [18].

The aim of this study is to determine the usefulness of the UPSIT, SS-16 and B-SIT for assessing smell identification in a Mexican population and its accuracy in discriminating control subjects from patients with PD.

2. Methods

One hundred ninety-nine consecutive nondemented PD patients, who fulfilled the Queen Square Brain Bank criteria [22], were recruited at the movement disorder specialist clinic at the National Institute of Neurology and Neurosurgery in Mexico City. One hundred ninety-nine controls matched by gender were recruited among visitors and patients.

Subjects with history of seasonal allergies, nasal illness or surgery, severe head trauma or current upper respiratory tract infection were excluded from the study. Subjects with a Montreal Cognitive Assessment score <26 were excluded from the study. Subjects were randomized to either the UPSIT or the SS-16 testing. Data from the B-SIT were obtained from a previous report by our group [18].

The local ethics and research committee approved the study. All participants provided written informed consent.

2.1. Smell testing

The Spanish version of the University of Pennsylvania smell identification test (UPSIT, Sensonics, Haddon Heights, New Jersey, USA) was used. The test was applied by scratching each micro-encapsulated odorant strip with a pencil tip and the strip was immediately sniffed by the subject. The subjects were offered four possible multiple-choice responses for each odor and were asked to select one of the options even if no smell was perceived or identified.

The sniffin sticks odor-identification test (SS-16) (Burghart Medizintchnik, Gemany) consists of 16 pens filled with common odorants: orange, leather, cinnamon, peppermint, banana, lemon, licorice, turpentine, garlic, coffee, apple, cloves, pineapple, rose, anise, and fish. During the test, the experimenter removed the cap and participants were asked to smell the pens with both nostrils. They were asked to identify the odorant from a list of four options given by the examiner for each pen. An answer was required even if the subjects were unable to identify the smell (forced multiple-choice task identification test). Nostrils were not tested independently.

A total of 199 subjects with PD and 199 controls were included. Additionally, the information of 70 PD patients and 70 healthy controls from the B-SIT study was included for comparison and analysis. The main demographic and clinical characteristics of all three groups is shown in Table 1.

The UPSIT was applied to 100 healthy controls and 100 PD subjects. Smoking status were similar between both groups (11% were current smokers among control subjects and 8% in PD subjects, $p = 0.52$).

2.2. Statistical analysis

Demographic data were reported as frequencies, means and standard deviation. The percentage of control and PD subjects who correctly identified each item of the smell tests was compared using a Chi-square test. Receiver operating characteristic (ROC) curves were used to determine sensitivity and specificity of the UPSIT and the SS-16. A multiple regression analysis was used to determine factors that impact total score in the UPSIT and the SS-16. Discriminant factor analysis was carried out to obtain predicted and actual group membership (PD or control group) for the UPSIT, SS-16 and B-SIT. STATA 12 (StataCorp) software was used for all analyses. A p value <0.05 was considered significant.

Table 1
Demographic and clinical characteristics between Parkinson's disease subjects tested by the UPSIT, SS-16 and BSIT.

	UPSIT	BSIT[a]	SS-16
n	100	70	99
Male Gender *n* (%)	55 (55%)	41 (58.5%)	64 (64.6%)
Age (years ± SD)	63 ± 10.2	66 ± 9.0	62.5 ± 9.2
Smoker status *n* (%)			
Never smoker	57 (57%)	36 (51.4%)	52 (52.5%)
Former smoker	32 (32%)	18 (25.7%)	30 (30.3%)
Current smoker	11 (11%)	16 (22.8%)	17 (17.2%)
Age at PD Onset (years ± SD)	56.6 ± 13.4	59.7 ± 9	56.1 ± 12.5
Disease duration (years ± SD)	7.4 ± 6.1	6.7 ± 5	7.3 ± 7
Hoehn and Yahr *n* (%)			
Mild (1–2)	73%	61.4%	69.9%
Moderate (3)	20%	34.2%	25%
Severe (4–5)	7%	4.4%	5.1%

BSIT: brief smell identification test; PD: Parkinson's disease; SS-16: sniffin sticks test; UPSIT: University of Pennsylvania smell identification test.
[a] [18].