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Differences Between Essential Tremor Developing Parkinson's Disease and Essential Tremor

Parkinson Hastalığı Geliştiren Esansiyel Tremor ile Esansiyel Tremor Arasındaki Farklılıklar

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ABSTRACT

Objective: Essential tremor (ET) is the most prevalent extrapyramidal disorder and some ET patients may later develop Parkinson's disease (PD). However, up to date, precise association was not determined. To understand the relationship between ET and PD, we investigated differences between patients with ET and ET developing PD (ETPD) in terms of demographic and clinical characteristics.

Methods: One hundred forty-four patients with ET and 336 PD patients were retrospectively assessed from their clinical charts, and their current age, gender, onset age of ET, family history of ET, asymmetrical or symmetrical tremor and history of REM-Sleep Behavior Disorders (REM-SBD) were recorded.

Results: Thirty-three patients who had ET prior to PD were evaluated as ETPD patients based on previous clinical records. The mean duration from ET to PD was 12±11.4 years (range: 1-47). There was no difference in gender between the groups. The mean age, the mean age at ET onset, asymmetrical tremor and REM-SBD history were significantly lower in ET patients compared to ETPD patients. The family history of ET and head tremor was more frequent in ET patients than in ETPD.

Conclusions: Our results point out that some patients with ET, having asymmetrical tremor, late onset and REM-SBD history may develop PD. *(Archives of Neuropsychiatry 2010; 47: 101-4)*

Key words: Essential tremor, Parkinson's disease, demographic and clinical characteristics

ÖZET

Amaç: Esansiel tremor (ET) en yaygın ekstrapiramidal hastalıktır ve bazı ET hastaları sonradan Parkinson Hastalığı (PH) geliştirebilirler. Ancak bugüne kadar kesin bir birliktelik tanımlanmamıştır. Biz ET ve PH arasındaki ilişkiyi anlamak için, ET ile ET sonrası PH geliştiren hastalar arasındaki farklılıkları demografik ve klinik açıdan araştırdık.

Yöntemler: Yüz kırk dört ET ve 336 PH hastası retrospektif olarak klinik kayıtlarından değerlendirildi ve yaş, cinsiyet, ET başlama yaşı, ailede ET öyküsü, asimetrik veya simetrik tremor REM-uyku davranış bozukluğu (REM-SBD) öyküsü kaydedildi.

Bulgular: Otuz üç PH öncesi ET'si olan hasta önceki klinik kayıtlarına dayanarak ETPD hastası olarak değerlendirildi. ET'den PH'e dönme süresi ortalama 12±11.4 yıl idi (1-47). Gruplar arasında cinsiyet farklılığı yoktu. ET hastalarında ETPD hastaları ile karşılaştırıldığında ortalama yaş, ET başlama yaşı, asimetrik tremor ve REM-SBD öyküsü anlamlı olarak daha azdı. ET hastalarında ailede ET öyküsü ve baş tremoru ETPD'den daha fazla idi.

Sonuç: Bizim sonuçlarımız asimetrik tremor, geç başlangıçlı ET ve REM-SBD öyküsü olan ET hastalarının sonradan PH geliştirebileceğine dikkati çekmiştir. *(Nöropsikiyatri Arşivi 2010; 47: 101-4)*

Anahtar kelimeler: Esansiel tremor, Parkinson Hastalığı, demografik ve klinik özellikler

Introduction

Essential tremor (ET) is known to be the most common progressive movement disorder characterized by rhythmic shaking of the arms, head, tongue, limbs and voice, and its prevalence range is between 2.8% and 4% (1,2). However, there is still no definitive test or biological marker to confirm the diagnosis of ET, nor definite pathology remarks are assigned (3).

Although a clinical diagnosis of idiopathic Parkinson's disease (PD) and ET are very straightforward, to estimate what kind of ET will develop PD is difficult.

There are many studies indicating a relationship between ET and PD (4-10) and there is a risk of PD in ET patients (11). Moreover, such patients developing PD after ET were named as ETPD for a long time (7). Nevertheless, despite accepting such a relationship, there is still no definite data showing the

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differences between the patients with ET and ET developing PD (ETPD). To distinguish between ET and ETPD is important in determining the prognosis and in treatment decision-making.

We reanalyzed data related to this relationship from the literature and decided that one way to determine the relationship between ET and ETPD patients is to investigate the differences between them and aimed to compare ET and ETPD patients in terms of demographic and clinical characteristics and to find whether there is a passing from ET to PD or a risk of PD in ET patients.

Methods

One hundred forty-four patients with ET and 336 PD patients between 1996 and 2009 at Istanbul University, Istanbul Faculty of Medicine Neurology Department, Movement Disorders Unit were evaluated with their retrospective clinical records by two neurologists specializing in movement disorders. The clinical records of all patients conceived as ETPD were reviewed again and after arranging a settlement between the same neurologists were diagnosed as ETPD. At the following visit, their ETPD diagnosis was confirmed. All patients' demographic, clinical characteristics and historical data were retrospectively assessed from their clinical charts and their current age, gender, age at ET onset, family history of ET, symmetrical or asymmetrical tremor and history of REM-Sleep Behavior Disorders (REM-SBD) were recorded after his/her bed partner/informant questionnaire using the clinical criteria of the International Classification of Sleep Disorders (ICSD) (12). The demographic data and clinical characteristics of the patients are summarized in Table 1.

In our movement disorders clinic, all patients had underwent neurological examination, including UPDRS and ET evaluation at least four times in one year and in each visit all data and diagnosis for all PD and ET patients were updated. The diagnosis of PD was made according to the UK Parkinson's Disease Society Brain Bank criteria (13) and the diagnosis of ET was based on the presence of a tremor of the upper extremities and on the ET criteria (14). For ETPD patients, because of the absence of definitive diagnostic test for ET, the diagnosis of pre-existing ET had been made by either us or by referring the subjects to other medical centers, and the age of tremor onset was confirmed by self-history. Because our study was designed to investigate the differences between ET and ETPD, when describing the patients we did not determine specific ETPD features, which involve precise interval and clinic differences between ET and PD. Therefore, we did not exclude the patients, whose interval was very short or long. The patients, who were diagnosed as ET diagnosis in our Movement Disorders Unit, had no bradykinesia and rigidity, but no data were available concerning the absence or presence of other Parkinsonian symptoms in the patients referred from different medical centers. Almost all other causes for tremor, such as hyperthyroidism, medical intoxication, drug withdrawal and chronic alcoholism were excluded by the patients' history and blood tests. All ET patients had had tremor during drinking or while holding something, which had increased with stress. The presence of findings, which were thought to represent Parkinson's plus syndrome were exclusion criteria and none of the ET or PD patients had pallidotomy, thalamotomy or deep brain stimulation. Cranial computed tomography or magnetic resonance imaging was normal in all PD patients.

Statistical analyses were performed using SPSS for Windows, version 11.5 (SPSS Inc., Chicago, IL). Two-group independent t-test was performed. Significance level for all statistical methods was set at $p<0.05$.

Table 1. Demographic and clinical characteristics in ET and ETPD patients

	ET	ETPD	
Number	144	33	Significance
Gender (F/M)	68/76	20/13	p>0.05
Age (Years)			p=0.03
mean±SD	57±17.4	67±12.6	
(min-max)	(12-91)	(39-91)	
Age at ET Onset (Years)			p=0.003
mean±SD	46±19.7	55±13.8	
(min-max)	(3-87)	(29-80)	
REM-SBD History	4 (%2.8)	5 (%15)	p=0.000
Family History of ET	82 (%57)	8 (%24)	p=0.000
Asymetrical Tremor	47 (%33)	31 (%94)	p=0.000
Head Tremor	36 (%25)	0	P=0.000

Results

Of the 336 patients with idiopathic PD, 33 were evaluated as ETPD patients based on previous clinical records. All had ET prior to PD. Patients with PD having no detailed clinical records were excluded from the study due to insufficient data.

In ETPD patients, the mean total Unified Parkinson's Disease Rating Scale (UPDRS) score at the diagnosis of PD was 20±6.2 (14-26), which favored early PD.

There was no gender difference between groups. Compared to ET patients, ETPD patients were older (p=0.03). The mean duration from ET to PD was 12±11.4 (range: 1-47). The mean age at ET diagnosis was significantly lower in ET patients than ETPD patients (45.7±19.7 vs. 54.7±13.8, p=0.003). Family history of ET was more frequently seen in ET patients, in contrast with ETPD patients (24% vs. 57%, p=0.0001). We found a significantly higher risk of REM-SBD in ETPD patients compared with ET patients (15% vs 2.8%, p=0.0001). In addition, patients with ETPD had higher asymmetrical tremor than ET patients (33% vs 94%, p=0.0001). Head tremor was present in 36 (25%, p=0.00001) ET patients.

Discussion

An overlap between PD and ET has been suggested previously by many studies (4-10). However, there is no agreement among movement disorders specialists for ETPD. Determining the differences between ET patients and ETPD patients may contribute to better understanding of the underlying pathogenic mechanisms of ET and to investigating the possible existence of a subset of ET predisposing to PD.

Different data on gender in both PD and ET are available, however, male preponderance in PD (17-20) and female in ET (19,20) have been known for a long time. Contrary to two studies (10,21), investigating ETPD patients and in which male predominance was observed, and to the generally accepted idea, our finding was consistent with a more recent study reported by Spanaki et al. (22). The incidence of both ET and PD increases with advancing age (23,24,25). Nevertheless, the mean age of onset of ET is younger than PD (22). Our findings remained consistent with this evidence, because the mean age of ETPD, approximately the age accepted for PD, is greater than the mean age of ET.

Besides the increased risk of PD (11,26,28), there are some other differences between young-onset and late-onset ET. Late-onset ET have larger amplitude and lower frequency tremor (27,28) and Louis et al.(28), in very recently their study, found that rate of tremor progression was higher in late-onset ET than in young-onset and claimed that old-onset ET had more degenerative pathology.

Asymmetrical resting tremor is one of the cardinal diagnostic features of PD (29). ET, however, is characteristically symmetrical (29). This study confirms the results of previous similar clinical studies indicating that there was asymmetry in ET patients developing PD. The mechanism for differences of asymmetric and symmetric tremor in ET could not be precisely known, but can be concern for the fact that asymmetric ET may be initiator for PD.

ET patients developed PD either after very short time or after very long time. In Chaudhuri series (9) with 13 ETPD patients presenting with asymmetric postural tremor at the onset of ET, the mean latency was 19.2 years. In another study investigating ETPD patients, this mean period was 6.0 years (range: 0.5-52.0 years) (21). Similar to latter study, in our series of 33 patients with ETPD, we found very wide period from 1 year to 47 years. Whether there are different pathogenic mechanisms for short and long period is not clear and further studies are needed to clarify this issue.

In many clinical and epidemiological studies, an increased risk of ET was reported among first-degree relatives of both ET and PD patients when compared to controls (5,10,30-34). However, this risk is higher in ET patients than in PD (35). In our series, we found increased incidence for family history of ET in ET patients than in ETPD patients.

There are different data in the literature regarding the rate of ETPD patients among PD patients. A retrospective study of 100 PD patients found that only 3% had a history of ET symptoms prior to the onset of Parkinsonism (15). Only 2% of incident ET cases were later diagnosed with PD in a 45-year longitudinal study (16). In more recent studies, investigating an island population and a population-based study in Spain, this proportion was also low compared to our sample (9.8%) (11,22). This may be associated with the fact that this kind of cases are frequently referred to tertiary centers, having neurologists specializing in movement disorders.

REM-SBD is commonly associated with PD (36,37) compared to ET, but we found that it is also more prevalent in ET patients than in the population (0.5% (12) vs. 2.8%). However, when we searched the literature, there was no data regarding more frequent history of REM-SBD in ET patients. At this point the question arises whether ET patients having REM-SBD later develop Parkinson's disease. The reason that underlies this increased ratio is not clear and could be further assessed by following such patients.

It is known that head tremor is a classical feature of ET (38,39), contrary to PD (40,41). However, there is a study reporting head tremor in PD (40). Although one-fourth of ET patients had head tremor, all ETPD patients had no head tremor. This observation that head tremor in ET patients was more frequent than in ETPD patients may serve as one of rationales for confirming the links between some ET cases and PD.

This study had some limitations. Clinical records were retrospectively collected, therefore, some data might be missed. One of the strengths of this study is large sample of ETPD. Another one is that such comparison has not been used in similar studies.

In the light of our findings, we notice that special attention should be paid while establishing the diagnosis of ET, if there is asymmetry, late onset, REM-SBD in ET patients and we suggest that there might be a subtype of ET predisposing to PD.

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References

1. Louis ED, Ottman R, Hauser WA. How common is the most common adult movement disorder? Estimates of the prevalence of essential tremor throughout the world. Mov Disord 1998; 13:5-10. [Abstract] / [PDF]
2. Doğu O, Sevim S, Camdeviren H et al. Prevalence of essential tremor: door-to-door neurologic exams in Mersin Province, Turkey. Neurology 2003; 61:1804-7. [Abstract] / [Full Text] / [PDF]
3. Bhidayasiri R. Differential diagnosis of common tremor syndromes. Postgrad Med J 2005; 81:756-62. [Abstract] / [Full Text] / [PDF]
4. Yahr MD, Orosz D, Purohit DP. Co-occurrence of essential tremor and Parkinson's disease: a clinical study of a large kindred with autopsy findings. Parkinsonism Relat Disord 2003; 9:225-31. [Abstract] / [Full Text] / [PDF]
5. Louis ED, Levy G, Meja-Santana H et al. Risk of action tremor in relatives of tremor dominant PD and postural instability gait disorder PD. Neurology 2003; 61:931-6. [Abstract] / [Full Text] / [PDF]
6. Ondo WG, Lai D. Olfaction testing in patients with tremor-dominant Parkinson's disease: is this a distinct condition? Mov Disord 2005; 20:471-5. [Abstract] / [Full Text] / [PDF]
7. Geraghty JJ, Jankovic J, Zetusky WJ. Association between essential tremor and Parkinson's disease. Ann Neurol 1985; 17:329-33. [Abstract] / [PDF]
8. Shahed J, Jankovic J. Exploring the relationship between essential tremor and Parkinson's disease. Parkinsonism Relat Disord 2006; 13:67-76. [Abstract] / [Full Text] / [PDF]
9. Chaudhuri KR, Buxton-Thomas M, Dhawan V et al. Long duration asymmetrical postural tremor is likely to predict development of Parkinson's disease and not essential tremor: clinical follow up study of 13 cases. J Neurol Neurosurg Psychiatry 2005; 76:115-7. [Abstract] / [Full Text] / [PDF]
10. Barbeau A, Pourcher E. New data on the genetics of Parkinson's disease. Can J Neurol Sci 1982; 9:53-66. [Abstract]
11. Benito-Leon J, Louis ED, Permejo-Pareja F. Risk of incident Parkinson's disease and parkinsonism in essential tremor: a population-based study. J Neurol Neurosurg Psychiatry 2009; 80:423-5. [Abstract] / [Full Text] / [PDF]

12. Boeve B. REM sleep behavior disorder. Ann. N.Y. Acad. Sci. 1184 (2010) 15–54 c_ 2009 New York Academy of Sciences.
13. Movement Disorder Society Task Force on Rating Scales for Parkinson's disease. UPDRS: status and recommendations. Mov Disord 2003; 18:738-50. [Abstract] / [Full Text] / [PDF]
14. Bain P, Brin M, Deuschl G et al. Criteria for the diagnosis of essential tremor. Neurology 2000; 54:7. [PDF]
15. Cleeves L, Findley LJ, Koller W. Lack of association between essential tremor and Parkinson's disease. Ann Neurol 1988; 24:23-6. [Abstract] / [PDF]
16. Rajput AH, Offord KP, Beard CM, Kurland LT. Essential tremor in Rochester, Minnesota: a 45-year study. J Neurol Neurosurg Psychiatry 1984; 47:466-70.
17. Lyons KE, Hubble JP, Tröster AI et al. Gender differences in Parkinson's disease. Clin Neuropharmacol. 1998; 2:118-21. [Abstract]
18. Wooten GF, Currie LJ, Bovbjerg VE et al. Are men at greater risk for Parkinson's disease than women? J Neurol Neurosurg Psychiatry. 2004; 75:637-9. [Abstract] / [Full Text] / [PDF]
19. Mayeux R, Marder K, Cote LJ et al. The frequency of idiopathic Parkinson's disease by age, ethnic group, and sex in northern Manhatıootan, 1988-1993. Am J Epidemiol 1995; 142:820-7. [Abstract] / [PDF]
20. Benito-Leo´n J, Bermejo-Pareja F, Morales JM, Vega S, Molina JA. Prevalence of essential tremor in three elderly populations of central Spain. Mov Disord 2003; 18:389-94. [Abstract] / [PDF]
21. Mia T. Minen, Elan D. Louis. Emergence of Parkinson's Disease in Essential Tremor: A Study of the Clinical Correlates in 53 Patients. Movement Disorders 2008; 23:1602-12. [Abstract] / [Full Text] / [PDF]
22. Spanaki C, Plaitakis A. Essential tremor in Parkinson's disease kindreds from a population of similar genetic background. Mov Disord 2009; 24:1662-8. [Abstract] / [Full Text] / [PDF]
23. Moghal S, Rajput AH, D'Arcy C et al. Prevalence of movement disorders in elderly community residents. Neuroepidemiology 1994;13:175-8. [Abstract]
24. Louis ED, Marder K, Cote L et al. Prevalence of a history of shaking in persons 65 years of age and older: diagnostic and functional correlates. Mov Disord 1996; 11:63-9. [Abstract] / [PDF]
25. Findley LJ. Epidemiology and genetics of essential tremor. Neurology 2000; 54:8-13. [Abstract]
26. Louis ED, Ford B, Barnes LF. Clinical subtypes of essential tremor. Arch Neurol 2000; 57:1194-8. [Abstract] / [Full Text] / [PDF]
27. Elble RJ. Essential tremor frequency decreases with time. Neurology 2000; 55;1547-51. [Abstract] / [Full Text] / [PDF]
28. Louis ED, Faust PL, Vonsattel JP et al. Older onset essential tremor: More rapid progression and more degenerative pathology. Mov Disord 2009; 24:1606-12. [Abstract] / [Full Text] / [PDF]
29. Louis ED. Clinical practice. Essential tremor. N Engl J Med 2001; 345:887-91. [Abstract] / [Full Text] / [PDF]
30. Lang AE, Kierans C, Blair RD. Family history of tremor in Parkinson's disease compared with those of controls and patients with idiopathic dystonia. Adv Neurol 1986; 45:313-6. [Full Text]
31. Jankovic J, Beach J, Schwartz K et al. Tremor and longevity in relatives of patients with Parkinson's disease, essential tremor, and control subjects. Neurology 1995; 45:645-8. [Abstract]
32. Semchuk KM, Love EJ, Lee RG. Parkinson's disease: a test of the multifactorial etiologic hypothesis. Neurology 1993; 43:1173-80. [Abstract] / [PDF]
33. Lang AE, Kierans C, Blair RD. Association between familial tremor and Parkinson's disease. Ann Neurol 1986; 19:306-7.[Abstract] / [PDF]
34. Roy M, Boyer L, Barbeau A. A prospective study of 50 cases of familial Parkinson's disease. Can J Neurol Sci 1983; 10:37-42.[Abstract]
35. Louis ED, Ottman R. How familial is familial tremor? The genetic epidemiology of essential tremor. Neurology 1996; 46:1200-5.[Abstract] / [Full Text] / [PDF]
36. Boeve BF, Silber MH, Ferman TJ et al. Association of REM sleep behavior disorder and neurodegenerative disease may reflect an underlying synucleinopathy. Mov Disord 2001; 16: 622-30. [Abstract] / [Full Text] / [PDF]
37. Gagnon JF, Bedard MA, Fantini ML et al. REM sleep behavior disorder and REM sleep without atonia in Parkinson's disease. Neurology 2002; 59:585-9. [Abstract] / [Full Text] / [PDF]
38. Bain PG, Findley LJ, Thompson PD et al. A study of hereditary essential tremor. Brain 1994; 117:805-24. [Abstract] / [PDF]
39. Benito-Leon J, Louis ED. Clinical update: diagnosis and treatment of essential tremor. Lancet 2007; 369:1152-4. [Abstract] / [Full Text] / [PDF]
40. Roze E, Coelho-Braga MC, Gayraud D et al. Head tremor in Parkinson's disease. Mov Disord 2006; 21:1245-8. [Abstract] / [Full Text] / [PDF]
41. Gan J, Xie-Brustolin J, Gervais-Bernard H et al. Possible Parkinson's disease revealed by a pure head resting tremor. J Neurol Sci 2009;279:121-3. [Abstract] / [Full Text] / [PDF]