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Prognostic System for Parkinson Disease (An overview)

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Abstract: Today, with existing complexities and ever increasing Parkinson Disease (PD), it has become difficult to track the progression of the disease. Through a study we try to provide a prognostic system to track the progression of Parkinson disease. With an aim to study the progressive nature of PD, in this paper we have proposed an Expert system which aids the specialist in the prognosis of PD. In this, three key issues are identified – i) that identifies and distinguish PD from other Parkinson syndrome, ii) that evaluates the risk of getting PD and iii) that evaluates the progression of PD. In this paper, we have studied how the various features (attributes) are associated with the progressiveness of PD.

Keywords: Parkinson disease, Diagnostic, Prognosis, Expert system, Progression of PD, Rating

I. INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disease caused by a loss of dopaminergic neurons in the substantia nigra, as well as other dopaminergic and non-dopaminergic areas of the brain. PD is a chronic, slowly progressive and the PD symptoms continue and worsen over a period of years. The way it progresses, it is different for everyone. Depending on person's difficulties it is categorized as Mild, Moderate and advanced stage of Parkinson's.

Advances in the field of AI lead to the emergence of Expert system. The aim of work is to propose an expert system which aids the specialist in the prognosis of Parkinson's disease. The Prognostics System report the risk percentage of getting the Parkinson's disease based on evaluating the Genetic factors, Environmental factor and symptoms experienced by the people. As this disease is slowly progressive, this system evaluate the progression of disease in a person from first level (Mild) to second level (Moderate) and from the second level to third level (Advanced) of the disease. Also this system evaluate whether the progression is benign or rapid progression.

II. PARKINSON'S DISEASE

Parkinson's disease is a neurodegenerative disorder. Like Parkinson's there are many other neurodegenerative disease such as Alzheimer's disease, Arthritic disease, Dementia with Lewy bodies, Corticobasal degeneration, Progressive supra nuclear palsy, Prion disorders, and so on. Among all of these neurodegenerative diseases, Parkinson's disease (PD) is second most common disease after Alzheimer's.

PD is caused by a loss of dopaminergic neurons in the substantia nigra, as well as other dopaminergic and non-dopaminergic areas of the brain. Although PD is common, it can be difficult to diagnose in early stages, and approximately 5 to 10% of patients with PD are misdiagnosed. Conversely, up to 20% of patients are diagnosed as PD reveal that they are affected by other neurodegenerative disease.

A. *Causes of Parkinson's disease*

The two main cause of Parkinson's disease are Genetic factors and Environmental Factors

1) Genetic factor: Researchers have discovered several gene mutations that can cause the disease directly, but these affect only a small number of families. Some of these mutations involve genes that play a role in dopamine cell functions. Parkinson's has developed at an early age in individuals with mutations in genes for parkin, PINK1, LRRK2, DJ-1, and glucocerebrosidase. The two categories of genes are causal and associated genes.

Causal genes are very rare which actually causes the disease accounting one to two percent of people with PD. A causal gene alone, without the influence of other genes or environmental factors, guarantees that a person who inherits it will develop PD [11]. *Alpha-synuclein is a Causal Gene.*

Associated genes do not cause Parkinson's disease on its own, but increases the risk of developing it. A person may have these genes and never develop PD, while people who do not have these genes may have Parkinson disease. However, those who have the gene are more likely to develop PD then those without it. PD may be triggered when they are combined with other *genetics* or environmental factors [11]. *LRRK2 is an Associated Genes*

2) Environmental Factors: It includes environmental toxin or injury. Epidemiological research has identified several factors that may be linked to Parkinson's, including rural living, well water, manganese and pesticides. It is noted that a simple exposure to an environmental toxin is never enough to cause Parkinson's.

Reference [11] specifies that prolonged occupational exposure to certain chemicals is associated with an elevated risk of PD. They are

- insecticides permethrin
- beta-hexachlorocyclohexane (beta-HCH)
- herbicides paraquat
- 2,4-dichlorophenoxyacetic acid
- Fungicide maneb.

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- Agent Orange
- A synthetic neurotoxin agent called MPTP (Parkinson's in the general population are exceedingly rare.)

B. *Symptoms of Parkinson's disease*

Each person with Parkinson's will experience symptoms differently. Some people have symptoms on one side of the body for many years; eventually the symptoms begin on the other side. Symptoms on the other side of the body often do not become as severe as on the initial side.

The various categories of symptoms experienced by the people are Primary Motor Symptoms, Secondary Motor Symptoms, Non motor Symptoms and Other non motor symptoms. The most common symptom among the people with the disease is motor symptom.

1) *Primary Motor Symptoms:* The primary motor symptoms are Resting Tremor, Bradykinesia (slow movement), Rigidity and Postural Instability. Many people experience tremor as their primary symptom, while others may have problems with balance.

2) Secondary Motor Symptoms: The secondary motor symptoms are Freezing, Micrographia, Mask-like Expression and Unwanted Accelerations

3) *Non motor symptoms:* Many researchers believe that non motor symptoms may precede motor symptoms. The most recognizable early symptoms are loss of sense of smell, constipation, REM behavior disorder (a sleep disorder), mood disorders and orthostatic hypotension (low blood pressure when standing up).

4) *Other Non motor Symptoms:* The other non motor symptoms included are sleep disturbances, constipation, bladder problems, sexual problems, excessive saliva, weight loss or gain, vision and dental problems, Fatigue and loss of energy, depression, fear and anxiety, skin problems, cognitive issues, such as memory difficulties, slowed thinking, confusion and in some cases, dementia and medication side effects, such as impulsive behaviors.

The diagnosis of Parkinson's does not come from a test, but instead requires a careful medical history and physical examination to detect the cardinal signs of the disease (symptoms). If a person has one or more of these symptoms, it does not necessarily mean that individual will develop Parkinson's, but these markers are helping scientists to better understand the diagnosis and prognosis process.

III. RATING SCALE

The rating scale is used to measure the severity and the stage of the Parkinson's disease. The various rating scale used are

- Unified Parkinson's Disease Rating Scale Motor Examination (UPDRS-ME)
- Hoehn & Yahr rating scale (HY)
- Schwab and England Activities of Daily Living Scale (SE)
- AMC Linear Disability Score (ALDS)

A. Parkinson's disease Quality of Life questionnaire (PDQL)

B. Unified Parkinson's disease Rating Scale Motor Examination (UPDRS-ME)

C. The severity of PD symptoms was rated using the UPDRS-ME. The UPDRS-ME was subdivided into two domains: Motor subscore A and Motor subscore B.

Motor subscore A ranges from 0-88 and represented relatively levodopa responsive motor signs of PD. It includes facial expression, rigidity, bradykinesia (combination of finger movements, hand movements, rapid alternating movements of hands, leg agility, and body bradykinesia and hypokinesia) and tremor score which is calculated by adding tremor at rest and action or postural tremor of hands.

Motor subscore B ranges from 0-20 and represented relatively levodopa non-responsive motor signs of PD. It includes speech and score for axial impairment (adding arising from a chair, posture, gait and postural stability)

Based on the UPDRS-ME, patients were classified in one of three clinical subtypes

- akineticrigid
- tremor-dominant
- mixed (features of akinetic-rigid and tremor)

D. *Hoehn & Yahr rating scale (HY)*

This scale is used to determine the stage of disease. It is a widely used clinical rating scale, which defines broad categories of motor function in Parkinson's disease (PD). Progression in HY stages has been found to correlate with motor decline, deterioration in quality of life and neuroimaging studies of dopaminergic loss. Also it does not provide any information concerning nonmotor aspects of PD.

E. *Schwab and England Activities of Daily Living Scale (SE)*

It is used to evaluate the Disability. The SE is specifically designed for patients with PD and reflects the patient's ability to perform daily activities in terms of speed and independence. ADL ability is measured on an 11-point index: ranging from 0% (vegetative function) to 100% (complete independence).

F. *AMC Linear Disability Score (ALDS)*

The ALDS item bank is developed to quantify functional status in terms of the ability to perform ADL. The original units of the ALDS scale are (logistic) regression coefficients, expressed in logits. To make the results easier to interpret, the logit scores are linearly transformed into values between 10 and 90. The value 10 represents the lowest level and the value 90 the highest level of functional status.

G. *Parkinson's disease Quality of Life questionnaire (PDQL)*

Quality of life (QoL) was evaluated using this disease-specific instrument. The PDQL, which has adequate clinometric support, is a self-administered measure which contains 37 items allocated to four subscales: parkinsonian symptoms, systemic symptoms, social functioning and emotional functioning. The total PDQL score is 37-185, with higher scores indicating better QoL.

IV. PROGNOSTICS SYSTEM OF PARKINSON'S

The Prognostics System report the risk Percentage of getting the Parkinson's disease based on evaluating the Genetic factors, Environmental factor and symptoms experienced by the people. As this disease is chronic,

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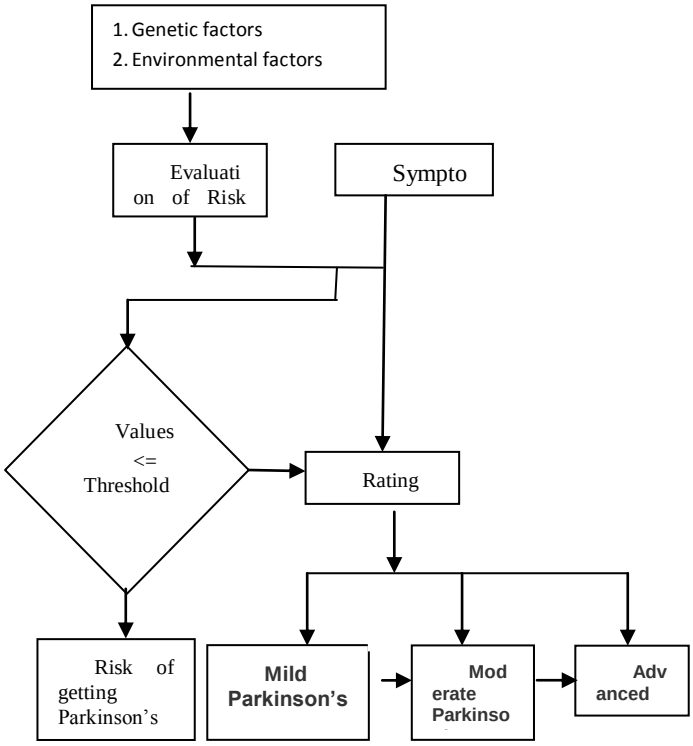
slowly progressive and worsen over a period of years, this system evaluate progressive of the diseases in a person from first level (Mild) to second level (Mid) and from the second level to third level (Advanced) of the disease. Figure 1 shows the Expert system for Prognostics of parkinson's disease.



1 – Progressive of the diseases from Mild level to Moderate level
2 – Progressive of the diseases from Moderate level to Advanced level

Fig. 1 Expert system for prognostics of parkinson's disease

A. *Key Issus*

In this prognostic system, three key issues have to be addressed.

- Which feature identifies and distinguishes PD from other Parkinson syndrome
- Which feature is used to evaluate the risk of getting PD
- Which feature is used to evaluate the progressive nature of PD

1) Feature that identifies and distinguish PD from other Parkinson syndrome: The different parkinson syndrome are Multiple System Atrophy (MSA), Progressive Supranuclear Palsy (PSP), AD-type pathology, CorticoBasal Degeneration (CBD), Dementia with Lewy bodies (DLB), PD and cerebrovascular disease. Diagnoses of different parkinsonian conditions revealed that falling within 1 year of diagnosis was a strong predictor of other forms of Parkinsonism. Recurrent falling within the first year was a strong predictor of PSP, whereas time to onset of falling was more delayed in CBD, DLB, and MSA and most prolonged in PD [2], [4].

Reference [2] specifies certain clinical features that should be considered to distinguish PD from other parkinsonian syndromes in early stages of disease are Falls at presentation and early in the disease course, Poor response to levodopa, Symmetry at onset, Rapid progression, Lack of tremor and Dysautonomia (urinary urgency/incontinence and fecal incontinence, urinary retention requiring catheterization, persistent erectile failure or symptomatic orthostatic hypotension)

The clinical tests that may not be useful in differentiating PD from other parkinsonian syndromes are GH stimulation with clonidine, Electrooculography and SPECT scanning.

Olfaction testing should be considered to differentiate PD from PSP and CBD, but not PD from MSA. Levodopa and apomorphine challenge should be considered for confirmation when the diagnosis of PD is in doubt. MRI is possibly useful in distinguishing PD from MSA. Although PD patients have decreased smell as compared to MSA, these differences are not as pronounced. Thus, a significant loss of smell is suggestive of PD rather than other parkinsonian syndromes.

2) Features that are used to evaluate the risk of getting PD: The features that are used to evaluate the risk of getting PD are Age and Age of Onset, Sex Differences, Lifestyle Risk Factors, Occupational Risk Factors and Multi-Factorial Models.

Various studies suggest that most cases of PD have multi-factorial etiologies consisting of both genetic and environmental components. The model produced by several studies reveal the difference between risk factor and protective factor. Smoking remains a protective factor. The risk factors in multi-factorial model are Exposure to pesticides, direct exposure in specific occupations such as farming, indirectly as an environmental toxin in well water, Family history of PD, Medical history and Psychiatric history. As in [11], the following are the risk percentage for Parkinson's disease among population

- People over age 60 is 2:4
- People age less than 60 is 1:2
- People with Parkinson's report having a relative with the disease is 15 to 25 percent
- A person's chance of developing PD if their family members have disease, as compared to the general population is 4 to 9 percent
- Male get the disease more than female members

Risk percentage for Parkinson's disease among population = Risk percentage due to genetic factor + Risk percentage due to environmental factor

3) Feature that are used to evaluate the progressive of PD: PD is a progressive disease and heterogeneous across the population. For some people the disease progresses quickly, and in others it does not. The two types of progressive of PD are Rapid and Benign progression. Rapid progression was defined as those subjects who reached Hoehn and Yahr stage 3within three years or H&Y stage 4 or 5 within five years. Benign progression was defined as those subjects who were still in Hoehn and Yahr stage 1 or 2, after having PD for more than 10 years [2], [4].

The factors that are possibly useful for predicting a more rapid rate of motor progression of PD are Older age of onset (variably defined as over age 57-78 years), Rigidity/hypokinesia, Presence of associated comorbidities, Features of PIGD and Male gender

The factor useful in predicting slower progression and a longer response to levodopa therapy is Tremor as the initial presentation

The factors useful in predicting earlier development of cognitive decline and dementia are Older age of onset and Initial manifestations of hypokinesia/rigidity

The factors that are useful in predicting an increased risk for nursing home placement and shorter survival are Older age of onset, Dementia and Decreased dopamine responsiveness. As specified in [4], the following table describes how the progression is associated with the various clinical features.

TABLE I
ASSOCIATION BETWEEN PROGRESSION TYPE AND CLINICAL FEATURES

Progressive Type	**Negatively associated**	**Positively associated**
Benign progression	Older age of onset Past history of smoking Current or past use of levodopa Mild to severe rigidity	disease duration male sex current smoking habit
Rapid progression	disease duration male sex mild to severe resting tremor	older age of onset mild to severe rigidity

V. PERFORMANCE MATRICES

Three performance matrices are used to evaluate the performance of the diagnostic and prognostic methods. They are accuracy, sensitivity and specificity.

- Accuracy: It defines relationship between predicted and actual value i.e., how closes a predicted value to actual value. It is evaluated as Accuracy → (TP + TN)/(TP + TN + FP + FN)
- Sensitivity: It is also used to determine which attribute is more important to obtained correct output value. It is evaluated as Sensitivity → TP/(TP + FN)
- Specificity: It can be defined as high degree of confidence. It can be evaluated as Specificity → TN/(TN + FP)

VI. CONCLUSION

Early detection of the progressive nature of PD in a person is an essential factor. This review paper, studies and analyses the prognostic system of PD and defines all the features that were involved in progression of PD from mild to mid level and mid to advanced level. In addition, the features that were involved in rapid and benign progression were identified. This study tries to present an automatic method of finding the progression type in a person with Parkinson disease and the progressiveness of the disease from mild to mid level and mid to advanced level of Parkinson disease.

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