Detection of Parkinson's Disease Using Clinical Diagnostic Tools

Angana Saikia¹, Masaraf Hussain², Amit Ranjan Barua³, and Sudip Paul¹,⁴*

¹Department of Biomedical Engineering, North-Eastern Hill University, India
²Department of Neurology, North Eastern Indira Gandhi Regional Institute of Health and Medical Science, India
³Department of Neurology, GNRC Hospitals, India
⁴School of Computer Science and Software Engineering, The University of Western Australia, Perth

Abstract

The present paper emphasizes the early detection of any neurodegenerative disorder using clinical diagnostic tools. It has become increasingly important to stop the future risk of death. Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease. It is a progressive neurological condition that causes motor and non-motor manifestations. Treatment provides symptomatic benefit but no current treatment has been proven to slow disease progression. Research studies of PD require a means of rating the severity of disease by measurement of motor manifestations, assessment of ability to perform daily activities, and symptomatic response to medication. Advances in clinical recognition of early symptoms and signs, development of new neuroimaging technologies, identification of new neuropathological markers of PD, are gradually translating into better understanding of predisposing and preclinical factors that lead to progressive neurodegeneration. Neurodegeneration is the progressive loss of structure or function of neurons, including death of neurons. Many neurodegenerative diseases such as Alzheimer's disease and Huntington's disease are incurable, resulting in progressive degeneration and/or death of neuronal cells. As research progresses, many similarities appear that relate these diseases to one another on a sub-cellular level. Neurodegeneration can be found in many different levels of neuronal circuitry ranging from molecular to systemic.

In this study, we have used three different diagnostic scales for the analysis of various clinical parameters (Cognitive impairment, depression, and fatigue, oxygen level in brain and grip strength) for early detection of Parkinson's disease. The tools used were: Mini Mental state Examination (MMSE), Geriatric Depression Scale (GDS), Fatigue Severity Score (FSS). One way ANOVA in Origin 8 software.

INTRODUCTION

Parkinson's disease (PD)

Parkinson's disease is a neurodegenerative disorder which mostly seen in people after the age 50yrs. It is also a progressive disorder that causes many motor and non-motor dysfunctions [1,2]. The symptoms of PD are: Motor Symptoms [3]:

- Bradykinesia: Bradykinesia means "slow movement". A defining feature of Parkinson’s, Bradykinesia also describes a general reduction of spontaneous movement, which can give the appearance of abnormal stillness and a decrease in facial expressivity. Bradykinesia causes difficulty with repetitive movements, such as finger tapping.

- Rigidity: Rigidity causes stiffness and inflexibility of the limbs, neck and trunk. Muscles normally stretch when they move, and then relax when they are at rest. In Parkinson’s rigidity, the muscle tone of an affected limb is always stiff and does not relax, sometimes contributing to a decreased range of motion. People with PD most commonly experience tightness of the neck, shoulder and leg. A person with rigidity and Bradykinesia tends to not swing his or her arms when walking. Rigidity can be uncomfortable or even painful.

- Tremor: Tremor, or shaking, often in a hand, arm, or leg, occurs when you’re awake and sitting or standing still (resting tremor), and it gets better when you move that body part. Tremor is often the first symptom that people with Parkinson’s disease or their family members notice. At first the tremor may appear in just one arm or leg or only on one side of the body. The tremor may spread to both sides of the body. But in some cases the tremor remains on just one side. Emotional and physical stress tends to make the tremor more noticeable. Sleep, complete relaxation, and intention movement or action usually reduce or stop the tremor.

- Postural instability one of the most important signs of Parkinson’s is postural instability, a tendency to be unstable when standing upright. A person with postural instability has lost some of the reflexes needed for maintaining an upright posture, and may topple...
backwards if jostled even slightly. Some develop a dangerous tendency to sway backwards when rising from a chair, standing or turning. This problem is called retropulsion and may result in a backwards fall. People with balance problems may have particular difficulty when pivoting or making turns or quick movements.

Non-Motor Symptoms [3,4]:

- Neuropsychiatric: Neuropsychiatric symptoms such as depression, dysphoria, apathy, irritability, anxiety, agitation, aberrant motor behavior, and parkinsonian-like signs [5].
- ICDs: Impulse control disorders (ICDs) are behavioral disturbances in which a person fails to resist the drive to behave in ways that result in distress or impaired social and occupational functioning. In Parkinson’s disease (PD), ICDs most commonly include pathological gambling, excessive spending and hypersexuality.
- Sleep disorder: Sleep disturbances affect up to 60% of PD patients. Sleep disorders can result from motor-related aspects as well as from non-motor-related aspects and medications. Nocturnal dystonia and cramping may cause sleep fragmentation and could be treated by a dopamine agonist at bedtime.
- Autonomic dysfunction: Autonomic nervous system dysfunction symptoms in PD include sexual dysfunction, swallowing and gastrointestinal disorders, bowel and bladder abnormalities, sleep disturbances, and derangements of cardiovascular regulation, particularly, orthostatic hypotension.
- Sensory: Parkinson patients had sensory complaints of numbness, coldness, burning, or pain. There was no objective sensory loss, and sensory symptoms did not correlate with specific motor or autonomic signs.

Parkinson’s disease occurs due to loss of a neurotransmitter known as dopamine in the substantia nigra of the human brain. Dopamine is a neurotransmitter which helps a person to coordinate the signals from brain to muscles. Basically, dopamine inhibits human movement. A person with Parkinson’s generally loss this coordination, as a result its limb movements are disturbed. Loss of this dopamine results in abnormal nerve firing patterns within the brain that cause impaired movement [6]. Environmental and Genetic factors are also responsible for PD. Familial cases of Parkinson disease can be caused by mutations in the LRRK2, PARK7, PINK1, PRKN, or SNCA gene, or by alterations in genes that have not been identified. Environmental factors such as exposure to certain toxins such as exposure to MPTP, an illicit drug, or in people working in mining industries. These miners are mostly exposed to the metal manganese, which are also responsible for the cause of PD. Farmers exposed to insecticides and pesticides have high risk of PD. Many genetic factors are also responsible for PD. Researchers have identified different genetic mutations associated with PD, including the alpha synuclein gene, and many more genes have been also associated with this disorder. Studying the genes responsible for inherited cases of PD can help researchers understand both inherited and sporadic cases [7].

Clinical aspects of PD

Stages in PD: The UPDRS (Unified Parkinson’s disease rating score), Hoehn &Yahr and Schwab & England scales are the scales in common practice for Parkinson’s disease [8]. Their utility is that they objectively rate an individual patient’s disability at a particular moment in time. Each scale score is a reflection of disease burden on the individual patient and is useful in describing disease progression and treatment response with time.

Unified Parkinson’s disease Rating Scale (UPDRS):

This scale has multiple ratings that measure mental functioning, behavior and mood; activities of daily living and also the motor functions. The UPDRS are used to measure how individuals are fairing and how much treatments are helping them. The UPDRS is scored from a total of 195 points; higher scores reflect worsening disability [9].

- Modified Hoehn and Yahr Staging [10] Table 1

Scales in PD: Three types of scales are generally used to clinical diagnosis of the PD patients. They are:

- The Geriatric Depression Scale (GDS): It is a self-report assessment used to identify depression in the elderly. The short form consists of 15 items. Of the 15 items, 10 indicated the presence of depression when answered positively, while the rest (question numbers 1, 5, 7, 11, 13) indicated depression when answered negatively. Scores of 0-4 are considered normal, depending on age, education, and complaints; 5-8 indicate mild depression; 9-11 indicate moderate depression; and 12-15 indicate severe depression. The Short Form is more easily used by physically ill and mildly to moderately demented patients who have short attention spans and/or feel easily fatigued [12].
- Mini-Mental State Examination (MMSE) or Folstein test: It is a 30-point questionnaire that is used extensively in clinical and research settings to measure cognitive impairment. It is commonly used in medicine and allied health to screen for dementia. It is also used to estimate the severity and progression of cognitive impairment [13] and to follow the course of cognitive changes in an individual over time [14].
- Fatigue Severity Scale (FSS): Subjective fatigue was evaluated in all subjects using the Fatigue Severity Scale (FSS), a 9-item statement rating the severity of fatigue. Verbally the statements were asked to all the subjects and the ratings were given accordingly. FSS is rated between 1-7 points and higher the fatigue more is the score [15].
- Webster rating scale: Webster developed a rating scale for patients with Parkinson’s disease based on 10 clinical findings. The scale indicates the severity of disease and the clinical impairment. Changes in the scale over time can reflect changes due to disease progression or therapeutic interventions [16].

**Methodology**

**Subjects:** 60 subjects both male and female were recruited for the study from different hospitals in Shillong, Meghalaya and Guwahati, Assam, out of which 30 subjects (10 males and 15 females) were in the early stage (1 and 1.5 Stage) of Parkinson’s disease and 30 subjects (10 males and 15 females) were healthy. PD patients under study were diagnosed with neurological disorder in their family history. Most of them were exposed to insecticides and pesticides for more than 10 years. There was history of using well water for long period of time. PD subjects were also found to be non-smokers. Subjects with metallic implants and paralysis were not recruited for the study. The healthy subjects were without any neurological disorders. The mean age group was 60 ± 10 years and weight was 45 ± 20 kgs. Written consent form was taken before carrying out the study from each subject. Subjects were asked to sit in a comfortable position and all data’s were recorded during in the Out Patient departments of the hospitals during the morning hours.

**Procedure:** Three of the rating scales (MMSE, GDS, and FSS) were used for diagnosing each subject individually in presence of their guardians. SpO₂ levels were calculated for each patient using pulse oximeter for 15 mints. Also the grip strength was taken by applying the maximum force and then holding it for 4 sec. A pre-calibrated ready to use strain gauge based isometric dynamometer with a linear response in the range 0-800 N was used to determine the Handgrip force. When force is applied to the metal bar an output calibrated in units of Newton’s is recorded in Lab Chart. A green LED on the connector housing indicates the transducer is receiving power and is ready for use. Three trials were taken for each subject for a period of 5 seconds and the average value of the three trials was considered. A rest period of 10 seconds was given between consecutive contractions. The flowchart below gives the outline of the procedure carried out:

**Analysis**

The analysis was carried out using one way ANOVA in Origin PRO 8 software. ANOVA is a kind of parametric method for means comparison and is an extension of t-test. When there are more than two groups to be compared, pair wise t-test is not appropriate and ANOVA should be used. ANOVA requires normality and equal variance. There are two main modes of datasets in Statistics - indexed and raw. Here in our analysis we have used raw mode. For the means comparison Turkey test was used and the significance value was kept at 0.05 and the Levene test for equal variance. In addition, box charts were drawn for comparison between the groups for each of the diagnostic tools [17,18].

The results were given in the Tables (3-5) and box plots Graphs (1-5) below.

**RESULTS**

**One Way ANOVA**

a) Fit statistics (Table 3)  

b) Means comparisons:  

Turkey test (Table 4)  

c) Homogeneity of variance:  

Levene’s test (Absolute Deviations) (Table 5)
DISCUSSION

One-way ANOVA using ORIGIN PRO 8 was carried out for all the 60 subjects to compare the various clinical parameters. The parameters were: GDS, MMSE, FSS, SpO₂, and Grip Strength. The MMSE and GDS scores of the two groups were compared and it was detected that a person with PD has a higher score of GDS which indicates that a person with PD suffers from severe depression. The MMSE of the Parkinson’s patients is less than 23 which indicates cognitive impairment compared to non-Parkinson patients. It was also found that the healthy persons have a higher value of grip strength and lower fatigue than a Parkinson’s patient. As PD is directly related to weakening of muscle, hence their strength as well as ability to perform task like grasping is very low and they get fatigue very frequently. The SpO₂ level of PD is very low as compared to normal subject which signifies that patient with PD suffers from sleep disorder as the supply of oxygen to the brain is very less. The box plots show the comparison between PD and healthy subjects (Graphs 1-5).

Following were the outcomes of one way ANOVA analysis:

- Homogeneity of Variance Test was carried out using Levene’s test (Absolute Deviations). In statistics, Levene’s test is used to assess the equality of variances for a variable calculated for two or more groups [18]. Our analysis shows that the two groups (PD and Control) have equal variance, since the p-value is bigger than 0.05 for all the clinical parameters (Table 5). Tests for equal variance determine whether or not two or more population variances (rather than population means) are significantly different.
- Turkey test is a single-step multiple comparison procedure and statistical test. It can be used on raw data or in conjunction with an ANOVA (post-hoc analysis) to find means that are significantly different from each other [19]. From Turkey test, SIG value is 1 for all the

<table>
<thead>
<tr>
<th>Table 3: Fit statistics.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameters</td>
</tr>
<tr>
<td>MMSE</td>
</tr>
<tr>
<td>GDS</td>
</tr>
<tr>
<td>FSS</td>
</tr>
<tr>
<td>SpO₂</td>
</tr>
<tr>
<td>Grip Strength</td>
</tr>
</tbody>
</table>
parameters for both PD and healthy subjects (Table no. 4). This indicates that the means difference is significant at the 0.05 level.

- The F-Statistic is the ratio of between-groups to within-groups variances. F-statistics are the ratio of two variances that are approximately the same value when the null hypothesis is true, which yields F-statistics near 1 [20]. In Fit statistics, the R-Square value is near to 1 (Table 3) for all the clinical parameters for both PD and healthy subjects.

**CONCLUSION**

Clinical assessment is a way of diagnosing and planning treatment for a patient that involves evaluating the patient in order to figure out the abnormalities. There are many types of psychological assessments, all of which have their own strengths and weaknesses. Hence, clinical assessment is very much necessary for the early diagnosis of various diseases. Here in our work clinical assessment of PD is been done by using various tools. They were GDS to determine the level of depression, MMSE to determine the mental state and cognition level, FSS to determine the fatigue level of the patient, SpO₂ to determine the level of oxygen supply in the brain to assessment to detect the sleep behavior and lastly grip strength to determine the patient strength or capability to perform task with the help of his/her hand. It was found that these clinical parameters (MMSE, GDS, FSS, SpO₂ and GRIP STRENGTH) can be a useful tool for the early detection of Parkinson’s disease. It will help the clinicians and the caregivers to know the present state of patient and appropriate clinical interventions can be done at the earliest.

**CONFLICT OF INTEREST**

None of the authors have potential conflicts of interest to be disclosed. But the authors used the computational support from North-Eastern Hill University, India and The University of Western Australia, Perth, Australia; Clinical/Medical supervision/patients support was made from GNRC, Assam and NEIGRIHMS, Shillong, India.

**ACKNOWLEDGMENT**

We would like to acknowledge the Department of Neurology of Guwahati Neurological Research Center, Guwahati and North Eastern Indira Gandhi Regional Institute of Medical and Health Science, Shillong for their immense help and support during data collection. Also my sincere gratitude to the Department of Biomedical Engineering, North Eastern Hill University, Shillong for providing the required data collecting Instrument and laboratory space. Finally we got help from The University of Western Australia for software and other computation part.

**REFERENCES**

9. Ivey FM, Katzel LJ, Sorkin JD, Macko RF, Shulman LM. The Unified...


