EFFECTS OF LONG-TERM ANAESTHESIA ON AUDITORY EVOKED POTENTIAL AMPLITUDE AND LATENCY

Naoki Mori, Shoichi Sawada, Richard J. Mount and Robert V. Harrison
The Auditory Science Laboratory, Department of Otolaryngology,
The Hospital for Sick Children, University of Toronto

INTRODUCTION

In auditory science, a number of experimental techniques involve the use of anaesthetized animal models. In some studies anaesthesia is maintained for many hours, for example during electrophysiological mapping or optical imaging experiments. We, and others, have often noted a deterioration in auditory function during such long-term experiments. Here we explore systematically these effects with the particular interest in whether changes observed result from effects on central auditory pathways, or are caused by deterioration in cochlear function. We report here the effect of long-term anaesthesia, using a ketamine-xylazine combination, on auditory evoked potentials. We have monitored auditory brainstem evoked responses (ABRs) and middle latency responses (MLRs) from the chinchilla during 12 hours of anaesthesia, and we describe the deterioration in auditory function which results over this period.

MATERIAL AND METHODS

Adult chinchillas weighing between 460 g and 700 g and free from ear disease were used in this experiment. All procedures were carried out within the guidelines of the Canadian Council on Animal Care.

For induction of anaesthesia, atropine 0.04 mg/kg, xylazine 2.4 mg/kg and ketamine 15 mg/kg were injected i.m. Supplemental xylazine 1.2 mg/kg and ketamine 7.5 mg/kg were given at approximately one hour intervals to maintain level of anaesthesia during the experiment.

ABR and MLR potentials were recorded using skin needle electrodes in a mastoid-vertex configuration. The ABR was elicited using a range of tone pip frequencies between 2 and 24 kHz. The responses were amplified and filtered by convention methods. Responses were realized by averaging 300 sweeps with a 20 ms time window (Bio-Sig; Tucker-Davis Technologies). The MLR was elicited using 8 kHz tone bursts at 80 dB SPL. Responses were average of 1,000 sweeps using a 50 ms time window. ABR responses were recorded ten minutes after the initial injection of anaesthetic, ten minutes later, MLR were recorded. This protocol was repeated for 12 hours (Figure 1). Then the anaesthesia was stopped. Twenty four hours later, ABR and MLR were again measured.

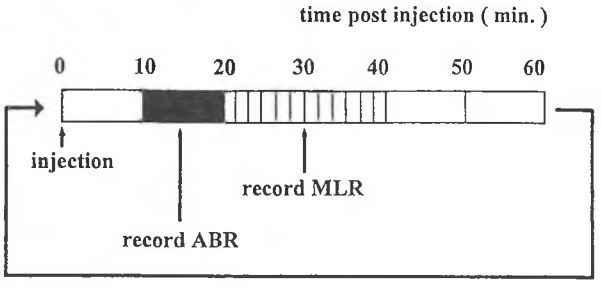

Figure 1. The protocol for recording ABR and MLR.

RESULTS

Figure 2 shows typical results from one subject. The waveforms of MLR, recorded at hourly intervals, are plotted. Early and late peaks are identified (small arrow symbols). These peak latencies gradually increased as the period of anaesthesia was prolonged. Whilst all peaks in the waveform

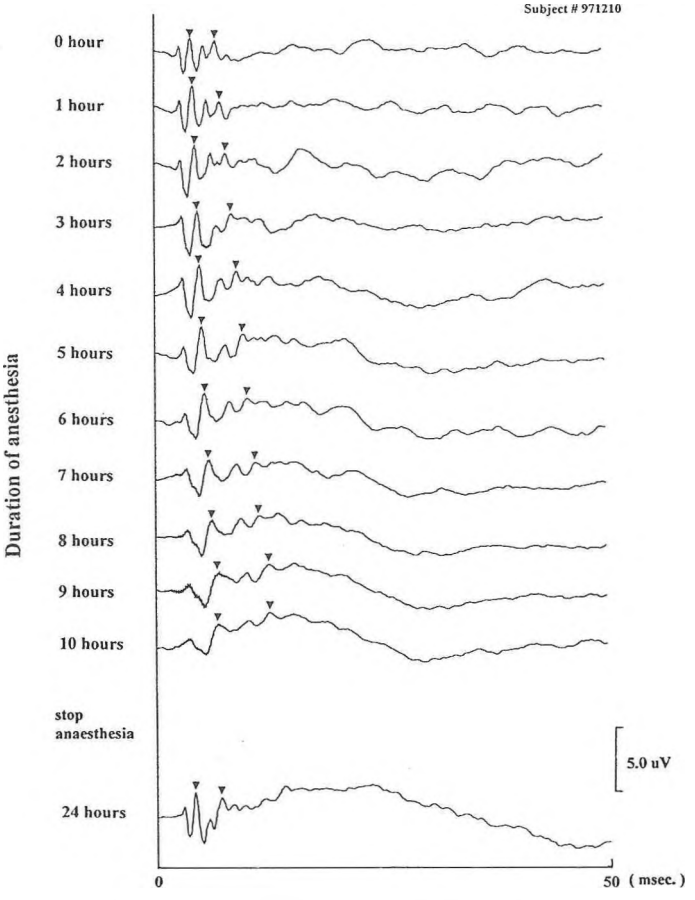

Figure 2. Auditory evoked potentials during long-term ketamine anaesthesia.

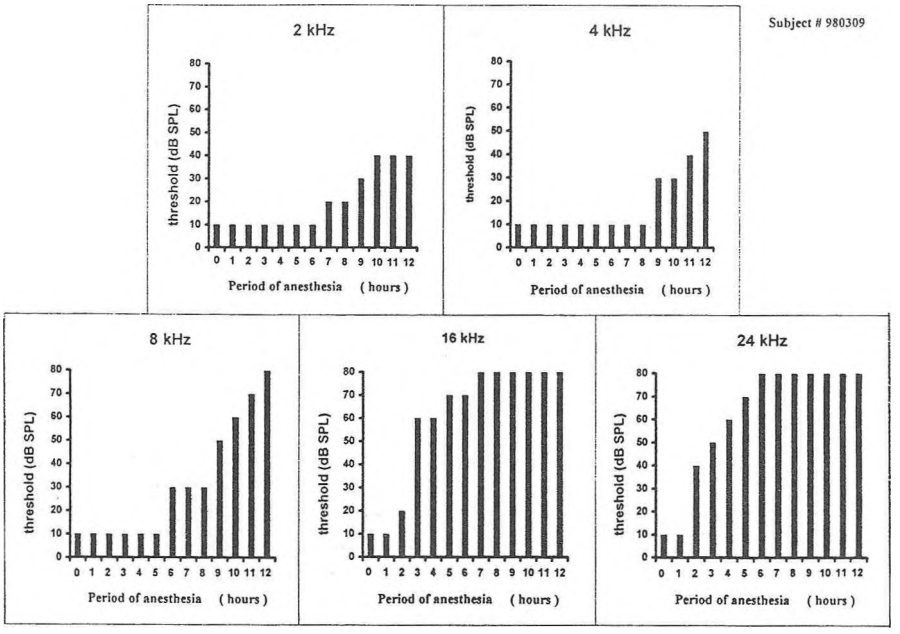

Figure 3. Effects of long-term ketamine anaesthesia on ABR thresholds.

showed increased latency over time, the change in the later peaks was most obvious. One day after the end of the anaesthetic period the waveforms appear normal as indicated in the lower trace of fig. 2. This indicates the reversible nature of the anaesthetic effects.

Figure 3 shows graphs of the ABR thresholds to 2, 4, 8, 16 and 24 kHz tone stimuli, as a function of time during anaesthesia. The threshold increase during anaesthesia was greater on ABR thresholds evoked by high frequency stimuli than by lower frequencies. The threshold shift at 24 kHz and 16 kHz occurred after two hours of anaesthesia. The thresholds increased rapidly reaching 80 dB SPL after six or seven hours. At 8 kHz, threshold changes started after six hours of anaesthesia and gradually increased over c.7 hours to reach 80 dB SPL. At lower frequencies, 4 kHz and 2 kHz, the changes occurred later, between seven and nine hours. The increase in threshold occurred less rapidly, and reached only 40 - 50 dB SPL.

DISCUSSION

The changes reported here agree with related work reported on by others. Sohmer et al. [1] have shown that experimental hypotension depressed ABR in cats. The ABR loss began with the later waves and progressed to the earlier waves. He suggested that hypotension induced cerebral ischaemia and decreased the oxygen supply and that the oxygen supply was the important factor for ABR.

Sanford and Colby [2] reported that in the rabbit, a ketamine-xylazine combination produces a drop in blood pressure and respiratory rate and a reduction of heart rate which recovers between four and six hours following injection. These conditions could influence cochlear function and therefore auditory evoked potentials. In contrast, in a human study it has been reported that ketamine does not suppress auditory evoked potentials in either peak latency or amplitude [3].

Billett et al. [4] reported damage in the cochlea during ischaemia. The damage appeared first in the cells of the basal turn of the cochlea and gradually progressed towards the apex with increasing period of ischaemia. Our results match these findings in that the ABR threshold change appeared first in the responses evoked by higher frequencies and only later progressed to affect responses evoked by lower frequencies.

We interpret our results as indicating that the changes originate at the cochlear level, because all parts of the ABR including the earliest peaks of the waveform show changes. We believe that the changes shown here occur because long-term anaesthesia can result in metabolic or ionic changes which affect haircells and/or nerve cells and their synapses. Functionally the cells in the basal turn of cochlea appear to deteriorate earlier than those apically. Our interest in this study is mainly practical. We are currently exploring a number of different anaesthetic techniques (e.g. barbiturate, halothane) to find the most effective agent for long term studies in chinchilla. There is also a clinical issue. Does long-term surgery in human subjects cause cochlear changes, and are these changes temporary (reversible) or not?

ACKNOWLEDGMENTS

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