Hearing Research 330 (2015) 147–154

Contents lists available at ScienceDirect

Hearing Research

journal homepage: www.elsevier.com/locate/heares

High frequency bone conduction auditory evoked potentials in the guinea pig: Assessing cochlear injury after ossicular chain manipulation

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ARTICLE INFO

Article history:
Received 4 March 2015
Received in revised form
11 October 2015
Accepted 12 October 2015
Available online 29 October 2015

Keywords:
Bone conduction
Evoked potentials
Guinea pigs
Otologic surgical procedures
Cochlear injury
Magnetostrictive transducer

ABSTRACT

Permanent high frequency (>4 kHz) sensorineural hearing loss following middle ear surgery occurs in up to 25% of patients. The aetiology of this loss is poorly understood and may involve transmission of supra-physiological forces down the ossicular chain to the cochlea. Investigating the mechanisms of this injury using animal models is challenging, as evaluating cochlear function with evoked potentials is confounded when ossicular manipulation disrupts the normal air conduction (AC) pathway. Bone conduction (BC) using clinical bone vibrators in small animals is limited by poor transducer output at high frequencies sensitive to trauma. The objectives of the present study were firstly to evaluate a novel high frequency bone conduction transducer with evoked auditory potentials in a guinea pig model, and secondly to use this model to investigate the impact of middle ear surgical manipulation on cochlear function. We modified a magnetostrictive device as a high frequency BC transducer and evaluated its performance by comparison with a calibrated AC transducer at frequencies up to 32 kHz using the auditory brainstem response (ABR), compound action potential (CAP) and summating potential (SP). To mimic a middle ear traumatising stimulus, a rotating bur was brought in to contact with the incudomalleal complex and the effect on evoked cochlear potentials was observed. BC-evoked potentials followed the same input–output function pattern as AC potentials for all ABR frequencies. Deterioration in CAP and SP thresholds was observed after ossicular manipulation. It is possible to use high frequency BC to evoke responses from the injury sensitive basal region of the cochlea and so not rely on AC with the potential confounder of conductive hearing loss. Ongoing research explores how these findings evolve over time, and ways in which injury may be reduced and the cochlea protected during middle ear surgery.

This article is part of a Special Issue entitled <IEB Kyoto>.

1. Introduction

This study has two principal aims. The first is to evaluate the use of a magnetostrictive bone conduction (BC) transducer to measure auditory function (cochlear potentials and auditory brainstem responses) in guinea pigs across a greater frequency range than is possible with conventional BC transducers. The second aim is to use this transducer to investigate the acute impact of a controlled, repeatable middle ear manipulation on cochlear function, as may occur as a consequence of middle ear surgery. A key purpose of developing this approach is to study the extent and mechanisms of sensorineural hearing loss following middle ear surgery. Bone conduction stimulation of evoked auditory potentials enables inner ear injury to be measured following middle ear surgical manipulations where there may also be some damage to the middle ear air conduction pathways.

The risk of postoperative sensorineural hearing loss following middle ear surgery is cited as 0.5% for a total loss and up to 5% for a partial loss (Dawes and Curry, 1974; Shea, 1998). However, the

Abbreviations: ABR, Auditory brainstem response; AC, Air conduction; BC, Bone conduction; CAP, Compound action potential; dBSPL, Decibel sound pressure level; dBSPLeq, Decibel sound pressure level equivalent; DC, Direct current; kHz, Kilohertz; I/O, Input–output (function); SP, Summating potential

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http://dx.doi.org/10.1016/j.heares.2015.10.009
0378-5955/

definition of partial loss greatly influences the apparent incidence of injury and there is substantial variation in definition within the literature (Berliner et al., 1996). In particular, as the higher audiometric frequencies are more sensitive to insult (Domenech and Carulla, 1988), definitions of loss which include the lower frequencies have less apparent injury (de Bruijn et al., 2001). In humans, nearly a quarter (4.6–60%) of patients undergoing stapes surgery have a postoperative sensorineural hearing loss at 4 kHz (Boonchoo and Puapermpoonsiri, 2007; Hausler et al., 1999; Lesinski and Stein, 1989; Liden et al., 1981; Shambaugh, 1963). In contrast, and using data from their same patient cohort, Lesinski and Stein (1989) showed that if thresholds were averaged over the lower frequencies of 0.5, 1 & 3 kHz only, there was no sensorineural loss (>10 dB).

The aetiology of this postoperative sensorineural hearing loss is not well understood. Potential mechanisms include noise exposure (Kylen et al., 1977), drill contact with the ossicular chain (Hallmo and Mair, 1996; Helms, 1976; Smyth, 1976; Smyth et al., 1971), infection (Brahe Pedersen and Felding, 1991; Sheehy and Crabtree, 1973), antisepsis (Packer et al., 1982) or the transmission of manipulation forces directly to the cochlea via the stapes and oval window (Kylen et al., 1980; Smyth, 1976; Smyth et al., 1971; Vartiainen and Seppa, 1997). Understanding the mechanisms of injury is essential to develop appropriate therapeutic or preventative interventions.

The otologic drill has been implicated in postoperative sensorineural hearing loss either by direct contact with the ossicular chain (Hallmo and Mair, 1996; Helms, 1976; Smyth, 1976; Smyth et al., 1971), or noise injury from prolonged drilling (Kylen et al., 1977). It may be that the final common pathway of assault on the cochlea is the same, and that drill contact with the ossicular chain simply represents a higher intensity noise, albeit over a much briefer period. Drilling on an intact ossicular chain can transmit over 130 dB eardrum pressure to the inner ear (Helms, 1976) and in humans, the short process of the incus is most susceptible to injury (Urquhart et al., 1992). However, despite peak noise levels of 125 dBA, with mean noise levels of greater than 100 dBA recorded in mastoid drilling (Holmquist et al., 1979), most authors have not found any association between postoperative sensorineural hearing loss and drill noise (Hallmo and Mair, 1996; Man and Winerman, 1985; Urquhart et al., 1992).

Animal studies are an important way to model the injury by using auditory evoked potentials to evaluate the functional loss from induced traumatic middle ear manipulations. This would then enable investigations of the mechanisms of inner ear injury in animal models. However, potential problems with air-conducted evoked potentials arise when the middle ear has been disturbed, as any conductive loss associated with surgical exposure or middle ear manipulation may attenuate sound transmission to the inner ear.

Bone conduction (BC) provides a stimulus to the cochlea that mostly bypasses the middle ear structures, although in humans the external and middle ear influence bone conduction in the lower frequencies up to about 3 kHz (Stenfelt and Goode, 2005). However, bone conduction using a conventional bone vibrator can provide useful information on cochlear status only up to around 5 kHz because the power output of most of these transducers falls away markedly above this frequency (Frank and Richards, 1980). Small mammals, which are used as models of inner ear injury and disease, have a higher hearing frequency range, up to 50–90 kHz depending on the species (Fay, 1988; Warfield, 1973), and thus the conventional human bone vibrator is only capable of stimulating the more robust apical regions of the animal cochlea. Subsequently, these standard bone conductors are inadequate for the sensitive detection of cochlear injury in small mammals by auditory evoked potentials, and particularly high frequencies where injury from middle ear manipulation is more apparent.

Magnetostrictive BC transducers have a much greater frequency range than standard electromagnetic BC transducers due to their ability to change shape in the presence of a magnetic field (Popelka et al., 2010). Popelka et al. (2010) used this device in the clinical setting to extend BC measurements from the 4–6 kHz range up to 16 kHz. Sakai et al. (2006) used such a magnetostrictive bone conductor to evoke potentials up to 30 kHz in rats, which lies in the sensitive high frequency basal turn.

In comparison with the mouse and rat, which have upper limits of hearing at ~90 and ~75 kHz respectively, the guinea pig hearing frequency spectrum spans a much lower range (0.054–50 kHz, Fay, 1988; Warfield, 1973). This brings the sensitive high frequency basal region much closer to the upper limits of a magnetostrictive bone conductor.

Here we report on the use of a magnetostrictive transducer to produce bone-conducted sound evoked potentials in the guinea pig and provide initial data on the impact of a surgical middle ear manipulation on the cochlea as a model of acute cochlear injury from middle ear manipulation.

2. Materials and methods

2.1. Study 1: bone-conduction device

In these studies we used non-mated, Tricolour Dunkin–Hartley female guinea pigs (6–8 weeks), mean weight 396 g ± 23 g (n = 13). This study was approved by the University of Auckland Animal Ethics Committee.

Response to sound was qualitatively assessed preoperatively with the Preyer's reflex in response to a clap and the external auditory canal was examined to exclude animals with any obvious underlying infection. Anaesthetic pre-medication (0.05 mg/kg buprenorphine (Temgesic)) was administered before anaesthesia was induced with 1500 mg/kg ethyl carbamate (Urethane). Top up anaesthesia was provided with a 50 mg/kg ketamine and 2 mg/kg xylazine mixture. Animals were euthanised with ketamine/xylazine overdose following the completion of recordings.

All experiments were performed in an acoustically and electrically shielded booth. The auditory evoking and potential recording hardware was a modular TDT System 3 (Alachua, FL) with a sampling rate of 200 kHz. Auditory brainstem responses (ABR) were recorded via the RA4 preamplifier (250× amplification) and RA4LI head stage (20× amplification) with subdermal platinum electrodes. The sampling rate of the RA4 is 25 kHz so this was only used for ABR where the target waveforms are below the Niquist value of ~10 kHz. The transducer used for air-conducted (AC) sound was a TDT closed field electrostatic speaker coupled to the animal's external auditory canal by a 10 cm plastic tube. AC latencies were adjusted by 0.3 ms to account for the delay in sound transmission along the tube. The non-linear output from this speaker was corrected with TDT's System 3 calibration software SigCal.

The magnetostrictive bone-conduction transducer was derived from commercially available BC headphones HP-F200 (TEAC, Tokyo, Japan). The transducer was extracted and coupled to the TDT System 3 (Alachua, FL). The input amplifier which is provided with the headphones was removed as this limited the performance of the transducer to frequencies below 24 kHz. The HP-F200 has an output of 2.8 W and a driving calibration voltage of 80 dB = 5 V (peak) was used for all frequencies. No direct current (DC) bias voltage was required.

To correct for BC transducer non-linearity a post-hoc analysis was performed for every animal whereby BC ABR wave I and II input–output (I/O) functions at each frequency were compared