

Combined Accelerometer and EMG Analysis to Differentiate Essential Tremor from Parkinson's Disease

Nooshin Haji Ghassemi*, Franz Marxreiter*, Cristian F. Pasluosta, Patrick Kugler, Johannes Schlachetzki, Axel Schramm, Bjoern M. Eskofier, *Member, IEEE, EMBS*, Jochen Klucken

Abstract— In this study, we intended to differentiate patients with essential tremor (ET) from tremor dominant Parkinson disease (PD). Accelerometer and electromyographic signals of hand movement from standardized upper extremity movement tests (resting, holding, carrying weight) were extracted from 13 PD and 11 ET patients. The signals were filtered to remove noise and non-tremor high frequency components. A set of statistical features was then extracted from the discrete wavelet transformation of the signals. Principal component analysis was utilized to reduce dimensionality of the feature space. Classification was performed using support vector machines. We evaluated the proposed method using leave one out cross validation and we report overall accuracy of the classification. With this method, it was possible to discriminate 12/13 PD patients from 8/11 patients with ET with an overall accuracy of 83%. In order to individualize this finding for clinical application we generated a posterior probability for the test result of each patient and compared the misclassified patients, or low probability scores to available clinical follow up information for individual cases. This non-standardized post hoc analysis revealed that not only the technical accuracy but also the clinical accuracy limited the overall classification rate. We show that, in addition to the successful isolation of diagnostic features, longitudinal and larger sized validation is needed in order to prove clinical applicability.

I. INTRODUCTION

Tremor is defined as rhythmic, oscillating and involuntary movements and often involves the upper extremities. Differential diagnosis of tremor commonly comprises essential tremor (ET) and Parkinson disease (PD) amongst other rare forms. The prevalence of ET is high with up to 5% with people over 65 years old [1]. PD has an overall prevalence of approximately 0.5 increasing up to 2% with age [2]. Tremor is one of the core symptoms in PD patients and the initial clinical presentation of the tremor dominant PD phenotype.

* These authors contributed equally to this work.

This study is supported by the FAU Emerging Fields Initiative (EFIMoves, 2_Med_03).

N. Haji Ghassemi, P. Kugler, C. Pasluosta and B. M. Eskofier are with the Digital Sports Group, Pattern Recognition Lab, Department of Computer Science, Friedrich Alexander University Erlangen-Nürnberg (FAU), Erlangen, Germany.

F. Marxreiter, J. Schlachetzki, C. Pasluosta, and J. Klucken are with the Department of Molecular Neurology, University Hospital Erlangen, Erlangen, Germany.

Axel Schramm is with the Department of Neurology, University Hospital Erlangen, Erlangen, Germany.

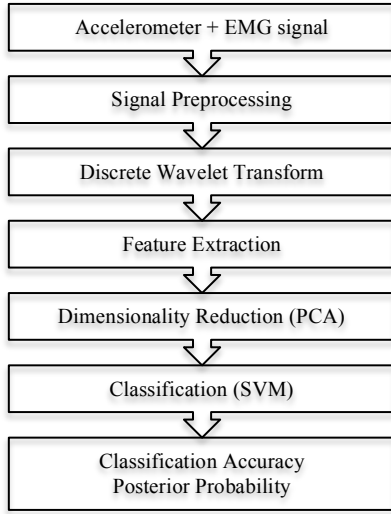
Prototypically, tremor in ET features a symmetric postural and kinetic tremor of the arms, whereas tremor in PD is characterized by an often unilateral resting and postural tremor. Differential diagnosis however, especially in early disease stages remains problematic because tremor in PD may not only occur at rest, but also at posture and/or during action. Further, tremor at rest is not pathognomonic for PD and has been also observed in ET. Due to these overlapping symptoms, misdiagnosis of ET and PD tremor may occur in 20-30% of the cases [3]. In light of the difference in prognosis as well as current and evolving treatment options for PD and ET, an accurate and reliable diagnosis is urgently needed. Despite these challenges, the diagnostic evaluation is highly dependent on the experience of the clinician and typically includes medical history and physical examination. Neuroimaging [4] has been considered as one potential diagnostic option to discriminate of PD and ET. However, ability, costs, and invasiveness of this diagnostic option have to be taken into consideration [5].

There is a growing interest in methods based on accelerometer and surface electromyography (EMG) electrodes, since they are readily available, non-invasive and cost-efficient diagnostic tools. Combination of these signals can be used to detect frequency and muscle activity [6]. Several studies differentiated ET from PD based on accelerometer and EMG signals [6] [7]. These studies yield reasonable differentiation between PD and ET and overall classification accuracy was used as the main metric for evaluation of performance. However, high classification accuracy is not enough to support clinical decision-making. A physician should be able to clinically validate classification results. Thus, classification procedure should be translated into an individual report for the patients. In this work, we propose using posterior probability to assess the classification result in an individual manner. This meta information is essential for us to integrate our method in clinical assessment. We utilized a SVM-based classifier, by which we can compute the posterior probability of both diseases. To the best of our knowledge, this is the first attempt to develop such a method for differential diagnosis.

II. METHODOLOGY

Our classification system is composed of the following steps: (1) signal preprocessing, (2) discrete wavelet transform, (3) feature extraction, (4) dimensionality reduction, and (5) classification. The schematic diagram of the system is shown in Fig 1. We implemented the entire procedure in Matlab R2015a (MathWorks).

Figure 1. Block diagram of the automated classification



A. Data Acquisition

Data acquisition was performed as part of a standard diagnostic tremor test in the neurophysiology lab of the Department of Neurology, University Hospital Erlangen, Erlangen, Germany. Typically, tremor frequencies and synchronization of agonist/antagonists are reported providing only a limited amount of information from the raw data recorded. Subjects were comfortably seated and placed their arms in a resting position on their legs. Prior to electrode placement, the skin was cleaned by cotton and ethanol. Two calibrated accelerometers were placed on the dorsal side of both hands of the subjects. Bipolar Ag/AgCl surface EMG electrodes were placed on the extensor and flexor muscles of the left and right forearm by an electrophysician. A total of six channels were recorded, two accelerometer signals and four surface EMG signals. All signals were recorded at 1000 Hz using a Schwarzer Topas EMG system, Natus, USA. Three 30-seconds tests were performed for each patient, the first with the arms fully relaxed and rested on the legs (rest), the second with their arms and hands extended in a horizontal position (hold) and the third in the same position with weights of 1 kg attached to the forearm (weight). To discard transitions from the recorded data, we considered only the signal from 10 to 25 seconds.

13 PD patients (tremor dominant forms) and 11 ET patients were included for this study. For our experimental procedures, we followed the declaration of Helsinki 1975, as revised in 2000. Initial diagnosis was made by a movement disorder specialist prior to tremor analysis. If possible, patients received clinical follow up examinations to confirm or change the initial diagnosis. PD and ET were diagnosed according to consensus criteria of the German Society of Neurology. Consensus criteria for PD are similar to the UK PDS Brain bank criteria for diagnosis of PD [3] Consensus criteria for ET are based on the consensus criteria of the movement disorders society [9] Patients' demographics and clinical characteristics are summarized in Tab I. PD severity of patients was staged using the Hoehn & Yahr scale and

motor performance was clinically evaluated using the UPDRS-III rating.

TABLE I. PATIENT CHARACTERISTICS.

	PD	ET
Number of Patients	13	11
Age at examination(Range)	67 $\pm$ 11 (45-88)	66 $\pm$ 13 (43-79)
Gender (Male/Female)	7/6	4/7
Disease duration	4 $\pm$ 4,6	13 $\pm$ 14,6
UPDRS III	17 $\pm$ 9,7	
H+Y	2 $\pm$ 0,9	

B. Preprocessing and Filtering

The recording physician visually inspected both EMG and accelerometer signals during data acquisition. Measurements with bad signal quality were either repeated or not included in the study. To remove non-tremor related high frequency components, the accelerometer signals and EMG signals were filtered with a Butterworth low pass filter with a cutoff frequency of 70 Hz. The EMG signals were additionally high pass filtered with a cutoff frequency of 20 Hz and DC-rectified to amplify the visibility of the tremor bursts in the signals.

C. Wavelet-based Feature Extraction

EMG signal is non-stationary, meaning that the characteristic of the signal changes over time. Discrete wavelet transform (DWT) [10] is widely used for analysis of non-stationary signals. DWT decomposes a signal to different level of coefficients corresponding to different frequency bands in a way that the coefficients include all information of the original signal. Each level of coefficients has different time-frequency resolution. In this work, we used Haar mother wavelet, since it has been widely used for wavelet analysis of EMG signal. The signals were decomposed in 10 levels in order to have an effective feature extraction from each coefficient in the next step.

Four EMG and two accelerometer signals were decomposed by DWT method. Then, a set of standard statistical features was extracted from the coefficients: mean, standard deviation, skewness, kurtosis, entropy, energy, root mean square, and mean absolute value. In the majority of PD and ET patients, one hand is more affected by the disease than the other hand. Feature extraction is performed based on the most affected side of the patients rather than left or right hand side, in order to obtain more descriptive features.

D. Dimensionality Reduction

Dimensionality reduction was performed to reduce the dimensionality of the feature vector and avoid overfitting in the classification step. This is particularly important in our study since the number of features (524 for each test) is much higher than the number of subjects (24). Feature reduction was achieved by using principal component analysis (PCA) [11]. PCA projects the feature space into principal components in the direction of maximum variance.

These new components compose a feature space with reduced dimensionality. In our experiment, the number of components was optimized empirically to achieve the highest classification performance.

E. Classification

We trained a binary Support Vector Machines (SVM) classifier [12] to distinguish between two classes: ET and PD. Two kernels, linear and radial basis function (RBF) were examined in this work. SVM has a cost parameter, which controls number of misclassification of training examples. The RBF kernel has an additional parameter, gamma, which controls how far the influence of a single training example reaches. A grid-search was employed as a method of model selection to adjust the SVM parameters. Since performing a complete grid-search is very time consuming, it was applied in two stages via coarse grid, and then, fine grid. In the coarse grid, the range of cost parameter was {0.001, 0.01, 0.1, 1, 10, 15, 20, 50, 100, 1000} and the range of gamma was {0.003, 0.03, 0.3, 3, 9, 15, 20}. In the fine, the parameters were examined in a range of $\pm 5\%$, $\pm 10\%$, $\pm 15\%$, and $\pm 20\%$ of their selected values. The input feature vector was normalized to zero mean and unit standard deviation.

As previously described, we considered the three tests, rest, hold and weight separately and trained a classifier for each test. From clinical point of view, it is important to investigate which of these tests yield a better differentiation between ET and PD.

F. Evaluation

Accuracy was computed for evaluating the performance of our method, meaning the rate of correctly classified patients. The evaluation was implemented using leave one out cross-validation (LOOCV). LOOCV was chosen due to the small number of data. Finding principal components and SVM parameters was performed for each training fold and the result was applied for the test subject. In addition, we computed the posterior probability of the classification. The SVM algorithm not only predicts the class of a data but can also report the posterior probability as an indicator of certainty of the classification. The posterior probability is a valuable piece of information in clinical applications since it allows for an individual result. It provides a measure of similarity for each patient assessed to the reference group. This information can complement the diagnostic workup for the clinician.

III. RESULTS

Tab. II shows the results for our classification method optimized for the number of PCA components and the parameters of SVM and the kernels. We analyzed each test of rest, hold and weight separately. The best performance was achieved for the weight test. Tab. III presents individual classification result for each patient and the posterior probabilities for each disease.

In order to better understand the misclassified patients and to associate different probability levels, we obtained additional clinical information from clinical records or

follow up visits if available in a non-standardized form to confirm the initial diagnose that was used in the classification experiments and to evaluate if the clinical heterogeneity of the small patient population might affect the classification outcome.

Table II. CLASSIFICATION ACCURACY RESULT

Tests	No. PCA Components	SVM Parameters	Accuracy
Rest	3	Linear kernel cost = 0.001	79%
Hold	3	RBF kernel cost = 14.25 gamma = 0.003	75%
Weight	3	RBF kernel cost = 10 gamma = 0.3	83%

IV. DISCUSSION

The preliminary results of this study suggest that our method is effective to discriminate patients with ET from PD patients. The best discrimination between ET and PD was achieved when there was a load in the subjects' hands. This finding underlines the ability of the diagnostic test, the sensor-paradigm and the algorithms used to identify characteristic differences between the two tremor forms. However, the classification accuracy is not sufficient to identify each patient with the reference group correctly, thereby limiting the individual diagnostic application. Therefore, we introduced a probability score for each patient and compared the resulting similarity levels with the available clinical information, in particular, for the misclassified patients.

TABLE III. INDIVIDUAL CLASSIFICATION RESULT and CLINICAL CONFIRMATION

No	Init. Diag.	Classific. result	Probability		Clinical confirm.
			ET	PD	
1	'ET'	'ET'	90,7%	9,3%	confirmed
2	'ET'	'ET'	61,1%	38,9%	confirmed
3	'ET'	'ET'	54,3%	45,7%	OTHER
4	'ET'	'ET'	75,5%	24,5%	confirmed
5	'ET'	'ET'	76,0%	24,0%	confirmed
6	'ET'	'ET'	63,0%	37,0%	no follow up
7	'ET'	'ET'	50,0%	50,0%	confirmed
8	'ET'	'ET'	95,6%	4,4%	no follow up
9	'ET'	'PD'	3,6%	96,4%	OTHER
10	'ET'	'PD'	43,2%	56,8%	no follow up
11	'ET'	'PD'	46,8%	53,2%	no follow up
12	'PD'	'ET'	83,0%	17,0%	confirmed
13	'PD'	'PD'	43,3%	56,7%	no follow up
14	'PD'	'PD'	31,4%	68,6%	confirmed
15	'PD'	'PD'	47,4%	52,7%	confirmed
16	'PD'	'PD'	46,4%	53,6%	confirmed
17	'PD'	'PD'	38,4%	61,6%	no follow up
18	'PD'	'PD'	40,4%	59,7%	confirmed
19	'PD'	'PD'	48,2%	51,8%	confirmed
20	'PD'	'PD'	34,5%	65,5%	confirmed
21	'PD'	'PD'	48,2%	51,9%	confirmed
22	'PD'	'PD'	42,1%	57,9%	confirmed
23	'PD'	'PD'	34,1%	65,9%	no follow up
24	'PD'	'PD'	39,7%	60,3%	confirmed

The accuracy of the clinical diagnosis “ET” is typically lower than “PD”, since the presence of other PD specific motor symptoms in addition to the tremor typically allow for higher accuracy for PD. In this work, three patients with initial diagnosis of ET (patient 9-11) and one PD patient (patient 12) were misclassified. Patient 9 is an important index patient for this clinical validation procedure since the probability for ET was extremely low (3,6%). Importantly, in the follow-up visits it became evident, that the initial clinical diagnosis “ET” could not be confirmed. In fact, the diagnosis was changed to cervical dystonia with irregular tremor. For patients 10 and 11 the probability “ET” was above 40%, but did not reach the 50% classification boundary. Further, patient 7 barely reached 50% probability for “ET”. Unfortunately, no follow up visits were documented for these patients, thus the clinical confirmation of the initial diagnosis could not be performed. Likewise, the diagnosis of ET for patient 3 was changed in follow-up examinations. Even though this patient was classified as ET, the probability was only 54,3% suggestion that probabilities around 50% generate another level of uncertainty for individual test results. The diagnosis of the misclassified PD patient 13 was clinically confirmed. Medical history did not reveal any signs that might explain the misclassification from the clinical point of view except that the patient was at the very first stage of PD (disease duration was 0 years), suggesting that at very early stage of tremor-dominant PD the classification accuracy might be limited.

Any pattern recognition method is bound to limitations. A major limitation of proof-of-concept studies is the small number of patients. Larger data set brings better generalization and as a result better classification result. Besides, our study also revealed that the validity of the ground truth is limited by the diagnostic accuracy of clinical examinations of PD as well as ET at a given time point, especially in early disease stages is not perfect. Therefore, careful reevaluation and the assessment of the response to treatment are often needed to finally decide upon the final diagnosis.

Despite of all limitations, our method brought good classification accuracy. Furthermore supporting that the study design and analysis enables the identification of different tremor forms. In this regard, the concept of probability definition is a first attempt to translate successful classification paradigms into individualized results that can complement the diagnostic workup in clinical settings. It is foreseeable that with increasing numbers of future patients that undergo the instrumented tremor testing the reference group can be increased and refined. This may also make lead to a better classification accuracy for patients in early disease stages. Moreover the acceptance of treating physicians and patients of the individual probability results can be evaluated in longitudinal studies.

V. CONCLUSION

In this work, accelerometer and EMG signals were analyzed to differentiate ET from PD using pattern recognition methods. With the proposed method we were able to discriminate ET from PD patient with an overall accuracy of

83%. Additionally, we propose the posterior probability of the classification outcome as a clinical indicator of patients presenting disease-specific symptoms. The clinical validation revealed that studies using clinically confirmed and small sized patient cohorts share the risk that the ground truth or gold standard for the classification experiment might be also affected by the clinical accuracy of the diagnoses. Thus, larger study cohorts, better clinical validation (e.g. neuroimaging, etc.) and/or standardized follow-up paradigms are required to clinically validate instrumented tests for diagnostic workup in the future. Our findings also underline that studies aiming at clinical translation of instrumented movement analysis have to include technical and clinical accuracy considerations in the study design to ultimately prove clinical applicability.

ACKNOWLEDGMENT

We would like to thank all participants of this study as well as the staff helping with data collection. First author acknowledges financial support from the Bavarian Research Foundation.

VI. BIBLIOGRAPHY

- [1] J. Benito-León and E. D. Louis, "Essential tremor: emerging views of a common disorder," *Nature Clinical Practice Neurology*, vol. 2, no. 12, pp. 666–678, 2006.
- [2] D. Hirtz, D. J. Thurman, K. Gwinn-Hardy, M. Mohamed, A. R. Chaudhuri, and R. Zalutsky, "How common are the 'common' neurologic disorders?," *Neurology*, vol. 68, no. 5, pp. 326–337, 2007.
- [3] A. J. Hughes, S. E. Daniel, L. Kilford, and A. J. Lees, "Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases," *Journal of Neurology, Neurosurgery, and Psychiatry*, vol. 55, no. 3, pp. 181–184, 1992.
- [4] L. Passamonti, A. Cerasa, and Q. Aldo, "Neuroimaging of Essential Tremor: What is the Evidence for Cerebellar Involvement?," *Tremor Other Hyperkinet Mov*, vol. 2, 2012.
- [5] K. Badiavas, E. Molyvda, I. Iakovou, M. Tsolaki, K. Psarrakos, and N. Karatzas, "SPECT imaging evaluation in movement disorders: far beyond visual assessment," vol. 38, no. 4, pp. 764–773, 2011.
- [6] J. Timmer, M. Lauk, and G. Deuschl, "Quantitative analysis of tremor time series," vol. 101, no. 5, pp. 461–468, 1996.
- [7] A. Hossen, M. Muthuraman, Z. Al-Hakim, J. Raethjen, G. Deuschl, and U. Heute, "Discrimination of Parkinsonian tremor from essential tremor using statistical signal characterization of the spectrum of accelerometer signal," *Bio-medical materials and engineering*, vol. 23, no. 6, pp. 513–531, 2013.
- [8] J. Raethjen, M. Lauk, B. Koster, U. Fietzek, L. Friege, J. Timmer, C. H. Lucking, and G. Deuschl, "Tremor analysis in two normal cohorts," *Clin Neurophysiol*, vol. 115, no. 9, pp. 2151–2156, 2004.
- [9] G. Deuschl, P. Bain, and M. Brin, "Consensus statement of the Movement Disorder Society on Tremor. Ad Hoc Scientific Committee," *Movement Disorders: Official Journal of the Movement Disorder Society*, vol. 13, no. 3, pp. 2–23, 1998.
- [10] C. S. Burrus, R. A. Gopinath, and H. Guo, "Introduction to Wavelets and Wavelet Transforms," *A Primer*, 1997.
- [11] S. Wold, K. Esbensen, and P. Geladi, "Principal component analysis," *Chemometrics and Intelligent Laboratory Systems*, vol. 2, no. 1–3, pp. 37–52, 1987.
- [12] M. A. Hearst, S. T. Dumais, E. Osman, J. Platt, and B. Scholkopf, "Support vector machines," *IEEE Intelligent Systems and their Applications*, vol. 13, no. 4, pp. 18–28, 1998.