Objective Assessment of Parkinson's Disease Symptoms Severity: A Review

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***Abstract*— Parkinson's disease (PD) is placed as second supreme neurodegenerative sicknesses after Alzheimer's. It is characterized by dopaminergic deficiencies in the mid brain that impair motor function. Due to rise in proportion of elderly people the number of patients with Parkinson (PWP) are expected to increase for the coming 25 years. Until now, there are still no solutions towards PD, although medication and surgical intervention can temporarily hold back the progression of the symptom. Therefore, early diagnosis is critical in order in improving PWP disease quality of life and prolong longevity, where many of them will be substantially dependent on clinical intervention. The investigators begin exploring motor disorders and the likelihood of applying various types of sensor to measure the significance of clinical involvements on the quality of movement observed while PWP accomplished different tasks. The focus of this review is to provide a discussion of the capabilities of wearable technology and audio sensors in the assessment of PD symptoms severity.**

***Index Terms*—Parkinson's Disease (PD), wearable sensors, speech signal, patients with Parkinson(PWP), Unified Parkinson Disease Rating Scale (UPDRS)**

I. Introduction

Parkinson's disease (PD) is described as among the commonest neurological illness profoundly affects the lifestyles of patients with Parkinson (PWP) and the people surrounding them. From the past research, it has suggested that one of the single most important risk factor for the onset of PD is age as the incidence of PD increases with age where it typically happens around age of 60 [1,2]. Based on the statistic conducted by the Malaysian PD Society, it is predicted that approximately 15,000 to 20,000 peoples are suffering from PD. As the quantity of elderly people in the population is growing, PD is classified as a major health problem to the society, where this figure of PWP is expected to upsurge in future years [3]. The classical characteristic features of PD are tremor, involuntary motions, rigidity, impaired balance and other general movement disorder [4, 5].

In clinical practice, managements of PD typically referred to patients' self-reports and diaries. This patient motor fluctuation's information is generally gained through patients reflecting back the amount hours of ON and OFF time they have gone through in the past. "ON time" represents the times when medications are active while "OFF time" represents the times when symptoms are present. However, these methods are subject to perceptual and recall bias. Although the usage of patient diaries can recover dependability, but the features captured are not beneficial for the clinicians to make their decisions. While, direct observation from the specialist is not practical as the motor fluctuations cover the time span of several hours between medication dosages. Conventional methods have many shortcomings such as frequent physical visits of patients to the clinic may be difficult [4, 6].

Due to this aspect, several rating scales which are mapped to the gold-standard clinical metric, the Unified Parkinson Disease Rating Scale (UPDRS), have been designed and used that reflects the presence and severity of PD symptom. This evaluation measures symptoms of PD based on a 5-points scoring scheme where 0 represents no sign of the severity and 4 as the highest severity of the symptoms). However, usage through UPDRS scaling grants some limits like intra and inter observer irregularities while there are still many doctors that are not familiar with such rating scales. These scales can takes up an extensive duration of administer and can be influenced by subjectivity concerns linked to patient historical data. They can be hardly be applied for continuous registration procedures done in the clinic. Furthermore, the PD symptom's pattern and severity can differ significantly during daytime, while UPDRS only offer evaluation of the particular moment only. Lastly, assessments of motor fluctuation conducted in medical centre may not precisely imitate the actual functional disability experienced by the PWP while they are at homes [6, 7].

The long duration of stays in hospital contribute to cost increase that will cause burden to the patients and their family members in term of their financial status. At present, this matter is one of the most demanding challenges faced when dealing with PD as the proper medical care is increasingly complex and expensive. With the current development, quantitative methods for detecting and assessing the symptoms severity of motor disorders in PD are quite limited. The evaluation of PD can be conducted through clinical and technological tools. Figure 1 shows the overall summary of the different types of assessments that are applicable in monitoring motor abnormalities in PD. In this review, our focus will be on research conducted previously using wearable sensors and audio sensor for early detection of PD symptoms severity.

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The main aim of this paper is to provide a discussion of the capabilities of wearable technology and speech signal which are presented in the following section.

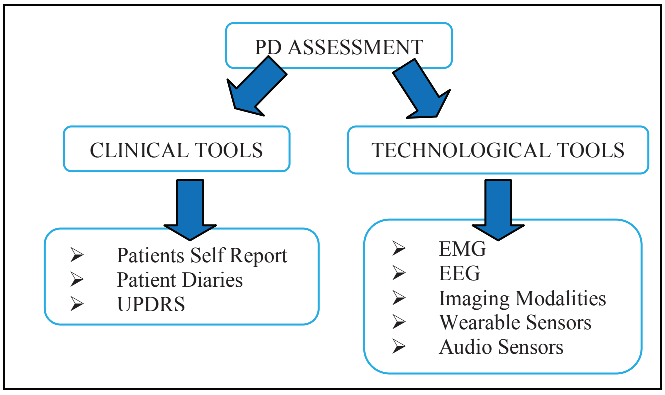

Fig 1: Summary of overall assessment of PD

II. RELATED WORK ON PD THROUGH WEARABLE SENSORS

A. Detection of Levopoda Induced Dyskinesia (LID) in PD

Keijsers et al. [8] had demonstrated research using trained neural networks for assessing dyskinesia and evaluating the performance of neural networks to differentiate dyskinesia from voluntary actions. The research was conducted using triaxial accelerometer, which was positioned at six locations of the subject's body. Assessment of the severity of levopoda induced dyskinesia (LID) was conducted using numerous features from the signal obtained through accelerometer. Multilayer perceptron (MLP) neural network was selected as the classifier in this study. Comparison between the scores obtained from the neural network, obtained through linear transfer function that had rating in the range from 0 to 4 representing the Abnormal Involuntary Movement scale (AIMS) score and assessment by physicians, who made the evaluation of the PWP condition through video.

For every 1-minute interval signal, there will be several parameters extracted from the accelerometer signals before being passed to the classification stage. These parameters will be used as the input for the classification and evaluation points provided by the physicians as the output. Table 1 showed the list of parameters used in this research and their description [9]. Figure 2 illustrates the overall approach in evaluating severity of dyskinesia. Different body parts was trained using different neural network architecture. This architecture was initiated through the forward selection technique for neural networks with several numbers of hidden units.

A main benefit of applying neural networks using this forward selection technique is that this method search for the most useful parameter without any extra information and restriction. The neural network classification was considered accurate if the neural network output and the points provided by the physicians was lower than 0.5. This classifier correctly categorized dyskinesia from absence of dyskinesia in 15-minute intervals with accuracy of 93.7% for arm, 99.7% for trunk and 97.0% for leg [8, 10].

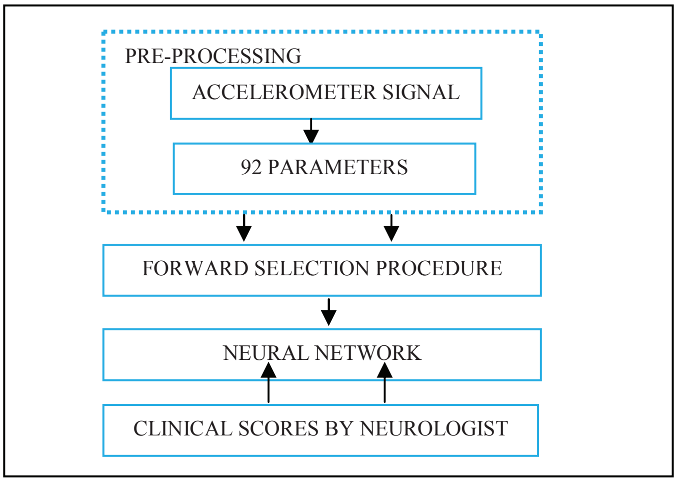

Fig 2: Schematic overview in the assessment severity of dyskinesia

B. Quantification of Tremor and Bradykinesia in PD

An ambulatory system for quantifying tremor and bradykinesia in PWP had been presented by Arash et al. [11]. Movement of the upper extremities of the subjects were continuously recorded while they followed a protocol of 17 tasks, each one representing a typical daily activity. The measurement system was conducted using sensors attached to the skin just above the wrist of the subjects which include three miniature uni-axial gyroscopes that measure the angular velocity of the forearm movements in roll, yaw and pitch direction. Tremor is generally characterized by rhythmic movements at a frequency of approximately 4-6 Hz that usually occurs at rest. Analysis of the angular velocity signals from each axis was conducted separately. The algorithm for detecting tremor found a high sensitivity of 99.5% and specificity of 94.2% compared to video recording while subjects performing typical daily activities based on the following calculation shown in Eq.1 and Eq. 2.

$$Sensitivity = \frac{\sum_n TP_{n,a}}{\sum_n \sum_i TP_{n,j}} \tag{1}$$

where

$TP_{n,a}$: The period of the tremor that was both visible in the video and correctly identified by the algorithm for each PD patient n and the three axes of the sensor a: $a \in \{p,r,j\}$

$TP_{n,i}$: Start and end of each period i of the visible tremor of the upper extremities of each patient, n

$$Specificity_{overall,a} = \frac{\sum_m Trec_m - FP_{m,a}}{\sum_m Trec_m} \tag{2}$$

where

$Trec_m$: Total duration recording of tremor for healthy subject, m

$FP_{m,a}$: The period of the tremor that was not clearly visible in some section of the video but correctly identified by the algorithm for each healthy patient m and the three axes of the sensor $a : a \in \{p,r,j\}$

Besides that, this investigation also studied on the correlation study between the UPDRS tremor subscore and the logarithm of the tremor amplitude reported by the algorithm and the correlation study between UPDRS bradykinesia subscore and the bradykinesia parameters (M_h, R_h and A_h). High correlation between tremor and bradykinesia related parameters and UPDRS subscore was achieved using Pearson's correlation and Partial correlation (for removing the effect of ON/OFF factor) whereby p-values above 0.05 were considered as non-significant for all statistical tests [11].

C. Quantification of Physical Activities in PWP

Arash et al. [12] suggested a novel ambulatory technique for physical activities observation in PWP using a transportable data logger with triaxial sensor (combination of gyroscope and accelerometer) to enable long term recording. The walking postures were sensed with two accelerometers placed on shanks and lying posture was sensed with gyroscope placed on the trunk. The main objectives of this research was the classification of PD patient's basic posture allocation such as sitting, standing, lying and walking durations. The detection of periods of body posture will deliver evidence on the level and range of activities the PWP giving a direct evaluation of their global motor function as a pointer of their PD symptom severity level. Besides that, this research also aims for the detection of Stand-Sit (StSi) and Sit-Stand (SiSt) transitions whereby several parameters of transitions pattern were extracted as described in Table 2. Then, two statistical classifiers constructed on a logistic regression model were applied to separate the transitions from non-transitions and differentiating between SiSt and StSi transitions. Logistic regression is an effective method for discrete outcome prediction (e.g., transition/non-transition) without any particular distribution assumptions for the predictors. The first classifier was used to allocate each candidate a probability of being a transition versus being a non-transition. The second classifier function to separate SiSt and StSi transitions by predicting a probability as the probability of a transition being of SiSt type. The durations of walking and lying were also detected using methods described in previous studies [12, 13].

Next, a fuzzy classifier has been proposed to differentiate the durations of sitting and standing according to data concerning the transitions and the activities conducted before and after. The link between the parameters defining the transition patterns and the UPDRS score of PD patients had shown high correlation. The classification of the basic activities, i.e. walking, standing, siting and lying had a sensitivity of 8.5%, 83.6%, 86.3%, and 91.8%, respectively, and specificity of 97.8%, 96.5%, 98.0%, and 99.8%, respectively, for PD patients while for the detection of StSi and SiSt transitions, the proposed algorithms had shown 83.8% sensitivity and a positive predicted value (PPV) of 87.0% for PWP [12].

D. Estimation of PD Symptoms Severity: Bradykinesia

In research conducted by Cancela et al. [15], they had presented a methodology for severity of bradykinesia automatic detection using wireless, wearable 3-axis accelerometer placed on the limbs, trunks and belt in PD patients. Evaluation of the procedure was conducted through the PWP daily living activities which were distinguished using an activity recognition algorithm. The results of the performance achieved between the ranges of 70%-86% based on the UPDRS severity classification of the algorithm depending on the classifier used. The determination of the severity of bradykinesia was determined as: 1) Data selection that links to the interest activity (e.g. walking and arm extension); 2) Resultant vector calculation based on data from the 3 axes; 3) Resultant vector filtering; 4) Feature extraction and 5) Feature classification.

As bradykinesia is only obvious when the patient moves, the filtered signal were analysed after running an activity recognition algorithm that aims to recognise time frames when the patient was either walking or extending/flexing his arms. Classification of the epochs was conducted using different classifiers: K-nearest neighbour classifier, binary decision tree, neural network classifiers by Back-propagation and support vector classifier whereby all the classification techniques used are characterized by high performances using its own technique providing different accuracies. The output of the implemented classifiers was given as the severity level of bradykinesia based on UPDRS score where 0 describes the absence of the bradykinesia and 4 describes the highest possible of having bradykinesia [14, 15].

III. RELATED WORK ON PD THROUGH SPEECH SIGNALS

Speech can be classified as a beneficial signal to remotely monitor Parkinson's symptoms severity on the basis of clinical proof that proposed huge mainstream of PWP typically expose to some form of vocal disorder. Speech disorders (vocal impairment) was among the initial indicator of PD symptom. It is reported that 90 % of PWP; moreover 29% of the patients themselves regard speech impairment as one of their most troublesome symptoms [16]. Assessing the degree of vocal impairment is usually conducted either using sustained vowel phonation [17, 18], or continuous speech [18]. The procedure of sustained vowels was the subject is asked to sustain the vowel for as long as possible, trying to maintain steady frequency and amplitude at a comfortable level. Research has revealed that sustained vowel "/a/" is satisfactory for many voice evaluation applications, which include prediction of PD grade and average monitoring of PD symptom [19, 20]. Max A. Little et al. [20] presented an evaluation for differentiating healthy subject from PWP by detecting dysphonia.

Table 1: List of input parameters for neural network [9]

Variables	Description
$\bar{V}$ segment	Mean of segment velocity
$\bar{V}_{<3\ Hz}$ segment	Mean of segment velocity for frequencies below 3Hz
$\bar{V}_{>3\ Hz}$ segment	Mean of segment velocity for frequencies above 3Hz
$\bar{V}_{<3\ Hz}$ segment/$\bar{V}_{>3\ Hz}$ segment	Ratio between $\bar{V}_{<3\ Hz}$ segment and $\bar{V}_{>3\ Hz}$ segment
SD(V) segment	Segment velocity standard deviation
% V_{θ} segment	Percentage of time of segment's movement
$\bar{V}_{\theta}$ segment	Mean segment velocity of segment's movement
$P_{1\text{-}3Hz}$ segment	Power for frequencies in the range between 1 and 3 Hz
$P_{<3Hz}$ segment	Power for frequencies in the range below 3Hz
$\bar{\rho}_{segment\text{-}segment}$	Mean value of the normalized cross-correlation between segment velocities of different segment
max ($\rho_{segment\text{-}segment}$)	Maximum value of the normalized cross-correlation between segment velocities of different segment
% sitting	Percentage of time during subject sitting posture
%upright	Percentage of time during subject upright posture

Table 2: List of posture transition related parameter [12]

Parameter	Description
TD (s)	Period of transition: Time break between the two positive peaks before and after the transition time in the trunk tilt, $\theta_{g\text{-}lp}$ signal
Min($\theta_{g\text{-}lp}$)(°)	Minimum amplitude of negative peak of flexion and extension tilt of the trunk that in general much higher in the real posture transition patterns compared to the non-transitions patterns
Max ($\alpha_{trunk\text{-}lp}$)(g x 10^{-3})	Signal $\alpha_{trunk\text{-}lp}$ was produced through the norm of the acceleration vector measured by the perpendicular accelerometers of the trunk sensor filtered using low pass filter.
Min($\alpha_{trunk\text{-}lp}$)(g x 10^{-3})	
Range($\alpha_{trunk\text{-}lp}$)(g x 10^{-3})	
T[Max($\alpha_{trunk\text{-}lp}$)](s)	
T[Min($\alpha_{trunk\text{-}lp}$)](s)	
Range($\theta_{g\text{-}lp}$)(°)	Range of flexion and extension tilt of the trunk where the value of this parameter was lower for the non-transitions than for the real posture transitions.

This research has presented a novel feature of dysphonia, known as pitch period entropy (PPE). Ten highly uncorrelated features were chosen, and an exhaustive search of different possibility combination had shown accuracy of 91.4%, applying kernel support vector machine (SVM) as the classifier. The results shown that the combination of nonstandard method with traditional harmonics-to-noise ratios had ability to differentiate healthy from PWP.

Research has also been conducted by Tsanas et al. [21] to test the accuracy of new algorithms that can be used to discriminate PWP from the healthy subjects. Exhaustive search through all potential measures subsets is computationally intractable, which has come out with development of feature selection (FS) algorithms which offer a rapid, principled approach to reduction of the number of features. In this research, they have compared four efficient FS: 1) least absolute shrinkage and selection operator

(LASSO), 2) minimum redundancy maximum relevance (mRMR), 3) RELIEF, and 4) local learning-based feature selection (LLBFS). The features selected were passed to classification stage applying two statistical classifiers: random forests and SVM. The results demonstrate that these new dysphonia measures can outperform existing results, reaching almost 99% overall classification accuracy using only ten dysphonia features. The use of four different FS to find only 10 features from the original 132 features has led to an informative feature subset for the binary classification task of this study, which may also tentatively suggest the most detectable characteristics of voice impairment in PD [21, 22-24].

IV. DISCUSSION AND CONCLUSION

In recent years, various technologies, methodologies and systems using variable types of sensors had been selected in monitoring and assessment of PD. Researchers have proposed several existing uni-modal approaches to distinguish PWP from control subjects with a single sensor platform. The investigators begins in investigation of motor disorders and chances of applying wearable technology in evaluating the effect of clinical interventions on the quality of movement observed while PWP accomplished functional activities.

Pursuing robustness and supporting more flexible, transparent, and powerful means of interaction between humans and computer has inspired the growing interest in multimodal interface platform design. Multimodal interface could potentially be applied to more inspiring usage, providing access to a wider range of users and provide more argumentative usage environments than before. The fusion and integration of multimodal sensors represents the co-operative combination of sensory data from various types of sensors to provide more reliable and accurate information. The advantages obtained through integration of multimodal sensors can be compiled into a combination of four fundamental aspects which are redundancy, complementarity, using less time and reducing cost of the information. A well-designed multimodal interface that fuse two or more information sources of redundant information can be an effective means of substantially reducing the recognition uncertainty and thus serve to obtain higher accuracy. Redundant information provided through fusion of groups of sensors can also serve to increase reliability in the case of sensor error or failure. Alternative information gained from different types of sensors allows additional features in the environment to be identified. In controversy, these features are impossible to be perceived from the information obtained using individual sensor that operates separately. Multiple sensors may also provide more timely information due to either the actual speed of each single sensor or the processing parallelism that had possibility to achieve as part of the integrating process [25-27].

Multimodal interfaces can function in a more robust and stable manner compare to unimodal systems that involves a single recognition technology. Perhaps, most importantly, multimodal system can achieve error suppression higher compared to unimodal system that improves the overall recognition rates. [28,29]. Realizing the potentials benefits in fusion and integration of multimodal sensors motivates the research in application involving early detection of PD symptoms severity. However, from the previous works, there is not much research on integration of different sensors in this applications. At the same time, the strength of existing signal processing and classification algorithms used in the research was not tested using the information from the multiple sensors. Although many advances have been done in the previous years, most of the studies were based on a single modality which was not an ideal diagnostic tool. This research is still in its early stage whereby at this beginning of the research it had not addressed it explicitly and only few published research papers had been done. In future, we will propose to develop an integrated multimodal system using several types of sensors for predicting the early symptom severity of PD.

ACKNOWLEDGMENT

All the authors would like to acknowledge the journal incentive research grants received from Universiti Malaysia Perlis (UniMAP) [Grant No: 9007-00071 and 9007-00117].

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