

Effects of exogenous neurotrophins in the deaf stimulated cochlea

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Summary

Do neurotrophins and chronic electrical stimulation affect spatial selectivity of cochlear implant stimulation?

Introduction

Infusion of neurotrophins (NT) into cochlear fluid prevents the degeneration of spiral ganglion neurons (SGNs) following hair cell loss^{1,2} and can promote the regrowth of SGN peripheral fibres². However, the regrowth appears to be disorganised, thereby disrupting the spatial organisation of SGNs. This may compromise the fidelity of auditory signals relayed by SGNs (Fig.1) and central structures following SGN stimulation by a cochlear implant (Fig.2).

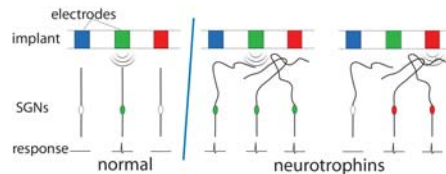


Figure 1. The spread of activation of SGNs by implant stimulation may be less spatially restricted in NT treated cochleae (right) than in normally organised SGN peripheral fibres (left).

Aim

To determine if the lateral deviation of SGN fibres following NT treatment affects the stimulation specificity of implant electrodes, and if concurrent chronic intracochlear electrical stimulation (ICES) has any interactive effects.

Methods

Adult guinea pigs were chemically deafened. After two weeks of deafness, left cochleae were implanted with a six electrode intracochlear stimulating array and drug delivery tube. The NTs BDNF and NT-3 (5µg each) or artificial perilymph (control) were delivered to the cochlea via an osmotic pump over 4 weeks. Chronic ICES on three bipolar electrode pairs was also delivered to half of the guinea pigs over the treatment period.

Following treatment, multi-unit cluster responses were recorded across the cochleotopic laminae of the central nucleus of the inferior colliculus (ICC) in response to ICES using a multi-channel recording array (Figs.2-4). Following recording, the neural tracer tetramethylrhodamine dextran (TMRD) was injected into the auditory nerve to trace single SGN peripheral fibres in order to examine their positions within the cochlea (Fig.5) The projection patterns are compared to the spatial distribution of ICC responses to ICES.

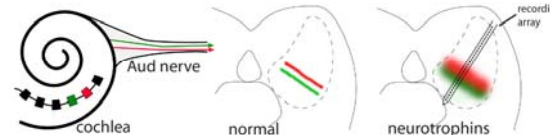


Figure 2. Distinct inferior colliculus (IC) subpopulations are normally excited, whereas NTs may produce overlapping sub-populations, indicating disrupted SGN organisation. Spatial excitation patterns can be recorded with a multi-channel recording array as shown.

Preliminary Results

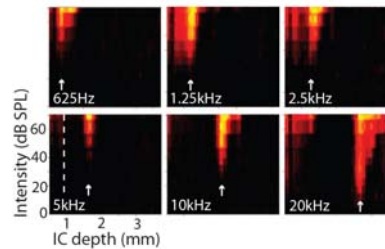


Figure 3. Multi-unit response intensities recorded from the IC to acoustic stimuli. The physiological boundary between the central (ICC) and external IC nuclei is shown by the dashed line. The tonotopic organisation is seen by the movement of frequency tuning to deeper ICC locations with increasing frequency (arrows).

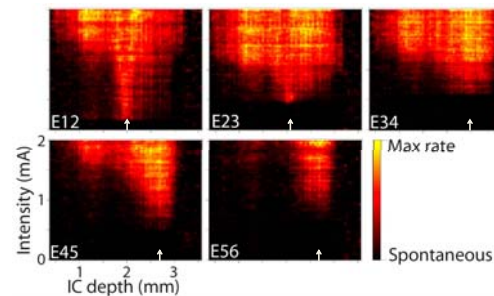


Figure 4. IC Spatial response intensities recorded to ICES stimuli in a 6 week deaf guinea pig. The active bipolar electrode pair is shown for each panel.

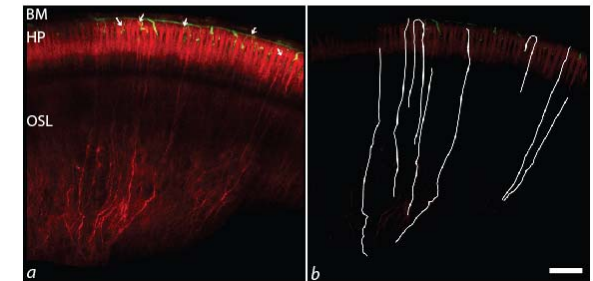


Figure 5. Basal cochlear turn of a 6 week deaf guinea pig. (a) Red fluorescence shows the tracer TMRD within some SGN fibres, and the green channel shows neurofilament. Double labeling is indicated by arrows. (b) Traced SGN peripheral fibres are shown in white. Scale bar = 50µm; BM = basilar membrane; HP = habenula perforata; OSL = osseous spiral lamina.

Discussion

The available data indicate that the spatial distribution of ICC responses to ICES were not affected by 6 weeks of deafness or NT treatment compared to normal. Thresholds were lower than normal in NT animals and higher in untreated animals. These animals did not receive chronic ICES. However, little data is presently available, so the above statements are preliminary. If these trends persist in future data and chronic ICES animals, this would suggest that NT treatment might not disrupt SGN organisation to an extent causing concern for cochlear implant performance.

References

- Gillespie LN et al. (2004). Neuroreport 15(7): 1121-5.
- Wise AK et al. (2005). J Comp Neurol 487(2): 147-65.

Acknowledgements

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