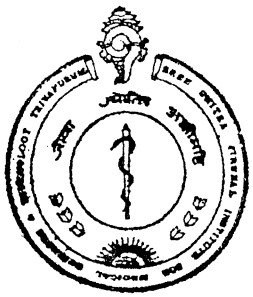

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY

THIRUVANANTHAPURAM - 695 011

PROJECT REPORT

NAME	:	DR.SUDEEP BALAKRISHNAN
PROGRAMME	:	D.M. Neurology
MONTH & YEAR OF SUBMISSION	:	NOVEMBER 1998

SREE CHITHRA THIRUNAL INSTITUTE FOR
MEDICAL SCIENCES & TECHNOLOGY

A PROSPECTIVE STUDY OF DEMENTIA AND DEPRESSION IN IDIOPATHIC PARKINSONS DISEASE

SUDEEP BALAKRISHNAN

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Dr.Sudeep Balakrishnan

CERTIFICATE

I, Dr. SUDEEP BALAKRISHNAN .....hereby declare that I have actually performed all the procedures listed/carried out the project under report.

Signature.....

Place : **Trivandrum**

Date :

Name in capital letters

SUDEEP BALAKRISHNAN

Forwarded. He has carried out the project under report.

Signature
Head of the Department

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PROJECT REPORT DONE

TITLE

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NAME : **DR. SUDEEP BALAKRISHNAN**

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Introduction

Parkinsons disease (P.D.) is a degenerative disease dominated by a disorder of movement consisting of tremor, akinesia or bradykinesia, rigidity, and postural instability. At least two of these should be present to make a diagnosis of clinically definite parkinsons disease. The major underlying pathology of P.D is the loss If neurons in the substantia nigra. Upto 80 percent of dopaminergic neurons are lost before the cardinal signs and symptoms first appear. This is due to the disruption of the dopaminergic nigrostriatal pathways that play a central role in controlling voluntary movements.

Parkinsons disease affects one percent of the population over the age of fifty five years.[1] It is typically a disease of middle to late years, beginning at a mean age of fifty to sixty years and progresses slowly over a ten to twenty year period. Roughly 5% of cases begin before the age of forty years (ie young onset P.D).

Dementia as a clinical symptom occurs only in patients with well established parkinsons disease, and is usually not a presenting feature. The incidence of dementia in P.D varies widely between 25% to 80%.[2] Typical cases of idiopathic P.D. manifest dementia in about 20% of cases, where as atypical cases have a higher incidence of 70% or above.[2] In 50% of patients with dementia, it is mild and not a significant problem. In general the severity of dementia correlates well with the severity.

Parkinsonian dementia is characterised by a general lack of activation. There is a general slowness and inefficiency in cognitive process (bradyphrenia), features

of a frontal lobe syndrome with indifference and social impropriety, lack of insight and poor judgement, difficulty in complex problem solving and concept formation.[3] There can be difficulty with constructional tasks and non verbal reasoning.

Earlier studies have found that patients who eventually became demented are the ones who developed P.D. at a later age, have the disease for a shorter time, and become more severely disabled with less response to levodopa.[4] Non demented patients with P.D. have a greater improvement with levodopa, but, have a higher incidence of involuntary movements and on-off phenomenon.[4]

Relevance of present study

To the best of our knowledge there are no previous Indian studies which has studied the frequency of dementia and depression or assessed the correlation to various known risk factors. Moreover a recent study has shown that normal Indian subjects have a lower nigral cell count compared to the western population.[5] The present study was therefore undertaken to study the frequency of cognitive impairment in our population and to determine the associated risk factors.

Pathophysiology of dementia in P.D.

Proposed mechanisms

In parkinsonian dementia, there is a disturbed caudate outflow which leads to defects in cognitive functions dependent on the integrity of the pre frontal cortex which is the cortical focus of caudatofugal signals.[6] There is also affection of the extrastriatal midbrain cells which reduces the extrinsic supply of dopamine to this cortical region. As the prefrontal cortex is thought to play a crucial role in self directed task planning, the validity of an outflow model in predicting the consequences of caudate nucleus dysfunction is supported.

Some studies have shown visuospatial impairment in P.D., which has been attributed to the affection of connections between the striatum and the parietal association cortex.[7]

Intellectual decline in P.D. is also thought to be due to the involvement of the ventral tegmental and mesocorticolimbic dopaminergic systems. Neuronal loss in locus ceruleus and nucleus basalis of meynert with norepinephrine and cholinergic depletion may be responsible for the impairment of memory and attention.[6]

A specific pattern of memory dysfunction is seen in P.D. Immediate memory, in general is spared. Recent memory is impaired in all patients where as remote memory gets impaired only in those who had a significant intellectual decline.[8]

Depression in P.D

Depression is by far, the most common psychiatric or neurobehavioural problem in P.D. It's prevalence is estimated in the range of 25 to 40%.[4] Most of it is endogenous depression, although an element of reactive depression is present.[9] Depression, is seen in both demented and non demented patients with a slightly higher incidence in the former group. Depression is more common in the pure P.D. patients who have primarily a subcortical dementia than in patients with global dementia seen in the combined P.D./A.D. State.[10]

There are also reports stating that depression occurs independent of dementia in P.D. and that the prevalence is similar in demented and nondemented patients and that it is not a prelude to dementia.[4]

In 15 to 20%, depression may manifest before the initial motor signs and symptoms. It is of a mild to moderate degree and is not necessarily correlated with disease severity. There has been no direct association noted with sex, age, disease

duration and anti parkinsonian drugs. A good objective motor response to levodopa without parallel mental satisfaction should lead one to suspect depression. It may lead to insomnia, and may have a negative effect on cognition, particularly on memory.

Pathogenesis of depression in parkinsons disease

The pathogenesis of depression in P.D. is not clearly know. One hypothesis is that it may be secondary to the loss of dopaminergic innervation in specific parts of basal ganglia or in the limbic system.[11] In patients with response fluctuation to levodopa, the off periods are associated with severe depression that rapidly disappears when the dose of levodopa turns them on.[10]

Another hypothesis is that serotoninergic mechanims are involved. In depressed parkinsonian patients, a reduction in the CSF 5- HIAA has been documented, thus indicating a reduced central serotoninergic transmission.[12]

Aims of study

1. To conduct a prospective study of the frequency of dementia and depression in our cases of P.D.
2. To study the patterns of cognitive dysfunction and the spheres of involvement.
3. To examine the relation between occurence of depression and dementia with
   a. Age at onset of disease.
   b. Clinical characteristics of the disease.
   c. Duration of levodopa treatment.
   d. Presence of motor fluctuations and dyskinesias
   e. Presence of depression.

Materials and Methods

50 consecutive cases of idiopathic P.D were selected from the `Movement disorder clinic' at Sree Chitra Thirunal Institute of Medical Sciences and Technology. Clinically definite cases were included in the study. Idiopathic P.D was defined as the primary form of the disease in which review of the medical history and physical signs indicated no other disease process that could be considered as the cause of the disorder. At least, two of the following four cardinal features of P.D were present on clinical examination - resting tremor, bradykinesia, rigidity or postural instability, one of which was either rest tremor or brady kinesia . All the patients were levodopa responsive.

Exclusion criteria included more than one affected relative, a remitting course, neuroleptic use within the past year, a previous history of encephalitis or repeated head trauma, cerebellar signs supra nuclear gaze palsy, prominent pyramidal signs, oculogyric crisis, early autonomic neuropathy and evidence of cerebrovascular disease.[13]

Control data

Thirty control subjects (18 males and 12 females) were also recruited. Their education and socioeconomic status were noted. The mean age at presentation of the control group was 57.41 ± 8.27 yrs (range 22-73 years). The control group was screened for any neurological disease and secondary causes of cognitive impairment, such as history of alcoholism, head trauma, psychiatric illnesses or drug abuse were

excluded. The control subjects were administered a battery of neuropsychological tests from which the normal range was ascertained (detailed below).

All patients at entry were staged according to the 'Hoehn and Yahr' staging.[14] Young onset cases of P.D were defined as those with an age of onset below 50 years. The severity of the disease was assessed using the `Unified Parkinsons Disease Rating Scale' (UPDRS) motor subset scoring system. The anti-parkinsonian drugs that the patient received, duration of levodopa treatment, side effects to levodopa including the presence of drug induced dyskinesias and motor fluctuations were noted at the time of evaluation.

The patients were initially screened for dementia using 'Folsteins' Mini mental status examination. This was followed by the administration of detailed neuropsychological tests enlisted below. Dementia was diagnosed provided they satisfied the DSM-4 criteria given below.[15]

SPECIFIC CRITERIA

Impairment of memory

Impairment in at least one other cognitive function. (language, visuospatial, apraxia etc.)

Significant disturbance in work or social function due to cognitive deficits not occuring during delirium.

Depression was assessed using Becks self inventory. An over all score of more than 14 was taken as indicating significant depression.

All tests were applied in the 'ON' state. The battery of neuropsychological tests administered to assess individual lobe functions included the following.

Frontal lobe functions

1. **Category test :** It is a subset of 'Halsteads battery' designed to measure frontal lobe functions. Problems were presented visually and the subject was asked to look for similarities and differences in the stimulus material, and to formulate a hypothesis as to the correct concept (variables include size, shape, position etc.) and to respond to it. Test was scored as accurate or not accurate.

2. **Verbal fluency :** Subjects were asked to tell as many words as possible in one minute begining with a particular letter (Normal > 12).

3. **Attention :** Tested using the 'digit span' subset of Wechsler Adult Intelligence Scale (WAIS). Normal values taken were forwards - 6, backwards - 4.

4. **Digit symbol subset (of WAIS) :** Transcription of numbers into symbols (Normal > 60)

5. **Serial subtraction :** Eg. 100 - 7, scored as having error or no error.

6. **Bender - Gestalt test :** Is a test of visuomotor ability. Subjects were asked to copy 9 geometric figures. Errors in reproduction were noted. Poor reproduction by a co-operative patient with intact visuomotor function was taken as indicative of frontal dysfunction.

7. **Visual scanning :** Tests right frontal function, with the aid of scanning of symbols. Patients were asked to cancel out circles and triangles from an array of symbols. The test was scored as having error on no error.

8. **Ideation fluency :** Tests left frontal function. Patients were asked to repeat as many words, in different categories as possible in one minute. A score less than 12 was taken as abnormal.

9. **Delayed response ability :** Using the digit span. Scored as having error or no error.

Temporal lobe functions

1. **Visual integration :** Tested using 'block design' subset of WAIS. Patients were asked to arrange blocks to form specific patterns. This tests both visuomotor ability ad integration. A score of >30, was taken as normal.

2. **Object assembly :** Tests both frontal and temporal lobe functions but is more sensitive for the latter. Patients were asked to assembe parts to make up a profile. A score of >25, was taken as normal.

Memory was tested as follows:

Immediate memory : Using the digit span subset of WAIS.

Recent memory : was tested using the 'logistic passage' subset of Wechsler memory scale (WMS). A passage containing 21 clauses were read out which the patient had to reproduce after 5 minutes. A score of > 14 was taken as normal.

LTM : Tested using the delayed recall of the above passage after 30 minutes.

STM (Visual) : Using ROCF. Test was scored as either having error or no error.

Parietal lobe functions

Right parietal functions (Visuospatial tasks)

1. Drawing and copying : Spatial neglect, distortion, fragmentation, lack of integration etc. were looked for.
2. Modified ROCF
3. WAIS block design and digit symbol subsets

Left parietal :

Focal neurological signs

Sentence repetition

Statistical methods

Statistical correlation between the variables was assessed using Chi-Square test. This was confirmed with Pearsons method and Fishers Exact testing.

Review of literature

Dementia in P.D.

In the initial description of P.D, by James Parkinson, there was a categorical denial of cognitive impairment. It was Charcot and Vulpian who first opined that the mental faculties are impared in P.D. Subsequently Lewy (1923), reported the occurrence of dementia in 64% of 86 Parkinsonism patients.

In the past 2 decades, controversy regarding dementia in P.D, has continued with varying incidence quoted by different authors.

Lees A.J et al,[16] studied 30 right handed patients with idiopathic P.D. They found that 76% of patients had difficulty in shifting of conceptual set patterns and showed perseveration on Wisconin Card Sorting Test (WCST) and verbal fluency tests.

Boller et al,[17] in a study of 30 patients with idiopathic P.D, showed significant impairment in visuospatial tasks. Cognitive impairment was noted overall in 55%, with good correlation to the stage of P.D.

Liberman A et al,[18] in a study of 520 patients with Parkinsonism seen over 8 years reported that 168 (32%) had moderate to marked dementia. Demented patients in addition to being older, developed the disease later, were more severely involved in a shorter time and less responsive to levodopa. Non demented group showed greater response with more fluctuations and on-off phenomena.

Girotti F et al,[19] studied the frequency of dementia, clinical characteristics and pattern of cognitive impairment in 147 unselected P.D patients. 14.28% were found to be demented. They had severe and widespread cognitive deficits especially in those tests that already discriminated Parkinsonian patients from controls.

Stern J et al,[20] studied the intellectual changes in 6 patients with MTP induced Parkinsonism. They found impaired frontal lobe tasks especially 'category naming' along with constructional apraxia. They postulated that changes in the dopaminergic system is responsible for at least some of the intellectual changes of P.D.

Ann E. Taylor(5) after detailed neuropsychological tests proposed a striatal outflow model to explain the significant impairment of frontal lobe function in these patients.

Mayeux R[21] in a population based study found crude prevalence of P.D with dementia to be 41.1 per 1 lakh which increased with age from zero for <50 years to 787 per 1 lakh for above age of 80 years. Dementia was seen to be strongly related to the age at onset of motor manifestations. The frequency was clearly age dependent and increased with each decade of life.

Dubois et al,[22] compared two groups of P.D. patients treated with and without anticholinergics. The former group showed severe impairment on frontal lobe tests thus suggesting that involvement of ascending cholinergic neurons may play a role in the behavioural changes.

Mayeux R et al,[23] in an 18 month follow up study found that demented patients were older, had a later age at onset of motor manifestations and more rapid progression. In addition the demented group showed poor response to levodopa and more drug related adverse effects. There was no correlation noted with disease duration, clinical subtype and associated depression.

The same author in another population based study later on concluded that dementia in P.D patients is more frequent than previously considered and is strongly related to age at onset of motor manifestations.

Another study reported an increased risk of dementia in P.D. patients who belonged to the lower socioeconomic strata with poor educational levels.[24]

Biggins et al,[25] in a controlled study of patients with idiopathic Parkinsonism found correlation with older age at disease onset and inclusion into study as well as with disease duration.

In a follow up study of 249 patients with idiopathic P.D, Ebmeier S.A et al,[26] reported a 24% incidence of dementia. They concluded that probability of dementia was associated with disease severity, independent of age.

Another prospective study conducted by Stern et al,[27] evaluated 250 patients with idiopathic P.D for a 5 year follow up period. The antecedent clinical features associated with dementia were age >70 years, UPDRS rating scale >20, depression and drug related side effects.

Aarsland et al,[28] in another study found an incidence of dementia in idiopathic Parkinsons disease of about 28%. The chief variables associated were depression, older age at onset, institutionalization and atypical neurological features.

Marder K et al,[29] in a prospective cohort based study found that patients with severe extrapyramidal signs have almost twice the risk of developing dementia.

In a population based study Tison F et al,[30] reported depression in 33% and dementia in 40%. The frequency of dementia increased with age and was higher in institutionalized patients.

In another study, Caperros et al,[31] found that cognitive decline in P.D, was significantly greater in the late onset group and in patients with dyskinesias and poor response to levodopa.

A cross sectional study of 70 consecutive patients with P.D found a significant association between incidence of dementia, age and duration of anticholinergic therapy.[32]

Glatt S.L et al,[33] found a significant association between risk of dementia in P.D to the severity of motor defecits (UPDRS motor score >20), age at onset of disease and lack of education.

Friedman et al,[34] in a study reported that the demented patients with Parkinsons disease was significantly older at the time of evaluation and also at disease onset. They had a more severe illness and were more prone to the psychotic effects of levodopa.

Hakim A.M et al,[35] in a retrospective study of Parkinsonian patients found a relatively high incidence of dementia (62%). They proposed that this could be explained by presence of associated early AD in some of their patients.

Similar observations in P.D patients with associated A.D like changes at autopsy have been also noted by Boller et al.[36]

In another study by Losanger W et al,[37] a high frequency of intellectual impairment was noted in P.D patients, with over 80% having deficits on WAIS and visuospatial tasks. There was a positive correlation between degree of dementia and disease severity. No association was noted with either the onset age, age at study or duration of disease.

Montimer et al,[38] after detailed neuropsychological testing, of 60 P.D patients showed that almost 90% performed poorly with moderate dementia in 80%. They concluded that a spectrum of intellectual impairment can occur in P.D. patients.

In a previous review Drachman et al,[39] had also stressed on the wide variation in the reported frequency of dementia (25-80%).

Depression in P.D

Hantz P et al,[40] assessed the prevalence of major depression among idiopathic P.D. patients. They concluded that the prevalence was no greater than other age and sex matched disabled persons.

However Haltenttof et al,[41] reported that depressive disorders occur in around 40% of patients with idiopathic P.D. These patients in addition had a severe akinetic rigid syndrome, lower age at onset and a positive family history.

Cumings et al,[42] in a review noted 40% incidence of depression in idiopathic P.D. This was more common in patients with the akinetic rigid subtype and with postural imbalance. In addition, female sex, younger age at disease onset and greater (L) hemispheric involvment were reported as risk factors.

Sergio E et al,[43] found that the severity of depression was the single most important factor associated with severity of cognitive impairment. In another study they also noted a positive association between degree of depression and rate of progression of motor signs.

Tandberg et al,[44] conducted a community based study for assessing incidence of depression in idiopathic Parkinsons disease. Although severe depression was noted in only 5.1%, the overall frequency of depression was 52%.

Another study by Troster et al,[45] concluded that depression exacerbates the memory and language impairment associated with P.D. The effect was more quantitative rather than qualitative.

Chia L.G et al,[46] in a study from Taiwan showed that Parkinsonian depression parallels both the disease duration and severity of motor disability.

Kostic V.S et al,[47] in a study of 169 patients compared the frequency of depression in idiopathic P.D patients with age of onset less than and more than 50 years. Major depression was found in 36% with early onset, and in 16% with late onset P.D. They also found a correlation between severity of depression and impairment of ADL.

In a recent study of 78 patients with P.D, Starkstein.[48] showed that even though prevalence of dysthymia was similar in both the classic and akinetic rigid subtypes, major depression was more frequent in the latter group (38% or 15% $P < 0.001$). In addition, bradykinesia was the sign showing maximum correlation with Hamilton scale scores.

In a Chinese study including 109 patients, of P.D, depression was noted in 42.2%. There was good correlation between the severity of depression and ADL.[49]

Other studies have shown a much lower incidence of depression in patients with idiopathic P.D.[50]

Results

Out of the fifty patients with idiopathic P.D studied, 35 patients had age of onset >50 years and 15 had younger age of onset (<50). 35 patients (70%) showed evidence of congnitive impairment of which 33 patients (66%) had impaired frontal lobe functions and 26 patients (52%) had impaired temporal lobe functions. 24 patients of these 35(69%) showed involvement of both lobes. Depression was noted in 28 patients (56%)

Table 1

Demographic characteristics

	P.D patients	Controls
Male	32(64%)	18(60%)
Female	18(36%)	12(40%)
Mean age at presentation	59.54 ± 11.55 yrs (range 26-81 yrs)	57.41 ± 8.27 yrs (range 22-73 yrs)
Mean duration of symptoms	5.4 ± 4.09 yrs (range 1-20 yrs)	

Table 2

	Akinetic-rigid	Tremor dominant	Mixed
Subtype of P.D	23(46%)	11(22%)	16(32%)

Table 3

Treatment characteristics

Fluctuators	Levodopa Treatment			Mean duration SD
	Stable	<3 yrs.	>3 yrs.	
18(36%)	32(64%)	29(58%)	21(42%)	3.47 ± 3.05 yrs Median 3 yrs

Table 4

Educational characteristics

	Primary	Secondary	College
Controls	3	10	17
P.D Patients	2	21	25
Demented	2	17	14
Non-demented		4	11

* 2 P.D patients with dementia had not attended school.

Table 5

Frontal Lobe Tests in P.D Patients

	Impaired (%)	Not impaired (%)	Controls
Verbal fluency	26(74)	9(26)	>12
Category test	11(31)	24(69)	No error
Attention	12(34)	23(66)	No error
Digit symbol	25(71)	10(29)	> 60
Serial subtraction	10(29)	25(71)	No error
Bender Gestalt	24(69)	11(31)	No error
Visual scanning	16(46)	19(54)	Normal
Ideation fluency	25(71)	10(29)	< 12
Delayed response	9(26)	26(74)	No error

Table 6

Temporal Lobe Tests P.D. patients

	Impaired (%)	Not impaired (%)	Controls
Visual integration	23(66)	12(34)	> 30
Object assembly	23(66)	12(34)	> 25
Sentence repetetion	4(11)	31(89)	Normal
Immediate memory	10(29)	25(71)	Normal
Recent memory	16(46)	19(54)	> 15
LTM	16(46)	19(54)	> 15
ST visual memory	29(83)	6(17)	no error

Table 7

Correlation with age at onset

Age at onset	<50 yrs (n = 15)	≥ 50 yrs (n = 35)	p-value
Dementia	10(67%)	25(71%)	0.71
Depression	9(60%)	19(54%)	0.58

n = total number of P.D. patients in the study.

No correlation was noted between either dementia or depression and the age of onset of P.D.

Table 8

Correlation with gender

	Male	Female	p-value
Dementia	19(59%)	16(89%)	0.038*
Depression	15(47%)	13(72%)	0.042*

Both depression and dementia showed an increased incidence in females, the association being statistically significant.

Table 9

Correlation with duration of disease

Disease duration	<3 yrs	≥ 3 yrs	p-value
Dementia	7(41%)	28(85%)	0.032*
Depression	10(59%)	18(55%)	0.52

Dementia was more common in P.D patients having a longer disease duration. No similar association was noted for depression.

Table 10

Duration of levodopa treatment

Dur. of Levodopa treatment	< 3 yrs	≥ 3 yrs	p-value
Dementia	19(66%)	16(75%)	0.43
Depression	16(55%)	12(57%)	0.72

Neither dementia nor depression showed any significant correlation with the duration of levodopa treatment.

Table 11

Subtype of P.D

	Akinetic-rigid	Trem.dominant	Mixed	P-value
Dementia	20(84%)	6(54%)	9	0.048*
Depression	16(69%)	8(72%)	4	0.65

The incidence of dementia showed a statistically significant correlation with the disease subtype, being more common in the akinetic-rigid variant. This was not applicable to depression.

Table 12

Severity of P.D

UPDRS score (motor)	< 15	> 15	p-value
Dementia	8 (53%)	27 (77%)	0.01*
Depression	8 (53%)	20 (57%)	0.37

Dementia was seen to be significantly higher in patients having more severe disease, as measured by the UPDRS motor score in the 'on state'.

Table 13

Presence of fluctuations and dyskinesias

	Fluctuations & Dyskinesias	Stable	p-value
Dementia	12 (66%)	23(71%)	0.51
Depression	8 (44%)	20 (62%)	0.28

No significant association was noted for either dementia or depression with the presence or absence of motor fluctuations.

Table 14

Correlation of Dementia to presence of depression

Depression	Present	Absent	p-value
Demented P.D	26 (74%)	9 (26%)	0.001*
Non-demented P.D	2	13	---

There was a significant correlation between the incidence of dementia and the presence of depressive symptoms.

Discussion

The present study is probably the first Indian study which prospectively assessed the frequency of dementia and depression in clinically definite cases of idiopathic P.D. The study was also carried out on patients selected from a speciality clinic(Movement disorder clinic of SCTIMST) which ensures a high degree of diagnostic accuracy of the cases selected.

We applied internationally accepted neuropsychological tests used in previous studies for the assessment of demintia in P.D. We tested on our normal controls and formulated our nomative data for the Indian population. We then compared the results of our study group, with our normal data.

In the present study, 70% of patients had dementia and 56% had depression. Presence of dementia was seen to correlate with the female sex, longer disease duration, akinetic rigid subtype of P.D, severity of the disease and the presence of coexisting depression. No correlation was noted with the age at disease onset, duration of levodopa treatment or to the presence of motor fluctuations and dyskinesias. Depression was more frequent in the female sex. No correlation of depression with the other variables were noted.

In this study 35 patients (70%) showed evidence of cognitive impairment. Although the frequency is rather high, similar incidences have been reported by previous workers.[16, 35] Others have noted an even higher incidence of 80%.[37,38 & 51] Some workers have observed a lower incidence in the range of 30-40%.[13,18] The

variability in the frequency of dementia could be due to factors such as differing patient selection criteria, differences in the tests administered and non-uniform criteria in defining dementia in various studies.[16,18] In studies with high frequencies of dementia in P.D, the authors have attributed this to the presence of coexisting AD and improved life expectancy of patients.

The relatively small number of patients (50 patients) and controls (30 subjects) was a drawback of our study.

In the present study, 33 patients (66%) had imparied frontal lobe functions as opposed to 26 patients (52%) with impaired temporal lobe functions. This is consistent with earlier studies.[6,22] In our study, depression was noted in 28 patients (56%) which is similar to the incidence reported by other workers.[44,45]

In the present study, no correlation was noted between the presence of dementia and the age at onset of P.D (Table 7). This is in contrary to certain earlier reports which had associated dementia with a later age at disease onset.[18,21 & 28] Compared to those studies,[21,25] our study had a relatively smaller number of patients with young onset P.D. This probably explains the lack of association with the age at onset noted in the present study.[44,45]

Although the incidence of depression showed a trend favouring a younger age at disease onset, it did not reach statistical significance, as noted in some of the previous studies.[41,47]

In the present study, neither the incidence of dementia nor depression showed any correlation with the duration of levodopa treatment (Table 10). This may be due to the fact that we did not have sufficient number of patients who had received levodopa for a longer duration.

The incidence of both dementia and depression was significantly more in the female sex in our study (P = 0.38 and .042 respectively; Table 8). This is inspite of having male predominance. There are not many studies quoting a higher incidence of dementia in the female sex.

The incidence of dementia was more in P.D. patients having disease duration > 3 years, the association being statistically significant (P<.04) (Table 9). Similar observations have been made by other workers.[21,25] No association was noted between depression and disease duration. Only a few studies have shown a significant correlation of depression with disease duration.[46]

In this study, correlation was noted between incidence of dementia and subtype of P.D, being significantly more in the akinetic rigid subtypes (P=.048, Table 11). This is not in agreement with previous observations of Mayeux. R[23] who found no association of dementia with disease sub type. Other workers have found an association with the akinetic rigid subtypes of P.D.[41,42]

No association was noted for presence of depression with disease subtype. We noted an increased incidence of dementia in idiopathic P.D patients having greater disease severity (UPDRS score > 15) (Table 12) (P<0.01). This is in agreement with most of the earlier studies that show an increased incidence of dementia in P.D patients with greater disease severity.[18,26 & 33] Unlike the study by Chia et al,[46] no such association was seen for depression.

Both dementia and depression showed no significant correlation to presence of motor fluctuations or drug induced dyskinesias. A previous study by Liberman et al,[18] had shown that the non demented group had a greater response to levodopa with motor fluctuations and peak dose dyskinesias. Others have also made similar

observations.[23] No similar associations have been found for depression in idiopathic P.D. patients.

Another finding in the present study was that depression was a significant risk factor for development dof dementia in P.D patients (P<.001) (Table 14). Similar observations have been made by earlier workers.[27,28 & 45] Sergio E et al, found depression to be the single most important risk factor for dementia[43] as in our study. However others have found no association between the two.[23]

Conclusion

Ours is probably the first Indian study which has prospectively assessed the frequency of dementia and depression in idiopathic P.D. cases.

The frequency of dementia and depression in the present study showed a relatively higher incidence compared to some of the western studies. The occurrence of dementia and depression represent major management problems. Since both levodopa and anticholinergics can contribute to cognitive impairment, medical management of such cases becomes dificult and needs to be tackled seperately.

A high proportion of our patients with idiopathic P.D had depression. This underlies the importance of identifying the presence of depression early on so that it can be treated, thus improving the `Quality Of Life' (QOL) of these patients.

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A PROSPECTIVE STUDY OF DEMENTIA AND DEPRESSION IN IDIOPATHIC P.D. CASES SEEN AT S.C.T.I.M.S.T

Principal investigator : **Sudeep Balakrishnan**

Co-investigator : **Asha Kishore**

Name :

Address :

Occupation :

Column	Code	Item
	_____	SCTIMST Number
	_____	Study number
	_____	Age
	_____	Gender
	_____	Exact age at onset
	_____	Duration of disease
	_____	Duration of levodopa treatment

Predominant symptom and sign (1= Yes, 2= No)

	_____	Tremor dominant
	_____	Rigidity and bradykinesia
	_____	Postural instability
	_____	Mixed pattern

Cognitive/Neuropsychiatric symptoms (1= Yes, 2= No)

_____ Anxiety

_____ Bradyphrenia

_____ Depression

_____ Dementia

Educational status (1= yes, 2= No)

_____ Primary school

_____ High school

_____ College

UPDRS motor score (on/off) _____

Disease severity and staging (Modified Hoehn and Yahr staging) (1=Yes, 2= No)

_____ Stage 0

_____ Stage 1

_____ Stage 1.5

_____ Stage 2

_____ Stage 2.5

_____ Stage 3

Drug therapy - past (1= Yes, 2=No)

_____ Levodopa

_____ Anticholinergics

_____ Dopaminergic agonists

_____ Selegeline

_____ Others

Drug therapy at the time of study (1= Yes, 2= No)

_____ Levodopa

_____ Anticholinergics

_____ Dopaminergic agonists

_____ Selegeline

_____ Others

Response to Levodopa (1= Yes, 2= No)

_____ Stable

_____ Fluctuator

_____ Dyskinesias

_____ Wearing off

_____ On - off phenomena

Severity of depression (rated on Hamilton's scale) (1= Yes, 2= No)

_____ Absent

_____ Mild

_____ Moderate

_____ Severe

_____ Very severe

Dementia (rated on MIMSE) (1= Yes, 2= No)

_____ Present

_____ Absent

Grade of dementia (DSM IV) (1=Yes, 2= No)

_____ Absent

_____ Mild to moderate

_____ Severe

Neuropscychological tests

Frontal lobe functions (1- Normal, 2= Impaired)

_____ Verbal fluency

_____ Category test

_____ Attention

_____ Digit symbol subset

_____ Serial subtraction

_____ Bender Gestalt

_____ Visual scanning

_____ Ideation fluency

_____ Delayed response

Temporal lobe functions (1= Normal, 2= Impaired)

_____ Visual integration

_____ Object assembly

_____ Sentence repetetion

_____ Immediate memory

_____ Recent memory

_____ LTM

_____ ST visual memory

Parietal lobe functions (1= Normal, 2= Impaired)

_____ Visuospatial impairment

_____ Constructional apraxia

_____ Dressing apraxia

_____ Acalculia

_____ Finger agnosia

_____ R - L disorientation

CT Scan (0 = Not done, 1 = Done, normal; 2 = Done, abnormal)

Site of lesion _____

Nature of abnormality _____

MRI (0 = Not done; 1=Done, normal; 2=done, abnormal)

Site of lesion _____

Nature of lesion _____