DEVELOPMENTAL PLASTICITY OF CENTRAL AUDITORY PATHWAYS: FREQUENCY REPRESENTATION AFTER NEONATAL HIGH FREQUENCY HEARING LOSS

Robert V. Harrison, Susan G. Stanton, Danyal Ibrahim, Sachio Takeno and Richard J. Mount
Auditory Science Laboratory, Department of Otolaryngology,
Hospital for Sick Children, Toronto.

INTRODUCTION

Cochleotopic (or tonotopic) organization is the systematic representation of the sensory epithelium of the cochlea within central auditory pathways including cortex. This central mapping of the sensory surface is a feature of all sensory systems. The organization of these sensory maps can be significantly modified by abnormal patterns of excitatory input, particularly during early stages of development. This has been shown most extensively in studies on the visual system [1] and in the somatosensory system [2,3]. More recently, studies in the auditory system have revealed that alterations to cochleotopic maps in primary auditory cortex can result from cochlear haircell lesions [4,5]. Our previous work has shown that ototoxic poisoning of the basal cochlear region (i.e. partial deafferentation) in newborn kittens results in the development of major changes to the frequency map in primary auditory cortex. Thus, regions of cortex which would normally contain neurons coding high frequencies (activity originating at cochlear base) has neurons tuned to lower frequencies. It appears that the establishment of cochleotopic maps in auditory cortex depends on the integrity of the pattern of ascending input from the cochlea. In this study, we ask if this reorganization is a feature only of the auditory cortex or whether it also exists at the midbrain level (inferior colliculus; IC).

MATERIALS AND METHODS

Newborn chinchilla pups were treated with the ototoxic aminoglycoside amikacin, 400 mg/kg/day for 2-4 days s.c., resulting in bilateral lesions to the base of the cochlea. We monitored auditory threshold elevation using auditory brainstem evoked responses to tone-pip stimuli (ABR audiograms). At maturity (6 months) the subjects were used in single unit electrophysiological recording studies in which the frequency representation (the cochleotopic map) at the level of IC was determined. (All procedures were carried out within the guidelines of the Canadian Council on Animal Care).

RESULTS AND DISCUSSION

Figure 1 shows the cochleotopic or tonotopic map in IC of the normal chinchilla. Dorsally, neurons respond best to low frequencies of sound; in ventral areas, they respond best to high frequencies. Figures 2 & 3 show the frequency maps in IC of two subjects treated with amikacin, i.e. with long-term neonatal high frequency hearing loss (as indicated by the ABR audiograms). Note in both these examples that the frequency region corresponding to the border of the cochlear lesion, and therefore the high frequency cut-off of the audiogram, is over- represented. In the subject of Figure 2, this cut-off is at 10 kHz; note the "expanded" region (cross-hatched area) containing neurons all tuned 10 kHz. In Figure 3 the cut-off slope of the audiogram is at about 5kHz; again and the IC contains a larger than normal region in which all cells are tuned to 5 kHz. It should be noted, however, that the tuning and threshold characteristics of the neurons in these expanded regions are pathological, i.e. thresholds are elevated and frequency tuning is abnormally broad (this is consistent with previous work on the threshold and tuning properties of neurons from damaged cochleas, [e.g. 6,7,8].

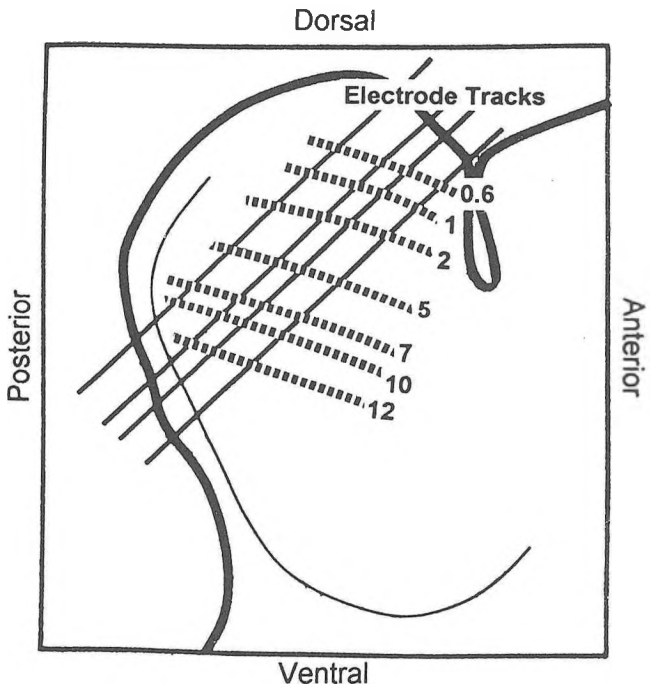

Figure 1. Saggital section through inferior colliculus indicating cochleotopic organization in the normal chinchilla midbrain.

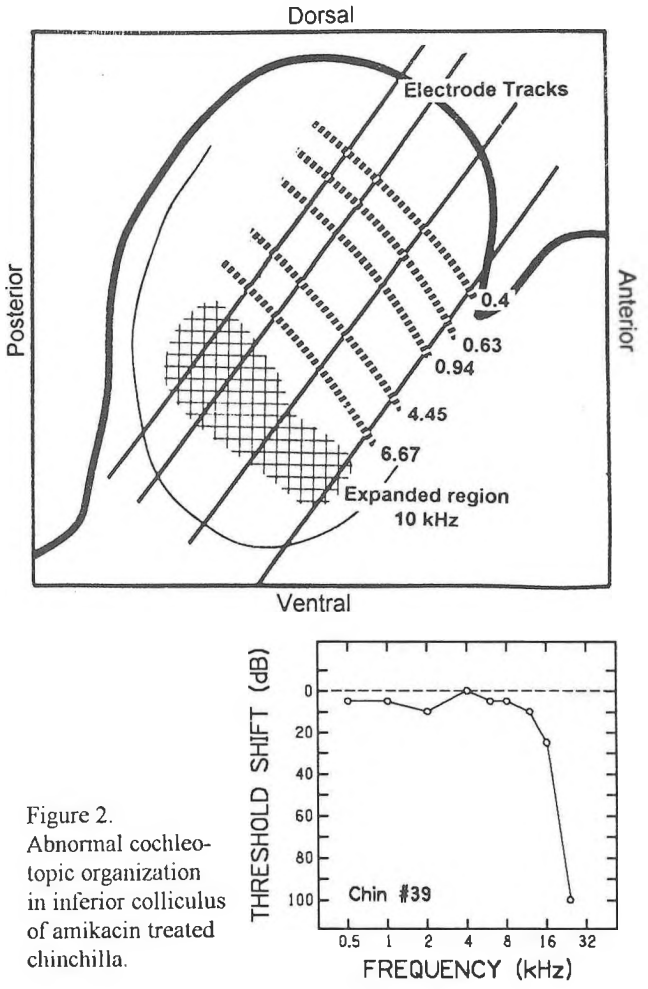

Figure 2.
Abnormal cochleotopic organization in inferior colliculus of amikacin treated chinchilla.

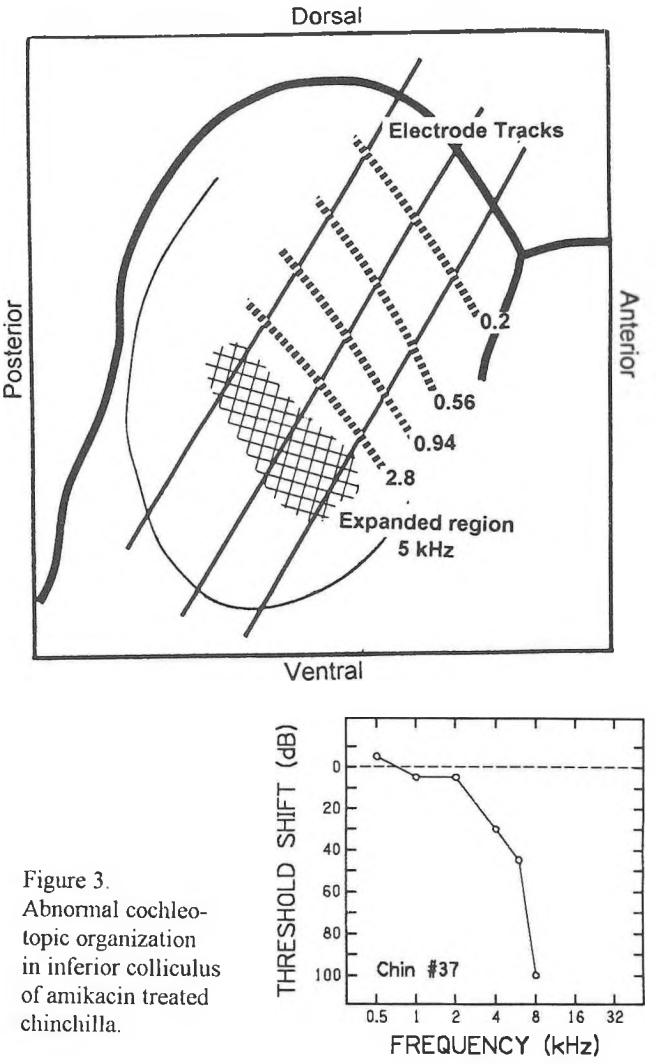

Figure 3.
Abnormal cochleotopic organization in inferior colliculus of amikacin treated chinchilla.

These experiments give us new information in relation to the basic mechanisms of plasticity of the central nervous system. The integrity of the cochlea is important for the development of central frequency maps; changes to auditory sensory input, particularly from an early age can significantly alter cochleotopic maps not just at cortex but at the midbrain level. Furthermore, our experimental subjects are animal models of human sensorineural hearing loss. Thus we believe that the changes to central cochleotopic maps that we observe are to be found in humans with long-term cochlear hearing loss. There are still many important questions in relation to this developmental plasticity. First, is there a developmental critical period when the central auditory pathways are most susceptible to changes in cochlear afferent input? Secondly, are these changes reversible? The answers to both questions have direct relevance to the treatment and rehabilitation of hearing loss, particularly in infants.

ACKNOWLEDGMENTS

This work was funded by the Medical Research Council of Canada, and the Masonic Foundation of Ontario.

REFERENCES

[1] Wiesel TN, Hubel DH (1963) Single cell responses in striate cortex of kittens deprived of vision in one eye. J Neurophysiol 26:1003-1017. [2] Waite PMS, Taylor PK (1978) Removal of whiskers in young rats causes functional changes in cerebral cortex. Nature 274:600-602. [3] Merzenich MM, Kaas JH (1982) Reorganization of mammalian somatosensory cortex following peripheral nerve injury. Trends Neurosci 434-436. [4] Robertson D, Irvine DRF (1989) Plasticity of frequency organization in auditory cortex of guinea pig with partial unilateral deafness. J Comp Neurol 282:456-471. [5] Harrison RV, Nagasawa A, Smith DW, Stanton SG, Mount RJ (1991) Reorganization of auditory cortex after neonatal high frequency cochlear hearing loss. Hear Res 54: 11-19. [6] Kiang NYS, Moxon EC, Levine RA (1970) Auditory nerve activity in cats with normal and abnormal cochleas. In: Wolstenholme et al. eds. Sensorineural Hearing Loss, CIBA Found Symp London Churchill pp241-268. [7] Dallos P, Harris D (1977) Properties of auditory nerve responses in absence of outer hair cells. J Neurophysiol 41:365-383. [8] Harrison RV, Evans EF (1979) Cochlear fibre responses in guinea pigs with well defined cochlear lesions. Scand Audiol Suppl 9: 83-92.