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Evoked Potentials as an Electrophysiological Marker of Postural Instability in Parkinsonism Patients - An Exploratory Study

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Abstract

Background: The term parkinsonism includes Parkinson's disease (PD) and other neurodegenerative diseases presenting with bradykinesia, rest tremor, rigidity and loss of postural reflexes. Such patients may have clinically subtle sensory disturbances demonstrable only by electrophysiological studies. This study aimed to correlate visual, auditory and somatosensory evoked potentials in patients with parkinsonism with presence and severity of postural instability (PI).

Methods: Thirty patients with parkinsonism and 28 healthy controls were enrolled. Disease severity scores- H and Y staging and MDS-UPDRS and scales for PI- PIGD score, FOGQ score and BBS score were assessed. Evoked potentials (EP) [(visual evoked potentials (VEP), brainstem auditory evoked potentials (BAEP), somatosensory evoked potentials (SSEP)] were done.

Results: Mean age was 59.17 ± 9.43 and 57.54 ± 5.81 years for cases and controls, respectively. Mean age of disease onset was 55.93±9.81 years. Majority showed moderate disease severity and moderate PI. A definite negative association was established between SSEP and freezing, VEP and PI, and BAEP latencies with falls and positive pull test. Our study demonstrated lower BAEP latencies with higher PIGD score or a greater risk of PI, shorter VEP and BAEP latencies with higher FOGQ scores and longer freezing episodes and lower VEP and BAEP latencies with lower BBS scores or higher degree of imbalance.

Conclusion: Freezing and PI is a significant cause of disability and morbidity in parkinsonism warranting early recognition and proper management. Significant association exists between PI and EP latencies suggested by our novel observations and may be used to assess disease progression.

Keywords: Postural Instability; PIGD Score; FOGQ Score; BBS Score

Introduction

Clinical features of parkinsonism including Parkinson's disease (PD) constitute both motor (bradykinesia, rest tremor, rigidity and loss of postural reflexes) and non-motor features [1,2]. Non motor symptoms are increasingly recognized as significant cause of morbidity, predating motor symptoms by several years [3]. Postural instability (PI) due to loss of postural reflexes, is highly prevalent in PD and an important cause of morbidity. Previously thought to be due to involvement of dopaminergic pathways, the current hypothesis is the cortical cholinergic degeneration [4]. Cholinergic neurons in the pedunculopontine nucleus have a powerful influence on motor control of gait and posture. Thalamic acetylcholinesterase activity, derived mainly from neuronal terminals in the pedunculopontine nucleus, reflects cholinergic activity and is reduced in early PD and more severely reduced in PD fallers compared with non-fallers [5].

Brain cholinergic activity can be estimated with short-latency sensory afferent inhibition, that non-invasively assesses the inhibitory circuit in sensorimotor cortex [6]. Patients with parkinsonism may also have sensory disturbances which may not be clinically apparent but demonstrable by electrophysiological studies [7]. Existing literature on evoked potentials (EP) has elucidated that significant delays in EP latencies were observed in parkinsonism, suggesting central conduction abnormalities. Based on above hypothesis, the current study aimed to identify any association between EPs and PI in parkinsonian disorders.

Methods

The study was an observational cross-sectional study conducted over 18 months. Purposive sampling was done from patients of PD attending out-patient and in-patient departments. Recruitment of patients was started after seeking approval from Institutional Ethics Committee (AIIMS/IEC/2022/4121,23/09/2022) and written informed consent from subjects. Patients satisfying the following criteria were enrolled-

Inclusion Criteria

1. Patients with age of 18 or more

2. Patients presenting with hypokinetic extrapyramidal disorder with rigidity, bradykinesia with or without tremor were recruited into the study and divided into typical and atypical parkinsonism.

3. Patients willing to provide written informed consent

Exclusion Criteria

1. Patients with CNS demyelinating disease

2. Patients who are uncooperative for tests

3. Patients with associated dyskinesias

4. Patients with pre-existing peripheral neuropathy, visual or hearing problems

5. Patients who are bedbound and unable to perform tests

Demographic details, clinical history and examination findings, Hoehn & Yahr stage (H and Y stage) and Movement Disorder Society Unified Parkinson's Disease rating scale (MDS-UPDRS) was recorded. Ophthalmological evaluation, audiometric assessment and nerve conduction studies were done to rule out subclinical involvement. EPs namely visual evoked potential (VEP), brainstem auditory evoked potential (BAEP), and somatosensory evoked potential (SSEP) were done. PI was assessed using PIGD, FOGQ, and BBS score. Those patients fulfilling the UK Parkinson's disease society brain bank clinical diagnostic criteria were included in the typical parkinsonism group (PD) and 2 patients having onset less than 40 years were considered as early onset parkinsonism but had asymmetric onset and were included along with PD group. Atypical parkinsonism patients were recruited if fulfilling validated clinical diagnostic criteria [8,9]. Two patients with hypokinetic rigid syndrome with preceding history of vaccination and improvement with steroids were considered post vaccineal and included in atypical parkinsonism group. Another two patients with symmetric akinesia and rigidity without significant tremors were considered as drug induced parkinsonism and includ-

ed in the atypical parkinsonism group [10].

Statistical Analysis

IBM SPSS software version 21.0 and jamovi version 2.5.5 was used for statistical analysis. Qualitative and quantitative variables were represented using frequency and mean and standard deviation respectively. Data was represented using tables, graphs and charts. Unpaired (students) t-test was employed for comparing mean between two groups. Spearmans correlation test was used to find association between EPs and PI severity scores. A p value of less than 0.05 was taken as statistically significant.

Results

A total of 30 cases with clinical diagnosis of parkinsonism were included. Mean age group was 59.17 ± 9.43 years. The mean duration of illness was 3.23 ± 2.31 years and mean age of onset was 55.93 ± 9.81 years. Assessment of clinical features at presentation revealed that tremor, tightness, bradykinesia, and PI/imbalance affected majority patients (Figure 1). While freezing was also common, falls were the least common symptom. Of the 30 cases, 20 were diagnosed to have PD and 10 had atypical parkinsonism.

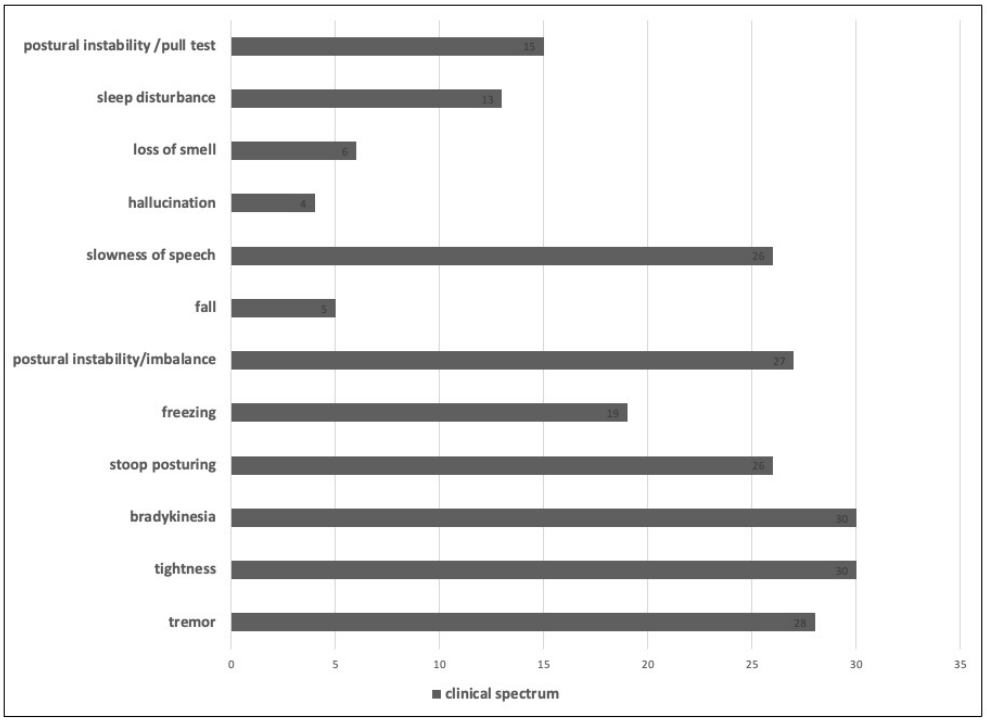

Figure 1: Clinical spectrum of motor features of parkinsonism in study group

Different severity scores were used to assess severity of disease and PI. Mean value of MDS-UPDRS sum score was 76.00 ± 26.04 and mean H & Y stage was 2.80 ± 0.51. Mean values of PIGD, FOGQ and BBS scores were 7.60±4.95, 11.26 ±5.91 and 37.13 ± 12.03 respectively. This indicates that majority of patients in our study had moderate to severe PI.

The mean values of disease severity scores- H and Y stage and MDS-UPDRS, and PI severity scores- PIGD, FOGQ and BBS scores were compared by correlation analysis between PD and atypical parkinsonism cases (Table 1). The mean values of all disease severity scores were more in patients with atypical parkinsonism indicating a higher disease severity though not statistically significant. However, a statistically significant difference was observed for FOGQ (higher score) and a trend towards significance for BBS (lower score) in patients with atypical parkinsonism. Patients having freezing, PI and falls were noted to have higher disease severity in terms of H and Y stage and MDS-UPDRS scores (Table 2).

Table 1: Comparison of clinical scoring in subgroups of PD and atypical parkinsonism

	Atypical parkinsonism (N=10) MEAN±SD	PD(N=20)MEAN±SD	t	P value
H & Y	2.750±0.3536	2.825±0.5911	0.368	0.716
MDS-UPDRS	81.40±23.277	73.30±27.488	0.798	0.432
PIGD	8.30±4.218	7.45±5.206	0.447	0.658
FOGQ	13.10±5.259	10.35±6.133	1.210	0.236
BBS	35.50±8.017	37.95±13.736	0.519	0.608

*- statistically significant

Table 2: Disease severity scores- H and Y stage and MDS-UPDRS and PI symptoms

		H & Y STAGEMEAN ± SD	p value	UPDRS SUM SCOREMEAN ± SD	p value
Freezing	present (N=19)	2.95±.55	0.038*	83.21±25.27	0.044*
	Absent (N=11)	2.55±.35		63.55±23.42	
Postural Instability	present (N=27)	2.89±.47	0.003*	79.30±25.13	0.035*
	Absent (N=3)	2.00±.00		46.33±12.66	
Fall	present (N=5)	3.20±.45	0.057	96.00±25.81	0.058
	Absent (N=25)	2.72±.50		72.00±24.67	

*- statistically significant

Frequency distribution of subjects based on presence and duration of freezing episodes, PIGD score, FOGQ score, and BBS scores are depicted in Figure 2A-D. Only a minority of patients had moderate (10%) and severe freezing (3%). Patients were grouped into four categories based on PIGD scores: 0-5, 6-10, 11-15 and 16-20 (Figure 2B). The majority had only mild to moderate PI as per PIGD score <10 (66%), while a very small proportion of patients (7%) had very severe PI. Severity of freezing was categorized into 3 groups based on FOGQ score (Figure 2C). Mild gait impairment was observed in 50% (FOGQ scores 1-10), and only 7% had severe gait impairment. Balance was scored based on BBS score and patients divided into three categories- the proportion of patients with low risk of falls was 46%, while 7% had high risk of falls. (Figure 2D).

The mean values of VEP, BAEP and SSEP latencies were compared among patients with and without clinical PI based on falls, freezing of gait, PI, and pull test positivity. No significant difference was noted for VEP among patients with (N=19) and without freezing. However, BAEP I-III IPL left and SSEP P37, N45 left were noted to be shorter in patients with freezing (p values 0.041, 0.033, and 0.042 respectively). Thus, a negative correlation was observed between BAEP/ SSEP latencies and freezing of gait. Amongst the 5 patients having falls, comparison of VEP latencies with those who did not have falls showed prolonged mean N75 and P100 latencies in patients without falls but the difference was not statistically significant. On comparing SSEP latencies, slightly shorter latencies were noted in patients with falls without significant difference. However, BAEP latencies were prolonged in patients without falls with statistical significance for I and I-III IPL right (p values 0.022 and 0.042, respectively).

Further on comparison between patients with and

without historical PI, most VEP latencies were shorter in patients with PI. Mean N75 and P100 left latencies were lesser in patients with PI (p values 0.015 and 0.036). On comparing BAEP, all individual wave latencies on left I, II, III, IV, V and I-III IPL, III-V IPL on both sides were more in patients with PI, though not statistically significant. No statistically significant changes were demonstrable in SSEP latencies. Hence, we demonstrated definite negative correlation between VEP and PI.

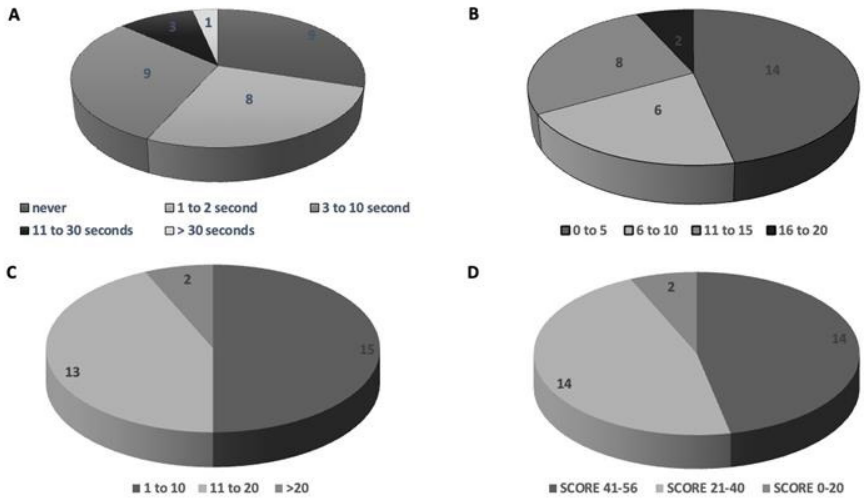

Figure 2: Distribution of cases with different A. duration of freezing B. PIGD score C. FOGQ score And D. BBS score

Similarly, EP latencies were compared between those with positive pull test (N=15) and without. VEP (N75, P100, and N145) and SSEP latencies showed no statistically significant differences between these groups. On the other hand, latencies of BAEP waves I, II III right, both wave V and I-III IPL left showed statistically significant differences (p values 0.033, 0.015, 0.013, 0.011, 0.039 and 0.027, respectively), with lower latencies in patients with positive pull test. Thus, an association of lower BAEP latencies with presence of positive pull test was observed.

The duration of freezing was also compared with EP (Table 3). Mean P100 right was significantly associated with duration, decreasing as freezing duration increased. Likewise, I-III IPL and III-V IPL left showed statistically significant correlation with freezing duration. Overall, a significant negative correlation was observed between VEP and BAEP latencies and duration of freezing of gait.

Table 3: Evoked potentials and association with duration of freezing

PARAMETER / DURATION OF FREEZING	(NEVER)MEAN ± SD (ms)(N=9)	(1–2 S)MEAN ± SD (ms)(N=8)	(3–10 S)MEAN ± SD (ms)(N=9)	(11–30 S)MEAN ± SD (ms)(N=3)	(MORE THAN 30 S) MEAN ± SD (ms)(N=1)	SPEARMAN COEFFICIENT	P VALUE
N75 RIGHT	77.11±17.59	74.13±10.65	69.00±14.00	74.67±16.50	78.00	-0.156	0.411
N75 LEFT	78.11±17.50	76.25±8.730	65.00±6.538	69.33±7.572	77.00	-0.335	0.070
P100 RIGHT	114.11±16.811	108.88±6.06	107.33±11.874	104.67±6.35	105.00	-0.307	0.099
P100 LEFT	114.67±16.439	110.25±6.86	103.89±11.73	106.67±8.96	105.00	-0.426	0.019*
N145 RIGHT	154.78±21.742	143.75±9.07	144.44±11.50	135.00±22.91	158.00	-0.286	0.121
N145 LEFT	153.56±18.96	147.00±14.68	148.78±11.63	143.33±14.57	159.00	-0.125	0.511
I RIGHT	1.88±.32	1.64±.31	1.49±.14	1.70±.70	1.60	-0.348	0.060

I LEFT	1.71±.34	1.74±.36	1.57±.41	2.30±.26	1.60	0.117	0.536
II RIGHT	2.68±.27	2.75±.27	2.49±.13	2.43±.81	2.40	-0.262	0.163
II LEFT	2.90±.45	2.77±.17	2.53±.43	2.97±.30	2.40	-0.216	0.252
III RIGHT	3.58±.35	3.87±.27	3.51±.13	3.23±.72	3.30	-0.277	0.139
III LEFT	3.94±.40	3.79±.36	3.48±.44	3.80±.10	3.70	-0.326	0.079
IV RIGHT	4.60±.52	5.00±.39	4.58±.34	4.40±.69	4.30	-0.142	0.454
IV LEFT	4.88±.53	4.90±.54	4.74±.30	4.93±.35	4.70	-0.109	0.568
V RIGHT	5.52±.43	5.95±.67	5.50±.60	5.33±.38	5.20	-0.180	0.342
V LEFT	5.71±.36	5.80±.60	5.81±.50	5.77±.21	5.40	-0.043	0.820
I-III IPL RIGHT	1.70±.34	2.11±.43	2.02±.20	1.50±.36	1.70	0.071	0.709
I-III IPL LEFT	2.24±.40	2.05±.39	1.92±.33	1.47±.15	2.10	-0.447	0.013*
III-V IPL RIGHT	1.97±.18	2.10±.58	1.96±.54	2.10±.35	1.90	-0.042	0.825
III-V IPL LEFT	1.77±.26	2.01±.53	2.34±.53	1.97±.11	1.70	0.377	0.040*
N20 RIGHT	19.57±2.29	19.45±4.08	20.87±3.16	25.83±1.15	17.80	0.273	0.144
N20 LEFT	20.62±2.18	21.65±2.45	21.89±3.68	19.13±1.80	16.40	-0.144	0.449
P22 RIGHT	23.17±3.15	23.20±5.93	24.14±3.44	26.23±5.44	20.30	0.122	0.522
P22 LEFT	24.09±2.76	25.30±3.38	25.33±3.17	24.90±1.90	20.10	0.019	0.923
P37 RIGHT	38.22±8.30	39.74±2.55	41.04±5.59	31.803.36	40.70	-0.052	0.784
P37 LEFT	37.78±6.14	38.97±3.18	37.53±4.34	36.50±4.7	38.60	-0.183	0.334
N45 RIGHT	45.25±7.50	46.64±3.36	46.81±4.56	36.77±5.01	45.40	-0.195	0.302
N45 LEFT	44.36±6.40	46.84±3.51	42.96±5.01	41.23±5.26	46.30	-0.201	0.287

*- statistically significant

Table 4: Evoked potentials and association with PIGD scores

PARAMETERS	PIGD (0-5)MEAN ± SD (ms) (N=14)	PIGD (6-10)MEAN ± SD (ms)(N=6)	PIGD (11-15)MEAN ± SD (ms)(N=8)	PIGD (15-20)MEAN ± SD (ms)(N=2)	SPEARMAN COEFFICIENT	p value
N75 RIGHT	74.14±16.56	75.00±6.45	73.25±15.37	68.00±14.14	-0.030	0.876
N75 LEFT	75.29±15.84	74.83±8.52	67.12±6.91	71.50±7.78	-0.188	0.320
P100 RIGHT	110.21±14.63	113.00±8.46	107.00±9.914	103.00±2.83	-0.207	0.271
P100 LEFT	110.43±13.60	113.67±12.88	105.00±10.156	103.00±2.83	-0.350	0.058
N145 RIGHT	148.71±16.58	152.50±17.44	140.13±15.113	144.00±19.80	-0.270	0.149
N145 LEFT	148.21±17.55	155.17±12.43	148.00±12.201	148.00±15.56	-0.025	0.897

I RIGHT	1.81±.28	1.58±.35	1.50±.4106	1.650±.070	-0.483	0.007*
I LEFT	1.68±.34	1.58±.50	1.90±.4209	1.850±.35	0.231	0.219
II RIGHT	2.73±.28	2.57±.16	2.42±.4334	2.60±.28	-0.379	0.030*
II LEFT	2.87±.35	2.52±.53	2.73±.30119	2.65±.35	-0.207	0.273
III RIGHT	3.76±.30	3.52±.34	3.39±.4121	3.50±.28	-0.487	0.006*
III LEFT	3.83±.37	3.67±.71	3.65±.2070	3.70±.00	-0.213	0.258
IV RIGHT	4.85±.52	4.57±.25	4.46±.4897	4.55±.35	-0.342	0.064
IV LEFT	4.95±.47	4.75±.58	4.77±.3012	4.65±.07	-0.138	0.467
V RIGHT	5.87±.59	5.42±.32	5.31±.5489	5.40±.28	-0.418	0.022*
V LEFT	5.95±.53	5.53±.32	5.66±.2774	5.50±.14	-0.221	0.241
I-III IPL RIGHT	1.88±.26	1.93±.65	1.89±.4121	1.80±.14	0.059	0.758
I-III IPL LEFT	2.16±.41	2.12±.377	1.72±.2915	1.85±.35	-0.424	0.019*
III-V IPL RIGHT	2.16±.43	1.80±.179	1.92±.5418	1.90±.00	-0.235	0.212
III-V IPL LEFT	2.11±.58	1.90±.518	2.01±.229	1.80±.14	-0.103	0.589
N20 RIGHT	19.75±3.66	18.95±1.48	22.47±2.999	22.40±6.51	0.358	0.050*
N20 LEFT	21.16±2.69	20.70±1.93	21.47±3.817	18.70±3.25	-0.107	0.574
P22 RIGHT	23.26±4.95	22.60±2.98	24.86±3.405	25.15±6.86	0.180	0.341
P22 LEFT	24.44±2.87	24.43±1.73	25.89±3.835	23.05±4.17	0.063	0.741
P37 RIGHT	40.10±6.18	37.13±4.19	39.31±6.849	34.35±8.98	-0.255	0.174
P37 LEFT	38.80±5.70	37.22±3.06	37.325±3.457	36.30±3.25	-0.308	0.098
N45 RIGHT	46.70±5.85	43.28±2.61	45.933±6.105	38.20±10.18	-0.292	0.117
N45 LEFT	44.91±6.13	44.92±4.22	43.238±4.681	43.15±4.45	-0.202	0.284

*- statistically significant

The various scales for PI and balance were subsequently analysed with respect to EP latencies. No significant association was noted in VEP parameters. Waves I, II, III, V latencies on right and I-III IPL on left showed a significant negative correlation with PIGD scores (Table 4). On comparing SSEP latencies, N20 right showed positive correlation with PIGD score. On subgroup analysis of groups with PIGD scores more than and less than 5, VEP and SSEP parameters showed no statistically significant difference. However, BAEP latencies were more in patients with lesser PIGD scores, the differences in wave I, II, III, IV, V latency on right and V left was statistically significant (p values 0.036, 0.051, 0.018, 0.050, 0.011, 0.027, respectively). Thus, lower BAEP latencies correlated with PIGD score or a greater risk of PI.

On comparison with FOGQ score, significant negative correlation was noted between FOGQ scores and P100 left and N145 right latencies (Table 5). For BAEP, wave I, III right, I-III and III-V IPL left was found to decrease as FOGQ score increased. Further subgroup analysis was done to study the relationship between severity of freezing (FOGQ scores more than and less than 10) and EP. N145 latency right was more in patients with less FOGQ (p = 0.035). BAEP latencies were more in patients with lesser FOGQ, the differences in wave I, II, III, IV latencies on right being statistically significant (p values 0.006, 0.039,

0.018, 0.010, respectively). However, no significant difference was observed in SSEP. Thus, VEP and BAEP latencies were more prolonged with lesser FOGQ scores.

Table 5: Evoked potentials and association with FOGQ scores

PARAMETERS	FOGQ (0-10)MEAN ± SD (ms)(N=15)	FOGQ (11-20)MEAN ± SD (ms)(N=13)	FOGQ (>20)MEAN ± SD (ms)(N=2)	SPEARMAN COEFFICIENT	p value
N75 RIGHT	75.93±15.36	71.92±13.00	68.00±14.14	-0.194	0.305
N75 LEFT	76.60±14.72	68.54±8.36	71.50±7.78	-0.248	0.186
P100 RIGHT	113.33±11.90	105.92±11.54	103.00±2.83	-0.357	0.053
P100 LEFT	113.20±11.44	105.38±12.83	103.00±2.83	-0.425	0.019*
N145 RIGHT	153.07±13.03	140.15±17.70	144.00±19.80	-0.380	0.038*
N145 LEFT	152.67±15.46	146.15±14.17	148.00±15.56	-0.221	0.241
I RIGHT	1.83±.29	1.48±.34	1.65±.07	-0.465	0.010*
I LEFT	1.73±.37	1.71±.45	1.85±.35	0.174	0.357
II RIGHT	2.73±.27	2.47±.35	2.60±.28	-0.322	0.083
II LEFT	2.78±.21	2.72±.55	2.65±.35	-0.139	0.465
III RIGHT	3.75±.30	3.43±.37	3.50±.28	-0.391	0.033*
III LEFT	3.83±.35	3.65±.49	3.70±.00	-0.211	0.263
IV RIGHT	4.89±.38	4.44±.50	4.55±.35	-0.228	0.226
IV LEFT	4.88±.51	4.83±.37	4.65±.07	-0.068	0.722
V RIGHT	5.79±.57	5.41±.54	5.40±.28	-0.275	0.141
V LEFT	5.81±.48	5.75±.45	5.50±.14	-0.069	0.717
I-III IPL RIGHT	1.85±.36	1.95±.44	1.80±.14	0.057	0.767
I-III IPL LEFT	2.10±.33	1.94±.48	1.85±.35	-0.401	0.028*
III-V IPL RIGHT	2.09±.40	1.93±.49	1.90±.00	-0.130	0.493
III-V IPL LEFT	1.99±.41	2.10±.57	1.80±.14	0.362	0.050*
N20 RIGHT	19.38±3.28	21.48±3.16	22.40±6.51	0.362	0.050*
N20 LEFT	21.26±2.69	21.02±3.09	18.70±3.25	-0.067	0.724
P22 RIGHT	23.05±4.64	24.18±3.59	25.15±6.86	0.213	0.258
P22 LEFT	24.31±2.60	25.48±3.32	23.05±4.17	0.130	0.493
P37 RIGHT	38.08±5.55	40.64±6.27	34.35±8.98	-0.075	0.694
P37 LEFT	37.73±5.21	38.39±3.94	36.30±3.25	-0.083	0.664
N45 RIGHT	45.03±5.28	46.58±5.64	38.20±10.18	-0.125	0.509
N45 LEFT	44.71±6.06	44.11±4.39	43.15±4.45	-0.124	0.513

* statistically significant

The association between BBS and EP latencies was studied (Table 6). P100 left and BAEP waves I, II, III, IV, V latencies right and I-III IPL left showed a significant negative correlation with BBS scores. However, only N20 right SSEP latency showed a positive correlation with BBS (p value 0.020). Thus, based on these results association between EP latencies and BBS score demonstrated that a lower VEP and BAEP latencies correlated with a lower BBS scores or higher degree of imbalance.

Table 6: Evoked potentials and association with BBS

PARAMETERS	BBS (41-56)MEAN ± SD (ms)(N=14)	BBS (21-40)MEAN ± SD (ms)(N=14)	BBS (0-20)MEAN ± SD (ms)(N=2)	SPEARMAN COEFFICIENT	p value
N75 RIGHT	75.50±15.75	71.71±11.90	74.50±23.33	-0.134	0.481
N75 LEFT	77.21±15.41	69.43±7.59	65.00±1.41	-0.326	0.078
P100 RIGHT	112.71±12.16	107.36±11.69	101.00±.00	-0.318	0.087
P100 LEFT	113.21±11.87	106.14±12.44	101.50±.71	-0.387	0.035*
N145 RIGHT	151.71±12.04	145.50±17.90	122.50±10.61	-0.323	0.082
N145 LEFT	151.50±15.46	149.64±14.42	135.00±2.83	-0.149	0.433
I RIGHT	1.78±.33	1.61±.31	1.35±.49	-0.427	0.019*
I LEFT	1.69±.34	1.71±.46	2.15±.07	0.155	0.415
II RIGHT	2.77±.25	2.51±.18	2.15±.92	-0.484	0.007*
II LEFT	2.81±.19	2.67±.53	2.80±.14	-0.231	0.219
III RIGHT	3.84±.22	3.42±.18	3.05±.92	-0.726	0.001*
III LEFT	3.81±.29	3.66±.52	3.75±.07	-0.286	0.125
IV RIGHT	4.95±.35	4.46±.40	4.20±.85	-0.534	0.002*
IV LEFT	4.88±.43	4.82±.48	4.75±.21	-0.159	0.400
V RIGHT	5.89±.52	5.36±.50	5.25±.49	-0.549	0.002*
V LEFT	5.84±.44	5.69±.48	5.65±.07	-0.198	0.295
I-III IPL RIGHT	1.99±.37	1.81±.39	1.65±.35	-0.266	0.155
I-III IPL LEFT	2.14±.35	1.95±.43	1.55±.07	-0.419	0.021*
III-V IPL RIGHT	2.07±.44	1.92±.43	2.20±.42	-0.092	0.629
III-V IPL LEFT	2.02±.40	2.04±.58	1.90±.00	-0.058	0.760
N20 RIGHT	19.24±3.37	20.99±3.09	25.85±1.62	0.424	0.020*
N20 LEFT	21.06±2.68	21.17±3.18	19.20±2.55	-0.057	0.763
P22 RIGHT	22.84±4.66	24.33±3.56	25.00±7.07	0.204	0.280
P22 LEFT	23.99±2.59	25.29±3.48	26.00±.00	0.254	0.176
P37 RIGHT	39.09±5.17	39.94±6.56	30.50±3.54	-0.239	0.203
P37 LEFT	37.89±5.27	37.94±3.86	38.00±5.66	-0.057	0.763
N45 RIGHT	45.79±5.08	46.09±5.68	35.50±6.36	-0.262	0.162
N45 LEFT	44.84±6.10	43.98±4.43	43.50±4.95	-0.148	0.435

*- statistically significant

Table 7: Evoked potential latencies in PD and atypical parkinsonism

PARAMETERS	Atypical parkinsonismMEAN ± SD (ms)(N=10)	PDMEAN ± SD (ms)(N=20)	t	p value
N75 RIGHT	71.00± 17.192	75.00± 12.448	0.730	0.471
N75 LEFT	72.50± 17.044	72.90± 9.668	0.082	0.935
P100 RIGHT	109.00± 13.266	109.65±11.394	0.140	0.890
P100 LEFT	109.60±17.989	108.90±8.602	0.146	0.885
N145 RIGHT	147.50±19.398	146.55±15.066	0.148	0.883
N145 LEFT	150.70±15.514	148.95±14.709	0.302	0.765
I RIGHT	1.55±0.347	1.73±0.328	1.391	0.175
I LEFT	1.700±0.4422	1.745±0.3832	0.288	0.775
II RIGHT	2.59±0.191	2.62±0.376	0.197	0.845
II LEFT	2.90±0.42	2.67±0.36	1.581	0.125
III RIGHT	3.54±0.23	3.62±0.42	0.562	0.578
III LEFT	3.77±0.35	3.73±0.44	0.280	0.781
IV RIGHT	4.55±0.48	4.73±0.47	0.979	0.336
IV LEFT	4.93±0.33	4.80±0.48	0.769	0.449
V RIGHT	5.53±0.60	5.64±0.56	0.473	0.640
V LEFT	5.88±0.45	5.70±0.44	1.041	0.307
I-III IPL RIGHT	1.99±0.46	1.84±0.34	1.049	0.303
I-III IPL LEFT	2.09±0.55	1.98±0.32	0.730	0.471
III-V IPL RIGHT	1.92±0.53	2.06±0.38	0.807	0.427
III-V IPL LEFT	2.10±0.59	1.99±0.41	0.622	0.539
N20 RIGHT	21.60±2.51	19.94±3.81	1.243	0.224
N20 LEFT	21.91±3.38	20.53±2.54	1.260	0.218
P22 RIGHT	25.12±2.81	22.96±4.67	1.340	0.191
P22 LEFT	25.57±3.17	24.32±2.89	1.085	0.287
P37 RIGHT	40.44±5.26	38.15± 6.45	0.970	0.340
P37 LEFT	38.70±3.89	37.54± 4.82	0.663	0.513
N45 RIGHT	46.67±4.79	44.53± 6.33	0.938	0.356
N45 LEFT	43.95±4.98	44.55±5.36	0.296	0.770

*- statistically significant

On multivariate analysis of EP latencies between PD and atypical parkinsonism, most of the SSEP latencies were prolonged in atypical parkinsonism group whereas in the case of VEP and BAEP latencies we could not establish a correlation with the type of parkinsonism as shown in Table 7. Though we observed differences between the two groups, they were not statistically significant.

Discussion

This observational, cross-sectional study in patients with clinically diagnosed parkinsonism brought important insights into EP variations that occur in parkinsonism. Distinct differences were observed with respect to type of parkinsonism and severity of PI. Existing literature revealed limited studies on individual EPs in parkinsonism. Our research has focused on all three EPs- VEP, BAEP and SSEP and tried to explore their association with imbalance and PI in parkinsonism.

Demographically, the mean age of onset of parkinsonism in our study was similar to most studies. This aligns with the observations made by Ozek et al, Shalash et al and Roy et al where majority of the study population had onset of disease beyond 50 years of age [11,13].

Apart from clinical features of imbalance and freezing, PI was studied among cases in terms of PIGD, BBS, and FOGQ scores. Our subjects had higher mean PIGD score (7.60±4.95) compared to other studies. Shalash et al reported an average PIGD score of 5.20±4.06 [12]. This indicates that our patients had more severe disease and greater PI. The mean FOGQ score in our study was 11.26 ±5.91 and average BBS score 37.13 ± 12.03, both indicating a moderate to severe disease and greater risk of falls. Klunk et al found average BBS scores to be 54.6±2.0 and 34.7±22.7 among PD and atypical parkinsonism, respectively [14]. We have similarly observed lower BBS scores in patients with atypical parkinsonism compared to IPD. While higher FOGQ were additionally noted in atypical parkinsonism in our study, we did not find literature comparing FOGQ scores between different types of PD. However, Lieberman et al studied freezing of gait in IPD and atypical parkinsonism and observed earlier onset and greater freezing of gait in atypical parkinsonism [15].

A significant negative correlation was established between EP latencies, and historical freezing, PI and falls in our study. A definite negative association was established between SSEP and freezing, VEP and PI and BAEP latencies with falls and positive pull test. This exemplified the fact that a significant correlation exists between increased imbalance and gait issues seen in moderate to severe parkinsonism with a progressive decrease in EP latencies within the group. A detailed literature review did not reveal any contemporary studies on associations between all three EP modalities with PI and freezing.

Using objective scoring of PI, freezing and imbalance, a significant negative correlation was noted with VEP and BAEP parameters and FOGQ and BBS scores. Similar observations were made for PIGD scores, where BAEP parameters showed significant negative correlation. Thus, we have observed an increased objective severity of PI, freezing and imbalance associated with significant reduction in EP latencies mainly for VEP and BAEP parameters. When analyzing between PD and atypical parkinsonism patients, SSEP latencies were more prolonged in atypical parkinsonism patients who also had higher mean disease severity and PI severity scores. This aligns with observations made by Roy et al. On comparing VEP and BAEP latencies with type of parkinsonism, we could not establish a definite correlation. So, this requires further studies.

Our findings are novel as no other literature supports our observations comparing PIGD, FOGQ and BBS scores with all three modalities of EP. However, a few similar studies that were related to our observations are reported. Roy et al compared EP latencies between tremor dominant PD and PIGD variety of PD and observed that BAEP latencies III, V, III-V were more prolonged in PIGD variant [13]. This observation was also statistically significant and it indicated that PI is positively associated with prolongation of BAEP latencies. On the other hand, negative correlation was found by Klunk et al between VEMP amplitude and BBS scores [14].

The major highlight of our study is the consistent lowering of EP latencies in patients with longer duration of parkinsonism and more severe PI and freezing. The pathophysiology behind this observation is unclear at present. While motor impairments in PI were earlier thought to be predominantly caused by dopaminergic neuronal deficits, lack of response of PI and freezing to dopamine therapy may indicate that other neurotransmitters may also be involved. It is currently postulated that gait disturbances in PI maybe linked to cholinergic system mediated cortical and subcortical connections and their degeneration [5]. Bohnen

et al showed lower levels of cholinergic activity and increased acetylcholine hydrolysis rates in PD fallers compared to non-fallers [16]. It maybe speculative that while severity of imbalance increases with duration and type of parkinsonism due to the above mechanisms, relative shortening of EP latencies may be influenced by alternate pathways and higher doses of dopaminergic medications that this subgroup is usually subjected to. Higher disease severity would have lead to more severe motor impairment and hence a higher dose of dopamine being used for treatment, the effect of which was not considered in our study. This is a relatively novel concept which needs further exploration as prior studies have contrary observations regarding disease severity and EP latencies [17].

Major limitation of our study was the sample size. The study was primarily designed to analyse relation between EP latencies and parkinsonism with postural instability and the recruitment of study subjects between different disease severity stages was not equal. The number of PD and atypical parkinsonism cases were also not similar (20 vs 10) and hence the observations made cannot be generalised to all PD and atypical parkinsonism patients and limits applicability of our findings. Similarly, most of the patients recruited had moderate disease and moderate PI. Hence the EP latencies in patients with early PD and early PI cannot be commented upon here. Though none of the patients were drug naïve, the effect of dopamine agonists and other drugs on EP latencies were not considered in this study. Some patients were observed to have prolongation of latencies on one side only. Whether this correlates with the side of symptoms has to be further studied in detail and currently we did not analyze the EP latencies based on laterality of clinical feature.

But this study highlights the existence of such associations between disease severity and degree of PI and EP latency and paves the way for future research and breakthroughs. Further studies are required comparing all three EP modalities with different disease stages of PD and atypical parkinsonism with patients recruited based of type and stage of parkinsonism and compared with drug effect and across time and if same association is proven, then EP latencies can be used as a marker for disease progression. This novel study has paved the way for future research which might lead to non-invasive investigations such as EPs being used for assessment of disease progression in PD.

Conclusions

EP abnormalities are common in PD and significant associations exist between PI and its severity and all three modalities of VEP, BAEP and SSEP. Our study revealed shorter EP latencies in patients with more severe PI. Thus, EPs maybe a useful marker of severity of disease and possibly predict PI. However, the exact pathophysiological mechanisms behind this observation cannot be explained with current knowledge, mandating more research.

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Disclaimer

NIL

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Patient Consent

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We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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