NEURO-GLIA-CI

Peripheral process health and regrowth for cochlear implant candidates

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Projektbeschreibung

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Background: Cochlear Implants (CIs) are the most successful bionic prostheses to restore severe hearing impairments but rely on a functional auditory nerve. Its bipolar spiral ganglion neurons (SGNs) are located in the bony center of the cochlea and send out peripheral processes (PPs) to contact the sensory hair cells. PP pathology and retraction after afferent synapse loss or postsurgical implantation trauma, decreases specifity of electrical stimulation. Although promising clinical trials aim to preserve hair cells, little attention is given to preserve the PPs that govern the fidelity of CI function.
Mission: Protecting neurons and regrowing their PPs with drugs such as neurotrophic factors (NTFs) shall enhance CI function with an improved human:machine interface. Reducing the gap between the CI and auditory nerve and prevent neuron loss is the key to boost CI performance.
Previous work: We showed in-vitro and in-vivo animal experiments, that Brain Derived Neurotrophic Factor (BDNF) and Neurotrophin-3 (NT-3) effectively protect SGNs and promote resprouting of PPs. In addition, glia cells play a key role in the protection mechanisms and closely associate with neurons as satellite glia and Schwann cells. We previously showed also that NTFs preserve glia-like supporting cells that embrace hair cells in the sensory epithelium.
Aim: This project aims to describe PP loss in human & animal models and identify parameters for a maturation of regrown neurites into axons with actively excitable components and a myelin insulation. This study shall proof positive effects of the NTFs Glia Cell Derived Neurotrophic Factor (GDNF) and Ciliary Neurotrophic Factor (CNTF) with & without BDNF on neuron-glia cell interaction and growth in murine SGN explants and in an already accomplished in-vivo guinea pig model. Hair cell survival shall be analyzed in the GDNF treated guinea pigs. We will support our data on health status and survival of deafferenciated PPs with data from aged mice/gerbils and human temporal bones to lay the basis for a pharmacologic treatment post CI implantation. This regrowth shall enable to design electrodes with more channels.
Methods: With histological methods, from automated quantitative immunohistochemistry to electron microscopy, we will characterize PP health in animal models and human temporal bones. Murine in-vitro SGN explant cultures shall identify the best NTF mix for neuronal and glial function to produce regenerated, myelinated and functional PPs.
Expected Outcome: This preclinical exploratory study will look in depth at PP pathology in cochlear implant candidates and

factors with a potential to improve the neural status and electrode/nerve interface. The expected outcome is to lay a knowledge base for a clinical pharmacologic treatment post CI implantation to improve the interface with the auditory nerve and ensure long-term survival of regrown PPs.

Projektpartner

- Medizinische Universität Innsbruck