

Evaluation of Brainstem Auditory Evoked Response (BAER) in Parkinson's Disease

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ABSTRACT

Background: Parkinson's disease (PD) is a progressive long-term, neurodegenerative disorder of central nervous system which mainly affects the motor system, caused by loss of dopaminergic neurons in the substantia nigra, but also in other dopaminergic and non-dopaminergic areas of the brain and mainly in the brainstem. Brainstem Auditory Evoked Response are routinely used in clinical practice to evaluate the function of the auditory nerve and auditory pathways in the brainstem. **Objective:** The aim of this study was to evaluate the Brainstem Auditory Evoked Response in patients with Parkinson's disease.

Methods 30 subjects (18 males and 12 females) with Parkinson's disease. And same number of healthy age-matched subject control group was assessed. Age of Control Group was 61.2±11.6 & of Test Group 61.7±10.4. A complete & detailed neurological examination (CNS) were performed in all individuals clinically especially of motor system to evaluate the severity of the disease for the occurrence of Parkinson's disease. Recordings of BAERs were performed with Neurostim Plus software of Medicaid Company, using 70 dB HL in the form of rarefaction

clicks were used in each ear obtain good quality BAER recording. **Results.** The BAER results were interpreted for the latencies and Interpeak latencies. The result of this study shows that the waves II, III, IV, V and IPL III-V were significantly delayed. **Conclusion.** Parkinson's disease population showed significant differences to Brainstem Auditory Evoked Response.

Key words: Parkinson disease, Brainstem Auditory Evoked Response and Auditory Pathways.

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INTRODUCTION

Parkinson's disease (PD) is a progressive long-term, neurodegenerative disorder of central nervous system which mainly affects the motor system, caused by loss of dopaminergic neurons in the substantia nigra, but also in other dopaminergic and non-dopaminergic areas of the brain and mainly in the brainstem.^[1,2] Parkinson's disease is not an uncommon disorder encountered by physicians in elderly

people, though it may occur in young as well. It is a syndrome and was first described by James Parkinson in 1817 while presenting his paper entitled. "The Shaking palsy".^[3]

Parkinsonism is defined as a syndrome comprising of tremor, rigidity, bradykinesia characteristic gait and postural disturbance. Bradykinesia or hypokiniesis describes the slowness in initiating and repeating voluntary movements, the muscle strength being normal, chronic progressive disorder in which idiopathic parkinsonism occurs without the evidence of wide spread neurological involvement is given the name Parkinson's disease.^[4]

Parkinson's disease occurs due to the insufficient formation

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and action of dopamine. Human beings have always had the potential for insufficient dopamine. Although Parkinson's disease has increased in its prevalence over time, it must have existed to some extent for as long as human existence. There are references found to Parkinson's disease symptoms throughout history.

Parkinsonism is associated either with defective release of impaired postsynaptic response to the neurotransmitter dopamine in the corpus striatum. The histopathological presentation of the disease is depletion of pigment neurons in substantia nigra, presence of eosinophilic inclusions (Lewy bodies) in nigral cells, atopic changes in substantia nigra and depletion of neurons in Locus coeruleus.^[5,6]

The primary symptoms of Parkinson's disease result from greatly reduced activity of dopamine-secreting cells caused by cell death in the pars compacta region of the sub-stantia nigra.

There are five major pathways in the brain connecting other brain areas with the basal ganglia. These are known as the motor, oculo-motor, associative, limbic and orbito-frontal circuits, with names indicating the main projection area of each circuit. All of them are affected in PD, and their disruption explains many of the symptoms of the disease since these circuits are involved in a wide variety of functions including movement, attention and learning. Parkinsonism generally occurs in middle or late years of life with gradual progression and a prolonged course and has an equal sex distribution. The disease incidence is approximately 01 in every 1000 people. With the increase in age, its incidence also increases proportionally being raised to 01 in every 100 persons older than 65 years (1%).^[7] However, according to a recent report more and more patients in their late 30s are being diagnosed with the disease and it is stated that about 10% cases in India suffering from Parkinsonism are in their late 30s and 40s.^[8] Disability in Parkinson's disease is mostly due to motor impairment.^[9,10] but sensory symptoms are frequent complaints and many patients experience pain during the course of their illness.^[11] The types of deficits inevitable with the progression of PD suggest that the basal ganglia are critical for sensorimotor agility.^[12]

However, of late there is ever increasing evidence that the spectrum of clinical manifestation of PD is more extensive, also including Non-Motor Symptoms (NMS). NMS of PD comprised a variety of cognitive, neuropsychiatric, sleep, autonomic, and sensory dysfunctions.^[3] The NMS may occur prior to or after the onset of motor symptoms.^[14] The symptoms which usually precede motor symptoms are rapid eye movement sleep behavior disorder (RBD), constipation, depression and olfactory dysfunction. NMS are being recognized as an important part of PD symptoms as they amount to significant disability and affect the quality of life of PD patients.

Of all the changes in the senses that occur with age, deterioration in hearing is perhaps the most expected and indeed the most accepted decline. Hearing serves several functions: it permits communication through speech,

provides warning of potentially injurious events occurring outside the visual field, and serves an aesthetic function as in the appreciation of music or nature. The wider impact of hearing loss may therefore be profound, with consequences for the social, functional, and psychological wellbeing of the person.^[15]

Results of animal studies implicate the role of oxidative stress in age related hearing loss. Cumulating oxidative stress damages the mtDNA in the cochlea causing apoptosis of cochlear cells. Source of oxidative stress could be general aging process, exposure to noise, relatively hypoxia involving cochlea as in atherosclerosis, genetically weak antioxidant defence system. Supplementation with antioxidants in laboratory animals have been shown to slow the AHL progression.^[16]

Brainstem Auditory Evoked Response is routinely used in clinical practice to evaluate the function of Auditory Pathways in the Brainstem, which depicts and locates exact loss of unmyelinated fibers during the course of disease.

Brainstem auditory evoked potentials (BAEP) are short-latency potentials recorded from the surface of the head during a brief acoustic stimulation. These potentials which consist of a series of positives and negatives waves recorded within 10 ms of the stimulus onset, are routinely used in clinical practice to evaluate the function of the auditory nerve and auditory pathways in the brain stem.^[17]

Brainstem Auditory Potentials and Parkinson's disease: Studies of Brainstem Auditory Potentials in Parkinson's disease auditory function were variable. Carmine Vitale et al.^[18] found normal latencies but M.J. Gawel et al.^[19], Süleyman Yılmaz et al.^[20], Fradis et al.^[21] and Daniel et al.^[22] have reported prolonged Brainstem Auditory Response whereas Prasher et al.^[23] found no significant difference between PD with healthy controls. The aim of this study was to evaluate the Brainstem Auditory Evoked Response in patients with Parkinson's disease.

BERA results across various studies were varying. All the BERA studies were on small sample size. Only Yılmaz et al studied both BERA and PTA in 20 PD patients and 24 controls. There has been no study on a purely younger cohort of PD patients. The limited number of studies on hearing assessment in PD patients especially with confounding factors of presbycusis, paves the way for further targeted research into this aspect of non-motor symptoms.

METHODS

The present study was done in the Neurophysiology Lab of Department of Physiology, Jawaharlal Nehru Medical College and Hospital, AMU, Aligarh. Informed consent (in accordance with the NINDS & NIMHANS, Bangalore) was taken from the Patient Group (PD) and Controls Group (CG) for participation in the study with approval of Institutional Ethical Committee. In this study 30 subjects (18 males and 12 females) with Parkinson's disease. And same number of healthy age-matched subject control group was assessed. Age of Control Group was 61.2±11.6 and of Test Group 61.7±10.4. A complete & detailed neurological

examination was performed in all individuals and clinically evaluated the deficit in Central Nervous System (Sensory & Motor). The Parkinsonian patients were staged according to Hoehn and Yahr's classification and diagnosed according with United Kingdom Parkinson's Disease Society Brain Bank Diagnostic Criteria for Parkinson's Disease. Recordings of BAERs were performed with Neurostim Plus software of Medicaid Company. In both the groups, in each case (Control & Parkinson's disease) we performed the Brainstem Auditory Evoked Response; the recordings were plotted for statically analysis using, appropriate statistical tests with the help of SPSS 17.0 for Windows Software

RESULTS

BAER FINDINGS

BAER was recorded in 30 PD patients. Taking the standard cut off for BAER latencies, there was abnormal latencies in Parkinson's Disease Group (PD). Among the PD Group nine had prolongation of latencies of wave IV and prolonged interpeak latencies III- V bilaterally. The other case had prolonged latencies of wave III, IV, V and prolonged interpeak latencies III- V. Among the controls one subject had prolonged latencies of III, IV, and V in right ear, and the other subject had prolonged latencies of wave V and prolonged interpeak latencies III-V bilaterally. Both the cases and controls with abnormal latencies had sensorineural hearing impairment.

Carmine et al¹⁸ observed that in PD patients, hearing impairment was more common in the elderly and in males. It was noted that PD patients with hearing impairment were of higher H and Y stage. There was no effect of duration of the disease, and side of onset of PD.

DISCUSSION

The BAER is an objective way of eliciting Brainstem Potentials in response to Audiological click stimuli. There are five well described waves in the auditory evoked responses; the corresponding anatomical localization are as described earlier (Table 1)

Prolonged wave latencies would help localize the site of involvement. The results of BERA in PD patients have been varying across various studies (Table 3). The delay in latencies of Waves III, IV, V and IPL III-V, which we founded (Table 4), is indicative of a central conduction delay at the brainstem-to-midbrain level.

Hypothesis for mechanism of hearing impairment: The localization of site of auditory impairment in PD cases is debatable. Alpha synuclein has been demonstrated in the inner ear and the alpha synuclein dysfunction could which could possibly explain a peripheral mechanism of hearing loss.^[24,25] Studies showing prolonged peak latencies postulated that there the involvement of the central auditory pathways. There are studies of brain perfusion SPECT and fMRI showing basal ganglia involvement on auditory stimulation. Outputs from basal ganglia are directed to the inferior colliculus, medial geniculate nucleus, and temporal cortex.^[26-29]

Table 1: WAVE and its origin along the course of Auditory Pathway

| WAVE | ORIGIN |
|------|-----------------------------------|
| I | COCHLEAR NERVE |
| II | DORSAL & VENTRAL COCHLEAR NUCLEUS |
| III | SUPERIOR OLIVARY COMPLEX |
| IV | NUCLEUS OF LATERAL LEMNISCUS |
| V | INFERIOR COLLICULUS |
| VI | MEDIAL GENICULATE BODY |
| VII | AUDITORY RADIATION(CORTEX) |

Table 2: Mean Latencies of Individual Waves and Inter-Peak

| WAVE LATENCY (MS) | CHIPPA ET AL. | MISRA & KALITA |
|-------------------|---------------|----------------|
| I | 1.7 ± 0.15 | 1.67 ± 0.17 |
| II | 2.8 ± 0.17 | 2.78 ± 0.21 |
| III | 3.9 ± 0.19 | 3.65 ± 0.22 |
| IV | 5.1 ± 0.24 | 5.72 ± 0.3 |
| V | 5.7 ± 0.25 | 5.72 ± 0.3 |
| I – III IPL | 2.1 ± 0.15 | 1.99 ± 0.25 |
| III – V IPL | 1.9 ± 0.18 | 2.08 ± 0.3 |
| I – V IPL | 4.0 ± 0.23 | 4.04 ± 0.225 |

Table 3: BERA based studies in PD patients

| Findings | Subject number | Parameters | Conclusion |
|----------------------|-------------------------------------------------------------------|------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Gawel (1981) | PD – 20 Controls – 24 | BERA | Prolonged latency of V in PD patients (p < 0.005) |
| Prasher (1986) | PD – 20 Controls – 32 | BERA | No significant difference compared with healthy controls. |
| Fradis (1988) | PD – 18 treatment withheld ,17 on levodopa Controls – 60 | BERA | In PD with withheld Levodopa, there is prolonged I-III, III-V, I- V latencies versus controls Prolonged III-V latencies in PD with treatment withheld versus treatment not withheld. |
| Yylmaz (2009) | PD – 20 Controls - 24 | BERA | Prolonged latencies of V and I-V in PD. (p < 0.05) |
| Carmine Vitale(2012) | PD-118 | BERA | Normal Waves and Latencies |
| Daniel (2013) | PD – 34 Controls – 29 | BERA | Prolonged latencies of II, III, IV, V, III-V in PD. (p < 0.05) |

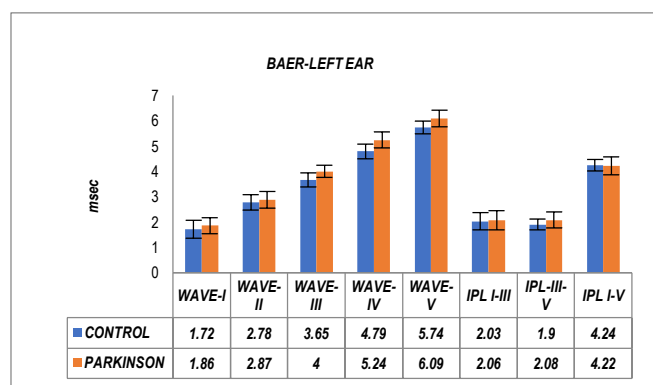
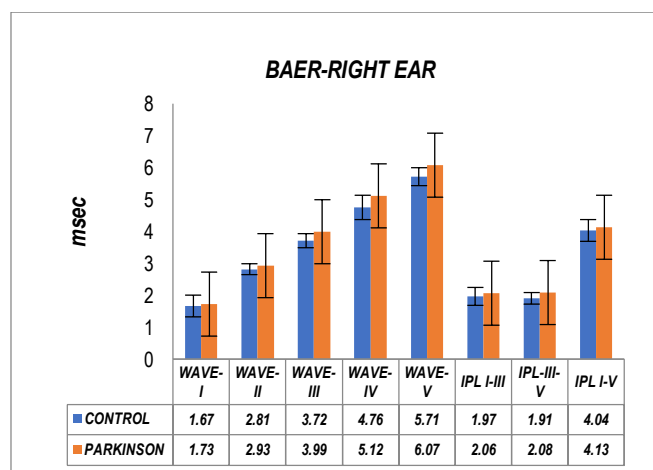
CONCLUSION

Hearing impairment is an under-recognized non-motor manifestation in Parkinson's disease (PD). There are only few studies on hearing impairment in PD. These studies reported a frequency of SNHL(Sensorineural Hearing Loss) upto 71 % in PD, but failed to account for presbycusis which is common in the elderly. The current study aimed to investigate the association of hearing impairment with PD, eliminating the potential confounders like presbycusis.

Table 4: Comparison of Control Subjects & Parkinson's disease Brainstem Auditory Evoked Response Latencies (in msec)

| BAER Latencies | Control Group Mean ±SD | Parkinson Group Mean ± SD | P value |
|------------------|------------------------|---------------------------|---------|
| RIGHT EAR | | | |
| I | 1.67±0.34 | 1.73±0.33 | 0.4907 |
| II | 2.81±0.17 | 2.93±0.32 | 0.0749 |
| III | 3.72±0.22 | 3.99±0.29 | 0.0001* |
| IV | 4.76±0.38 | 5.12±0.34 | 0.0003* |
| V | 5.71±0.28 | 6.07±0.29 | 0.0001* |
| I-III | 1.97±0.28 | 2.06±0.32 | 0.2511 |
| III-V | 1.91±0.18 | 2.08±0.34 | 0.0187* |
| I-V | 4.04±0.34 | 4.13±0.55 | 0.4489 |
| LEFT EAR | | | |
| I | 1.72±0.35 | 1.86±0.32 | 0.1113 |
| II | 2.78±0.30 | 2.87±0.33 | 0.2736 |
| III | 3.65±0.28 | 4.00±0.25 | 0.0001* |
| IV | 4.79±0.29 | 5.24±0.32 | 0.0001* |
| V | 5.74±0.25 | 6.09±0.32 | 0.0001* |
| I-III | 2.03±0.34 | 2.06±0.38 | 0.7484 |
| III-V | 1.90±0.22 | 2.08±0.32 | 0.0138* |
| I-V | 4.24±0.22 | 4.22±0.36 | 0.7961 |

*Significant (P<0.05)



The BAER was abnormal only in a majority of patients. There was significant association of hearing impairment with especially in males, duration of illness, H and Y stage. SNHL was present in all patients with familial PD, though the sample size was too small to detect a statistically significant association. The limitation was that auditory evaluation was restricted only to BERA.

The delay in the central conduction time in PD may be related to the neurodegenerative changes occurring in these patients. Although many parkinsonian patients had asymmetric clinical manifestations, there were no differences between the left and right ear. Also, the age of patient or duration of disease does not correlate with the abnormalities of BAER. It is increasingly recognized that degenerating neurons in PD, such as dopaminergic neurons of the nigrostriatal pathway, do not live in isolation. These neurons receive a variety of afferents and are surrounded by a large number of non-dopaminergic neurons like GABAergic and cholinergic neurons and non-neuronal cells such as astrocytes and microglia.^[30,31] Thus, it is the current belief that the neurodegeneration in PD occurs in response to a mixture of deleterious mechanisms taking place both inside the degenerating neurons and outside the degenerating neurons. It is possible that this neurodegenerative process to affect the functionality of central auditory pathway leading to a prolongation of wave latencies and peak intervals of auditory evoked potentials. Further research into the pathophysiological mechanisms of hearing loss, both peripheral and central, are needed.

Ethical Approval: The study was approved by the Institutional Ethics Committee

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