A mouse model of the auditory nerve to study cochlear synaptopathy

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Publication date:
2018

Document Version
Publisher's PDF, also known as Version of record

Citation (APA):
**Introduction**

Several non-human animal studies have demonstrated a permanent loss of auditory nerve (AN) fiber synapses after noise over-exposure, termed cochlear synaptopathy, without causing hair cell loss or altering normal auditory thresholds (e.g., Kujawska and Liberman, 2009). Studies in humans are generally inconclusive, mainly because assessing the status of the AN in humans represents a major challenge. In a previous study, we proposed the use of evoked frequency responses (EFRs) as a tool to investigate synaptopathy both in mice and humans (Encina-Llamas et al., under review; Parbasiathathy et al., 2017). Similar patterns of synaptopathy in mice and humans were found. The use of a “humanized” version of the AN model by Zilany et al. (2009-2014) could qualitatively account for the patterns obtained in human listeners. Nevertheless, the use of the original animal version of the AN model (based on the cat) failed to simulate EFRs in mice. It was argued that a species-specific AN model could improve the non-human animal simulations. Given that the mouse is the most used and best characterized species in connection with cochlear synaptopathy, the present study proposes a modification of the original AN model by Zilany et al. (2009, 2014) based on cat data adapted to the mouse.

**Aim of the project**

- Modify the AN model by Zilany et al. (2009, 2014) based on the cat to adapt it to the mouse.
- Due to the complexity of the AN model, it was intentionally decided to modify as few parameters as possible.
- Three main blocks were modified: the middle-ear filter, the cochlear tuning (Q values), and the range of sensitive characteristic frequencies (CFs).
- The ultimate goal was to use the model to simulate EFRs in non-synaptopathic and synaptopathic mice.

**Methods**

**Model:**
- "Modified" version based on the AN model by Zilany et al. (2009-2014):
  - 296 characteristic frequencies (CFs), ranging from 1 to 12.1 kHz.
  - Synapses per IC are simulated by independent synaptic connections of each of the 18 CF (86 fibers per CF with a total of 24 CFs).
  - Synaptic CFs are selected using a random selection method.

**Simulated EFRs using the CAT model:**

**Simulated EFRs using the MOUSE model:**

**References**


Zilany et al. (2014). Hearing Res. 329, 33-44. DOI: 10.1016/j.heares.2014.03.006.


**Fig. 3** Magnitude and phase responses of the middle-ear EFRs. Panels A & B show the ME filters in the cat model. The solid lines correspond to the original L1562 model filter (Bruce et al., 2001). The dashed lines correspond to the simplified ST filter in Zilany & Bruce (2004).

**Fig. 8** Simulated AN threshold in the healthy mouse. The solid line corresponds to the threshold obtained by calculating the distance to the nearest CF in the AN model by Taberner & Liberman (2017). The dashed line represents the AN threshold calculated for the model with synaptopathy (Zilany et al., 2014).

**Fig. 9** Simulated EFR level-growth functions in the MOUSE model using strongly (blue) and shallowly (red) amplitude modulated tones. Color bars show simulated EFR level-growth functions at 10 offset frequencies. Plot shows simulated EFRs for different types of CFs.