Opposing Gradients of Ribbon Size and AMPA Receptor Expression Underlie Sensitivity Differences among Cochlear-Nerve/Hair-Cell Synapses

Leslie D. Liberman, Haobing Wang, and M. Charles Liberman

Journal of Neuroscience, 31(3):801-808
Jan 19, 2011

Authors

- M. Charles Liberman
- Leslie D. Liberman
- Haobing Wang

Eaton Peabody Laboratory, Massachusetts Eye & Ear Infirmary
Department of Otology and Laryngology, Harvard Medical School
Program in Speech and Hearing Biosciences and Technology, Harvard-MIT

The Ear

The Cochlea

Nolte (1990) The Human Brain 3rd Ed. Fig. 8-34A, p. 213

3/8/2011
Inner and Outer Hair-cells

Tuning Curves


Threshold Sensitivity


Synaptic Ribbons

- Presynaptic electron-dense body surrounded by large number of synaptic vesicles
- C-terminal Binding Protein 2 (CtBP2 is major component
- Functional variation
- Help in coordinating vesicle release
Previous studies

- Threshold sensitivity and spontaneous discharge rate (SR) vary by position around hair cell circumference
- Higher discharge on pillar side than modiolar side
- Fibers on pillar side are larger and contain more mitochondria
- Larger ribbons associated with lower SR, smaller ribbons associated with higher SR

What is the mechanism for the differences in threshold sensitivity?

- No presynaptic intracellular compartmentalization for receptor potentials to differ on the two sides of the cell
- Inverse correlation of ribbon size and SR seems paradoxical
- Fiber size difference is probably an effect of the high metabolic cost of higher synaptic activity

Methods

- Dissection and epithelial whole mount of mouse cochlea
- Immunostain ribbons with anti-CtBP2 (red) and AMPA with anti GluR2/3 (green)
- High-power confocal microscopy for 3D imaging
- Data compiled from 1243 synapses from 22 confocal z-stacks of ~100 inner hair cells (2.0-50 kHz), 3 different ears

Major Results

1. Complementary gradients of ribbon and AMPA receptor patches
2. Spatial separation of ribbon and AMPA receptor patch sizes in modiolar and pillar side

Immuno staining of Inner Hair-cells
Opposing gradient of Ribbon and AMPA Receptor patches

Spatial segregation of gradients

Modiolar Side: Larger ribbons, smaller AMPAR patches
Pillar Side: Smaller ribbons, larger AMPAR patches

Spatial segregation of gradients

Gradient ratios along the Cochlea

Ribbon synapse Morphology
### Summary

<table>
<thead>
<tr>
<th>Modiolar side</th>
<th>Threshold sensitivity</th>
<th>Spontaneous rate of discharge</th>
<th>Ribbons size</th>
<th>AMPA receptor patch size</th>
<th>Different Fiber size</th>
</tr>
</thead>
<tbody>
<tr>
<td>high</td>
<td>high</td>
<td>large</td>
<td>small</td>
<td>LARGE</td>
<td>Low</td>
</tr>
<tr>
<td>low</td>
<td>low</td>
<td>LARGE</td>
<td>small</td>
<td>LARGE</td>
<td>High</td>
</tr>
<tr>
<td>leisure</td>
<td>leisure</td>
<td>leisure</td>
<td>leisure</td>
<td>leisure</td>
<td>leisure</td>
</tr>
</tbody>
</table>

### Discussion

- Greater ribbon size and vesicle count for low-SR seems paradoxical
- Ribbon size may contribute to Excitatory Postsynaptic current (EPSC) waveform shape
  - Small ribbons promote coordinated vesicle release and cause monophasic EPSC
  - Large elongated ribbons are less coordinated and cause multiphasic EPSC
- AMPA receptor patches likely underlie sensitivity differences

### Bibliography