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Dexamethasone modulates the wound healing process in an in vitro cochlear implantation trauma model

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Background: In the cochlear implant (CI) procedure as a treatment for profound deafness, an electrode array is surgically inserted to provide electrical stimulation to the auditory nerve. Mechanical trauma from insertion of a cochlear implant electrode into the scala tympani can lead to inflammation and a high level of oxidative stress, which can initiate the apoptosis of auditory hair cells (HC) and intracochlear fibrosis. Hair cell apoptosis and intracochlear fibrosis are thought to be causes of poor cochlear implant functional outcomes.

Methodology: In order to gain insight into the molecular mechanisms that initiate HC apoptosis and scala tympani fibrosis following electrode insertion trauma (EIT), and the otoprotective effects of dexamethasone (DXM) observed in previous studies, an in vitro model of EIT was designed. Here we present and characterize a novel, reproducible in vitro model for the study of cellular and molecular events that occur following an EIT procedure. Cochleae from 3 day-old rats were subjected to a cochleostomy and were then divided into three groups: 1) Control; 2) EIT; 3) EIT+DXM (20 μg/ml). In groups 2 and 3, a 0.28 mm diameter monofilament fishing line was introduced through the small cochleostomy located next to the round window area, allowing for an insertion of between 110-150º. HC counts, gene expression for pro-inflammatory cytokines (i.e. TNFα and IL-1β), pro-inflammatory inducible enzymes (i.e. iNOS and COX-2) and growth factors (i.e. TGFβ1, TGFβ3 and CTGF), oxidative stress (i.e. CellROX), and analyses of apoptosis pathways (i.e. Caspase-3, AIF and Endo G) were carried out on all explants at different time points.

Results: The results of this EIT in vitro model show the initiation of wound healing in which an inflammatory response is followed by a proliferative-fibrosis phase. Moreover, DXM treatment of EIT explants inhibited the inflammatory response and promoted a non-scarring wound healing process.

Conclusions: The novel in vitro model described here will improve our understanding of mechanisms underlying CI insertion trauma and protective strategies such as DXM treatment.