On the value of brief sound audiometry as a diagnostic tool for cochlear synaptopathy

Enrique A. Lopez-Poveda[1], Peter T. Johannesen[1], Byanka C. Buzo[1], Filip Rønne[2], Niels H. Pontoppidan[2], James M. Harte[3]

[1] University of Salamanca, Salamanca, Spain, [2] Eriksholm Research Centre, Denmark, [3] Interacoustics Research Unit, Denmark

E-mail: ealopezpoveda@usal.es

Motivation

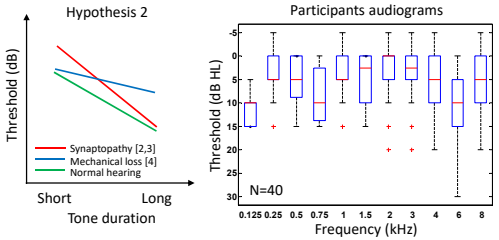
Cochlear synaptopathy (or the loss of primary auditory synapses) [1] remains a subclinical condition of uncertain prevalence in living humans. Here, we investigate (1) whether it occurs in listeners with normal audiometry, and (2) whether it may be diagnosed using brief-tone audiometry, as has been suggested by a perceptual model [2].

Assumptions

1. In rodents, noise exposure causes synaptopathy [1]. In human cadavers, the number of spiral ganglion cells decreases with increasing age at death [3]. Based on this, we assume that noise exposure and/or aging cause synaptopathy in humans.
2. We assume that synaptopathy reduces the rate of growth of ABR wave-I amplitude with increasing intensity, as it does in rodents [1].

Hypotheses

1. If synaptopathy occurs in humans, then the rate of growth of ABR wave-I amplitude with increasing intensity should be negatively correlated with age and/or noise exposure.
2. If it were possible to diagnose synaptopathy using brief-sound audiometry, then brief-tone thresholds should be abnormally high for synaptopathic patients.



Methods

Absolute thresholds

- Pure tones.
- 3AFC, one-up, two-down [5].
- 1-ms onset/offset $\cos^2$ ramps.

kHz	0.5	1.5	4.0	8.0	12
Short (ms)	5	2	2	2	5
Long (ms)	500				

ABR recording params.

- ER-3A insert phones.
- Rarefaction clicks.
- 90:5:110 ppe dB SPL
- Rate: 11 clicks/sec.
- Filtering: 0.1-3 kHz.
- 2048 to 8192 sweeps.

Noise exposure

Questionnaire estimating years (NAYE) of acceptable yearly exposure (AYE = 8 h at 85 dBA over 220 days) [6].

Participants

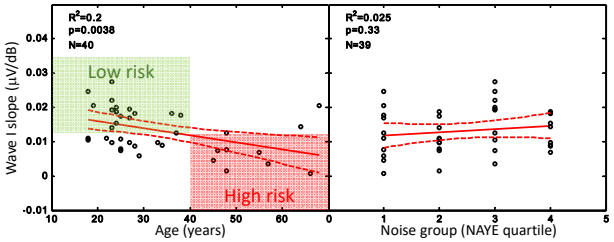
- N=40
- < 20 dB HL at 0.5 to 8 kHz.
- 24-68 yr. (median = 25 yr.)

Analyses

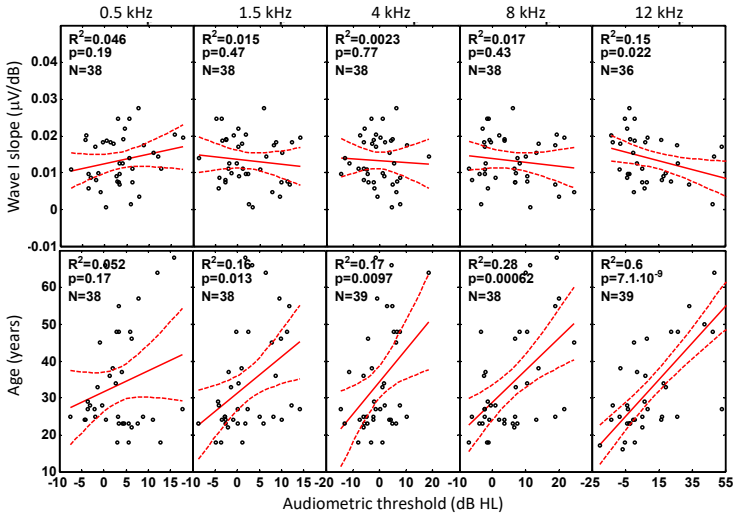
- Participants were grouped in four quartiles according to noise exposure.
- Straight lines were fitted to individual wave-I amplitude-level functions (slope in μV/dB).

Results. Hypothesis 1

Decreasing wave-I slope with age is consistent with synaptopathy:



But wave-I slope and age are also correlated with thresholds:



A multiple linear regression model suggests that once 12-kHz threshold was accounted for, age was not an additional predictor of wave-I slope. Hence, age and 12-kHz threshold are equivalent predictors of slope.

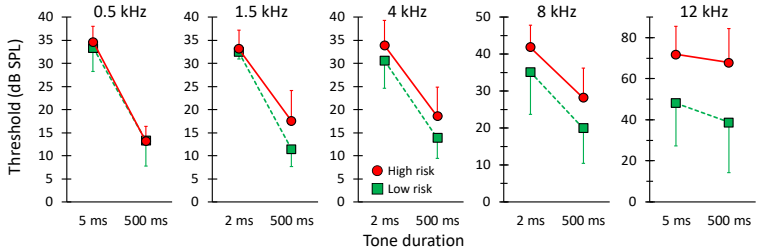
Order	Predictor	P-value	Adj. R^2
1	Thresh. (12 kHz)	0.022	0.12
2	Age	0.075	-

Discussion

- Either wave-I slope and 12-kHz threshold are both indicators of synaptopathy, or slope was reduced by high-frequency (12 kHz) loss.
- The latter cannot be ruled out because (1) wave I amplitude reflects basal cochlear responses [7, 8], and (2) ER3s excitation rolls off at 5 kHz but high-level clicks might excite all cochlear regions.

Results. Hypothesis 2

- Participants were classified into high-risk (7 older, shallow wave-I slope) and low-risk (17 younger, steeper wave-I slope) of synaptopathy, as in the left figure.
- Disproportionately larger thresholds for short than long tones may indicate synaptopathy.



- Mixed, repeated measures ANOVA with two factors: group and duration.
- The effect of duration was significant at all frequencies ($p < 0.001$).
- The effect of group was significant at 8 ($p = 0.043$) and 12 kHz ($p = 0.003$) only.
- The interaction duration×group was significant at 1.5 ($p = 0.003$) and 12 kHz ($p = 0.006$), but the pattern indicated mechanical loss rather than synaptopathy (see Hypothesis).

Discussion

- Either synaptopathy does not affect threshold-duration functions (or it affects long- and short-tone thresholds equally).
- Or the effect of synaptopathy on short-tone threshold is washed out by cochlear mechanical losses or by measurement variability.
- Or synaptopathy is less prevalent than is assumed to be.

Key findings

1. We saw (inconclusive) signs of synaptopathy in aged listeners.
2. Synaptopathy in humans may be diagnosed using the slope of ABR wave-I.
3. We saw no signs of noise-induced synaptopathy. But are noise-exposure questionnaires reliable?
4. Brief-tone thresholds appeared more consistent with cochlear mechanical loss than with synaptopathy.

Acknowledgements

Work funded by the Oticon Foundation, MINECO (ref. BFU2015-65376-P), and CNPQ.

References

[1] Kujawa & Liberman, 2009, J. Neurosci. 29:14077:14085.
[2] Marmel et al., 2014, Front. Aging Neurosci. 7:63
[3] Makary et al., 2011, JARO. 12:711-717.
[4] Florentine et al., 1988, JASA 84:195–203.
[5] Levitt, 1971, JASA 49:466-477.
[6] Beach et al., 2013, Int. J. Audiol, 52: S20-S25.
[7] Don & Eggermont, 1978, JASA, 63:1084–1092.
[8] Eggermont & Don, 1980, JASA, 68:1671–1675.

To access this poster: