Age-Related Changes of Myelin Basic Protein in Mouse and Human Auditory Nerve

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Introduction

Age-related hearing loss (sensorineural) affects nearly half the population over 75 years of age.1 Studies of temporal bones from older humans have shown that one of the most common pathological changes seen in age-related hearing loss is the degeneration of spiral ganglion neurons (SGNs).2,3 The degeneration of the spiral ganglion neurons is distributed in various glial cells, and may play an important role in the maintenance of inner ear function and repair processes.4-7 It is known that age-related degeneration of the spiral ganglion neurons in human ears may contribute to the decline of auditory nerve function in presbyacusis. Currently, electron microscopy (EM) is the standard procedure used to examine changes in the structure of myelin. Unfortunately, the results demonstrate that humans are not sensitive to human artifacts, rendering temporal bone preparations unsuitable for EM analysis.8-10 Thus, alternative non-ultrastructural approaches are necessary to assess pathological changes. The aim of this study was to determine the age-related alterations of myelin in mouse and human auditory nerves using immunohistochemical staining techniques. This specifically targeted myelin basic protein (MBP), a core component of myelin comprising 30% of the total protein and about 10% of the dry weight of myelin.11

Methods

Animal model: CBA/CaJ mice were used for studies of age-related functional and pathological alterations of the auditory system. Mice aged 1-3 months (young adult group, n = 17) and 23-27 months (aged group, n = 14) were included. Aged CBA/CaJ mice were also used as a comparison to the human tissue.

Functional analyses (Mice): ABR thresholds and ABR wave 1 amplitude (input/output (IO) functions) were performed.

Human temporal bones: We examined 13 temporal bones from 10 human subjects (9-13 Based on these observations, we hypothesized that age-related degeneration of the myelin encompassing human SGNs may contribute to the decline of auditory nerve function in presbyacusis. Mice aged 1-3 months (young adult group) and 26-month-old mouse. Dual labeling with anti-MBP (green) and anti-class III β-Tubulin (TuJ1, neuronal marker for type I SGNs) was performed to target both peripheral and central SGN processes in humans. A significant age-related reduction in MBP+ fiber density was found within the apical and basal turn. Mean density of MBP+ fibers within the OSL of young and aged mouse ears (n = 3-5 per group). A significant age-related reduction in MBP+ fiber density within the apical and basal turn.

Table 1. Antibody Characterization

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Isotype</th>
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<td>MBP</td>
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<td>Sigma</td>
<td>N0142</td>
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<tr>
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<td>IgM</td>
<td>Mouse</td>
<td>Sigma</td>
<td>N0142</td>
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<tr>
<td>Class III β-Tubulin (TuJ1)</td>
<td>IgG1</td>
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</tr>
</tbody>
</table>

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Conclusions

- Changes in the MBP immuno-staining pattern and reductions in MBP+ fiber density around SGNs were demonstrated in the older CBA/CaJ mice.
- By EM analysis, age-related degenerative changes of the myelin sheath were observed in older mice compared to the young adults.
- Auditory nerve function in the older mouse group was significantly reduced compared to that in young adult controls.
- Significant reductions in MBP+ fiber density were found in both peripheral and central SGN processes in older human cochleas.
- Older human cochleas also showed marked reductions in staining of neurofilament proteins denoting SGN degeneration.
- The results suggest that myelin degeneration may play a role in SGN loss and the subsequent decline of the auditory nerve function in presbyacusis.

Acknowledgments

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