

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) can prevent SGN degeneration and even promote regrowth. Furthermore, combining chronic intracochlear electrical stimulation (ICES) with NTs 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 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 produce NTs and were encased in alginate capsules that enabled the diffusion of NTs 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 compared to the contralateral untreated cochlea. Importantly, chronic ICES in combination with NTs provided greater SGN protection than NTs alone or chronic ICES alone (ANOVA $P < 0.003$). Treatment with NTs 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 ICES 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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