Smell Identification in Japanese Parkinson's Disease Patients: Using the Odor Stick identification Test for Japanese Subjects

Mutsumi Iijima¹, Tatsu Kobayakawa², Sachiko Saito³, Mikio Osawa¹,
Yukiko Tsutsumi¹, Shiori Hashimoto⁴ and Makoto Iwata¹

Abstract

Objective The purpose of the present study was to clarify the olfactory functions of Japanese patients with idiopathic Parkinson's disease (IPD) using the odor stick identification test for Japanese (OSIT-J).

Methods Fifty-four non-demented IPD patients (33 men and 21 women), ranging in age from 43 to 81 years (69.7±8.1 years) and 50 age- and gender-matched healthy controls who reported having no olfactory complaints were enrolled. OSIT-J consisted of 12 odorants familiar to Japanese subjects. Each subject sniffed each odor that was applied to paraffin paper. Next the subject chose 1 of 6 answers: 4 pictures associated with the odors labeled with their names, one of which was correct, and 2 other ones ("unknown" and "not detected").

Results The number of correct answers was significantly lower in the IPD group (4.4±2.7) than in the normal group (8.3±2.2) ($p<0.0001$). Even in IPD patients who could smell normal strength odors in subjective symptom, the number of correct answers decreased. The number of correct answers was not correlated with motor function, disease duration, or medication.

Conclusion The present study demonstrated that the smell identification ability of Japanese IPD patients was impaired based on the OSIT-J.

Key words: Parkinson's disease, olfaction, odor identification, smell test

(Inter Med 47: 1887-1892, 2008)

(DOI: 10.2169/internalmedicine.47.1345)

Introduction

Since Ansari and Johnson (1) first reported that the olfactory threshold was impaired in patients with idiopathic Parkinson's disease (IPD), many studies dealing with olfactory dysfunction in Parkinson's disease patients have been reported in the United States and Europe (2-19). Nowadays, olfactory dysfunctions are recognized as non-motor symptoms in PD, and are makers for a preclinical diagnosis of PD because pathological changes of olfactory systems start before motor symptoms develop (20). Doty et al (4, 5) employed the 40-odorant, University of Pennsylvania Smell Identification Test (UPSIT) and the 12-odorant, cross-

cultural, smell identification test (CC-SIT) to test IPD patients. They found that the impairment of olfactory function was independent of disease stage and duration. The 12-odorant Sniffin's Sticks test, which is the standard tool used by the German Otological Society, is used for smell identification testing in Europe (19). However, these smell identification tests consist of several odors that are unfamiliar to Japanese people, such as wintergreen, pumpkin pie, and pizza; thus, these tests are not directly applicable to Japanese patients (21). Therefore, there are only a small number of studies dealing with olfactory function in Japanese IPD patients. These studies of olfactory detection and recognition thresholds used T&T olfactometry, which tests recognition thresholds for 5 odorants and is the standard olfactory test

¹Department of Neurology, Tokyo Women's Medical University, Tokyo, ²National Institute of Advanced Industrial Science and Technology, Tsukuba, ³Saito Sachiko Taste and Smell Institute, Tsukuba and ⁴Medical Research Institute, Tokyo Women's Medical University, Tokyo
Received for publication May 27, 2008; Accepted for publication July 27, 2008

Correspondence to Dr. Mutsumi Iijima, mutumi@nij.twmu.ac.jp

in Japan (22, 23). T&T olfactometry is suitable for screening for olfactory disturbances; however, it has disadvantages due to the length of time required for the test and air contamination from the diffusion of odors (24). Recently, the odor stick identification test for Japanese (OSIT-J) was developed by Saito, Ayabe-Kanamura (25, 26) as a new type of smell identification test; it consists of 13 odorants that are all familiar to Japanese subjects. A significant correlation coefficient between the identification rate of OSIT-J score and the results of T&T olfactometry has been reported both in normal Japanese subjects and in patients with olfactory disturbances (27, 28). The OSIT score has been shown to be significantly correlated with the CC-SIT score, but the average identification rate using the OSIT was significantly higher than that using the CC-SIT (26). In 2003, OSIT-J was exhibited as a Technical Report for Japanese Industrial Standard; since 2004, it has been marketed by the Daiichi Yakuhin Co., Ltd., (Tokyo, Japan) as the odor identification test of the 12 odorants (excluding the putrid smell). The purpose of the present study was to document the olfactory functions of Japanese IPD patients using the OSIT-J.

Methods

Subjects

From June 2006 through February 2007, fifty-four non-demented consecutive outpatients with IPD (33 men and 21 women), ranging in age from 43 to 81 (mean $\pm$ SD, 69.7 $\pm$ 8.1) years, and 50 age- and gender-matched healthy controls who reported having no olfactory complaints (30 men and 20 women, 43 to 81 years of age; mean $\pm$ SD, 69.3 $\pm$ 7.3) were enrolled. The diagnosis of IPD was made based on the Criteria of the United Kingdom Brain Bank (29) and a negative family history of PD. The patients' disease duration ranged from 5 to 216 (mean $\pm$ SD, 56.2 $\pm$ 51.3) months. The motor performance of the IPD patients was assessed in the "on" stage using the Hoehn and Yahr Staging scale (H&Y), and the motor section (part III) of the Unified Parkinson's Disease Rating Scale (UPDRS): 9 patients were in H&Y stage I, 31 were in stage II, 9 were in stage III, and 5 were in stage IV. The mean UPDRS part III score was 14.5 points (range 4-31). The patients' mental functions were evaluated using the Mini-Mental State Examination (MMSE), and their mean MMSE score was 28.6 (range, 24-30) points. At the time of testing, 46 of the IPD patients were taking anti-parkinsonian medication: 32 took levodopa (100-400 mg/day), 35 took pramipexole (0.25-4.5 mg/day), 10 took cabergoline (0.75-4.0 mg/day), 3 took pergolide (750-1000 μ g/day), 10 took amantadine (50-200 mg/day), 5 took trihexyphenidyl (2-4 mg/day), 4 took droxidopa (200-400 mg/day), and 3 took selegiline hydrochloride (3.0-7.5 mg/day). Eight patients were newly-diagnosed patients who were not on any medications.

Healthy controls were examined at the National Institute of Advanced Industrial Science and Technology. Written in-

formed consent was obtained from all subjects following a full explanation of the study. This research was done in accordance with the guidelines of the Committee of Medical Ethics of Tokyo Women's Medical University.

OSIT-J

This test included 12 odorants: perfume, rose, condensed milk, Japanese orange, curry, roasted garlic, fermented beans/sweaty socks, gas for cooker, menthol, India ink, wood, and Japanese cypress (*hinoki*). These odors were chosen from the clusters of Japanese everyday life odors, which were odors familiar to the Japanese population. Each odorant was selected from among the essential oils, pure chemicals, or mixed odorants produced by Takasago International Corporation, Ltd. (Tokyo, Japan). Each odorant was enclosed in microcapsules made of melamine resin. These microcapsules were mixed into an odorless solid cream and then shaped like a lipstick. The examiner painted each odor stick in a 2-cm circle on a thin paraffin paper, folded the paraffin paper in half, rubbed the paper to grind the microcapsules, and then passed it to the subject. The subject opened the paraffin paper and sniffed it. Next, the subject chose 1 of 6 possible answers: 4 pictures of entities associated with the odors labeled with their names, 1 of which was correct, and 2 other ones ("unknown" and not detected"). The subjects were directed to avoid eating and smoking 30 minutes prior to being examined. The order in which the odorants were presented was randomized.

Subjective symptoms ranging from normosmia to anosmia were assessed on a 5-point scale: 1, could smell normal strength odors; 2, could smell only weakly; 3, could smell only strong odors; 4, could smell hardly at all; and 5, no sense of smell.

Data analysis

The number of correct answers was compared between the normal control group and the patient group using non-parametric analysis (Mann-Whitney *U* test); the correct rate for each odorant was assessed using the chi square test for independence. Factorial ANOVA was used to examine correlations between the data of OSIT-J and age, duration of illness, UPDRS scores, sex, and medication dosage in PD group.

Results

Subjective symptoms of olfactory disturbance

Twenty-six IPD patients (48.1%) had a score of 1, 7 (13.0%) had a score of 2, 13 (24.1%) had a score of 3, 8 (14.8%) had a score of 4, and none had a score of 5.

OSIT-J

The number of correct answers was significantly lower in the IPD patient group (mean $\pm$ SD, 4.4 $\pm$ 2.7) than in the normal subject group (mean $\pm$ SD, 8.3 $\pm$ 2.2) ($p < 0.0001$)

(Fig. 1). The answers for each odorant in the IPD group are shown in Fig. 2. The number of correct answers for almost all odorants, except for Japanese orange and roasted garlic, was significantly lower in the IPD group than in the normal subject group. The identification ratios of the Japanese orange and the roasted garlic were lower in PD than in normal subjects, but did not reach a statistical difference (Table 1). The number of correct OSIT-J answers decreased even in several patients who subjectively detected odors at normal strength (Fig. 3). In the IPD group, the mean number of incorrect answers was 3.4, the mean number of “unknown” answers was 2.4, and the mean number of “not detected”

answers was 1.7. The number of correct answers was not significantly correlated with disease duration ($p=0.70$) (Fig. 4), UPDRS scores ($p=0.81$) (Fig. 5), sex ($p=0.21$), or anti-parkinsonian drugs.

Discussion

Although many studies dealing with olfactory dysfunction in PD patients have been previously reported, in the present study, the smell identification ability of Japanese IPD patients was assessed using a new olfactory test. The present study demonstrated that the smell identification ability of Japanese IPD patients was impaired, and that the impairment was not correlated with motor function, disease duration, or medication. These results are in line with previous studies (4, 9).

The identification ratio of the roasted garlic tended to be lower in PD than in normal subjects, but did not reach a statistical difference. The identification ratio of Japanese orange was 40% in normal subjects, and 31.5% in PD, respectively in our study. Previous studies showed that the identification ratio of Japanese orange was lowest in normal subjects (26, 27), and was below 70% in normal subjects aged from 20 to 80 years, and was also lower in patients with olfactory dysfunction (28) because subjects chose “apple” in error (26, 28). In the present study, the reason why the identification ratio of Japanese orange in normal subjects was lower than that in the previous studies was that the age of normal subjects was older (mean age 69.7 years). We sug-

Figure 1. Comparison of correct odor stick identification test for Japanese (OSIT-J) answers between the normal subjects and patients with Parkinson's disease

Figure 2. Answers for each odorant in patients with Parkinson's disease. The correct answer rates were compared between the IPD group and the normal control group, C: correct answer, I: incorrect answer, U: unknown, N: not detected.

* $p<0.05$, ** $p<0.01$, *** $p<0.001$

Table 1. The Comparison of Identification Ratio of OSIT-J between Normal Subjects and Patients with Parkinson's Disease

Odorant	Normal subjects (%)	Parkinson's disease (%)	p value
Perfume	82.0	51.9	0.0023
Rose	78.0	42.6	0.0005
Japanese orange	40.0	31.5	0.48
Condensed milk	52.0	18.5	0.0007
Curry	100.0	48.1	< 0.0001
Roasted garlic	66.0	46.3	0.068
Sweaty socks/Fermented beans	74.0	51.9	0.033
Cooking gas	68.0	29.6	0.0002
Indian ink	80.0	35.2	< 0.0001
Wood	56.0	27.8	0.0065
Japanese cypress	66.0	20.4	< 0.0001
Menthol	79.0	40.7	0.005

Figure 3. Comparison between subjective symptoms of olfactory disturbance and the number of correct odor stick identification test for Japanese (OSIT-J) answers in patients with Parkinson's disease. Subjective symptoms ranged from: 1, could smell normal strength odors; 2, could smell only weakly; 3, could smell only strong odors; 4, could hardly smell at all; and 5, no sense of smell.

gested that there was no difference to the identification ratio of the Japanese orange because it was difficult for elderly normal subjects and patients with PD to identify the smell of the Japanese orange.

A significant correlation coefficient between the OSIT-J identification rate and the CC-SIT has been reported for Japanese normal subjects and Japanese patients with diseases affecting olfaction, but the average identification rate using the OSIT-J was significantly higher than that using the CC-SIT (26, 28). In particular, normal Japanese subjects had lower identification rates for "turpentine", "paint thinner", "rose", "lemon", and "smoke" on the CC-SIT (26). The familiarity score for the odorants was significantly higher on the OSIT-J than on the CC-SIT. Kobayashi et al (30) tested odor identification functions using OSIT-J in American and Japanese subjects with normal olfactory function. The

Figure 4. Comparison between disease duration and the number of correct odor stick identification test for Japanese (OSIT-J) answers. **Figure 5.** Comparison between the Unified Parkinson's Disease Rating Scale (UPDRS) (part III) scores and the number of correct odor stick identification test for Japanese (OSIT-J) answers.

American subjects had a significantly lower OSIT-J score than the Japanese subjects, suggesting that these results reflected the cultural differences in odor experience between American and Japanese subjects. The OSIT-J identification rate has been calculated for 10-year age groups; it has been shown to be lower in the elderly (identification rate: about 70% in the 70s and 50% in the 80s) than in young people (26). Therefore, the present study's results dealing with the smell identification ability of Japanese IPD patients using the OSIT-J were in line with previous results.

The present study showed that the number of correct OSIT-J answers decreased even in several patients who subjectively detected odors at normal strength. These results suggest that olfactory dysfunction in IPD patients was not simply due to an increased threshold for olfactory stimuli, but it was also related to impairment of odor identification. The olfactory processing in humans is transmitted from the olfactory receptors located in the nasal mucosa to the olfactory bulb and then to the primary olfactory cortices, consisting of the piriform cortex, the entorhinal cortex (ENT), and the periamygdaloid cortex (30, 31). The primary olfactory cortices project to the hippocampus and the mediodorsal nucleus of the thalamus (31-33). In IPD patients, olfactory dysfunction appears to be primarily due to degenerative

changes in the olfactory bulb, notably in the anterior olfactory nucleus, where Lewy bodies first develop (20, 34, 35). Cortical Lewy bodies are mainly found in the anterior cingulate gyrus and the parahippocampus (36). Masaoka et al (23) identified inspiratory-related potentials that reflect the response to odor stimuli and are located in the ENT, the hippocampus (HI), amygdala (AMG), and the orbitofrontal cortex (OFC). They found that detection scores in T&T olfactometer were not statistically different between normal subjects and Japanese IPD patients, but that odor identification was lower in Japanese PD patients than in normal subjects; inspiratory-related potentials showed less activation in the HI, AMG, and OFC in IPD patients. In addition, since impairment of odor identification is a cognitive task of olfactory judgment, olfactory dysfunction in IPD patients could also in part be the result of semantic processing impairment and could be associated with disruption of olfactory areas situated in the temporal lobes and prefrontal cortex (14).

In conclusion, the present study is the first to report that the odor identification abilities in Japanese IPD patients are estimated accurately using the OSIT-J. The OSIT-J is a convenient test that is suitable for clinical use in Japanese IPD patients.

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