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ANIMAL AND HUMAN PHYSIOLOGY

A Standardized Test for Evaluation of Olfactory Function for the Russian Population

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Abstract—We have tested the original version of the University of Pennsylvania Smell Identification Test (UPSIT) on a population of Central Russia including groups of different ages residing in the city area and in the rural part of the country. Our results demonstrate that the UPSIT is applicable for evaluation of olfactory function within the population of Central Russia and allows us to detect age-related differences in olfactory function. However, several odor samples presented within the original UPSIT proved to be unfamiliar to the subjects due to cultural differences. We have identified and tested odor items that may replace poorly recognizable items of the original UPSIT. Thus, we have developed a culturally adapted version of the UPSIT to be used within the population of Central Russia.

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INTRODUCTION

Studies of recent decades have left no doubts about underestimation of the importance of olfaction in human life, and referring humans to microsmatics is wrong (Laska et al., 2005; McGann, 2017). Humans are able to differentiate multicomponent mixtures of odorants and recognize up to a trillion odors, which exceeds the estimations of the resolution abilities of visual and auditory analyzers (Bushdid et al., 2014; Gerkin and Castro, 2015). Currently the timeliness of investigation of the role of olfactory signals in organization of human behavior and regulation of physiological status is undeniable. In addition, olfaction has a considerable impact on the quality of human life and accomplishes a protective function. The loss of olfaction or decrease of sensitivity to odors predisposes one to food and natural gas poisonings, loss of appetite, and a change in food preferences and diet. In a number of industries, for instance, the chemical or gas sectors, continuous monitoring of olfactory function is crucial for healthcare. The evaluation of olfactory function is necessary in routine practice of ENT specialists and clinical trials in rhinological, endocrinological, and pharmacological areas. The assessment of olfactory function is valuable for early diagnostics of several neurodegenerative diseases. For example, a typical early sign of Alzheimer's and Parkinson's diseases is a decrease in olfactory acuity (Doty, 2007; Djordjevic et al., 2008; Voznesenskaya et al., 2011b; Woodward et al., 2017). In 2006 the American Academy of Neurology approved the examination of olfactory sensitivity for differential diagnostics of Parkinson's disease (Suchowersky et al., 2006).

However, currently there is no standardized test for quantitative assessment of human olfactory function in Russia. The University of Pennsylvania's Smell Identification Test (UPSIT) is broadly used abroad and is based on identification of odors. UPSIT was developed in the United States in 1984 and allowed researchers to detect the majority of olfactory impairments (anosmia, hyposmia, parosmia) and to exclude simulation of olfactory dysfunction (Doty et al., 1984). The advantages of the test are its reliability, relatively low cost, ease of use, and possibility of distant testing of patients (Doty et al., 1984, 1995). The test is characterized by very high reproducibility of the results ($r = 0.9–0.92$) (Doty et al., 1984, 1995). Although due to cultural differences in odor perception, this test is impossible to be mechanically transferred to a different culture. UPSIT has already been successfully adapted in several countries including Brazil, Japan, Australia, and Taiwan (Mackay-Sim and Doty, 2001; Ogihara et al., 2011; Fornazieri et al., 2015; Hsu et al., 2015). Development of a national version of the test is essential for both medical practice and fundamental research. A test of this kind is needed for major population studies, as well as application in field and expeditionary conditions. The purpose of this study is to adapt UPSIT for the Russian population.

Table 1. Identification of 40 UPSIT odor samples in the Central Russian population ($n = 252$)

Percent of correct answers, %	Odor samples (percent of correct answers, %)
<75	Fruit punch (23), lime (24), lilac (30), cheddar cheese (39), grass (48), cedar (71)
75–90	Pizza (78), cinnamon (78), chocolate (78), clove (79), strawberry (79), cherry (81), soap (83), bubble gum (84), menthol (84), turpentine (84), grape (84), pineapple (87), mint (88), Root beer (88), pickle/dill (88), motor oil (89), orange (89), rose (89)
>90	Banana (92), coconut (92), gingerbread (92), peanut (92), licorice (93), wintergreen (93), natural gas (93), peach (94), paint thinner (94), pine (94), petrol (95), watermelon (96), lemon (96), leather (97), onion (97), smoke (100)

Table 2. Identification of additional odor samples, candidates for inclusion in the test

Odor	Percent of correct answers, %	
	city ($n = 45$)	village ($n = 41$)
Apple	51.1	78.1
Raspberry	73.3	82.9
Garlic	100	100
Baby powder	93.3	80.5
Grapefruit	95.6	97.6
Rubber tire	82.2	95.1
Coffee	97.8	100

MATERIALS AND METHODS

This study was conducted on the territory of the Central Federal District with the largest population in the Russian Federation. Over 340 people between the ages of 18 and 87 years volunteered for participation in the study. Test subjects have permanently resided in a metropolitan city (Moscow) or in rural areas.

To evaluate general olfactory sensitivity, we used the North American version of UPSIT (Sensonics, Inc., United States). The full version of the test consists of 40 different odor samples (Table 1), with each of them accompanied by four alternative variants of answers. The odor samples are represented by platelets of microgranules layered on thick paper that provides gradual release of odor by scratching with a sharp pencil. The test is accompanied by calculated scores corresponding to the condition of the olfactory function. The overall score in UPSIT depends on the number of correctly recognized odors. Standard scores of the test have been developed for the adult population in North America for each age–sex group in increments of five years based on a large group of test subjects (about 4000) including those with clinically identified olfactory impairments. Criteria characterizing normal olfactory function, or normosmia, were presented by the authors of the original test using calculation of the interquartile range (25th–75th percentile) of UPSIT scores in every age–sex group (Doty et al., 1984). The test results can also be assessed by an absolute normative scale for all the adult subjects. The norm of olfactory function equals to a score of 34–40, microsmia of different intensity scores 19–34, and complete anosmia is 6–18 points (Doty et al., 1984). For example, a 73-year-old man, a resident of North America, who scored 31 points, would be diagnosed with mild microsmia by the absolute rating scale, while in his age–sex group his olfaction would be normal. According to standardized data, women have higher scores, on average. The number of points in UPSIT normally decreases with age in both men and women (Doty, 1995).

The test was translated into Russian by the authors. In a number of cases, we corrected the descriptions of smells referring to national cultural features (Voznesenskaya et al., 2011a; Klyuchnikova et al., 2017). Participants were asked to fill in a questionnaire specifying their habitation, sex and age, education, ethnicity, problems with olfaction and taste, treatment received, administration of medications, and smoking habits. The variants of answers and the UPSIT questionnaire in Russian were printed in large font on A4 paper. The testing took place in a room in the presence of the researcher giving oral explanations and releasing odors in accordance with the original instructions. The participants were told that one variant had to be chosen despite their uncertainty. The majority of subjects filled in the answer sheet independently and marked a chosen answer, however, if desired, some of the seniors were tested orally, which is also acceptable (Doty, 1995). Most of the subjects ($n = 193$) were instructed to mark unfamiliar odors among all (correct and incorrect) alternative answers ($n = 51$) after completion of UPSIT in order to replace unfamiliar variants.

An additional group of subjects ($n = 86$) was tested to replace unfamiliar odors. The average age of megapolice residents was 46.9 ± 24.1 years ($n = 45$), and the residents of rural areas were aged 45.3 ± 20.8 years ($n = 41$). We used seven odor samples (Table 2) from the manufacturer's catalog, which were not included in the UPSIT but were equivalent to the replaced odors.

Statistical analysis was conducted in the Statistica 8.0 software using descriptive statistics unit and generalized linear models. We analyzed the following main factors: sex, age, place of permanent residence, and

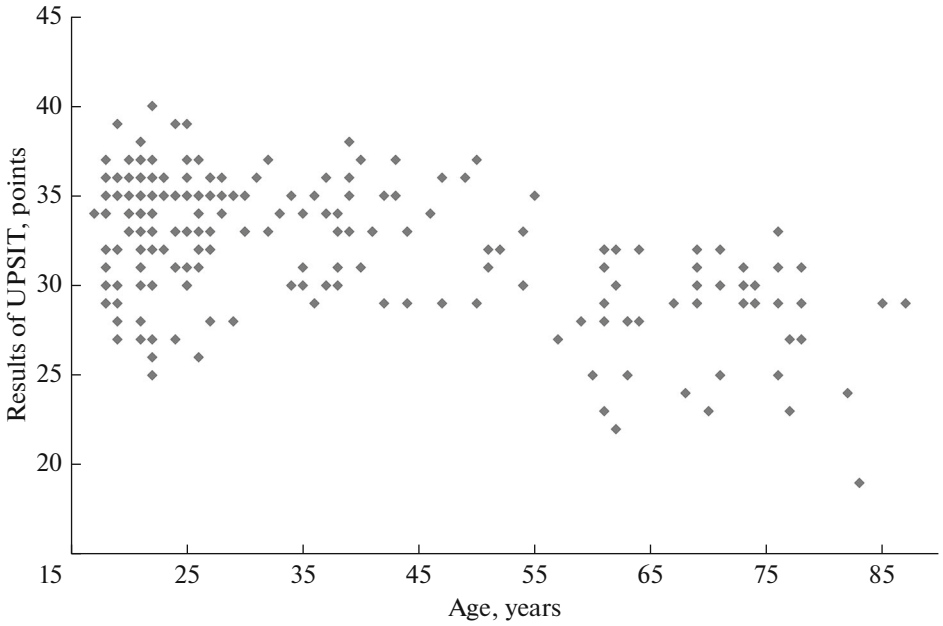

Fig. 1. Age-related differences in olfactory function according to UPSIT in residents of Central Russia ($n = 252$, n is the number of subjects).

smoking habits. Data are presented as the mean ± standard deviation.

RESULTS AND DISCUSSION

In the group studied ($n = 252$, average age 34.9 ± 18.8 years) the mean score was 32.6 ± 3.5 points in the North American version of the UPSIT. The distribution of scores related to age is presented in Fig. 1. This score was 32.5 ± 3.4 in women ($n = 162$), while in men ($n = 90$) it was 32.7 ± 3.8 points. The average UPSIT score in urban residents ($n = 156$) was 33.1 ± 3.3, while in habitants of rural areas ($n = 96$) it was 31.7 ± 3.7 points. The average UPSIT score significantly decreased in dependence on age ($F(1, 247) = 102.9$, $p < 0.001$), while sex $F(1, 247) = 0.001$, $p = 0.98$) and place of permanent residence ($F(1, 247) = 1.1$, $p = 0.29$) showed no impact; in addition, no significant interaction between these factors (interaction of sex and place of permanent residence) was found ($F(1, 247) = 0.04$, $p = 0.83$)). Moreover, we did not reveal any significant influence of smoking on success of test completion ($F(1, 199) = 2.7$, $p = 0.1$). Age-related decline of the olfactory function observed in this work using UPSIT (Fig. 1) are in good agreement with the literature data. It is known that human olfactory function starts dramatic decrease from the age of 60–65 years, in contrast to the relatively stable level of olfactory sensitivity in the age group of 18–60 years (Doty et al., 1984; Murphy et al., 2002; Doty and Kamath, 2014). From the example of our sample, the number of correct answers among subjects older than 60 years was significantly lower than among subjects aged 18–60 years (33.4 ± 3.2, $n = 208$ against 28.4 ± 2.9, $n = 44$; $F(1, 250) = 105.7$, $p < 0.001$). Women of the North American population demonstrated better results of UPSIT (Doty, 1995). The absence of sex differences in our sample size does not correspond with numerous literature data and our evaluation of olfactory sensitivity to certain substances for the Russian population (Voznesenskaya and Klyuchnikova, 2017). This difference is associated with the presence of unfamiliar, and consequently, unrecognizable odors among the original samples. For example, sex differences were revealed in Turkey during the process of test adjustment only after replacement of unknown odors (Altundag et al., 2015). Similarly, a more significant effect of smoking was found after replacement of unfamiliar odors (Altundag et al., 2015).

During development of the North American version of the test, one of the inclusion criteria for a particular odor was correct recognition by at least by 75% of respondents. Table 1 contains data on each of the 40 test samples. The majority of odors (34) was correctly identified in over 75% of cases. However, for six odorants (cedar, lime, fruit punch, lilac, cheddar, and grass), the mentioned criterion was not achieved. Apparently, the main reason here is cultural differences. According to the results of an additional test ($n = 193$), more than 10% of subjects noticed that odor of cedar, lime, cheddar, and fruit punch were unfamiliar to them, while the samples of lilac and grass did not correspond to the expected smell. "Soap," an alternative variant for "fruit punch," was a source of confusion for that odorant. In all, 95% of respondents chose

that answer. The test subjects associated the perceived fruit smell with perfume compositions used in the production of the popular "wild strawberry soap." For this reason we changed the name of the sample from "fruit punch" to "wild strawberry soap." The exclusion of five poorly recognizable odors resulted in reduction of the sample number from 40 to 35. In several countries shortened versions of UPSIT (Maremmani et al., 2012) are applied for assessment of olfactory function, though the full version is preferable for purposes of diagnostics. Application of the shortened version of UPSIT in Russia requires recalculation of the standard scores for the test. In our sample size the values of the lower quartiles were counted similarly to the original method. For the group of women at the age of 20–30 years ($n = 84$), the score was 32; for men ($n = 41$), it was 33 points. The threshold score of normosmia in the analogous age group of the North American population for both men and women is 36 points. Therefore, we suggest to lower the original age–sex limits of the normal range by four points in women and three points in men in case of application of the shortened North American version of UPSIT for population of Central Russia. The norm in absolute scale for Russian seniors should be considered 31 points or more. A score lower than 23 points might indicate a severe olfactory impairment.

However, as mentioned above, the application of a shortened version of UPSIT is limited, and for medical and scientific purposes the full version is preferable. From that perspective, the next phase of investigation included replacement of the five poorly recognizable odors for ones well recognizable. The results of testing of seven additional samples in order to find the replacements for poorly identifiable UPSIT odor items, are presented in Table 2. Five out of seven odors (garlic, baby powder, grapefruit, rubber tire, coffee) were identified by over 75% of respondents, which corresponds with the criterion of inclusion of samples into UPSIT. For each of the five samples, three alternative variants of answers were chosen. As a result, we completed the full set of studies to maintain a full version of the test consisting of 40 odor items.

The results of our studies suggest that the adapted UPSIT is applicable for quantitative assessment of olfactory function in the population of the Russian Federation in both cities and rural areas. Currently an essential set of studies has been conducted to produce a trial version of the Russian Smell Identification Test which would allow in the future to diagnose olfactory dysfunctions as well as to determine the risk groups for neurodegenerative diseases at early stages and conduct major population studies.

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