ORIGINAL ARTICLE

Difference of Disability Between Electrophysiologic Subgroups of Essential Tremor*

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ABSTRACT: ***Objective:*** The aim of the study was to test the validity of the controversial subdivision of essential tremor (ET) patients into electrophysiological subgroups. ***Methods:*** We evaluated a hundred patients with ET using surface electromyographic (EMG) recordings of antagonist forearm muscles and distinguished three groups: the first group showed synchronous activity of antagonistic muscles, the second showed alternating activity of antagonist muscles; and the third group consisted of patients whose EMG recordings were not compatible with the other two groups. We compared patients with synchronous and alternating activity in terms of sex, age at onset, duration of illness, family history of tremor, symmetry and frequency of tremor, and the scores of a disability scale. ***Results:*** The only significant difference between the patients with synchronous and alternating activity was that the patients with synchronous activity were more disabled. ***Conclusion***: This result adds to the evidence for distinct electrophysiological subgroups of ET with distinct clinical properties.

RÉSUMÉ: Différences dans le degré d'invalidité entre des sous-groupes électrophysiologiques de patients présentant un tremblement essentiel. ***But:*** Le but de cette étude était d'évaluer la validité d'une subdivision controversée des patients présentant un tremblement essentiel (TE) en sous-groupes électrophysiologiques. ***Méthodes:*** Nous avons évalué cent patients présentant un TE au moyen d'enregistrements électromyographiques (ÉMG) de surface des muscles antagonistes de l'avant-bras et nous les avons divisés en trois groupes. Le premier groupe avait une activité synchrone des muscles antagonistes alors que le second avait une activité alternante des muscles antagonistes. Le troisième groupe était composé de patients dont l'enregistrement ÉMG n'était pas compatible avec ceux des deux autres groupes. Nous avons comparé les patients présentant une activité synchrone à ceux qui présentaient une activité alternante quant au sexe, à l'âge de début, à la durée de la maladie, à l'histoire familiale de tremblement, à la symétrie et à la fréquence du tremblement ainsi qu'au score à l'échelle d'invalidité. ***Résultats:*** La seule différence significative entre les patients présentant une activité synchrone et une activité alternante était que les patients présentant une activité synchrone avaient un degré d'invalidité supérieur à ceux qui présentaient une activité alternante. Conclusion: Ces observations sont en faveur de l'existence de sous-groupes électrophysiologiques distincts, avec des caractéristiques cliniques distinctes, chez les patients atteints de TE.

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Essential tremor (ET) is a common neurological disorder with slow progression over years, characterized by tremor under postural and action conditions without additional severe neurological findings and complaints.[1] In the last two decades there have been attempts to classify ET on the basis of agonist-antagonist muscle interaction and other electrophysiological data with the hope of identifying subgroups with good responses to specific drugs.[2] Several authors have reported findings suggesting that ET could be categorized into two types: one with synchronous, and the other with alternating activity of antagonist muscles.[1,2,3,4] This classification of ET has been criticized and it is now generally accepted that such classification is not yet possible,[5,6] but the controversy still goes on.[2]

The aim of this study was to further investigate whether ET can be categorized into subtypes with synchronous and alternating contractions of antagonist muscles on the basis of clinical variables.

Materials and methods

A hundred consecutive consenting ET patients from the movement disorders clinic, whose duration of tremor was at least three years, were included in the study. We used the diagnostic criteria for definite ET proposed by the Tremor Research Investigation Group (TRIG)[7] as follows: 1) Presence of postural tremor in the arms that worsens with action, in the absence of any condition or drug known to cause enhanced physiologic tremor,

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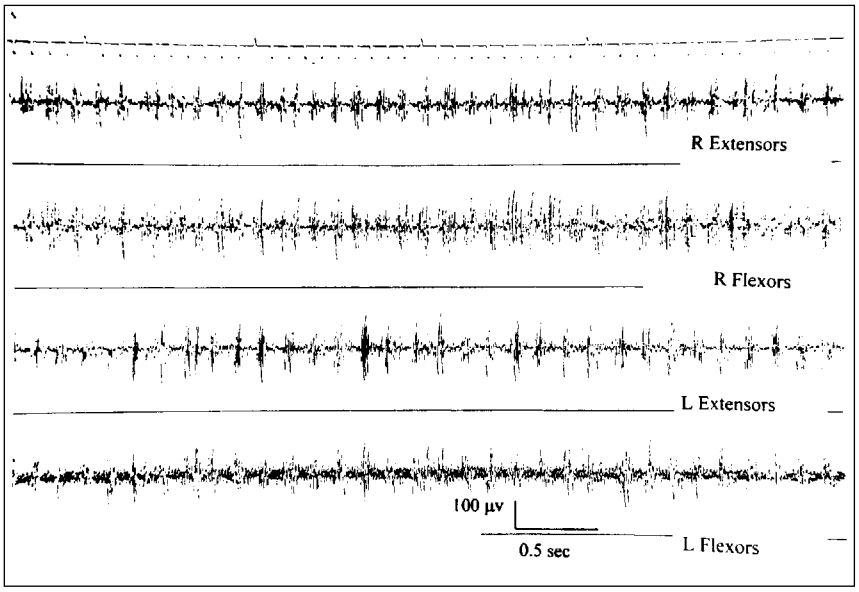

Figure 1: *Synchronous activity of antagonist muscles of forearm. R: Right, L: Left*
Note the simultaneous contraction of flexors and extensors

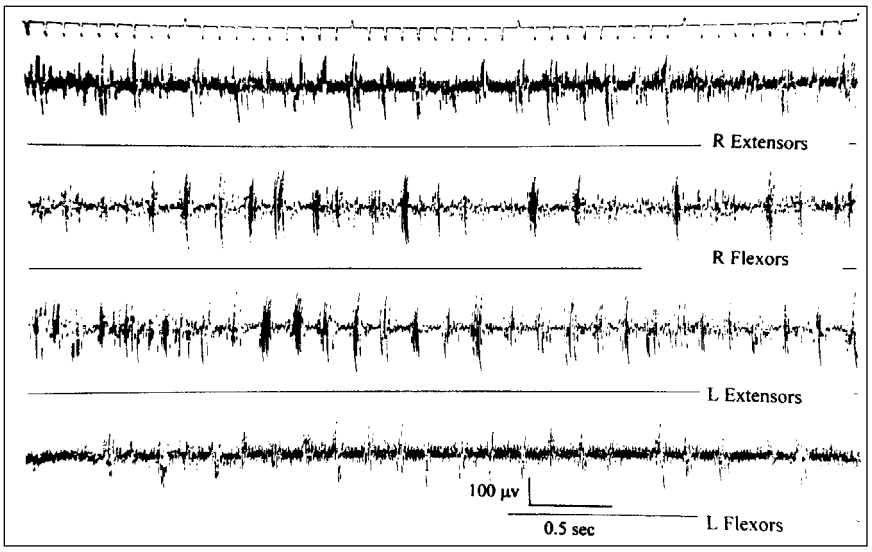

Figure 2: *Alternating activity of antagonist muscles of forearm. R: Right, L: Left*
Flexor and extensor muscles contract one after another

in the absence of cerebellar symptoms and signs, and in the absence of Parkinson's disease, dystonia, hyperthyroidism, chronic alcoholism, peripheral neuropathy, and an anxiety state, or 2) Postural tremor of the arms without action tremor, plus head (neck) tremor, in the absence of cerebellar symptoms and signs, and in the absence of Parkinson's disease, and dystonia.

The EMG recordings were made with a San-ei EEG 1A96 electroencephalograph, using 1-cm diameter Ag-AgCl surface electrodes from the extensor and flexor surfaces of the forearm in regions where optimum traces were obtained. The region where optimum traces was obtained frequently occurred on the extensor surface, to the distal end of the proximal one third of the distance between lateral epicondyle and radial styloid process (while the forearm was in pronation); and on the flexor surface, to one or two centimeters lateral aspect of the point on the distal end of the proximal one third of the distance between medial epicondyle and ulnar styloid process. The reference electrode was placed four centimetres distal to the active one. Crosstalk between extensor and flexor muscle groups was avoided by having the patient extend her/his wrist voluntarily and observing the continuous EMG activity from the extensor surface, provided that the recording from the flexor surface was silent. The opposite manoeuvre and the observations were done for wrist flexion. The myoelectric signals were band-pass filtered (53 to 3000 Hz).

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During the recording procedure the patients were seated with their arms outstretched horizontally in pronation. The recordings were made from both hands simultaneously. The recording sessions consisted of three periods each lasting ten minutes separated by ten-minute intervals without recording. Three groups were distinguished in terms of the phasic relationships of antagonist muscles: the first group showed only synchronous activity, the second showed only alternating activity, and the third consisted of patients without a uniform activity pattern in both arms throughout the recording session. We evaluated the patients with only synchronous or only alternating activity during all three recording periods (Figures 1 and 2). We did not include the third group in the analysis for reasons explained below.

Tremor frequency was calculated as the average frequency of tremor-related EMG bursts on three epochs of one-minute duration.

Family history of tremor was accepted to be present when there was at least one first degree relative with symptoms suggesting ET.

Each patient completed a self-questionnaire to document the extent of his or her tremor-induced disability. The questionnaire consisted of an inventory of 25 activities of daily living each scaled from 0 (able to do the activity without difficulty) to 4 (cannot do the activity by yourself). The version of the scale adapted for patients with tremor by Bain et al[8] was used. Patients always filled in the questionnaire form with the help of a study physician who was blind to the neurophysiological results to avoid the inappropriateness of the fact that the rating scale lacks Turkish standardization.

Data were analyzed to disclose any association between the two groups of patients having only synchronous or only alternating activity with respect to gender, family history of tremor, age of onset, disease duration, symmetry of tremor, the impact of tremor to activities of daily living, and tremor frequency.

Table 1: Clinical and neurophysiological characteristics of patients with synchronous and alternating activity of antagonist muscles.

	Synchronous	Alternating	Total
n	25	23	48
Gender (male/female)	14/11	13/10	27/21
Mean Age	54.4±16	51.7±18.2	53±17
Mean Age of Onset	46.8±16	45.6±19.7	46.1±18
Mean Disease Duration	7.6±9	6.1±4.6	6.9±6.8
Family History of Tremor Present/Absent	12/13	12/11	24/24
Tremor Symmetric/Asymmetric	15/10	13/10	28/20
ADL* Rating Scale Score**	49± 16	40± 10	45± 14
Mean Frequency (Hz)	7.4 ±1.3	7.7± 1.5	7.5± 1.4

*ADL: Activities of daily living.

** Significant difference, Mann-Whitney U, p=0.03.

The means of different groups were compared by Mann-Whitney U, and Fisher's exact test was used in the analysis of nominal variables.

Results

Forty-eight of 100 patients had either only synchronous or only alternating activity. Table 1 shows the clinical and neurophysiological characteristics of the patients.

There was no difference between the groups with synchronous and alternating activity in terms of sex, age at onset, duration of illness, family history of tremor, and symmetry and frequency of tremor.

The only significant difference between the groups of patients with synchronous or alternating activity was that the tremor-induced disability of the patients with synchronous activity was higher than that of the patients with alternating activity (Mann-Whitney U, p=0.03) (Table 1).

Discussion

Alternating activity of antagonist muscles in a trembling limb is characteristic of Parkinsonian rest tremor, while synchronous muscle activity is associated with ET.[3]

Patients with ET might also have alternating activity of antagonist muscles, and these patients could constitute a subgroup with different clinical, pharmacological, and neurophysiological characteristics. Table 2 shows the characteristics of ET patients with synchronous and alternating activity of antagonist muscles.

The clinical significance of classifying ET according to EMG patterns of antagonistic muscles has been questioned for three reasons:

1) The phasic relationship of antagonist muscles could not always be defined as synchronous or alternating, since there are patterns that reside somewhere between synchronous or alternating activity.[2,11]
2) The presence of either synchronous or alternating patterns has been shown to vary from patient to patient, from task to task, from minute to minute, and could even be different in the right and left hand of the same patient at the same time.[2,12]
3) In a relatively large series (61 patients), neither synchronous nor alternating pattern correlated significantly with other clinical or neurophysiological characteristics of ET.[5]

We designed the present study taking the criticisms mentioned above into consideration. Elble[11] and Boose et al[2] reported intermediate patients who did not show exclusively synchronous or alternating activity, and indeed such intermediate patients constituted 52% of patients in our study. We evaluated the patients with *only* synchronous or *only* alternating activity, thinking that these represented the extremes of the spectrum (if such grouping exists), so any associations would be stronger and easy to detect.

To detect and exclude patients whose contraction pattern changed with time, we used a long recording period (3 x 10 minutes). This is longer than the 3 x 6 minute-long period of Elble,[11] which he said was atypically long. We also recorded from both arms simultaneously and excluded the patients who show different types of contraction patterns in different upper extremities.

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Table 2: The characteristics of reported patients with essential tremor with synchronous and alternating activity of antagonist muscles.

Reference	Characteristic	Synchronous	Alternating
Shahani and Young[3]	Percent	95%	5%
		No clinical differences	
Sabra and Hallett[4]	Number of patients		12
	Frequency		Low
	Propranolol response		Poor
Deuschl et al[1]	Number of patients	18	13
	Long latency reflexes	Normal	Enhanced LLRI*
	Frequency	High	Low
	Propranolol response	Good	Poor
Hsu et al[9]	Percent	73%	27%
	Burst duration	Not mentioned	Short
	Amplitude	Not mentioned	Low
	Propranolol response	Good	Poor
Koguchi et al[10]	Number of patients	10	9
	Frequency	High	Low
	Silent period following PS**	Normal	Prolonged
	Type of tremor	Postural only	Postural + rest
	Beta blocker response	Good	Poor
	Primidon response	Not studied	Good
	Hypothesized mechanism	Peripheral	Central
Boose et al[2]	Number of patients	6	2
	Amplitude	Low	High
Deuschl et al[6]	Number of patients	58	
	Age	Younger	Older
	Sex preponderance	Male	Female
Present Study	Number of Patients	25	23
	Disability	High	Low

*LLR I: Long latency reflex I.
**PS: Peripheral stimulation

One disadvantage of the present study is the relative lack of objectivity of the visual inspection method (when compared with computerized techniques) that was used to categorize the phasic relations of antagonistic muscle groups; however, the method has been used effectively in similar studies.[1,3,4,5]

The only statistically significant difference between patients with synchronous or alternating activity was that the average activities of daily living score was higher in patients with synchronous activity (Table 1). Only Koller et al[5] evaluated patients with a functional disability scale. They found no difference in disability between the patients with different phase relationships. This discrepancy with the present results may be due to two methodological differences:

1) We evaluated patients with synchronous and alternating activity of antagonist muscles, and we did not include the patients with flexor-only contractions, while Koller et al[5] included patients with flexor-only contractions as a third group.
2) Koller et al[5] assessed tremor using three ratings (a self-reporting disability scale, a motor task/function rating, and a scale of tremor severity). They did not mention if they analyzed only the total score or if they also analyzed the disability subscore separately.

It has been shown that voluntary movement in tremulous patients always begins simultaneously with an EMG burst of tremor.[13] In patients with synchronous activity of the antagonistic muscles, both the agonists and antagonists contract at the same time on the initiation of voluntary movement, without reciprocal inhibition of the antagonist muscle group. This probably makes the performance of the movement more

difficult and might render the patient disabled. On the other hand, reciprocal inhibition of the antagonist muscles is possible for patients with alternating activity, since the agonists and antagonists do not contract at the same time. Voluntary movement, therefore, takes place more easily than in patients with synchronous contraction of the antagonist muscle groups.

Conclusion

ET patients with synchronous contractions were more disabled than patients with alternating contractions. We think this result contributes to the evidence for distinct electrophysiological subgroups of ET, with distinct clinical properties.

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