Does oxygen deficit to the cerebral blood flow caused by subdural hematoma and/or increased intracranial pressure affect the variations in auditory evoked potentials in white New Zealand rabbits?

Jae Joong Im, Byung Rim Park

*Division of Electronics and Information Engineering, Chonbuk National University, Chonju, 561-756, South Korea
Department of Physiology, School of Medicine, Wonkwang University, Iksan, 570-749, South Korea

Received 15 September 2001; received in revised form 8 October 2001; accepted 27 October 2001

Abstract

The experiment entails surgically placing two subarachnoid bolts and a subdural balloon through the skull of white New Zealand rabbits. One bolt is used to raise the intracranial pressure (ICP) by continuously infusing lactated Ringer’s solution (LRS) into the subarachnoid space to maintain the desired level of ICPs, and the second bolt is to monitor the ICP. A subdural balloon is inflated with a known volume of LRS to simulate a subdural hematoma condition. Using various levels of ICP and/or different sizes of balloons, auditory evoked potentials (AEPs) were recorded from a rabbit. The results indicate that a major correlation of changes in AEP peak latencies is due to mechanical forces of a mass (inflated balloon simulating a hematoma) on the brain matter rather than increased ICP. The AEP peak latencies are relatively insensitive to an increase in ICP without the simulated intracranial hematoma. This study provides evidence that oxygen deficit to the cerebral blood flow caused by deformation of certain parts of the brain could be identified using AEPs. © 2002 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Intracranial pressure; Subdural hematoma; Oxygen deficit; Auditory evoked potential; Noninvasive measurement

The most frequent cause of death in head injury is intracranial hypertension following cerebral contusion and subdural hematoma. In a head-injured patient, the most critical factor governing prognosis is the damage sustained by the brain. In the development of brain damage after head injury, there are two basic stages [10]: (1) brain damage occurring at the moment of injury, and (2) brain damage which does not present clinically for a period of time after the injury, e.g., intracranial hemorrhage, brain swelling, raised intracranial pressure (ICP), and infection. ICP of greater than 20 mmHg, which is considered abnormal, will cause neurologic dysfunction and impairment of the brain's electrical activity.

As a result of accumulating blood within the skull following head injuries, normal homeostatic mechanisms controlling the ICP level are disturbed, leading to a significant increase in ICP with compression of brain tissue. When the brainstem is forced inferiorly by increasing ICP, control of heart rate, respiration, and blood pressure is lost and there is a noticeable change in the patient's level of consciousness. Since the ICP limits the cerebral blood flow and deprives the oxygen supply to the brain, ICP must be measured and controlled from the moment of injury [6,13]. However, several major disadvantages are associated with current methods of ICP monitoring such as the invasive method, which poses a risk to the patient and has technical problems in determining reliable ICPs. Current medical practice precludes all head-injured patients from ICP measurement by an invasive pressure transducer, and a major clinical problem in neurosurgery is the inability to assess ICP by noninvasive means. If a noninvasive means of measuring ICPs were developed and found to have a linear relationship with the ICP, then the noninvasive method would be the preferred method for use on all traumatic head-injured and hydrocephalic patients.

Damage along the eighth nerve or brainstem pathway impedes the neural ability to conduct electrical impulses. One indication of neurological dysfunction revealed in the
auditory evoked potential (AEP) trace is prolonged peak latencies [12]. The latency referred to the time interval between the onset of the click stimulus and a specific point on the AEP waveform. Within the last decades, several studies have evidenced an interest in evoked potentials (EPs) [1,5,8] and attempted to establish a relationship between increased ICP and the parameters of multimodality EPs (AEP, visual evoked potentials, and somatosensory evoked potentials) [7]. Normal and hydrocephalic (surgically induced increased ICP) rabbits were used for the study in which ICP was elevated by infusing Ringer’s solution, during which the brain stem auditory evoked responses (BAERs) were recorded. Increased ICP in the hydroceplhalic model showed an increase in the latencies of AEP components [2]. Continuous monitoring of BAERs provided a useful physiological counterpart to physical parameters such as ICP, and an increase in ICP frequently affects the electrical activity in the brainstem [3,4]. In the absence of ICP changes, a changing pattern of brain stem auditory evoked potential (BAEP) reflects secondary ischemia in sensitive brainstem areas [11].

However, no research efforts appear to have been conducted to evaluate whether the subdural hematoma accompanied by an increase in ICP causes the oxygen deficit and results in the changes in AEP latencies. Moreover, development of a noninvasive intensive care system calls for the use of EPs as a means of diagnosing traumatic head-injured patients who have a reduced oxygen supply. This is important since the variations in AEP latencies could be explained in two different ways: deformation of the certain part of the brain and just an increment of the ICP level without deformation of local parts of the brain. That is, the increment of the ICP level could possibly appear without hematoma, mechanical deformation of local parts of the brain matters. Therefore, the main cause for the variations in AEP latencies should be defined prior to finding the relationship between the ICP level and AEP latencies. This study with an experimental animal group focuses on the analysis of AEP parameters and different sizes of simulated hematoma with corresponding levels of increased ICP.

The experiment was devised for three groups of white New Zealand rabbits: group 1 and group 2 were used as control groups (two rabbits for each group). Control group 1 was used to establish/measure the control for examining the effects of anesthesia on AEP parameters for the duration of the experiment (2 h). Group 2 was used as a control for examining the effects of anesthesia and sham surgery on AEP parameters for the duration of the experiment (2 h). Rabbits in group 3 (eight rabbits) were used as an experimental group to study the changes in the AEP’s parameters under various levels in ICP and/or different inflated sizes of the subdural balloon.

The experimental conditions were divided into four major categories of treatment: baseline ICP (post-surgery without balloon inflation or ICP infusion), variation of ICP without balloon inflation, variation of balloon size without ICP infusion, and variation of balloon size with variation in ICP infusion. The ICP-only experiment consisted of four predetermined levels of increased ICP (15, 20, 25, and 30 mmHg) without balloon inflation. The balloon-only experiment was further categorized into three subcategories which used three different sizes of balloons, 0.2, 0.4, and 0.6 ml. The experiment with each of the three sizes of balloon consisted of five consecutive steps. Step 1, inflating the subdural balloon only, created the simulated hematoma condition without increasing ICP. Steps 2 through 5 corresponded to maintaining the balloon size constant while varying the levels of ICP, i.e., 15, 20, 25, and 30 mmHg.

Anesthesia was induced with ketamine (20 mg/kg) and xylazine (Rompun, 10 mg/kg) administered intramuscularly and was maintained by incremental intramuscular injection of both agents. An incision was made in the trachea between two tracheal rings, located six rings distal to the larynx. A plastic endotracheal cannula was inserted and secured with circumferential ligatures to provide adequate pulmonary ventilation (E&M’s small animal respirator, #5KGR). A cannula was made from an 18 gauge stainless steel hypodermic needle and attached to a fluid-filled flexible tube to monitor the blood pressure.

A 5 cm midline skin incision was made from just distal to the nuchal crest to 2 cm proximal to the orbit, and an incision of equal length was also made through the peristeum. Three twist drill craniotomy holes were made in the skull with the use of a 4 mm diameter drill bit. The first hole was made in the coronal suture of the left parietal bone, 8 mm lateral from the midline. A subarachnoid bolt was screwed firmly to the hole so that the open inner end protruded into the subarachnoid space, and the open end of the bolt was connected to a pressure transducer for ICP monitoring. A second drill hole was also made in the left parietal bone, 15 mm caudal to the coronal suture and 8 mm lateral from the midline. An open end of the subarachnoid bolt through this hole was attached to a 1000 ml bag of lactated Ringer’s solution (LRS) (Vialflex type 2B2324), with an adjusting knob for the drops to alter the ICP. A subdural balloon was placed through the third hole, drilled in the right parietal bone, 6 mm caudal to the coronal suture and 8 mm lateral from the midline. A 1.0 ml syringe was attached to a stopcock extending from the subdural balloon.

Physiological signals, arterial blood pressure (ABP), ICP, and AEP, were collected from the rabbits using a Narco Biosystems physiograph (desk model #DMP-4B). Monopolar recordings of the AEP signals were obtained using 20 gauge needle electrodes, located at the midline of the motor cortex Cz (reference electrode), the left temporal T3 (active electrode) and the right hind-foot (common electrode). An ipsilateral recording of the AEP was performed by placing an earphone in the left ear canal. The rabbit’s auditory system was stimulated by clicks (0.1 ms pulse duration) with a repetition rate of five clicks per second. The program performed data collection and averaged the AEPs until 500 clicks were presented.
In the first statistical study, group 1 (anesthesia only) and group 2 (anesthesia and sham surgery) showed no significant changes in peak latencies. This infers that there is no significant adverse effect caused by anesthesia and/or surgery. The changes in P3 and P5 latencies during an experiment show that they return to normal baseline values of ICP 30 min after the LRS infusion for an ICP of 30 mmHg is stopped and the balloon is deflated (Fig. 1). This infers that a minimum of 30 min is necessary for the AEP to return to "normal"; otherwise, successive treatment conditions would be dependent and affected by the previous treatment. As shown in Fig. 1, the P5 latencies reach their highest values of 2.07 ms (ICP of 30 mmHg with balloon deflated), 2.23 ms (ICP of 30 mmHg with 0.2 ml balloon), and 2.23 ms (ICP of 30 mmHg with 0.4 ml balloon), respectively. It was observed that as the balloon size is increased more time is required for the AEP latencies to return to their normal values.

The changes in AEP positive peak latencies (P1, P3, P5) under combined experimental conditions were compared (Fig. 2). Mean differences increase gradually between different sizes of the balloons, but there is no definite increase in mean differences between ICP levels. This implies that the main cause of the mean differences in AEP peak latencies is the size of the balloon rather than the ICP increase. A possible explanation for the effect is that the inflated balloon results in compression or mechanical forces (pressure) to the brainstem, which affect the control center for the blood supply to the brain, i.e., as the size of the balloon is increased, the oxygen supply to the brain is restricted resulting in abnormal electrical brainwave activities.

Multiple regression analyses were performed to determine best fitting parameters and the relationship between the ICP and positive/negative peak latencies. The $R^2$ and Cp statistics were used to find the relationship between variables and to select the combination of variables that would provide the best fitting model [9]. Based on the best subset
of variables selected for each experimental treatment, the best fitting regression model was extracted using multiple regression analysis. Table 1 summarizes the multiple regression results including probabilities ($P > F$) and $R^2$ values for each experimental treatment. The regression model for the treatment in which the ICP was varied without balloon inflation had the lowest squared correlation coefficient value of 0.225. The ICP variation gives a better fitting model with a higher $R^2$ value as the balloon size is increased. The experimental treatment in which the ICP is varied while maintaining the balloon size at 0.6 ml had the highest $R^2$ value of 0.608. Changes in AEP latencies do not have higher predictability just with the variations of ICP alone or with the variations of balloon size alone. This leads to the conclusion that the larger effect on the variations in AEP latencies appears with the bigger balloon size together with the high levels of ICP values.

The results obtained from this study suggest that the major correlation of changes in AEP peak latencies is due to reduced oxygen supply to the brain (mechanical forces of a mass by inflating the balloon simulating a hematoma) in the distortion of the temporal lobe of the brain matter. This implies that the variations in AEP parameters, the abnormal brain's electrical activity, have predictability on ICP changes with a bigger balloon size simulating a hematoma.

<table>
<thead>
<tr>
<th>Experimental conditions</th>
<th>Cp value</th>
<th>Variables</th>
<th>$P &gt; F$</th>
<th>$R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variation of ICP without balloon Inflation</td>
<td>5.025</td>
<td>P1 P2 P5 N2 N4</td>
<td>0.1079</td>
<td>0.225</td>
</tr>
<tr>
<td>Variation of ICP with 0.2 ml of balloon</td>
<td>5.350</td>
<td>P1 P3 N3 N4 N5</td>
<td>0.0148</td>
<td>0.329</td>
</tr>
<tr>
<td>Variation of ICP with 0.4 ml of balloon</td>
<td>5.077</td>
<td>P1 P3 N1 N2 N4</td>
<td>0.0038</td>
<td>0.389</td>
</tr>
<tr>
<td>Variation of ICP with 0.6 ml of balloon</td>
<td>6.171</td>
<td>P1 P2 P3 N2 N3 N5</td>
<td>0.0001</td>
<td>0.608</td>
</tr>
<tr>
<td>Variation of balloon size at baseline ICP</td>
<td>4.658</td>
<td>P4 P5 N3 N5</td>
<td>0.0028</td>
<td>0.440</td>
</tr>
<tr>
<td>Variation of balloon size at 15 mmHg</td>
<td>1.944</td>
<td>N2 N5</td>
<td>0.0255</td>
<td>0.224</td>
</tr>
<tr>
<td>Variation of balloon size at 20 mmHg</td>
<td>1.910</td>
<td>P5 N1</td>
<td>0.0027</td>
<td>0.338</td>
</tr>
<tr>
<td>Variation of balloon size at 25 mmHg</td>
<td>1.681</td>
<td>P3 N3</td>
<td>0.0255</td>
<td>0.224</td>
</tr>
<tr>
<td>Variation of balloon size at 30 mmHg</td>
<td>2.663</td>
<td>P4 P6</td>
<td>0.0173</td>
<td>0.224</td>
</tr>
</tbody>
</table>


