Temporal Processing Deficits due to Noise-Induced Synaptopathy
Studied Using Envelope-Following Responses

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INTRODUCTION
Noise exposure can produce temporary and permanent changes in threshold sensitivity. Predictive threshold shifts (PTS) are typically associated with hair cell loss or damage. In contrast, complete post-exposure recoveries of thresholds has been assumed to indicate cochlear recovery, without delayed changes as noise-exposed individuals age.

Our recent work in mouse models of noise and aging challenges this view. We have described an age-progressive cochlear synaptopathy, that is exacerbated by a noise exposure1 and is the basis for this study. We describe here, for the first time, a computational model of the auditory nerve (AN)6, to better understand the contributions of different SR neurons, as well as the role of the SNR neurons in noise-induced synaptopathy.

RESULTS
I. Thresholds recover with synaptopathic noise but neural amplitudes do not

In the first experiment, growth functions of EFRs showed altered amplitude modulated tones of low (red line) and high (blue line) modulation depth. The hypothesis is that if the low-SR neurons are preferentially affected by the noise exposure, it would affect the shallower modulation depth adversely (yellow line). The results support this hypothesis.

II. Synaptopathy causes a reduction in EFR amplitudes

In the second experiment, an AM tone with 100% modulation depth (25kHz) was presented at a low sound level while the background noise was systematically varied. The results demonstrated that if the low-SR neurons are preferentially targeted by the noise, encoding of stimulus in background noise would be more significantly affected than at lower modulation depths. This is supported by the fact that EFR amplitudes were reduced in the presence of noise.

A complementary model of the cochlea was implemented to simulate the effects of noise exposure on the auditory system. The model was able to reproduce the altered EFRs seen in the animals, and the results suggest that the off-channel, contributions had a major impact in the temporal processing.

III. Aging may affect the same neuronal sub-population as synaptopathic noise

EFRs were compared between 32 week old animals that received a single synaptopathic noise exposure at 16 weeks vs unexposed cohorts. In this way, very early aging time point, the difference in amplitudes due to noise exposure was reduced in both experiment 1 and experiment 2, suggesting that the aging process and the acute noise trauma may be targeting similar subpopulations of neurons in the auditory nerve.

IV. Computational model of the AN can recreate EFRs in normal and synaptopathic conditions

A computational model of the AN was used to recreate the EFRs seen in normal and synaptopathic rats. Center frequencies of the synaptopathic and non-synaptopathic conditions were adapted to correspond to the cat cochlear frequency map, and the model was able to recreate the EFRs seen in the animals, and the results suggest that this off-channel, contributions had a major impact in the overall response characteristics.

CONCLUSIONS
Synaptopathy noise exposure causes persistent declines in suprathreshold auditory processing even when counteracted and neural based thresholds recover. This decline has been measured previously using the wave 1 amplitude of the ABR. Here we extend this result to show that temporal processing measures like EFRs are also affected by this noise exposure.

Exposure to noise trauma caused a reduction in EFR amplitudes at various modulation depths - level combinations, as well as depression of the dynamic range of cochlear neurons. AM stimulation is known to exert effects on both cochlear and aging and are both thought to affect a specific subset of low-SR auditory nerve neurons.3 Some evidence for this has been seen in this study, where the difference in EFR amplitudes between species show a change that were smaller when compared to the younger animals.

When measuring population responses like the EFRs, it is important to consider the off-channel contributions to the lower frequency tails of higher CF responses. The computational model was able to recreate the EFRs seen in the animals, and a further analysis of the components of the response revealed that these off-channel contributions had a major impact in the overall response characteristics.

Taken together these results reveal the temporal processing deficits due to noise-induced synaptopathy, and the utility of this model to understand the underlying mechanisms behind the generation of non-invasive population responses.

REFERENCES
1. Furman, A. C., Kujawa, S. G. & Liberman, M. C. Noise-induced cochlear neuropathy is selective for the subset of auditory nerve fibers with low spontaneous rates (SR) of firing: important for suprathreshold processing of sound, particularly in noise.
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