BRAINSTEM AUDITORY EVOKED POTENTIALS IN PARKINSON'S DISEASE

Daniel Alexa[1], Laura Alexa[2], Livia Popa[3], Dan Nicolae Paduraru[4], Bogdan Ignat[1,5] Aurora Constantinescu[1,5], Doru Baltag[5], Alexandrina Rotar[5], Cristian Dinu Popescu[1,5]

[1]University of Medicine and Farmacy "Gr.T. Popa", Iasi
[2]Arcadia Hospital, Iasi
[3]Center for Diagnostic and Treatment Euromedic, Iasi
[4]University of Medicine and Pharmacy "Carol Davila", Bucharest
[5]Rehabilitation Hospital, Iasi

ABSTRACT

Background. Parkinson's disease is a neurodegenerative disorder caused by loss of dopaminergic neurons in the substantia nigra, but also in other dopaminergic and nondopaminergic areas of the brain and mainly in the brainstem. Auditory evoked potentials are routinely used in clinical practice to evaluate the function of the auditory nerve and auditory pathways in the brainstem. The aim of this study was to investigate the auditory brainstem pathways in patients with Parkinson disease.

Materials and methods. In this study was included 34 patients with Parkinson's disease. The control group was composed of 29 healthy age- and sex-matched subjects. Detailed examination were performed in all individuals and the parkinsonian patients were stage between 2 and 4 according to Hoehn and Yahr's classication. Recordings of BAEPs were performed with Nihon Kohden Neuropack using 80 dB HL alternating polarity clicks in each ear at a rate of 10 s-1.. Averaged potentials to 1,000 clicks were obtained.

Results. The BAEP results were interpreted for the latencies of waves I, II, III, IV, V and Interpeak Latencies (IPL) I-III, III-V and I-V. The results of our study have shown that the waves II, III, IV, V and IPL III-V were significantly delayed bilaterally. This modifications does not correlates with the age or duration of disease

Conclusion. This study showed some modifications of auditory evoked potentials wich can be determined by the neurodegenerative process that affects the brainstem.

Key words: Parkinson disease, auditory evoked potentials, auditory pathways

INTRODUCTION

Parkinson's disease (PD) is a common adult-onset neurodegenerative disease characterized by the relatively selective death of neuronal subtypes, notably those of the nigrostriatal dopaminergic pathway. However, damage is not restricted to these structures but there is multifocal involvement of the central, peripheral and autonomic nervous system and other organs associated with widespread occurrence of Lewy bodies and dystrophic Lewy neurites. The vast majority of the neurons lost or displaying signs of pathology in early- and mid-stage PD patients are found in the brainstem. Levy pathology and cell loss have been reported in the region of the dorsal motor nucleus of vagal nerve, the medullary reticular formation, the raphe nuclei, the locus coeruleus, the pedunculopontine nuclei, the substantia nigra pars compacta, and, to a lesser extent, the ventral tegmental area and retrorubral area. (1,2)

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. (3) Brainstem auditory evoked potentials (BAEPs) of Parkinson patients are reported by a number of authors. Some of them found normal latencies in

Author for correspondence:
Daniel Alexa, MD, University of Medicine and Farmacy "Gr.T. Popa", 16 Universitatii Street, Zip Code 700115, Iasi, Romania
e-mail: alexadaniel2004@yahoo.com

BAEPs and some investigators have reported prolonged auditory brainstem responses (ABRs) (4,5,6). The aim of this study was to investigate the auditory brainstem pathways in patients with Parkinson disease.

MATERIALS AND METHODS

In this study was included 34 patients with Parkinson's disease, diagnosed according with United Kingdom Parkinson's Disease Society Brain Bank Diagnostic Criteria for Parkinson's Disease. Exclusion criteria were: present or past audiological diseases and a family history of otological disorders; concomitant neurological diseases or other medical disorders known to negatively affect hearing function and the ABRs (ie, cardiovascular diseases, hyperlipidemia, diabetes, vasculitis, polyneuropathy due to other diseases, multiple sclerosis); and clinical features consistent with a diagnosis of atypical parkinsonism, such as multiple system atrophy, progressive supranuclear

palsy, and corticobasal degeneration. The control group was composed of 29 healthy age- and sex-matched subjects. Detailed examination were performed in all individuals and the parkinsonian patients were stage between 2 and 4 according to Hoehn and Yahr's classication.

Brainstem auditory evoked potentials study was done in a semi-dark room with quiet surroundings. The subjects were made to sit comfortably in a chair, whose back was turned towards the recording machine. The participants were asked to avoid unnecessary movement and to remove all the metallic ornaments that they were wearing. Recordings of BAEPs were performed with Nihon Kohden Neuropack using 80 dB HL alternating polarity clicks in each ear at a rate of 10 s-1. Masking white noise (40 dB) was delivered to the unstimulated ear. Averaged potentials to 1,000 clicks were obtained. Percutaneous silver disc electrodes were used and the active electrodes were placed at the left and right ear lobes (A1, A2), reference electrode was placed at vertex (Cz position of the 10-20 International system of EEG electrode placement), while the ground electrode was placed on the scalp, in the midline frontal location (Fz position of 10-20 system). Electronic impedance was kept below 5KOhms. Two or more responses were obtained for both the ears separately, to show replicability. The BAEP results were interpreted for the latencies of waves I, II, III, IV, V and Interpeak Latencies (IPL) I-III, III-V and I-V.

RESULTS

The 34 participating patient's median age was 55 (interquartile range[IQR] 45.5 to 67.5), with a median disease duration of 8 years (IQR 5 to 12.5). The most patients were male (n=19). Patients were in Hoehn & Yahr stage 2 (n=19), 3 (n=10) and 4 (n=5). The data was analyzed statistically by using modules of MedCalc softwere. In this purpose there was done statistical description of samples to obtain descriptors of interest and checking normality of data distribution. Data were statistically analyzed using MedCalc software modules working. For statistical analysis were applied Student t-test for independent samples with equal variances, Student t-test for independent samples with unequal variance and Mann-Whitney test.

***TABLE 1**. Comparison of brainstem auditory evoked potentials latencies (in msec) between Parkinson and control subjects*

BAEP latencies	Control Group Mean ± SD	Parkinson Group Mean ± SD	*P* value Two-tailed probability
Right ear			
I	1.69 ± 0.35	1.93 ± 0.32	0.1920
II	2.71 ± 0.39	2.96 ± 0.28	0.0372*
III	3.71 ± 0.30	3.99 ± 0.28	0.0072*
IV	4.77 ± 0.37	5.24 ± 0.33	0.0004*
V	5.61 ± 0.29	6.07 ± 0.29	< 0.0001*
I-III	1.99 ± 0.26	2.07 ± 0.26	**0.4490**
III-V	**1.92 ± 0.16**	2.06 ± 0.34	**0.0277***
I-V	**3.92 ± 0.33**	**4.13** ± 0.50	**0.1422**
Left ear			
I	1.73 ± 0.32	1.87 ± 0.30	0.1850
II	2.70 ± 0.30	2.90 ± 0.26	0.0431*
III	3.75 ± 0.28	4.00 ± 0.25	0.0091*
IV	4.79 ± 0.36	5.24 ± 0.42	0.0017*
V	5.64 ± 0.18	6.09 ± 0.37	0.0002*
I-III	2.03 ± 0.32	2.18 ± 0.31	**0.1589**
III-V	1.89 ± 0,20	2.10 ± 0.33	**0.0318***
I-V	**3.92 ± 0.342**	**4.28 ± 0.38**	**0.1054**

**Significant (P<0,05)*

***TABLE 2**. Comparison of brainstem auditory evoked potentials latencies (in msec) between the right and left ear in parkinsonian patients*

BAEP latencies	Right ear Mean ± SD	Left ear Mean ± SD	*P* value Two-tailed probability
I	1.93 ± 0.32	1.87 ± 0.30	0.5291
II	2.96 ± 0.28	2.90 ± 0.26	0.5418
III	3.99 ± 0.28	4.00 ± 0.25	0.9340
IV	5.24 ± 0.33	5.24 ± 0.42	0.9746
V	6.07 ± 0.29	6.09 ± 0.37	0.8592
I-III	2.07 ± 0.26	2.18 ± 0.31	0.2724

BAEP latencies	Right ear Mean ± SD	Left ear Mean ± SD	*P* value Two-tailed probability
III-V	2.06 ± 0.34	2.10 ± 0.33	0.7633
I-V	4.13 ± 0.50	4.28 ± 0.38	0.3426

None of the differences between any of the latencies is statistically significant (P>0,05)

***TABLE 3**. Pearson's correlation between the brainstem auditory evoked potentials latencies, duration of disease and the age of patient*

BAEP latencies	Control Group Age	Parkinson Group Age	Duration disease
Right ear			
I	**0.2749**	**0.1363**	**0.3074**
II	**0.7668**	**0.1191**	**0.0854**
III	**0.1517**	**0.6890**	**0.2649**
IV	**0.3614**	**0.7114**	**0.4767**
V	**0.3742**	**0.8969**	**0.4760**
I-III	**0.5634**	**0.1466**	**0.9006**
III-V	**0.0885**	**0.7429**	**0.1389**
I-V	**0.7349**	**0.3206**	**0.2863**
Left ear			
I	**0.8387**	**0.1839**	**0.3480**
II	**0.7630**	**0.3923**	**0.5614**
III	**0.1966**	**0.8664**	**0.4910**
IV	**0.2521**	**0.9100**	**0.6678**
V	**0.5902**	**0.9036**	**0.4685**
I-III	**0.3619**	**0.5545**	**0.4565**
III-V	**0.1935**	**0.7442**	**0.1391**
I-V	**0.9194**	**0.4307**	**0.5152**

None of the differences between any of the latencies is statistically significant (P>0,05)

As seen in Table 1 patients with Parkinson's disease showed significantly increased latencies in wave II, III, IV, V compared with control subjects ($P < 0.05$) but there was not significant difference in peak latencies in wave I. As well, there was a significant increase in III–V IPLs for PD patients when compared with control subjects ($P < 0.05$) although no significant differences were noted in I–III or I–V IPLs. This modifications are not influenced by age or duration of disease as is shown in Table 3.

DISCUSSIONS

BAEP waveforms include a series of fluctuant farfield potentials occurring during the first 10 ms following a transient acoustical stimulation. They reflect synchronous activity of auditory cells populations. Structures which generate wave I are spiral ganglion cells of the cochlea. Wave II is generated by the cochlear nucleus cells. The globular cells of the posterior part of the anteroventral cohlear nucleus and of the anterior part of the posteroventral cohlear nucleus are the main cell population involved in wave II generation. Waveform III originates both from cochlear nucleus and contralateral superior olivar complex cells. In the cohlear nucleus, spherical cells of the anterior part of the anteroventral cohlear nucleus generate a part of wave III whereas in the contralateral superior olivar complex, principal cells of medial nucleus of trapezoid body contribute to wave III generation. Ipsi and contralateral cells of the superior olivar complex participate in wave IV generation with medial superior olivar principal cells identified as wave IV generators. Cellular generators of wave V are located in the lateral lemniscus and:or the inferior colliculus. The neurotransmitter of these neurons are glutamat with excitatory effect and GABA or glycin with inhibitory effect. (1)

The results of our study have shown that the waves II, III, IV, V and IPL III-V were significantly delayed bilaterally. The latency of wave I were found to be comparable between both the groups, indicating that the auditory nerve transmission is normal in patients with PD. On the other hand, the delay in latencies of waves III, IV, V and IPL III-V, I-V that we founded is indicative of a central conduction delay at the brainstem-to-midbrain level. The delay in the central conduction time in PD may be related to the neurodegenerative changes occurring in these patients. Although the majority of parkinsonian patients had asymmetric clinical manifestations, there were no differences between the left and right ear as we can see in table 2. Also, the age of patient or duration of disease does not correlates with the abnormalities of BAEP.

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 nondopaminergic neurons like GABAergic and cholinergic neurons and nonneuronal cells such as astrocytes and microglia. (7,10) 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.

CONCLUSIONS

This study showed some modifications of auditory evoked potentials wich can be determined by the neurodegenerative process that affects the brainstem

This modifications are not influenced by the duration of disease or the age of subjects

The auditory system is involved equally on the both sides, regardless the asymmetry of motor manifestation

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