DELAYED NEUROTROPHIN TREATMENT SUPPORTS AUDITORY NEURON SURVIVAL IN DEAFENED GUINEA PIGS

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The cochlear implant provides auditory cues to patients with a severe-profound hearing loss by direct electrical stimulation of the auditory nerve. As such, the total number and integrity of the surviving auditory neuron population may govern the benefits that patients can derive from the implants. Therefore, the rescue of auditory neurons from degeneration following the loss of hair cells is of great therapeutic significance.

Neurotrophic factors are known to be important for the development and maintenance of the auditory system\(^1\), and have also been reported to act as survival factors for auditory neurons in animal models of deafness. However, while studies have demonstrated that the application of neurotrophins into the inner ear shortly following deafening can prevent auditory neuron degeneration\(^2\), much less is known about the survival effects of delayed neurotrophin treatment, which is a clinically more realistic model.

This study therefore examined the effects of delayed neurotrophin treatment on auditory neuron survival following deafening. Specifically, we aimed to determine if any or all of the neurotrophins – BDNF, NT-3, NT-4/5 and NGF – could rescue neurons from degeneration after a period of two weeks of deafness. Normal hearing guinea pigs were bilaterally deafened using a combination of the aminoglycoside kanamycin and the loop diuretic frusemide. Two weeks later the left cochleae were implanted with a cannula attached to a mini-osmotic pump, which delivered 10\(\mu\)g of neurotrophin over a period of 28 days. The right cochleae acted as deafened and untreated controls.

Despite the delayed treatments, each of the four neurotrophins prevented the degeneration of auditory neurons that is normally seen following loss of hair cells. When compared to normal hearing animals, the neuronal survival rates of deafened, neurotrophin-treated animals ranged between 79-87%; in contrast, deafened, untreated controls displayed only 52% neuronal survival. Current work is also investigating the expression patterns of the neurotrophin Trk receptors in relation to these findings, and these results will also be discussed.

The results of this study provide further support to the theory that neurotrophic factors may be able to be used as therapeutic agents for the benefit of the hearing impaired community.

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