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Somatosensory Evoked Blink Reflex in Patients with Parkinson's and Parkinson's Plus Disease

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Abstract

Introduction: Patients with degenerative neurological diseases involving the basal ganglia may present with functional abnormalities of brainstem reflexes, resulting from disturbed activity of loops between the thalamus and the investigated circuits. The Somatosensory Evoked Blink Reflex is a release phenomenon transmitted *via* the brainstem reticular formation. This response may be clinically relevant in disorders associated with brainstem lesions.

Materials and methods: Totally 54 subjects were included. We performed somatosensory evoked blink response in these patients.

Inclusion criteria:

- Age between 18-80 years.
- PD patients diagnosed according to the MDS criteria.
- Parkinson plus syndrome (DLB, PSP, MSA) patients.

Exclusion criteria:

- Patients with associated peripheral neuropathy.

Results: We observed that the presence of somatosensory evoked blink reflex was more common in IPD patients and dyskinesia, postural instability, dysarthria, dysphagia and bowel/bladder abnormality showed positive correlation with SSEBR.

Conclusion: In Parkinson's disease patients the presence of SSEBR was associated with increased probability of dyskinesia, postural instability, dysarthria, dysphagia and bowel/bladder abnormality.

Keywords: Blink reflex • Parkinson's plus disease • Neurological diseases • Dyskinesia

Introduction

Parkinsonian syndromes are progressive debilitating neurodegenerative diseases that affects dopaminergic and other neurotransmission, resulting predominantly in bradykinesia, rest tremor and rigidity [1]. These disorders have a prevalence of 1 to 2% above the age of 60 years and typically develops between the ages of 55 and 65 years. In initial period these disorders have a similar clinical picture and have response to dopaminergic treatment and in these stages it will be difficult to differentiate the sub type based on clinical symptoms alone. However, as the disease becomes more advanced the other clinical symptoms will become more apparent and will be helpful in differentiating the different Parkinsonian syndromes.

The clinical symptomatology, response to dopaminergic therapy and natural course of the disease are the features which help in identifying the sub type of the Parkinson's disease with help from

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imaging which includes Magnetic Resonance Imaging (MRI), Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET) which allow brain imaging of structural, functional and molecular changes in vivo in patients with PD. Structural MRI is useful to differentiate PD from secondary and atypical forms of Parkinsonism. 123I-ioflupane (DaTSCAN (TM)) SPECT is a valid tool in the differential diagnosis between PD and essential tremors, while cardiac 123I-metaiodobenzylguanidine SPECT and 18F-fluorodeoxyglucose PET are valid in the differential diagnosis between PD and atypical Parkinsonism (MSA-P, PSP). But the availability of these modalities are limited and are expensive. Ultrasound imaging has been tried in visualizing the basal ganglia structures.

In this study we would like to evaluate the clinical picture, electrophysiological findings (somato sensory evoked blink reflex) in patients of Idiopathic Parkinson's disease, progressive supranuclear palsy, multiple system atrophy and DLBD and assess the findings in these disorders.

Materials and Methods

The study was conducted in the department of neurology, Nizam's Institute of Medical Sciences, Hyderabad. It is a prospective single center cross sectional study of patients attending department of neurology in OPD and IP basis and diagnosed as Parkinson's disease from December 2021 to March 2023. In the present study various clinical aspects such as demographics, clinical presentations are analyzed. Data is analyzed from the data collection forms [2].

53 subjects (32 males and 21 females) with an age range of 38 to 80 years (mean age of 57.2 years) were included in the study.

All the patients with IPD, PSP, MSA, DLB meeting the diagnostic criteria (MDS for IPD, PSP and MSA and consensus criteria for DLB) and attending the OPD/IPD at department of neurology at NIMS and given consent to be included in the study and undergoing the SSEBR procedure.

Patient not willing to participate in the study and Parkinson's disease patient not meeting the diagnostic criteria for IPD or PSP or DLB or MSA and patient having peripheral neuropathy ascertained with NMSS questionnaire were excluded, however routine NCS was not done in all patients to exclude neuropathy.

The study protocol was subjected to clearance and approval from the Institutional Ethics Committee (IEC) was obtained.

SSEBR was obtained on Nicolet EDX synergy machine. For SSEBR stimulation of median nerve was done and presence of R^2 component of blink reflex was assessed on Ipsilateral side.

The data on categorical variables is shown as n (% of cases) and the data on continuous variables is presented as mean and Standard Deviation (SD) for normally distributed variables and using median and minimum-maximum for non-normally distributed variables. The inter-group statistical comparison of distribution of categorical variables is tested using *Chi-square* test or Fisher's exact probability test if more than 20% cells have expected frequency less than 5. The inter-group statistical comparison of medians of non-normally distributed continuous variables is done using Mann-Whitney U test. The underlying normality assumption was tested before subjecting the study variables to Mann-Whitney U test. All results are shown in tabular as well as graphical format to visualize the statistically significant difference more clearly.

In the entire study, the p-values less than 0.05 are considered to be statistically significant. The entire data is statistically analyzed using Statistical Package for Social Sciences (SPSS ver 24.0, IBM Corporation, USA) for MS Windows [3].

Results

Patient characteristics

In our study a total of 53 subjects were included. Detailed clinical history and demographic data of these patients were collected. Our study group of 53 patients was divided into 4 groups: 39 with Idiopathic Parkinson's disease, 7 with PSP, 6 with MSA, 1 with DLB

All the patients had a detailed clinical evaluation done and 53 subjects (39 IPD, 7 PSP, 6 MSA, 1 DLB) had undergone brain stem electrophysiological evaluation including Somatosensory Evoked Blink Reflex in the morning after stopping the medications for 24 hrs.

All patient's cognitive assessment was done. ACE 3 scores, NMSS and PDQ 39 scores were assessed. The data collected were filled in data charts and collected and the investigation findings were collected from all these patients [4,5].

A total of 53 patients that satisfied inclusion criteria were included in the study. The mean ± SD of age of cases studied was 57.40 ± 10.29 years and the minimum-maximum age range was 38-80 years. Out 53 cases, 32 (60.4%) were males and 21 (39.6%) were females.

The following section shows the detailed statistical analysis along interpretation and the graphical representation of the available data (Table 1).

Table 1. Age distribution of cases studied.

Age group (years)	No. of cases	% of cases
<40	1	1.9

41-50	16	30.2
51-60	19	35.8
61-70	10	18.9
71-80	7	13.2
Total	53	100

Age distribution of cases studied

Out of 53 cases studied, 1 case (1.9%) had age below 40 years, 16 cases (30.2%) had age between 41-50 years, 19 cases (35.8%) had age between 51-60 years, 10 cases (18.9%) had age between 61-70 years and 7 cases (13.2%) had age between 71-80 years in the study group.

The mean ± SD of age of cases studied was 57.40 ± 10.29 and the minimum maximum age range was 38-80 years (Figure 1 and Table 2) [6,7].

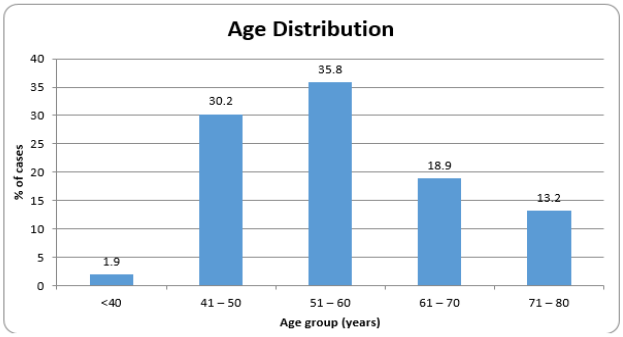

Figure 1. Age distribution of cases studied.

Table 2. Sex distribution of cases studied.

Sex	No. of cases	% of cases
Male	32	60.4
Female	21	39.6
Total	53	100

Sex distribution of cases studied

Out of 53 cases studied, 32 cases (60.4%) were males and 21 cases (39.6%) were females. The male to female sex ratio was 1.52: 1.00 (Figure 2 and Table 3).

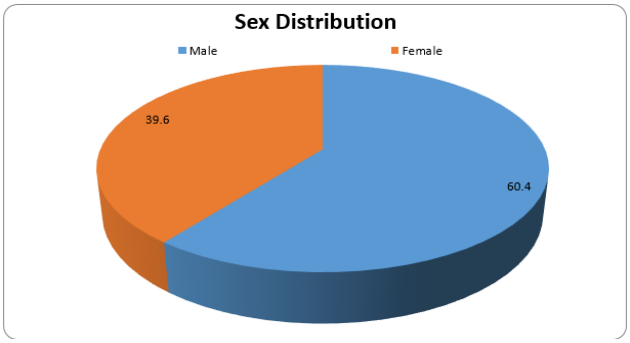

Figure 2. Sex distribution of cases studied.

Table 3. Distribution of duration of disease among the cases studied.

Duration (years)	No. of cases	% of cases
1-4 years	41	77.4
5-8 years	12	22.6
Total	53	100

Table 3. Distribution of duration of disease among the cases studied.

Duration (years)	No. of cases	% of cases
1-4 years	41	77.4
5-8 years	12	22.6
Total	53	100

Distribution of duration of disease among the cases studied

Out of 53 cases studied, 41 cases (77.4%) had duration of disease between 1-4 years and 12 cases (22.6%) had duration between 5-8 years in the study group (Figure 3 and Table 4) [7].

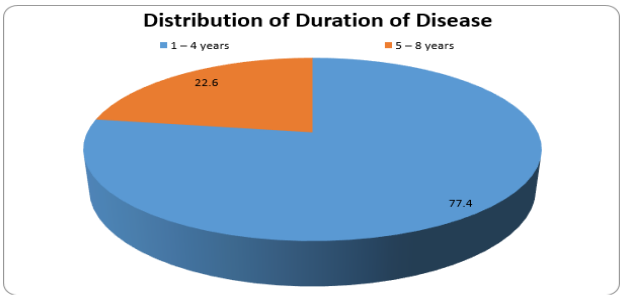

Figure 3. Distribution of duration of disease among the cases studied.

Figure 3. Distribution of duration of disease among the cases studied.

Table 4. Distribution of co-morbidity among the cases studied.

Co-morbidity	No. of cases	% of cases
Nil	28	52.8
Diabetes mellitus	9	17
Hypertension	13	24.5
Diabetes mellitus+hypertension	3	5.7
Total	53	100

Co-morbidity distribution among the cases studied

Out of 53 cases studied, 28 cases (52.8%) had no co-morbidity, 9 cases (17.0%) had diabetes mellitus, 13 cases (24.5%) had hypertension and 3 cases (5.7%) had both diabetes mellitus and hypertension in the study group (Figure 4 and Table 5) [8].

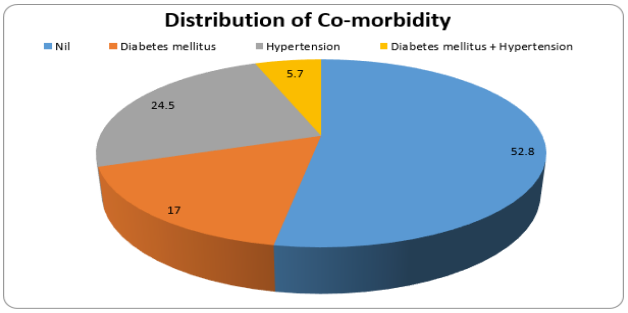

Figure 4. Distribution of co-morbidity among the cases studied

Table 5. Distribution of type of PD among the cases studied.

Type of PD	No. of cases	% of cases
PD	38	71.7
PD plus	15	28.3
Total	53	100

Distribution of type of PD among the cases studied

Out of 53 cases studied, 38 cases (71.7%) had IPD and 15 cases (28.3%) had Parkinson plus disease in the study group (Figure 5 and Table 6).

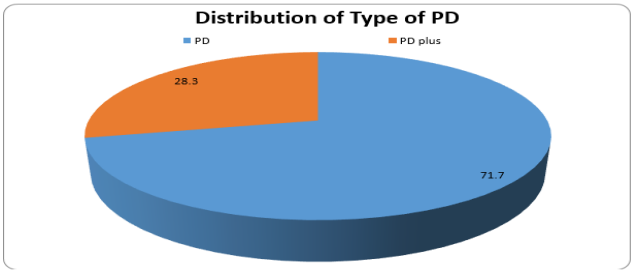

Figure 5. Distribution of type of PD among the cases studied.

Table 6. Distribution of status of Somatosensory Evoked Blink Reflex (SSEBR) among the cases studied.

SSEBR status	No. of cases	% of cases
Absent	37	69.8
Present	16	30.2
Total	53	100

Distribution of status of Somatosensory Evoked Blink Reflex (SSEBR)

Out of 53 cases studied, 37 cases (69.8%) had the absence of SSEBR and 16 cases (30.2%) had the presence of SSEBR in the study group (Figure 6 and Table 7) [9].

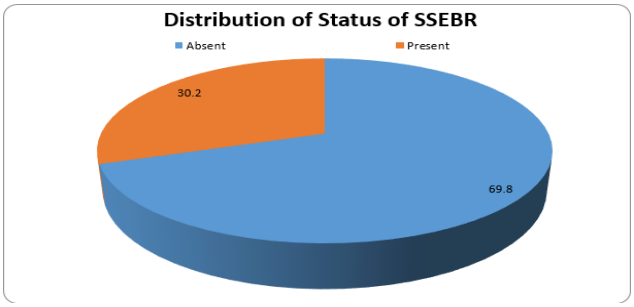

Figure 6. Distribution of status of Somatosensory Evoked Blink Reflex (SSEBR) among the cases studied.

Table 7. Distribution of various symptoms among the cases studied.

Symptoms	No. of cases	% of cases
Tremor	28	52.8
Rigidity	50	94.3
Bradykinesia	50	94.3

Dyskinesia	19	35.8
Postural Instability	27	50.9
Ataxia	5	9.4
Dysarthria	22	41.5
Oculomotor abnormality	18	34
Dysphagia	3	5.7
Recurrent falls	6	11.3
Dystonia	15	28.3
Sleep disturbance	22	41.5
Bowel/Bladder abnormality	25	47.2
Orthostatic hypotension	4	7.5

Distribution of various symptoms among the cases studied

Out of 53 cases studied, 28 cases (52.8%) had tremor, 50 cases (94.3%) had rigidity, 50 cases (94.3%) had bradykinesia, 19 cases (35.8%) had dyskinesia, 27 cases (50.9%) had postural instability, 5 cases (9.4%) had ataxia, 22 cases (41.5%) had dysarthria, 18 cases (34.0%) had oculomotor abnormality, 3 cases (5.7%) had dysphagia, 6 cases (11.3%) had recurrent falls, 15 cases (28.3%) had dystonia, 22 cases (41.5%) had sleep disturbance, 25 cases (47.2%) had bowel/bladder abnormality, 4 cases (7.5%) had orthostatic hypotension in the study group (Figure 7 and Table 8) [10].

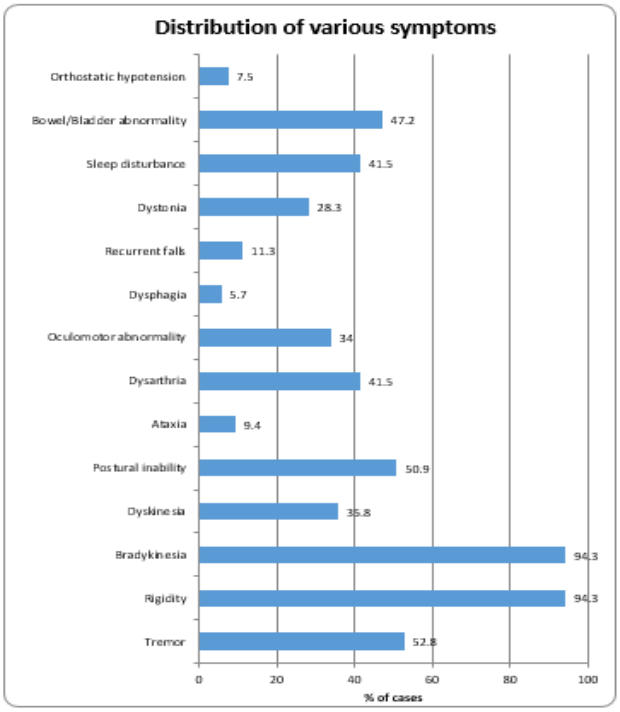

Figure 7. Distribution of various symptoms among the cases studied.

Table 8. Descriptive statistical measures of clinical and cognitive parameters studied.

Parameters	Statistical measure	PD (n=38)	PD Plus (n=15)	Total (n=53)
MOCA	Mean	24.1	20.13	22.98
	Standard deviation	3.25	5.07	4.21
	Median	25	20	25
	Minimum-Maximum	15-28	14-29	14-29
UPDRS (ON)	Mean	20.5	22.8	21.15
	Standard deviation	7.62	10.93	8.64
	Median	19.5	18	18
	Minimum-Maximum	13-40	13-51	13-51
ACE 3	Mean	77.68	65.8	74.32
	Standard deviation	12.31	17.36	14.77
	Median	82	66	80
	Minimum-Maximum	50-94	44-92	44-94
NMSS	Mean	42.18	45.67	43.17
	Standard deviation	37.75	40.89	38.29
	Median	28	33	30
	Minimum-Maximum	8-160	9-160	8-160
Latency (milliSec)	Mean	85.17	81	84.13
	Standard deviation	11.65	8.41	10.82
	Median	88	82	85
	Minimum-Maximum	65-100	70-90	65-100
Amplitude (microVolts)	Mean	95.17	96	95.38
	Standard deviation	11.35	8.48	10.44
	Median	96	95	96
	Minimum-Maximum	75-110	88-106	75-110

Descriptive statistical measures of clinical and cognitive parameters studied

- The median MOCA in group of cases with IPD and group of cases with Parkinson plus disease was 24.10 and 20.13 respectively and in the whole group it was 22.98.
- The median UPDRS (ON) in group of cases with IPD and group of cases with Parkinson plus disease was 19.50 and 18.00 respectively and in the whole group it was 18.00.
- The median ACE 3 score in group of cases with IPD and group of cases with Parkinson plus disease was 82.00 and 66.00 respectively and in the whole group it was 80.00.
- The median NMSS score in group of cases with IPD and group of cases with Parkinson plus disease was 28.00 and 33.00 respectively and in the whole group it was 30.00.
- The median Latency score in group of cases with IPD and group of cases with Parkinson plus disease was 85.17 and 81.00 respectively and in the whole group it was 84.13.
- The median Amplitude score in group of cases with IPD and group of cases with Parkinson plus disease was 95.17 and 96.00 respectively and in the whole group it was 95.38 (Figure 8 and Table 9).

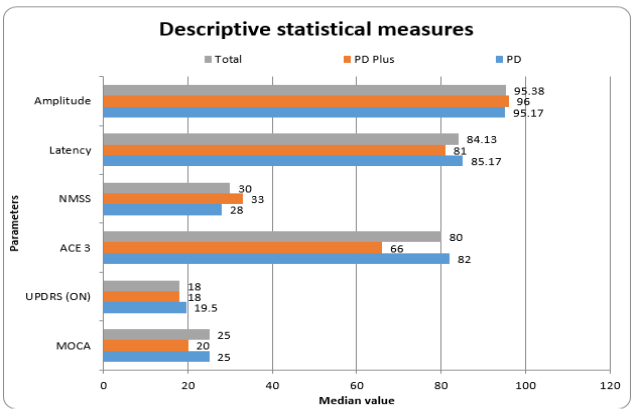

Figure 8. Descriptive statistical measures of clinical and cognitive parameters studied.

Table 9. The status of Somatosensory Evoked Blink Reflex (SSEBR) according to type of PD.

	PD		PD Plus		Total		P-value
SSEBR status	**No. of cases**	**% of cases**	**No. of cases**	**% of cases**	**No. of cases**	**% of cases**	
Absent	26	68.4	11	73.3	37	69.8	0.999^{NS}
Present	12	31.6	4	26.7	16	30.2	
Total	38	100	15	100	53	100	

Note: P-value by *Chi-Square* test; P-value<0.05 is considered to be statistically significant; NS-Statistically non-significant

The status of Somatosensory evoked blink reflex (SSEBR) according to type of PD

Out of 38 cases with IPD, 26 cases (68.4%) had absence of SSEBR and 12 cases (31.6%) had the presence of SSEBR. Out of 15 cases with Parkinson plus disease, 11 cases (73.3%) had absence of SSEBR and 4 cases (26.7%) had the presence of SSEBR [11].

Distribution of prevalence of presence of SSEBR did not differ significantly between group of cases with PD disease and group of cases with PD plus disease (P-value>0.05) (Figure 8 and Table 10).

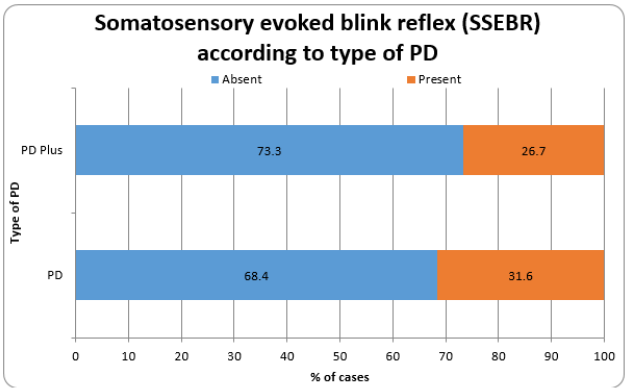

Figure 8. The status of Somatosensory Evoked Blink Reflex (SSEBR) according to type of PD.

Table 10. The status of Somatosensory Evoked Blink Reflex (SSEBR) according to various symptoms among the cases studied.

		Somatosensory Evoked Blink Reflex (SSEBR)						
		Absent		Present		Total		
Symptoms		**n**	**%**	**n**	**%**	**n**	**%**	**P-value**
Tremor	No	20	80	5	20	25	100	0.127^{NS}
	Yes	17	60.7	11	39.3	28	100	
Rigidity	No	2	66.7	1	33.3	3	100	0.999^{NS}
	Yes	35	70	15	30	50	100	
Bradykinesia	No	2	66.7	1	33.3	3	100	0.999^{NS}
	Yes	35	70	15	30	50	100	
Dyskinesia	No	30	88.2	4	11.8	34	100	0.001^{***}
	Yes	7	36.8	12	63.2	19	100	
Postural instability	No	26	100	0	0	26	100	0.001^{***}
	Yes	11	40.7	16	59.3	27	100	

Ataxia	No	33	68.8	15	31.2	48	100	0.999^{NS}
	Yes	4	80	1	20	5	100	
Dysarthria	No	26	83.9	5	16.1	31	100	0.008**
	Yes	11	50	11	50	22	100	
Oculomotor abnormality	No	26	74.3	9	25.7	35	100	0.322^{NS}
	Yes	11	61.1	7	38.9	18	100	
Dysphagia	No	37	74	13	26	50	100	0.024*
	Yes	0	0	3	100	3	100	
Recurrent falls	No	32	68.1	15	31.9	47	100	0.655^{NS}
	Yes	5	83.3	1	16.7	6	100	
Dystonia	No	27	71.1	11	28.9	38	100	0.754^{NS}
	Yes	10	66.7	5	33.3	15	100	
Sleep disturbance	No	24	77.4	7	22.6	31	100	0.152^{NS}
	Yes	13	59.1	9	40.9	22	100	
Bowel/bladder abnormality	No	27	96.4	1	3.6	28	100	0.001***
	Yes	10	40	15	60	25	100	
Orthostatic hypotension	No	34	69.4	15	30.6	49	100	0.999^{NS}
	Yes	3	75	1	25	4	100	

Note: P-value by *Chi-square* test; P-value<0.05 is considered to be statistically significant; *P-value<0.05; **P-value<0.01; ***P-value<0.001; NS-Statistically non-significant.

Distribution of prevalence of presence of SSEBR did not differ significantly between group of cases with or without the presence symptoms such as tremor, rigidity, bradykinesia, ataxia, oculomotor abnormality, recurrent falls, dystonia, sleep disturbance and orthostatic hypotension in the study group (P-value>0.05 for all) [12,13].

The prevalence of presence of SSEBR is significantly higher in group of cases with presence of symptoms such as dyskinesia, Postural instability, dysarthria, dysphagia and bwel/bladder abnormality compared to group of cases who did not have these symptoms in the study group (P-value<0.05 for all) (Figure 10 and Table 11).

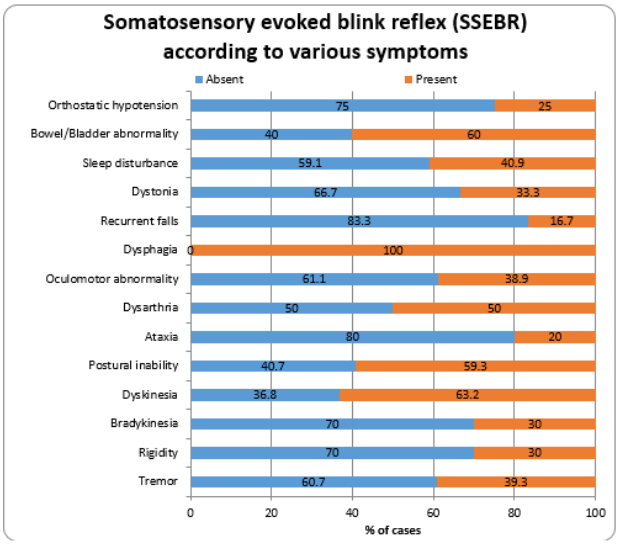

Figure 10. The status of Somatosensory Evoked Blink Reflex (SSEBR) according to various symptoms among the cases studied.

Table 11. Distribution of median ACE 3 and NMSS parameters according to the status of Somatosensory Evoked Blink Reflex (SSEBR).

	Somatosensory evoked blink reflex (SSEBR)				
	Absent (n=37)		Present (n=16)		
Parameters	Median	Min-Max	Median	Min-Max	P-value
ACE3	84	44-94	67.5	50-92	0.014*
NMSS	25	8-47	69	32-160	0.001***

Note: P-value by Mann-Whitney U test. P-value<0.05 is considered to be statistically significant. *P-value<0.05, ***P-value<0.001.

Distribution of median ACE3 and NMSS parameters according to the status of Somatosensory Evoked Blink Reflex (SSEBR)

The median ACE3 score in group of cases with absence in group of cases and with presence of SSEBR was 84.00 and 67.50 respectively. The distribution of median ACE3 score is significantly higher in group of cases with absence of SSEBR compared to group of cases with presence of SSEBR (P-value<0.05).

The median NMSS score in group of cases with absence in group of cases with presence of SSEBR was 25.00 and 69.00 respectively. The distribution of median NMSS score is significantly higher in group of cases with the presence of SSEBR compared to group of cases with absence of SSEBR (P-value<0.05) (Figure 11) [14].

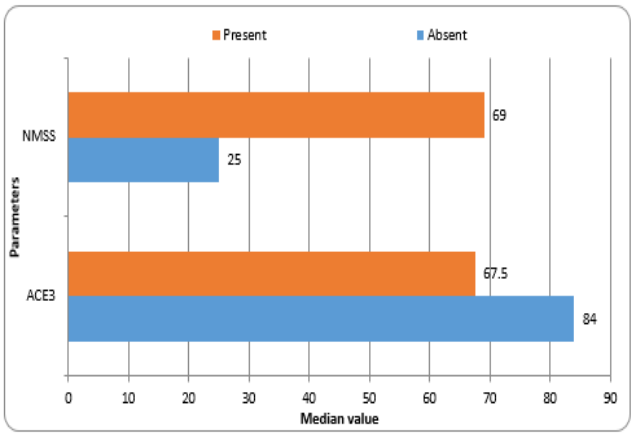

Figure 11. Distribution of median ACE3 and NMSS parameters according to the status of Somatosensory Evoked Blink Reflex (SSEBR).

Discussion

Parkinsonian syndromes are progressive degenerative disorders with major brunt on basal ganglia structures also involving the cortical, subcortical, brain stem and cerebellum structures to varying extent based on the sub type and stage of the disease. Patients with degenerative neurological diseases involving the basal ganglia may present with functional abnormalities of brainstem reflexes, resulting from disturbed activity of loops between the thalamus and the brainstem and cortical circuits. Brain stem interneuron excitability can be assessed by recording the Somatosensory Evoked Blink Reflex (SSEBR).

The clinical symptomatology in patients of different sub-types of Parkinsonian Syndromes in advanced stages is quite varied and can be clearly differentiated but in early stages the symptoms can be subtle and overlapping hence may be difficult to differentiate. There are no definite investigations to differentiate the sub types of Parkinson's disease patients [15].

Demographics

- The mean age in the study was 57 years with standard deviation of 10 years.
- Around 60% were males in the study group.
- Around 22.6% of patients had disease duration of more than 5 years.
- 71.7 % of them were IPD patients and remaining were PD plus.
- The demographic characters in this study were almost similar to study by Hideto Miwa etal.
- DM and HTN were the most common co-morbidities noted.
- There was no significant difference between mean age, sex, duration of disease and comorbidities among PD and PD plus patients.

Conclusions

- Somatosensory Evoked Blink reflex is more frequently elicitable in patients with Parkinson's disease.
- In patients with IPD somatosensory evoked blink reflex was positive in 31.5% of patients and it was observed that patients with IPD had more probability of being SSEBR positive when compared to other Parkinsonian syndromes (26.6%)
- Presence of dyskinesia, postural instability , dysarthria, dysphagia and bowel/bladder abnormality showed positive correlation with presence of positive SSEBR.
- Median ACE 3 score was significantly lower in patients with presence of SSEBR
- Median NMSS score was significantly higher in patients with presence of SSEBR.

Limitations

- The limitations in this study include that we have included patients in all stages of the disease and almost all the patients have been started on dopaminergic medication and other medication even though we have stopped the drug for 24 hrs prior to the SSEBR there is still a possibility of the drugs interfering with these electrophysiological responses.
- Subset of PD plus patients were less compared to IPD patients and hence were not analysed separately.
- There was no control population studied.
- There was no correlation done with imaging findings or other investigations.

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