

Smell identification scores of patients with essential tremor

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Abstract

It has been reported that patients with essential tremor have a much higher risk of Parkinson's disease; moreover, olfactory dysfunction is common in Parkinson's disease and becomes apparent early in the disease process. We aimed to investigate the olfactory function of essential tremor patients using the Short Smell Test Battery of GATA Haydarpaşa (GULTEST), which consists of five odors (banana, lemon, mint, rose, and chocolate). The participants in the study were 155 male essential tremor patients, 20–36 years of age (mean age: 21.2), and 290 male control subjects, 20–35 years of age (mean age: 21.1). The two groups were similar in terms of age, gender, and smoking history; their mean GULTEST scores were 3.41 and 3.4, respectively. Our results showed no loss of olfactory function in young male essential tremor patients.

INTRODUCTION

Essential tremor (ET) is the most common movement disorder. It is a syndrome characterized by slowly progressing postural and/or kinetic tremors, usually affecting both upper extremities, although it can also affect the head, chin, and voice. The prevalence of ET is estimated at 0.3–5.6% of the general population.^{1,2}

There has been growing interest in olfactory dysfunction in patients with neurodegenerative disorders since it was revealed that olfactory disorder is a common feature of Parkinson's disease (PD) and Alzheimer's type dementia (AD).^{3,4} In addition, ET and PD share some pathological and clinical features, and some ET patients are diagnosed with PD after a long clinical process. Both diseases can cause smell disorders, but they are more prominent in PD than in ET.⁵

Olfactory dysfunction in PD is common, and it occurs before the classical symptoms of the disease become clear.⁶ Patients with PD have profound olfaction disorder^{3,6}, and olfactory event-related potentials are often absent or delayed.^{3,7} A

pilot smell identification study involving 15 ET patients⁸ reported normal results, but a subsequent study found impairment of the University of Pennsylvania Smell Identification Test (UPSIT), which has been proposed to reflect cerebellar dysfunction.⁹ In a later study¹⁰, patients with ET and resting tremor exhibited olfactory defects, but not as severely as PD patients. However, data regarding olfaction dysfunction and ET is scarce and controversial. In this study, we aimed to re-investigate the odor identification scores of ET patients. The study population was unique in that all the participants were male and young, between the ages of 20 and 36.

METHODS

This study was approved by the Institutional Review Board of GATA Haydarpaşa Training Hospital, and informed consent was obtained from all participating subjects. The patients were recruited sequentially from clinics over 12 months. ET patients and the severity of tremor were diagnosed according to the "Washington

Heights-Inwood Genetic Study of Essential Tremor: methodologic issues in essential-tremor research” by neurologists.¹¹

Patients with psychogenic tremor or other tremor types were excluded from study, such as tremor concomitant to any severe systemic disease, metabolic diseases (e.g. hyperthyroidism), other neurological disorders than ET, psychiatric disorders, use of medications to increase tremor or drug abuse. Detailed physical examination and laboratory studies were performed for detecting and excluding the other types of tremor.

All of the subjects were asked to answer a questionnaire and provide information regarding age, education, cigarette smoking, history of congenital anosmia or acquired olfactory dysfunction due to nose surgery, recent upper respiratory illness, and severe head trauma history. Patients who answered “yes” to any of the last four questions were not included in the study. After an otorhinolaryngologic examination patients with nasal polyposis or rhinosinusitis were also not included in the study. The study subjects were administered olfactory testing.

Psychophysical testing of olfactory function

The participants were taken to the test room to be screened with the Short Smell Test Battery of GATA Haydarpa a (GULTEST).¹² To prepare the GULTEST, three layers of high-quality blotter paper were cut to fit the bases of Fonart brand airproof pallet containers, and pure odor essences were placed inside, without diluting them with water. To keep the subjects blinded to the test, the bottom of each container was marked with a number assigned to that specific odor.

The odor samples used in the GULTEST are presented in Table 1; these odors are well-known

by every segment of our society. The olfactory test scale is presented in Figures 1a and 1b. During the test, each patient was asked to smell an odor, selected randomly from the tray, for five seconds, and then name it. The answers were marked on an answer sheet. When evaluating the test results, similar names for the odors, such as “nice flower” instead of “rose” and “cocoa” instead of “chocolate,” were accepted as correct answers. For every correct answer, one point was recorded in the scoring section. The test was conducted in a ventilated, air-filtered area, in order to prevent any extraneous odors that could affect the test. The patients were not tested consecutively in the same area. The scores of the healthy participants were used to determine normal GULTEST values.

Statistical analysis

Data analysis was performed using SPSS 21.0 (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL). The normal distribution of considered variables was first evaluated using the Shapiro–Wilk test. Data were shown as mean \pm standard deviation for continuous variables and number of cases for categorical ones. Demographic data of the subjects were compared with a t test or chi-square test. A t test was used to evaluate the relationship between independent variables and grouping status (ET group or healthy group). The level of significance was set at 0.05.

RESULTS

A total of 155 ET patients 20-36 years of age (mean age: 21.2) were enrolled in the study, and 290 healthy subjects 20-35 years of age (mean age: 21.1) were chosen for the control group (Table 2). The two groups were similar in terms of age, gender, and smoking habits.



Figure 1a & 1b. Odor samples used in the study (GULTEST)

Table 1: Odor samples used for olfactory testing (GULTEST)

	Odor	Description accepted
1	Banana	Lovely fruit
2	Mint	Menthol
3	Rose	Lovely flower
4	Lemon	Orange
5	Chocolate	Cacao

There was no co-existence of movement disorders or related disabilities within the two groups. The initial symptom was tremor in 100% of the ET group, and the initial findings were 92% bilateral. Neurological examinations revealed no paresis, but two ET patients exhibited pathological reflexes. The tremor intensity distribution was 92% moderate, 5% marked, and 3% severe.

The mean GULTEST score of the ET group was 3.41, and that of the control group was 3.4 (Table 2); there was no statistically significant difference between the groups. The odor identified correctly most often by both groups was mint.

DISCUSSION

The pathophysiology of ET is not known, and no pathological findings are known to be consistently associated with ET.¹³ There is conflicting data regarding whether ET is a neurodegenerative disease, like PD, and the relationship between ET and PD is controversial. In a clinical study of 130 ET patients, Geraghty *et al.* concluded that the risk of PD in ET patients was 24 times greater than in normal controls.¹⁴ On the other hand, some studies have found no correlation between ET and PD.¹⁵

Some researchers have found olfactory deficit in ET patients, but the physiopathology is unclear. Family history is not a determinant factor for olfactory deficit in tremor-dominant PD patients, and the ranges of olfactory loss in ET patients with

rest tremor are different from those of PD patients. These factors strengthen the case for a different entity called ET-PD syndrome.^{16,17}

Classical ET is typically diagnosed without difficulty, particularly when there is a strong family history. However, there can be confusion between ET and benign tremulous PD when cogwheeling is absent or vague and, in a minority of cases, when the tremor appears to be dystonic or there is coexisting rigidity.¹⁸

In the first effort to evaluate olfaction in relation to this condition, the University of Pennsylvania Smell Identification Test (UPSIT) scores of 15 ET patients were assessed, and they were all shown to be within the normal range.⁸ A decade later, Louis *et al.* reported that a significant proportion of ET patients had mild impairment on the UPSIT⁹, leading to the suggestion that the defect might be related to the role of the cerebellum in olfactory function. However, a subsequent study of ET patients with isolated rest tremor found that their UPSIT scores were no different from those of typical ET patients.¹⁰ In accordance with the findings of Busenbark *et al.*, recent studies have found normal UPSIT scores in ET patients^{19,20}, leading to the suggestion that errors could occur if apparent ET is confused with benign tremulous PD, a condition associated with smell dysfunction. Shah *et al.* compared the UPSIT scores of 59 persons with ET to those of 64 persons with tremor-dominant PD, and a nearly complete separation of the two groups was made on the basis of the UPSIT scores and, to a lesser degree, measures from odor event-related potentials.¹⁹ Paradoxically, ET subjects with a first-degree relative family history of tremor actually scored significantly better than age- and gender-matched controls did, suggesting possible resistance to the effects of olfactory aging in these subjects.

Recently, Quagliato *et al.* conducted a study aiming to characterize olfactory identification in 40 ET patients with UPSIT, correlate UPSIT scores with clinical and epidemiological data,

Table 2: Demographic and other characteristics of the study groups

Characteristics	Normal control	Essential tremor	p value
Number of subjects	290	155	
Mean age in years	21.1	21.2	0.5
Gender	All male	All male	
Smoking history	31/65	92/155	0.2
Family history of movement disorders	None	80%	
Duration of tremor	None	4 years	
GULTEST score	3.4 ± 0.9	3.41 ± 0.88	0.87

and compare them to 89 aged-matched controls. They found that ET severity did not correlate with the UPSIT scores; rather, the study demonstrated normal olfactory identification in ET patients.²⁰

Literature support the idea that olfactory dysfunction is associated with PD and usually has its onset only a few years before the onset of PD motor symptoms.²¹⁻²⁶ One important study suggested that olfactory dysfunction was associated with an increased risk for development of PD within four years.²⁷ As known, PD is more common in older people, with most cases occurring after the age of 50. This study and the similar ones, evaluating the relationship between olfactory functions and PD or dementia, were performed in elderly individuals. In contrast to these studies, our study was performed in young individuals with ET (mean age 21.2 years) who were free of age-related neurodegeneration and according to our results we did not find a relationship between olfaction and ET in young males.

Our study had some limitations. Firstly, different from previous studies, our study population was all male. This patient composition was a result of study center. Our study was performed in military hospital, that's why the majority of the patients were young males. Female patients with ET did not reach sufficient numbers for statistical analysis. Secondly, the study group composed of individuals with a shorter duration of tremor symptoms. Therefore, one reason for not finding a significant relationship between ET and olfactory dysfunction might be the short duration of the ET disease. However, no significant relationship has been found between duration of ET and olfactory dysfunction.⁹

The participants were young male individuals, making the study group unique. The age and gender factors were not studied in terms of this subject, but this situation prevented the confounding effects of gender and age. Second, the odor battery consisted of a limited number of odors, all of which were well known by the population. However, there was no other validated smell test available for our population in our country.

According to previous publications^{28,29}, ET patients presented high familial incidence of ET (82.5%). We also found a high familial incidence (80%) in our ET patients.

In conclusion, the present findings suggest that young, male ET patients have no olfactory dysfunction, raising the question of whether or not ET is a neurodegenerative disease, like PD.

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DISCLOSURE

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