Clinical Value of Brainstem Auditory Evoked Potential in the Diagnosis of Vertebrobasilar Ischemia

Xiao-Jing Zhang, Li-Jun Zhang, Jing Zhu, Min He, Ze Wang, Jun Wang, Min-Jian Zhang, Fang-Li Li, Jian Shen, Yu Bai, Ji-Wei Cheng

Departments of Brain Function, Neurology, ENT, Traditional Chinese Internal Medicine and General Internal Medicine, Putuo Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, China

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Vertebrobasilar ischemia · Brainstem auditory evoked potentials

Abstract
Objective: The objective of this study was to explore the clinical value of brainstem auditory evoked potential (BAEP) in the diagnosis of vertebrobasilar ischemia (VBI). Methods: The subjects were divided into the 2 following groups: an observation group of 300 VBI patients and a control group of 100 normal healthy volunteers. BAEP examination was carried out in both groups, and then the results were analyzed and compared. Results: BAEP abnormalities were observed in 59% (177 out of 300) of the patients in the observation group: brainstem type 64.4% (114 cases), inner-ear type 7.4% (13 cases), and mixed type 28.2% (50 cases). In the control group, abnormalities were observed in only 9% (9 cases): inner-ear type 66.7% (6 cases) and mixed type 33.3% (3 cases). There was a statistically significant difference between the 2 groups in their total abnormality rates (p < 0.05). After the neck twisting test, the BAEP abnormality rate of the observation group rose to 85% (255 cases) and was significantly different from that of normal BAEP (p < 0.05). Conclusion: BAEP is an easy but effective auxiliary means for the noninvasive examination of VBI with a high positive rate, thus providing objective evidence for the diagnosis of VBI that may be useful in future clinical application.

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X.-J. Zhang and L.-J. Zhang are co-first authors.
Introduction

Vertebrobasilar ischemia (VBI) refers to the occurrence of transient vertebrobasilar ischemic blood circulation disorders. Its clinical manifestations tend to disappear quickly; as a result, by the time the patient seeks medical help, the episodes are only intermittent, hence making it difficult to detect positive symptoms. Even imaging probes such as skull CT and MRI may not discover any obvious responsible foci. In recent years, there have been reports [1–4] claiming that brainstem auditory evoked potential (BAEP) has a unique diagnostic value and is able to provide objective evidence for the diagnosis of VBI. However, this has not yet been determined. Therefore, we carried out systematic BAEP examinations of 300 patients clinically diagnosed with VBI at the Department of Neurology at our hospital as well as of 100 healthy volunteers. The examination results were analyzed and compared so as to further clarify the value of BAEP in the diagnosis of VBI.

Material and Methods

Subjects

The observation group was comprised of 300 patients clinically diagnosed with VBI at the Department of Neurology at our hospital from July 2012 to June 2014. There were 146 males and 154 females aged 40–80 years (average age 60 ± 2.5 years). Among the patients, there were 89 cases with hypertension, 70 with diabetes, 56 with hyperlipidemia, 212 with cervical spondylosis diagnosed by cervical spine plain films or CT, and 195 cases with carotid or vertebral atherosclerosis or plaque formation diagnosed by ultrasonography.

The control group consisted of 100 normal healthy volunteers (48 males, 52 females, aged 38–75 years, average age 58 ± 2.3 years) selected by our hospital from July 2012 to June 2014. Among the controls, 15 cases had hypertension, 12 diabetes, 14 hyperlipidemia, 17 cervical spondylosis diagnosed by cervical spine plain films or CT, and 10 carotid or vertebral atherosclerosis or plaque formation diagnosed by ultrasonography. There were no statistically significant differences in age or gender between the 2 groups (p > 0.05; table 1).

The VBI diagnostic criteria were as follows [5]: (1) neurological deficit signs and symptoms must be located in a particular vertebral-basilar artery distribution region; (2) the onset is abrupt, will reach its peak within a few minutes and usually eases off in 24 h – in the case history, at least two brief seizures accompanied by other signs and symptoms mainly involving the brainstem should be found; (3) during the intermission between brief seizures, there should be no abnormal neurological signs and symptoms (except for patients with previous cerebral infarction); (4) at least 2–3 incidences of signs and symptoms such as complaints of dizziness, vomiting, nystagmus, ataxia, perioral numbness, difficulty in swallowing, and sudden deafness; (5) vertebral-basilar artery stenosis [6, 7] diagnosed by vertebral artery ultrasonic-B, transcranial Doppler, BAEP, or digital subtraction angiography, and (6) having ruled out systemic disease factors (low blood pressure, anemia, hematopathy, craniocerebral trauma, intracranial tumor, etc.).

Examination Methods and Criteria for Judgment

BAEP Conventional Examination Method

BAEP was performed using Keypoint 4 (Model, 33A04) Evoked Potential Equipment produced by Dantec Company in Denmark. According to the international 10-20 lead method, the reference electrode was placed on the forehead, the recording electrode was attached to the ear mastoid for sound stimuli, the ground electrode was connected to the nasal root, and skin electrode impedance was less than 5 Ω. The auditory stimulus consists of polarity-alter-
nating clicks with a frequency of 8.9 Hz and a stimulus intensity of 60 db HL. The signal was filtered and amplified. Vernier was used to measure peak latency (PL), interpeak latency (IPL) of waves I–V, and the amplitude of waves I and V.

**Neck Twisting Test**

In order to enhance the positive rate in evoked potential testing, when the conventional BAEP had been performed, we carried out the induced neck twisting test in the subjects, where the specific approach was to ask the subject to turn his/her neck to the maximum extent in both the right and left directions, while the BAEP examination was going on at the same time. Test parameters, electrode placement, and BAEP abnormality determination were identical to the conventional BAEP examination.

**Criteria for Judgment of BAEP Abnormalities [8]**

1. The absolute values of PL of waves I–V and/or IPL of waves I–III, III–V, and I–V are larger than those of the control group; (2) the wave V and I amplitude ratio (V/I) is <1 or the amplitude on one side is smaller than that on the opposite side by over 50%; (3) the IPL ratio between III–V and I–III (III–V/I–III) is >1, and (4) poor differentiation or failure to differentiate waves I, III, and V makes it difficult to measure PL or IPL. Satisfying any one of these criteria is considered abnormal.

**Statistics**

SPSS 14.0 was used to determine differences between the groups. Data are presented as means ± SD. The χ² test was used for comparison of the age and gender between the 2 groups and the t test was used to compare PL and IPL as well as the amplitudes of waves I and waves V between the 2 groups. A significant difference was set at a p value of <0.05.

**Results**

Among the 300 patients in the observation group, a BAEP abnormal rate was seen in 59% (177 cases) of the patients; the brainstem type accounted for 64.4% (114 cases), the inner-ear type for 7.4% (13 cases), and the mixed type for 28.2% (50 cases). The corresponding rate in the control group was only 9% (9 cases), of which the inner-ear type accounted for 66.7% (6 cases) and the mixed type for 33.3% (3 cases). There was a significant difference between their total abnormality rates (p < 0.05). In the observation group, the PL of waves I, III, and V, the IPL of waves I–III, III–V, and I–V, and the III–V/I–III ratio were all higher than those of the control group (p < 0.05; table 2). The amplitudes of wave I and wave V were lower than those of the control group (p < 0.05), but the difference in the V/I ratio between the 2 groups was not statistically significant (p > 0.05; table 3).

After the neck twisting test, the BAEP abnormal rate in the observation group increased to 85% (255 cases), and the difference with conventional BAEP was statistically significant.
(p < 0.05). The abnormal rate of the control group increased to 16% (16 cases), and the difference compared to conventional BAEP was not statistically significant (p > 0.05). After the neck twisting test, the amplitude of both groups decreased. The decrease was more evident in the observation group, whose amplitude of wave I and wave V was lower than that of the control group (p < 0.05; table 3).

**Discussion**

VBI is a common neurological disease with a high incidence rate. Its etiological causes are quite complicated, and because of its frequent recurrence, it can seriously affect the daily life of a patient. Owing to the fact that there is a lack of objective means of identifying the disease, its diagnosis chiefly depends on the neurologist’s clinical experience and is thus liable to result in misdiagnosis. At present, many studies have shown [1–4] that BAEP can provide objective evidence for VBI diagnosis and is of discriminating value with regard to aural vertigo and VBI. A pair of vertebral arteries runs in parallel through the transverse foramen on both sides of the cervical vertebrae, upward into the skull, where the two blood vessels converge in the brain to form the basilar artery. From the vertebral artery and the basilar artery a number of small blood vessels of various diameters come off which supply blood to the occipital lobe, cerebellum, brainstem, and thalamus as well as the inner ear and other areas. The vertebral artery and basilar arteries together with their ramification are collectively
referred to as the vertebrobasilar system. The vertebral artery is tortuous in form and hence is vulnerable to cervical impact and prone to ischemic symptoms. Due to a different range of blood supply to the affected blood vessels, VBI can be expressed variously as signs and symptoms at the midbrain, pons, medulla oblongata, and cerebellum that clinically occur as a paroxysmal manifestation. VBI onset will cause a transient shortage of blood supply in brainstem neurons and lead to an increase in ATP consumption, resulting in increased decomposition and neuronal cell polarization at the same time. There was a large influx of calcium ions into neurons, consequently damaging them, slowing down conduction, and weakening electrical activity, which are exactly the pathophysiological events that cause abnormal BAEP.

The blood supply to the inner-ear labyrinth and brainstem which is precisely the representative region of waves I, III, and V of BAEP all comes from the vertebrobasilar system. Some researchers [9–11] have reported that BAEP can sensitively reflect the functional abnormality caused by changes in blood supply to brainstem neurons and that the remission of clinical symptoms of VBI is consistent with the BAEP electrophysiological reversal. The complete BAEP comprises 7 waves, and clinical analysis mainly deals with waves I, III, and V. Wave I is involved in auditory nerve action potentials, wave II stems from the intracranial section of the auditory nerve and the cochlear nucleus, wave II I originates from the olivary nucleus of the pons, VI wave is related to the lateral lemniscus, and wave V stems from the central nuclei of the inferior colliculus of the midbrain. Thus, according to the abnormal waves the diseased site can be located. In the present study, the brainstem type accounted for 64.4% (114 cases), which mainly manifested as a normal wave I, PL of wave III and wave V being extended or with a poorly differentiated waveform, IPL of waves I–III, III–V, and I–V all being extended, and the ipsilateral V/I amplitude ratio <1. The inner-ear type accounted for 7.4% (13 cases), which mainly manifested as extended PL of wave I, with a poorly differentiated waveform and a decreased amplitude. The mixed type accounted for 28.2% (50 cases), which mainly manifested as an extension of PL of waves I, III, and V or an extension of IPL of waves I–III, III–V, and I–V. In the observation group, PL of waves I, III, and V, IPL of waves I–III, III–V, and I–V, and the ratio of III–V/I–III were all higher than those in the control group.

The BAEP diagnosis of VBI can produce a higher abnormal rate and hence has been widely used clinically. In the present study, the BAEP abnormal rate was as high as 59%, and the abnormal rate after the neck twisting test increased to 85%, which corroborates the relevant literature [3–5, 8, 12]. After neck twisting, the cervical vertebral artery is squeezed by cervical vertebrae and its accessory tissues, resulting in poor blood flow in the vertebral artery. This causes the onset of VBI, particularly in patients suffering from combined cervical spondylopathy or carotid sclerosis, whose vertebral artery is in a poor state and, in the event of it being squeezed, is more likely to cause vascular stenosis or even occlusion, thus leading to VBI. For this reason, when checking BAEP, we try to combine it with the neck twisting test in order to enhance the positive rate of the VBI diagnosis. However, it is advisable that the neck twisting test should be performed gently and slowly in order to avoid injury to the cervical spine. For patients with severe cervical spondylosis or a spinal cord injury and who are therefore vulnerable to neck twisting, the neck twisting test should under no circumstances be forcibly performed.

In conclusion, BAEP is an easy but effective auxiliary means for the noninvasive examination of VBI with a high positive rate, thus providing objective evidence for the diagnosis of VBI and possible clinical applications. However, the BAEP diagnosis of VBI still needs to be conducted in association with iconographic examinations such as craniocerebral CT or MRI, and with the precondition of having ruled out any organic intracranial diseases such as cerebral infarction, cerebral hemorrhage, and brain tumors. Only then can a diagnosis of VBI be considered.
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References