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Evaluation of the presence of re-emergent tremor and its effect on clinical features in Parkinson's disease

Mumune Bozdag Kiraz[a], Nevra Oksuz[a,*], Okan Dogu[a]

[a]*Mersin University, Faculty of Medicine, Department of Neurology, Mersin, Türkiye*

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Abstract

Aim: Re-emergent tremor (re-t), an examination finding specific to Parkinson's disease (PD), is a type of postural tremor that occurs after a period of time when the arms are extended forward. Its frequency and severity are similar to the resting tremor seen in PD. In our study, it was planned to investigate the incidence of re-t in PD, its latency, the severity of motor and non-motor symptoms in patients with re-t, and whether there is a difference with patients without re-t.

Materials and Methods: 72 Parkinson's patients diagnosed according to Queen Square Bank diagnostic criteria were included in the study. The patients were divided into two groups as those with and without re-t. Hoehn-Yahr (H&Y) Scale, Unified Parkinson's Disease Rating Scale (UPDRS), Nonmotor Symptoms Scale (NMMS), Montreal Cognitive Assessment Scale (MoCA), and Geriatric Depression Scale (GDS) were applied to all patients. All patients were evaluated at on-period and re-emergent latency was measured with a stopwatch.

Results: Re-t was observed in 17 patients, mean re-t latency was 9.3±4.4 seconds and severity was 2.2±1.2. No difference was observed between the two groups in terms of H&Y stage, UPDRS, and NMMS scores. Similarly, no difference was found in MoCA and GDS scores.

Conclusion: Different from the literature, in this study PD patients with and without re-t were compared with GDS and MoCA tests for the first time, and similar cognitive impairment and depression were found between the two groups. This study showed that the course of PD was similar in patients with and without re-t.

Introduction

Parkinson's disease (PD) is a neurodegenerative disease with cardinal symptoms of resting tremor, bradykinesia, rigidity, and postural instability. Parkinsonian tremor classically occurs at rest, but also postural tremor can also occur in many patients. Resting tremor is the classic tremor seen in PD with a frequency of 3-7 Hz. Resting tremor is the initial finding in 70-80% of patients. Clinical observations describe re-emergent (re-t) tremor, which is thought to have mechanisms similar to resting tremor [1]. Re-t is a finding specific to PD that was first described by Jankovic and is known to resemble resting tremor [2,3]. Postural tremor in PD are heterogeneous in appearance and re-t is a type of postural tremor that occurs after the arms are extended forward, is also seen in PD [4]. Approximately two-third of PD patients have re-t [5]. PD and essential tremor (ET) may co-exist frequently and may be confused with postural tremor re-t seen in ET [4]. It can be distinguished from postural tremor observed in ET, with its frequency similar to resting tremor and its latency (the onset of tremor after posturing). The mean latency of re-t varies between 8-10 seconds, and its prevalence varies between 38.2% and 75% [2,3,6,7]. Re-t is also similiar to the typical rest tremor in PD. They share many features such as 3 to 5-Hz frequency, and good response to dopaminergic therapy [8]. Since PD is complex diseases accompanied by motor and non-motor symptoms, PD patients with and without re-t have been compared in many studies using UPDRS, H&Y, and Standardized Mini Mental Test (SMMT). However, no difference was found between the two groups [3,9].

In this study, it was aimed to investigate the clinical characteristics of patients with re-t and to compare their clinical features with patients without re-t. For this purpose, GDS and MoCA were applied to the patients. 72 Parkinson's patients were included in the study. The patients were divided into two groups as those with and without re-t.

*Corresponding author:
Email address: nevraoksuz@mersin.edu.tr (Nevra Oksuz)

H&Y Scale, UPDRS, NMMS, MoCA, and GDS were applied to all patients.

Materials and Methods

In our study, 72 patients who applied to the movement disorders outpatient clinic of Mersin University Hospital between January 2017 and July 2017 and were diagnosed with PD according to Queen Square Brain Bank Criteria were included. Patients younger than 18 years of age and who had cerebrovascular disease, normal pressure hydrocephalus, Parkinson's plus syndromes, and secondary parkinsonism were excluded. Before the study, the G*Power program was used to determine the sufficient number for statistical analysis. After reviewing the literature, it has been determined that at least 70 patients need to be included with 80% power and type I error, to obtain a difference of 0.27 units between the two groups. A random selection was made among Parkinson's patients who admitted to our clinic. Disease severity was evaluated with the H&Y scale and UPDRS, while NMSS was used for non-motor symptoms, GDS for mood assessment, and the Turkish version of the MoCA (MoCA-TR) for cognitive functions.

GDS consists of 30 questions in total. Patients are asked to answer "Yes-No" by asking "How they have felt in the last week?" and the evaluation is carried out over a total of 30 points. In the scoring criteria, 0-10 points are defined as "no depression", 11-13 as "probable depression" and above 14 as "definite depression". The MOCA scoring consists of 7 parts. In part 1, visual-spatial/executive functions (0-5 points), In part 2, naming (0-3 points), In part 3, attention (0-6 points), In part 4, language (0-3 points), In part 5, abstract thinking (0-2 points), In part 6, memory (0-5 points), In part 7, orientation (0-6 points) were evaluated. The lowest score that can be obtained from the scale is 0, and the highest score is 30 [10,11]. The H&Y scale evaluates the disease in 5 stages according to its clinical features. As the stage progresses, the severity of the disease increases. UPDRS consists of four parts. Patients are evaluated using the examination method consisting of 4 questions for mental functions, behavior and affect in the first part, 13 questions for daily living activities in the second part, 16 questions for the motor examination in the third part, and 3 questions for the treatment complications in the fourth part. NMSS consists of 30 questions in total. The frequency of non-motor symptoms was evaluated over the 0-4 points and the severity was evaluated over 1-3 points. The frequency and severity points obtained are multiplied then result was evaluated over a total of 360 points.

Similar to previous studies, to evaluate re-t, patients were asked to rest for 60 seconds in a sitting position, then extend their arms forward and stay in the same posture for 90 seconds. Tremor occurring after at least 1 second was defined as re-t [12]. Two groups were formed as re-t and non-re-t. All patients were evaluated in ON periods. In patients with re-t, latency (time between arm extension and the onset of tremor) was recorded in seconds. The severity of re-t was graded in the range of 0-4 according to UPDRS3. The kinetic tremor was evaluated with finger-nose and finger-finger tests 15 times for each side. Mersin University ethics committee approval and written consent were obtained from all participants for the study (2017/49).

Statistical analysis

In descriptive statistics; numbers and percentages are given for quantitative variables, the mean and standard deviation values are given for qualitative variables. Shapiro-Wilk test was used to control the normality of continuous variables. Comparison of normally distributed features in 2 independent groups was evaluated with Student's t test, and comparison of non-normally distributed features in 2 independent groups was evaluated with Mann Whitney U test. Chi-Square test was used in the analysis of categorical data. For data entry and analysis, we used the TIBCO Statistica version.13.5.0.17 program The results are given as 95% confidence intervals (CI), and $p<0.05$ was considered significant.

Results

In our study, 72 PD patients were included and re-t was detected in 17 patients (23.6%). In the group with and without re-t, the mean age was 64.6±12.3 and 61.6±12.2, respectively. No difference was found between the two groups in terms of age ($p=0.461$) and gender ($p=0.174$). In the group with and without re-t disease duration, 7.3±3.2 and 6.1±4.3 were found, respectively, and this difference

Table 1. Initial symptoms of PD.

Initial symptom	Non-Re-t group (n,%) (55.76.3%)	Re-t group (n,%) (17.23.6%)	Total (n,%) (72.100%)
Pain	1 (1.8%)	0 (0%)	1 (1.4%)
Bradykinesia	17 (30.9%)	1 (5.9%)	18 (25%)
Falls	1 (1.8%)	0 (0%)	1 (1.4%)
Weakness	1 (1.8%)	0 (0%)	1 (1.4%)
Tremor	33 (60.0%)	15 (88.2%)	48 (66.7%)
Paresthesia	1 (1.8%)	1 (5.9%)	2 (2.8%)
Gait disturbance	1 (1.8%)	0 (0%)	1 (1.4%)

Table 2. H&Y, UPDRS, NMSS, GDS, MoCA-TR scores.

	Re-t group Mean±SD (median) n=17	Non-Re-t group Mean±SD (median) n=55	P*
H&Y scale	2.4±1.1 (2)	2.4±0.9 (2)	0.699
$UPDRS_1$	12.8±6.0 (12)	15.1 6.2 (14)	0.144
$UPDRS_2$	12.4±9.1 (10)	9.5 7.8 (7)	0.140
$UPDRS_3$	25±12.5 (20)	19.9±8.3 (17)	0.93
$UPDRS_4$	0.2±0.7 (0)	1.2±3.0 (0)	0.105
$UPDRS_{total}$	50.9±22.5 (45)	45.9±17.6 (41)	0.524
NMSS	93±61.4 (78)	86.1±46.5 (80)	0.776
GDS	12.9±6.7 (13)	13.2±8.4 (12)	0.979
MoCA-TR	19.1±5.7 (21)	18.7±5.2 (19)	0.568

H&Y: Hoehn-Yahr, UPDRS: Unified Parkinson's Disease Rating Scale NMSS: Nonmotor Symptoms Scale, GDS: Geriatric Depression Scale (GDS), MoCA-TR: Turkish version of Montreal Cognitive Assessment Scale, *P<0.05 was accepted as significant.

was not statistically significant (p=0.364). Tremor was the most common symptom in the group with and without re-t, and was observed as the initial symptom in 15 (88%) and 33 (60%) patients, respectively. Initial symptoms are shown in Table 1. In the group with re-t; The mean re-t latency was 9.3±4.4 seconds, and the mean severity was 2.2±1.2. Tremor was detected on the right side in 41.2% of the patients with re-t, on the left side in 35.3%, and bilateral in 23.5%.

H&Y scores were found to be 2.4±1.1, 2.4±0.9 in the group with and without re-t, respectively, and UPDRStotal scores were 50.9±22.5, 45.9±17.6. There was no significant difference between the two groups in terms of the H&Y scale, UPDRS, NMMS, GDS, and MoCA-TR scores (Table 2).

The number of patients with a GDS score of ≥14 was 7 (41.1%) in the group with re-t and 26 (47.3%) in the group without re-t, and this difference was not statistically significant (p=0.288). The number of patients with a MoCA-TR score <21 was found to be 9 (52.9%) and 20 (36.4%) in the group with and without re-t, respectively (p=0.223).

Discussion

In the study of Jankovic et al., 66.7% of 18 tremor-dominant PD patients and in the study of Mailankody et al, 38.2% of 63 tremor-dominant PD patients had re-t [2,3]. In the other two studies with larger patient groups, this rate was found to be 75% and 81%, respectively [6,13]. In this study, the re-t rate was 23.6%. We think that this rate is lower than other studies because Parkinson's patients were included without tremor-dominant discrimination. The mean re-t latency ranged between 8-10 seconds in previous studies [2,3,14]. Similarly, in our study, it was found to be 9.3±4.4 seconds.

Similar to previous studies, the H&Y stage was not different in the group with and without re-t. Belvisi et al. in his study, the UPDRS3 scores differed in the group with and without re-t [3,12]. However, Aytürk et al. and Mailankody et al. found no difference between the two groups in terms of UPDRS scores similar to our results [3,9]. In this study, NMSS scores were not different between the two groups. Similar results were obtained in previous studies [3,14,15]. This finding showed that the presence of re-t did not affect nonmotor symptoms in PD. Again, in the study of Mailankody et al., SMMT scores did not differ between the two groups [3]. We, on the other hand, used MoCA-TR and we did not find any difference between the two groups in terms of MoCA-TR scores. The fact that the rate of cognitive impairment was close to the expected rate in PD suggested that re-t did not affect the cognitive functions of the patients. Depression is seen at a rate of approximately 50% in PD [16,17]. We could not find any study in the literature comparing groups with and without re-t in terms of depression. In our study, depression was found in 41.1% of patients with re-t and 47.3% of patients without re-t. This made us think that the risk of developing depression is not higher in patients with re-t than in those without.

As a result, no difference was found in the groups with and without re-t in terms of H&Y stage, UPDRS, and NMMS scores. In addition, different from the literature, GDS and MoCA-TR tests were used for the first time, and similar rates of cognitive impairment and depression were detected between the two groups. This study showed that the course of PD was similar in patients with and without re-t.

Conclusion

Re-t is a clinical feature of PD that is still up-to-date and continues to be researched. We investigated the nature of postural tremor and the effect of the presence of re-t on the clinic of PD. We did not find any difference, but the limited sample size may have caused insignificance. New studies to be conducted in a larger patient population will contribute to this issue.

Ethical approval

Ethical approval was obtained from Mersin University Clinical Research Ethics Committee for this study (Date: 23.02.2017 Decision number: 49).

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