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Research paper

Effects of deafening and cochlear implantation procedures on postimplantation psychophysical electrical detection thresholds

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ABSTRACT

Previous studies have shown large decreases in cochlear implant psychophysical detection thresholds during the weeks following the onset of electrical testing. The current study sought to determine the variables underlying these threshold decreases by examining the effects of four deafening and implantation procedures on detection thresholds and implant impedances. Thirty-two guinea pigs were divided into four matched groups. Group I was deafened and implanted Day 0 and began electrical testing Day 1. Group II was deafened and implanted Day 0 and began electrical testing Day 45. Group III was deafened Day 0, implanted Day 45 and began electrical testing Day 46. Group IV was not predeafened but was implanted Day 0 and began electrical testing Day 1. All groups showed threshold decreases over time but the magnitude of change, time course and final stable threshold levels depended on the type and time course of treatment. Impedances increased over the first two weeks following the onset of electrical testing except in Group II. Results suggest that multiple mechanisms underlie the observed threshold shifts including (1) recovery of the cochlea from a temporary pathology caused by the deafening and/or implantation procedures, (2) effects of electrical stimulation on the auditory pathway, and (3) tissue growth in the implanted cochlea. They also suggest that surviving hair cells influence electrical threshold levels.

1. Introduction

Previous studies involving chemical deafening and implantation of the cochlea in animal research on cochlear implants showed large fluctuations in psychophysical detection thresholds to electrical stimuli for a period of time following surgery. In nonhuman primates, thresholds increased within days after surgery, then decreased over a period of one to several months, eventually stabilizing at or below the originally measured levels (Pfingst et al., 1979; Pfingst, 1990). In guinea pigs, threshold decreases were observed several days after surgery culminating in stable, relatively low thresholds after 30–40 days (Miller et al., 2000). It is important to understand the functional condition of the auditory system during these periods of change, particularly if that condition is changing rapidly over time, and to understand its relationship to the longer term, more stable periods that characterize patients with cochlear implants. This study aims to define variables responsible for these postimplantation fluctuations and considers several possible hypotheses for mechanisms underlying the observed changes.

One hypothesis is that postimplantation threshold changes may reflect a temporary pathology and subsequent recovery of the cochlea from trauma caused by the deafening agent and/or the physical insertion of the implant. In our cochlear implant animal models, the cochlea is deafened through the administration of ototoxic drugs (aminoglycosides) intended to destroy hair cells and produce a cochlea similar to that found in human cochlear implant candidates. Aminoglycoside infusion into guinea pig cochleae has been shown to produce histological changes in the auditory nerve within hours (Leake-Jones et al., 1980; Dodson, 1997). Some of these changes, such as the swelling of neurons, might be reversible over time resulting in the observed early increases and later decreases in thresholds. Threshold decreases have been observed in implanted humans with long-term deafness as well (Michelson, 1971; Eddington et al., 1978), implying that implantation alone may also result in the observed changes. However, reported observations are sparse because implants in humans are usually not activated until roughly 1 month after implantation. Thus most postimplantation changes might be over before testing of these subjects begins. Further studies are required to determine the relative effects of the deafening agent versus effects of implantation alone. To test the effects of these procedures we formed groups of animals that differed in the timing of the implantation and/or deafening procedures, as detailed in Section 2.

Abbreviations: ABR, auditory brainstem response; dB, decibel; mA, milliamperes; rms, root-mean-square; SPF, specific pathogen free

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Effects of electrical stimulation on the auditory nerve or central auditory neurons comprise additional mechanisms that could be hypothesized to underlie the threshold changes observed. Many studies have shown that both peripheral and central changes in the auditory pathway, such as improvements in the neurochemical environment and expansion of the central representation of the stimulated region, occur as a result of postdeafening electrical stimulation (reviewed by Miller, 2001). These physiological changes or other effects of electrical stimulation could result in an increase in sensitivity to electrical stimuli over time. To test this hypothesis, we compared thresholds of animals in which electrical stimulation began shortly after deafening and implantation with those in which the onset of electrical stimulation was delayed in order to determine if thresholds would decrease over time in the absence of electrical stimulation.

The process of learning to listen to an electrical signal may also play a roll in the threshold changes observed. Since electrical stimuli undoubtedly sound different from their acoustic counterparts, some practice in listening to the electrical signal might be necessary before subjects begin responding optimally. The possibility that learning plays a role in the observed threshold decreases will be discussed in the context of results from these and previous experiments.

Finally, we considered that tissue growth in the scala tympani might affect detection threshold levels. Tissue growth including fibrous tissue and new bone formation is commonly observed in the implanted cochlea (Pfingst et al., 1981; Duckert, 1983; Kawano et al., 1998). These alterations could affect current pathways from the electrodes to the neurons, resulting in changes in the amount of current that reaches the sites of action potential initiation. These changes also affect the impedances of the current passed between electrodes (Newbold et al., 2004) so we used impedance to estimate the time course of tissue growth around the implant.

2. Materials and methods

In this study four distinct subject groups, comprised eight animals each, were tested. Psychophysical detection thresholds and implant impedances were measured as a function of time. The four groups allowed us to examine the effects of (a) the deafening procedure, (b) the implantation procedure, and (c) postimplantation electrical stimulation and psychophysical testing.

2.1. Subjects

Subjects tested in this experiment were adult pigmented guinea pigs born in a specific pathogen free (SPF) environment and then maintained in the laboratory under a modified SPF protocol. At the time of their arrival from the Elm Hill breeding facility, animals weighed approximately 250–300 g. They were gradually acclimated to a sound-attenuating chamber and a restraint harness that kept them oriented towards the front of the test chamber. Their diet remained unrestricted until they weighed approximately 400 g. At this time their food was rationed to 25 g per day, which they would receive after each testing session. This regime ensured the animals motivation in the positively reinforced task while maintaining a healthy weight. Also at this time, hearing was assessed physiologically at 2, 8 and 16 kHz using auditory brainstem responses (ABRs) in order to minimize preimplant variation in the condition of the implanted ear. Only animals with ABR thresholds that fell within the normal range in at least one ear were included in the study. Normal ranges were established using data from over 200 previously tested ears. After the animals reached 600 g in weight, the food allowance was increased to 30 g per day. On this diet, weights stabilized around 800–1200 g. Animals were always allowed free access to water.

This study was performed in accordance with National Institutes of Health Guidelines (Guide for the Care and Use of Laboratory Animals, 1996). The University Committee on the Use and Care of Animals at the University of Michigan approved the animal protocols. Veterinary care and animal husbandry were provided by the Unit for Laboratory Animal Medicine, in facilities certified by the Association for Assessment and Accreditation of Laboratory Animal Care, International (AAALAC, Intl.). After completing the current experiment, the animals were used in other psychophysical and/or neurophysiological experiments before they were euthanized.

2.2. Psychophysical procedures

Subjects were trained in increments using positive reinforcement procedures. They were trained to perform a psychophysical task in which they initiated a trial by pressing a button (the observing response) and reported detection of an acoustic signal by releasing the button. They learned to press and hold down the button through a randomly-variable foreperiod (1–6 s) and then to release it within 1 s of the auditory stimulus onset. Button releases within 1 s of stimulus onset (the detection response) were rewarded by delivery of a food pellet (Noyes/Research Diets). Once the animals responded reliably at moderate sound pressure levels, they were trained to respond to very soft sounds. Animals were considered trained when they could reliably detect and respond to various types of stimuli at threshold and suprathreshold levels. The entire training process took 3–6 months.

For both acoustic and electrical detection threshold determinations, the method of constant stimuli was used. Stimulus tables consisted of six to eight levels of attenuation at a step size of 5 dB for acoustic and 2 dB for electrical stimuli. Stimuli were arranged in descending order from the most to the least audible stimulus, but presented in random order. Stimulus levels were selected to maintain a relatively constant rate of reinforcement across conditions in order to avoid situations that might lead to a change in response strategy. The percentage of correct responses as a function of attenuation level was assessed and threshold was defined as the level at which the animal responded correctly 50% of the time, as determined by linear interpolation from the psychometric function. Guess rates (releases of the response button during a 1 s unmarked observation period on trials where no stimulus was presented) were measured during all sessions. Thresholds were considered valid if subjects completed at least 15 trials at each stimulus level, generated a smooth psychometric function and had a guess rate that was no greater than 20%. Daily testing sessions lasted from one to three hours.

2.3. Experimental groups

Trained animals were assigned to one of four groups. Animals were matched across groups in regards to sex, age, and implant type. That is, for each animal in Group I, there were sex, age, and implant matched counterparts in Groups II, III, and IV.

Procedures and time courses for the four groups are summarized in Table 1.

Animals in Group I were chemically (neomycin) deafened and implanted in the same surgery and electrical threshold testing was initiated the next day. Animals in Group II were chemically deafened and implanted in the same surgery, but electrical threshold testing was not initiated until 45 days after implantation (similar to the time of activation relative to implantation in clinical practice). Animals in Group III were chemically deafened and then