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THE EFFECTS OF EXPERIMENTAL HYDROPS VERSUS INCREASED INTRACOCHLEAR PRESSURE ON AUDITORY FUNCTION IN THE GUINEA PIG

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Abstract - In order to investigate the physiological consequences of hydrops on auditory function an animal model has been developed in which endolymphatic hydrops is surgically induced and electrophysiological responses are monitored preceding during and following hydrops induction. These studies have revealed that experimental hydrops systematically results in a fluctuant low frequency hearing loss (below 4 kHz) which is apparent within a few days of surgery. After about two months there is in addition a very high frequency loss (16 kHz and above). A final mid frequency loss (including 8 kHz), after a further lapse of one month, results in a flat audiogram.

In order to investigate whether increased endolymphatic pressure is responsible for the electrophysiological changes observed in endolymphatic hydrops we have recently placed a canula in the endolymphatic canal of normal hearing guinea pigs and hence increased the intracochlear pressure to investigate the effects on the audiogram. There is an immediate high frequency loss which includes 8 kHz, followed by a low frequency loss below 2 kHz and finally a mid frequency loss around 4 kHz.

These two experimental procedures result in cochlear pathologies which differ in two principal aspects. The immediate effect of experimental hydrops is a deterioration of the low frequencies whilst that of increased pressure is a deterioration of the high frequencies. Experimental hydrops appears to preserve the functioning of the cochlea best around 8 kHz whilst increased pressure applied at the base of the cochlea appears to preserve the 4 kHz region. The data suggest that increased intracochlear pressure is not likely to account for early low frequency fluctuant hearing losses in experimental hydrops and in Menière's disease but could account for the evolutive nature of the deafness to include the higher frequencies.

1 - INTRODUCTION

Ever since Hallpike and Cairns (1938) demonstrated an excess of endolymph in the inner ear of Menière's patients "endolymphatic hydrops", it has been assumed that hydrops could account for the characteristic symptoms: tinnitus, vertigo and fluctuant low frequency hearing loss. The generally held conception has been that the excess endolymph increases pressure in the endolymphatic spaces and hence various clinical approaches to the treatment of Menière's disease are aimed at reducing the pressure. Diuretic treatment or
approaches to the treatment of Meniere's disease are aimed at reducing the pressure. Diuretic treatment or endolymphatic sac decompression have not however proven as successful as might have been expected if excess endolymphatic pressure were the key element involved. In fact there is some evidence that surgical intervention has a placebo effect (Bretlau et al., 1983). Indeed Tran ba Huy (1984) has demonstrated that the removal of a small volume of endolymph in two Meniere's patients resulted in a further deterioration of audition rather than an improvement.

The aim of the present study was to compare the deterioration of auditory function in guinea pigs with confirmed endolymphatic hydrops (experimentally-induced) with that provoked by augmenting the endolymph pressure in guinea pigs without hydrops. If excess endolymphatic pressure is implicated in the pathology of hydrops which develops over a period of months then the pressure experiment should reveal the same type of auditory deterioration over the duration of the experiment which lasts several minutes.

2 - EXPERIMENTAL METHODS

Induction of endolymphatic hydrops

Pigmented guinea pigs (n=6) were chronically implanted with a round-window platinum ball electrode using standard techniques. The animals were anaesthetised (1 ml/kg) for the duration of the surgery using a Ketalar/Rompun mixture in the ratio of 2:1 (ketamine 50 mg/ml, xylazine 2%). The animals were allowed to recover and two weeks later the compound action potential (CAP) audiogram was determined using tone pip stimuli (2ms rise/fall, 30 stimulations/s) presented via a headphone (Sennheiser, HD424X) in the free field at 1 cm from the ear pinna. For the determination of the audiogram the animals were awake but sedated (Rompun 0.5ml/kg) with the body and head movements restricted by the use of a body-holder with a nose-ring. When the audiogram was shown to be normal the animals were then anaesthetised (as above) and operated to provoke endolymphatic hydrops. The posterior fossa was opened, the dura mater deflected laterally, the cerebellum displaced medially, the endolymphatic sac visualised and the endolymphatic canal opened using a pointed instrument. Bone wax was forced into the opening in order to block the canal. A piece of gel-foam was then placed on the exposed cerebellum and the skin sutured in place. The animals recovered within the hour and showed no behavioral signs of vertigo. The CAP audiograms were tested repeatedly during the 4 months which followed hydrops induction.

Increasing endolymphatic pressure

Under anaesthesia the animals (n=15) were implanted acutely with a platinum ball electrode on the round window. The CAP audiogram was immediately determined. When the audiogram was judged to be normal the endolymphatic sac was exposed in the same manner as described above. The proximal end of the sac/endolymphatic canal was pierced using a pointed instrument and a needle (0.5mm) was forced into the opening in order to cannulate the endolymphatic canal. The needle was connected to a length of tubing filled with endolymph-like solution (330 mosmole/kg H2O, K+ 153 mM, pH 7.4) (16), which in turn was connected to screw-type syringe. The syringe had a double exit with one opening towards the electrode using standard techniques. The animals were anaesthetised (1 ml/kg) for the duration of the surgery using a Ketalar/Rompun mixture in the ratio of 2:1 (ketamine 50 mg/ml, xylazine 2%). The animals were allowed to recover and two weeks later the compound action potential (CAP) audiogram was determined using tone pip stimuli (2ms rise/fall, 30 stimulations/s) presented via a headphone (Sennheiser, HD424X) in the free field at 1 cm from the ear pinna. For the determination of the audiogram the animals were awake but sedated (Rompun 0.5ml/kg) with the body and head movements restricted by the use of a body-holder with a nose-ring. When the audiogram was shown to be normal the animals were then anaesthetised (as above) and operated to provoke endolymphatic hydrops. The posterior fossa was opened, the dura mater deflected laterally, the cerebellum displaced medially, the endolymphatic sac visualised and the endolymphatic canal opened using a pointed instrument. Bone wax was forced into the opening in order to block the canal. A piece of gel-foam was then placed on the exposed cerebellum and the skin sutured in place. The animals recovered within the hour and showed no behavioral signs of vertigo. The CAP audiograms were tested repeatedly during the 4 months which followed hydrops induction.

The CAP audiogram was determined repeatedly during the experimental procedure: after the dura mater was deflected, after the cannula was in place, and at intervals following the application of a fixed pressure.

3 - RESULTS -

Endolymphatic hydrops typically provoked a sequential loss of auditory sensitivity which is exemplified in figure 1. Immediately following the operation there is a low frequency hearing loss with an abrupt threshold shift between 8 kHz and 6.4 kHz. This typical hydropic form of early hydrops is still evident at 4 weeks post operation. At 8 weeks there is an additional very high frequency loss which results in a typical "V" shaped audiogram with the best frequency being 8 kHz. At 8/12 weeks the 8 kHz becomes affected and at 16 weeks post operation the audiogram approaches a flat conformation.

The augmentation of the hydrostatic pressure of the scala media typically provoked a sequential loss of auditory sensitivity which was different from that described above following hydrops induction. An example is presented in figure 2. Immediately after the application of the pressure there is a very high frequency loss. This loss extends down to and including 8 kHz in general. There then follows a very low frequency loss which is most evident at 500 Hz and 1/2 kHz. These losses give the audiogram a "U" shaped form with the best frequency around 4 kHz. As the pressure endures further the thresholds for all frequencies appear to be effected by the pressure and the "U" shaped audiogram becomes more raised.
Figure 1. Experimentally-induced hydrops of the inner ear. A typical sequence of CAP audiograms from an individual animal (GP394). Note the low frequency loss, high frequency loss and finally the mid frequency loss with "best" frequency at 8 kHz.

Endolymp-like Solution 0.5 cm Hg (GP345)

Figure 2. Increase of hydrostatic pressure of the inner ear. A typical sequence of CAP audiograms from an individual animal (GP34). Note the high frequency loss, low frequency loss and finally the mid frequency loss with "best" frequency at 4 kHz.

4 - DISCUSSION

We have observed that blocking of the endolymphatic duct in the guinea pig systematically results in a low frequency hearing loss within days of the operation and this hearing loss evolves to a flat loss within months. The model presents a number of features which are particularly interesting since they show a certain similarity to symptoms of Menière's disease. The low frequency hearing loss is fluctuant (Horner and Cazals, 1987). The abrupt threshold shift between the 8 kHz and 6.4 kHz, as demonstrated here, is also very intriguing and in particular since a similar form of audiogram (with a two octave shift) is often observed in Menière's patients (Martin and Martin, 1982; Morrison, 1984).
Until now it has been generally assumed that the hearing loss in Menière's patients was due in some way to the increased pressure within the scala media. Despite this generally held conception there has been no real evidence for an increased pressure. In fact it has been demonstrated that withdrawal of endolymph in two Menière's patients did not improve but rather provoked a deterioration of hearing which recovered to the preoperative values in days or weeks (Tran ba huy, 1984). In addition there is some evidence that endolymphatic sac decompression surgery has a placebo effect (Bretlau et al., 1983). In the experimental model the presence of hydrops can be checked (which is not the case for Menière's patients) and so experimentally induced hydrops should present a good model for investigating possible intracochlear pressure changes. However in the experimental model Long and Morizono (1987) could not detect any pressure difference between the endolymph and the perilymph in early hydrops and only a very small pressure difference of less than 1 cm H2O was detected in long-standing hydrops (Ito et al., 1987; Bohmer et al., 1989).

The technique for measuring intracochlear pressure, however, can be criticised on the grounds that a small hole must be pierced in the cochlear wall in order to introduce a measuring device and hence there is possibly a sudden pressure release which could go undetected. In order to avoid this technical problem we have introduced the pressure device within the endolymphatic duct – leaving the cochlea untouched. We have reasoned that if pressure is implicated in the pathology of hydrops, increasing the hydrostatic pressure in normal cochleas should produce hydropic-like audiograms. As demonstrated here this does not seem to be the case – at least in early hydrops. On the other hand increased pressure might partially account for the later high frequency loss associated with hydrops.

These conclusions fit well with some earlier observations made by us. We have demonstrated that the volume of hydrops in the model can be reduced by the oral administration of a diuretic but that the hearing loss is not prevented (Horner at al., 1989a). Those data suggested that the hydrops and the hearing loss due to hydrops may be considered separately. In fact the low frequency hearing loss (above the first cochlear turn) associated with hydrops does not correlate with the distribution of hydrops observed throughout the cochlea nor with the hair cell loss in the apical turn (Kimura and Schuknecht, 1965, Aran et al., 1984). On the other hand we have recently demonstrated a new outer hair cell stereocilia pathology in two Meniere's patients did not improve but rather provoked a deterioration of hearing which recovered leaving the cochlea untouched. We

5 REFERENCES


