Tremor in Parkinson's Disease with Mechanical Devices

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Parkinsonian tremors are sometimes confused with essential tremors or other conditions. Researchers conducted several studies on tremor evaluation using wearable sensors and devices, which may support an accurate diagnosis. Mechanical devices are also commonly used to treat tremors and have been actively researched and developed. Mechanical devices for tremor suppression include deep brain stimulation (DBS), electrical muscle stimulation, and orthosis. Adaptive DBS and optimization of stimulation parameters have been studied to improve treatment efficacy further. Due to developments using state-of-the-art techniques, effectiveness in diagnosing, evaluating, and suppressing tremors using these devices is satisfactorily high in many studies.

Parkinson's disease essential tremor diagnosis

1. Introduction

Parkinson's disease (PD) is a progressive degenerative disorder primarily characterized by the degeneration of dopamine neurons in the substantia nigra [1][2]. Its main symptoms include tremor, rigidity, bradykinesia, akinesia, and postural instability [3]. Tremors are one of the most common motor symptoms of PD. PD can be classified into different subtypes as follows: patients with predominant akinesia/rigidity, which is an akinetic-rigid type (ART), and those with a tremor-dominant type (TDT) [4]. PD-ART displays greater cognitive impairment and faster progression than TDT-PD [5]. This warrants understanding the status of tremors, considering their role in diagnosing the disease and its symptoms. Non-pathological, slight physiological tremors can be found in normal individuals. Pathological tremor affects more than 0.4% of the population [6], and its incidence and prevalence increase substantially with age [7].

Tremor is caused by a variety of conditions [8], and its exact underlying mechanism is not understood [9]. Among several causes of tremor, the most common and incidental types of tremor are seen in patients with PD and essential tremor (ET) [6]. ET is a major differential diagnosis. According to the 2018 Movement Disorders Consensus Criteria, ET is characterized by isolated bilateral upper limb movement tremor with a duration of at least 3 years without other neurologic signs [9]. Tremor in patients with ET and PD is sometimes confusing. PD is a complex neurodegenerative disorder, usually characterized by asymmetrical onset bradykinesia, muscular rigidity, postural instability, and tremor. Patients with PD present with resting tremor, as well as other symptoms, except during the early stages. Resting tremors are often enhanced by walking and performing tasks, such as calculation. In contrast, tremor severity tends to increase during kinetic tasks in patients with ET. Despite the lack of a test to confirm diagnosis, medical interviews, physical examinations, and blood tests should exclude other common causes of action tremors, such as the side effects of certain medications or hyperthyroidism.

Tremor assessment is based on physical examination by a neurologist. Current diagnostic methods and quantification are based on the phenomenological demonstration of tremor, principally with the help of movement disorder scales, such as the essential tremor rating assessment scale [10], Fahn–Tolosa–Marin scale [11], and Unified Parkinson’s Disease Rating Scale (UPDRS) [12]. The correct diagnosis of the different tremor types is essential for treatment, which may depend on the specific etiology of each type. However, tremor misdiagnosis owing to confusion between PD and ET can occur in 20% to 30% of cases [13][14]. Thus, technological solutions may improve the quality of diagnosis and quantify the disease stage.

2. Tremor Diagnosis Using Devices

2.1. Distinguishing between Patients with PD and Healthy Individuals, Using Devices

With regard to tremor diagnosis, distinguishing between ET and PD is sometimes challenging. Therefore, researchers are actively identifying ways to support differential diagnosis by device-based objective evaluation. The first step in diagnosis is to distinguish a patient from a healthy individual. Giulia et al., used a wearable inertial sensor to discriminate between patients with PD and healthy participants [15]. Thirty-six patients with PD and 29 healthy controls performed the following seven motor tasks from the Movement Disorder Society-Sponsored Revision of the Unified Parkinson’s Disease Rating Scale (MDS-UPDRS) III wearing inertial sensors: resting tremor, postural tremor, rapid alternating hand movement, foot tapping, heel-to-toe tapping, timed up and go test (TUG), and a pull test. Of these endpoints, SVM was performed using highly relevant items, namely, tremor, bradycardia, pull test, and TUG, and was able to distinguish between patients with PD and healthy controls with a high accuracy of 97%. Channa et al., also developed the A-WEAR bracelet for diagnosis using 3D acceleration and gyroscopes, which accurately identified PD with a 91.7% probability by K-nearest neighbors [16]. Such research has been applied to smartphones and smartwatches. Kostikis et al., developed a smartphone-based tool to assess upper limb tremor in patients [17]. Using machine learning, the system correctly classified 82% and 90% of the patients and healthy participants, respectively, based on data from a smartphone’s accelerometer and gyroscope. Prototypes have also been developed using smartwatches [18]. This system was tested with artificial neural networks, random forests, and SVM, and trained on a sample comprising 192, 75, and 51 patients with PD, other movement disorders, and healthy participants, respectively. Artificial neural networks displayed the best results in distinguishing healthy participants from others, including those with PD and other movement disorders, with precision and recall of 0.94 (SD 0.03) and 0.92 (SD 0.04), respectively. Moreover, SVM demonstrated the best performance in distinguishing patients with PD from those with other motor disabilities, and healthy participants, with precision and recall of 0.81 (SD 0.01) and 0.89 (SD 0.04), respectively. Moreover, there are other validations of diagnostics using commercially available smartwatches [19]. A study which used the Apple Watch series 3 and 4, which are commonly distributed smartwatches, first evaluated their accuracy by comparing it with the Nanometrics seismometer. Both series 3 and 4 were confirmed to be accurate, with a maximum error of <0.01 Hz from the seismograph. The patient performed a test designed by a disability specialist to obtain acceleration data while wearing the smartwatch. Machine learning was used to discriminate between patients with PD, healthy participants, and those with motor impairments other than PD (ET, Parkinsonism, etc.). The machine learning classifiers used were as follows: SVM, CatBoost, multilayer perceptron, and simple deep learning architecture. SVM, CatBoost, and multilayer perceptron displayed a balanced accuracy of >80% and precision and recall rates of >90% for patients with PD and healthy participants. In an advanced task that distinguishes PD and non-PD motor impairment, the multilayer perceptron demonstrated a balanced accuracy, precision, and recall of 74.1%, 86.5%, and 90.5%, respectively. Thus, considerable identification accuracy can be achieved, even with consumer products. Another study used inertial data from a commercially available smartwatch to investigate eating behavior and evaluate the reduction in motor symptoms in PD [20]. They evaluated plate-to-mouth (PtM) in seven healthy participants and 21 patients with PD. PtM is a measure related to the average time for the hands to transfer food from the plate to the mouth when eating. Those with PD had higher PtM values than healthy participants. Furthermore, a model using PtM was used to classify patients and revealed precision, recall, and F1 (harmonic mean of fit and recall) of 0.882, 0.714, and 0.789, respectively. However, some of the aforementioned methods are difficult to use because they require expertise in system operation and maintenance. Junior et al., developed a device that can be combined with a regular pen as an approach for easier and simpler diagnosis [21]. It can distinguish patients with PD from healthy individuals through a simple diadochokinetic paper test, which assists in diagnosing the early stages of PD. The device was equipped with an accelerometer and gyroscope, and the acquired data were classified using linear discriminant analysis, logistic regression, classification and regression trees, K-nearest neighbors, SVM, and naive Bayes. The results confirmed that the overall accuracy was approximately 100% for multiple classifiers.

2.2. Distinguishing between PD and ET Using Devices

The classic method of differentiating PD tremor from ET involves iodine-123-labelled N-omega-(fluoropropyl)-2beta-carbomethoxy-3beta-(4-iodophenyl) tropane and iodine-123-labelled 2β-carbomethoxy-3β-(4-iodophenyl) tropane dopamine transporter imaging with single-photon emission computed tomography using nuclear imaging techniques [22][23][24]. However, its accuracy may be less than that of clinical diagnosis by movement disorder specialists [25]. In addition, nuclear imaging techniques are widely unavailable because they involve radiopharmaceuticals and are expensive and time-consuming. This warrants considering the mechanism of relatively inexpensive and widely available wearable devices to identify PD and ET. Despite an overlap between the frequency ranges exhibited by PD and ET tremors, the accelerometer power spectrum analysis signals can effectively distinguish between PD and ET [26][27][28][29][30][31]. Thanawattano et al., proposed a novel method for extracting temporal features based on variations in the frequency of tremors with state [26]. They attached six-axis inertial sensors to the index fingers of the participants and requested them to perform three tasks as follows: kinetic, postural, and resting. Each task took 10 s to complete. The elliptical regions of two-dimensional representations of the resting task for those with PD and ET were significantly different ($p < 0.05$). Locatelli et al., developed a small, low-cost, wearable device with an inertial sensor [32]. The device was worn on the wrist, and four standardized tasks were performed to acquire data and build a classification model, which achieved an average accuracy of >90%. Researchers have also used the acceleration from a smartwatch to identify PD and ET

[27]. The use of the mean harmonic peak power obtained from the accelerometer could facilitate calculation of the optimal discrimination threshold by a receiver operating characteristic (ROC) analysis (sensitivity 90.9%, 95% CI 58.7–99.8%; specificity 100%, 95% CI 76.8–100%; and Cohen’s kappa = 0.91, SE = 0.08). In addition, the accuracy of the smartwatch was evaluated using an analog accelerometer and provided consistent estimates of the peak frequency and proportional harmonic power. Studies have also been conducted using smartphones: Woods et al., performed a task while holding a smartphone in the hand to obtain acceleration information [30]. This application used discrete wavelet transforms and SVM to classify the data and found an accuracy rate of over 96%. Barrantes et al., also used smartphones to identify PD and ET [33]. Patients with an undecided diagnosis were included in the evaluation and were re-evaluated after 1 year. For the experiment, smartphones were placed on the dorsal side of the hand, and recordings were obtained for epochs of 30 s at rest and 30 s during arm stretching. They calculated the ROC of the total spectral power to establish a threshold to separate participants with and without tremors. The results demonstrated an accurate diagnosis of PD or ET in 27 of 32 patients (84.38% discrimination accuracy). Of the patients with undecided diagnoses, all PD cases (two) and two of four ET cases were correctly classified. Duque et al., also performed machine learning classification using the linear acceleration of tremor recorded by the smartphone’s built-in accelerometer, and showed performances ranging from 90.0% to 100.0% sensitivity, and 80% to 100% specificity [34]. Thus, the smartphone, a familiar device, is expected to be utilized. Moon et al., evaluated the performance of several machine-learning methods, including neural networks, SVM, K-nearest neighbor methods, decision trees, random forests, and gradient boosting [35]. They used six inertial sensors (on the wrist, back of the foot, sternum, and hip) to analyze balance and gait characteristics to distinguish between PD and ET. The F1 score (harmonic mean of fit and recall), which is the most commonly used performance metric in machine learning, was 0.61, 0.59, 0.56, 0.55, 0.53, and 0.49 for neural networks, gradient boosting, random forest, SVM, decision tree, and K-nearest neighbors, respectively. It was superior to conventional logistic regression, thus confirming the usefulness of machine learning for diagnosis. Most studies were diagnostic, based on data obtained from inertial sensors, although some studies were conducted using EMG. A study investigating the EEG characteristics of resting tremor in patients with ET and PD confirmed that the parameter that best differentiated the two disorders was the pattern of muscle activation [36]. Vescio et al., developed a μEMG device worn on the wrist to record resting tremor [37]. Comparison with common EMG recordings confirmed a good correlation between tremor frequency (r = 0.93, $p < 0.001$) and phase difference (r = 0.92, $p < 0.001$). Thus, wearable devices have been used to classify PD and ET with high accuracy. Further validation may provide more efficient diagnostic and prognostic tools that can assist clinicians in decision-making processes.

3. Tremor Evaluation Using Devices

3.1. Tremor Evaluation Using Wearable Sensors

Raethjen et al., and Zhang et al., used EEG and EMG data to characterize tremors in patients with PD [38][39]. Currently, surface electromyography (sEMG) is the standard technique used for the characterization and monitoring of tremors in patients with PD [40]. Researchers have assessed the severity of tremors to determine the diagnostic usefulness of sEMG. They compared 30 patients with PD with a healthy age-matched control group by attaching bipolar sEMG to the biceps brachii muscle and evaluated muscle activity. The recurrence and determinism rates were significantly higher in the PD group than in the control group, and were correlated with the UPDRS scores [41]. Inertial sensors have been increasingly used in recent years [42][43][44][45]. A study comparing the accuracy of inertial sensors and EMG motion tracking showed that inertial sensors were more accurate [46]. Data-processing approaches vary across studies. Rigas et al., successfully estimated tremor severity based on acceleration acquired using accelerometers attached to body segments and features extracted from a hidden Markov model [47]. Using a gradient descent algorithm, Cai et al., isolated the acceleration caused by pure translational motion. A multiple regression model of UPDRS was created from the features extracted from these accelerations and angular velocities [48]. The performance of this model was r^2 = 0.95 for resting tremor and r^2 = 0.93 for postural tremor. Kim et al., developed SNUMAP, a wrist-mounted evaluation device with a three-axis accelerometer and gyroscope [49]. They trained recordings from 92 patients with PD using a convolutional neural network (CNN) to create an estimated UPDRS model. The results displayed an average accuracy of 85%, with a linearly weighted kappa of 0.85. CNNs could achieve higher accuracy than simple machine learning methods, such as SVM or regression. Such machine learning-based methods have been a trend in recent years, and numerous studies have been conducted. Wu et al., extracted characteristic values from acceleration signals in the time, frequency, and spectral domains, and tested multiple machine learning methods. The results showed that the neural network model was more accurate than the SVM, random forest, and multivariate linear regression models [50]. Another method using CNNs is to learn a convolved 2D image of the frequency response of the tremor signal [51]. The results showed an average accuracy of 91%, with a linearly weighted kappa of 0.91. Moreover, researchers have proposed an approach to estimate UPDRS using fuzzy inference rather than machine learning [52]. The fuzzy theory postulates that the truth value is not binary, true, or false but rather deals with all intermediate values. Moreover, it considers uncertainty. This method is scalable and easily tunable because it is modeled in a manner similar to the human inference process. Garza-Rodríguez et al., also used fuzzy inference to evaluate UPDRS from hand pronation/supination exercises, and found that in most cases the results were consistent with expert evaluation [53]. While wearable sensors have the advantage of monitoring patients in several situations, devices that do not require attachment to the patient are also useful while measuring behavioral tremors under specific conditions. This led to the development of Rehapiano, an ergonomically designed tremor evaluation device with strain gauges placed on a two-handed handle [54]. The performance evaluation also confirmed that the sensitivity was sufficient to quantify the tremor. The other product is the TREMITAS-System, a pen-type device with an accelerometer, 3D gyroscope, and 3D magnetometer [55]. This device was able to quantify tremors and was significantly correlated with UPDRS and the tremor research group essential tremor assessment scale subscores.

3.2. Tremor Evaluation Using Smartphones and Smartwatches

Smartphones have become the most popular devices in recent years, and studies have been conducted on the evaluation of tremors using these devices. This is partly attributable to the rapid increase in their computing power. Lemoyne et al., used a common smartphone to evaluate tremor frequency in patients with PD [56]. Araujo et al., demonstrated good consistency between a clinically obtained EMG, and accelerometer data obtained using smartphone applications (Pearson > 0.8, $p < 0.001$) [57]. Bermeo et al., developed an Android application that could assess the status of patients with PD based on three tests in the MDS-UPDRS [58]. Kostikis et al., used a smartphone's gyroscope and accelerometer to detect and quantify tremors. The smartphone detected data on hand tremors, and the UPDRS hand tremor scores revealed a good correlation ($r > 0.7$ and $p < 0.01$) [17]. These studies have often been conducted in controlled environments, such as laboratories; however, some studies were performed in free-living environments. Researchers have proposed an algorithm for tremor classification using a multiple-instance learning method based on smartphone acceleration to cope with noisy data, which demonstrated good classification performance [59]. van Brummelen et al., compared laboratory-grade and consumer product accelerometers and suggested that the amplitude at peak frequency varied among the sensors, indicating that distal worn sensors tended to measure higher amplitudes relative to proximal ones. Thus, the placement of sensors may be an important part of evaluating tremor amplitude [60]. Thus, tremors can be detected and evaluated with high precision without using dedicated sensors, besides having considerably lower hurdles for their use.

In addition to smartphones, several smartwatches have become popular in recent years, with the availability of numerous models. Smartwatches may be suitable for tremor assessment because they are worn on the wrists. Several studies evaluated tremors using sensors attached to the wrist. López-Blanco et al., quantified resting tremors by obtaining the parameters of tremor intensity from the root mean square of angular velocity acquired from a smartwatch [61]. Furthermore, they simultaneously performed a statistical analysis of the quantified data with the UPDRS-III score, which revealed a strong correlation with a Spearman's correlation coefficient (ρ) of 0.81 ($p < 0.001$). In addition, satisfaction associated with the device was high. Tremors can also be classified using machine learning based on triaxial acceleration data from commercially available smartwatches [62]. Investigators have achieved high tremor detection performance using a multitasking CNN that uses both raw signals and spectral data representations as inputs. They are exploring data measurement characteristics necessary for the accurate detection of PD symptoms [63]. Following a comparative evaluation of commercially available smartwatches and measurement sensors with multiple functions, accelerometer data from the smartwatch alone were sufficient to detect tremors. A sampling rate ≥ 30 Hz was required to detect tremors using acceleration. In addition, they investigated the impact of the features used in machine learning (time, frequency, entropy, correlation, and derivative) on accuracy. Entropy was identified to be important for tremor detection. Entropy is computationally expensive and affects real-time performance and battery consumption. Taken together, tremor detection using smartwatches has reached a practical level and is expected to be utilized. The use of affordable wearable technology is less burdensome and the most useful approach for routine care and assessment of patients with PD.

4. Tremor Monitoring

Despite the variety of novel devices being designed to assess tremors at specific times, several studies have aimed at continuous monitoring. Assessments in clinics and other settings are time-limited and may not reflect routine symptoms. This warrants an evaluation with prolonged monitoring to accurately assess disease status. Such monitoring is also expected to be used as screening for the application of advanced treatments, such as DBS [64]. In the early studies, there was a type of study in which tests were taken several times a day [65]; however, in recent years, a continuous monitoring system has also been realized. Pulliam et al., attached motion sensors to the limbs and obtained data for six daily activities, such as eating and brushing teeth [66]. Assessments of 13 patients with PD revealed that the ratings by ROC curves were consistent with the clinician's UPDRS-III ratings of the video recordings (ROC area > 0.8). Similarly, Hssayeni et al., measured tremor severity from activities of daily living with wrist- and ankle-mounted three-axis gyroscopic sensors; results from 24 patients with PD displayed the maximum correlation of 0.96 in gradient tree boosting [67]. Researchers have proposed wearable sensors attached to the wrist and chest combined with questionnaire-based assessment for continuous monitoring of PD symptoms in daily life [68]. Overlapping frequency components make it difficult to distinguish between daily activities and tremors; nonetheless, a method has been proposed for detecting tremors using a two-step algorithm [69]. Another device that can detect PD hand tremors from daily movements is the PD-Watch [70]. This device enables detection by checking for movement frequency and supination–pronation characteristics. The index calculated from 24 h of data obtained from this device was shown to correlate with the UPDRS score. Furthermore, a system was proposed as a machine learning approach to detect tremors in daily life data using a CNN and other techniques from a wearable accelerometer system worn on the wrist [71]. This technology enabled the quantification of the number of tremors in daily life. For a more user-friendly and complete sensor, researchers developed the biosensor patch NIMBLE (MC10, Inc., Lexington, MA, USA) with an accelerometer and myoelectric system [72]. It can adhere to the skin using adhesive stickers. In addition, the measurements can be wirelessly transmitted to a smartphone or tablet and a cloud server. Prediction scores using acquired data were within the range of ±1, with a probability of 91%. Moreover, their adhesion and safety were evaluated. Such techniques may allow for better treatment by assessing tremors at higher frequencies in daily activities.

5. Treatments for Tremor

5.1. DBS

DBS has been established as the standard of care for patients with movement disorders, such as PD, ET, and dystonia. DBS is an effective and widely used treatment for these patients, and the majority of them achieve good clinical results following surgery [73][74][75]. DBS improves bradykinesia [73], gait freezing in PD [76][77], camptocormia [78][79], and tremor [80]. Moreover, it is a safer treatment with lower complication rates than stereotactic thalamotomy [81][82]. The subthalamic nucleus (STN) and internal globus pallidus (GPi) are the most common targets for PD stimulation [83]. A meta-analysis evaluating the effect of DBS on tremor suppression compared DBS ON and OFF conditions and found a significant standardized difference mean effect (effect size = 0.36; 95% CI = 0.316–0.395; $p < 0.0001$) [84]. The sum of UPDRS III, items 20 and 21, was used for this measure. These results indicate moderate effectiveness. Z-test results showed no significant difference in effect size between STN and GPi ($p = 0.56$). A 12-month follow-up study also confirmed its effectiveness in reducing action/postural tremor and resting tremor [85]. The method of electrode placement is also important. Diffusion tensor imaging and tractography guided lead placement have been shown to provide more stable placement and better tremor control compared to conventional methods of lead placement [86]. Other targets include the ventral intermediate nucleus of the thalamus (VIM), caudal zona incerta, and posterior subthalamic area, which have a striking effect in improving tremors [87][88][89][90][91][92]. Therefore, if tremor is the main problem, rather than bradykinesia for patients with PD, these targets are warranted to be considered as first choice. A study of 98 patients with PD and ET showed sustained improvement in tremor scores (UPDRS III, items 20 and 21; Fahn–Tolosa–Marin Tremor Rating Scale) with VIM stimulation (mean improvement, 70% and 66% at 1 year and 63% and 48% at >10 years, respectively, $p < 0.05$) [92]. There was no significant loss of a stimulation effect over time ($p > 0.05$). Thus, the effects of DBS are long-lasting. Tremor can be controlled by maintaining the activities of daily living, and there was high patient satisfaction during the 10-year follow-up [93]. However, DBS is not effective in all patients, and patients need to determine whether they are appropriate candidates.

aDBS

Advances in DBS technology are ongoing, and novel research and development are underway. aDBS is one of the most innovative techniques. An aDBS device operates on the principle of closed-loop interaction, which can determine the effect of stimulation and adjust it, in response to the observed effect. LFPs are used as biomarkers to achieve a closed loop in aDBS. aDBS with LFPs has the advantage of being achieved by the online analysis of deep brain recordings, without the need for additional measurement channels. It is effective and is currently being used to treat patients with PD [94][95][96][97].

With regard to tremor suppression, an aDBS device has not been used clinically. Performing DBS only after the appearance of symptoms may reduce battery consumption. Power consumption is important because battery replacement requires surgery. aDBS necessitates the detection of tremors from the LFP. Reliable symptom detection is important for the implementation of aDBS. Tremor-related activity occurs throughout the motor network [98][99]. Specifically, it includes the basal ganglia, thalamus, cerebellum, and primary motor cortex, which coherently respond at tremor frequencies of 3–7 Hz upon their presentation [100]. Other findings include an increase in low gamma power (31–45 Hz) [101][102] and changes in high-frequency fluctuations in the subthalamic nucleus [103]. Advanced techniques, such as machine learning, are required to capture the aforementioned complex features. Hirschmann et al., used a hidden Markov model to classify tremors [104]. They obtained the LFP from the STN of 10 patients with PD, which was evaluated using four frequency domains (power at the individual tremor frequency ± 1 Hz, beta power, low gamma power, and high-frequency oscillations power ratio). The results indicated a mean area under the ROC curve of 0.82 and a SD of 0.15. Furthermore, it displayed good accuracy, even without training, for individual patients. High-frequency domain is the most useful feature for detecting tremors. Camara et al., developed a system that simultaneously recorded LFP in the subthalamic nucleus and electromyographic activity in the forearm and used fuzzy inference to detect tremors based on the relationship between the signals [105]. The system displayed 100% accuracy in detecting tremors in four of 10 patients with PD and attained >98.7% accuracy in seven patients.

The Optimization of Stimulation Parameters

The optimization of stimulation parameters is important for the efficient use of DBS. Setting general DBS parameters often relies on subjective evaluation, which may not yield optimal effects. In addition, multiple parameters, such as frequency, pulse width, and amplitude, must be set appropriately within the time constraints. Thus, researchers proposed next-generation methods to quantify tremors using wearable sensors as objective indicators for determining stimulation parameters. Pulliam et al., proposed an algorithm in which motion sensors, including accelerometers and gyroscopes, were attached to the fingers to acquire motion data, which were subsequently used to set the DBS parameters [106]. There were two algorithms, as follows: one to maximize the treatment effect and the other to optimize the battery life. The algorithm that maximized the treatment effect reduced motor symptoms by 13%; however, it increased the stimulus amplitude, compared with the usual setting method. In contrast, the algorithm that optimized battery life successfully reduced the stimulus amplitude by an average of 50% while maintaining the level of therapeutic effect. Currently, the intraoperative parameter setting is subjectively performed. A system was developed to assist in electrode placement and test stimulus settings during DBS implantation surgery for awake patients. The system facilitated the quantitative real-time visualization of neural activity recorded by microelectrode and motor symptoms, such as tremors, recorded by an inertial measurement unit during surgery [107]. Dai et al., also developed a glove-type system that uses an inertial measurement unit and force sensitive resistor to measure the immediate effects of DBS by tremors, bradykinesia, and rigidity assessments [108]. In addition, highly functional inertial sensors with conformal, wireless, and data upload functions, and the Food and Drug Administration (FDA)-approved BioStamp nPoint, have been developed [109]. These technologies will realize next-generation methods of optimizing stimulation parameters in clinical settings.

5.2. EMS

EMS Controlled by Motion Detectors

EMS, used to alleviate resting tremor, is based on modifications by changes in peripheral mechanical conditions, external joint motion, or EMG [110]. Jitkritsadakul et al., developed a glove-shaped portable device that detected and suppressed tremors [111]. It consisted of three components, as follows: a glove with an embedded inertial sensor and an EMS module, a control box that can be worn on the waist belt, and an Android smartphone. An inertial sensor attached to the glove was used to detect and stimulate tremors. EMS was performed via two electrodes placed over the short thumb abductor muscle and the first and second dorsal skeletal muscles. They evaluated the performance of this device using a double-blind, 1:1 pair-designed, randomized, placebo-controlled design in 30 patients with PD. The tremor glove effectively suppressed intractable resting hand tremors in these patients, without serious adverse events. Specifically, they identified a significant reduction in the root mean squared angular velocity (as a percentage) in every axis, in peak magnitude in the axis (x-, y-), and in UPDRS tremor scores (glove: 5.27 ± 2.19, sham: 4.93 ± 2.37) during stimulation with Tremor's glove, compared with the sham groups ($p < 0.05$, each). Gallego et al., developed a device that integrated neurostimulation electrodes, gyroscopes, and control electronics [112]. It analyzed the characteristics of the tremor (instantaneous amplitude and frequency) from the gyroscope recordings and regulated the level of muscle co-contraction by injecting current into the antagonist pair, as appropriate. They obtained significant attenuation of the tremor ($p < 0.001$) in patients with PD and ET, reducing its amplitude to 52.33 ± 25.48%.

EMS Controlled by EMG Signals

Researchers have proposed a method for detecting tremors from the EMG signals of muscles. Dosen et al., proposed a method of detecting tremors from the EMG of the muscles causing the tremor and counteracting it by applying an out-of-phase electrical stimulation to a similar muscle [113]. The device was evaluated in four and two patients with PD and ET, respectively, and demonstrated an average tremor reduction of 46% to 81% and 35% to 48% in the five patients, respectively. In one patient, the system did not attenuate the tremor. Myoelectric sensors implanted in muscles have been developed to improve diagnostic accuracy [114]. The sensor can acquire EMG signals near muscle fibers, and the implantable system ensures a stable relationship between the source and electrodes. It has the advantage of being unaffected by external factors, such as sweat. Intramuscular electrodes can be placed using a hypodermic needle. These electrodes usually have only the function of a single recording; however, in recent years, investigators have developed multichannel electrodes made of thin polyimide films [115][116][117]. In addition, a device that not only records, but also simultaneously stimulates, has been developed [118]. It was built on a polyimide substrate and comprises 12 recording sites and three stimulation sites made of platinum. This device was tested on six patients with ET and three healthy participants to assess basic information, such as perceptual thresholds and current limits. Furthermore, the application of this electrode to the system created by Dosen et al., [113] suppressed tremors and wrist angles by an average of 58%.

5.3. Other Devices

Tremor Suppression Using Orthosis

Several studies have used suppressive orthoses for tremor suppression [119][120] Herrnstadt and Menon developed a one-degree-of-freedom elbow brace that can be worn by people with tremors [121]. This system consisted of a suppression motor, gears, sensors, including force transducers and encoders, and braces on the upper arm and forearm. They evaluated the brace in nine patients diagnosed with mild to severe tremors, including PD, and observed a 94.4% ($p < 0.001$) reduction in the mean power of the tremor [122]. This type of tremor-suppression device requires a power supply and is termed an active device. In contrast, researchers have developed passive devices that operate by damping or absorbing vibration energy [123]. Buki et al., developed a passive device based on energy absorption, termed a Vib bracelet [124]. This device absorbs vibrations in the frequency range associated with tremors using the principle of a dynamic vibration absorber. This technology is widely used to absorb vibrations caused by earthquakes in bridges and high-rise buildings. It has a simple structure, weighs 280 g, and has a small and lightweight outer radius of 57 mm. The evaluation of the mechanical forearm enabled attenuation of the vibration in the range of 4 Hz to 5.75 Hz, with an amplitude attenuation of 86% (approximately one in 7.3) at 4.75 Hz. Further performance improvement can be achieved by personalizing the device according to the frequency of the tremor. Faizan et al., developed a passive bracelet-type device [125] that comprised a dual-parallel configuration passive vibration absorber. Their theoretical evaluation revealed that the device reduced the amplitude of angular motion of the wrist by 57.25%. Furthermore, an evaluation of patients with PD confirmed that rectangular sketching partially improved the tremors while using the device. While most of these studies have targeted wrist tremor, a glove-type device that independently controls tremor in each finger joint has also been proposed [126][127]. This device is designed to manage tremor in the index metacarpophalangeal joint, thumb metacarpophalangeal joint, and the wrist. Results show overall suppression of 73.1%, 80.7%, and 85.5% in resting tremor, 70.2%, 79.5%, and 81% in postural tremor, and 60.0%, 58.7%, and 65.0% in kinetic tremor in the index finger metacarpophalangeal joint, the thumb metacarpophalangeal joint, and the wrist, respectively. In addition, Wanasinghe et al., developed a lighter and less bulky glove-type device based on layer jamming [128]. When a vacuum is supplied to the layer jamming elements, which contain a stack of attached layers, this device increases the stiffness of the glove and suppresses hand tremor. An assessment of 11 tremor patients revealed mean frequency power reductions of 41.74, 41.99, and 24.7% for the index and middle fingers and in grasping, respectively, with a maximum power reduction of 59.15%. The above-mentioned studies are examples of reports on the impacts of engineering solutions.

Tools with Tremor Control Function

Additional approaches include research that incorporates a mechanism to suppress unintended movements in tools rather than the tremor itself. For example, researchers developed a tray to transport objects, which included a vibration stabilization function [129]. This tray includes a mechanical platform and an electronic system to suppress the vibration of the base plate. It is stabilized by controlling three servomotors in a direction that counteracts the changes based on the data acquired by the inertial sensors. Some tableware contains a tremor control function. The Liftware Steady^{TM} (Liftware, Inc., San Francisco, CA, USA) comprises an electronically controlled stabilizing handle and numerous attachments, including a spoon, fork, and spork, to facilitate eating for patients with tremors. A pilot study demonstrated an improvement in tremor with the Liftwear Steady^{TM} using the Fahn–Tolosa–Marin Tremor Rating Scale [130]. In addition, investigators have attempted to use such spoons for tremor assessment [131]. The tremors were assessed using a linear model trained from motion signals that recorded the tremors. A modified Fahn–Tolosa–Marin scale was used for the assessment, and the correlation coefficient between the expert rating and the model score was 0.91 ($p < 0.001$). It demonstrated practical accuracy and can be used for daily objective monitoring. In addition, technologies have been proposed to assist in computer mouse control [132]. This method uses adaptive path smoothing via the B-spline to provide a smooth mouse path.

6. Conclusions

Due to developments using state-of-the-art techniques, effectiveness in diagnosing and evaluating tremor and suppressing it using these devices is satisfactorily high in many studies. However, other than DBS, no devices are in practical use. To acquire high-level evidence, large-scale studies and randomized controlled trials are needed for these devices.

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