Differentiating tremor patients using spiral analyses*

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Abstract— **Essential tremor follows an autosomal dominant type of inheritance in the majority of patients, yet its genetic basis has not been identified. The age of onset in this tremor is bimodal, one in young age and another when they are old. The old onset is referred to as senile tremor in this study. The precise pathology is still not completely understood for both these tremors. We wanted to develop an easy diagnostic tool to differentiate these two tremors clinically. In this study, the spirals were asked to be drawn by 30 patients, 15 from each group. The spirals were recorded digitally from each hand, with and without the spiral template, using a Wacom intuos version 4 tablets. The aim of the study was to look at the easy diagnostic measures from these spirals to distinguish the two cohorts of patients. The first measure was to use the well-known clinical scores like the number of complete circles without the template, width, height, axis, and degree of severity. The second measure was to estimate the peak frequency and the peak amplitude for the position, velocity, and acceleration data, in the frequency domain. The well-known clinical scores, most of them, did not show any significant difference between the two patient cohorts except the degree of severity which showed significant difference. The peak frequency and the peak amplitude in most of the data were not significantly different between the two cohorts of patients, only the peak amplitude from the acceleration data showed significant difference. Thus, we could use these two parameters to differentiate between the two tremors patient groups, which would be an easy clinical diagnostic tool without the need for any complicated analyses.**

I. INTRODUCTION

Essential tremor (ET) is the most common movement disorder. From clinical experience and epidemiological studies we know that it follows an autosomal dominant type of inheritance in the majority of patient [1, 2]. The old onset type of tremor, namely, the senile is not much discussed in the tremor literature. The pathophysiology of ET tremor has been largely discussed earlier with EEG or MEG correlates being coherent with the tremor oscillations [3, 4]. The spiral analysis has been looked up in earlier studies for essential tremor [5] and other tremors [6]. The parameters like the spiral width variability index (SWVI), height, and axis have been extensively studied in essential tremor [7-9]. All the above parameters have shown reasonable accuracy in differentiating essential tremor patients from other tremor patients. The degree of severity has also been looked up in essential tremor and dystonia patients [10] which has also shown good accuracy in discrimination. However, the peak frequency and the peak amplitude have not yet been looked up in detail in these tremors. So, to search for the best parameter and to have an easy diagnostic tool for distinguishing the two cohorts of tremors, we tested all the above parameters. The spirals can be easily recorded in these patients and it is not a cumbersome process like EEG or MEG recordings. The distinction of these tremors with these non-complicated analyses could help us in building a robust diagnostic tool for clinical usage. Most of the above studies have used the parameters SWVI, height, and axis, which have been analyzed using human intervention and the values were estimated by experienced neurologists. However, it would be nice to have more data-driven approach without any human intervention like the frequency domain analyses used in this study. We therefore looked at both of these approaches to see whether they complement each other or we get some additional information that supplements the well-known clinical scores.

II. METHODS

A. Data Acquisition

In this study, nine female and six male with senile tremor (ST) were included. The mean age of the patients was 76.3±5.31 years. In the case of essential tremor patients, we included six female and nine male with a mean age of 62.3±11.1 years. The study protocol used was approved by the local ethics committee and all patients have signed a written consent regarding the procedure. We collected in total eight spirals from each patient, four from the right hand and four from the left hand. In those four spirals, two of them were with the template of the spiral boundaries as shown in Figure 1 (with template) and the other two spirals without template as shown in Figure 1 (without template), with patients seated comfortably at a digitizing tablet. The tablet used was Wacom intuos version 4. This tablet has a resolution of 2540 points per inch, an output rate of 200 points per second which translates into 65-70 Hz per axis. It has 2048 levels of measurable pressure and can collect spiral

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data in a virtual tri-axial setup $(X, Y, \text{and pressure})$. A writing pen is held in a normal fashion without constraints to allow the most clinically meaningful results. Eight spirals were collected for both hands and all tracings were monitored on-line for error control. The eight spirals were drawn on A4 size white papers and were documented for visual analysis.

B. Spiral analysis

All the parameters with the visual interpretation were checked by the two independent reviewers (KL and MM) from the data, namely, the number of spirals which was the first parameter for the ones without the template, for each hand as shown in figure 1. The number of spirals was counted with full circles. So, in this case (without template), for the left hand it will be 6 and for the right hand it will be 4. The second and the third parameter was the width and height of the spirals (without template), in centimeters, measured from the documented spirals for each patient, respectively. The fourth parameter was the axis for looking at the nature of the spirals (without template) as shown in figure 1. For the left hand it was 30° (equivalent to number 2 in a clock) and for the right hand there was no specific axis direction, so it is 0° (equivalent to number 12 in a clock). The fourth parameter which is the degree of severity (DOS), we need first to estimate some mathematical indices, namely, the first and second-order smoothness, tightness, and first and second order zero crossing. Initially, the freely drawn spiral was transformed into a linear format. An ideal spiral can be written as follows:

$$x = a\theta \cos(\theta + c) \tag{1}$$

$$y = a\theta \cos(\theta + c) \tag{2}$$

Where x, y are the Cartesian co-ordinates, a is a constant parameter, θ is an angle parameter and c is a constant representing the initial angle. The polar expression of an ideal spiral can be defined as follows:

$$r = a\theta \tag{3}$$

Where $r = \sqrt{x^2 + y^2}$. This transformation into a linear relation between r and θ gives us the starting point for the further analysis of the spirals. The first order smoothness can be defined by how close the linear transformation remained to its own mean and this can be mathematically written as follows:

$$i_1 = \frac{1}{\Theta}\sum\left(\frac{\Delta r}{\Delta\theta} - \bar{r}_\theta\right)^2 \left|\Delta\theta\right. \tag{4}$$

$$I_1 = \ln i_1$$

Where I_1 is the first index, which is the natural logarithm of the equation (4); Θ is the total angular change; $\bar{r}_\theta$ is the average slope of $r \sim \theta$; and $\Delta\theta$ is the difference operator reflecting discrete changes caused by the sampling in the digitizing tablet. The second order smoothness is obtained by taking the first derivative which can be expressed as follows:

$$i_2 = \frac{1}{\Theta}\sum\left(\frac{\Delta\frac{\Delta r}{\Delta\theta}}{\Delta\theta} - d\bar{r}_\theta\right)^2 \left|\Delta\theta\right. \tag{5}$$

$$I_2 = \ln i_2$$

Where $d\bar{r}_\theta$ is the average slope of $\frac{\Delta r}{\Delta\theta} \sim \theta$.

The next index is the tightness which can be defined by the number of turns of the spirals over its total angular change within a 10-cm square, normalized to 7 (or 14π because of each full loop = 2π), and to the largest radius, R which can be written as:

$$I_3 = \left(\Theta/R - 14\pi\right)/2\pi \tag{6}$$

The zero-crossing rates are the measures of how frequently the linear transformation $\Delta r/\Delta\theta$ crosses its own mean indicating the irregularity of the spiral and can be written as follows:

$$I_4 = \frac{1}{2(J-1)}\sum_{j=1}^{j-1} sign\left(\frac{\Delta r}{\Delta\theta}\Big| j+1 - \bar{r}_\theta\right) - sign\left(\frac{\Delta r}{\Delta\theta}\Big| j - \bar{r}_\theta\right)\cdot 100\,\% \tag{7}$$

Where j is the total number of points collected, $sign$ is a Sign function defined by:

$$y = sign(x) = \begin{cases} 1 & x > 0 \\ 0 & x = 0 \\ -1 & x < 0 \end{cases} \tag{8}$$

The second-order (first derivative) zero-crossing rate can be written as follows:

$$I_5 = \frac{1}{2(J-1)}\sum_{j=1}^{j-1} sign\left(\frac{\Delta\frac{\Delta r}{\Delta\theta}}{\Delta\theta}\Big| j+1 - d\bar{r}_\theta\right) - sign\left(\frac{\Delta\frac{\Delta r}{\Delta\theta}}{\Delta\theta}\Big| j - d\bar{r}_\theta\right)\cdot 100\,\% \tag{9}$$

These indices with the most significant, highest r^2, and lowest residuals $I_2, I_3, and\ I_5$ were then used to define a "degree of severity", which is a clinically relevant score ranging from 0-4:

$$DOS = 0.4615 \times I_2 + 0.0544 \times I_5 - 0.2331 \times I_2^2 - 0.0726 \times I_3^2 - 0.001 \times I_5^2 + 0.2539 \times I_2 \times I_3 + 1.3668 \quad (10)$$

All the measured parameters were statistically tested for significance, between the two cohorts of patients, using a non-parametric Mann-Whitney test with significant difference identified with (p < 0.05).

The linear transformed signals were taken as time series for the estimation of the power spectrum using the Welch periodogram method [11]. In this method the spectral estimate $\hat{P}(f_n)$ is the average of the periodograms and can be written as:

$$\hat{P}(w_L) = \frac{1}{M}\sum_{n=0}^{M-1}\left|A_w(n)e^{-jwn}\right| \quad (11)$$

Where L is the length of the segments, and M is the number of segments into which the time series were epoched, and $A_w(n)$ can be written as follows:

$$A_w(n) = w(n)\cdot A(n) \quad (12)$$

Where w is the window used to estimate the spectrum. After estimating the spectrum the maximum peak frequency and the corresponding peak amplitude was estimated for each of the spirals. Finally, the mean and standard deviation was calculated over all the patients in each group.

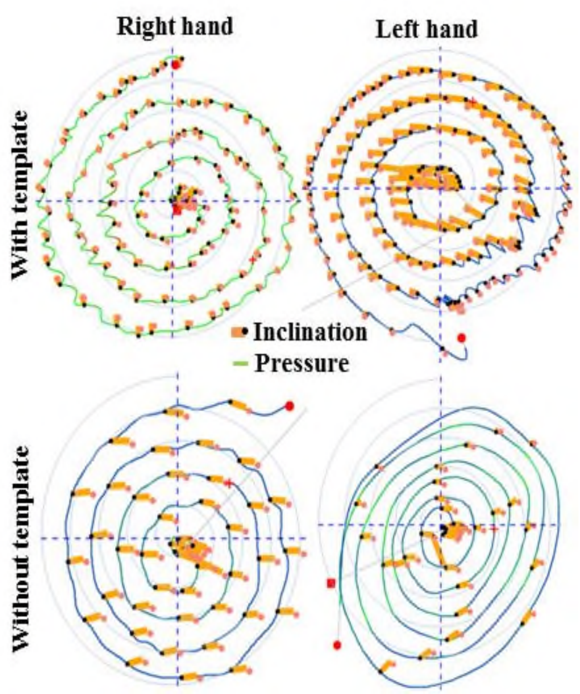

Figure 1. Shows the spirals from a single essential tremor patient. The first colum shows the spirals for the right hand and the second column for the left hand. The firt row shows the spirals with the template and the second row shows the spirals without the template. The blue bold lines are the drawn spirals, green lines represent the pressure exerted, and the black dots with the orange cubes show the inclincation of the pen at those points. The red dots indicate the beginning and end of the spiral drawing.

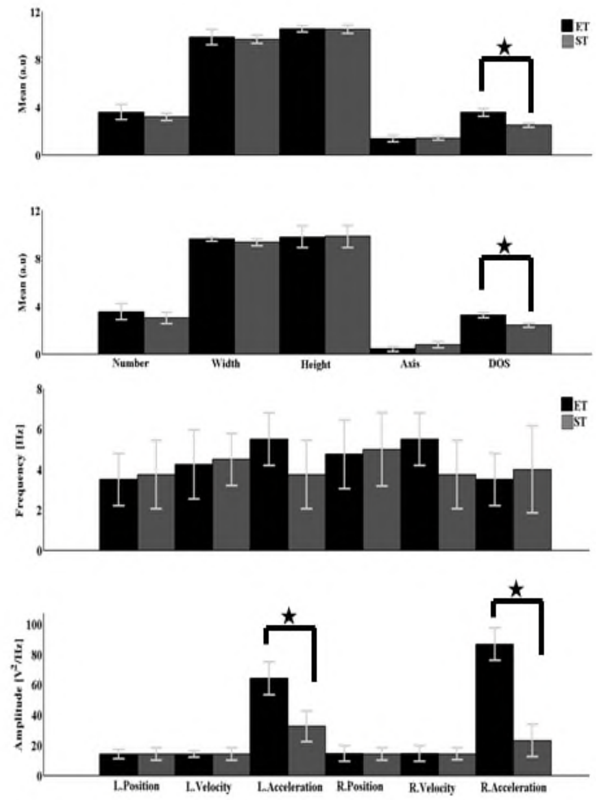

Figure 2. The first subpplot (left hand) shows the results from the parameters measured with the spirals without template, namely, the number of spirals, width, height, axis, and degree of severity. The second subplot shows the reults from the parameters for the right hand. The third (peak frequency) and fourth (peak amplitude) subplots are parameters measured from the spiral with the template. The mean and standrad deviation are shown for the data taken from the poistion, velocity, and aceeleration. The asteriks (*) shows the parameters which showed significant difference(s) between the two cohorts of patients.

III. Results

A. Clinical and data-driven results

The clinical estimated parameters, namely, the number of spirals for the left hand (p = 0.67) and right hand (p = 0.24) did not show any significant difference between the two cohorts of patients. The width for the left hand (p = 0.78) and right hand (p = 0.59) followed by the height for the left hand (p = 0.57) and right hand (p = 0.69) also did not show any significant difference. The parameter axis was also not significantly different between the two patient groups for both the left hand (p = 0.46) and right hand (p = 0.38). However, the degree of severity showed significant differences between the two group pf patients for the left hand (p = 0.014) and right hand (p = 0.035). In essential tremor patients, the degree of severity was higher compared to the senile tremor patients. In case of the peak frequency, none of the three recorded data, namely, the position (Left Hand L: p =0.78; Right hand R: p =0.57), velocity (Left Hand L: p =0.54; Right hand R: p =0.49), and acceleration (Left Hand L: p =0.38; Right hand R: p =0.49) were significantly different. The peak amplitude was also not significantly different for the position (Left Hand L: p =0.62; Right hand R: p =0.84), and the velocity (Left Hand L: p =0.84; Right hand R: p =0.47), between the two patient groups. However, the peak amplitude for the acceleration data (Left hand L: p = 0.009; Right hand R: p = 0.006), showed significant differences between the two patient groups. In both hands, the peak amplitude was higher for the essential tremor patients compared to the senile tremor patients.

IV. Discussion

The spiral analyses using degree of severity, axis, width, and height have shown good accuracy in classifying essential tremor patients from other tremor patients [2, 5, 6]. In this study, we have looked into these parameters for our group of patients and found out that the degree of severity could be the optimal parameter for differentiation. The additional analyses using the peak frequency and the peak amplitude have also shown us that they are also useful parameters which can be extracted from these data. The peak amplitude from the acceleration data looks like an optimal parameter for the classification. The limitation of the study is the limited number of patients from each group. For the future study, in order to introduce both the above parameters as diagnostic tools, we need to test them in larger cohorts. These parameters can be used to quantify motor dysfunction in patients with variety of movement disorders [10].

In conclusion, the spiral analyses can be an easy diagnostic tool in differentiating these two patient groups. However, all the parameters should be tested with larger cohort of patients.

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