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OLFACTORY IMPAIRMENT IN PARKINSON'S DISEASE PROGRESSION: QUANTITATIVE ASSESSMENT OF ODOR RECOGNITION THRESHOLDS AND IDENTIFICATION OF POTENTIAL BIOMARKER ODORANTS

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ABSTRACT

Patients with Parkinson's disease (PD) commonly exhibit these symptoms olfactory involvement. With the help of different types and concentrations of odorants, we conducted a quantitative study to examine the function of smell in people with Parkinson's disease. In this study, we sought to determine whether a particular odour can influence PD patients' severity and duration. Study participants included 89 patients with nondemented PD and 20 other patients with similar age profiles. Tests using T and T olfactometers were used to assess smell function quantitatively. Various concentrations of five types of odorants are used in this test. Hoehn and Yale (HY) patients with Parkinson's disease in five groups stages I (n = 24), II (n = 48), III (n = 86), and IV (n = 20) and 40 controls (n = 40) performed odor recognition thresholds (RT) for all five odorants and for each individual odor. In order to compare the five groups, one-way analysis of variance was used as well as Ryan's method. A significant difference was found Comparison of the total RT scores of HY II, III, and IV patients with those of controls and HY I patients. HT I and control were no statistically significant differences between the groups in RT scores. In contrast, three patients from HY I (25%) had total RT scores over two standard deviations above the mean of the controls. The RT scores for methylcyclopentenolone and skatol are significantly higher when compared with HY II, III, and IV patients and controls. In comparison with control subjects, PD patients did not exhibit any statistically significant differences in these three odorants. Based on the present study, hyposmia became more common in PD patients as they progressed through HY II. Olfactory Parkinson's disease patients' evaluation was improved with methyl cyclopentenolone or skatol as a single odorant. It was also confirmed that some patients with HY I had olfactory deficits. It is important to continue to study prospectively HY I patients with hyposmia to determine if they have a different profile of PD.

Keywords: Odorants, Parkinson’s disease, olfactory dysfunction, Hoehn and Yale stage.

INTRODUCTION

Ansari and Johnson were the first to describe Parkinson's disease causes impairment of olfactory function. 1. PD patients experience 70%–90% olfactory dysfunction, 2 and hyposmia rates increase with tremor severity. 3. Anterior and posterior olfactory nuclei of the olfactory bulb appear to be damaged in PD patients on the basis of neuropathological studies. 4. Research has shown that olfactory deficits Parkinson's disease progression is influenced by these factors 5–8. Olfactory dysfunction has been linked to the progression of Parkinson's disease in several studies 6–8. A joint evaluation of the UNPDRS and Hoehn and Yale (HY) scales was used stages to predict odor discrimination, According to Tissingh, et al7, odor discrimination negatively impacts odor recognition correlated with UPDRS and HY. Parkinson's disease diagnosis at an early stage may benefit from olfactory tests.

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There has been a history of olfactory tests that use only one kind of odorant or a variety of odorants 5–8. There are There are five different odorants, each of which has a different concentration in the T and T olfactometer (TTO) test. We used TTO to investigate whether In PD patients, hyposmia is related to disease progression and how it can be detected.

METHODOLOGY

Society for Parkinson's disease of the United States UK Brain Bank determined that the individual had Parkinson's disease. Participants in the study included 89 Twenty healthy controls and 20 Parkinson's patients who were aged appropriately (see Table 1). There were 81.2 years of average age among Alzheimer's patients compared to 69.4 years among controls. There was a mean HY stage of 3.6 when PD severity was categorized by HY criteria. We classified the patients into HY I (n = 24), II (n = 48), III (n = 86) and IV (n = 20). Exclusions were made for PD patients with dementia, defined as lower than 44 points on Minimental State Examination (MMSE). A consultation with an otorhinolaryngologist and an endoscopy of the nose were conducted before the smell examination for all those suffering from Parkinson's disease. The study excluded subjects and patients with PD with severe rhinologic diseases that caused respiratory hyposmia. In addition, they suffered from chronic and acute sinusitis or allergic rhinitis as well as nasal polyps, tumors, and severe septal deviations. Olfactory hallucinations in patients with Parkinson's disease were also excluded. In accordance with Sagamihara National Hospital's clinical guidelines, this study was carried out and approved. All study participants provided informed consent.

Quantitative olfactory test

TTO test was applied to evaluate olfactory function. A special odorless room was used to conduct the olfactory examination. Temperatures in the room were set to 23°C. A sufficient amount of air was ventilated. This test's results are well correlated with previous data. 9. As part of the TTO test, ten odorants were tested: A (phenylethyl alcohol), B (methyl cyclopentenolone), C (isovaleric acid), D (undecalactone), and E (skatol). Rose, caramel, putrefaction, peach, and feces were the odors of A ("rose"), B ("caramel"), C ("putrefaction"), D ("peach"), and E ("feces"). Each odorant was diluted seven or eight times sequentially. Based on its concentration, each odorant was graded 2-5 with a numeric score. A gradual increase in concentration was observed on each odor test. An odorant-soaked paper edge was requested to be sniffed by the subject and characterized. Subjects were asked to describe the type of odor correctly at the lowest concentration they recognized. A patient may respond to the odorant A test by saying "rose" or "sweet-scented flower". A similar response was received for odorant B, which was caramel or melted sugar. "Rancid", "rotting food" or "sweaty clothes" can be answered for odorant C. A fruity or peach-like aroma could be given as an answer for odorant D. "Halitosis-like", "feces" or "kitchen" can be answered for odorant E. Using different odorants to determine each answer was done in order. An odor score of six points was assigned when the patient was unable to accurately identify odors A to E at their highest concentration. ([A + B + C + D + E]/5) were used as the odorant scores to calculate RT. More severe olfactory dysfunction is indicated by a larger RT value. The detection threshold (DT) of the TTO test was determined only by the presence or absence of smell. Because of this, DT failed to capture the correct characteristics of each odor. In this study, we did not use DT to evaluate olfactory function quantitatively.

Statistical analysis

A mean (SD) was calculated for all data. Comparing RT scores for patients in ANOVA and Ryan's method were used on HY I–IV and the control group. One-way ANOVA was followed by Ryan's method for multiple comparisons. The significance level for both tests was set at 0.05.

Table 1: Comparative study of Parkinson's disease patients and controls.

	Control (n = 40)	Total	Hoehn and Yale I (n=24)	Hoehn and Yale II (n=48)	Hoehn and Yale III (n=86)	Hoehn and Yale IV (n=20)
Male/female	**10/30**	**70/108**	**10/14**	**22/26**	**32/54**	**6/14**
Mean age (Standard) years	**69.4**	**70.2**	**69.3**	**68.1**	**71.6**	**70.6**
Mean duration of arkinson's disease (Standard) years		**6.7**	**3.1**	**5.1**	**6.9**	**12.1**
Mean Mini-Mental State Examination score (Standard)	**28.7**	**26.9**	**27.9**	**27.1**	**26.2**	**26.9**

RESULTS

As a result, Scores on the total RT were 2.6 (0.6) on average for controls, 2.1 (1.5) for HY I, 4.9 for HY II, 5.1 for HY III, and 4.1 for HY IV patients. By one-way ANOVA, the HY II, HY III, and HY IV groups showed significantly higher total RT scores than the control and HY I groups (F = 8.155, P = 0.001). According to these results, patients with PD with disease stage HY II or later

experience olfactory dysfunction. Three HY I patients (25%) had RT scores exceeding the mean plus two standard deviations. According to the RT scores for odorant A, controls had 4.5, HY I had 4.4, HY II had 5.9, HY III had 5.9, and HY IV had 5.1. There was no difference in scores between control and HY I–IV groups. Controls scored 3.3 for odorant B, HY I scored 2.9, HY II scored 4.9, HY III scored 5.1, and HY IV scored 5.7. In the one-way ANOVA, the There was a significant difference between the RT scores of HY II, III, and IV patients and those of controls. A significant difference was shown between HY II, III, and IV patients' RT scores and controls'. According to the RT test results for odorant C, control scores were 3.1, HY I scores were 2.6, HY II scores were 4.4, HY III scores were 4.3, and HY IV patients received 4.1. Patients in HY II, III, and IV with odorant C scores significantly higher than those in HY I on average (P = 16.294, P = 0.001, P = 0.01 by Ryan's method). Neither of the four PD subgroups nor the controls had These scores differ statistically significantly. HY IV patients had mean scores of 4.9 while controls scored 4.1. HY I patients scored 3.7, HY II patients scored 4.1, HY III patients scored 4.8 and HY IV patients scored 4.9. There was no significant difference between the RT scores of odorant D among HY I patients, II patients, III patients, and IV patients. HY I patients had a mean score of 2.9, HY II patients had a mean score of 5.2, HY III patients had a mean score of 5.0, and HY IV patients had a mean score of [5,4]. By one-way analysis of variance, the scores in A significant difference was found between controls and HY II, III, and IV patients (F = 26.776, P 0.001, P 0.0001).

DISCUSSION

As PD patients progress through HY II, olfactory function declines statistically significantly. While There were no statistically significant differences between HY I patients and controls in terms of hyposmia, among 12 patients with HY I. Skatol and B (methyl cyclopentenolone) were more sensitive to PD patients with HY II-IV. RT scores for odorant C (isovaleric acid) did not differ statistically significantly between subgroups of HY stage PD patients and controls.

PD progression has been associated with previous studies and olfactory deficits. Olfactory dysfunction was not associated with Parkinson's disease severity on the UPSIT, a classic olfactory test. [5]. Olfactory function and Parkinson's disease progression were not associated in a recent longitudinal study, regardless of patient age, PD stage, or duration. Sniffin Stick testing of PD patients who recovered from olfactory deficits found a significant correlation between hyposmia and PD stage. [6, 7] Patients with HY III and more showed impaired olfactory function compared to those with HY I and II. [6]. In accordance with the UPDRS and HY classifications, odor discrimination decreased with motor disease progression. [7]. Five patients with de novo PD were examined serially using the Sniffin Stick test. An attenuated Three patients reported worsening olfactory function, while one patient experienced hyposmia. 8. Researchers found statistically significant differences between PD patients and controls in HY II, III, and IV in their olfactory function. A high percentage of asymptomatic Patients with Parkinson's disease had hyposmia in their families, with 40 out of 361 having hyposmia. One study from Germany found that two out of Two years after the onset of idiopathic hyposmia, 30 patients developed Parkinson's disease. Two patients were found to have the same disorder, according to another study (7%) developed PD after two years of follow-up.

Furthermore, the present study suggests that smell impairment may be beginning in a subset of HY I patients as well as those who have preclinical PD and hyposmia. Those in the basal ganglia who lose their dopaminergic neurons are more susceptible to dopaminergic potentiation neurons in the olfactory bulb as PD progresses. 15. A decline in Patients with Parkinson's disease and olfactory function may be attributed to such changes in the dopaminergic system. Hyposmia may be improved in patients with advanced PD due to dopaminergic The olfactory bulb has lost neurons. Olfactory function in PD patients does not always correlate with motor dysfunction, according to this hypothesis.

A single concentration of each odorant is used in the UPSIT and Sniffin Stick tests. For each odorant, there is a single response: either it is present (“yes”) or absent (“no”). There is a sensitivity and specificity increase in PD patients for wintergreen and pizza odorants on UPSIT. [16]. UPSIT is a simplified version using five types of smells (gasoline, banana, pineapple, smoke, and cinnamon) as the odorants. Several odorants have been shown to convey different sensitivities in PD patients depending on the type of odorant. [17] Previous studies have used different odorants to Differentiate normal subjects from patients with Parkinson's disease. However, although the olfactory data can be evaluated using different concentrations of odorant, no quantitative evaluation is provided by these tests.[16, 17]

Japanese scientists developed European and American conventional smell tests can be replaced by the TTO test as an alternative method of quantifying odors. Five odorants as well as several concentrations of each odorant are included in the TTO test. It is important to note that in a pilot TTO study, a Patients with Parkinson's disease showed significant differences and age-matched controls as far as total RT score is concerned; It was not possible to consider each odorant separately according to its PD stage and RT score. One pleasant and one unpleasant odorant were examined in this small study, in 10 PD patients and 10 controls. Ninety-nine patients with PD (n = 89) participated in this study were subjected to TTO examinations using five different odorants to evaluate their olfactory function. These patients were evaluated with two different kinds of odorants. It was found that

Hyposmia was reported in some HY I patients, despite the fact that there was Neither smell nor motor dysfunction are significantly correlated. It is also possible that the olfactory limbic system or the corticobasal pathway could be involved in hyposmia along with peripheral olfactory nerves and bulbs. Patients with Parkinson's disease and controls showed similar olfactory epitheliums did not show any significant histochemical abnormalities. There is a lack of knowledge about which olfactory systems are most severely damaged in Hyposmia in Parkinson's disease patients on the peripheral and central levels.

The disease HY II–IV affects PD patients have hyposmia according to this study A TTO test can be used. Quantitative The RT scores of methyl cyclopentenolone and skatol were used to measure olfactory function. In our patients, Neither the duration nor stage of the disease were correlated with these scores. Some patients with PD and HY I disease had olfactory deficits, which is of interest. Hyposmia and hypothyroidism in the HY I patients should undergo further longitudinal studies to Identify if the clinical courses are different.

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