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QUANTITATIVE MOTOR ASSESSMENT, DETECTION, AND SUPPRESSION OF PARKINSON'S DISEASE HAND TREMOR: A LITERATURE REVIEW

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ABSTRACT

Parkinson's disease (PD) is difficult to detect before the onset of symptoms; further, PD symptoms share characteristics with symptoms of other diseases, making diagnosis of PD a challenging task. Without proper diagnosis and treatment, PD symptoms including tremor, bradykinesia, and cognitive problems deteriorate quickly into patients' late life. Among them, the most distinguishable manifestations of PD are rest and postural tremor. Tremor is defined as an involuntary shaking or quivering movement of the hands or feet. Unified Parkinson's Disease Rating Scale (UPDRS), Hoehn and Yahr (H&Y) scales are the most common rating scales that quantify the severity of PD. Due to the lack of consistency in these diagnostic tests, researchers are looking for devices for quantification and detection that can provide more objective PD motor assessments. Additionally, since there is currently no cure for PD, temporary PD symptom suppression is an active research area for improving patients' quality of life. In this survey, the current state of research on Parkinson's disease hand tremor quantification, detection, and suppression is discussed, especially focusing on electromechanical devices. The future direction of research on these devices is also considered.

Keywords: Parkinson's disease; motor assessment; hand tremor; symptoms.

INTRODUCTION

Parkinson's disease (PD) was first formally documented in "an essay on the Shaking Palsy" published in 1817 by a London physician named Parkinson (1). Today, PD is interpreted as the loss of dopamine-secreting neurons in the substatia nigra, a region in the basal ganglia inside the brain. The degeneration of these neurons results in motor function abnormalities including bradykinesia (slowness of movement), akinesia (impairment of voluntary movement), rigidity and tremor. PD commonly occurs in the middle or late life, usually after the age of 50.

Rest tremor is the most distinguished symptom of PD. The tremor is most prominent when the limbs are at rest and diminishes when intentional movements occur. Rest tremor is more visible at distal parts of the body including the hands and feet. 75% of individuals with PD experience rest tremor and rest tremor is within the frequency range 3-7 Hz (2). Although PD is distinguished from similar diseases by tremor at rest, tremor has been reported to remain visible even during posture or movement (3, 4 and 5). This behavior makes distinguishing PD with other diseases a challenging task.

Approximately seven to ten million people worldwide are living with PD (6), but its causes remain poorly understood (7). Researchers are still looking for a legitimate explanation for the death of dopamine-generating cells in the brain and how such loss can cause motor dysfunctions. The lack of fundamental knowledge about the origin of PD leads to difficulties in both diagnosis and treatment.

The main diagnostic tools for PD are the Unified Parkinson's Disease Rating Scale (UPDRS) (8) and the Hoehn and Yahr (H&Y) scale (9). UPDRS comprises six sections that evaluate different aspects of PD patients' performance. Among them, section III focuses especially on motor evaluation. The H&Y rating scale assesses overall severity of PD on a scale of one to five. The problem associated with UPDRS and H&Y scales is that they are based on self-reports from patients' daily experience and subjective assessments from clinical professionals (10). Inconsistency and variation in motor and cognitive assessments can lead to misdiagnosis or assigning an incorrect PD severity score, further leading to incorrect medication prescription. For this reason, researchers are currently looking for a more systematic, quantitative assessment of motor symptoms in possible PD patients.

While PD currently cannot be completely treated, there are some temporary symptom solutions that significantly relieve motor dysfunction. Levodopa (L-dopa) therapy supplements dopamine to alleviate motor problems by activating motor receptors (11), but most patients develop motor complications as a result (12). Another common solution for PD patients at advanced stages is deep brain stimulation (DBS). DBS is an invasive neurosurgery treatment performed by installing microelectrodes to stimulate the globus pallidus and subthalamic nucleus inside the brain to reduce debilitating motor symptoms (13, 14). DBS, however, is both expensive and susceptible to post-surgery complications (13). The short-comings of current treatments result in several methods proposed to suppress rest and postural tremors noninvasively in upper extremities of PD patients.

The purpose of this paper is to review current methods for the assessment, detection, and suppression of rest tremor in PD patients. Section 2 of this work discusses different methods for PD hand tremor assessments, including comparing and contrasting tremor symptoms under different conditions (with or without cognitive load and scripted or unscripted motor tasks). Section 3 covers studies using different hand tremor features to differentiate among PD and similar conditions. Section 4 addresses hypotheses and theories concerning the possible causes of PD tremor, and section 5 considers methods for suppressing PD hand tremor.

PD TREMOR ASSESSMENT

While no permanent treatment for PD currently exists, PD assessment plays a fundamental role in both understanding the behavior of this disease and providing patients proper temporary treatments. The current lack of complete understanding of PD and an objective, accurate PD assessment partially stem from the disease itself. Patients with PD often have differing tremor amplitudes and frequencies. This, along with the fact that the standard clinical assessments are based on subjective decisions of both healthcare professionals and patients, often leads to inconsistency in assigning PD assessment scores. Recent research has attempted to build different mechanisms or wearable devices along with feature extraction techniques and classification algorithms to quantitatively assess the motor performance of PD patients.

Protocol

In order to examine hand motor performance, several tasks that require either hand movements or finger-exerted forces are the fundamental component of motor assessments. Grip force tracking has been extensively used to assess motor performance, especially PD tremor, as an attempt to quantify the severity of PD. Brewer et al. (15) proposed the Assessment of Parkinson's Disease Protocol (ASAP) to quantitatively measure motor impairment in early to moderate PD. The patients were requested to use the index finger and thumb to exert force on the six-axis force/torque sensors. Data from 26 PD patients were retrieved from their grip forces when they tracked sinusoidal or pseudorandom target forces that were displayed on the computer screen. Three main variables for tremor quantification, tremor integral, root mean square error between the target wave and subject's force response, and the lag between the target wave and the subject's force response, were recorded. Also to analyze hand motor performance (16), a palmar grip test was conducted on 35 PD patients and 42 healthy (HT) controls, and signal strength was recorded as a function of time. The palmar grip signals are decomposed into five characteristic phases: reaction, contraction, maintenance, release and relaxation. These phases represent the static and dynamic characteristics of hand function. Another novel approach, using an instrumented twist cap device which consists of six-axis force/ torque transducers to assess the hand's precision and power grips, was applied to quantify PD patients' motor performance by analyzing the peak force level and time to reach peak force (17). Participants were asked to twist a small cap (the same size as a soda bottle cap) and a large cap (the same as peanut butter jar lid) in clockwise and counter clockwise directions under conditions of varying external resistance.

Assessment of kinematic movements also reflects insight into how PD tremor debilitates motor activities. A special wrist robot, using back-drivable hardware and impedance control, was developed to test motor function of PD patients (19). The robot could move, guide or perturb movements of the subject's limb and could record motion and mechanical information including position, velocity and torque applied. Patients were requested to move the robot hand to targets noted on the screen. The targets were presented with a center target and eight peripheral ones. Another system, Kinesia (20), integrated accelerometers and gyroscopes into a wrist worn device to examine kinematic movement by having subjects perform three tremor tasks: hand resting on the lap for 30 seconds, arm extending in front of the body for 20 seconds, and finger repeatedly touching the nose from an extended arm position for 15 seconds.

In another attempt to assess hand rest tremor (RT), Rigas et al. (21) introduced the SHIMMER platform, which received signals wirelessly from tri-axial accelerometers on the wearers. Five HT people simulated rest tremor with severity from 1 to 4 on the UPDRS scale. A rest tremor metric was created to classify the tremor severity into one of four bins, where each bin represented a severity level of tremor. An artificial neural network was chosen to classify the signals recorded from five HT subjects and compared against the rest tremor metric results.

The effect of load

In order to improve motor performance assessment, some studies employed either cognitive loads or external forces. Cognitive loads encompass activities that involve thinking or mental processing. Cognitive loads are known to cause distraction when the subjects are performing motor tasks and are powerful for magnifying motor complication in PD patients (17). This is especially important for early stage PD when detection and quantification using sensors and algorithms can be difficult. Brewer et al. (15) requested patients to count down from 100 by 1 or 3 while tracking target waveforms. In another work, patients performed the auditory analog of the Stroop test while performing the motor tasks (17). In this test, participants listened to a series of the words ''high'' or ''low'' in either high or low pitches. They were instructed to indicate the pitch of the word. Pradhan et al. (18) showed a decrease in motor performance of patients who were tested on isometric pinch grip force between the thumb and index finger along with cognitive load.

External loads have also been used extensively to magnify the motor complications of PD patients. The effect of perturbing force on kinematic movement of PD patients is clearly reflected in Figure 1 (19). The forces used are proportional to the subject's wrist velocity, and are perpendicular to it. For the twist cap device (17), external resistance is applied in addition to cognitive loads. The force required to twist the two caps was between 5 and 10 N.

Purpose of assessment

PD tremor assessment is further classified into two subcategories, based on their applications: to predict and assign PD assessment scores and to evaluate the effect of treatments. Several studies assessing PD motor performance compared their results with the current standard, UPDRS. With ASAP protocol, the mean prediction error was approximately 3.5 UPDRS points out of the total score of 147 from 26 PD patients (15). Kinesia was used to collect data from 60 PD subjects as they completed a subset of the UPDRS upper extremity motor exam including rest, postural, and kinetic tremor (20). There was a high correlation between the results from the tremor scoring algorithm and UPDRS scores.

Functional Independent Measure (FIM) is a test that investigates performance of the execution of 18 daily living activities. The score for this test ranges from 1 (total assistance) to 7 (complete independence). Tinetti A test assesses the balance while the Tinetti B test assesses the gait. The three assessment methods were combined into one score from 0 to 1. The authors concluded that there was a high correlation between parameters related to dynamics and the tests (16).

There are major differences between PD severities during ON and OFF DBS, as well as ON and OFF L-dopa medication. In the study from Krebs et al. (19), five patients took the UPDRS and Hoehn and Yahr tests during two conditions, OFF DBS (DBS was not activated) and ON DBS (DBS was activated). The results clearly showed a large discrepancy between the two cases for these patients. With the wrist robot, the ability to complete the tasks was visually identified (Figure 1).

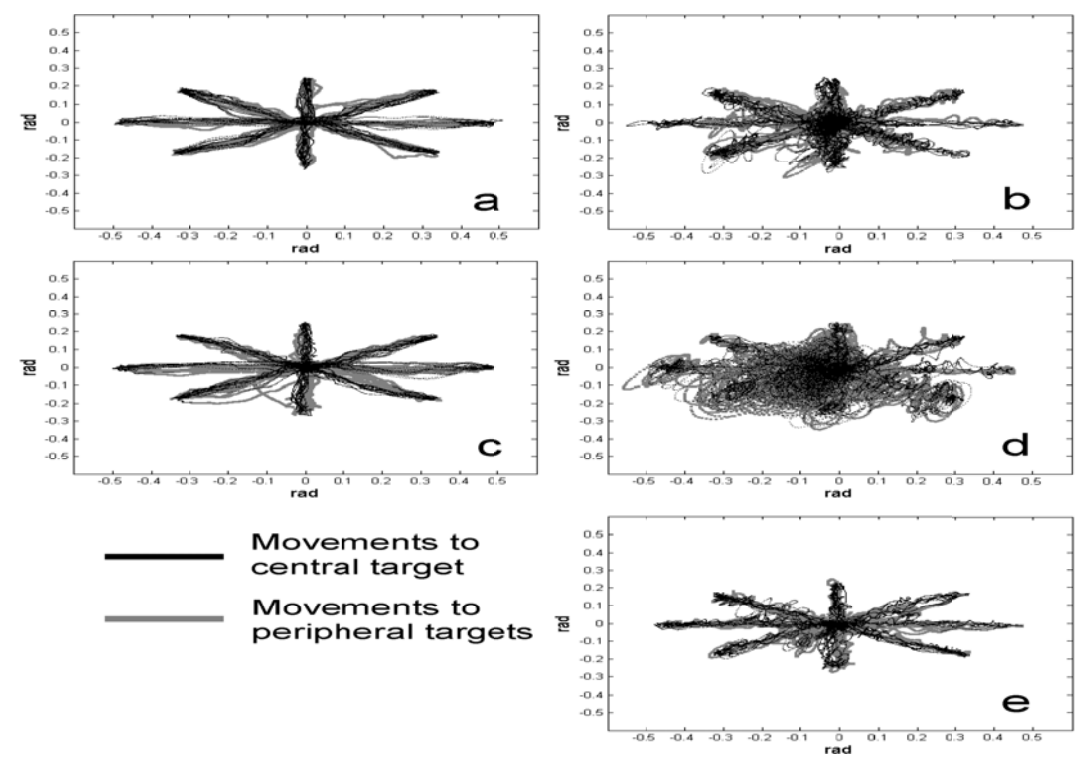

Figure 1. Movement traces of patient A in the DBS ON (left column) and DBS OFF (right column) conditions. (a) DBS ON, block 2 (No load); (b) DBS OFF, block 2 (No load); (c) DBS ON, block 3 (Load type A); (d) DBS OFF, block 3 (Load type A) and (e) DBS OFF, block 6 (Load type A). (19)

One study attempted to differentiate the severity of PD while ON and OFF medication (17). According to the authors, OFF medication leads to longer response time to auditory tasks and increased cost to perform simultaneous tasks, measured by the percent difference between combined auditory/motor tasks and auditory only tasks.

Table 1. Summary of studies in PD tremor assessment.

Authors	Purpose	Subjects	Protocol	Load
Brewer et al., 2009	Compare with UPDRS	26 PD	ASAP: Thump-index Force exertion to track target forces	Counting down
Attivissimo et al., 2009	Compare with FIM and Tinetti	35PD-42HT	Palmar grip	---
Pradhan et al., 2011	ON vs OFF L-dopa	9 PD	Twist Cap: Precision and power grip	Stroop test. Resistant loads
Krebs et al., 2007	ON vs OFF DBS	10 PD with DBS implant	Wrist Robot: kinematic movement	Perturbing loads
Giuffrida et al., 2009	Compare with UPDRS	60 PD	Kinesia: Rest, postural and kinematic tasks	---
Rigas et al., 2009	Compare RT Metric and ANN	5 HT	Shimmer: Simulating tremor with 4 severity levels	---

Conclusion

Table 1 summarizes all studies in PD tremor assessment and quantification. The fact that no treatments for PD currently exist leads to research on quantifying motor deficiency as a fundamental step to slow the progress of PD. The earlier the accurate assessment of PD is, the better healthcare professionals can delay PD progression. As an attempt to replace the UPDRS motor section, several studies have been proposed with several benefits over current standard tests including assessing motor function along with loads and objectively quantifying motor performance. Current standard PD rating scales are neither accurate nor consistent due to the subjective nature of the tests. To resolve this issue, a new PD assessment method that is both consistent and universally accepted should be introduced or the consistency of the current standard, UPDRS, should be improved. The current goal of motor assessment research is to build consistent, test-retest reliable features into the UPDRS, making the assessment more accurate.

Due to the lack of subjects for device performance testing, how reliably the device can measure PD motor performance is still in question. The fact that many studies only have a few PD patients, and others have to have HT patients simulating tremor, can lead to inaccurate results. Test-retest reliability with a large number of samples is one of the important future directions of research.

DETECTING PARKINSON'S DISEASE TREMOR

The loss of dopamine-generating cells begins long before the first symptom of PD becomes apparent. For this reason, early detection of PD is crucial for better PD treatments. On the other hand, PD tremor exhibits several similar characteristics with other diseases including essential tremor (ET) or enhanced physiological tremor (EPT). For this reason, healthcare professionals frequently misdiagnose PD patients and assign improper treatment. The similarity among the tremors of PD, ET, and EPT is the major obstacle for current research in differential diagnosis of these diseases.

Protocol and features

Similar to the protocol applied in tremor assessment, several studies used different hand movement tasks to detect tremor behavior in PD. De Oliveira et al. (22) introduced a micro-electro-mechanical system (MEMS) based capacitive accelerometer to retrieve signal from a motor test in which subjects were asked to move their predominant tremor hands along a 20-cm linear trajectory in a horizontal plane. Mutual information to evaluate the interdependency between x and y movements of hand in the horizontal plane is the main distinguishing feature between PD andH In a study from Melillo et al. (23), the subjects (3 PD, 3 ET, and 7 HT) started placing their arms on their upper legs for 30 seconds (static motor task). Then, the subjects performed an ascending and descending arm movement, with a continuous frequency, for 30 seconds (kinetic motor task) and returned to a relaxed position for another 30 seconds. A custom-made accelerometer was built for acceleration signal acquisition of 11 task segments to analyze the differences among PD patients, ET patients and HT group. Similarly, rest, postural and action tasks were recorded in 7 PD, 7 HT, and 7 ET patients (24). Four metrics, root mean square, peak to peak, approximate entropy, and power ratio values were calculated from the acceleration signal of the hand.

González et al. (25) requested more than 50 patients to perform static tasks (for postural tremor detection), kinetic tasks, 3D patterns and dynamic tasks. Subjects were asked to guide the PHANToM device to perform specific tasks on the monitor screen. Power spectral density and other parameters were then recorded to characterize PD and ET.

The above studies focused on scripted motor examination of PD tremors. In a scripted environment, subjects are asked to perform a predefined, guided set of tasks for specific types of motor evaluations. By contrast, unscripted environments allow subjects to participate in daily, regular activities without being constrained. In the study from Cole et al. (26), subjects wore EMG sensors and accelerometers for both scripted and unconstrained home-like environments. Features were extracted from tri-axial accelerometers and surface EMG sensors (sEMG). sEMG data showed that tremor was characterized with periodic bursts of energy while dyskinesia was represented by spontaneous bursts of energy that varied in amplitude and duration.

Samà (27) used a tri-axial accelerometer, a magnetometer, and gyroscope at 200 Hz to record tremor data. Subjects performed a set of scripted activities as well as unscripted activities in their own homes/apartments. A set of features, such as fast Fourier transform, peak frequency and amplitude, and median and mean amplitude, were calculated to detect the period of tremor.

Classification

Classification algorithms are pattern recognition methods/machine learning methods that guide computers to make decisions or choices or to recognize certain patterns in data based on a set of predefined rules and guidelines. Artificial neural network (ANN), support vector machine (SVM), and hidden Markov models (HMM) are several classification algorithms that are used extensively in pattern recognition applications. ANN is based on the mapping patterns of the brains and very effective for non-linear data classification. SVM is a differential classifier defined by separating hyper-planes. HMM is a statistical and probabilistic algorithm in machine learning.

Classification algorithms have been used extensively in detecting and differentiating tremor symptoms. Cole et al. (26) compared three classifiers, dynamic neural networks, dynamic support vector machines, and HMM, in terms of performance in detecting PD tremor and dyskinesia. The dynamic neural network performed the best with an error rate of less than 10%. Hossen et al. (28) calculated power spectral density of hand signals from piezoelectrical sensors and EMG sensors which served as input for the ANN. The ANN architecture had 16 input nodes, 3 hidden nodes, and one output to distinguish PD and essential tremor (ET). The error rate in this study was also below 10%. González et al. (25) used high-order statistics, combined with power spectral density, to extract 26 parameters. These parameters served as input to the multilayer perceptron neural network, and there were 3 outputs: PD, ET, or HT with value of 1 or 0 (yes or no). While the error rate was less than 20%, the result could be more reliable due to a larger number of subjects, 210 HTs, 34 ET, and 120 PD, which could result in better training and testing for the neural network algorithm.

Samà (27) attempted to compare the performance of a SVM with a linear kernel in two cases, one employing only the frequency-related features and the other with the frequency-related features and non-frequency related features. The research also evaluated both SVMs with an RBF kernel and a linear kernel. The results indicated that adding non-frequency features did not necessarily improve the accuracy. Also, a linear kernel was sufficient to detect tremor with only slightly lower sensitivity and specificity. Another study compared the performance of 2D-SVM and 3D-SVM (24). For the 2D-SVM, the input attribute vectors were the rest tremor RMS value and postural tremor peak-to-peak value. For the 3D-SVM, the input attribute vectors were the RMS value, postural tremor peak-to-peak value and action tremor power ratio. The overall result was that the misclassification rate for both SVMs was 9.5% but the 2D-SVM performed better than 3D-SVM when differentiating PD and ET.

According to Das et al. (29), supervised learning frameworks such as SVMs or ANNs were difficult for unscripted, uncontrolled home environments. The authors proposed multiple instant learning, a weakly supervised learning framework which does not require the exact instances of symptom occurrences for training, for PD tremor detection. Features included mean, energy, high frequency energy content, correlation, frequency domain entropy, and a five-bin histogram representation of the spectral contents over all three axes.

Application of information theory is a novel approach for differentiating between PD patients and a HT control group (22). The purpose of this study was to evaluate the hypothesis that a temporal interdependent processes exists between axial and perpendicular acceleration of the forearm during unconstrained upper limb movements. Authors also believed that the interdependence is lower in PD. By applying mutual information (MI) on the data analysis, they found the MI on HT subjects significantly differs from that observed in the PD group.

Conclusion

A summary of studies on PD tremor detection is shown in Table 2. One of the main obstacles researchers currently face is the differentiation between PD and ET. While some papers provided a clear visual difference in acceleration and EMG related signals between PD and ET, a systematic methodology for distinguishing between PD and ET with high sensitivity and specificity is lacking. This issue could be explained by the nature of these two diseases. Firstly, while rest tremor is the most prominent characteristic of PD, rest tremor is not obvious in all PD patients. Secondly, both PD and ET can exhibit postural tremor, making diagnostic tests challenging. Thirdly, the magnitude and frequency of acceleration signals in PD and ET tremors are similar. Resolving these three problems is the primary goal of current PD tremor detection research, ultimately developing reliable systems that can differentiate between PD and ET.

Current research focusing on unscripted protocol does not commonly include quantifying tremor. The algorithms can only record when and for how long tremor occurs but not the severity of each tremor occurrence. The unscripted protocol, however,

Table 2. Summary of studies in PD tremor detection and differentiation.

Authors	Purpose	Subjects	Protocol	Classification Algorithm
De Oliveira et al., 2011	PD vs HT	8PD – 8 HT	x-y movement horizontal plane	Information Theory
Cole et al., 2014	Tremor vs Dyskinesia	Training Set: 11 PD Test Set: 8 PD- 4HT	Unscripted task	DNN, DSVM, HMM
González et al., 2014	PD vs ET	>50 Patients	Following 2D and 3D patterns on screen	High Order Statistics + ANN
Melillo et al., 2014	PD vs ET vs HT	3PD – 3 ET – 7 HT	Ascending and descending arm	Kruskal-wallis (ANOVA)
Hossen et al., 2012	PD vs ET	training set: 21 ET, 19 PD Test set: 20 ET, 20 PD	---	ANN
Samà, 2014	Detect Tremor	Training set 12 PD Test Set 64 PD	Scripted + Unscripted	Support Vector Machine with linear kernel
Aubin et al., 2012	PD vs ET vs HT	7 PD- 7ET- 7HT	Rest, postural, action tasks	2D and 3D SVM
Das et al., 2012	Detect Tremor	2 PD for 4 days	Unscripted	Multiple Instance Learning

exhibits certain advantages over scripted motor assessments since UPDRS evaluation depends largely on the patients' self-reports. Hand tremor detection in daily activity could yield an objective and reliable standpoint for UPDRS evaluation. Unscripted tremor detection not only provides doctors with a complete picture of motor performance in various home situations but also takes into account the effect of medication or therapy, helping healthcare professionals to adjust the medication prescription if necessary.

THE CAUSE OF PD TREMOR

Several researchers have attempted to determine the origin of PD (30, 31, 32 and 33), yet there is limited information as to how the defects in the brain can result in motor complications such as PD tremor. Palanthandalam-Madapusi and Goyal (34) published a research paper explaining that PD tremor could be characterized by the limit cycle of the nonlinear dynamic system. In this system, the motor response was considered as a closed-loop feedback control system, with the feedback path represented by sensory feedback and the controller considered as the neural system that controlled the muscle movements. Within this context, the reaction time was a transport delay in the closed-loop system, which was known to be higher in PD patients (35). The authors then elaborated further that such delay, when greater than a certain threshold, resulted in an unstable system. The natural frequency ultimately saturated at a certain amplitude due to saturation in actuation and may result in a limit cycle. The hypothesis helped explain why a patient trying to keep his/her hand still (intended velocity = 0) would exhibit limit cycle oscillation, or rest tremor.

This hypothesis might be able to explain a role of DBS in tremor alleviation, whose mechanism is still unknown. The authors asserted that the perspective of the closed-loop system on PD tremor could help differentiate PD tremors with other similar diseases and develop new monitoring methods and treatments.

PD TREMOR SUPPRESSION

Because the origin and the treatment of PD are yet to be found, improvement of patients' quality of life is a temporary but essential current research topic. PD patients enduring prolonged rest tremors encounter muscle fatigues and impairment of motor functions. They also report several problems associated with postural tremor, a less common feature of PD, when fine motor tasks such as shirt buttoning and dining are required. Several methods including L-dopa therapy and DBS are currently the standard for PD relieving symptoms, yet their side effects could be great.

Several suppression devices have been proposed to alleviate vibrations from PD hand tremors. However, since PD tremor behaves nonlinearly in both time and frequency domains and PD tremors are different in different people, it can be difficult to build orthotic devices that adaptively suppress tremors. Researchers are looking for better and more robust control algorithms that can precisely detect and attenuate tremor without interfering with intentional movements, which is further complicated due to the fact that tremor signals and intentional movement signals are constantly distorted with noise.

Functional Electrical stimulation (FES) was introduced in 1992 as an early attempt to suppress tremor (36, 37). The main principle of this method was to apply electrical stimulation to antagonistic muscles during involuntary activation of agonist muscles. Maneski et al. (38) introduced the TremUNA system, an adaptive and programmable FES platform, that could suppress hand tremor in more than one joint. In order to track tremor frequency, amplitude and phase lag, the system was implemented with a Butterworth second-order adaptive band-pass filter. By applying multi-pad electrodes on one muscle group instead of a single cathode, the system reduced fatigue and achieved an average tremor suppression of 67%. A similar approach was used by Dosen et al. (39). The authors provided a comparison between two versions of FES and revealed a novel application of electrical stimulation toward PD hand tremor suppression. The performance of electrical stimulation above and below the motor threshold on tremor suppression were compared. Even though the extent of tremor suppression using sensory stimulation (35%-48%) is less than that using motor stimulation (46%-81%), sensory stimulation could prevent muscle fatigue and discomfort for the patients.

Hao et al. (40) hypothesized that the propriospinal neurons (PN) network transmitted the tremor command to the peripheral muscles. The authors used electrical stimulation to examine the motor response in PD hand tremors. A positive correlation between cutaneous afferents with a reduction in tremor amplitude and frequency was found. When transcutaneous electrical stimulation (TES) was applied to the dorsal hand skins of PD patients, there was an instant suppression of tremor amplitude and frequency, but the tremor amplitude quickly recovered to prior levels after stimulation while the frequency took longer to recover. One possible reason for this behavior is that the stimulation inhibited the effect of cutaneous afferents on PNs, thus reducing tremor amplitude and EMGs.

Piezoelectric devices are important for bridging the gap between electrical and mechanical applications. Piezoelectric actuators convert electrical signals, usually voltage, into mechanical output, usually force and motion, and vice versa. A piezoelectric actuator integrated smart glove was introduced to suppress hand tremor vibration (41). In order to evaluate the performance of this novel device, two experiments were conducted: actual human hand tremor suppression, and Intra Vernacular (IV) Training Arm tremor suppression. The IV Training Arm was a hand tremor simulator, whose tremor was generated by using two DC motors with unbalanced masses as a source of vibration. The result of this study showed that the percentage of tremor suppression was dependent on the piezoelectric actuator vibration frequency. At a vibrating frequency of 9Hz, the glove suppressed 76.16% of the acceleration magnitude peak in actual human hand tremor.

Teixeira et al. (42) proposed a self-tunable Dynamic Vibration Absorber (DVA) that could alter the DVA's mass. In a mass-spring-damper system, there are three main components whose changes in value could change the oscillating behavior: mass, damping coefficient, and stiffness coefficient. According to the authors, mass tuning for tremor suppression was easier than stiffness tuning and made the system lighter and smaller. In order to tune the DVA mass, the device was equipped with a fluidic-system with micro-pumps. The control algorithm changed the water flux of the mass element by analyzing the RMS of the amplitude at the oscillation's predominant frequency over time. An oscillating body, implemented with sinusoidal and PD's waveforms to emulate the desired movements, was used to evaluate the DVA's performance. The dampened DVA was able to suppress 57% of tremor in a particular PD patient's tremor signal.

In another novel design, Richer and Hurmuzlu (43) developed a non-linear force controller for a pneumatic actuator consisting of a double-action pneumatic cylinder. Taheri et al. (44) introduced the control algorithm to suppress tremor using the system developed by Richer and Hurmuzlu (43). The motion in the PD hand tremor frequency range was estimated to be 4-6 Hz (fundamental frequency) and 8-12 Hz (second harmonics) (44). Therefore, the range of 3-12 Hz was chosen as the tremulous frequency which was subjected to suppression. Then by using a back-stepping method, a suppressive torque moved the human arm joint such that the output of the high-pass filter converged to zero. A human arm joint simulator was built for the experiment. In the experiment, the suppressing device was tested for two cases: sinusoidal intentional motion with tremor, and arbitrary intentional motion with tremor. The overall result of 97.5-99.2% tremor suppression was achieved in this study.

Due to a lack of fundamental knowledge about the origin of PD tremor, hand tremor suppression relies mainly on tremulous movement features such as amplitudes and frequencies. Tremor suppression devices are temporary solutions for PD tremors because they tackle the symptoms rather than the cause of this disease. Furthermore, motor stimulation using FES could cause muscle fatigue and discomfort for the wearer. Current tremor suppression algorithms have phase lag and signal filter issues that cause either delays in tremor suppression or suppressing intentional motions. Improvements to the signal analysis system and suppression algorithms which robustly and effectively control PD hand tremors are still needed.

Discussion and Conclusion

As the size of the elderly population increases thanks to the better medications and healthcare systems, the number of PD patients also increases. While UPDRS III and H&Y scales remain the standard for PD motor quantification, there is a need for a better, less subjective motor assessment. UPDRS and H&Y scales depend on the self-reports from patients and the subjective perception of healthcare professionals, causing the assessments to be fluctuating and inconsistent. Different hand tremor assessment devices have been proposed to make the process of quantification more objective and consistent.

The shift toward unscripted, uncontrolled motor quantification seems to be a direction for future diagnostic tools. Unscripted motor estimation reflects most accurately the daily activity of patients. Patient tremor behavior fluctuates with time, thus making scripted motor task assessment less reliable. Further, unscripted motor assessment can take into account the changing effects of medication and treatments. Since it usually takes several hours to fully see the changing effect of L-dopa, unscripted motor assessment could objectively record all occasions when motor performance fluctuates. This method also eliminates the need for patients to manually log their tremor behavior versus time, which they sometimes forget.

The search for a wearable PD tremor suppression device that is light weight, inexpensive, aesthetically pleasing, and comfortable is the main challenge of current research. For many designs, extraneous weight might interfere with intentional movements during daily activities. Some methods using FES are reported to cause muscle fatigue and discomfort to the wearer. Many devices encounter phase lag that suppress tremor a few seconds after it occurs while other devices suppress intentional motion due to a blurred boundary between intentional motion and tremor. Even though tremor suppression studies are still preliminary, several studies report that the devices are able to suppress hand tremor significantly, both in tremor models and real PD and ET patients. However, more and actual PD subjects and test-and-retest reliability might be necessary to confirm the really positive impact of PD tremor suppression devices.

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REFERENCES

1. Parkinson, J. (2002). An Essay on the Shaking Palsy. Journal of Neuropsychiatry, 223-236.
2. Morrison, S., Kerr, G., & Silburn, P. (2008). Bilateral tremor relations in Parkinson's disease: Effects of mechanical coupling and medication. Parkinsonism & Related Disorders, 14(4), 298-308.
3. Forssberg, H., Ingvarsson, P., Iwasaki, N., Johansson, R., & Gordon, A. (2000). Action tremor during object manipulation in Parkinson's disease. Mov. Disord. Movement Disorders, 15(2), 244-254.
4. Wenzelburger, R., Raethjen, J., Loffler, K., Stolze, H., Illert, M., & Deuschl, G. (2000). Kinetic tremor in a reach-to-grasp movement in Parkinson's disease. Mov. Disord. Movement Disorders, 15(6), 1084-1094.
5. Duval, C. (2006). Rest and postural tremors in patients with Parkinson's disease. Brain Research Bulletin, 70(1), 44-48
6. Statistics on Parkinson's. (n.d.). Retrieved November 4, 2015. http://www.pdf.org/en/parkinson_statistics
7. Jankovic, J. (2008). Parkinson's disease: Clinical features and diagnosis. Journal of Neurology, Neurosurgery & Psychiatry, 79(4), 368-376.
8. Fahn, S., Elton, R.L., Members of the UPDRS development committee. (1987). Unified Parkinson’s disease rating scale, recent developments in Parkinson’s disease 2. 153–164.
9. Hoehn, M., & Yahr, M. (1967). Parkinsonism: Onset, progression, and mortality. Neurology, 17(5), 427-442.
10. Geminiani, G., Cesana, B., Tamma, F., Contri, P., Pacchetti, C., Carella, F., Caraceni, T. (1991). Interobserver reliability between neurologists in training of Parkinson's disease rating scales. A multicenter study. Movement Disorders Mov Disord., 6(4), 330-335.
11. Standaert, D., & Young, A. (2001). Treatment of central nervous system degenerative disorder. In J. Hardman & L. Limbird (Eds.), Goodman and Gilman's Pharmacological Basis of Therapeutics (10th ed., pp. 549-620). McGraw-Hill.
12. Chase, T. (1998). Levodopa therapy: Consequences of the nonphysiologic replacement of dopamine. Neurology, 50(5), S17-25
13. Aziz, T. and Yianni, J. (2003). Surgical treatment of Parkinson's Disease. Advances in Clinical Neuroscience and Rehabilitation, 2(6), 21-22.
14. Eberle, W., Penders, J., & Yazicioglu, R. F. (2011). Closing the loop for deep brain stimulation implants enables personalized healthcare for Parkinson's disease patients. 2011 Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 1556-1558.
15. Brewer, B. R., Pradhan, S., Carvell, G., & Delitto, A. (2009). Application of modified regression techniques to a quantitative assessment for the motor signs of Parkinson’s disease. IEEE Transactions on Neural Systems and Rehabilitation Engineering : A Publication of the IEEE Engineering in Medicine and Biology Society, 17(6), 568–575.
16. Attivissimo, F., Cavone, G., Lanzolla, a. M. L., & Savino, M. (2009). Application of hand grip signals for an objective evaluation of Parkinson disease: Analysis and comparison with standard functional clinical tests. Measurement: Journal of the International Measurement Confederation, 42(8), 1123–1130.
17. Pradhan, S. D., Scherer, R., Matsuoka, Y., & Kelly, V. E. (2011). Use of sensitive devices to assess the effect of medication on attentional demands of precision and power grips in individuals with Parkinson disease. Medical and Biological Engineering and Computing, 49(10), 1195–1199.
18. Pradhan, S., Brewer, B., Carvell, G., Sparto, P., Delitto, A., & Matsuoka, Y. (2010). Assessment of fine motor control in individuals with Parkinson’s disease using force tracking with a secondary cognitive task. Journal of Neurologic Physical Therapy, 34(1), 32-40.
19. Krebs, H. I., Shils, J. L., Apetauerova, D., & Arle, J. E. (2007). Parkinson’s disease : a motor control study using Wrist Robot. Advanced Robotics, 21(10), 1201–1213.
20. Giuffrida, J. P., Riley, D. E., Maddux, B. N., & Heldmann, D. a. (2009). Clinically deployable kinesia technology for automated tremor assessment. Movement Disorders, 24(5), 723–730.

21. Rigas, G., Tzallas, A. T., Tsalikakis, D. G., Konitsiotis, S., & Fotiadis, D. I. (2009). Real-time quantification of resting tremor in the Parkinson's disease. Proceedings of the 31st Annual International Conference of the IEEE Engineering in Medicine and Biology Society: Engineering the Future of Biomedicine, EMBC 2009, 1306–1309.
22. De Oliveira, M. E., Menegaldo, L. L., Lucarelli, P., Andrade, B. L. B., & Büchler, P. (2011). On the use of information theory for detecting upper limb motor dysfunction: An application to Parkinson's disease. Physica A: Statistical Mechanics and Its Applications, 390(23-24), 4451–4458.
23. Melillo, P., Scala, P., Santoro, D., Vadursi, M., & Pecchia, L. (2014). The International Conference on Health Informatics, 42, 110–113.
24. Aubin, P. M., Serackis, A., & Griskevicius, J. (2012). Support vector machine classification of Parkinson's disease, essential tremor and healthy control subjects based on upper extremity motion. 2012 International Conference on Biomedical Engineering and Biotechnology, 900–904.
25. González, R., Barrientos, A., del Cerro, J., & Coca, B. (2014). DIMETER: A haptic master device for tremor diagnosis in neurodegenerative diseases. Sensors (Switzerland), 14(3), 4536–4559.
26. Cole, B., Roy, S., De Luca, C., & Nawab, S. (2014). Dynamical learning and tracking of tremor and dyskinesia from wearable sensors. IEEE Transactions on Neural Systems and Rehabilitation Engineering : A Publication of the IEEE Engineering in Medicine and Biology Society, 4320(c), 982–991.
27. Samà, A. (2014). Is "frequency distribution" enough to detect tremor in PD patients using a wrist worn accelerometer? Proceedings of the 8th International Conference on Pervasive Computing Technologies for Healthcare.
28. Hossen, A., Muthuraman, M., Raethjen, J., Deuschl, G., & Heute, U. (2012). A neural network approach to distinguish parkinsonian tremor from advanced essential tremor. Advances in Intelligent and Soft Computing 130, 1051–1060.
29. Das, S., Amoedo, B., Torre, F., & Hodgins, J. (2012). Detecting Parkinsons' symptoms in uncontrolled home environments: A multiple instance learning approach. 2012 Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 3688-3691.
30. Fahn, S., & Cohen, G. (1992). The oxidant stress hypothesis in Parkinson's disease: evidence supporting it. Annals of Neurology Ann Neurol., 32(6), 804-812.
31. Hallett, M., Jasper, R., Daube, J.R., Mauguire, F. (2003), Movement Disorders, Elsevier Health Sciences.
32. Stefanis, L. (2011). α-Synuclein in Parkinson's disease. Cold Spring Harbor Perspectives in Medicine, 2(2).
33. Science News. (2015, July 14). Parkinson's Disease Foundation. Retrieved November 4, 2015. http://www.pdf.org/en/science_news/release/pr_1436895968.
34. Palanthandalam-Madapusi, H. J., & Goyal, S. (2011). Is parkinsonian tremor a limit cycle? J. Mech. Med. Biol. Journal of Mechanics in Medicine and Biology, 11(05), 1017-1023.
35. Visanji, N., Brooks, P., Hazrati, L., & Lang, A. (2015). The prion hypothesis in Parkinson's disease: Braak to the future. Acta Neuropathologica Communications Acta Neuropathol Commun, 15(5), 28-28.
36. Prochazka, A., Elek, J., & Javidan, M. (1992). Attenuation of pathological tremors by functional electrical stimulation I: Method. Annals of Biomedical Engineering Ann Biomed Eng, 20(2), 205-224.
37. Javidan, M., Elek, J., & Prochazka, A. (1992). Attenuation of pathological tremors by functional electrical stimulation II: Clinical evaluation. Annals of Biomedical Engineering Ann Biomed Eng, 20(2), 225-236.
38. Maneski, L. P., Jorgovanović, N., Ilić, V., Došen, S., Keller, T., Popović, M. B., & Popovic, D. B. (2011). Electrical stimulation for the suppression of pathological tremor. Medical and Biological Engineering and Computing, 49(10), 1187–1193.
39. Dosen, S., Muceli, S., Dideriksen, J., Romero, J., Rocon, E., Pons, J., & Farina, D. (2014). Online tremor suppression using electromyography and low level electrical stimulation. IEEE Transactions on Neural Systems and Rehabilitation Engineering : A Publication of the IEEE Engineering in Medicine and Biology Society, 4320(c), 1–11.
40. Hao, M. Z., He, X., Kipke, D. R., & Lan, N. (2013). Effects of electrical stimulation of cutaneous afferents on corticospinal transmission of tremor signals in patients with Parkinson's disease. International IEEE/EMBS Conference on Neural Engineering, NER, 355–358.
41. Kazi, S., Azizan, Zain, Z. M., & Mailah, M. (2010). Performance evaluation of smart glove applied to experimental rig to control human hand tremor for parkinson disease. Recent Advances and Applications of Computer Engineering: Proceedings of the 9th WSEAS International Conference (ace 10), Univ Kebangsaan.
42. Teixeira, C., Bicho, E., Rocha, L., & Gago, M. (2013). A self-tunable dynamic vibration absorber: Parkinson's Disease's tremor suppression. 2013 IEEE 3rd Portuguese Meeting in Bioengineering (ENBENG).
43. Richer, E., & Hurmuzlu, Y. (1999). A high performance pneumatic force actuator system: Part I—Nonlinear mathematical model. J. Dyn. Sys., Meas., Control Journal of Dynamic Systems, Measurement, and Control, 122(3), 416-425.
44. Taheri, B., Case, D., & Richer, E. (2014). Robust controller for tremor suppression at musculoskeletal level in human wrist. IEEE Transactions on Neural Systems and Rehabilitation Engineering, 22(2), 379–388.

