Changes in peripheral and subcortical auditory processes in response to small arms fire-like noise exposure

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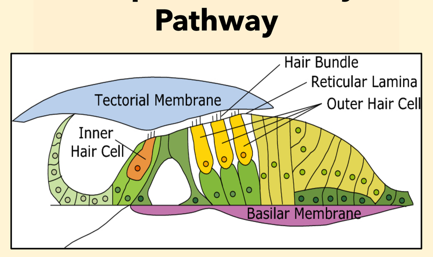
BACKGROUND

- Hearing loss (HL) caused by different auditory stressors have been shown to possess distinct damage profiles (e.g. age-related HL may show gradual cortical gain changes, while noise-induced HL may result in acute loss of hearing sensitivity).[2,3,4,5]
- Treatment often only addresses hearing sensitivity, rendering it suboptimal. *It is important to understand underlying mechanisms of different auditory stressors to best optimize treatments for each patient.*
- In 2019, Altschuler et al. showed exposure to small arms fire-like (SAF) noise induced persistent outer hair cell damage (OHC), a reduction in cochlear synapses, and threshold increases.[1]
- *However, the early adaptations (<10 weeks post-exposure) to SAF noise in the peripheral and central auditory pathways are not well understood. During these early periods, dynamic region-specific changes in gain may occur that distinguishes the damage profile and therefore, the best treatment options.*
- **PURPOSE: Identify biomarkers sensitive to underlying mechanisms responsible for SAF noise-induced hearing loss in the peripheral and central auditory system to better inform and optimize individual treatment options.**

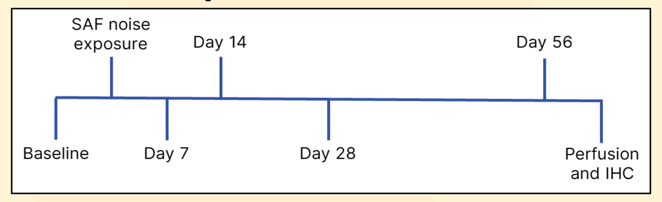
METHODS

- **Subjects**: 3–6-mth-old F344 rats (SAF–F=4, M=4; Sham–F=2, M=2)
- **SAF noise exposure**: 50 biphasic 0.3 ms pulses (1 every 3 s) for 2.5 min; SAF = 120 dB pSPL, Sham = 60 dB pSPL; bilateral presentation; ketamine (60mg/kg) and dexdomitor (0.1 mg/kg)[1]
- **OHC function → Distortion product otoacoustic emissions (DPOAEs)**: presentation of two frequencies that cause the emittance of a third frequency called a distortion product
- **Hearing sensitivity → Thresholds**: lowest sound level at which all auditory brainstem response (ABR) peaks (*Ch 1 – W1, W3; Ch 2 – W1, W4, W5)* can be distinguished
- **Central auditory processing → ABRs** : auditory evoked potentials representing subcortical neuronal population activation in response to sound *(Ch 1 W1 = auditory nerve (AN), W3 = cochlear nucleus; Ch 2 W1 = AN, W4 = superior olivary complex, W5 = inferior colliculus (IC))*

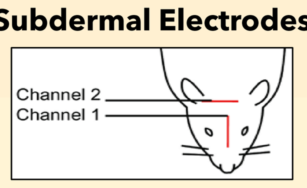
Peripheral Auditory Pathway



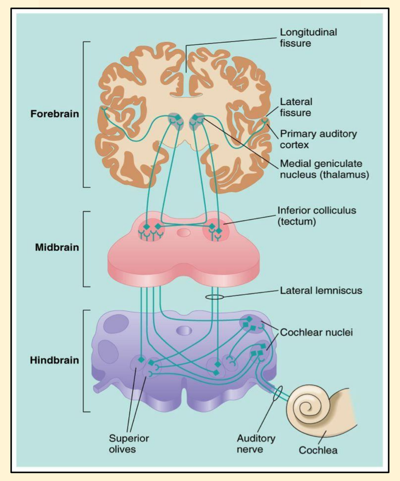
Experimental Timeline



Subdermal Electrodes



Central Auditory Pathway

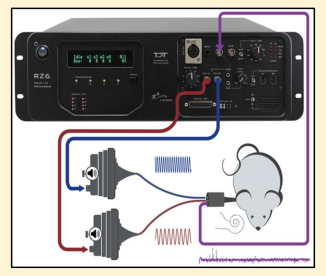


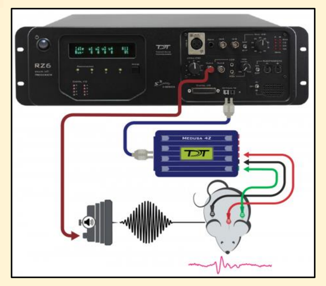
DPOAEs

$f_1/f_2 = 1.22$; L1-L2 = 10
f_2 = 4kHz, 8kHz, 10kHz
L1 = 60dB & 70dB

ABRs

Click ABR: 0.3ms pulse at 30Hz
8kHz: 2ms pure tone
1500 avgs.





CONCLUSIONS

- OHC damage progression following SAF exposure shows persistent damage, with possible slight regain of function at L_1=60dB. Thresholds and neural measures demonstrate day-specific responses that have a period of damage (D7-14) followed by recovery (D28) before possible further damage or stabilization (D28-D56).
- Persistent OHC function with possible recoveries in W1/W5 amplitudes suggest an initial period of damage followed by a delayed alteration in information propagation along the central pathway

SAF noise induced HL may be characterized by acute initial OHC damage, followed by mild OHC recovery and delayed, persistent alterations on the impulse transmission throughout the subcortical auditory pathway.

	D7	D14	D28	D56
8K OHC Function	- - -	- - -	- -	-
Click Thresholds	+ +	+ +	+	+ +
Click ABR W1/W5	-	- -	+	+ + +
8K Thresholds	+ + +	+ + +	+	+
8K ABR W1/W5	- - -	-	0	- - -

Future directions: Correlate functional electrophysiological changes with neuroanatomical structural effects of SAF noise induced HL using immunohisto-chemical methods.

ACKNOWLEDGEMENTS

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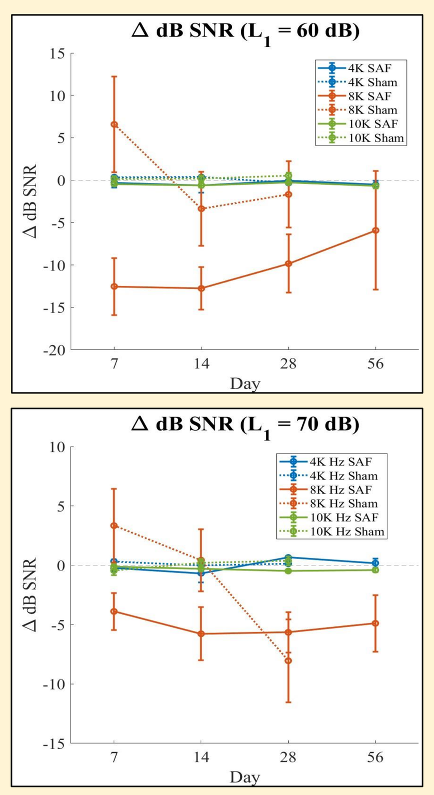
RESULTS

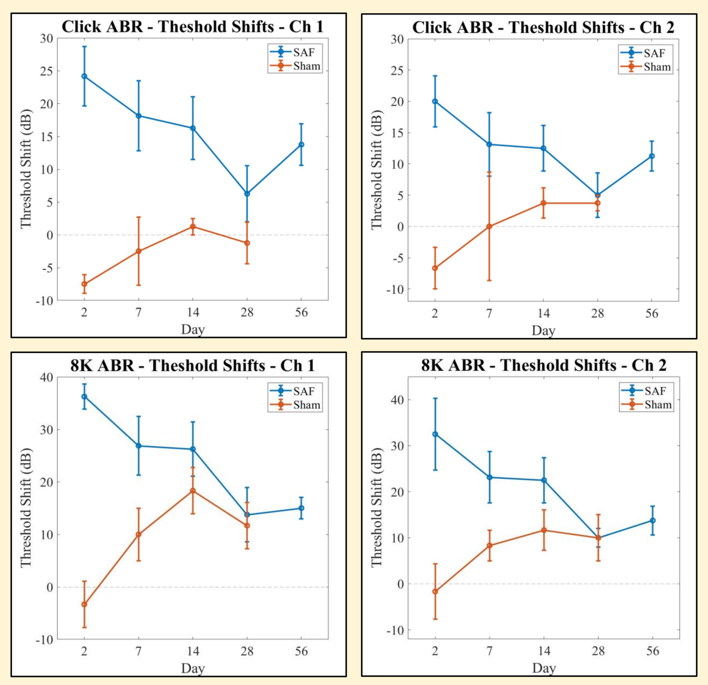
DPOAEs
OHC Health



- 8K shows acute decrease in dB signal-to-noise (SNR) ratio followed by slight recovery. *4K & 10K* show no change between sham and SAF or between days *(top – L1=60dB, bottom – L2=70dB)*

Suggests damage preference to 8K section of cochlea.

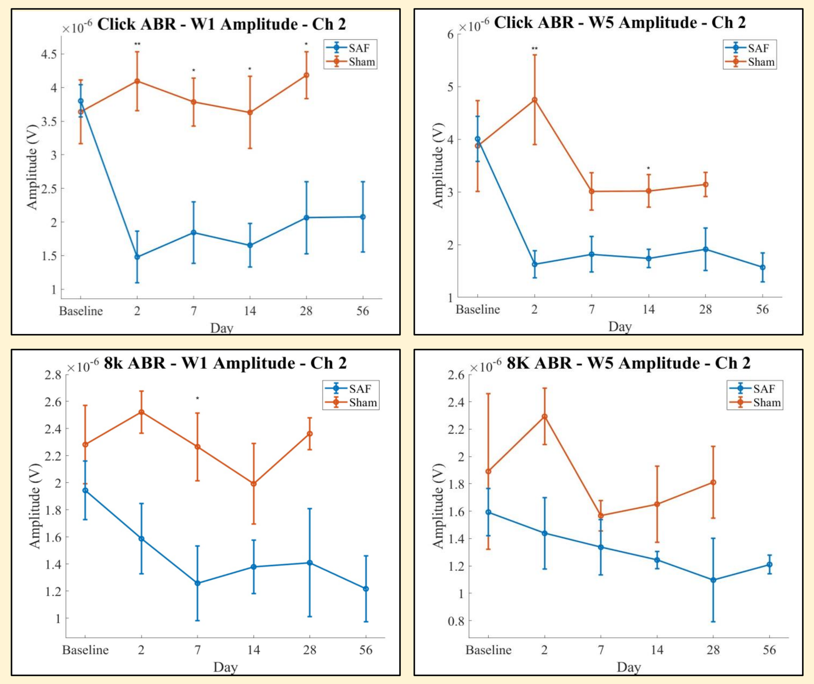
Thresholds
Hearing Sensitivity



- All graphs show threshold shifts *(top – click, bottom – 8K; left – Ch 1, right – Ch 2)* and demonstrate an immediate increase in threshold at D2, followed by incremental decreases from D7-28, and either mild recovery or stabilization on D56.

Suggests possible phases of damage consisting of acute injury, gradual recovery (not quite to baseline), and stabilization.

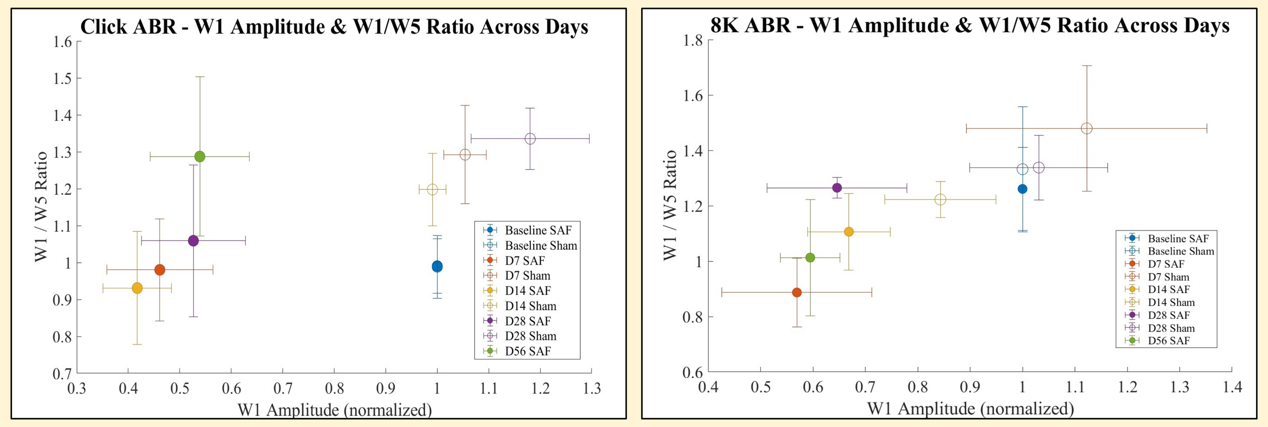
W1 & W5 Amplitudes
AN and IC population response



- *(top row)* Both W1 and W5 amplitudes demonstrate a precipitous decrease at D2 before stabilization
- *(bottom row)* Both 8K W1 and W5 amplitudes decrease steadily after SAF exposure

Suggests possible unique mechanisms of damage responsible for neural responses to broad band auditory stimuli (clicks) and pure tone frequencies (8K)

W1/W5 Ratios
Relative contribution of AN and IC to the neural response



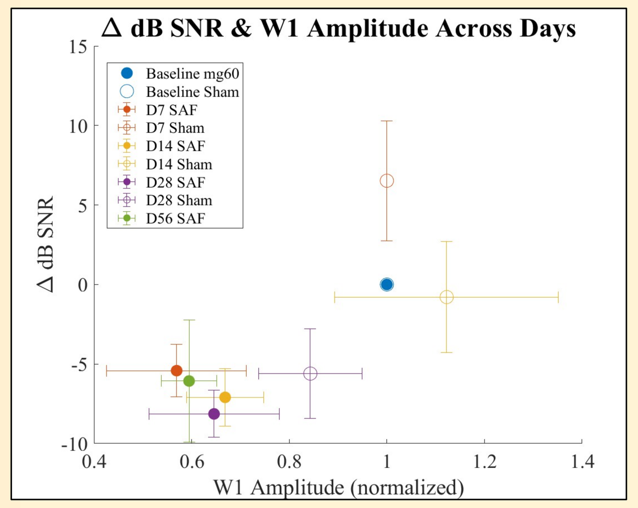
- *(left)* Click – W1 amplitudes are significantly different between SAF and sham groups. D7-14 show decreased W1 amplitudes and W1/W5 ratios compared to baseline, but D56 show decreased W1 amplitude with an increase in W1/W5 ratio.
- *(right)* 8K – W1 amplitudes are show a smaller decrease. Compared to D56 of click, D56 of 8K does not show W1/W5 ratio increase to baseline levels.

Suggests SAF exposure alters the relative strength of the AN and IC to the overall ABR. It shows a general decrease in W1 amplitude after the exposure, and a delayed decrease in W5, possibly occurring around D56 of click ABR D28 and 8K ABR.

Δ dB SNRs & W1 Amplitude
Relationship between OHC health (DPOAEs) and AN function (ABRs)

- *(right)* Δ dB SNR and W1 amplitude for 8K Ch 2 shows a marked decrease in amplitude and dB SNR following SAF exposure

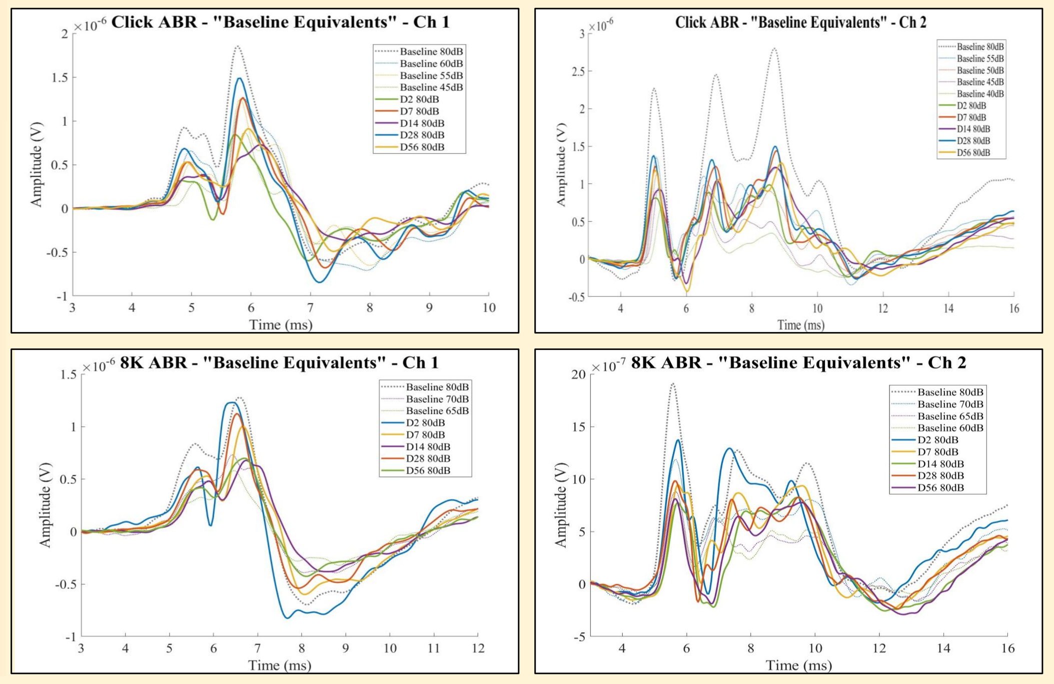
Suggests proportional relationship between DPOAEs and W1 amplitudes, notably not reflected in W1/W5 ratios.

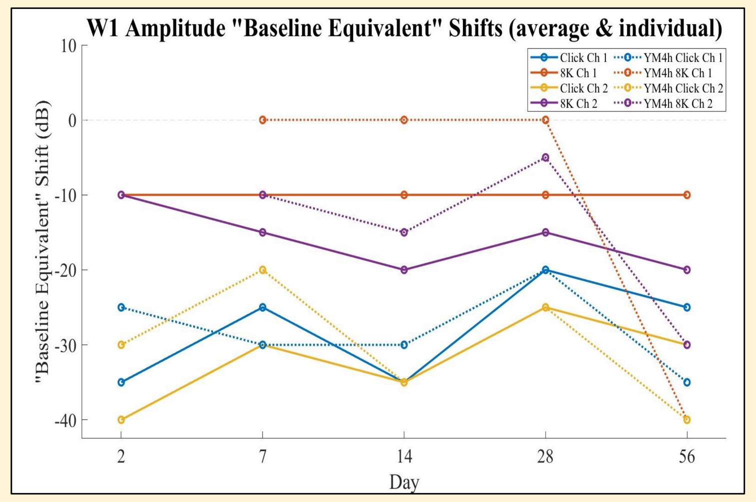


ABR "Baseline Equivalents"
Neuronal strength comparison

- *(top row)* Click – Ch 1 (left) and Ch 2 (right) show an equivalent 20-40dB shift when matching averaged W1 amplitudes
- *(bottom row)* 8K – Ch1 (left) and Ch 2 (right) show an equivalent 10-20dB shift when matching averaged W1 amplitude
- (right-most) Average and individual (rat ID – YM4h) shifts in W1 amplitude "baseline equivalents"

Suggests persistent decrease in function and inability to return to baseline. Sustained damage may perpetuate delayed alterations to impulse transmission through the subcortical auditory system.





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