Effect of temperature and cardiopulmonary bypass on the auditory evoked response†

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Summary

We have recorded auditory evoked potentials before and during cardiopulmonary bypass in 10 adult patients undergoing cardiac surgery under moderate hypothermia to 27–28 °C. The immediate effect of bypass was a small decrease in latency and increase in amplitude of the early cortical response. We also studied two adults and two children during profound hypothermia with circulatory arrest during cardiopulmonary bypass. Reduction in core temperature to 25 °C resulted in an increase in latency and amplitude of the brain stem responses; below this temperature the amplitude decreased but latency continued to increase until the auditory evoked response trace became completely flat between 21 and 19 °C. These changes were reversible on rewarming. (Br. J. Anaesth. 1995; 75: 293–296)

Key words


The auditory evoked response (AER) is the EEG response to a repetitive sound stimulus. The AER is extracted from the EEG by computer averaging, and consists of a series of waves representing the passage of electrical activity along the auditory pathway from the cochlea to the cortex (fig. 1). The early cortical AER, in the time window between 10 and 80 ms after the auditory stimulus, changes in a similar manner in response to increasing anaesthetic concentration, independent of the agent used [1]. These changes are reversed partially by surgical stimulation [1, 2], giving credence to the concept of depth of anaesthesia as the balance between cerebral depression caused by anaesthesia and arousal caused by surgical stimulation. Using the isolated forearm technique, the characteristic change from the three-wave early cortical AER pattern (latency of the Nb wave <44.5 ms) to the two-wave pattern (Nb latency >44.5 ms) represents the transition from the awake to the anaesthetized state [3].

Awareness is a particular problem in obstetric anaesthesia, total i.v. anaesthesia and during cardiopulmonary bypass, especially during the rewarming period. However, if the AER is to be used as a reliable monitor of depth of anaesthesia during cardiopulmonary bypass, the effect of bypass on the AER needs to be clearly understood. The aim of this study was to define the effects of moderate and profound hypothermia on the AER during cardiopulmonary bypass.

Patients and methods

After obtaining approval from the Southampton Joint Ethics Committee and informed consent, we studied 14 patients. Ten adults (seven male), aged 55–75 yr, were planned admissions for elective cardiac surgery requiring a period of cardiopulmonary bypass with active cooling to 28 °C. Six patients were undergoing coronary artery bypass grafting and four valve replacements. The four other patients (two adults, two children) required a period of profound hypothermia (nasopharyngeal temperature 19–21 °C) with circulatory arrest during cardiopulmonary bypass.

All adult patients were premedicated with lorazepam 1–2 mg, papaveretum 10–20 mg and hyoscine 0.2–0.4 mg. Anaesthesia was induced with midazolam 50–100 μg kg⁻¹, thiopentone 0–1 mg kg⁻¹, fentanyl 10 μg kg⁻¹ and pancuronium was used for neuromuscular block. Anaesthesia was maintained with a further 5–10 μg kg⁻¹ of fentanyl, and 50 % nitrous oxide in oxygen with <1 % inspired concentration of isoflurane. While on bypass a propofol infusion was given at a rate of 100 mg h⁻¹.

The children were premedicated with Triatro- morph (trimiprazine 3 mg ml⁻¹, atropine 60 μg ml⁻¹, morphine 1 mg ml⁻¹ in aqueous syrup) 0.5 ml kg⁻¹. Anaesthesia was induced and maintained as above, with up to 30 μg kg⁻¹ of fentanyl, but propofol was not used.

Monitoring during surgery included invasive arterial pressure, ECG, pulse oximetry, central venous pressure, and nasal and oesophageal temperatures. We used the Northwick Park AER system, which records EEG with a prototype amplifier, digital signal processor system (Loughborough Sound Instruments, Loughborough) with a band-
width of 400 Hz and sampling rate of 1 kHz, and bespoke software running on a 386SX personal computer. With this system, it is not possible to discriminate the individual components of the brain stem response and a composite peak, which is predominantly wave V of the brain stem response, is seen immediately preceding the early cortical waves. The AER system was set up and connected to the patient before anaesthesia was induced. Silver–silver chloride electrodes (Medicotest Blue Sensor P-00-S) were placed on the vertex and on both mastoid processes after rubbing the skin with gauze soaked in acetone. Electrode impedance was \(58 \pm 9024\) k\(\Omega\) for each patient. Rarefaction clicks at 6.12 Hz and 105 dB peak equivalent sound pressure level (approximately 65–70 dB loudness relative to the normal hearing threshold) were played into both ears via moulded ear pieces. The EEG was recorded between one mastoid electrode and the vertex electrode, with the other mastoid electrode acting as ground. A total of 1024 sweeps of the EEG signal following each click were filtered (0 Hz high pass, 25 Hz low pass) and averaged by the software, and the resulting AER was displayed on the computer screen in real time. The raw EEG was also stored on magnetic disk for re-processing at a later date. Baseline AER were obtained after induction of anaesthesia, and the AER was then recorded continuously during the remainder of the operation until the patient was separated from cardiopulmonary bypass.

The bypass circuit was of standard construction; we used a membrane oxygenator and arterial line filter. The circuit was primed with 2 litres of compound sodium lactate solution, to which was added 500 u. of porcine heparin. Bypass was conducted with a flow index of 2.4 litre min\(^{-1}\) m\(^{-2}\) at 37 °C, reducing to 1.6 litre min\(^{-1}\) m\(^{-2}\) at 25–28 °C; in those patients having deep hypothermic arrest the flow index was maintained at 2.4 litre min\(^{-1}\) m\(^{-2}\) for the duration of the bypass period to enable efficient cooling, as is standard practice in the Wessex Cardiothoracic Unit. The acid–base status of the patients was controlled on bypass using the o-stat principle.

The amplitude and latency of the brain stem and early cortical evoked potentials were analysed and tabulated in relation to nasopharyngeal temperature.

The amplitude of each of the waves was determined by drawing a line between the preceding and succeeding peaks of the opposite polarity, and then drawing a vertical line from the peak of the wave to this line (see fig. 1). Measurements were obtained at the following times: before bypass, at a nasopharyngeal temperature of 35–36 °C; immediately after going on bypass, with the nasopharyngeal temperature still at 35–36 °C; and at each 1 °C change in temperature during the cooling and rewarming phases of bypass.

Results were analysed by repeated measures analysis of variance or the Friedman test where appropriate. Individual comparisons or contrasts were analysed with Scheffé or Meddis tests.

**Results**

After induction of anaesthesia we obtained the standard AER trace (fig. 2, top panel). As surgery progressed, before cardiopulmonary bypass was established, the amplitude of the AER decreased progressively and the latencies of all early cortical waves gradually increased. Immediately cardiopulmonary bypass was established, before any change in nasopharyngeal temperature, the amplitude of the early cortical AER, especially wave Nb, increased and the latencies of the early cortical waves decreased, but in no patient was the latency of the Nb wave less than 55 ms.

**AMPLITUDE: BRAIN STEM RESPONSES**

There was no change in the amplitude of the brain stem response as bypass was established. The mean amplitude of the brain stem response increased progressively during cooling to 28 °C, when it was...
Temperature, cardiopulmonary bypass and the AER

The mean amplitude of wave Pa did not change significantly as bypass was established, although the amplitude of Pa did increase significantly in some patients. During cooling to 28 °C, the mean amplitude of wave Pa decreased significantly compared with the values before bypass \((P < 0.05)\) and immediately on bypass \((P < 0.01)\). There was a significant increase in mean amplitude of wave Nb as bypass was established \((P < 0.05)\) but otherwise the pattern of change in wave Nb was similar to Pa (table 1).

### Table 1

<table>
<thead>
<tr>
<th>Component</th>
<th>Pre-bypass</th>
<th>On bypass</th>
<th>At 28 °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain stem</td>
<td>0.62 (0.10)</td>
<td>0.63 (0.13)</td>
<td>1.00 (0.13)</td>
</tr>
<tr>
<td>Wave Pa</td>
<td>0.31 (0.05)</td>
<td>0.39 (0.05)</td>
<td>0.11 (0.03)</td>
</tr>
<tr>
<td>Wave Nb</td>
<td>0.21 (0.05)</td>
<td>0.31 (0.04)</td>
<td>0.16 (0.13)</td>
</tr>
</tbody>
</table>

### Table 2

<table>
<thead>
<tr>
<th>Component</th>
<th>Pre-bypass</th>
<th>On bypass</th>
<th>At 28 °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain stem</td>
<td>10.0 (1.7)</td>
<td>10.3 (1.8)</td>
<td>14.5 (2.0)</td>
</tr>
<tr>
<td>Wave Pa</td>
<td>40.0 (2.9)</td>
<td>35.0 (2.4)</td>
<td>64.5 (6.0)</td>
</tr>
<tr>
<td>Wave Nb</td>
<td>80.0 (5.8)</td>
<td>75.0 (2.9)</td>
<td>106.0 (7.7)</td>
</tr>
</tbody>
</table>

**Discussion**

Hypothermia produces neurophysiological changes which include slowing of axonal conduction and depression of synaptic transmission as a result of impaired transmitter release [4–6]. These two mechanisms probably explain the increased latency of the brain stem and early cortical AER with profound hypothermia.

In all four patients undergoing deep hypothermic circulatory arrest, the amplitude of the brain stem responses continued to increase until the core temperature reached 25 °C, when the mean amplitude was 1.6 µV, while the amplitude of the early cortical responses continued to decrease. Below 25 °C the amplitude of all waves decreased, with a corresponding increase in their latency, until at 19–21 °C the AER trace was flat. These changes were completely reversible on rewarming (fig. 3).

**LATENCY: BRAIN STEM RESPONSE**

There was no change in the latency of the brain stem response as bypass was established, but during cooling to 28 °C the latency increased significantly \((P < 0.01)\).

**LATENCY: EARLY CORTICAL RESPONSE**

The latencies of waves Pa and Nb were significantly greater at 28 °C compared with pre-bypass and immediately on bypass \((P < 0.01)\). There were no differences between latencies before and immediately on bypass (table 2).

**PROFOUND HYPOTHERMIA**

In all four patients undergoing deep hypothermic circulatory arrest, the amplitude of the brain stem responses continued to increase until the core temperature reached 25 °C, when the mean amplitude was 1.6 µV, while the amplitude of the early cortical responses continued to decrease. Below 25 °C the amplitude of all waves decreased, with a corresponding increase in their latency, until at 19–21 °C the AER trace was flat. These changes were completely reversible on rewarming (fig. 3).
reduction in temperature. The effect of hypothermia on the amplitude of brain stem responses is harder to explain. Similar changes have been reported by other workers in both animal and human studies [7–9], and it has been suggested that moderate hypothermia causes decreased activity of inhibitory olivocochlear bundles which terminate on the cochlear hair cells [10]. The olivocochlear bundles are considered to be inhibitory because electrical stimulation suppresses cochlear nerve activity. In our study the amplitude of the brain stem response increased as the temperature decreased to 25–26 °C, and therefore control should maintain the balance between cerebral temperature of each patient. Alpha-stat acid–base control should maintain the balance between cerebral blood flow directly, but we did maintain cardio-
lation [11–13]. However, during reperfusion after cardiac arrest with inadequate cerebral perfusion, the brain stem response is broadened, while the early cortical potentials recover normally [13]. The reduction in amplitude of the brain stem AER below 25 °C, together with the generalized decrease in amplitude of the early cortical AER during cooling, is probably caused by a temperature-related reduction in cerebral metabolic rate. Hypothermia produces generalized cerebral depression, with loss of consciousness at about 30 °C. Cerebral blood flow is reduced by 7 % per 1 °C decrease in temperature, associated with a corresponding reduction in cerebral metabolic rate [14]. We did not measure cerebral blood flow directly, but we did maintain cardiopulmonary bypass flow rates appropriate for the core temperature of each patient. Alpha-stat acid–base control should maintain the balance between cerebral blood flow and cerebral metabolic rate, and therefore further work is required to establish if the changes we have demonstrated are related directly to blood flow or temperature.

Our anaesthetic technique for cardiac surgery comprised moderate doses of fentanyl (20–30 μg kg–1) supplemented with either less than 1 MAC of a volatile agent or a low-dose (1–3 mg kg–1 h–1) infusion of propofol. This technique produces an AER of small amplitude with an N2 wave latency of approximately 80 ms before cardiopulmonary bypass is established. These patients should be well anaesthetized with little possibility of awareness according to the criteria established by the Northwick Park group [2, 3]. It is interesting to speculate on whether or not current cardiac anaesthetic practice produces patients who are too deeply anaesthetized in our attempt to control the haemodynamic responses to cardiac surgery by suppressing cardiovascular reflexes, rather than by manipulating the cardiovascular system directly.

Acknowledgements
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References