Animal Model of Cochlear Hair Cell Loss after Ischemia and Reperfusion Injury

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Introduction

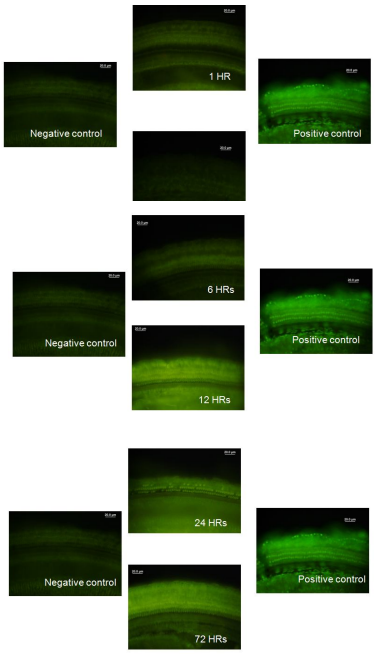
The cochlea plays a key role in converting the mechanical sound energy into electrical potential and sensory inputs. Cochlear hair cell loss is the main cause of sensorineural hearing impairment.. Cochlear is an end-artery organ and mainly supplied by the labyrinthine artery, which is a branch of anterior inferior cerebellar artery (AICA).[1] Therefore, the cochlea is sensitive to disturbance of blood flow. Disturbance of cochlear microcirculation leading to local hypoxia is thought to contribute to a variety of otologic disorders, e.g. age related, noise-induced and sudden hearing loss. However, there is no animal model of cochlear cell loss after ischemia and reperfusion injury. This study sets out to build an animal model of cochlear hair cell loss after ischemia and reperfusion injury.

Materials and Methods

Because of the anatomical feasibility of cochlea, guinea pigs are the most common experimental animals used in the hearing research. In this study, we choose the ventral approach to occlude the labyrinthine artery through the tympanic bulla cavity. In order to produce reversible cochlear ischemia, a tailored made microclamp (S&T Micro Clamps B-2, No. 00398-02) was used. The labyrinthine artery was clamped by this microclamp for 60 minutes. The effects of labyrinthine artery occlusion were verified by ABR(Auditory Brainstem Response) threshold shift. ABR threshold is collected before, immediate after sugery and pre-sacrifice. The experimental cochlea is harvested 1, 3, 6, 12, 24, 72 hrs after ischemia and reperfusion procedure. The cochleaswere then dissected in 0.1 M phosphate buffered saline (PBS) and the organs of Corti collected for analysis. Cell death occurs by two ways. One is necrosis and the other one is apoptosis. Apoptosis can be detected by TUNEL assay. Hair cell death in the organ of Corti, not depending on the apoptosis, can be evidenced by the presence or absence of stereocillia with the help of phalloidin, a marker for F- actin in hair cell stereocillia. The number of TUNEL-positive nuclei of IHC and OHCs is counted under fluroscense microscopy.

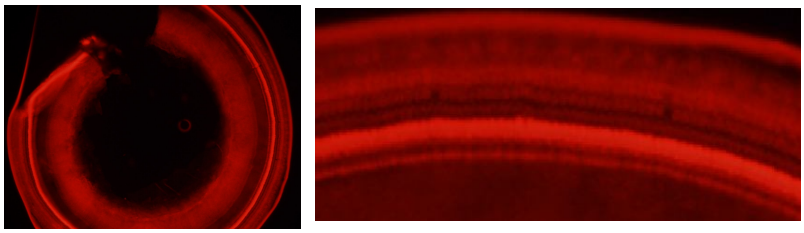
Results

Time course of TUNEL stain of cochlea after ischemia and reperfusion



1. Apoptotic cell death appears 6 hours after ischemia and reperfusion.
2. Both outer and inner hair cells exhibited apoptotic changes.

Phalloidin staining characteristic to F-actin in the stereocillia.6 hours after cochlea ischemia and reperfusion.



The ratio of lost cochlear hair cells is low 6 hours after ischemia and reperfusion

No	1.00(reference)	1.00(reference)	1.00(reference)
Yes	6.15(5.11-7.39)	6.03(5.00-7.26)	3.80(3.13-4.62)
Allergic rhinitis			
No	1.00(reference)	1.00(reference)	1.00(reference)
Yes	3.34(3.13-3.56)	3.44(3.22-3.68)	2.94(2.74-3.16)
Chronic otitis media			
No	1.00(reference)	1.00(reference)	1.00(reference)
Yes	2.05(1.85-2.27)	2.27(2.03-2.53)	1.74(1.55-1.95)
URI			
No	1.00(reference)	1.00(reference)	1.00(reference)
Yes	1.77(1.54-1.89)	1.70(1.53-1.88)	1.65(1.48-1.84)
Pneumonia			
No	1.00(reference)	1.00(reference)	1.00(reference)
Yes	1.96(1.72-2.24)	2.02(1.76-2.32)	1.34(1.15-1.55)
Asthma			
No	1.00(reference)	1.00(reference)	1.00(reference)
Yes	2.04(1.86-2.25)	2.17(1.96-2.39)	1.23(1.10-1.37)
COPD			
No	1.00(reference)	1.00(reference)	1.00(reference)
Yes	1.77(1.44-2.18)	1.92(1.54-2.40)	1.22(0.97-1.55)
Hypertension			
No	1.00(reference)	1.00(reference)	1.00(reference)
Yes	1.13(1.04-1.23)	1.22(1.09-1.36)	1.12(1.00-1.25)
Rheumatoid arthritis			
No	1.00(reference)	1.00(reference)	1.00(reference)
Yes	1.55(1.10-2.20)	1.63(1.15-2.31)	1.22(0.84-1.76)

Discussion

This study is the first attempt to investigate the cell death type and time course of cochlea hair cell after ischemia and reperfusion injury. Previous literatures shows both OHCs and inner hair cells exhibited mostly apoptotic and less necrotic changes after either noise trauma or ototoxic drug administration. Our findings revealed deviated nasal septum, allergic rhinitis, chronic otitis media, prolonged URI, pneumonia, asthma (patients had change in the lower airways as measured by physiological changes and the presence of inflammatory mediators) are the considerablely prior diseases consequently cause the later chronic sinusitis.

Conclusion

Deviated nasal septum, allergic rhinitis, chronic otitis media, prolonged URI, pneumonia, or asthma are risk factors to the later sinusitis. When patients are diagnosed with chronic sinusitis, we should trace the possible history of deviated nasal septum, allergic rhinitis, chronic otitis media, prolonged URI , pneumonia, asthma history. Proper management of these prior diseases may reduce the occurrence of later sinusitis.

References

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