NEUROCOGNITIVE AND PSYCHOPHYSIOLOGICAL AND STUDY OF PATIENTS OF PARKINSONISM & PARKINSON'S DISEASE IN CENTRAL INDIA

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ABSTRACT: To evaluate the patients of Parkinson's disease in the Indian tertiary setup it was necessary to weigh the multivaried presentation of PD for the motor disorders as well as neurocognitive and various grades of psychophysiological inadequacies with emphasis on cognitive deficits. Two groups of patients consisting of 41 subjects in each of case and control group were analyzed for the psycho-neurophysiological functions using AIIMS battery (in Hindi) and MMSE scoring system. The case and controls had appreciable difference in MMSE scoring with almost 2.5% of patients having very low score (<10) compared to none in control scoring less than 10.80% of cases presented with disease in upper or lower limbs. Disability scoring on Hoehn & Yahr scoring was stage 2(34%) or stage 3(27%) for most of the patients in the study. 85.4% patients presented with tremors, 13% patients had history of early falls and 63% patients had urinary bladder involvement at the time of presentation. 20% (6/35) of the cases categorized as Idiopathic Parkinson's disease presented with conspicuous gaze abnormality. The different lobes were evaluated categorically for dysfunction in both the hemispheres and an estimate of dysfunction distribution was obtained. Right frontal lobe had the highest psychocognitive score while the right parietoccipital had the least score of all the lobar regions evaluated on AIIMS neuropsychiatric battery scoring. The score differences of cases with controls the RSM-right sensorimotor and LT-left temporal were the maximum. In overall hemispherical comparison, right lobe scored 335.50 as compared to 315.90 of left lobe. All four subdomains of MMSE were subnormal in cases as compared to controls with remarkable impairment of execution functions and memory. The AIIMS test battery was more sensitive for cognitive evaluation in this study with 70% cases of impaired patient had scored normal on MMSE scoring system.

KEYWORDS: Parkinsons, Parkinsonism, Neurocognitive, Psychophysiologocal.

INTRODUCTION: Parkinson's disease (PD) is the second most common neurodegenerative disorder, after Alzheimer's disease.¹ James Parkinson is attributed with rendering the first description of PD in his monograph, The Shaking Palsy (1817). He identified the hallmark features of the illness through cases observed in the streets of London as well as his own patients.² In community-based series, PD accounts for more than 80% of all Parkinsonism, with a prevalence of approximately 360 per 100,000 and an incidence of 18 per 100,000 per year.³ Among the subjects with Parkinsonism visiting the movement disorder clinics, approximately 80-85% have PD, the rest belonging to the categories of atypical Parkinsonism and secondary Parkinsonism.⁴ PD afflicts approximately one million individuals in the United States (~ 1% of those over 55 years).⁵ Another study reported that about 1% of population above the age of 65 years and about 5% above the age of 80 years suffer from PD.⁶ It can, therefore, be calculated that in India alone with an estimated population of over one billion by the turn of the century, approximately 700 million people will be above the age of 65 years, of which about 7 million will suffer from PD.⁶ The Parkinson's disease (PD) is stereotypically branded with motor abnormalities attributed commonly to neurodegenerative infliction of nigro-striatal pathways.⁷ But PD

appears to be a multifocal or even global neurodegenerative involvement leading to myriads of psychophysiological^{8,9,10} and neuro-cognitive¹¹⁻¹³ presentation revealed as subtle to major loss of executive functions, deterioration of various higher reflexes, learning and adaptations in general and with regards to sensory perception. The Parkinson's disease may also present with hallucinations, anxiety, psychosis,¹⁴ autonomic disturbance,¹⁵ sleep disturbance,¹⁶ attention deficits, low conceptualization scoring and all spectrum of memory loss.^{8,17-20} The deficits might also be in immediate recall of verbal material, language production and semantic fluency, set-formation, cognitive sequencing and working memory and visuomotor construction.²¹⁻²⁴ However the immediate memory span,²⁵ long-term forgetting,²⁶ naming, comprehension and visual perception etc. may be intact.¹¹⁻¹² Language deficits²⁷ and more severe frontal lobe impairments was observed in patients with abnormal MMSE score.

The present study aimed at the neurocognitive profiling of patients with Parkinsonism with forty one (41) patients and the age and sex matched controls that fulfilled the chosen inclusion criteria were enrolled in this study from the Neurology outdoor patient department.

In this study a small sample of patients with PD were assessed with instruments that evaluate relevant aspects of cognitive impairment in PD without being sensitive to motor symptoms. In comparison with the controls, all four cognitive sub domains were impaired in our study patients. In this study 80% (33 out of 41) of patients with impaired cognition had disease duration of less than 5years. Our results show that poorer cognitive performance is associated with more severe impairments in other domains of PD. In line with finding of others, we found that patients with tremor predominance showed higher cognitive scores. Thus our study revealed significant impairment of lobar functions in patients with PD with predominantly right hemispheric dysfunction in patient's at stage 2 and above.

The complaints of patients with Parkinsonism were not limited to the motor system. Various grades of Dementia might be observed in a various cases of Parkinsonian syndrome. Cognitive changes in the majority of patient with PD could be subtle and may restrict to attention and retrieval deficits. It is only by using appropriate neuropsychological evaluation tests that these cognitive changes could be detected. The tests mainly concerned with: (a) executive function, (b) memory (c) visuospatial domain. Depression and anxiety was encountered in about 30% of patients and apathy is not infrequent in PD and has repercussion on cognitive function, affect, and behavior. Drug-induced psychiatric disorders frequently found in PD mainly consist of hallucination and delusion. These disorders are however, much more frequent in PDD or DLBD. Cognitive changes are mild in the Parkinsonian variant of MSA, Psychiatric disorder have been poorly studied in MSA-P. In PSP cognitive and behavioral changes are consistent even in the early stages of the disease. Dynamic apraxia may be observed. Bilateral apraxic errors for transitive and intransitive movements have been reported, but they are much less severe than in Corticobasal degeneration.

MATERIALS AND METHODS:

The following diagnostic inventories were utilized in this study for patient inclusion:

- 1. British Brain Bank Clinical Criteria (Hughes et al.).
- 2. Unified Parkinson's disease Rating Scale (Christopher G., et al).
- 3. Diagnostic Criteria for PSP As Proposed by Golbe et al.
- 4. Multiple System Atrophy Consensus Criteria (Gilman, Low, et al).
- 5. Proposed Research Criteria for the Diagnosis of the Clinical Syndrome.
- 6. Consensus Diagnostic Criteria for Dementia with Lewy Bodies (McKeith, Dickson et al).

- 7. Mini-Mental State Examination.
- 8. The AIIMS Comprehensive Neuropsychological Battery Developed By Gupta (1992).

PROCEDURE: The study was carried out in two groups. The first group of subjects with a probable diagnosis of Parkinsonian syndrome underwent thorough clinical examination by administering various scale and a detailed neuropsychological testing with help of MMSE and AIIMS Neuropsychological Battery. The neuropsychological battery and the MMSE was utilized also on control group to assess the control cognitive functioning. All the scales were applied to the subjects at the time of admittance to the Out Patient Department or IPD of Department

The present study will exploit the empirical investigation of localization of deficits with AIIMS Comprehensive Neuropsychological Battery in Hindi (Adult Form) using the eight lobar scales for both the right and left hemispheres used in each patient. The patients should have studied at least up to class V which is the requirement for applying the AIIMS Comprehensive Neuropsychological Battery.

The standard procedure consisted of the 160 item AIIMS Comprehensive Neuropsychological Battery defining the following eight lobar scales – Left Frontal (LF; 42 items); Left Sensory-Motor (LSM; 14 items); Left Parietal-Occipital (LPO; 17 items); Left Temporal (LT; 24 items); Right Frontal (RF; 21 items); Right Sensory-motor (RSM; 16 items); Right Parieto–Occipital (RPO; 12 items); and Right Temporal (RT; 15 items) administered to a sample size of 41 patients. The AIIMS Battery was also administered to an equal sample of 41 normal subjects.

Eight scales of items for localizing brain damage were derived by computing multiple T-test comparing the performance of each brain damage group with normal group on each 160 items of AIIMS comprehensive neuropsychological Battery. Items which significantly discriminated only one brain damaged group from the normal group were assigned to that group's scale. Then items which significantly discriminated only two groups from the normal were assigned to those two groups' scale. Items number 62 and 143 were such which were retained in three scales: (1) items 62 in the right frontal, right parieto-occipital and right temporal scale and (2) item 143 in the left parieto-occipital, left temporal and right parieto-occipital scales. This could be done because these two items discriminated the three groups from normal beyond. 001 level. Otherwise in case of all the remaining 158 items, no two scales had more than two items in common. The items retained finally provide high discrimination of each brain damaged group from the normal.

The raw scores for individual subjects in the brain damaged groups with localized brain lesion and the normal group were determined. Means and standard deviation of the raw scores for each of these groups were computed on each scale.

In the next step, T-scores were computed based upon the means and standard deviations of the normal group on each scale.

The results were compared with age & gender matched control subjects. Data has been presented here in the form of mean and standard deviation of T score values of different variables. Student t test has been used to find out the significant difference in the mean levels of various lobar scales in cases with control group mean level.

OBSERVATION AND RESULTS: On the basis of distribution at diagnosis IPD (85.4%) comprised the majority of cases followed by PSP (12.2%) and CBGD (2.4%).

Most of the cases (81%) presented within 2-5 years of the disease onset. Majority (80%) of disease presentation was with an abnormality in right or left upper limbs. On Hoehn & Yahr disability

scoring most of the patients presented in stage 2 (34%) or 3(27%). As many as 85.4% cases presented with tremors while the rest presented with rigidity. Nearly 13% patients had presented with history of early falls and all of them were of PSP type, as much as 63% cases presented with urinary bladder involvement. 20% (6\35) of IPD presented with gaze abnormality.

Significant difference in MMSE scores was obtained in two test groups with more deteriorated score in older age groups (>50 years) all the control had score more than 10.

The mean Mini Mental Status Examination (MMSE) score in the patient's group came out to be 21.70 ± 2.87 and in the control group it was 26.46 ± 1.07 .

Neuropsychological testing revealed that the mean T scores of the lobar scales (both right and left hemispheres) in patient group (LF–77.33; LSM–76.57; LPO–79.26; LT-82.74; RF–95.14; RSM–92.05; RPO–73.86; RT-74.45) are remarkably significant as compared to the controls (p<0.0005).

Symmetry of Lobe Dysfunction: Of the dysfunctions of all lobes examined involvement of the right hemispheric and in that mainly right frontal region was observed distinctly significant in patients with disease stages of 2 and above (mean score of right hemisphere was 335.50 being more than mean score of left hemisphere which has been 315.90). The mean score of right frontal lobe was also found greater than the mean score of other individual lobes.

DISCUSSION: Parkinsonism patients conspicuously present with motor dysfunctions as is already commonly known but it may also present with various grades of neurocognitive features which could be accurately discerned at an early stage by using sensitive tests early in disease course. The patients of PD can present with hallucination, depression, anxiety, sleep disturbance etc. And a significant fraction of PD patients develop dementia in all the spectrum of presentation. Earlier estimates of the prevalence of dementia in PD have been highly varied ranging from 20%²⁶ to 80%.²⁷ The Dementia in PD is primarily of the subcortical type.²⁸

In this study a small sample of patients with PD were assessed with instruments that evaluate relevant aspects of cognitive impairment in PD without being sensitive to motor symptoms.

The finding of this study, however, should be reviewed against the following background. Firstly this is a clinical based study with a selection preoccupation of onset and disease duration. Therefore, the results in this study cannot be generalized to the PD population at large.

The percentage of patients with impaired cognitive functions in this study cannot be interpreted as a prevalence estimate, which limits the possibility to compare our findings with prevalence rates of other studies.

In many studies on cognitive functioning in PD, the MMSE score is applied as a gross measure of cognitive impairment.²⁹ The MMSE includes items from domains which generally are less severely affected in PD (Temporal orientation and language)³⁰ whereas the AIIMS comprehensive neuropsychological battery in Hindi focuses on domains which are frequently affected in PD. Therefore, the AIIMS comprehensive neuropsychological battery is expected to be more sensitive to cognitive deficits of PD. This is demonstrated by fact that in our study >70% of patients with abnormal AIIMS comprehensive neuropsychological battery scores had normal MMSE scores.

In this composition, both scores were corrected for age and years of education, indicating that the MMSE may substantially underestimate the degree of cognitive impairment in PD. In comparison with the controls, all four cognitive sub domains were impaired in our study patients.

In accordance with³⁰ executive functioning was most prominently affected, followed by memory. In our study both patients and control had relatively low scores on memory sub domain, indicating that items of this sub domain are more difficult to execute compared with other studies, more advanced disease (Higher Hoehn & Yahr stage, higher battery score) was associated with poor cognitive performance^{19,31} indicating an additional influence of the disease process on cognitive performance.

In this study 80% (33 out of 41) of patients with impaired cognition had disease duration of less than 5 years. Generally it is assumed that cognitive impairment may develop early in the disease process³² but clinical symptoms of dementia as detailed in the DSM-IV criteria appear only late in the disease course.³³

Our results show that poorer cognitive performance is associated with more severe impairments in other domains of PD. In line with finding of others, we found that patients with tremor predominance showed higher cognitive scores. Thus our study revealed significant impairment of lobar functions in patients with PD with predominantly right hemispheric dysfunction in patient's stage 2 and above.

Although the study population is small in number a larger population study is required to predict and support the pattern of cognitive function.

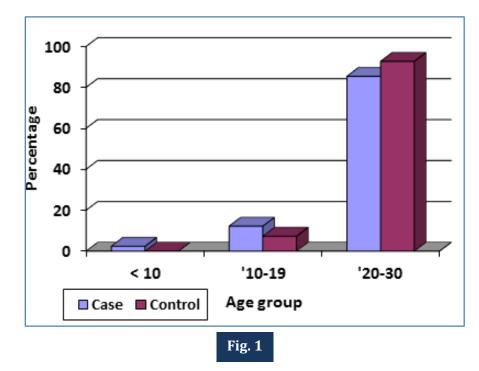
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MMSE score	Case	(n=41)	Control(n=41)		
	No.	%	No.	%	
< 10	1	2.4	0	0.0	
10-19	5	12.2	3	7.3	
20-30	35	85.4	38	92.7	
Total	41	100.0	41	100.0	
Table 1					

Distribution of cases and control according to MMSE score:



T-score comparison among case and control according to AIIMS Neuropsychiatric battery (Hindi).

Lobar distribution	Category	N	Mean	Std. Deviation	t-value p-value
LF	Case	41	77.33	16.12	t-value-13.558
	Control	41	43.22	2.954	p-value-0.0005
LSM	Case	41	76.57	20.79	t-value-7.765
	Control	41	50.73	6.907	p-value-0.0005
LPO	Case	41	79.26	22.87	t-value-11.158
	Control	41	40.61	3.499	p-value-0.0005
LT	Case	41	82.74	23.58	t-value-11.747
	Control	41	41.41	2.757	p-value-0.0005
RF	Case	41	95.14	21.27	t-value-12.903
	Control	41	48.61	8.826	p-value-0.0005
RSM	Case	41	92.05	22.70	t-value-10.156

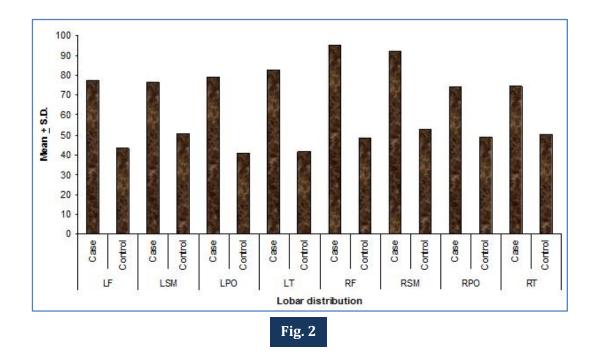
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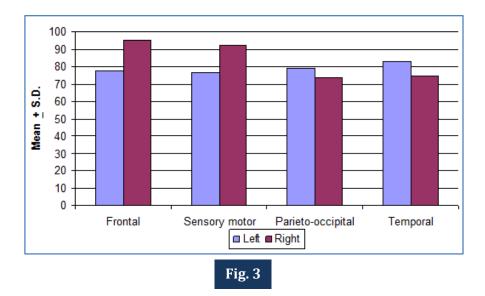
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	Control	41	52.80	9.837	p-value-0.0005
RPO	Case	41	73.86	19.46	t-value-7.856
	Control	41	48.78	7.977	p-value-0.0005
RT	Case	41	74.45	12.23	t-value-10.654
	Control	41	50.22	7.715	p-value-0.0005
Table 2					



Neuropsychological testing revealed that the mean T scores of the lobar scales (both right and left hemispheres) in patient group (LF–77.33; LSM–76.57; LPO–79.26; LT-82.74; RF–95.14; RSM–92.05; RPO–73.86; RT-74.45) are remarkably significant as compared to the controls (p<0.0005).

Lobe	Left	Right	t-value	p-value		
	Mean±S.D.	Mean±S.D.	t-value			
Frontal	77.33±16.12	95.14±21.27	9.12	0.000		
Sensory motor	76.57±20.79	92.05±22.70	7.58	0.000		
Parieto-occipital	79.26±22.87	73.86±19.46	2.33	0.025		
Temporal	82.74±23.58	74.45±12.23	3.36	0.002		
Total	315.90±78.66	335.50±68.91	3.84	0.000		
Table 3						



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