

# Effects of cochlear hypoxia on otoacoustic emissions compared with auditory evoked potentials

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## PURPOSE

The purpose of this study was to investigate the effects of mild systemic hypoxia on inner haircell (IHC) and outer haircell (OHC) function. A number of studies have explored the effects of anoxia/hypoxia and ischemia of the inner ear [e.g. 1,2,3,4,5] but have not addressed whether there is a dissociation between IHC and OHC function during such an insult. To monitor OHC activity we recorded otoacoustic emissions (OAEs) which are known to originate at OHC level. IHC/cochlear afferent nerve function was assessed indirectly from auditory brainstem evoked responses (ABR). We hypothesize that in chronic cochlear hypoxia, IHC (and cochlear afferent nerve) activity deteriorates before that of OHCs. Our study represents a model for effects of perinatal hypoxia or anoxia on the inner ears of high risk neonates which may be a contributing factor to the hearing deficits seen in auditory neuropathy [6,7]. We show that changes in IHC and OHC function during mild hypoxia occur with different time courses.

## METHODS

All experiments were carried out in a sound-attenuating booth. Five adult chinchillas weighing from 400 to 600g, free from ear disease, were used. All animals were anesthetized with ketamine (15mg/kg, IM) and xylazine (25mg/kg, IM). To prevent airway obstruction by secretions, atropine (0.1mg/kg, IM) was injected. Half doses of ketamine and xylazine were given for maintenance for anesthesia. All animals were tracheotomized and a small tube was inserted into trachea. To produce systemic hypoxia, a dead space was added to the tidal volume by connecting a syringe with a small hole at the distal end to the tracheal tube. A 20ml volume of dead space was sufficient to change ABR thresholds [3]

## Otoacoustic emissions measurement

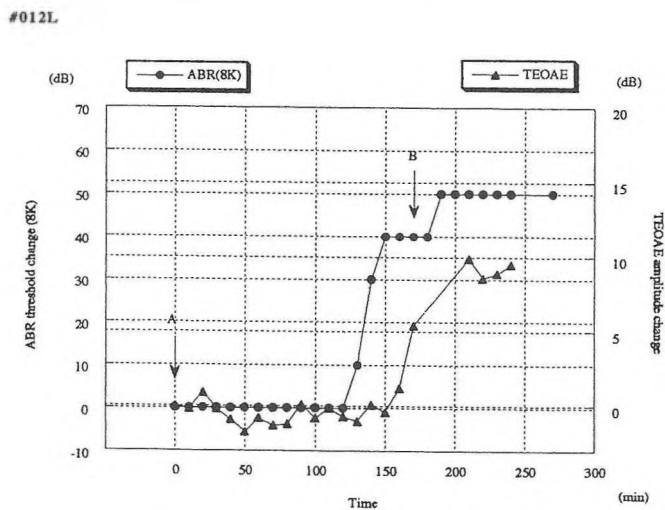
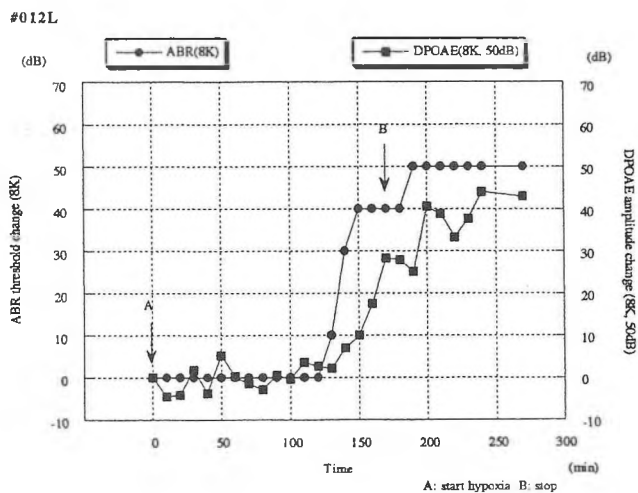
For transient evoked otoacoustic emissions (TEOAE) and distortion product otoacoustic emissions (DPOAE) recording, we used ILO88/92 systems (Otodynamics). TEOAE and DPOAE were measured at 10 minute intervals before and during the period of experimental hypoxia. The parameters for TEOAE were the default protocol for human measurements in the non-linear mode. Stimuli were 80  $\mu$ s clicks at 80 dB peSPL. The responses were the average of 260 sweeps. For DPOAE measurement, test stimuli of  $f_2$  was at 8kHz, from 35 to 80dB SPL. The emissions were generated by presentation of the same level ( $f_1=f_2$ ) at a separation ratio of  $f_2/f_1=1.22$ . To plot the time course (see figure), we selected amplitudes at 50 dB SPL. (We have also measured emission input/output functions to verify that thresholds were not changing independently of these amplitude values.)

## Auditory brainstem evoked response measurement

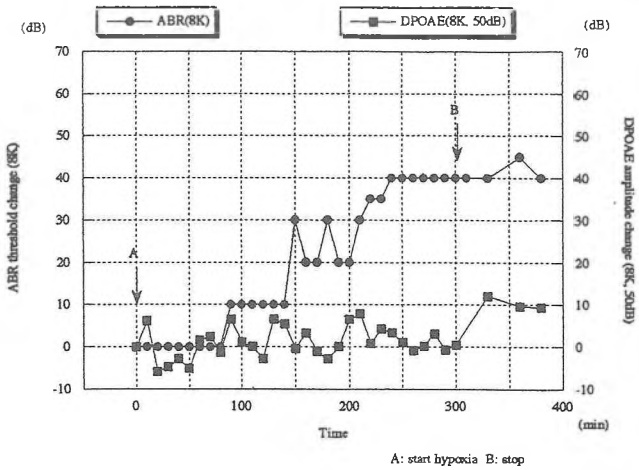
ABR responses were recorded with needle electrodes in standard vertex - bulla (mastoid) configuration. Stimuli were from 0 to 80 dB SPL tone bursts, presented through a calibrated sound system. The responses were amplified and filtered conventionally, and waveforms were averaged (BioSig; Tucker-Davis Technologies). Before and after hypoxia, we measured six frequencies (0.5, 1, 2, 4, 8, 16 kHz). During hypoxia, thresholds at 8 kHz were measured at 10 minute intervals.

## RESULTS

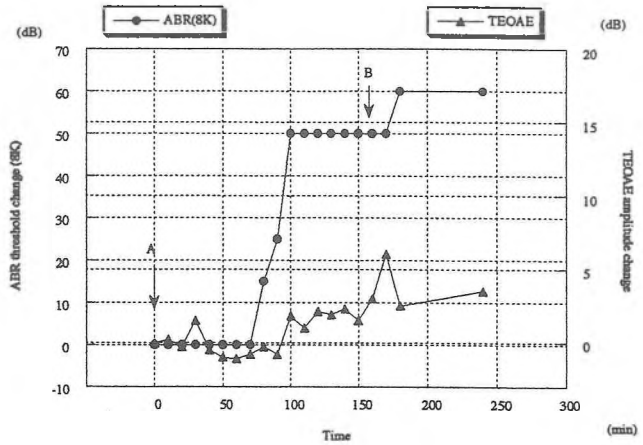
The figures show the time courses of ABR thresholds and of and DPOAE (left panels) TEOAE amplitudes (right panels) during many hours of sustained hypoxia (start and finish of hypoxic period indicated by arrows A and B). In all animals, ABR thresholds were significantly increased within 90-150 minutes, whilst otoacoustic emission amplitudes showed either little deterioration (e.g. #013R, #014L) or lagged behind ABR changes (#012L). It is of importance to note the general correspondence between TEOAE and DPOAE amplitude changes measured from the same cochlea.



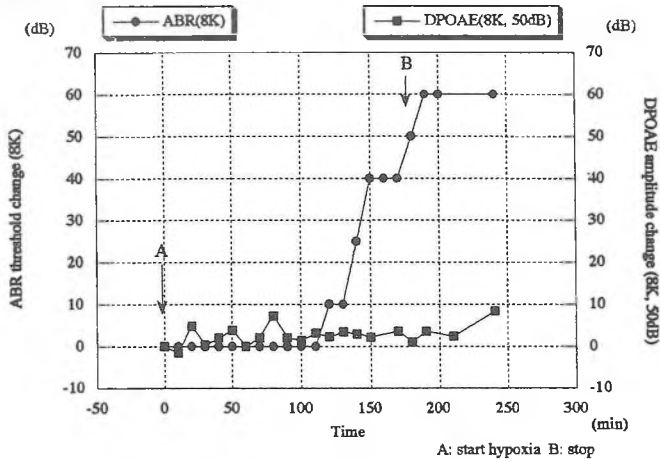
#013R



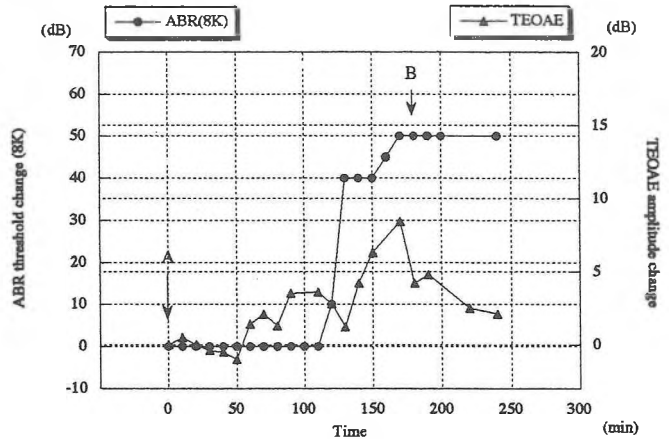
#014L



#016L



#017R



## DISCUSSION

We show that IHC/cochlear afferent function as reflected in neural evoked responses are more sensitive to prolonged, mild cochlear hypoxia than the activity of OHCs as revealed in otoacoustic emission measures. Our focus on cochlear hypoxia relates to the clinical issue of possible IHC/cochlear afferent damage as a result of hypoxia in high risk infants, either resulting from difficult birth, or circulatory insufficiency in utero. Such IHC damage could result in auditory neuropathy [6], a hearing disorder which appears to result from a sub-total depletion or desynchronization of cochlear afferent neurons, but in which OHC function (as shown by otoacoustic emission or cochlear microphonic recording) is much less damaged. The present study which shows that hypoxia can have an initial effect on the IHC/cochlear afferents supports our theory [7] that hypoxia is an important etiological factor in some types of auditory neuropathy.

## REFERENCES

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