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Changes of Brainstem Auditory Evoked Responses (BAERs) in a Brain Stem Ischemic Model Using Embolization Technique in Cats, a Preliminary Study

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ABSTRACT

In order to evaluate brain stem dysfunction related to ischemic process, the authors monitored the Brainstem Auditory Evoked Responses (BAERs) with time in a brain stem ischemic model.

19 adult mongrel cats were divided into two groups: embolization (n=14) and sham operated control (n=5). Embolization was done by injecting cylindrical silicone embolus to the right vertebral artery. Each successful embolization of the basilar artery was then confirmed by vertebral angiography. BAERs were monitored before embolization and then 5-10 min, 15 min, 30 min, 60 min, 3 hr and 6 hr after embolization. The presence of ischemic lesion caused by embolization was confirmed by injecting 2% Evans blue solution 30 min before sacrificing the animals. Leakage of the dye was observed.

In embolized animals, significant (Student t test, $p<0.05$) delay of interpeak latencies of waves 1-3, 3-5, and 1-5 was observed 15 min after embolization. This delay became more significant ($p<0.01$) 30 min after embolization.

These results provide evidence for the usefulness of BAERs monitoring which can be used to complement other diagnostic methods for patients with vertebrobasilar insufficiency and/or infarction.

Key words: *Brain stem Auditory Evoked Responses, Brain stem ischemia, Embolization*

Study of neuroelectrical activity is a method of assessing central nervous system function irrespective of the presence or absence of anatomical alteration[6]. Clinically, this is particularly useful in the uncooperative, confused, or comatose patient.

Brain stem Auditory Evoked Responses (BAERs) are low voltage electrophysiological events generated from the auditory pathways in response to specific acoustic stimulation[2,6]. These responses are seen as sequential series of waves or components representing electrical activity at various levels of the auditory pathway. BAERs monitoring is non invasive and allows frequent serial studies at low risk to the patient.

In 1971, Jewett and Williston[8] introduced a technique for non invasive scalp recording of auditory evoked potentials with short latency. In 1975, Buchwald and Huang[2] reported on short latency evoked potentials recorded from the vertex of adult cats in response to click stimulation. Several authors agree[6-8,11,15] that the first five peaks of the Brain stem Auditory Evoked Responses (BAERs) most likely arise from the eight nerve, cochlear nuclei, superior olivary complex, nuclei of the lateral lemniscus and inferior colliculus respectively.

During the past several years, the monitoring of BAERs has been practiced routinely for many purposes. BAERs are especially useful for evaluating auditory function or integrity of the brain stem, as in surgery of the posterior fossa with traction of the cerebellum and/or the brain stem[3,14]. BAERs has also been used to monitor patients with clinical or radiological signs of ischemic processes of the vertebrobasilar area. BAERs even have a prognostic value in the early evaluation of patients with brain stem ischemic strokes[15]. Abnormal BAERs were found in more than 90% patients with physical evidence of dysfunction of midbrain and pontine structures[4,11]. BAERs are more reliable than CT-scan in identifying ischemic process.

In order to evaluate brain stem dysfunction related to ischemic process, the authors established a brain stem ischemic model using an embolization technique in cats[13], and monitored the BAERs with time.

MATERIALS AND METHODS

19 adult mongrel cats, weighing about 2.5 and 4.0

kg were anesthetized with 30 mg/kg of sodium pentobarbital injected intraperitoneally and immobilized with 0.08 mg/kg of pancuronium bromide given intravenously.

Mechanical ventilation was adjusted so that the arterial pCO2 and pO2 remained in physiological values during the experiment. The vertebral artery was catheterized through the subclavian artery approached from the right axillary regoin. Vertebral angiography was done before embolization. The angiographic result was taken in order to determine the size of the embolus to embolize the top of the basilar artery in each cat. The cylindrical silicone emboli were 5 mm in length and 0.60, 0.65, and 0.70 mm in diameter. One of those was then injected to embolize the basilar artery. Location of the embolus was confirmed by vertebral angiography 30 min after embolization[13]. In order to observe the presence of ischemic lesion caused by embolization, 2 ml/kg of 2% Evans blue solution was injected intravenously 60 min before sacrifice. The animals were sacrificed 6 hr after the embolization and leakage of the dye was observed[15].

BAERs were recorded (using Neuropack 8, Nihon Kohden Corporation) unilaterally with 90dB alternating click. Contralateral ear was masked with 30dB white noise. Pass band filter was set between 100 and 1000 Hz. 1500 responses were averaged for each recording which was set before embolization and then 5-10 min, 15 min, 30 min, 60 min, 180 min, and 6 hr after each successful embolization. The random acoustic signal, with a duration of 0.1 msec and frequency 20 Hz, was conducted to the cat's auditory canal via a 2cm long conical speaker. For recording of BAERs, needle electrodes were inserted subcutaneously in the vertex (midpoint between bregma and lambda) as an active electrode, in the forehead as a grounding electrode and in both earlobes as reference electrodes.

The animals were divided into 2 groups. A: the embolization group (n=14), and B: sham operated group (n=5). The sham operated animals were exposed to all procedures except injection of the embolus.

RESULTS

The presence of embolus in the Basilar artery was confirmed angiographically in all group A cats (Fig. 1). The embolus stopped at the vertebrobasilar junction or proximal portion of the basilar artery in 3 cats, at the middle portion of the basilar artery in 4 cats, and at the basilar top or distal portion of the basilar artery in 7 cats.

Pre-embolization interpeak latencies (IPLs) of waves 1-3, 3-5, and 1-5 in group A cats were 1.678 ± 0.095 msec (mean ± SD), 2.134 ± 0.149 msec, and 3.811 ± 0.180 msec respectively. 15 min after embolization, IPL 1-3 changed significantly (Student's t test, $p<0.05$), and IPLs 3-5 and 1-5 changed very significantly (Student's t test, $p<0.01$) (Figs. 2, 6-8). They were 1.784 ± 0.154 msec, 2.334 ± 0.252 msec, and 4.074 ± 0.301

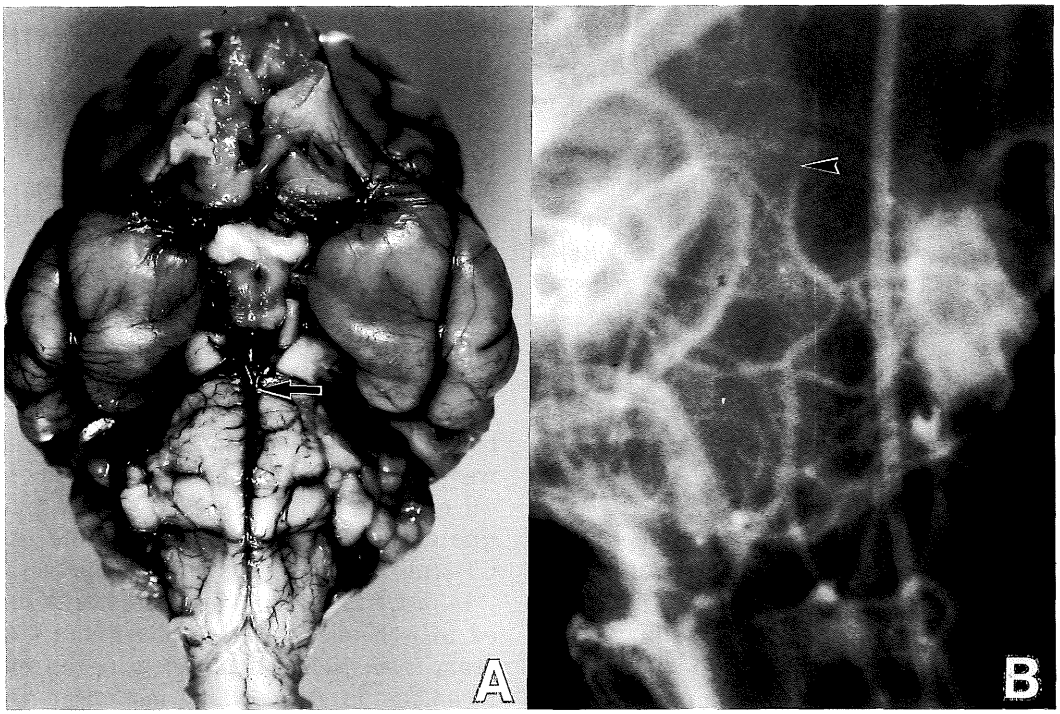

Fig. 1. A. Embolization of the basilar artery. Silicone rubber cylindrical embolus was lodged at the terminal portion of the basilar artery (arrow).
B. Vertebral angiogram of post-embolization.
The embolus stopped at the terminal portion of the basilar artery (arrow head).

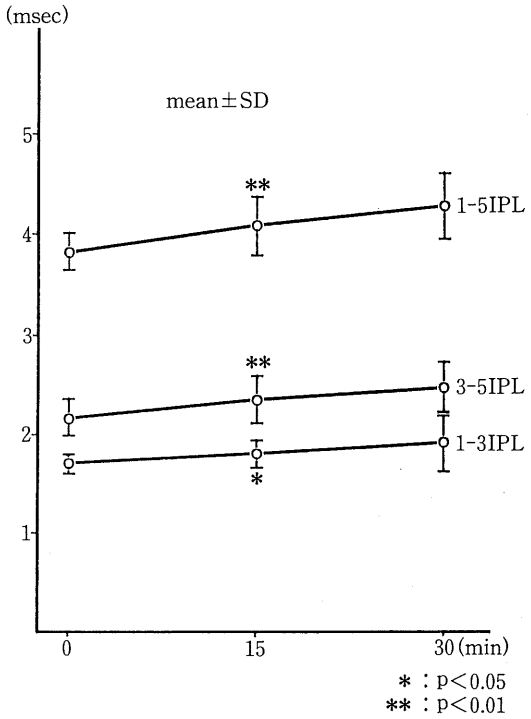

Fig. 2. Changes of interpeak latencies 1-3, 3-5, and 1-5 in embolized animals. Significant changes (Student's t test) were observed.

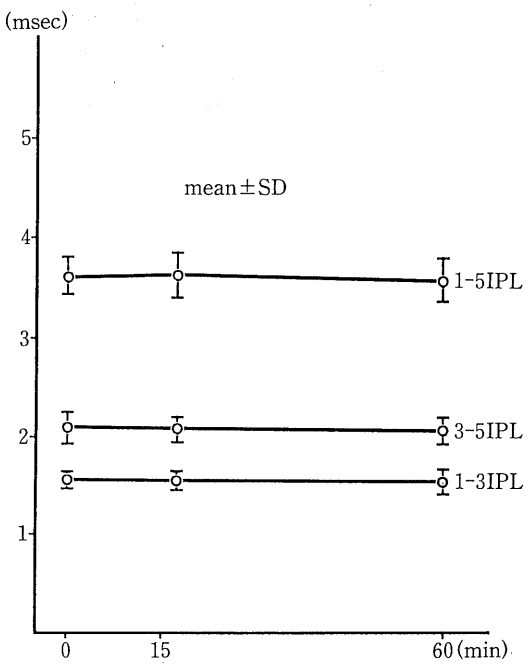

Fig. 3. Changes of interpeak latencies 1-3, 3-5, and 1-5 in sham operated animals. The interpeak latencies did not change during the experiment.

msec respectively. In group B, there was no significant change in any interpeak latencies (Fig. 3). Among all peak waves, peak V became the first to be significantly prolonged, followed by peak III, while peak I did not change significantly until the end of the experiment (Figs. 4, 6-8). After the

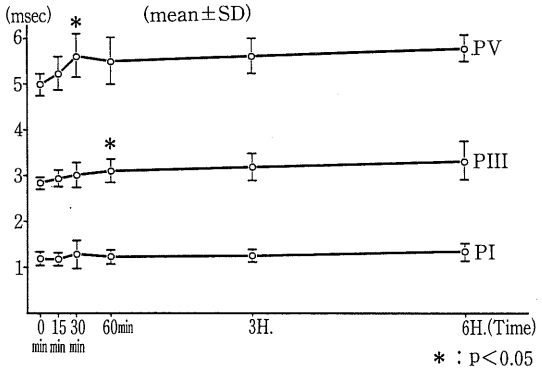

Fig. 4. Absolute latencies of peaks I, III, and V in embolization group (n=14). Significant changes (Student t test) first seen on latency of peak V and followed by peak III.

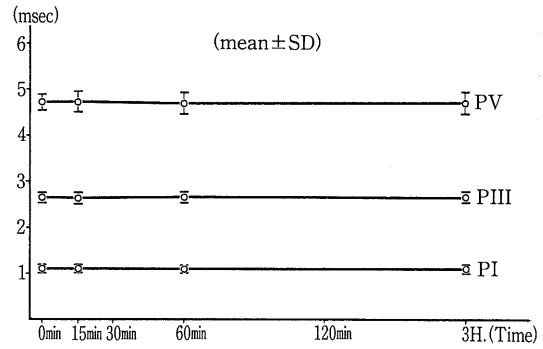

Fig. 5. Absolute latencies of peaks, I, III, and V in sham operated group (n=5). There was no significant change observed for all peak waves.

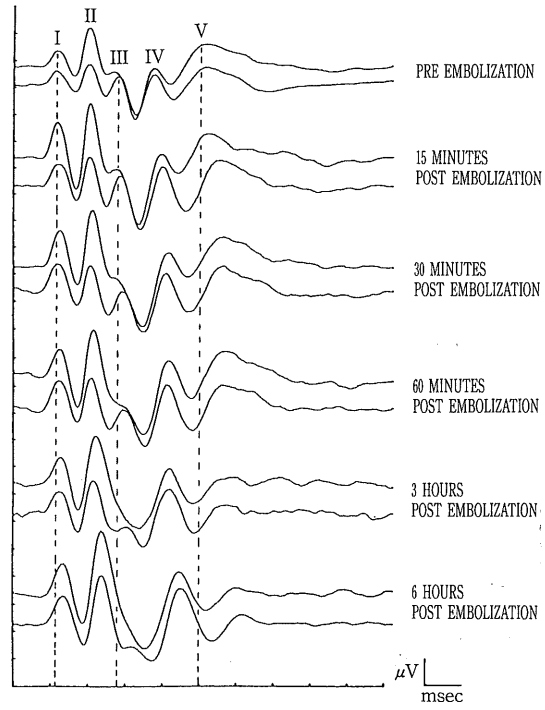

Fig. 6. Cat No.28; Embolus stopped at distal basilar artery. Marked prolongation in latencies of peaks III, IV, and V, and marked decrease in amplitude of peak III were observed.

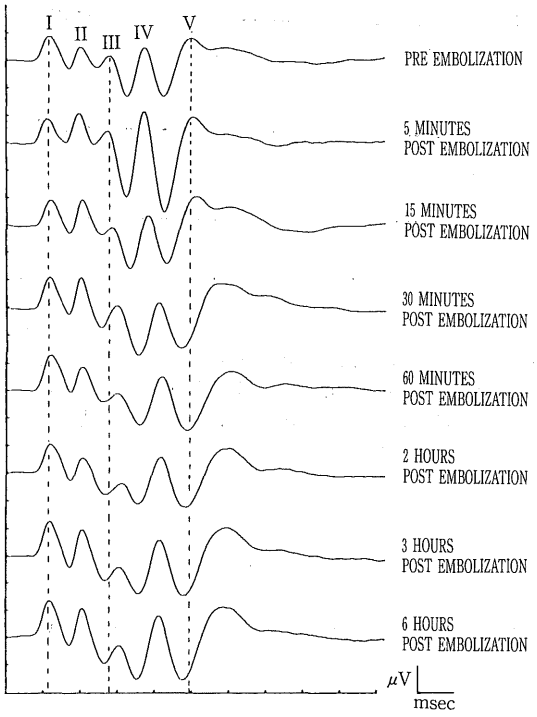

Fig. 7. Cat No.47; Embolus stopped at the top of basilar artery. Latencies of peaks III, IV, and V were markedly prolonged.

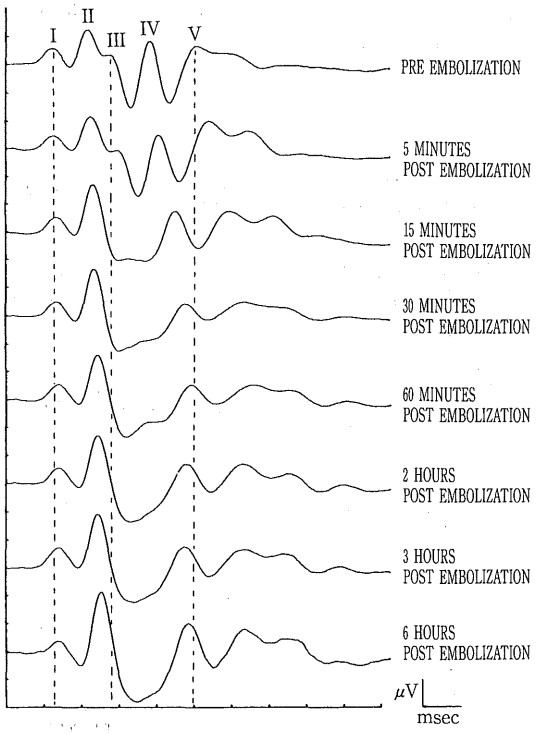

Fig. 8. Cat No.53; Embolus stopped at middle basilar artery. Marked prolongation of peaks III, IV, and V, and flattening of peak III were observed.

animals were sacrificed, group A showed leakage of the dye with different proportion at midbrain, pons, medulla oblongata and cerebellum (Fig. 9).

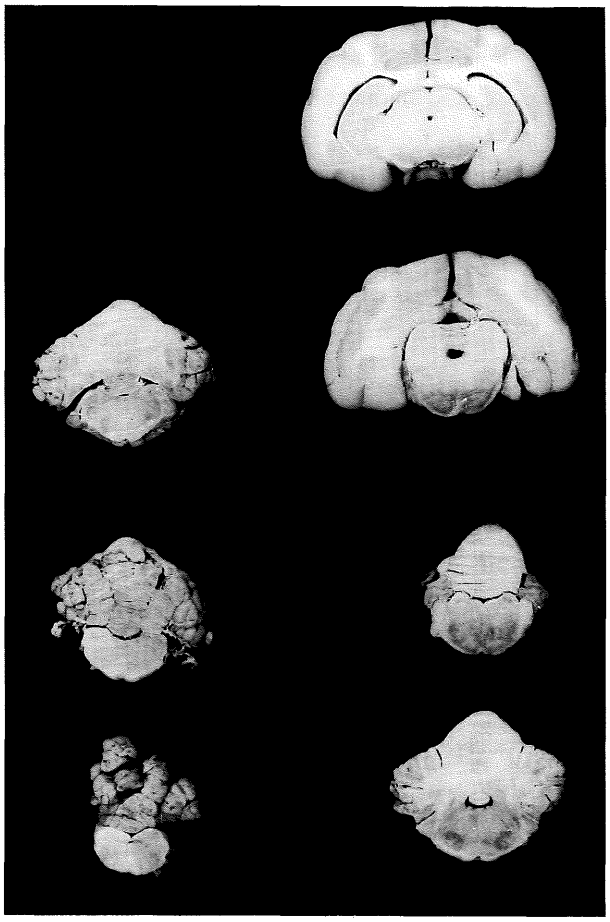

Fig. 9. Ischemic area of the vertebrobasilar system. When the embolus stopped at the top of basilar artery, leakage of the dye was observed especially at ventral portion of midbrain, pons, medulla oblongata, and cerebellum.

DISCUSSION

BAERs have been more readily observed in the cat than in those of humans. This is due to a shorter distance from the vertex electrode to the pons in the cat. In addition, the cat's auditory nerve has about 50,000 fibers compared to only about 25,000 fibers in man[5]. IPL 1-3 represents medullo-pontine segment and IPL 3-5 represents ponto-mesencephalic segment of the auditory pathway, while IPL 1-5 shows the intraaxial portion of the system. Prolongation of the IPLs of the recorded BAERs was consistently found in the embolized group, but deterioration and disappearance of a single peak was also sometimes seen. Since peak I represents activity of the cochlear nerve which is an extraaxial portion of the auditory system, prolongation of IPL 1-3 must be the result of alteration of IPL 2-3. These results are consistent with the clinical data provided in some authors[4,10,11,15].

In one animal, though the embolus stopped at the top of the basilar artery, significant alteration of the BAERs was not observed. The reason for this might be an incomplete obstruction of the arterial

lumen, or that the dysfunction took place in the medial portion of the brain stem. The major part of the auditory tract was laterally placed in pons and midbrain[4]. The leakage of the injected Evans Blue solution showed a breakdown of the blood brain barrier which was presumably caused by ischemic process resulting from embolization. This is also consistently found in the experimental group. Neurologically, infarction or hemorrhage in the vertebrobasilar system will produce a complex clinical syndrome due to the concentration of important cranial nerves, long tracts, and vegetative centers in the brain stem[12]. Some authors[1,9] have stated that an access to vascular disease of the vertebrobasilar territory is difficult, not only because of vague symptomatology, but developmental variations in origin, course, or caliber of vessels. The variations are so frequent that a given vertebrobasilar system will seldom, if ever, fit with ideal embryological patterns which symmetrically developed. In our model, unless the animals are allowed to recover from anesthesia and mechanical ventilation, it is impossible to evaluate the progression of the neurological changes caused by the embolization. Demonstration of basilar artery occlusion using routine CT or MRI is only rarely achieved, and posterior fossa remains a difficult area to visualize[1,9]. Since BAERs monitoring is non invasive and allows for frequent testing, it is an important tool to complement CT or MRI in the diagnosis and follow up of patients with vertebrobasilar insufficiency and/or infarction.

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