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Research Article

Electrophysiological Assessment of Essential Tremors' Severity by accelerometer: Frequency Domain Approach

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ABSTRACT

Background: Evaluation of tremors is critical in the management of essential tremors, starting from early diagnosis to initial medication and follow-up. Clinical rating scales, accelerometry, or electrophysiology can be used to determine the severity of tremors. However, clinical assessments are self-administered and may be influenced by intra- and inter-evaluator differences in experience and small changes in tremor severity.

Objectives: to demonstrate whether accelerometers are a valuable method for assessing patients with essential tremors.

Subjects and Methods: In the postural position, hand tremor was recorded using a unidirectional piezoelectric accelerometer placed on the dorsum of the index finger for 60 seconds. Fourier (spectral) analysis was used to determine the amplitude and frequency of the tremors.

Results: Significant correlations between log tremor amplitude and the Essential Tremor Rating and Assessment Scale were found.

Conclusions: unidirectional piezoelectric accelerometers can be used to objectively assess the intensity of essential tremors on routine basis, which may aid in treatment adjustment.

Introduction

The most prevalent type of tremor is the essential tremor, which has a frequency of (4 to 8 Hz) lower than the physiologic tremor and is unrelated to other neurologic alterations; Thus, it is named "essential." Typically, it is at the lower end of this frequency range and fluctuates. Essential tremor, like many other tremors, is exacerbated by emotion, exertion, and fatigue. The intensity of essential tremor may progress to the extent where the patients handwriting becomes unreadable (1) and they cannot bring a spoon or glass to their lips without spilling the contents. Eventually, all manual dexterity-required jobs become difficult or impossible (2). The Essential Tremors Rating and Assessments Scale (TETRAS) is extensively used clinical tool for assessing and quantifying the severity of the essential tremor. It contains a clinician-rated performance scale for determining the severity of tremors, which can be evaluated in amplitude or impact on a prescribed task such as hand-writing or draw a spiral shape (4,5).

The TETRAS scale is administered by a doctor who observes the patient's limbs in various postures and physical tasks. The physician rates the limb displacement caused by tremor on a scale of 0 to 4 (with a higher number indicating a more significant amplitude tremor) (5). While TETRAS is a robust and effective clinical instrument for diagnosing kinetic and postural tremors, like all clinician-reported outcomes, exhibits high inter and intra rater variability due to different experiences and individual differences in tremor interpretation and

perception (3). The reliability and validity of tremor scales vary (6,7). Even the most sensitive and objective clinical scales may be insensitive enough to detect mild abnormalities and exact changes of tremor severity or objective sufficient to see meaningful therapeutic responses, while the graphic evidence of tremor activity can be analyzed clinically by studying written or drawn spiral lines, (8) which are still subjectively perceived and are difficult to standardize across patients. Thus, the objective and quantifiable data analysis afforded by digitalised assessment of tremors can be an essential tool for research and specific clinical settings (9). The amplitude and frequency are the primary characteristics of each tremor type, which are used to classify and grade the severity of a human tremor
(10) The pathophysiological cause mainly determines the frequency of tremors. The tremor amplitude is variable in both short and long term and is also affected by disease progression and treatment efficacy (11). Accelerometry is widely considered as the gold standard since it objectively assesses tremor frequency and amplitude (13,14). The majority of published studies agree that the accelerometer-collected tremor signals stationary. The frequency and amplitude of tremors are frequently determined in the frequency domain using Fourier (spectral) transform methods (FFT, PSD) (14,15). For instance, the tremor frequency is defined as the prominent peak in the PSD, and the tremor amplitude is inferred from the area beneath this peak.
This study compares a unidirectional piezoelectric accelerometer-based method with (TETRAS) for clinical assessment and quantification of essential tremor severity.

Subjects and Methods

Forty-five patients (25 men) with postural tremors participated in the study at the neurophysiology unit in Ghazi Al-Hariri Hospital in Baghdad after informed written agreement was taken from all patients, the study was approved by a local ethical committee of the medical college/University of Baghdad according to Declaration of Helsinki. All patients had a prior diagnosis of classic essential tremor, as defined by the Movement Disorder Society in 1998 (16). The inclusion criteria were that the individual must be over 18 years old and is able to walk independently without assistance. Cardiologic illnesses and other conditions impairing mobility were excluded as an exclusion criterion. Hand tremor was graded on a scale of 0 to 4 by a movement disorders specialist using (TETRAS), which is based on the following tremor estimates:

- Grade 0; no visible tremor
- Grade 1; slight, amplitude >0.5 cm
- Grade 2; Moderate, amplitude 0.5 to >2.5 cm
- Grade 3; marked, amplitude 2.5 to 5 cm
- Grade 4; sever, amplitude<5 cm

To record a tremor signal in a postural position, the patient is sat comfortably on a special chair with both hands pronated and resting on the armrests, allowing the hands-free in the air to quantify hand tremor. This position is crucial to isolate the hand tremor from any other limbs movement that could potentially contaminate recordings of the accelerometers. Regarding the amplifier setup, a 2 Hz highpass and a 30 Hz lowpass filter were used for the accelerometer (17). A small unidirectional piezoelectric accelerometer was attached to the index finger of the hand, which exhibited a more severe tremor during the 60-second recording. The patient was informed to extend his wrist against the gravity while pronating his forearm that should be rested on the armrest and the hand extended beyond armrest. The obtained data will be a time series illustrating the change in acceleration over time. The signal will then be translated from the time domain to the frequency domain using Natus (KEYPOINT.NET) Software v. 2.40's Fourier (spectral) transformation (FFT, PSD). The prominent peaks in the accelerometry spectrum (frequency domain) corresponds to the tremor's frequency, and the amplitude is determined using the area beneath the peak. The relationship between (TETRAS) and the tremor amplitude was determined using the linear regression analysis using IBM's SPSS v25 software. Regression was performed with log10 transformation of the tremor amplitude or without it, (19) To acertain which relationship produced the best linear fit (greatest r2 and homoscedasticity).

Results

The patient's mean age was 43.20 ± 13.83 years (20–76 years). In addition, 85 percent of these individuals reported right-hand dominance. Eighty percent of subjects had a positive family history of tremor in a first-degree relative. Twenty patients were taking medication, including beta-blockers (10 patients), primidone (7 patients), and others (3 patients). Table 1 summarizes the patient's demographic characteristics.

Table 1: Demographic, clinical, and tremor measurement data collected from patients with Essential Tremors.
SD: standard deviation; TETRAS: Essential Tremors Rating and Assessments Scale

Number of patients	45
Gender (Male/Female)	25/20
Age (mean ± SD)	43.20 ± 13.83
Disease duration ± SD (years)	10.36 ± 6.98
Mean TETRAS scale ± SD	2.47 ± 1.14
Mean frequency (Hz)	7.20 ± 1.79
Mean amplitude(µv/√Hz)	7.48 ± 7.06

The forty-five patients evaluated had the following distribution of tremors ratings: 12 patients with TETRAS 1, 11 patients with TETRAS 2, 11 patients with TETRAS 3, and 11 patients with TETRAS 4. In 35%, there was a one-grade asymmetry between the hands, with the rightmost severely affected 90% of the patients. Two of the patients with asymmetry were lefthanded and had a more severe tremor in their left hand. The results of the study for each rating are summarized in Table 2. As the tremor becomes more severe, the tremor spectral peak becomes a more prominent component of the amplitude spectrum. Figure 1 illustrates examples of FFT amplitude spectra. Scatter plots (dots) revealed a nonlinear relationship between tremor amplitude and TETRAS scores when tremor amplitude was not log 10 transformed. However, when tremor amplitude was log 10 transformed, a significant correlation between TETRAS scores and the logarithm of tremor amplitude was observed ($r=0.97 p>0.001 n=45$), as illustrated in figure 2. The frequency of tremors was negatively correlated with the tremor score ($r = -0.87 p<0.001 n=45$). These values remained constant when log 10 of the peak frequency was used.

Table 2: Hand tremor frequency and amplitude corresponding to clinical rating scores

Rating score	Tremor type	Mean log10 amplitude ± SD	Mean frequency ± SD
TETRAS 1	Postural	0.34 ± 0.27	9.28 ± 0.96
TETRAS 2	Postural	0.56 ± 0.09	7.97 ± 0.70
TETRAS 3	Postural	0.84 ± 0.07	5.90 ± 0.93
TETRAS 4	Postural	1.23 ± 0.13	5.44 ± 0.74

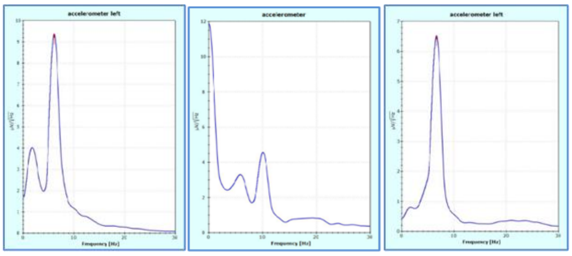

Figure 1: Representative amplitude spectra for a patient with TETRAS 2(left), TETRAS 3 (middle), and TETRAS 4 (right). Thisspectra were computed with an FFT. Amplitude is plotted versus frequency. The tremor spectral peak becomes a high dominant part of the amplitude spectrum with increasing tremor severity.

Figure 2: Linear regression and 95% confidence limits showing. a significant correlation between the TETRAS and the logarithm of tremor amplitude, Tremor amplitude was computed with an FFT. Without log10 transformation, the tremor amplitude and TETRAS relationships were nonlinear and heteroscedastic, with increasing variance in tremor amplitude with high TETRAS.

Discussion

In this study, we presented the method for assessing hand tremor using a unidirectional piezoelectric accelerometer placed on the index finger. This method allows us to determine tremor frequency and amplitude in the frequency domain using Fourier (spectral) analysis. The logarithmic relationship between accelerometer measures of amplitude of tremor and tremor ratings is predicted by the wellknown Weber Fechner law of psychophysics. (18,20) The smallest observable change in tremor, ΔT, is ΔT=K·T1, if T1 is the beginning amplitude of tremor and K is Weber's constant. It is logarithmically associated with a five-point tremor rating scale. These technologies have the ability to make the evaluation of tremor parameters more objective, Additionally, there is a strong association between the amplitude and frequency of tremors—which are often spectrally quantified using Fourier or Wavelet transformation—and clinical ratings, (21). We found that a unidirectional piezoelectric accelerometer is a highly accurate method for quantifying essential tremor. The logarithm of tremor amplitude was found to be a strong predictor of clinical tremor scores (19). Therefore, transforming instrument-based tremor data logarithmically plays an essential role as untransformed data didn't strongly correlate with tremor disability. (20) At least two factors could account for this occurrence. Instrumental measures, particularly those sensitive to three-dimensional movement within a volume, scale with tremor severity exponentially, whereas rating scales scale linearly. Additionally, all rating scales have a maximum value, whereas instrumental measures continue to increase even after the maximum clinical rating score is reached. The logarithmic transformation certainly provides general compensation by establishing a more linear relationship between these nonlinear variables. Furthe rmore Different from clinical rating scales, accelerometry offers a quantitative evaluation of upper limb tremors and has become a typical method for measuring tremors in clinical trials. It does, however, offer a precise means of determining two tremor indices: the magnitude (root mean square acceleration) of the primary peak in a spectrum and its frequency (22). Furthermore, we suggest that the application of artificial intelligence could facilitate the more precise application of unidirectional piezoelectric accelerometers in the evaluation of essential tremor for accurate results and to manage large amounts of data (23).

The weak ponit of the study is the lack of a control group and the small number of patients recruited. However, the total number of participants was sufficient to obtain adequate statistical evaluation.

Conclusion

This paper present that severity of essential tremors can be quantified validly during a postural task when the data are logarithmically transformed using automatic machine approach using accelerometer. Furthermore, we suggest that the method described here can help to facilitate clinical research by improving tremor evaluation with a highly accurate method, follow-up, and treatment adjustment. This method could be also very useful application to support the decision of clinicians that made according to the routine subjective clinical rating scales.

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Conflict of Interest

Authors declare no conflict of interest.

Data availability

Data are available upon reasonable request.

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