5THp: PROTECTION OF SPIRAL GANGLION NEURONS WITH NEUROTROPHINS AND CHRONIC ELECTRICAL STIMULATION

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In the deaf cochlea spiral ganglion neurons (SGNs) undergo continual degeneration that ultimately leads to neuron death. The exogenous application of neurotrophins (NTs) has been shown to prevent SGN degeneration and even promote regrowth. Furthermore, combining chronic intracochlear electrical stimulation (ICES) with NT administration can enhance the survival effects of NTs and lower electrical thresholds. However, following the cessation of NT delivery SGNs continue to degenerate. Therefore techniques that deliver NTs over a long period of time are required to maintain the therapeutic benefit of NT treatment.

We have used cell-based therapy to provide NTs in combination with an intracochlear electrode array in a long-term deafened cat model. Cats were neonatally deafened with daily injections of neomycin, and at two months of age were implanted with encapsulated porcine choroid plexus cells (NTCell, LCT Inc.) and the stimulating electrode array. The choroid plexus cells were encased in an alginate capsule that enabled the diffusion of neurotrophins (including Brain-Derived Neurotrophic Factor and Neurotrophin-3) into the cochlear fluids. Environmentally derived ICES was delivered chronically via a clinical stimulator (Nucleus CI24M, Cochlear™) and processor (Esprit 3G, Cochlear™). Five cats received chronic ICES only. Six cats received NTs without chronic ICES and six cats received NTs in combination with chronic ICES. Control animals (n=7) were normal hearing and were not implanted.

The results indicated that chronic ICES alone (without NTs) did not provide greater SGN survival when compared to the contralateral untreated cochlea. Importantly, chronic ICES in combination with NT delivery provided greater SGN protection than NT alone or chronic ICES alone (ANOVA $P<0.003$). Treatment with NT alone led to an improvement in thresholds from electrically evoked brainstem responses (ANOVA $P<0.003$). These results indicate that cell-based NT delivery in combination with electrical stimulation delivered by a cochlear implant can promote SGN survival. These findings have important implications for future strategies that will combine cochlear implantation with systems that deliver drugs safely to the cochlea.

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