Neurotrophic treatment of the degenerating auditory nerve; cochlear implants in deafened guinea pigs

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Direct electrical stimulation of spiral ganglion cells (SGCs)

More than 120,000 cochlear Implants worldwide

Factors that influence the performance

- Degeneration of the auditory nerve
- Reorganization of the central auditory system
- Cognitive skills of CI candidate
- Surgery
Release of neurotrophic factors by hair cells
Loss of hair cells and SGCs

normal 6 weeks deaf
Progressive degeneration of SGCs after deafening

normal

2 weeks deaf

4 weeks deaf

8 weeks deaf
Assumption
More and better functioning spiral ganglion cells (SGCs) result in better performance of the cochlear implant user.

Research Questions
Is delivery of brain-derived neurotrophic factor (BDNF) effective in preventing degeneration of SGCs?
What is the effect of cessation of BDNF treatment?
Are the rescued SGCs functional?
Application of brain-derived neurotrophic factor (BDNF)

Protocol

- Deafening
- Kanamycine 400 mg/kg (s.c.); furosemide 100 mg/kg (i.v.)
- Implantation
- BDNF treatment
- Cessation of BDNF treatment
Results

- 6 weeks deaf untreated
- normal
- 2 weeks deaf
- BDNF treatment
- 0
- 2
- 4
- 6

Deaf

BDNF treatment
Results

- 6 weeks deaf untreated
- 2 weeks after cessation
- 2 weeks after deafening
- 8 weeks after deafening

- Normal
- 2 weeks deaf
- BDNF treatment

- 0
- 2
- 6
- 8

Deaf BDNF treatment
Discrepancy between literature and our results

Possible explanation:
Measurements of electrically evoked auditory brainstem responses (eABR)

Protocol

- eABR measurement

Time in weeks:
- 0
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8

Deaf

BDNF treatment
Measurements of eABR
Assessment of the functionality with eABRs

Stimulus intensity (μA)

Amplitude of wave N1-P2 (μV)

- normal hearing
- deafened
- BDNF
- BDNF cessation

Stimulus

time (ms)

0 2 4 6 8 10 12

10 μV

400 μA

318 μA

252 μA

200 μA

159 μA

126 μA

BDNF cessation
Summary and Conclusions

- Delivery of brain-derived neurotrophic factor is effective in preventing degeneration of spiral ganglion cells

- After cessation of the BDNF treatment, the effect is still present (two weeks)

- The eABR amplitude in BDNF treated animals is larger than in untreated deafened animals and comparable with normal
Acknowledgements

- Prof. dr. G.F. Smoorenburg
- Prof. dr. F.W.J. Albers
- Prof. dr. V.M. Wiegant
- Ferry Hendriksen
- Frits Meeuwsen
- Kelly Maijoor
- Leone Nijman
- Lotte van Dijk

Heinsius-Houbolt Fonds

Cochlear®
Possible improvement of the performance with a cochlear implant

Results

8 weeks deaf
BDNF after cessation

SGC density (cells/mm²)

location

b1 b2 m1 m2 a1

n=5 n=6 n=5 n=5 n=2

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