Application of machine learning and numerical analysis to classify tremor in patients affected with essential tremor or Parkinson's disease

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N.D. Darnall, C.K. Donovan, H-Y. Tseng, P. Barthelmess, P.R. Cohen, D.C. Lin, Application of machine learning and numerical analysis to classify tremor in patients affected with essential tremor or Parkinson's disease. Gerontechnology 2012; 10(4):208-219; doi:10.4017/gt.2012.10.4.002.00 The overall goal of this study was to compare the accuracy of various data analysis techniques to quantify tremor severity (TS) in a clinical context, with the aim of improving the reliability (context consistency and inter-rater agreement) of tremor evaluation in patients with Parkinson's disease (PD) or essential tremor (ET). Ten patients with either PD or ET were asked to perform several tasks used in the clinical practice for the characterization of tremor. Three-axis gyroscopes in a Shimmer device measured angular velocities of the wrist of each subject for postural, kinetic, spiral tracing, and resting scenarios, and a digital pen recorded subjects' tracings of an Archimedes spiral printed on paper. Gyroscope data were used for training and testing a supervised machine learning algorithm to classify TS and for root mean squared (RMS) numerical rating of TS, while digital pen data were analyzed numerically to quantify tracing deviations from the spiral and obtain a tremor rating. We evaluated the performance of our proposed methods compared to clinicians' diagnostic rating. The machine learning method matched the clinical rating with 82% accuracy, the digital pen with 78% accuracy, and RMS with 42% accuracy. We obtained the best accuracy of 82% using the decision tree machine learning approach with gyroscope data measured with the Shimmer.

Keywords: tremor rating, spiral trace, digital pen, gyroscope, machine learning

Tremor can be defined as a rhythmic shaking and involuntary rhythmic movements of body segments. It occurs in healthy individuals, as so-called physiological tremor[1]. Tremor is composed of two oscillations, mechanical reflex and central neurogenic, which are superimposed on a background of irregular and involuntary fluctuations in muscle forces and displacements[2]. In patients with neurological disorders, tremor is clinically described as rest, postural, and kinetic tremor. Rest tremor appears during resting while postural tremor is triggered by maintenance of a posture or a position against gravity. Kinetic tremor is evoked by a voluntary movement and is maximal while near the movement target[1].

Parkinson's disease (PD) is a progressive neurodegenerative disorder. The motor symptoms of PD include rest tremor, bradykinesia, and rigidity, and these develop gradually during the progression of the disorder[3]. Motor (such as tremor) and non-motor (such as memory loss) PD impairments can be rated from a combination of self-reporting and subjective clinical assessments within different scales[4], including Unified Parkinson's Disease Rating Scale (UPDRS), Hoehn and Yahr Scale (HY), and Short Parkinson's Evaluation Scale (SPES). The severity ratings of these scales range from 0-4 (UPDRS), 1-5 (HY), and 0-3 (SPES)[5].

Essential tremor (ET) is a neurological disorder with no known cause and is characterized by postural and kinetic tremor[6]. The tremor can affect almost any part of the body, but it occurs most often in the hands, especially when the patients are maintaining a given posture or executing tasks, such as drinking from a glass, tying shoelaces, writing or shaving.

Tremor severity (TS) in ET or PD is commonly rated clinically using the Fahn-Tolosa-Marin Tremor Rating Scale (TRS), which is on a scale of 0 to 4[7]. The rating is based upon the clinician's observation of tremor location and amplitude, the patient's ability to perform motor functions (such as writing and drawing), and the patient's self-report of their functional disability resulting from tremor[8]. One of the most widely used clinical procedures for measuring the severity of arm tremor is tracings of Archimedes spirals[9]. Patients with tremor show irregularity with swerves compared to individuals without tremor[10].

More objective assessments of tremor have been made by quantitative measurement of tremor characteristics[11-13]. Namely, tremor frequency varies by both tremor type and tremor location. Rest tremor frequency is typically in the 3–6 Hz frequency range[3]. The frequency of postural tremor is between 4 and 12 Hz. Kinetic tremor has a frequency between 2 and 7 Hz. Mechanical-reflex tremor depends on limb inertia and joint stiffness. For example, normal elbow tremor occurs at 3-5 Hz while wrist tremor has a natural frequency of 8-12 Hz due to the lower inertia of the hand[14]. Arm and leg tremor frequency are 5.2 Hz and 3.8 Hz respectively[15]. Postural and kinetic wrist tremor in PD patients have a prominent coherence peak at 5-8 Hz, which is distinguishable from the 8-12 Hz peak of healthy controls[16]. These findings suggest a need to identify specific parameters through which assessment of tremor is independent of different types of tremor and of different body segments.

A general problem with the clinical rating of TS is the subjectivity due to inter-rater and patient self-reporting variability[17,18]. Inter-rater reliability for the TRS in ET patients has a Kappa statistic of k=0.53 (k=1 means complete agreement and k=0 means no agreement) for postural and action tremor and k=0.41 for handwriting[8]. Quantitative measurement of tremor is objective and context independent and could improve this low reliability. However, the bridge between these measurements and the commonly-used TRS clinical scale has not been well established.

Quantitative data collected during standard clinical tests have been used to classify on, off, and dyskinetic states in PD patients[19] or to classify the UPDRS score[20]. However, these methods require lengthy procedures for the patient and measurements from many different sensors and body segments. A link between quantitative data and clinical ratings specifically for tremor assessment would not have these drawbacks and still provide clinicians valuable information. Therefore, the study aim was to capture objective tremor data, quantify TS from the data, and assess the ability of different computational methods to classify TS by matching them to clinical diagnostic assessments.

Material and methods

Participant description

This study was approved by Washington State University Institutional Review Board (IRB). Patients signed both informed consent (IC) and The Health Insurance Portability and Accountability Act (HIPAA) authorization forms. Ten participants were selected at the clinics, Northwest Neurology and Inland Neurosurgery and Spine, three of which exhibited a history of ET, six of which exhibited a history of PD, and one of which exhibited a history of both PD and ET. Presence of predominant postural tremor in addition to a resting tremor, as observed in this last patient, has been described as a co-occurrence of PD and ET[21]. Two thirds of the patients were female. All patients had Deep Brain Stimulation (DBS) implants. 20 data sets were gathered; ten in which the participants performed tasks with DBS on, and ten in which they performed the same tasks with DBS off. Although some patients used various medications to treat their PD motor symptoms, information regarding their medication type, dosage, and medication schedule was not considered relevant to the purpose of this study. Clinicians rated TS for each patient with DBS on and again for the

Table 1. Comparison of tremor rating method results of patients taking part in the study; DBS=Deep brain stimulation; ET=Essential tremor; PD=Parkinson disease; SWSU=Shimmer wireless sensor unit; TRS= Fahn-Tolosa-Marin Tremor Rating Scale

Patient	Disease	DBS	Ratings			Rating errors		
			Spiral	SWSU	Clinician (TRS)	Spiral-clinician	SWSU-clinician	Spiral-SWSU
1	PD	off	4	2	1	3	1	2
1	PD	on	0	0	0	0	0	0
2	ET	off	2	2	3	-1	-1	0
2	ET	on	2	1	2	0	-1	1
3	PD&ET	off	0	1	1	-1	0	-1
3	PD&ET	on	1	1	1	0	0	0
4	PD	off	1	0	1	0	-1	1
4	PD	on	1	1	1	0	0	0
5	PD	off	1	1	1	0	0	0
5	PD	on	1	0	1	0	-1	1
6	PD	off	0	1	0	0	1	-1
6	PD	on	1	0	1	0	-1	1
7	PD	off	no data	4	0	no data	4	no data
7	PD	on	1	1	1	0	0	0
8	PD	off	1	1	1	0	0	0
8	PD	on	1	0	0	1	0	1
9	ET	off	2	2	4	-2	-2	0
9	ET	on	1	0	1	0	-1	1
10	ET	off	4	3	4	0	-1	1
10	ET	on	4	2	4	0	-2	2

same patient with DBS off, prior to each set of tasks each patient performed. Clinically rated TS ranged from 0-4 with mean TS of 1.40 for all patients under all conditions; 0-4 with mean TS 1.20 for DBS on, and 0-4 with mean 1.45 for DBS off (note TS is only rated on an integer scale in these methods). Participant description is listed in parallel to study results (*Table 1*).

Clinicians' tremor rating method

Immediately prior to performing each set of tasks for this study, each patient was evaluated by a clinician who rated their current clinical TS based on the TRS. A total of three clinicians participated in rating individual patients; one neurosurgeon and two nurse practitioners. Participants were asked to perform four tasks using their dominant hand while seated. Tasks included repeatedly extending the arm full length then touching nose five times, holding hand at full horizontal extension for five seconds, resting hand in lap for five seconds, and tracing a spiral print. During the spiral trace task, the patient traced a clinician-supplied spiral with a standard pen using the dominant hand. Clinicians established the clinical TS score on a scale from 0-4 for each patient at each condition (DBS on and DBS off) based on the patient's performance on the tasks as described in the TRS[5].

Deep brain stimulation device

A DBS device is a surgically implanted electronic device that emits low voltage pulses into the brain[21,22] and has been shown to reduce tremor[23,24]. For each patient, a clinician customizes the voltage, pulse width, electrode configuration, and frequency of the DBS signal to minimize tremor[25,26].

A clinician adjusted the settings of each participant's DBS device to optimally reduce tremor prior to tasks participants performed with their DBS device turned on. Clinicians determined the optimum DBS setting by changing the setting, then observing the change in the clinical tasks used to classify TS. A lower TS score was interpreted as resulting from a more optimal DBS setting. DBS settings were not recorded because the effect of DBS on tremor is not a primary topic of interest in this study.

Hardware and software

Four hardware devices were incorporated in this study: a gyroscope (an angular velocity sensor) contained in a Bluetooth wireless Shimmer unit, an Anoto digital pen, a laptop computer equipped with a Bluetooth receiver, and DBS devices specific to each patient. Data were collected from the Shimmer device via a Bluetooth link to the laptop, while the digital pen transmitted data to the laptop via a USB interface. Software used in the study included National Instruments Labview software, Weka machine learning tool, Adapx Capturx digital pen software, and Microsoft Excel.

The selection criteria for the Shimmer device were: low cost, wireless, containing a 3 axis gyroscope, lightweight, and small size. The Shimmer Wireless Sensor Unit (SWSU)[27] is lightweight (15g) with a small form factor (50x2x12.5mm) suitable for PD and ET patients. The SWSU also supports wireless communication through Bluetooth and 802.15.4 radio.

Digital pen

Adapx's Capturx™ system for digital paper and pen integrates standard digital pen technology with standard office software applications. Similar technology has been used in the medical field to quantify physical impairment of drivers under the influence of alcohol[28]. The pen records all the X-Y coordinates that it traverses and uploads the data to a computer via a USB interface.

Experimental procedure

Participants with the SWSU strapped to their wrist were asked to perform the same set of four tasks used in the clinical evaluation. Each set was performed twice by each participant: once with their DBS device on, once with it off. A period of 5 to 10 minutes between the first task (DBS on) and the second task (DBS off) was allowed for any residual effects of the DBS to wear off. Turning the DBS device off resulted in a visible resting tremor in PD patients, which was allowed to continue for about 2 minutes before beginning the second task.

Machine learning

Six classifiers were used: Random Forest, Decision Tree, Nearest Neighbor (NN), Bayes, Multilayer Perceptron (MLP), and Support Vector Machine (SVM). In a decision tree classifier, entropy is measured as:

$$\text{Entropy}(S) = -p_+ \log_2 p_+ - p_- \log_2 p_- \qquad (1)$$

where S is the set of data points, "p_+" is the number of data points that belong to the positive class and "p_-" is the number of data points that belong to the negative class.

The information gain for each attribute is described by the equation:

$$\text{Gain}(S,A)=\text{Entropy}(S)-\sum_{v\in \text{Values}(A)} \frac{|S_v|}{S} \text{Entropy}(S_v) \qquad (2)$$

where Values(A) is the set of all possible values for feature A. Gain(S,A) measures how well a given feature separates the training examples according to their target classification[29]. We used the J48 decision tree provided with the Weka software distribution to classify TS.

Random Forest is an ensemble classifier that consists of many decision trees and outputs the most popular class. A tree is grown from independent random vectors using a training set, resulting in a classifier. After a large number of trees is generated, random forest outputs the class that is the mode of the class's output by individual trees[30].

NN calculates instances using Euclidean distance and correspond to points in an n-dimensional space. The algorithm assigns a class label to a data point that represents the most common value among the k training examples nearest to the data point[31]. We used the IBK scheme from Weka with parameter n=1 in our experiment.

SVM maximizes the margin between the training examples and the class boundary. SVM generates a hyperplane which provides a class label for each data point described by a set of feature values[32].

Artificial Neural Networks (ANNs) are computational models mimicking a neuronal organizational structure[33]. ANNs are built from an interconnected set of sample units, which takes a number of real-valued inputs and produces a single real-valued output[31]. Using back propagation, ANN minimizes the squared error between the network output and target values. We applied this technique by using Weka's MLP algorithm to classify TS.

Naïve Bayes Classifier is a probabilistic classifier which assumes the presence of a particular feature of a class is independent of other features. It learns a classification label by mapping features with Bayes' theorem:

$$\text{argmax}_{t_i \in T} P(t_i|F)=\frac{P(F|t_i)P(t_i)}{P(F)} \qquad (3)$$

where T represents the tremor class label and F represents the features values. $P(t_i)$ is estimated by counting the frequency with which each target value t_i occurs in the training data. P(F) is calculated from the frequency of feature values. Based on the simplifying assumption that feature values are independent given the target values, the probability of observing the features is the product of the probabilities for the individual features[34].

Signal analysis

The SWSU signal processing overview (*Figure 1*) shows that data were gathered for three axes: yaw (perpendicular to the arm with positive pointing away from the back of the hand), pitch (perpendicular to the arm with positive pointing to the right), and roll (aligned with the arm with positive pointing away from the body). The gyroscope range for each axis is +/- 500°/s. The raw gyroscope data for each axis, in °/s, the power spectral density (PSD) for each axis, in $(°/s)^2$ / Hz, the peak frequency and magnitude for each axis, the RMS value for each axis and the TS were recorded by the computer.

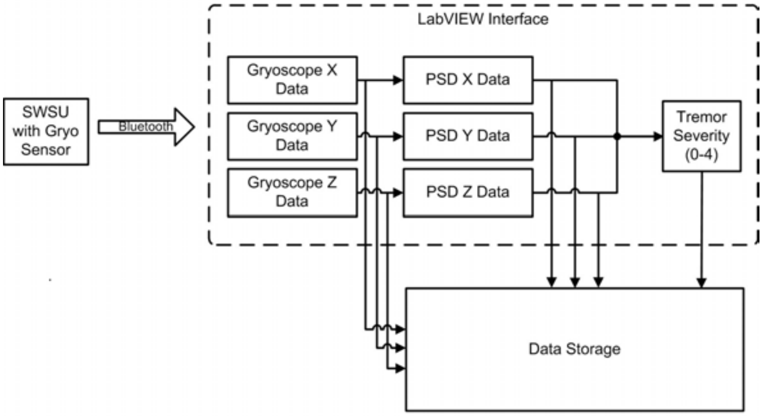

Figure 1. Shimmer wireless sensor unit signal processing

features over 10 samples. As an alternate approach, we considered each data feature as an instance, i.e., each sample at interval of 0.1s from the triaxial gyroscope was considered one instance. This instance was different because instead of averaging over 10 samples, each gyroscope-recorded feature is its own instance.

The TS was calculated using an RMS method with a 5s time window. The RMS for each gyroscope signal was calculated for a finite series $\{x_t+x_{t+1}+x_{t+2}+x_{t+n}\}$ using (4), where n designated the number of signals in the finite series. Data were sampled at 100Hz, but only written to file at 10Hz in order to reduce file size. Because PD tremor usually lasts at least a few seconds, selecting a short time window (less than 1s) could increase TS scores and give false positives. Selecting a larger time window, such as 10s, would reduce the TS resolution[35]. The RMS values for each axis are used to calculate TS which has units of (°/s) and a range of 0 to 4, where 0 represents no tremor and 4 represents severe tremor.

$$x_{RMS}=\sqrt{\frac{x_t^2+x_{t+1}^2+x_{t+2}^2+x_{t+n}^2}{n}} \qquad (4)$$

TS was scaled to a 0-4 scale based on maximum and minimum RMS values recorded for tremor.

We studied the effect of combinations of different features and different algorithms on the accuracy of computing TS. Each data point used to train and test a classifier was treated as an instance. We processed the six features from the gyroscope data in two different ways prior to applying machine learning algorithms. We first defined each instance as a combination of 10 samples in a 1s time window. To convert 10 samples into one data point, we calculated root mean square values for each of the six data

Using 10-fold cross validation, the accuracy of each classifier in classifying TS was obtained by comparing the categorizations of the learned classifier to the clinicians' evaluation. A cross-validation approach was used to estimate how accurately a model would perform in practice by separating the dataset into training and validation sets. Analysis was performed based on the data used for training and the result is validated on validation or test data set. To reduce variability, k-fold cross-validation approach was used in which cross validation was performed k different times, each time using a different partitioning of the data into training and validation sets. The results were then averaged[31]. We used the machine learning tool Weka [36] to perform 10-fold cross-validation approach on tri-axial gyroscope data for the six different classifiers.

In a second approach to measuring TS, we analyzed the patient's digital pen tracings of a printed Archimedes spiral. The printed spiral was generated by the Archimedes spiral equation (5), where the coefficient of offset (α) is a positive real number defining the magnitude θ increases for a given r. For the printed spiral, α=10.07.

$$\theta = \alpha \cdot r \qquad (5)$$

Successive spiral tracing data points were compared to the printed data points that were defined by (5) and linearized by (6).

Prior to analysis, we linearized both the printed and traced spirals by plotting spiral radius (r) vs. angle (θ), which were derived from x and y coordinates recorded from the pen in the case of the traced spiral. The radius r was calculated as shown in (6).

$$r = \sqrt{(x - x_0)^2 + (y - y_0)^2} \tag{6}$$

θ was calculated as shown in (7) from the polar expression where x_0 and y_0 were the spiral center coordinates.

$$\theta = \tan \frac{(y - y_0)}{(x - x_0)} \tag{7}$$

θ was returned as a series of increasing or decreasing positive or negative values depending on the Cartesian quadrant in which the data were recorded. Consequently, θ was recalculated by defining the active quadrant from the change in sign and value of θ, then adding the radian angle θ from the previous iteration. The result was a consistent progression of θ that correctly corresponded to the angular progression of θ on the spiral.

To determine a TS score for each spiral tracing, we calculated from the linearized pen tracing data, r vs. θ, five factors: maximum difference between the radius of the printed spiral and the tracing (Δr_{max}), the average radius difference between the printed spiral and tracing radius (Δr_{avg}), the square of the Pearson product moment correlation coefficient for tracing r and θ data points (R^2), the RMS of the radius difference, and the standard deviation (σ) of the radius difference between printed spiral and tracing[37]. We derived equations scaling each of the above factors to a 5-point TS scale from four spiral tracings rated for TS by plotting each factor vs. TS rating for that trace, then fitting a best-fit curve to data in Excel (*Figure 2*). This method resulted in five equations scaling TS from 0-4 for each of the five factors. We averaged the five tremor ratings derived from each of the five factors characterizing deviation from that spiral tracing to obtain a single rating of TS. This averaged TS rating was then rounded to the nearest whole number between 0 and 4. The resulting TS score was compared to the clinician's rating for the patient to determine the ability of the system to classify the same level of tremor the clinicians identified.

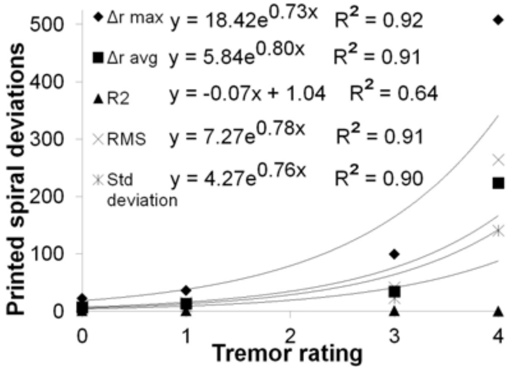

Figure 2. Digital pen tremor scaling

Results

TS ratings from the Shimmer, machine learning approach, and digital pen data analysis were compared to the clinician's tremor rating for each patient under each condition (DBS on or off) (*Table 1*). The accuracies of all three methods were compared to determine the most accurate method.

Comparison of accuracy was obtained for Random Forest, Decision Tree, Nearest Neighbor (NN), Bayes, Multilayer Perceptron (MLP), and Support Vector Machine (SVM) for both time-segmented data and raw data (*Figure 3*).

The accuracy of each classification method is reported for the entire data set, rather than for individual participants, due to the nature

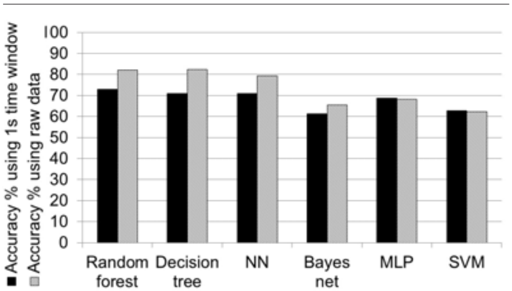

Figure 3. Machine learning accuracy

of 10-fold cross evaluation. The best value of accuracy has been obtained using a decision tree classifier on raw data: 82%.

Spiral tracings (*Figure 4*), were linearized and plotted versus the printed spiral (*Figure 5*). The numerical analysis methods were applied to each linearized spiral trace to determine a tremor rating. Tremor rating for patient 5 with DBS off, differs greatly from that of patient 5 with DBS on (*Table 2*). In both tables, each type of tracing deviation (Δr_{max}, Δr_{avg}, etc.) is listed for that tracing above the scaled TS score for that factor with the tremor rating averaged from the five scaled tremor severities.

Digital pen tracings yielded a match to clinicians' ratings with 74% accuracy.

We identified one outlier that was removed from the data set. Digital pen spiral tracing for one patient displayed very high tremor with tracings off the page due to tremor, yielding a TS rating of 4, as assigned by digital pen data analysis. However, when the clinician rated the patient, the patient traced a clinician-provided spiral with a standard pen, pressing his hand hard against the writing surface.

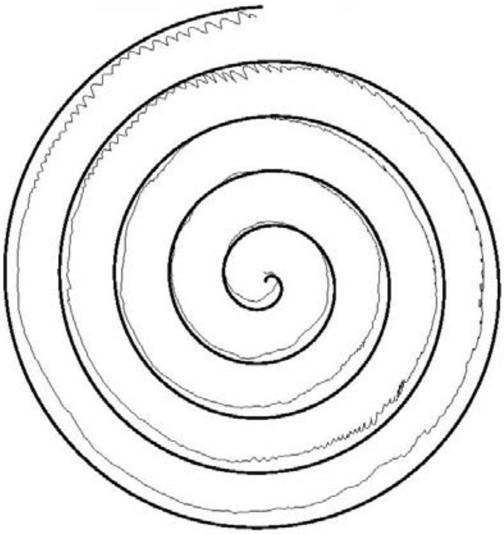

Figure 4. Spiral trace of patient 5, Deep brain stimulation off, Parkinson Disease

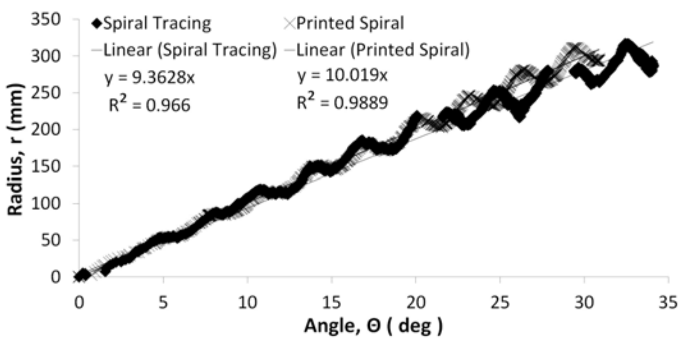

Figure 5. Linearized spiral trace of patient 5, Deep brain stimulation off, Parkinson Disease

Table 2. Tremor severity (TS) for digital pen spiral trace in patient 5; Δr max= maximum difference between the radius of the printed spiral and the tracing; Δr avg= average radius difference between the printed spiral and tracing radius; R2= square of the Pearson product moment correlation coefficient for tracing r (radius) and θ (angle) data points; RMS= root mean square of the radius difference; SD= standard deviation of the radius difference between printed spiral and tracing; DBS= Deep brain stimulation

Parameter	Spiral Trace Deviation Factors					TS Rating
	Δr max	**Δr avg**	**R^2**	**RMS**	**SD**	
DBS= off						
Patient spiral trace data	63.46	16.05	0.97	21.34	14.07	
Decimal TS average of 5 deviation ratings	1.69	1.27	0.86	1.37	1.58	1.35
Rounded TS rating						1
DBS=on						
Patient spiral trace data	26.75	11.03	0.99	13.32	7.47	
Decimal TS average of 5 deviation ratings	0.51	0.80	0.67	0.77	0.74	0.70
Rounded TS rating						1

This effectively dampened the tremor during the clinician-provided spiral trace and yielded a clinician tremor rating of 1. For all other tracings, it was insured that the patient did not press his hand hard against the paper. Because this one patient kept his hand off the paper during the digital pen spiral trace, this data collection was not conducted in the same manner as the others, and we concluded that data for patient 1 DBS off should be discarded as an outlier. Removing this outlier, the digital pen yielded exact match accuracy to the clinicians' rating of 78%.

Figure 6 shows the raw gyroscope data from the SWSU when patient 10 was resting. With the DBS device off the RMS value of the tremor was 23.35°/s and with the device on the RMS value was 11.21°/s. This showed a total RMS improvement of 12.14°/s when using DBS. These results parallel those of the literature, which report displacement RMS measured with accelerometers decreased by approximately half for DBS on vs. DBS off condition for medicated PD patients experiencing postural and kinetic tremor[38]. Frequency decreased by 0.8 Hz and power density of the tremor decreased by 25.26$(°/s)^2$ / Hz when the DBS device was on (*Figure 7*). Figure 8 shows patient 7's raw gyroscope data for the roll axis when the patient was resting. With DBS off, the RMS value of the tremor was 148.54°/s. With DBS on, the RMS value was 2.05°/s. This showed a total RMS improvement of 146.49°/s when using the DBS device. Figure 9 shows patient 7's power spectral density for the roll axis when the patient was drawing a spiral. With the DBS device off, a large power density of 779.18 $(°/s)^2$ / Hz occurred at 3.8 Hz. By contrast, when the DBS was on, very little tremor was noticeable.

Using the RMS method, the tremor severity was matched to the clinician assessment 42% of the time with the aforementioned outlier removed.

Discussion

We compared the spiral TS ratings with the clinicians' TS ratings and the SWSU TS ratings. Table 3 shows a match comparison for tremor ratings based on digital pen spiral tracings, SWSU data, and clinicians' analysis for ten patients, both for the DBS off con-

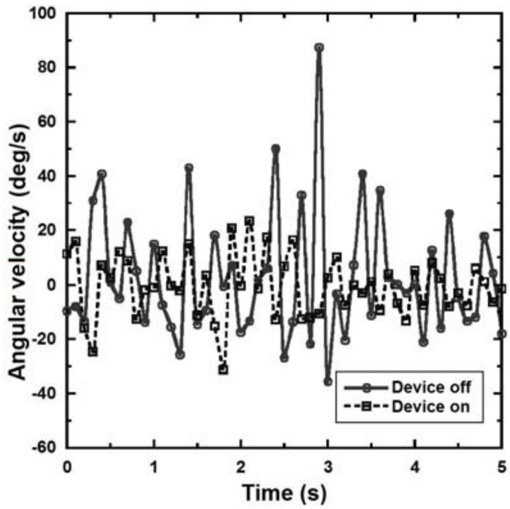

Figure 6. Raw gyroscope data at rest of patient 10

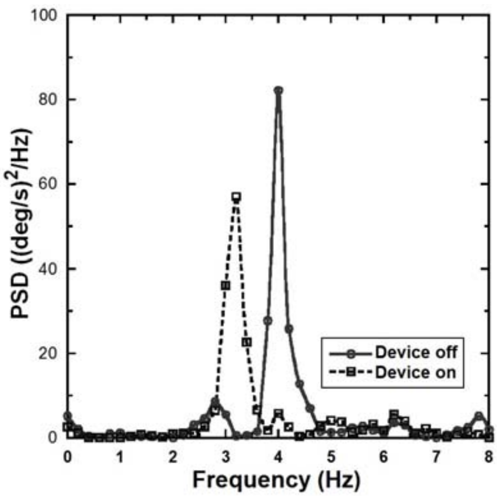

Figure 7. Power spectral density roll axis, spiral trace of patient 10

Table 3. Exact match accuracy

Parameter	Accuracy, %
Random Match Probability	20
Machine Learning Exact Match	82
Spiral-Clinician Exact Match; Outliers Removed	78
SWSU-Clinician Exact Match; Outliers Removed	42
Spiral-SWSU Exact Match; Outliers Removed	44

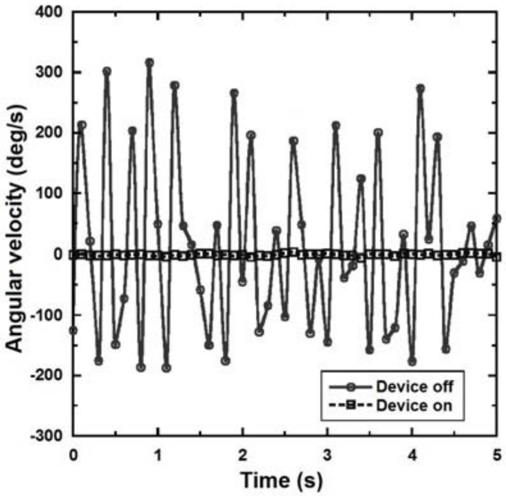

Figure 8. Raw gyroscope data roll axis at rest of patient 7

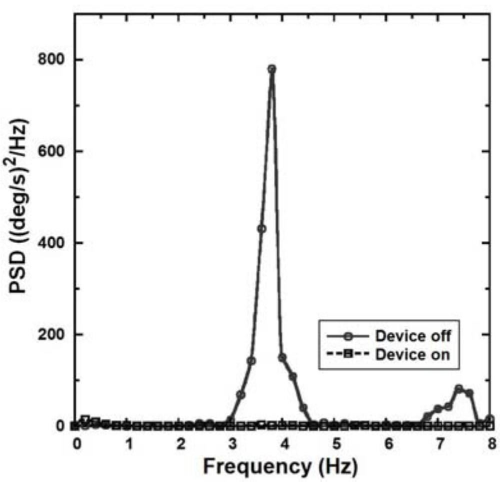

Figure 9. Power spectral density roll axis, spiral trace of patient 7

dition and the DBS on condition, with one missing data set for patient 7 with DBS off.

SWSU TS ratings matched clinicians' ratings with 42% accuracy, digital pen 78%, and machine learning 82%. It is important to note that a value equal to 20% is due to random effect. These results represent a substantial improvement over the clinical inter-rater reliability for the TRS (Kappa statistic =~0.5)[8]. Because the machine learning algorithms used the clinical rating from three different raters as the target data, a match of 100% would not be expected due to inter-rater variability. Although the upper limit for matching clinical ratings was not established due to the limited number of subjects, the 82% match (machine learning algorithms) and 78% match (digital pen) shows that these methods have the capability to provide more reliable assessments of the TRS scale.

Spiral to SWSU exact match accuracy was 44%, demonstrating poor correspondence between the two rating methods. We concluded that the RMS method applied to gyroscope method alone, at a sample rate of 10 Hz, was not an adequate assessment tool for TS. However, the same data were useful in classifying TS using a random forest machine learning algorithm.

We chose to record SWSU data at 10 Hz even though we sampled data at 100 Hz with the device. Although we initially sampled and recorded data at 100 Hz, we observed from our data a peak PSD at about 4 Hz and decreased the sample rate to 10 Hz in order to reduce file size. This methodology has been used in previous studies. For example, Wu et al.[16] reported a maximum concurrence peak below 4 Hz for postural and kinetic tremor in PD patients, with a lesser and secondary peak between 6 and 8 Hz. While our sample rate of 10 Hz most likely captured the maximum PSD peak for tremor, some of the lesser PSD data that occur around 8 Hz may been lost. This could have contributed to our poor accuracy in matching clinical TS ratings with the Shimmer RMS method.

This study presents a feasible approach to bridge objective measurements of tremor to ratings (TRS) familiar to clinicians. Furthermore, this approach used moderately demanding motor tasks in PD and ET patients who could accomplish these tasks with reasonable effort. However, due to the low number of samples (20 data sets from 10 participants under two DBS conditions), the impact of these methods could be more clearly defined with the inclusion of additional participants. Notably, our findings imply that machine learning algorithms can reliably classify TS in the wrist from gyroscope data into the same scale used by clinicians. Furthermore, the reliability could be further improved by incorporating digital pen data into the machine learning approach along with gyroscope data to achieve an even higher accuracy in the evaluation of TS.

Conclusions

Applying three computational methods to assess patient tremor, we discovered that we could match the qualitative clinical tremor rating 78% of the time with a digital pen spiral tracing analysis, 42% of the time with Shimmer data using RMS methods, and 82% of the time with a machine learning decision tree algorithm on gyroscope data. Combining machine learning with RMS tremor gyroscope data proved to be the most reliable method. This computational method has the potential to substantially increase the reliability of tremor assessment.

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References

1. Grimaldi G, Manto M. Neurological tremor: Sensors, signal processing and emerging applications: Sensors 2010;10(2):1399-1422; doi:10.3390/s100201399
2. Elbe R. Characteristics of physiologic tremor in young and elderly adults: Clinical Neurophysiology 2003;114(4):624-635; doi:10.1016/S1388-2457(03)00006-3
3. Cunningham L, Nugent C, Moore G, Finlay D, Craig D. Computer-Based Assessment of Bradykinesia, Akinesia, and Rigidity in Parkinson's Disease. ICOST 2009; LNCS 5597:1-8
4. Waters C. Diagnosis and Management of Parkinson's Disease. 5th edition. Caddo: Professional Communications Inc; 2006 pp 39-252
5. Fahn S, Tolosa E, Marin C. Clinical rating scale in tremor. In: Jankovic J, Tolosa E, editors. Parkinson's disease and movement disorders. Baltimore: Urban and Schwarzenberg; 1988; pp 225-234
6. Heldman D, Jankovic J, Vaillancourt D, Prodoehl J, Elble R, Giuffrida J. Essential tremor quantification during activities of daily living: Parkinsonism and Related Disorders 2011;17(7):537-542; doi:10.1016/j.parkreldis.2011.04.017
7. Kompoliti K, Comella C, Goetz C. Clinical rating scales in movement disorders. In: Jankovic J, Tolosa E, editors. Parkinson's disease and movement disorders (5). Philadelphia: Williams and Wilkins; 2007; pp 692-701
8. Stacy M, Elble R, Ondo W, Wu S, Hulihan J. Assessment of interrater and intrarater reliability of the Fahn–Tolosa–Marin Tremor Rating Scale in essential tremor. Movement Disorders 2007;22(6):833-838; doi:10.1002/mds.21412
9. Miotto G, Andrade A, Soares A. Measurement of Tremor Using Digitizing Tablets. Uberlândia: V CEEL; 26-28 September; 2007; pp 1-4
10. Factor S, Weiner W. Parkinson's disease: Diagnosis and clinical management. New York: Demos; 2002
11. Rubchinsky L, Kuznetsov A, Wheelock V, Sigvardt K. Tremor. Scholarpedia 2007;2(10):1379; doi:10.4249/scholarpedia.1379
12. Lo G, Suresh A, Stocco L, Gonzalez-Valenzuela S, Leung V. A Wireless Sensor System for Motion Analysis of Parkinson's Disease Patients. IEEE: PerCom 2011; pp 564-567
13. Someren E, Vonk B, Thijssen W, Speelman J, Schuurman P, Mirmiran M, Swaab D. A new actigraph for long-term registration of the duration and intensity of tremor and movement: IEEE Transactions on Biomedical Engineering 1998;45(3):386-395
14. Elbe R. Clinical mechanisms of tremor. Journal of clinical neurophysiology 1996;13(2):133-144; doi:10.1097/00004691-199603000-00004
15. O'Suilleabhain P, Matsumoto J. Time-frequency analysis of tremor. Brain 1998:121(11); 2127-2134; doi:10.1093/brain/121.11.2127
16. Wu P, Lin C, Wang C, Hwang I. Atypical task-invariant organization of multi-segment tremors in patients with Parkinson's disease during manual tracking. Journal of Electromyography and Kinesiology 2009;19:e144–e153; doi:10.1016/j.jelekin.2007.12.003
17. Siderowf A, McDermott M, Kieburtz K, Blindauer K, Plumb S, Shoulson I. Test–Retest Reliability of the Unified Parkinson's Disease Rating Scale in Patients with Early Parkinson's Disease: Results from a Multicenter Clinical Trial: Movement Disorders 2002;17(4):758-763; doi:10.1002/mds.10011

18. Bennett D, Shannon K, Beckett L, Goetz C, Wilson R. Metric properties of nurses' ratings of parkinsonian signs with a modified Unified Parkinson's Disease Rating Scale: Neurology 1997;49(6):1580-1587
19. Bonato P, Sherrill D, Standaert D, Salles S, Akay M. Data mining techniques to detect motor fluctuations in Parkinson's disease. Proceedings of the 26th Annual International Conference of the IEEE EMBS 2004; pp 4766-4769; doi:10.1109/IEMBS.2004.1404319
20. Papapetropoulos S, Katzen H, Scanlon B, Guevara A, Singer C, Levin B. Objective quantification of neuromotor symptoms in Parkinson's disease: Implementation of a portable, computerized measurement tool. Parkinson's Disease 2010;2010(760196):1-6; doi:10.4061/2010/760196
21. Deuschl G, Volkmann J, Raethjen J. Tremors: differential diagnosis, pathophysiology, and therapy. In: Jankovic J, Tolosa E, editors. Parkinson's disease and movement disorders (5). Philadelphia: Williams and Wilkins; 2007; pp 298-320
22. Fisman G, Herzog J, Fishman D, Tamma F, Lyons K, Pahwa R, Lang A, Deuschl G. Subthalamic nucleus deep brain stimulation: summary and meta-analysis of outcomes. Movement Disorders 2006;21(14):S290-S304; doi:10.1002/mds.20962
23. Benabid A, Pollak P, Gao D, Hoffmann D, Limousin P, Gay E, Payen I, Benazzouz A. Chronic electrical stimulation of the ventralis intermedius nucleus of the thalamus as a treatment of movement disorders. Journal of Neurosurgery 1996;84(2):203–214; doi:10.3171/jns.1996.84.2.0203
24. Obwegeser A, Uitti R, Witte R de, Lucas J, Turk M, Wharen R. Quantitative and qualitative outcome measures after thalamic deep brain stimulation to treat disabling tremors. Neurosurgery 2001;48(2):274-284; doi:10.1097/00006123-200102000-00004
25. Bronstein J, Tagliati M, Alterman R, Lozano A, Volkmann J, Stefani A, Horak F, Okun M, Foote K, Krack P, Pahwa R, Henderson J, Hariz M, Bakay R, Rezai A, Marks W, Moro E, Vitek J, Weaver F, Gross R, DeLong M. Deep brain stimulation for Parkinson disease. Archives of Neurology 2011;68(2):165-171; doi:10.1001/archneurol.2010.260
26. Obeso J, Olanow C, Rodriguez-Oroz C. Deep-brain stimulation of the subthalamic nucleus or the pars interna of the globus pallidus in Parkinson's disease. New England Journal of Medicine 2001;345(13):956-963; doi:10.1093/brain/124.9.1777
27. www.shimmer-research.com; retrieved July 19, 2011
28. Davies S, Beale R, Tiplady B. An Investigation into the Measurement of Driver Impairment at the Roadside Using a Logitech Digital Pen. 17th International Conference on Alcohol, Drugs, and Traffic Safety; Glasgow; August 2004
29. Quinlan J. Induction of decision trees. Machine learning 1986;1(1):81-106; doi:10.1007/BF00116251
30. Breiman L. Random forests. Machine Learning 2001;45(1):5–32; doi:10.1007/BF00116251
31. Mitchell T. Machine Learning. New York: McGraw Hill; 1997
32. Boser B, Guyon I, Vapnik V. A training algorithm for optimal margin classifiers. Proceedings of the 5th annual workshop on computational learning theory 1992; Pittsburgh ACM; pp 144-152
33. Zornetzer S, Davis J, Lau C. An introduction to neural and electronic networks. San Diego: Academic Press; 1990
34. Rish I. An empirical study of the naive Bayes classifier: IJCAI-01 workshop on empirical methods in AI; 2001
35. Salarian A, Russmann H, Vinterhoets FJG, Burkhard PR, Blanc Y, Dehollain C, Aminian K. An Ambulatory System to Quantify Bradykinesia and Tremor in Parkinson's Disease. 4th International IEEE EBMS Special Topic Conference on Information Technology Applications in Biomedicine; 2003; pp 35-38; doi:10.1109/TBME.2006.886670
36. Bouckaert R, Frank E, Hall M, Kirkby R, Reutemann P, Seewald A, Scusc D. WEKA Manual for Version 3-6-3; University of Waikato; Hamilton, New Zealand; July 27, 2010
37. Wang H, Yu Q, Kurtis M, Floyd A, Smith W, Pullman S. Spiral Analysis - Improved Clinical Utility with Center Detection. Journal of Neuroscience Methods 2008;171(2):264-270; doi:10.1016/j.jneumeth.2008.03.009
38. Sturman M, Vaillancourt D, Metman L, Bakay R, Corcos D. Effects of subthalamic nucleus stimulation and medication on resting and postural tremor in Parkinson's disease. Brain 2004;127(9):2131-2143; doi:10.1093/brain/awh237