



## Clinical & Neuropsychological profile in patients with Parkinson's disease and Parkinson's Plus syndromes: study from a tertiary care referral centre in a developing country

Abu Zafar Ansari,<sup>1</sup> Deepika Joshi,<sup>1\*</sup> Vijay Nath Mishra,<sup>1</sup> Rameshwar Nath Chaurasia,<sup>1</sup> Shailesh Gupta,<sup>2</sup> Baidanath Kumar,<sup>1</sup> Vijay Nandmer,<sup>1</sup> Arun Kumar,<sup>1</sup>

<sup>1</sup>Dept. of Neurology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, UP, India

<sup>2</sup>Dept. of Cl. Neurophysiology, Department of Physiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, UP, India

### ABSTRACT

**Background:** Cognitive dysfunction is an important cause of disability in Parkinson's disease (PD) and Parkinson's Plus syndrome (PD Plus). The development of dementia in PD has significant impact on the natural history of disease with rapid progression of disability and increased mortality. The present study aimed to evaluate the clinical and neuropsychological profile in patients with PD and PD Plus syndromes.

**Methods:** Forty-one patients with a diagnosis of probable PD, and Parkinson's Plus syndromes with minimum of fifth standard education were enrolled. They were evaluated with the UPDRS, Hoehn & Yahr staging, MMSE and AIIMS comprehensive neuropsychological battery in Hindi (adult form) using the eight lobar scales for the right and left hemisphere. Patients were then compared with age and gender matched controls.

**Results:** Parkinson's disease (85.4%) comprised

the majority of cases followed by PSP (12.2%) and CBGD (2.4%). The MMSE scores were significantly reduced in the patients as compared to controls. 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) were higher & remarkably significant as compared to the controls ( $p < 0.0005$ ) particularly stage II and above.

**Conclusion:** Our study revealed neuropsychological dysfunction involving right hemisphere more than the left. The AIIMS test battery was more sensitive for cognitive evaluation in this study, as about 70% patients who had impaired cognitive function with this battery had scored normal on MMSE.

### INTRODUCTION

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease.<sup>1</sup> Among the subjects with Parkinsonism visiting the movement disorder clinics, approximately 80-85% have PD, the rest belong to

\* Correspondence to: Dr Deepika Joshi, Professor, Department of neurology, Institute of medical sciences, Banaras hindu university, Varanasi, India. Email: drdeepikajoshi73@gmail.com.

the categories of atypical Parkinsonism and secondary Parkinsonism.<sup>2</sup> In addition to the typical motor symptoms the nonmotor dysfunctions in PD may antedate the motor dysfunction and are a major determinant of the quality of life and disease progression.<sup>3</sup> Subtle cognitive deficits, predominantly frontal lobe executive dysfunction present in patients with early PD can be detected with sensitive neuropsychological testing.<sup>4</sup>

The present study aimed to evaluate the clinical and neuropsychological profile in patients presenting with Parkinsonism at a tertiary care referral centre in India.

## METHODS

Patients presenting with features of Parkinsonism attending the neurology outpatient department and or admitted to the neurology ward from August 2009 to July 2011 were included. All patients with minimum of fifth standard education who gave a written informed consent were enrolled in the study.

The following diagnostic criteria were utilized in this study for patient inclusion: UK Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria; Unified Parkinson's disease Rating Scale;<sup>6</sup> Diagnostic Criteria for PSP as proposed by Golbe et al;<sup>7</sup> Multiple System Atrophy Consensus Criteria;<sup>8</sup> Mini-Mental State Examination;<sup>9</sup> The AIIMS Comprehensive Neuropsychological Battery.<sup>10</sup>

The study was carried out in two groups. The first group was comprised of patients with a diagnosis of probable Parkinsonism. Patients were evaluated clinically and were then scored by UPDRS and Hoehn and Yahr staging. Subsequently cognitive functions were assessed using MMSE and the AIIMS comprehensive neuropsychological battery in Hindi (adult form). The second group was the age and gender matched controls evaluated with MMSE and the AIIMS comprehensive neuropsychological battery.

The eight lobar scales for both the right and left hemispheres of the AIIMS battery were used in each patient. The patients were required to have studied at least upto 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. Each item was rated on a 5 point score with 0 being given for all correct answers and 4 for all incorrect responses. Ratings of 1, 2 and 3 suggest intermediate performance. A raw score was generated for all items of the lobar scales. Raw scores were converted to T scores, which were developed using means and SD of the scores yielded by a group of normal controls (N=175). Variables like age and education can alter performance in this battery, hence both these variables were considered. An expected T-score using regression analysis was evolved using a population of 175 normal controls. If the T score was more than the expected T score the performance was considered abnormal.

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.

## 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%). Majority of the cases (81%) presented within 2-5 years of the disease onset and had an upper limb onset (80%). 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, and 63% cases presented with urinary bladder involvement. Significant difference

**Table 1.** Distribution of cases and controls by MMSE score.

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

MMSE, Mini-Mental State Examination.

**Table 2.** 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:13.558, p: 0.0005
	Control	41	43.22	2.954	
LSM	Case	41	76.57	20.79	t: 7.765, p: 0.0005
	Control	41	50.73	6.907	
LPO	Case	41	79.26	22.87	t: 11.158, p: 0.0005
	Control	41	40.61	3.499	
LT	Case	41	82.74	23.58	t: 11.747, p: 0.0005
	Control	41	41.41	2.757	
RF	Case	41	95.14	21.27	t: 12.903, p: 0.0005
	Control	41	48.61	8.826	
RSM	Case	41	92.05	22.70	t: 10.156, p: 0.0005
	Control	41	52.80	9.837	
RPO	Case	41	73.86	19.46	t: 7.856, p: 0.0005
	Control	41	48.78	7.977	
RT	Case	41	74.45	12.23	t: 10.654, p: 0.0005
	Control	41	50.22	7.715	

in MMSE scores was obtained in two test groups with more deteriorated score in older age groups (>50 years). None of the controls had score below 10. The mean Mini Mental Status Examination (MMSE) score in the patient's group was  $21.70 \pm 2.87$  and in the control group  $26.46 \pm 1.07$  (Table 1).

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 ( $p < 0.0005$ , Table 2).

### Symmetry of lobe dysfunction

In examining the dysfunction of the lobes; involvement of the right hemispheric, mainly right frontal region was observed to be 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 (Table 3)

## DISCUSSION

Parkinsonism patients conspicuously presenting with motor dysfunctions 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 hallucinations, 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%<sup>11</sup> to 80%.<sup>12</sup> The Dementia in PD is primarily of the subcortical type.<sup>13</sup>

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 many studies on cognitive functioning in PD, the MMSE score is applied as a gross measure of cognitive impairment.<sup>14</sup> MMSE evaluates mainly orientation and language<sup>15</sup> and therefore can be normal in patients with right hemisphere and frontal

**Table 3.** Symmetry of lobe dysfunction.

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

lobe damage. Also an appropriate localization and lateralization cannot be done with MMSE. Thus it is a useful screening tool for cognitive impairment with sensitivity of 70% and specificity of 60%<sup>16</sup> but is not a diagnostic test for dementia. In patients with PD frontal lobe dysfunction as the predominant abnormality AIIMS battery had a better diagnostic utility, as it allowed for the comprehensive evaluation of all lobar functions.

Therefore, the AIIMS comprehensive neuropsychological battery appears to be more sensitive to detect 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 with other studies<sup>15</sup> executive functioning was most prominently affected, followed by memory. Patients with more advanced disease (higher Hoehn & Yahr stage, higher battery score) was associated with poor cognitive performance indicating an additional influence of the disease process on cognitive performance.<sup>17 18</sup>

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 process<sup>19</sup> but clinical symptoms of dementia as detailed in the DSM-IV criteria appear only late in the disease course.<sup>20</sup>

Our results show that poorer cognitive performance is associated with more severe impairments in other domains of PD. In line with findings 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.

## REFERENCES

- Przedborski S. Etiology and pathogenesis of Parkinson's disease. In: Jankovic J, Tolosa E, eds. *Parkinson's Disease and Movement Disorders* 5th ed. Philadelphia: Lippincott Williams and Wilkins; 2007;77-92.
- Mitra K, Gangopadhyaya PK, Das SK. Parkinsonism plus syndromes - A review. *Neurology India* 2003; 5:183-8.
- Santamaria J, Tolosa E, Valles A: PD with depression : a possible subgroup of idiopathic Parkinsonism. *Neurology* 1986;36:1130-1133.
- Hely MA, Moorris JG, Reid WG et al : Sydney multicentre disease of PD: non dopa-responsive problems dominate dominate at least 15 years. *Mov disorders* 2005; 20: 190-1995)
- Hughes et al. UK Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria. Hughes AJ et al. *J Neurol Neurosurg Psychiatry* 1992;55:181-4.
- Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Process, format, and clinimetric testing plan: Christopher G. Goetz<sup>1,\*</sup>, Stanley Fahn<sup>2</sup>, Pablo Martinez-Martin<sup>3</sup>, *Movement Disorders* Volume 22, Issue 1, pages 41–47, January 2007
- Golbe LI, Davis PH, Schoenberg BS et al: Prevalence and natural history of progressive supranuclear palsy. *Neurology* 1988;38:1031-1034.
- Consensus statement on the diagnosis of multiple system atrophy. S Gilman, PA Low, N Quinn, A Albanese, Y Ben-Shlomo, CJ Fowler, H Kaufmann, T Klockgether, AE Lang, PL Lantos, I Litvan, CJ Mathias, E Oliver, I Schatz, GK Wenning *J Autonomic Nervous System* 74 (1998) 189-192
- Folstein MF, Folstein SE, McHugh PR . ""Mini-mental state". A practical method for grading the cognitive state of patients for the clinician". *Journal of psychiatric research* 1975;12 (3): 189–98.
- Gupta S, Khandelwal PN, Tandon PN. The development and standardization of a comprehensive neuropsychological battery in Hindi (adult form). *J of Personality and Clinical Studies* 2000; 16: 75-109.
- Pollock M, Hornabrook RW. The prevalence, natural history and dementia of Parkinson's disease. *Brain*. 1966;89(3):429-448.
- Boller F. Mental status of patients with Parkinson's disease. *J Clin Neurophysiol*. 1980;2:157-172.
- Albert ML, Feldman RG, Willis AL. The subcortical dementia of progressive supranuclear palsy. *J Neurol Neurosurg Psychiatry* 1974;37:121-30.
- Aarsland D, Zaccari J, Brayne C. A systematic review of prevalence of studies in dementia in Parkinson's disease. *Mov Disord* 2005; 20: 1255-63.
- Emre M. Dementia associated with Parkinson's disease. *Lancet Neurol* 2003; 2: 229-37.
- Tombaugh TN, McIntyre NJ. The Mini Mental State Examination: A comprehensive review. *J Am Geriatr Soc* 1992; 40: 922-35.
- Aarsland D, Anderson K, Larsen JP, et al. The rate of cognitive decline in Parkinson's disease. *Arch Neurology* 2004; 61:1906-11
- Anderson KE. Dementia in Parkinson's disease. *Curr Treat Option Neurol* 2004; 6: 201-7.
- Muslimovic D, Past B, Speelman JD, et al. Cognitive profile of patients with new diagnosed Parkinson disease. *Neurology* 2005; 65: 1239-45.
- Fuchs GA, Gemenda I, Herting B, et al. Dementia in idiopathic Parkinson's syndrome. *J Neurol* 2004; 251(Suppl 6): VI: 28.