Turkish Journal of Endocrinology and Metabolism, (1999) 1 : 29-32 **ORIGINAL ARTICLE**

Brainstem Auditory Evoked Potentials in Patients with Type 2 Diabetes Mellitus

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The concept of central diabetic neuropathy has been described in the recent years. Peripheral and autonomic nervous system involvement in type 2 diabetes mellitus is evidenced by numbers of studies while evidence of central involvement in diabetes is scarce.

Evoked potentials can be used to central diabetic neuropathy. Of these, brainstem auditory evoked potential (BAEP) studies have come to the fore. In this study, BAEP responses of the 126 diabetic patients were compared to those of a control group of 30 (age and sex-matched) healthy subjects.

In the diabetics, latencies of waves I, III and V together with interpeak latencies I-III and I-V were found to be significantly more prolonged than those of controls.

Results were evaluated in wiew of literature knowledge and it was concluced that BAEPs might be a useful diagnostic tool in detecting central diabetic neuropathy.

KEY WORDS **Brainstem auditory evoked potentials, diabetes mellitus, central neuropathy**

Introduction

In the literature, although there are few studies on neuropathology it has been known since the 19 th century that in diabetics disorders caused by vascular and metabolic involvements take place in many organs (1).

Central diabetic neuropathy is a never concept and it can be detected by simple and noninvasive methods. One of these methods is brainstem auditory evoked potentials (BAEP) and interpretations of them (2,3). By this method, functional and autonomic pathologies from the acustic nerve to the upper part of the brainstem can be demonstrated at an early stage (3). Lesions on these levels result in changes in BAEP amplitudes and latencies. Evaluation of these changes might help to determine early subclinic injuries restricted to the afore mentioned regions (4).

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Materials and Methods

This study was performed in the electrophysiology laboratories of the Neurology Department of Selçuk University Medical Faculty on 126 type 2 diabetic patients (54 female and 72 male) aged 18-72 years, who were followed up by the Endocrinology and Metabolic Disorders Department. The illness interval of the diabetic patients was between 1-10 years. A control group was formed from 30 people with similar sex and age distribution. Neither group showed any central neuropathology. There was no subjective symptom which showed an auditory pathology in either the diabetics patients or the control groups. Also, neurological examination including Weber and Rinne tests was normal.

In the brainstem auditory evoked potentials (BAEP) study, subjects were in a supine position on the examination desk. Active electrodes were attached to A1 and A2 points, reference electrode to Cz, soil electrode into Fz points (Figure 1). Recordings were done by monoaural stimulation by giving 90 dB stimulation to both ears and 40 dB masking

rumbling sound to the contralateral ear. The duration of analysis was 10 msc and frequency range was 300-3000Hz. 2000 stimulations were applied to both ears and the average of them was accepted as BAEP response (Figure 2). The results of the patients and control groups were analysed statistically by using student's t-test.

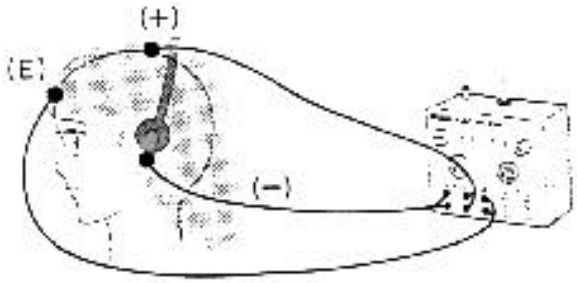

Figure 1. Electrode placement. Active (+): Vertex 'Cz' of the international "10-20" system, Reference (-): Earlobe, A1 left, A2 right, Ground: Forehead.

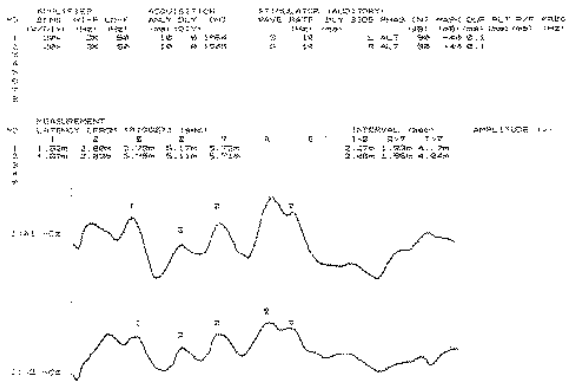

Figure 2. The BAEP found in a diabetic patient.

Results

Table 1 and 2a, 2b show statistical analysis of age, sex, blood glucose levels, HbA1C and blood pressure (mm Hg) of the patients and control group and BAEP latency averages. The amplitude was a changeable parameter, so it was not taken into consideration.

As seen in Table 2a, in diabetics, especially in the first wave latency ($p>0.01$), IIIrd ($p<0.05$) and Vth (0.01) wave latencies are longer than in the control group. In addition, we found that interpeak latencies of I-III, III-V and I-V (Table-2b) were longer than those of the control group ($p<0.05$).

There was no significant correlation between the duration of diabetes, blood glucose levels and the latencies (Table 3a,b).

Table 1. The distribution of the cases according to age and sex, blood glucose levels and HbA1C.

	Patient group	Control group
Age distribution	18-72	21-69
Age average	40.20±15.82	39.41±10.36
Sex (F,M)	54/72	13/17
Blood glucose levels	186±62	104±12
HbA1C	8.1±0.8	6±1.2
Blood pres. diastolic systolic	140±14-92±10	135±16-90±8
n	126	30

Table 2a. The statistical analysis of BAEP values obtained by a 90 dB stimulation of diabetic and control groups.

	Latence (mm./sc.)		
Waves	I	III	V
Patients (n: 126)	1.7075±0.190	3.8833±0.1750	5.8712±0.333
Controls (n: 30)	1.5859±0.1245	3.7520±0.1708	5.5565±0.2259
p	<0.001	<0.05	<0.01

Table 2b. The statistical analysis of BAEP values obtained by a 90 dB stimulation of diabetic and control groups.

	Interpeak latence (mm./sc.)		
Waves	I-III	III-V	I-V
Patients (n: 126)	2.2133±0.2245	2.04±0.2059	4.2373±0.310
Controls (n: 30)	2.1382±0.1729	1.9041±0.2076	4.0252±0.220
p	<0.05	>0.05	<0.05

Table 3a. The statistical analysis of blood glucose levels and latencies of BAEP waves in diabetics.

	Latence (mm./sc.)		
Waves	I	III	V
* 150 mg/dl ↓ (n: 49)	1.8210±1.0065	3.8490±0.110	5.8600±0.124
* 150 mg/dl ↑ (n: 87)	1.6900±0.1200	3.8176±0.180	5.7424±0.240
p	>0.05	>0.05	>0.05

* Blood glucose levels

Table 3b. The statistical analysis of the duration of diabetes and latencies of BAEP waves in diabetics.

	Latence (mm./sc.)		
Waves	I	III	V
1-5 year	1.6800±0.1820	3.8640±0.176	5.850±0.120
5-18 year	1.7355±0.195	3.919±1645	5.891±0.150
p	>0.05	>0.05	>0.05

Table 4. The structures of waves arising in BAEP.

Wave	I	II	III	IV	V
Origination structures	Acoustic nerve	Cochlear nucleus	Sup. olivery nucleus	Inferior brainstem	Superior brainstem

Discussion

Central and peripheral nerve damage in diabetes may be related to the microangiopathy of diabetes. In diabetes small precapillaries and capillaries develop thickened basement membranes which may interfere with their function (5). The second major metabolic derangement that may be involved in the development of diabetic neuropathy is the accumulation of alcohol sugars sorbitol and fructose. Conceivably, an excessive accumulation of alcohol sugar in the nerves might similarly damage nerve structures (5,6). Diabetic neuropathy may be due to a deficiency of myoinositol in the nerve. Nerve myoinositol levels are decreased by galactose feeding and in Wallerian degeneration (5,7).

That metabolic and vascular complications of diabetes causing multi-organ failure is a well known feature of the disease but the central nervous system changes were not mentioned in the literature until the second half of the 19th century. De Jung was first to make the description of diabetic encephalopathy. Later on, postmortem examination by Reske et al. disclosed leptomeningeal thickening, cortical gliosis, degenerative changes of the brainstem and cerebellum with axonal degeneration and demyelination of cranial nerves.

The functions of the 6th nerve are relevant to hearing and equilibrium. Makashima and Tonoka have also observed cochlear atrophy and demyelination of the 8th cranial nerve (7). Kan and Surenson reported vasculer changes in the cochlear and vestibular nucleus in the postmortem experiments on a diabetic patient who had vertigo and deafness (8).

There is little information about the vestibular function and central neuropathy in diabetics. In addition, it is thought that microangiopathy, orthostatic hypotension, complications of diabetes, sorbitol accumulation or electrolyte imbalance may cause central neuronal ischemia. As an addition the peripheral part of the vestibular system may be affected directly by acustic internal arter microangiopathy (6-9).

In past clinical studies, electroencephalography was used to explore the changes in electrocortical activity. But, by applying this method, it is impossible to obtain information on deep brain structure. In evoked potential studies used in recent years, it becomes possible to have detailed and adequate information on the central nervous system. Brain auditory evoked potantial is a useful investigation method in order to explore the early subclinical neurologic dysfunctions in metabolic disorders.

In order to evaluate acoustic nerve function clinically, Weber and Rinne tests are used. In laboratory conditions, audiogram and brain audotory evoked potential can be used. In audiogram, cooperation of the subject and external conditions effect the results and may give false results (10) That audiogram cannot give information about brainstem pathology is its further disadvantage. But in brain auditory evoked potential the cooperation of the subject and it has a simple technique to apply even subject is not needed and it is a simple technique to apply even to subjects who are asleep or in a coma. It is not affected by external conditions (2,4).

BAEP study relies on the measurement of latencies and amplitude of waves arising after giving a sound higher than the hearing threshold (3). An auditory stimulus delivered to the ear evokes consecutive stimulation of brainstem structures such as the cochlear nucleus and tracts of the lateral lemniscus and inferior colliculus. Localizations and latencies from which waves originate are seen in Table 4. Consecutive waves on a BAEP pattern from I to V reflect the electrical activity of the acustic nerve, cochlea, superior olives, lateral lemniscus, and inferior colliculus respectively (3,11). Patologies on this pathway from the

acoustic nerve to the mesencephalic may result in decreasing amplitude, lengthening of the latency or absence of the wave. Amplitudes were not taken into consideration because of their wide range of variability (11).

In this study, we found a longthening in I, III and V wave latencies and I-III and I-V interpeak latencies in patients compared to the control group ($p<0.05$). In III-V interpeak latency, there was minimal longthening and this was not significant statistically. Lengthening in teh first wave latency indicates that the disorder is peripheral (distal to the nucleus), whereas, lengthening in the Vth wave latency is specific for brainstem involvement (3,9). If the longthening in I-III interpeak latency occurs together with I-V interpeak latency, this indicates upper or lower brainstem pathology. Lengthening in I-III interpeak latency with normal III-V interpeak latency indicates that the pathology is in the lower brainstem or pons (3,9).

According to our results, lengthening in waves and interpeak latencies indicate that the pathology affected both the peripheral and the central nervous system structures. Some previous studies indicate similar results, and the main affected item is reported as BAEP interpeak latencies (12).

In our comparisions, there was no correlation between the lengthening in BAEP latency and metabolic control and this was compatible with the literature (13). There was a positive correlation between the duration of illness and lengthening of latency. This condition can be explained by subclinical ischemia which can develop during diabetic process (atherosclerosis, hypotension, sorbitol accumulation) (14,15).

According to these results and information in the literature, it can be suggusted that BAEP can demonstrate electrophysiologically any lesions from the acoustic nerve to the brainstem and can be used in diabetics to show subclinical variances and central neuropathy.

References

1. Martini A, Comacchio F. Auditory brainstem responses in clinical evaluation of diabetic encephalopathy. In: Evoked Potentials Neurophysiological and Clinical Aspect. (Ed. Morocitti C, Rizzo PA). Amsterdam Elsevier Science, 231-235.
2. Bergamaschi R, Versino M, Callieco R. Multimodal evoked potentials in diabetics. *Acta Neurol* **13 (3):** 228-235, 1991.
3. Chippa KH, Ropper HA. Evoked potentials in clinical medicine. *N Eng Med* **306:** 1140-1150, 1982.
4. Spehlman R. Evoked potential primer. Boston, Butterworth Publisher, 1987, 204-207.
5. Dick P, Low PA, Stewans JD. Diseases of peripheral nerves. Clinical Neurology. (Ed: Joynt RJ). Philadelphia JP Lippincott comp, 1982, 71-73.
6. Partenen J, Niskanen L, Lehtinen J, Mervaala E, Sıttanen O, Uusitura M. Natural history of peripheral neuropathy patients with non-insulin dependent diabetes mellitus. *N Eng Med* **333(13):** 89-93, 1995.
7. Reske Nielsen E, Lundbaeck K, Rafaelsen OJ. Pathological changes in the central and peripheral nervous system of young long-term Diabetic. *Diabetologia* **1:** 233-241, 1996.
8. Bosch EP. Disorders of peripheral neuropathy. Neurology Clinic Practice. 2. edition (Ed.Bradly GW, Daroff RB. Feniche GM). Boston, William-Wilkins, 1996, 1881-1952.
9. Kukichi S, Kaga K, Yamasoba T et all. Slow blood flow of the vertebrobasiler system in patients with dizziness and vertigo. *Acta Otolaryngol* **113(3):** 257-60, 1993.
10. Becker W, Naumann HH, Pfaltz CD. Kulak Burun Boğaz Hastalıkları (Çev. Bahbur Cevanşir) 1. baskı, İstanbul Cem Ofset, 1993.
11. Stockard JJ, Pope-Stockard JE, Sharbrrough FW. Brainstem auditory evoked potentials in neurology. Electrodiagnosis in Clinical Neurology. (Ed. Aminoff MJ) 3. edition. Boston, Churchill Livingstone, 1992, 503-536.
12. Broohler KH, Rubin W. Practical method of reporting test result in neurootologic disorders. *Am J Otol* **12(5):** 347-9, 1991.
13. Alexander M, Mohan PK,. Prolonged brainstem auditory evoked potential latencies in pancreatic diabetics with normal hearing. *Electromyogr Clin Neurophysiol* **35(2):** 95-8, 1995.
14. Martini A, Comacchio F, Fedele D. Auditory brainstem responses in clinical evaluation and follow up of insulin dependant diabetic subjects. *Acta Otolaryngol* **103:** 620-627, 1987.
15. Pozzessere G, Rizzo PA, Valle E.Early detection of neurologycal involvement in IDDM and NIDDM. Multimodal evoked potentials versus metabolic control. *Diabetes* **11(6):** 473-480, 1988.