Acute intracranial hypertension and auditory brain-stem responses

Part 3: The effects of posterior fossa mass lesions on brain-stem function

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The auditory brain-stem responses (BER's), infratentorial intracranial pressure (ICP), systemic blood pressure (BP), and heart rate were recorded before, during and after expansion of an infratentorial epidural mass in anesthetized cats. Two types of BER's to increasing posterior fossa pressure were noted. In Type 1, there was predominantly suppression of the electrical activity of the auditory nuclei of the upper brain stem (Waves V and IV) and upward transtentorial herniation of the midbrain. In Type 2, the neural activity of the lower brain-stem nuclei (Waves III and II) was affected as well as that of the upper brain stem. There was upward and foraminal impaction of the brain stem and cerebellum which was confirmed by the postmortem brain sections. The change in the amplitudes of BER Waves V and III proved useful in detecting upward transtentorial herniation of the midbrain and foraminal herniation of the cerebellum in acute expanding lesions of the posterior fossa. Medullary paralysis was also detected by observing Wave III.

KEY WORDS • auditory brain-stem responses • intracranial hypertension • brain stem • posterior fossa mass • upward transtentorial herniation • foraminal impaction

Patients with extra-axial mass lesions of the posterior fossa frequently demonstrate signs of brain-stem dysfunction. In these patients, brain-stem distortion, edema, and circulatory disturbance, due to upward transtentorial herniation of the brain stem and cerebellar herniation into the foramen magnum, have been recognized as causes for brain-stem dysfunction. Objective evaluation of the brain-stem functions in patients with such conditions is believed useful for detecting the severity of brain-stem impairment and the effectiveness of treatment. Also, by establishing an early diagnosis of impaired brain-stem function, one may often prevent brain-stem paralysis by appropriate therapy. Since the auditory brain-stem responses (BER's) are evoked in topographically specific brain-stem auditory nuclei, located between the lateral pontomedullary region and the rostral midbrain in cats and humans, measurements of BER's make it possible to demonstrate neuroelectrical alterations in the brain stem, and present objective parameters with which changes in brain-stem function can be assessed.

The purpose of this investigation is to study the near mass effect on brain-stem function by observing the changes in BER's in cats, and to correlate the results with displacement and distortion of the brain stem, posterior fossa mass volume, and infratentorial intracranial pressure (ICP).

Materials and Methods

Experiments were performed on 19 adult cats weighing 3 to 4.5 kg. The animals were anesthetized with thiamylal sodium (Surital), 25 mg injected intravenously, and the trachea was cannulated. After paralysis of the animals with gallamine triethiodide
At the termination of brain compression, the brain was perfused with 10% formalin, 200 ml, at a pressure of 100 mm Hg through a catheter placed in the thoracic aorta. The balloon was kept expanded. The cats' heads were frozen, then sectioned in mid-sagittal plane. Patterns of displacement and distortion of the brain stem were examined under the dissecting microscope and photographs were taken.

**Results**

**General Observations**

Representative changes in the infratentorial ICP, systemic arterial pressure, heart rate, BER's, and pupillary size during posterior fossa mass expansion are illustrated in Fig. 1. There are five components of BER's in cats, which originate in the following brainstem auditory pathways: Wave I: the acoustic nerve; Wave II: the cochlear nucleus; Wave III: the superior olivary complex; Wave IV: the ventral nucleus of the lateral lemniscus and preolivary region, or in and on either side of the inferior colliculus; and Wave V: the inferior colliculus.

As infratentorial ICP increased to approximately 40 mm Hg with a balloon volume (BV) of 0.6 ml, the amplitude of BER Wave V was suppressed to 50% of the control without any significant changes in the vital signs and pupillary size. When infratentorial ICP was further increased to 70 mm Hg by inflation of the balloon (1.2 ml), the typical vasopressor response occurred, with the beginning of pupillary dilatation. The heart rate initially decreased, then increased; BER Wave V completely disappeared and Wave III was suppressed. At an additional increment of 0.1 ml (BV 1.3 ml), the blood pressure fell. Pupils were fully dilated with complete deterioration of the animal. There was a remarkable change in the wave form of BER's, and the amplitudes of Waves III and II were markedly suppressed. Generally, once the amplitude of BER Wave III was suppressed, even a small increment of the BV resulted in rapid cardiocirculatory collapse and deterioration. There also seemed to be a close correlation between the suppression of Wave III amplitude and the pressor and depressor response of the systemic blood pressure. When the pressor response occurred, characterized by an increase in mean arterial pressure of 60% or more, the amplitude of Wave III was suppressed to 49.1 ± 16.1% of the control (mean ± SD, in nine cats). At the beginning of the progressive hypotensive stage, the amplitude of Wave III was 16.1 ± 8.2% of the control in seven cats.

The suppression of the amplitude of BER's during posterior fossa balloon expansion was classified into two types, as previously described (Fig. 2). In Type I (six animals), the amplitudes of Waves V and IV, which represent the neural activity of the auditory pathways in the rostral midbrain and lateral pons, respectively, were predominantly suppressed during...
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posterior fossa compression, and the amplitudes of Waves III and II were well preserved until the terminal stage. This suppression type was essentially the same as observed in supratentorial brain compression. In Type 2 (seven animals), the amplitude of Wave III (frequently concomitant with Wave II) progressively decreased from the start of balloon expansion in the posterior fossa, as well as those of Waves V and IV. When Wave V disappeared, the amplitude of Wave III was suppressed to less than 50% of the control. This type is considered to be specific for mass lesions of the posterior fossa because we never observed it in supratentorial brain compression.

To clarify the patterns of brain-stem displacement and distortion in Types 1 and 2, the animals were sacrificed when typical BER's of Type 1 (flat Wave V, and the amplitude of Wave III was still greater than 80% of the control) and Type 2 (flat Wave V, and

FIG. 1. Changes in pupillary size, infratentorial intracranial pressure (IICP), systemic arterial pressure (BP), heart rate, and auditory brain-stem responses (BERs) during posterior fossa balloon expansion in Cat 7. At a balloon volume of 1.2 ml, typical vasopressor response and pupillary dilatation occurred with suppression of BER Wave III and disappearance of BER Wave V. Only 0.1 ml of balloon increment (1.3 ml) caused a progressive fall in BP and marked suppression of BER Waves II and III. The animal deteriorated soon after.

FIG. 2. Typical changes in the auditory brain-stem responses during posterior fossa compression classified into two types. See text for explanation.
Wave III amplitude less than 20% of the control) were recorded.

The sagittal section of the posterior fossa of a normal cat demonstrates the inferior colliculus 1 mm caudal to the tentorial edge (Fig. 3 upper left). In Type 1, upward transtentorial herniation of the anterior lobe of the cerebellum through the posterior part of the tentorial space compressed the midbrain from behind, and the dorsal surface of the inferior colliculus was displaced 4 mm upward to the edge of the tentorium (mean 4.6 mm). However, downward shift of the cerebellum was less than upward movement, resulting in only slight impaction of the cerebellum into the foramen magnum (Fig. 3 upper right).

In Type 2, severe upward transtentorial herniation of the brain stem and cerebellum (inferior colliculus elevated 6 mm above the original position, mean value 6.2 mm) and marked foraminal impaction of the cerebellum occurred in all animals. The midbrain, pons, and medulla oblongata were compressed against the clivus and distorted in both upward and downward directions. Particularly striking was the flattening of the brain stem along its axis (Fig. 3 lower).

Amplitude Change

Changes in the amplitude of BER Waves I to V during balloon expansion in the posterior fossa are presented in Fig. 4. The ordinates are relative amplitude expressed as percentage of the control, and the abscissae are balloon volumes.

In Type 1, some facilitation in the amplitude was observed immediately after balloon expansion, especially in the early components of BER's. The amplitude of Wave III remained greater than 80% of the control throughout brain compression. A one-way analysis (ANOVA) with repeated measurements demonstrated that there was no difference in amplitude due to balloon volume. A post hoc test, Donnutt's test, confirmed that there was no significant difference from control in Waves I, II, and III.

The amplitude of Wave IV tended to decrease at a BV greater than 1.0 ml and was significantly suppressed at a BV of 1.4 ml (F(7,35) = 3.0, p < 0.05). Wave V was suppressed significantly at a BV greater than 1.0 ml (F(7,35) = 5.0, p < 0.01) and in a more stepwise pattern than Wave IV. Animals showed a flat
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Wave V at a BV of 1.0 ml to 1.8 ml. As the posterior fossa brain volume of cats is between 6 to 8 ml (calculated from the data of White, et al.,22 and Stern19) this BV equals 12% of the posterior fossa brain volume. In Type 2, from the start of brain compression, there was a gradual suppression in the amplitude of Waves II, III, IV, and V.

Statistical analysis showed that Wave II was suppressed significantly at a BV of 1.4 ml (F(7,42) = 2.4, p < 0.05); Wave III at a BV greater than 1.0 ml (F(7,42) = 12.2, p < 0.01), Wave IV at a BV greater than 1.0 ml (F(7,42) = 8.4, p < 0.01), and Wave V at a BV greater than 0.8 ml (F(7,42) = 6.6, p < 0.01), respectively. Most of the animals showed a flat Wave V at a BV 0.8 to 1.0 ml (10% to 12% of the posterior fossa brain volume). It is clear that in Type 2, neuroelectrical suppression of the brain-stem auditory pathways between the pontomedullary portion (Wave II) and rostral midbrain (Wave V) was more severe than that of Type 1.

The effects of increased infratentorial ICP on the suppression of the amplitude of BER Waves I to V are shown in Fig. 5. Suppression of the amplitudes of BER Waves I to V, expressed in percentage change of the control, are plotted against the magnitude of infratentorial ICP in eight animals (four animals in each group). In Type 1, statistical analysis indicated no correlation between changes in the amplitude of BER Waves I, II, and III and infratentorial ICP.

The regression equation relating the magnitude of infratentorial ICP (X) to percentage change in the amplitude of BER Wave IV (Y) showed a low correlation (Y = 116.4 - 0.55X, r = -0.64, p < 0.01). However, a high correlation between the two variables

Fig. 4. Alteration in the amplitudes of BER Waves I to V in Type 1 (six animals) and Type 2 (seven animals) as percentage of control during posterior fossa compression related to balloon volume. Note a clear dissociation of the changes in Wave III between the two types.

Fig. 5. The relationship between infratentorial ICP and the amplitudes of BER Waves I to V, expressed as percentage changes of the control during posterior fossa balloon expansion. Solid circles and solid lines refer to Type 1, open circles and dashed lines refer to Type 2.
existing in Wave V \(Y = 125.8 - 1.06X, r = -0.91, p < 0.001\). At an infratentorial ICP of 70 mm Hg, BER Wave V fell to approximately 50% of the control. The data imply that in this type, increased infratentorial ICP did not affect the amplitude of the lower brain-stem auditory pathways, but produced linear suppression of that of the rostral midbrain (inferior colliculus). In Type 2 (Fig. 5), no correlation was indicated between the two factors in Wave I. However, in BER Waves II, III, IV, and V, relationships between the suppression of the amplitude and the magnitude of infratentorial ICP were statistically significant which are as follows: Wave II, \(Y = 119.3 - 0.56X, r = -0.55, p < 0.05\); Wave III, \(Y = 119.1 - 0.93X, r = -0.86, p < 0.001\); Wave IV, \(Y = 113.5 - 0.93X, r = -0.72, p < 0.001\), and Wave V, \(Y = 119.2 - 1.33X, r = -0.93, p < 0.001\), respectively.

The amplitude of Waves III, IV, and V were nearly linearly suppressed by an increase in infratentorial ICP. At an infratentorial ICP of 50 mm Hg, Wave V was suppressed to approximately 50% of the control, and, at 70 mm Hg, Wave III fell to less than 50% of the control and some animals developed to flat Wave V. At a 90-mm Hg infratentorial ICP, Wave V completely disappeared.

Latency Change

In order to examine the effects of posterior fossa mass lesions on the conductance of the brain-stem auditory pathways, the differential latencies of Waves I-III, III-V, and I-V were evaluated in 13 animals (six of Type 1 and seven of Type 2) (Fig. 6).

The interwave latencies between Waves I-III demonstrate conduction delay between the acoustic nerve and superior olivary complex (lower brain-stem conduction), and those between Waves III-V also show delay between the superior olivary complex and inferior colliculus (upper brain-stem conductance). Central conductance delays in the whole brain stem were indicated as differential latencies of Waves I-V (acoustic nerve to inferior colliculus). The control values of the differential latencies of Waves I-III of Type 1 and Type 2 are 2.0 ± 0.2 msec (mean ± SD) and 2.0 ± 0.3 msec, respectively. The interweave latencies of Waves III-V of Types 1 and 2 are 2.9 ± 0.6 msec and 2.7 ± 0.4 msec; and those of Waves I-V of Types 1 and 2 are 5.0 ± 0.7 msec and 4.7 ± 0.6 msec, respectively. The differential latencies of Waves I-III gradually increased during posterior fossa balloon expansion, and significantly lengthened at a BV greater than 0.8 ml in Type 2 \(F(7,42) = 10.6, p < 0.01\), and at a BV 1.0 ml in Type 1 \(F(7,35) = 6.2, p < 0.01\). The latencies of Waves III-V increased significantly at a BV greater than 0.4 ml (5% of the posterior fossa brain volume) in Type 2 \(F(7,42) = 25.6, p < 0.01\), and at a BV of 1.2 ml in Type 1 \(F(7,35) = 4.0, p < 0.01\).

Conductance of the whole brain stem (I-V) was affected significantly in Type 2 at a BV greater than 0.4 ml \((F(7,42) = 32.9, p < 0.01)\), and at 0.8 ml in Type 1 \(F(7,35) = 16.9, p < 0.01\) (5% to 10% of the posterior fossa brain volume). The neural conductance of the lower and upper brain-stem auditory pathways was more severely affected in Type 2 than in Type 1.

Discussion

Changes in BER’s During Posterior Fossa Expanding Lesions

Axial mechanical distortion of the brain stem was thought to cause stress on the neural pathways of the brain stem and alter the electrical conductivity of neurons, resulting in changes in cardiorespiratory activity.\(^{21}\) Impairment of neural transmission of the pons by extrinsic compression was reported in patients with posterior fossa tumors as evidenced by alterations in the electrically evoked orbicularis oculi reflex.\(^{16,17}\)

Abnormal ocular movement due to functional interference in the posterior longitudinal bundles was
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also described as a result of pressure on the brain stem by a large tuberculoma of the cerebellum.19

These electrophysiological and clinical findings appear to result from altered neural transmission within the limited segment of the brain stem, and partially indicate the severity of the brain-stem paralysis due to acute expanding masses in the posterior fossa, especially its correlation with the mass volume and infratentorial ICP. As the early five components of BER’s of cats9,17 and humans20 originate in the auditory nuclei between the lateral pontomedullary portion and rostral midbrain, we endeavored to clarify in part the changes in function of the whole brain stem along its axis simultaneously, and assess the severity of brain-stem paralysis by an analysis of every component of BER’s in acute intracranial hypertension of the posterior fossa.

In our study, the results indicate that in Type 1 the rostral midbrain was initially and selectively compressed and displaced proportionately to balloon expansion, and the neural conductance and electrical activity of the inferior colliculus were significantly affected when the mass volume approached 10% to 20% of the posterior fossa brain volume.

In Type 2, the neural conductance and activity of the upper brain-stem auditory nuclei were first affected in a mass volume equivalent to 5% to 10% of the posterior fossa brain volume, and an increase in BV and infratentorial ICP resulted in linearly suppressed functions of either the lower or upper brainstem nuclei. There was marked distortion and displacement of the midbrain due to upward transtentorial herniation, and remarkable compression of the lower brain stem by foraminal impaction of the cerebellum when Waves V and III were suppressed. Knüpling, et al.14 suggested that, in patients with posterior fossa tumors, latency shifts of the BER’s, especially the components of the inferior colliculus and lateral lemniscus, were indicative of chronic ascending transtentorial herniation; however, it is clear that changes in the amplitude of BER’s corresponded well with the location and severity of brain-stem distortion and dysfunction in acute expanding lesions of the posterior fossa.

When BER Wave V became flat, complete upward transtentorial herniation of the midbrain and cerebellum was demonstrated in Types 1 and 2. Suppression of the amplitude of BER Wave V is thought to be an objective index of upward transtentorial herniation of the midbrain, as in downward transtentorial herniation reported before.15,16

The superior olivary complex (the origin of Wave III)2,8 is anatomically close to the presessor and depressor centers in the brain stem.1,7,18 There was a close relationship between the vasopressor and depressor response and the suppression of the amplitude of BER Wave III. When the amplitude of BER Wave III approached 50% of the control (infratentorial ICP 70 mm Hg), a vasopressor response (an increase in mean arterial pressure of 60% or more) was evoked. As it fell to less than 20%, circulatory collapse occurred, and the animals died soon after. These results strongly indicate that critical ischemia and neural damage7,24 due to compression and distortion of the lower brain stem are taking place in the medulla oblongata when the amplitude of BER Wave III approached 50% of the control. When it is suppressed below 20% of the control, irreversible medullary paralysis occurs immediately as a result of foraminal impaction of the cerebellum as demonstrated by brain sections.

In acute expanding lesions of the posterior fossa, the change in the amplitude of BER Wave III is considered to be a sensitive index for predicting medullary failure due to foraminal herniation of the cerebellum. It also indicates that a mass volume of 5% to 10% of the posterior fossa brain volume and an infratentorial ICP of 50 mm Hg (Wave V 50%) to 70 mm Hg (Wave III 50%) are the critical thresholds for the neural activity and conductance of the brain-stem auditory pathways. It is unclear why two different response patterns of BER’s were observed during posterior fossa compression. Many factors could be involved, including different degrees of force and directions of balloon expansion, interindividual differences of intracranial anatomy in the shape and size of the tentorial incisura and foramen magnum, and accommodation space to the mass and its ratio to brain size.

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