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Research Article

Non-motor Dysfunction in Idiopathic Parkinson's Disease - An Indian Perspective

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Abstract

Parkinson Disease (PD) was described by James Parkinson in his classic in 1817. Recently there has been a tremendous progress in our understanding of this complex and fascinating neurological disorder. It not only manifest motor symptoms but there is a whole range of non-motor features, including cognitive, psychiatric and autonomic impairments. The non-motor dysfunction of PD is an important cause of morbidity and increases the burden of the disease far beyond that caused by the classical motor symptoms..

Keywords: Parkinson Disease (PD); Parkinson Disease Dementia (PDD); Depression

Introduction

Parkinson Disease (PD) was described by James Parkinson in his classic 'Essay on the Shaking Palsy', in 1817. Since then, and especially in recent years, there has been a tremendous progress in our understanding of this complex and fascinating neurological disorder. We have learned that it is manifest not only by motor symptoms but also that there is a whole range of non-motor features, including cognitive, psychiatric, sleep, sensory, and autonomic impairments. In fact the non-motor dysfunction of PD is an important cause of morbidity and increases the burden of the disease far beyond that caused by the classical motor symptoms.

As the life expectancy of patients of PD became longer, cognitive dysfunction and dementia associated with the disease became more prominent. In fact, it was recently described by Foltynie., *et al*. [1], that 36% cases in an incident cohort of PD patients had evidence of cognitive impairment, suggesting that cognitive dysfunction is an inherent part of this disease. Parkinson Disease Dementia (PDD) is thus, increasingly more recognized and it has been revealed that PD is associated with a characteristic dementia, which differs from Alzheimer's Dementia in many ways.

Disorders of mood and affect, though receiving less attention than motor aspects of the disease, have long been recognized as a part of PD. Depression is common in PD, occurring in up to one-half of the patients

Anxiety disorders may be as common as depression [2,3] and the two are frequently co-morbid. Apathy, may overlap, but is usually distinct from depression. In addition, suicidal ideations, hallucinations, and delusions may be found [4,5].

When PD patients are carefully questioned, it becomes evident that fatigue, sleepiness, and sleep disturbances are major complaints independent of any medication and motor disability. Recent neuropathological publications demonstrate that neurodegeneration involves sleep regulation and daytime alertness to a large degree [6].

Clinical studies have shown that sensory symptoms, such as pain and anosmia, may precede the development of PD, sometimes by many years[5]. Central pain is usually associated with lesions in thalamus, and the intralaminar nuclei of thalamus which partici-

pate in the perception of pain, have major input to the basal ganglia [7].

Autonomic dysfunction occurs prominently in PD. This can manifest as dysphagia, constipation, urinary urgency, incontinence, erectile dysfunction, orthostatic hypotension, dyshidrosis, and impaired thermoregulation. Indeed, about nine out of ten patients of PD have one or more of these autonomic symptoms [8]. Autonomic problems appear to increase significantly with increasing disease severity [9].

Present study aims to investigate the non-motor dysfunction of PD in Indian patients.

Aims and Objectives

- To study the non-motor dysfunction among patients with idiopathic Parkinson's disease (IPD) in a tertiary care centre in North India.
- To study the correlation of non-motor dysfunction in patients with IPD with duration of the disease.
- To study the correlation of non-motor dysfunction in patients with IPD with severity of the disease as assessed by motor dysfunction scales (Hoehn and Yahr stage).

Material and Methods

Study design

Case-control comparative analysis of non-motor dysfunction in patients with idiopathic PD, and age and gender matched healthy controls.

Sample

The study sample consisted of 50 consecutive patients with idiopathic PD selected from the patients attending the Neurology outdoor/indoor services of the Institute of Human Behaviour and Allied Sciences, which is a tertiary care hospital.

The control group comprised of 50 age and gender matched healthy controls subjects, who were related or unrelated to the patients.

Inclusion criteria

- Idiopathic Parkinson's disease as defined by the UK Brain Bank criteria.
- Patients of age more than 20 years
- Patients of either gender.
- Patients willing to participate in the study after giving written informed consent.

Exclusion criteria

- Atypical Parkinsonian syndromes due to drugs (e.g.- metoclopramide, flunarizine), metabolic disorders (e.g.- Wilson's disease), encephalitis, or other degenerative diseases (e.g.- Progressive supranuclear palsy, Corticobasal degeneration, Dementia with Lewy bodies, Multiple system atrophy).
- History of dementia preceding the onset of PD.
- Systemic conditions known to be associated with autonomic dysfunction (diabetes, chronic alcoholism, chronic renal failure, etc).
- History of intake of medications other than antiparkinsonian medicines known to be associated with autonomic dysfunction.
- Pregnant female patients.
- Patients not willing to participate in the study.

Plan of study

- The study was approved by the medical ethics committee of IHBAS hospital.
- A written informed consent was taken from all subjects. After collecting the demographic data, all patients were subjected to comprehensive workup including history, general physical examination, and neurological examination. All patients fulfilled the United Kingdom PD Society Brain Bank criteria for idiopathic PD.
- They underwent routine investigations including complete blood counts, blood sugar, serum creatinine, total serum bilirubin, serum transaminases, serum electrolytes (sodium, potassium, calcium), lipid profile, resting electrocardiogram, and neuroimaging (magnetic resonance imaging).
- Severity of disease was assessed by dividing patients into strata based on the Hoehn & Yahr staging.
- Evaluation of motor and non motor aspects of Parkinson's disease was done using the MDS-UPDRS.
- There were 13 questions which assessed cognition, depression, psychosis, apathy, anxiety, feature of Dopamine Dysregulation syndrome, sleep problems, excessive day time sleepiness, pain fatigue and autonomic functions such as constipation, light headedness on standing and urinary problems.

- Five strata were constructed, based on age at onset (≤40 years and >40 years) and disease duration (<2 years, 2-5 years and ≥5 years). For reasons of comparability, all patients who used antiparkinsonian medication were assessed while they were clinically stable on their medication.
- Control subjects were selected to match the overall age and sex distribution of the patients, and had no documented illness.

- MRI-Brain was done in all patients on a GE HDX 3-Tesla MRI machine.
- Statistical Analysis was done using SPSS software.

Observations and Results

The present study was conducted to assess the non-motor dysfunction in patients with idiopathic Parkinson's disease.

The aim was to study the occurrence of non-motor dysfunction and its correlation, if any, with the duration, severity and medications used for the treatment of Indian patients with Parkinson's disease.

The study was conducted at Institute of Human Behaviour and Allied Sciences (IHBAS) which is a tertiary care centre for Neurology in Delhi.

A total of 50 consecutive patients with idiopathic Parkinson's disease were enrolled serially who attended either the outdoor services, or were admitted in the Neurology ward. At the same time 50 healthy age and sex matched control subjects, who were either related to the patients or volunteers from the Institute, were studied.

S. No.	Parameter	Cases (n = 50)	Controls (n = 50)	p
1	Age (years) Mean (S.D.)	53.86 (12.04)	48.0 (11.48)	0.42
	Range	(25-78)	(28-71)	
2	Sex Males	39 (78%)	41 (82%)	0.84
	Females	11 (22%)	9 (18%)	

Table 1: Age and sex distribution of cases and controls.

There were no significant differences in the mean age (p = 0.42) and sex distribution (p = 0.84) between cases and controls. As seen in table 1, both the groups were comparable.

S. No.	Parameter	Normal	slight	Mild	moderate	Severe
1.1	Cognitive impairment Frequency (%)	15 (30%)	16 (32%)	16 (32%)	3 (6%)	0
1.2	Psychosis and Hallucination Frequency (%)	35 (70%)	9 (18%)	5 (10%)	0	1 (2%)
1.3	Depressed Mood Frequency (%)	14 (28%)	4 (8%)	14 (28%)	13 (26%)	5 (10%)
1.4	Anxiety Frequency (%)	8 (16%)	10 (20%)	15 (30%)	16 (32%)	1 (2%)
1. 5	Apathy Frequency (%)	12 (24%)	21 (42%)	9 (18%)	6 (12%)	2 (4%)
1.6	Dopamine Dysregulation Syndrome frequency (%)	0	0	0	0	0
1.7	Sleep Problems Frequency (%)	17 (34%)	9 (18%)	16 (32%)	8 (16%)	0
1.8	Day time sleepiness Frequency (%)	26 (52%)	15 (30%)	7 (14%)	2 (4%)	0
1.9	Pain and other Sensations Frequency (%)	11 (22%)	9 (18%)	12 (24%)	14 (28%)	4 (8%)
1.10	Urinary Problems Frequency (%)	36 (72%)	2 (4%)	8 (16%)	4 (8%)	0
1.11	Constipation Problem Frequency (%)	26 (52%)	3 (6%)	12 (24%)	9 (18%)	0
1.12	Light Headedness on Standing Frequency (%)	41 (82%)	8 (16%)	1 (2%)	0	0
1.13	Fatigue Frequency (%)	2 (4%)	31 (62%)	9 (18%)	7 (14%)	0

Table 2: Frequency of non-motor parameters in cases of Parkinson's disease.

S. No.	Parameter	Cases (n = 50)	Controls (n = 50)	p
1.1	Cognitive impairment Mean (S.D)	1.36 (0.77)	0.24 (0.47)	< 0.001
1.2	Psychosis and Hallucination Mean (S.D)	0.46 (0.83)	0	< 0.001
1.3	Depressed Mood Mean (S.D)	1.82 (1.3)	0.28 (0.57)	< 0.001
1.4	Anxiety Mean (S.D)	1.84 (1.1)	0.62 (0.85)	< 0.001
1. 5	Apathy	1.30 (1.09)	0.58 (0.75)	< 0.001
1.6	Dopamine Dysregulation Syndrome Mean (S.D)	0	0	0
1.7	Sleep Problems Mean (S.D)	1.3 (1.1)	0.54 (0.83)	< 0.001
1.8	Day time sleepiness Mean (S.D)	0.70 (0.86)	0.34 (0.51)	< 0.013
1.9	Pain and other Sensations Mean (S.D)	1.82 (1.28)	0.22 (0.50)	<0.001
1.10	Urinary Problems Mean (S.D)	0.60 (1.03)	0.14 (0.40)	< 0.001
1.11	Constipation Problem Mean (S.D)	1.08 (1.2)	0.22 (0.58)	< 0.001
1.12	Light Headedness on Standing Mean (S.D)	0.20 (0.45)	0	< 0.001
1.13	Fatigue Mean (S.D)	1.48 (0.86)	0.06 (0.24)	< 0.001

Table 3: Comparison of non-motor parameters of cases and controls.

S. No.	Parameter	Cases (n = 50)	Controls (n = 50)	P
2.1	Speech Mean (S.D)	1.40 (1.12)	0	< 0.001
2.2	Saliva and Drooling Mean (S.D)	0.84 (0.99)	0	< 0.001
2.3	Chewing and Swallowing Mean (S.D)	0.52 (0.83)	0	< 0.001
2.4	Eating Task Mean (S.D)	0.96 (1.0)	0	< 0.001
2.5	Dressing Mean (S.D)	1.44 (1.23)	0	< 0.001
2.6	Hygiene Mean (S.D)	1.04 (0.78)	0	< 0.001
2.7	Handwriting Mean (S.D)	1.48 (0.95)	0.04 (0.19)	< 0.001
2.8	Doing Hobbies and other Activities Mean (S.D)	1.12 (1.04)	0.12 (0.32)	< 0.001
2.9	Turning in Bed Mean (S.D)	0.96 (0.78)	0.08 (0.34)	< 0.001
2.10	Tremor Mean (S.D)	2.42 (1.14)	0.06 (0.24)	< 0.001
2.11	Getting out of Bed, a Car or a Deep Chair Mean (S.D)	1.48 (1.03)	0.12 (0.32)	< 0.001
2.12	Walking and Balance Mean (S.D)	1.28 (0.80)	0.08 (0.27)	< 0.001
2.13	Freezing	0.92 (0.72)	0	< 0.001

Table 4: Comparison of motor parameters of cases and controls.

As shown in table 3, cases had significant non motor dysfunctions when compared with controls.

As shown in the table, there were no significant difference in non-motor parameters between male and female patients.

Discussion

It is well known that the motor symptoms of Parkinson's disease adversely affect the quality of life of the patients. But, the non motor features of this disorder are under-recognised and, consequently undertreated. Results from a recent international survey show that up to 62% of non-motor symptoms of Parkinson's disease, such as apathy, depression, pain, sexual dysfunction, mild cognitive dysfunction, bowel problems and sleep problems, might remain undeclared to health care professionals because patients are either embarrassed or unaware that the symptoms are linked to Parkinson's disease.

It is the co-existence of non motor dysfunctions in the disease that significantly adds to the burden of disease and also to the quality of life. Additionally, non-motor symptoms are a frequent cause of hospitalisation which can increase the cost of care of patients with Parkinson's disease by four times.

Present study was undertaken to know the spectrum of non-motor dysfunctions in Idiopathic Parkinson's disease in a tertiary care hospital in North India and to find any correlation of these symptoms with age of the patients, severity of motor dysfunction, antiparkinsonion medications used and with the duration of the disease.

The study sample consisted of 50 patients with idiopathic Parkinson's disease and 50 control subjects.

Data revealed that cases and controls were well matched for both age ($p = 0.42$) and sex ($p = 0.84$) distribution.

As expected patients had significant motor dysfunctions as compared to controls ($p < 0.001$). When non motor parameters were compared between cases and controls, cases showed significant impairment in cognition ($p < 0.001$) and patients had significantly more neurobehavior symptoms such as depression, anxiety and apathy ($p < 0.001$).

They also complained of significantly poor quality of sleep at night ($p < 0.001$) and significantly more day time sleepiness ($p < 0.013$), as compared with controls.

Patients had significantly more bodily pain ($p < 0.001$) and fatigue ($p < 0.001$). Patients had statistically significant more autonomic symptoms reported as urinary problems ($p < 0.001$), light headedness on standing ($p < 0.001$) and constipation ($p < 0.001$).

The non-motor parameters did not show any significant difference amongst male and female patients. When patients parameters were studied according to the age of onset of Parkinson's disease (≤40 years and >40 years), there were no significant difference in their speech involvement ($p = 0.31$), chewing and swallowing difficulties ($p = 0.26$), eating tasks ($p = 0.49$), dressing ($p = 0.11$), and maintaining hygiene ($p = 0.61$).There were statistically significant difference in saliva handling and drooling of saliva in patients with onset above 40 years of age ($p = 0.01$) and freezing of gait which was more common in younger age of onset ($p = 0.002$).

They had no significant difference in their cognitive function ($p = 0.73$), they also had comparable involvement in neuro-behaviour domain like psychosis, apathy, depression, anxiety with p value 0>.05. No significant difference was seen between their night time sleep quality and day time sleepiness ($p = 0.18$).

There was significant more pain in patients with onset after 40 years of age ($p = 0.01$); there was also statistically difference in fatigue between two groups ($p = 0.01$).

Both group had similar levels of autonomic dysfunctions as assessed by light headedness on standing ($p = 0.29$), constipation ($p = 0.57$) where as urinary problems were significant more pain in older patients ($p = 0.04$).

Patients parameters were also analysed after dividing them into three categories based on duration of their illness (<2 years, 2-5 years and >5 years). There was significant increase in motor dysfunction as assessed by Hoen and Yahr staging with longer duration of illness.

There was no significant difference in their cognitive decline ($p = 0.22$). There were no significant difference in occurrence of depression ($p = 0.92$) in three groups, depression was more common in patients with duration of disease less than 2 years suggests that non-motor symptoms may occur early in the course of disease. There was statistically difference in occurrence of anxiety ($p = 0.05$), but this parameter not followed linear relation with duration of disease; it was more common in patients with duration of disease between 2 to 5 years.

There were no significant difference in occurrence of other parameters like sleep problems ($p = 0.53$), pain ($p = 0.52$), fatigue ($p = 0.49$). There were no significant difference in autonomic symptoms as assessed by constipation ($p = 0.98$), light headedness on standing ($p = 0.60$) and urinary problems ($p = 0.24$).A significant percentage of Parkinson's disease patients develop dementia. In our study we found that Cognitive impairment was present in 70% of patients, most of the patient had mild impairment and none of the patient had severe cognitive impairment. Earlier estimates of prevalence of dementia in Parkinson's disease have been highly variable, ranging from 20% to 81% [10]. This might be due to different assessment techniques and different study populations. We used a five point scale of MDSUPDRS which assessed cognitive slowing, impaired reasoning, memory loss and deficit in attention and orientation. We found that 64% of the patients had mild impairment

in cognition with no interference or only minimal interference with the patient's ability to carry out normal activities and social interactions.

Parkinson's disease patients- even those with mild disease – exhibit patterns of cognitive deficits that include decrements in planning, sequencing, concept formation and working memory, which are all tasks associated with frontal lobe dysfunction [10]. Sullivan and colleagues [11] suggested that memory deficits were directly related to overall disease severity, with mildly impaired patients showing no decrements in memory performance, while Goldman and colleagues [12] found increasing memory deficits with increasing disease severity, including deficits among those very mildly affected.

The cognitive decline in Parkinson's disease is subtle initially, and frank dementia only occurs in very advanced stages. In patients with Parkinson's disease, the most consistent neuropsychological deficit is frontal/executive dysfunction [13]. Patients also have prominent perceptual and visuospatial deficits. A more recent survey indicated that 20% to 40% 0f PD patients ultimately demented, with an incidence of 10% per year [14]. We propose tools which specifically address these deficits, such as the recent SCOPA-COG [15] or detailed neuro-cognitive assessment should be applied to quantify the baseline deficits in patients who first present with Parkinson's disease.

When patients were divided according to severity of the disease as assessed by Hoen and Yahr staging and comparison of non-motor symptoms were done with the severity of the disease, following observations were made.

The duration of illness was significantly longer with greater severity of the disease. Importantly, more severe disease was significantly associated with greater depression ($p < 0.05$), apathy ($p < 0.05$); more cognitive impairment ($p < 0.05$), significantly more night –time sleep dysfunction ($p < 0.01$); more day time sleepiness ($p < 0.001$), more autonomic symptoms such as constipation and urinary problems.

Previous authors like Tandberg., *et al*. [16], Okun., *et al*. [17], and Cummings [18] have reported increased occurrence of depression in Parkinson's disease. Major depression was not a prominent finding and patients with Parkinson's disease had milder form of depression. This finding was also reflected in our study with only 5 patients out of 50 (10%) falling in the severely depressed category. In fact, 62% had symptoms of mild to moderate depression. Fourteen patients (28%) did not have any symptoms of depression. Our observation were similar to those reported in previous studies showing the prevalence of depression in Parkinson's disease ranging from 4% to 70%, with a mean of 40% approximately [18].

Reported prevalence and incidence rates for depression in PD are highly variable. This is in part due to different assessment techniques and populations studied. Previous studies showed high rates of under-recognition and under treatment of depression in Parkinson's disease. In a study by Weintraub., *et al*. [19], almost two third of subjects meeting criteria for depression were not treated. Shulman., *et al*. found that clinicians did not recognize or treat depression in 50% or more of significantly depressed Parkinson's disease patients [20].

We found depression in 72% of patients, though it was mild depression in majority of the patients. Mild depressive disturbances are associated with reduced functional ability, increased caregiver burden, and reduced quality of life [21]. Evidence suggests that the detection and treatment of mild depressive symptoms in PD may improve these outcomes.

Study patients were assessed for any relation of type of medication used (as dopamine replacement therapy) with the various study parameters. Patients were divided into three groups: those on no dopamine replacement therapy, those on levodopa monotherapy and those on both drugs (levodopa plus dopamine agonist).

Patients who were on combination therapy of levodopa and dopamine agonist had significantly less cognitive impairment ($p = 0.001$). This might be due to antidepressant effect of dopamine agonist or it might be possible that dopamine agonist have some cognitive enhancer effect.

Patients on dual therapy had more day time sleepiness ($p = 0.01$) as compared to patients on levodopa monotherapy. In a previous study too, Paus., *et al*. have reported that excessive day time sleepiness is best correlated with dopamine replacement therapy,

and is more frequent in combination therapy of levodopa with dopamine agonist, as compared to monotherapy [22].

Other neuropsychiatric symptoms in patients with Parkinson's disease, in order of descending frequency were: anxiety (84%), apathy (76%), depressed mood (72%), psychosis and hallucination by 30% of patients. No patient reported affirmative to the following symptoms: Delusions, Agitation/Aggression, Elation/Euphoria, Disinhibition, and Abberant motor behaviour.

Aarsland and colleagues [23] assessed neuropsychiatric symptoms in patients with Parkinson's disease and dementia. Their symptoms frequency was - depression (58%), apathy (54%), anxiety (49%) and hallucinations (44%).

In our study frequency of anxiety was much higher as compared to other study; this might be due to fact that most of the patients were not aware of the course of the disease, they had a lot of questions regarding the disease and management as they were not explained well to the patients. Amongst autonomic dysfunctions assessed in study population, we found constipation in 48% of our patients, urinary problems in 28% of patients and light headedness on standing in 18% of our patients. Patients with severe Parkinson's disease experienced significantly more constipation ($p < 0.01$) and urinary problems ($p < 0.02$) like urgency, frequency and incontinence, as compared to patients with mild to moderate Parkinson's disease. When autonomic functions were compared in those on levodopa monotherapy and on combination therapy, no significant differences were noted for urinary problems ($p = 0.14$), light headedness on standing ($p = 0.19$) and constipation ($p = 0.09$).

Verbaan and colleagues [24] noted that patients without dopamine replacement therapy experienced significantly less urinary problems and gastrointestinal problems compared to patients on combination therapy. Our study revealed that autonomic dysfunction is a prominent aspect of Parkinson's disease, being present in early stages of disease and increasing with increasing Hoen and Yahr stages. Constipation may occur as an early manifestation reflecting involvement of neuronal circuits of the gastrointestinal system or arise as a consequences of other factors, such as decreased water intake secondary too\diminished thirst sensation.

Two studies have supported the notion that PD may start with autonomic involvement. One study found that infrequent bowel movements were associated with an elevated risk of future Parkinson' s disease in men while another study reported that constipation preceded the onset of motor symptoms in the majority of patients with Parkinson's disease [25,26].

This is a clinic based study, autonomic symptoms were assessed in 50 patients with Parkinson's disease. To obtain an adequate distribution of important determinants of the disease course, patients were evaluated based on age of onset (≤/>40 years) and disease duration(<2 years, 2-5 years of disease and more than 5 years of disease). Because of this selection process, the results cannot be generalised to the general Parkinson's disease population. These autonomic symptoms are all embarrassing and have a severe impact on social life. Sialorrhea is generally noticed during follow up visits but patient may hesitate to report incontinence. Consequently, increased clinical awareness is warranted and may prevent under treatment of autonomic symptoms in PD. Although several therapeutic treatment options for the various autonomic dysfunction in PD are available, there is lack of evidence from randomised trials regarding their efficacy. The high frequency of autonomic symptoms in PD found in our study clearly indicates the need for more attention towards these symptoms.

Pain as assessed by asking regarding uncomfortable feeling of pain, aches, tingling and cramps over the past week, was reported by 78% of the patients. This was significantly more severe than in controls ($p < 0.001$). But, perception of pain was not significantly related to sex of the patients ($p = 0.01$), duration of illness ($p = 0.52$), and severity of illness ($p = 0.85$). Pain was significantly more in patients with disease onset after 40 years of age ($p < 0.01$).

Previous studies have also reported pain as a symptom in Parkinson's disease in 40% of patients. The NMS Quest study reported pain in 29% of patients, a recent study, the DOPAMIP survey in southwest France, found 62% of patients with Parkinson's disease had at least one form of chronic pain [27]. Similar figures were reported in a recent Italian case-control survey, which noted that, overall, 70% of the population studied had pain [28].

Pain is one of the common non motor symptom of Parkinson's disease and very much neglected because it may be due to other co-morbidities in old age like osteoarthritis, decrease threshold to pain etc. As pain is one of the symptom that responded to dopamine therapy, it should be assessed in every Parkinson' disease patients.

We did not find features of Dopamine Dysregulation syndrome in our patients of Parkinson's disease. Assessment of disorders like Compulsive Buying, atypical or excessive gambling, excessive sexual drive or interests, repetitive activities like dismantling objects or taking extra non-prescribed drugs for non-physical reasons was reported to be negative by all the patients and controls.

Previous study by Weintraub., *et al*. [29], has reported an increased prevalence of impulse control disorder in patients with Parkinson's disease on dopamine agonist therapy. Total of 6.6% patients reported such symptomatology in their study and these patients were on higher dosage of dopamine agonist and some had past history of such disorders. Our Indian patients may be a subset in which such symptoms are not seen so frequently.

We propose further larger studies are required in Indian patients with Idiopathic Parkinson's disease to confirm the increased presence or absence of Dopamine Dysregulation Syndrome in them.

Conclusions

Non motor symptoms are universal features of Idiopathic Parkinson's disease and involve dysfunction in the neuropsychiatric, cognition, sensory, sleep and autonomic domains. They add significantly to overall disability caused by PD and are critical determinants of health related quality of life of affected patients.

As effective treatment for motor symptoms of Parkinson's disease are available, non motor dysfunctions has developed into a major prognostic factor for overall disease burden and everyday function in PD. In addition, there is increasing evidence that non motor dysfunctions antedates clinical manifestations of motor symptoms of PD by years or even decades and may thus turn out to be critical target for early diagnostic paradigms and identification of at risk populations.

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