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Research paper

Delayed low frequency hearing loss caused by cochlear implantation interventions via the round window but not cochleostomy

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ABSTRACT

Cochlear implant recipients show improved speech perception and music appreciation when residual acoustic hearing is combined with the cochlear implant. However, up to one third of patients lose their pre-operative residual hearing weeks to months after implantation, for reasons that are not well understood. This study tested whether this "delayed" hearing loss was influenced by the route of electrode array insertion and/or position of the electrode array within scala tympani in a guinea pig model of cochlear implantation. Five treatment groups were monitored over 12 weeks: (1) round window implant; (2) round window incised with no implant; (3) cochleostomy with medially-oriented implant; (4) cochleostomy with laterally-oriented implant; and (5) cochleostomy with no implant. Hearing was measured at selected time points by the auditory brainstem response. Cochlear condition was assessed histologically, with cochleae three-dimensionally reconstructed to plot electrode paths and estimate tissue response. Electrode array trajectories matched their intended paths. Arrays inserted via the round window were situated nearer to the basilar membrane and organ of Corti over the majority of their intrascalar path compared with arrays inserted via cochleostomy. Round window interventions exhibited delayed, low frequency hearing loss that was not seen after cochleostomy. This hearing loss appeared unrelated to the extent of tissue reaction or injury within scala tympani, although round window insertion was histologically the most traumatic mode of implantation. We speculate that delayed hearing loss was related not to the electrode position as postulated, but rather to the muscle graft used to seal the round window post-intervention, by altering cochlear mechanics via round window fibrosis.

1. Introduction

Electroacoustic hearing (EAS) has led to improved speech perception and music appreciation in cochlear implant (CI) recipients (Gstoettner et al., 2006; Dorman et al., 2009; Adunka et al., 2013; Gantz et al., 2005; Kiefer et al., 2005; Gfeller et al., 2006). Yet up to one third of CI recipients experience a progressive loss of residual hearing (Gstoettner et al., 2006; Woodson et al., 2010) which threatens to erode the benefits of EAS. The cause(s) of this hearing loss remain elusive. Delayed hearing loss in humans typically occurs in the months after CI surgery, often following a period of stable hearing. This suggests that delayed hearing loss may be associated with either a chronic or slowly progressing intracochlear pathology. One such candidate is the tissue response to the intracochlear electrode array, which is typified by fibrosis, neo-osteogenesis, and an infiltrate of inflammatory cells such as mononuclear leukocytes and histiocytes (Cervera-Paz and Linthicum, 2005; Seyyedi and Nadol, 2014) – findings consistent with this being predominantly a foreign body reaction (Gstoettner et al., 2006; Dorman et al., 2009; Adunka et al., 2013; Gantz et al., 2005; Kiefer et al., 2005; Gfeller et al., 2006; Cervera-Paz and Linthicum, 2005; Nadol et al., 2008; Gstoettner et al., 2004; Ilberg Von

Abbreviations: EAS, electroacoustic hearing; CI, cochlear implant; ABR, auditory brainstem response; SV, stria vascularis; PTA, pure tone average; LBT, lower basal turn; UBT, upper basal turn; LT2, lower second turn; UT2, upper second turn; IHC, inner hair cell; OHC, outer hair cell; SGC, spiral ganglion cell; OSL, osseous spiral lamina

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et al., 1999; Turner et al., 2008). Giant cells within a foreign body reaction produce free radicals to degrade the implanted material, and have been implicated in some cases of "soft failure" of CI devices (Gstoettner et al., 2006; Adunka et al., 2013; Seyyedi and Nadol, 2014; Nadol et al., 2008; Choi and Oghalai, 2005). If similar mechanisms occur near the organ of Corti, it is conceivable that the sensory neuroepithelium could be damaged, resulting in delayed hearing loss.

Intracochlear fibrosis (or osteoneogenesis) could also potentially influence hearing by interfering with cochlear mechanics (Gstoettner et al., 2006; Woodson et al., 2010; Choi and Oghalai, 2005). Fibrosis within the basal turn of scala tympani is thought to dampen acoustic tuning (i.e. hearing) at the apex of the cochlea, while fibrosis of the basilar membrane is thought to dampen acoustic tuning locally (Cervera-Paz and Linthicum, 2005; Seyyedi and Nadol, 2014; Choi and Oghalai, 2005; O'Leary et al., 2013). Consistent with this, we have observed an association between extensive fibrosis and gradual progression of hearing loss in guinea pigs over the first month after surgery (O'Leary et al., 2013; Shepherd et al., 1983; Xu et al., 1993; James et al., 2008). In light of these considerations, intracochlear fibrosis could conceivably cause delayed hearing loss if its physical characteristics change over time.

This study intended to examine whether the trajectory of the electrode array within scala tympani might influence delayed hearing loss. We reasoned that the electrode array trajectory would determine the location and possibly the extent of the foreign body ("tissue") response, and therefore its effects upon cochlear mechanics or the organ of Corti. The electrode array trajectory was controlled by using the two main surgical approaches to cochlear implantation, namely insertion via the round window (to orient the electrode near to the basilar membrane), or a cochleostomy. To further control electrode array position, we developed a cochleostomy technique that caused the electrode array to traverse scala tympani either more medially or laterally relative to the modiolus. Auditory brainstem responses were recorded at selected time points over a 12 week period, at which time cochleae were harvested then subjected to histopathological analysis.

2. Materials and methods

2.1. Experimental design

All experiments were approved by and conducted according to the guidelines of the Animal Research Ethics Committee of the Royal Victorian Eye and Ear Hospital (principal investigator David Rowe; application 11/236AR). The study was performed on 35 Dunkin-Hartley tricolour guinea pigs (≥350 g). These were randomly allocated to five treatment groups. In two round window treatment groups, the round window membrane was incised, with an electrode array then inserted (round window insertion group) or not inserted (round window incision group) into the scala tympani. The remaining treatment groups all underwent scala tympani cochleostomy, followed in one group by laterally directed insertion of an electrode array (lateral insertion group), or by medially directed insertion of an electrode array in another group (medial insertion group). Auditory brainstem responses (ABRs) were recorded before surgery and 1, 4 and 12 weeks after surgery, after which subjects were euthanised and their cochleae harvested for histological analysis. . All subjects possessed normal hearing (defined here as an ABR threshold to a 100 μs click less than 48 dB peak–peak equivalent) before surgery.

2.2. Auditory brainstem responses

Subjects were anaesthetised with a intramuscular injection of mixed ketamine (40 mg/kg) and xylazine (4 mg/kg). The ABR recording system has been described previously (Shepherd et al., 1983; Xu et al., 1993; James et al., 2008; Merchant, 2010). Computer-generated acoustic stimuli (clicks and tone pips lasting 5 ms with 1-ms rise/fall times, with tone pips presented at frequencies of 2, 8, 16, 24 and 32 kHz) were delivered to anaesthetised subjects via a loudspeaker (Richard Allen DT-20, UK) placed 10 cm from the pinna. ABRs were recorded differentially using subcutaneous needle electrodes placed at the vertex and nape. A grounding electrode was placed further caudally in lateral subcutaneous tissue. Ear mould compound (Otoform, Dreve, Germany) was used to attenuate hearing in the contralateral ear. Using this method, the frequency-specific cross-head attenuation (measured from the occluded ear canal of the guinea pig) is 28, 27, 35, 45 and 28 dB at 2, 4, 8, 16 and 32 kHz, respectively.

Responses were amplified by a factor of 100,000 (DAM-5A, W–P Instruments Inc., USA) and band-pass filtered (Krohn-Hite 3750, Avon, USA) between 150 Hz and 3 kHz (6 dB/octave). The filter output was fed to a 16- bit analogue-to-digital converter (Tucker Davis Technologies, USA) and sampled at 20 kHz for a period of 10 ms following stimulus onset. Thirty stimuli were presented per second. Responses were averaged over 250 stimulus repetitions. Stimulus intensity was decremented in 5 dB steps from high stimulus levels to sub threshold. Waveforms were exported to a software analysis program (written by Dr. James Fallon, adapted by Prof. Stephen O'Leary using Igor 5.02, Wavemetrics Inc., USA) and analysed by the researcher who was blinded to subjects' identity and treatment group. Threshold was defined as the lowest intensity stimulus that evoked a response of >0.4 μV amplitude in wave III of the ABR (responses of this amplitude reliably exceeded background noise).

2.3. Electrode array

The electrode array comprised three platinum rings, each welded to a platinum wire 25 μm in diameter, all housed within a Silastic® carrier (MDX4-4210, Dow Corning Products, USA). The electrode tip was tapered to a diameter of 0.41 mm and had a maximum diameter of 0.45 mm. The three platinum rings, each separated by 0.75 mm, were situated near the tip of the electrode and served as visible markers of insertion depth. The total length of the array was 15 mm. All electrode arrays were sterilised before use.

2.4. Cochlear interventions

Guinea pigs were anaesthetised with an intramuscular injection of mixed ketamine (60 mg/kg) and xylazine (4 mg/kg). Local anaesthesia was induced at the target ear with a subcutaneous injection of 2% lignocaine. A curvilinear post-auricular incision was made through skin and subcutaneous tissues to expose the bulla. A #11 blade on a #3 handle rotated in the hand was used to make a bullostomy, through which the round window and basal turn were sighted. Care was taken not to disturb the ossicles or external auditory canal. The cochlea was accessed either by incising the round window membrane with a micro pick (round window groups) or by using a 1 mm diamond bur to drill a cochleostomy in the basal turn adjacent to the round window (cochleostomy groups). In the round window, medial and lateral insertion groups, an electrode array was inserted into the scala tympani until resistance was encountered. The round window or cochleostomy was then sealed with harvested muscle. In the lateral and medial