Acute intracranial hypertension and auditory brain-stem responses

Part 1: Changes in the auditory brain-stem and somatosensory evoked responses in intracranial hypertension in cats

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Changes in auditory brain-stem responses (BER's) and somatosensory evoked responses (SER's) were investigated to correlate mass volume, intracranial pressure, and neurological dysfunction in mass-induced intracranial hypertension in cats. As the intracranial pressure was raised by expansion of a supratentorial balloon, the late components of the SER's were suppressed first, followed by the early components of the SER's, then Wave V and Wave IV of the BER's, in that order. This suggests that the nonspecific reticular projections are most vulnerable to compression ischemia, and the specific somatosensory pathways are the next most vulnerable. Neural activity of the auditory pathways in the upper brain stem was also gradually suppressed, but less so than that of the somatosensory pathways. After complete transtentorial herniation, in spite of immediate mass evacuation, the function of the somatosensory pathways was greatly impaired, often irreversibly. The neural activity of the auditory pathways in the upper brain stem revealed progressive recovery during a 3-hour period. The measurements of BER Wave V is thought to be useful in predicting transtentorial herniation.

KEY WORDS • auditory brain-stem response • somatosensory evoked response • supratentorial mass • intracranial hypertension • transtentorial herniation • head injury

Cerebral evoked responses (somatosensory, visual, auditory, and auditory brain-stem responses) have recently been employed for monitoring severe head injury in humans. Despite this potential for the evaluation of patients with head injury, few basic studies with detailed analysis of these responses have been carried out, especially in the condition of intracranial hypertension and head injury. Since every component of the evoked responses is considered to relate to topographically specific neural structures, it is possible that the location and severity of brain dysfunction could be accurately defined by careful analysis of evoked responses.

We have investigated the electrophysiological changes of auditory brain-stem responses (BER's) and somatosensory evoked responses (SER's) during and after brain compression in cats, using a simulated epidural hematoma. We also correlated the relationships between mass volume, intracranial pressure (ICP), and the degree of neural dysfunction both during compression and after evacuation of the mass.

Materials and Methods

The study was conducted with 10 unselected mongrel cats, weighing between 3 to 4.5 kg. Anesthesia was induced with 30 mg ketamine hydrochloride, and the trachea was cannulated. The animals were paralyzed with 10 mg gallamine triethiodide (Flaxedil) administered intravenously, and maintained on a respirator* while the arterial pCO₂ was kept between 30 and 35 mm Hg. The arterial pO₂ was reviewed intermittently,† and main-

†Blood Micro System manufactured by Radiometer, Copenhagen, Denmark.
FIG. 1. Coronal (left) and sagittal (right) sections of a cat's brain immediately after the animal showed ipsilateral or bilateral pupillary dilatation and flat electroencephalogram. Note transtentorial herniation and marked caudal displacement of the dorsal brain stem predominantly in the upper brain stem. The supratentorial structures and midbrain are displaced and distorted. Arrows: tentorium cerebelli; arrowheads: herniated brain; I: inferior colliculus; M: midbrain.

A small balloon connected to a fine polyethylene tube was then placed in the epidural space in the right temporal region through a small parietal burr hole, and inflated with saline in increments of 0.2 ml to simulate an expanding mass. Intracranial pressure was continuously measured by the use of an epidural microballoon over the left temporal lobe connected to a pressure transducer.

For SER's, a small silver ball electrode was placed on the dura surface over the right primary sensorimotor cortex (compression side) through a small burr hole. A reference electrode was placed on the midline over the superior orbital ridge.

Square wave stimuli, 0.2 msec duration with 50 V intensity, were delivered at a rate of 0.5 Hz to the ulnar nerve in the left forearm. A stainless steel screw was secured at the vertex for the recording of BER's. A second reference lead was attached to the right mastoid tip. These electrodes also served to record the electroencephalogram (EEG). Click stimuli from a Grass stimulator at a 2-Hz rate and 0.2-msec duration were amplified by a Bogan amplifier,* and delivered by a speaker located 1.0 cm from the cats' right ear. The click intensity was 70 db (referenced to 0.0002 dyne/sq cm) measured on a sound level meter.†

The EEG was amplified‡ with a selectable gain of 10,000 Hz; the low frequency was 1 Hz for SER's and 100 Hz for BER's, respectively, and the high frequency was 10,000 Hz. The output of the amplifier was coupled to a Nicolet 1070 evoked response computer.§ The time constant was set at 0.1 msec, 200 msec for SER's and 20 msec for BER's, and a vertical display of 4096 for SER's and 2048 for BER's, respectively. An average of 64 sweeps was used. The summated evoked responses were then printed on a Hewlett Packard 7010 X-Y plotter.||

Both SER's and BER's were recorded each time the balloon was inflated, at approximately 10-minute intervals. During increase in ICP, direct compression of the primary sensorimotor cortex was avoided. The preliminary experiments included five animals. Each cat's brain was gradually compressed by the expanding balloon in the right middle fossa. When either the ipsilateral or bilateral pupil was dilated and fixed and

* Bogan amplifier manufactured by Bogan Company, Paramus, New Jersey.
† B-K Model 2303-1616 sound level meter manufactured by B-K Instruments Corp., Cleveland, Ohio.
‡ Statham P23 Db pressure transducer manufactured by Statham Laboratories, Inc., Oxnard, California.
§ Grass Model P 511 amplifier manufactured by Grass Instrument Company, Quincy, Massachusetts.
|| Hewlett Packard 7010 X-Y plotter manufactured by Hewlett Packard Corp., San Diego, California.
the EEG tracing became completely flat, 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 cats' heads were instantaneously frozen, then sectioned in coronal and mid-sagittal planes. Patterns of displacement and distortion of the brain and pathological changes of the brain stem were examined. These animals all demonstrated transtentorial herniation. In the experimental animals, the ICP was likewise increased until the ipsilateral or bilateral pupils were dilated and fixed, and the EEG's became completely isoelectric. The animals were kept in this condition for 5 minutes, then the balloons were deflated. After balloon deflation, both SER's and BER's were recorded at intervals of 5, 15, 30, 60, 90, 120, 150, and 180 minutes.

Results

Clinical electrophysiological-anatomical correlations were made in five animals. Figure 1 shows representative coronal and sagittal sections of the brain when the animals showed ipsilateral or bilateral pupillary dilatation and a completely flat EEG. In coronal section, supratentorial structures were markedly shifted by an expanded balloon, and the medial temporal lobe (often with a portion of the occipital lobe) had herniated beneath the tentorium in all animals. The midbrain was distorted and shifted laterally by direct compression of the herniated brain.

Transtentorial herniation and caudal displacement of the brain stem were also shown in the sagittal plane. The inferior colliculus was displaced caudally 5 mm from the edge of the tentorium (mean 6.6 mm). The normal position is 1 to 2 mm from the edge. The upper brain stem was directly compressed and displaced more than the lower brain stem.

Progressive changes in the appearance of the waveforms, amplitude, and latency of SER's and BER's as correlated with pupillary changes during balloon expansion and after evacuation in one animal are shown in Fig. 2. There were six peak components within 100 msec in the SER's, labeled by their surface polarity as P₁ (mean peak latency 9.4 msec), N₁ (14.8 msec), P₂ (18.7 msec), N₂ (23.4 msec), P₃ (37.4 msec), and N₃ (60.1 msec), respectively. Five positive components of BER's were identified within 10 msec, labeled in roman numerals in ascending order from the first component I to latest component V.
Amplitude Changes

As the balloon was inflated to 1.8 ml, the late component of SER (N₃) was suppressed and disappeared first (Fig. 2). The N₁ component was reduced only in amplitude. At this stage, the amplitude of BER Waves IV and V was moderately suppressed. When the ICP was raised further to 78 mm Hg (balloon volume of 2.4 ml), the ipsilateral pupil became dilated, indicating tentorial herniation. The amplitude of SER N₁ was markedly suppressed. At the same time BER Wave V abruptly became flat, and Wave IV was further suppressed in amplitude. After deflation of the balloon, BER Wave V reappeared within 15 minutes while the dilated pupil recovered simultaneously. Three hours later, the amplitude of the early components of the SER’s gradually improved, but the late component (N₃) did not reappear.

In general, the late component of SER’s (N₃) was easily and severely suppressed by supratentorial brain compression and showed almost no recovery. There also seems to be a correlation between pupillary change and BER Wave V, which is described below.

Somatosensory Evoked Responses. Stepwise suppression and recovery of amplitude of N₁ (from the peak of P₁ to N₁) and N₃ (from the peak of N₃ to subsequent positive peak) during balloon inflation and after evacuation in 10 animals are presented in Fig. 3.

As the balloon was inflated, amplitudes of N₁ were suppressed nearly linearly and, at a balloon volume of 1.0 ml (about 5% of the cat’s brain volume), mean values decreased to about 50% of the control.

Brain-Stem Responses. The amplitude of Waves IV and V was significantly and gradually suppressed during supratentorial compression, that of Wave V more...
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than Wave IV. Amplitudes of Waves I, II, and III were not influenced during and after brain compression (Fig. 4).

At a balloon volume greater than 1.4 ml, the amplitude of Wave IV was significantly suppressed. (F (7,63) = 5.9, p < 0.01). The amplitude of Wave V was suppressed significantly at a balloon volume greater than 1.2 ml (F (7,63) = 4.4, p < 0.01), and at a balloon volume of 1.4 ml (7% of the brain volume) the amplitude of Wave V approached 50% of the control value. At a balloon volume of 2.4 ml Wave V became flat, while Wave IV remained at about 50%.

After deflation of the balloon, the amplitudes of Waves IV and V were still significantly suppressed at 5, 15, and 30 minutes (Wave IV, F (8,48) = 3.2, p < 0.01, Wave V, F (8,48) = 2.6, p < 0.05). After 30 minutes they recovered in a stepwise fashion to a value not significantly different from the control value, that is, 70% to 80% of the control in 3 hours. The amplitude of Waves I, II, and III did not deviate significantly from the control value at an ICP of 80 mm Hg. The amplitude of Wave V was suppressed linearly by increases in the ICP (Y = -1.0X + 97.7, Y = -0.81, p < 0.001); it was reduced to 50% of control levels at an ICP of 50 mm Hg and became flat at an ICP higher than 80 mm Hg.

Latency Changes

The control latency of SER was as follows: P1, 9.4 ± 3.1 msec; N1, 14.8 ± 3.1 msec; P2, 18.7 ± 3.1 msec; N2, 23.4 ± 3.9 msec; P3, 37.0 ± 8.6 msec; and N3, 60.1 ± 11.7 msec (mean ± SD).

There was a significant increase in the latencies of SER's and BER's during brain compression as shown in Fig. 2. At a balloon volume of 1.8 ml, latencies of all components increased at a balloon volume of 1.4 ml. It seems that neural conductances of BER's were significantly altered at a balloon volume of 0.8 to 1.0 ml (4% to 5% of the brain volume). At 90 minutes after deflation, the latencies of BER's were not significantly different from the control except for Wave V.

Pupillary Changes and Brain-Stem Responses

A correlation between pupillary abnormalities and changes of electrical activity of BER Waves IV and V was investigated at the beginning of transtentorial herniation. For this purpose, changes of the latency and amplitude of BER Waves IV and V immediately before and after pupillary dilatation were statistically analyzed, with the following results. The latency of Wave IV decreased from 5.0 to 5.3 msec, and Wave V latency rose from 6.5 to 6.6 msec, both not significant. The amplitude of Wave IV decreased from 58.4% to 45.1% of the control value, which was not significant. However, the amplitude of Wave V fell from 52.6% to 22.8% of the control value, which was significant (t = 3.8, p < 0.01). Thus, only changes in amplitude of Wave V had a significant correlation to the pupillary changes. Furthermore, in five of 10 animals, Wave V disappeared simultaneously with pupil dilatation. After balloon deflation, dilated pupils returned to normal within 15 minutes in eight animals. In these animals, rapid reappearance and progressive recovery of the amplitude of Wave V corresponded with a return to normal pupil size.

Discussion

Changes in Auditory BER's and SER's in Brain Compression

Grossman, et al., observed suppression of the direct cortical evoked response, in relation to a decrease in cortical blood flow, in a model of increased ICP in baboons. Bennett, et al., reported the suppression of the SEP N1 component by brain retraction in dogs, with a linear correlation to a decrease in cerebral perfusion pressure, and increase in retraction pressure. In patients with intracranial hematomas, SER's were suppressed and tended to become monophasic and flat.

Our data show suppression of the early and late components of SER's and Waves IV and V of BER's...
by an increase in the supratentorial mass volume. Correlations between amplitude changes of the evoked responses and increase in the mass volume as well as the effect of balloon deflation are summarized schematically in Fig. 6.

It has been widely accepted that the early components of SER's including the N1 component, are generated by the specific somatosensory (medial lemniscal) pathways. The second negative sequence (N1 component of our data) is thought to originate either in the thalamocortical axons or in the somesthetic cortex: Thus, changes in the amplitude of SER N1 are considered indicative of electrical suppression in the thalamocortical fibers or cortical organization of the supratentorial specific somatosensory pathways.

In man and monkey, the late components of SER's are thought to originate in the non-specific somatosensory pathways predominantly passing via the reticular formation of the brain stem. In cats, there is a definite difference in afferent pathways between the primary cortical response and secondary cortical response (greater than 30 or 40 msec in latency) with sciatic nerve stimulation, and the ascending reticular formation (RF) are the most easily suppressed in the following 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, Wave V, the inferior colliculus. This suggests that changes in amplitudes of Waves II and III of BER's could be attributed to the neural suppression of the auditory pathways at the pontomedullary portion and lower pons, and those of Waves IV and V to suppression of pathways in the upper pons and rostral midbrain.

Applying these interpretations to our data, we find that the non-specific somatosensory pathways (ascending reticular formation (RF)) are the most easily and severely affected by supratentorial brain compression, followed by the specific somatosensory pathways and auditory pathways of the rostral midbrain and upper pons, respectively. After complete transtentorial herniation, in spite of balloon deflation, neural activity of the non-specific pathways (RF) showed almost no recovery for 3 hours, while medial lemniscal activities were poorly restored and remained at low amplitude. On the contrary, neural activity of auditory pathways of the upper brain stem (rostral midbrain and upper pons) recovered well. There were no significant changes in amplitude of the pontomedullary and lower pons auditory pathways during and after brain compression, whereas their latencies were lengthened.

In experimental concussion in the monkey, Foltz and Schmidt reported long-latency activity in the reticular formation which disappeared immediately after head injury with loss of consciousness, while short-latency medial lemniscal activity remained intact in response to peripheral stimulation.

Our data indicate that the late component of SER's, which might represent neural activity of the RF, was also suppressed earlier and more severely than medial lemniscal activities in gradual brain compression.

There were remarkable differences in the responses of BER Waves II and III and those of Waves IV and V during and after brain compression. A possible anatomical explanation may be that the lower brain stem, as shown in Fig. 1, is less moveable because of the upper cervical denticulate ligaments, while the upper brain stem adjacent to the tentorial hiatus can be easily and directly compressed by the herniated brain, and laterally or caudally displaced and rotated, resulting in narrowing of the dorsal upper brain stem. At the same time, mechanical compression of the upper brain stem causes interference with brain-stem circulation. On the other hand, the neural function of the lower brain stem appears preserved, as the pressure on it was reduced by the displacement and shortening of the upper brain stem.

After balloon deflation, the neural activity of the non-specific (RF) and specific somatosensory
pathways shown in SER N3 and N4, respectively, was almost completely or greatly suppressed. As these components represent the neural functions of the ascending reticular formation and supratentorial medial lemniscal pathways, severe damage to these pathways is indicated.

Spontaneous progressive improvement in amplitude of BER Waves IV and V was noted after balloon deflation. This may suggest that the suppression of neural activities of the auditory pathways in the upper brain stem during brain compression is the result of direct mechanical pressure and not secondary irreversible damage. If this proposal is true, changes in the amplitudes of BER Waves IV and V will give us an objective parameter with which to estimate the effectiveness of decompression procedures, medical or surgical, on the brain stem.

Our data show that the latencies of SER's and BER's, which represent changes in the neural conductance and conductance velocity in the somatosensory and auditory pathways, were significantly increased at a balloon volume greater than 4% to 5% of the brain volume, and the neuroelectrical suppression, described above, occurs when the supratentorial mass approached 10% of the brain volume.

**Transtentorial Herniation and Auditory BER's**

In our experimental model with middle fossa compression, a pupillary change has been shown to be one of the earliest clinical signs of transtentorial herniation, and this finding was confirmed by our preliminary experiments. Of the waves of BER's, statistical analysis showed that the change in the amplitude of Wave V alone was significantly correlated to pupillary change, which we believe correlates with the development of transtentorial herniation. In fact, amplitudes of Wave V became flat simultaneously with pupil dilatation in five of 10 animals. It was possible to predict pupillary changes by observation of the BER Wave V amplitude. After deflation of the balloon, normalization of dilated pupils corresponded well with restoration in amplitude of Wave V. The auditory pathways were superficial in the rostral midbrain (inferior colliculus). As the supratentorial mass expands, first the rostral midbrain is compressed directly by the herniated brain, then the dorsal surface of the brain stem is displaced caudally more than its ventral surface (Fig. 1). It is reasonable to assume that BER Wave V, which originates in the inferior colliculus, could indicate early changes of the brain-stem function and predict transtentorial herniation in acute supratentorial expanding lesions.

**Acknowledgments**

Grateful acknowledgments are made to Mr. Milton Fojtik for his skillful technical assistance and Mrs. Bettye J. Braswell for preparing the manuscript.

**References**


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