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Developing a stem-cell-based treatment for vestibular hypofunction

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Introduction

Vestibular hypofunction secondary to vestibular neuronitis can have a severe impact on a patient's quality of life, particularly when it is bilateral. There is an unmet need for treatments to restore end-organ function.

Method

There are almost no models of acquired, late-onset, bilateral vestibular hypofunction that would mimic the clinical condition. We developed a mouse model by applying ouabain bilaterally to the round window niche. The animals were then transplanted with human embryonic stem cell derived otic progenitors into Scarpa's ganglion.

Results

Animals underwent audiometric and weekly vestibular testing for 12 weeks after transplantation, followed by post-mortem histology. Bilateral ouabain application had damaged the vestibular neurons, and generated a persistent effect on hearing and balance function. The otic neural progenitor transplant was well tolerated, and the engraftment is currently under analysis.

Conclusion

Bilateral round window ouabain is a useful model for vestibular hypofunction and suitable to study cell transplantation.

Understanding factors that cause tinnitus: a Mendelian randomisation study of UK Biobank data

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Aims

To investigate the causal role of established risk factors and associated conditions in tinnitus and tinnitus severity.

Method

A prospective cohort study was conducted with a large dataset of more than 500 000 individuals (via UK Biobank). The study comprised an analytical sample of data from 129 731 individuals. Logistic regression and two-sample Mendelian randomisation were carried out.

Results

The prevalence of tinnitus was 20 per cent, with severe tinnitus in 3.8 per cent. Observational results were consistent with previous literature. Current tinnitus was

predicted by genetically instrumented hearing loss (odds ratio = 8.65 (95 per cent confidence interval (CI) = 6.12–12.23)), major depression (odds ratio = 1.26 (95 per cent CI = 1.06–1.50)), neuroticism (odds ratio = 1.48 (95 per cent CI = 1.28–1.71)) and higher systolic blood pressure (odds ratio = 1.01 (95 per cent CI = 1.00–1.02)). Lower odds of tinnitus were associated with a longer duration in education (odds ratio = 0.74 (95 per cent CI = 0.63–0.88)), higher caffeine intake (odds ratio = 0.89 (95 per cent CI = 0.83–0.95)) and being a 'morning person' (odds ratio = 0.94 (95 per cent CI = 0.90–0.98)). Severe tinnitus was predicted by a higher genetic liability to neuroticism (odds ratio = 1.15 (95 per cent CI = 1.06–1.26)) and schizophrenia (odds ratio = 1.02 (95 per cent CI = 1.00–1.04)).

Conclusion

Genetic analysis determined causal relationships with several factors; these findings expand our understanding of tinnitus aetiology.

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