NEONATAL SENSORINEURAL HEARING LOSS AFFECTS SYNAPTIC DENSITY IN THE AUDITORY MIDBRAIN

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We examined the effect of neonatal deafening on synaptic density in the inferior colliculus (IC), a major auditory relay station which receives binaural innervation. Eight adult cats were used in the study: two were normal hearing controls, and six were deafened at 10 days after birth. Of these deafened animals, two were bilaterally deafened and four were unilaterally deafened. Duration of deafness was approximately one year. Animals were deeply anaesthetised with sodium pentobarbital (40 mg/kg i.p.), transcardially perfused with 4% paraformaldehyde, and a core sample of tissue from the central nucleus of the IC was removed and immersed in Karnovsky's fixative. The samples were post fixed with 1% osmium tetroxide, immersed in 1% uranyl acetate, dehydrated in graded alcohols and embedded in Spurr's resin. Ultra-thin sections were mounted on uncoated 200 mesh copper grids, stained with Reynold's lead citrate and examined with a calibrated Jeol JEM-100S transmission electron microscope. Sections were systematically scanned at 30,000 times for synaptic contacts. Statistical analysis of synapse counts from the IC revealed a significant difference across the three groups (one-way ANOVA; p=0.013). Synaptic density in bilaterally deafened animals was significantly lower than the normal hearing animals (Tukey's post-hoc analysis; p<0.05). Interestingly, there was no significant difference between normal hearing animals and either IC of unilaterally deaf animals (p>0.05). Future studies will investigate whether synaptic density in the auditory midbrain of neonatally deafened animals is subject to regulation by chronic intracochlear electrical stimulation.

Growth factors from different superfamilies act in synergy when promoting the survival of auditory neurones in vitro.

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Several growth factor superfamilies have been implicated in normal inner ear development and in promoting auditory neurone survival. The neuronal promoting ability of neurotrophin-3 (NT-3), brain-derived neurotrophic factor (BDNF), leukemia inhibitory factor (LIF) and transforming growth factor β-5 (TGF-β5), alone and in combination, were evaluated in dissociated cell cultures of early postnatal rat auditory neurones. Rat pups were anaesthetised on ice and sacrificed by rapid decapitation, followed by removal of the cochleae under aseptic conditions. Here we provide evidence that synergistic relationships exist between growth factors from diverse superfamilies when promoting auditory neurone survival in vitro. Administered alone, all factors promoted survival of between 10-15% of initially plated neurones, with NT-3 the most potent of the factors. When used in combination, LIF + BDNF, NT-3 + TGF-β5, and BDNF + TGF-β5 all promoted auditory neurone survival in a synergistic fashion. In contrast, NT-3 + BDNF and LIF + TGF-β5 displayed additive survival effects. These results suggest that growth factors may act by interdependent mechanisms when sustaining neuronal integrity, and that a combination of several growth factors may provide a better approach than single factor therapy when developing pharmacological therapies for the treatment of deafness.
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