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TITLE: Mechanism-Based Prevention of Noise-Induced Tinnitus: Protection and Repair of Peripheral Auditory Neuropathy

PRINCIPAL INVESTIGATOR: Dr. Richard Altschuler

CONTRACTING ORGANIZATION: Regents of the University of Michigan

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Dr. Richard Altschuler, PhD
E-Mail: shuler@umich.edu

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Regents of the University of Michigan
1042 Wolverine Tower
3003 South State Street
Ann Arbor, Michigan 48109-1274

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14. ABSTRACT

Studies test a potential treatment for noise-induced tinnitus in the rat model. We hypothesize that noise-induced loss of synaptic connection between Inner Hair Cells (IHC) and the auditory nerve (AN) contributes to the induction of tinnitus and rapidly repairing this loss will therefore decrease the incidence of tinnitus. Treatment with the neurotrophic factor NT-3 was previously shown by our consultant Dr. Corfas to induce significant IHC-AN synapse reconnection after a different type of noise in his mouse model (Suzuki et al., 2016). During the first year of studies we have found that we can duplicate these results using a more military relevant small arms fire (SAF)-like noise in the rat model, showing a large and significant re-connection (described later in Section 3 of the Results Section). NT-3 in poloxamer was applied to the round window with the trans-tympanic approach that has been successfully applied in people for other treatments. These results show that it is possible to reverse noise induced synaptic loss from a military relevant noise exposure with a treatment paradigm that can be applied to those in the service. Such noise-induced synapse loss can cause a "Hidden Hearing Loss" that can impair speech understanding (Liberman et al., 2016, 2017). Therefore the ability to repair and reverse Hidden Hearing Loss has immediate impact. The major goal, however, is to test if such reconnection will decrease or prevent the later development of tinnitus and that is the focus of the next stage of our ongoing studies. Studies are now underway to determine if this rapid reconnection from NT-3 treatment will decreases the incidence of noise induced tinnitus compared to noise exposed rats without treatment. If successful, this would provide a military relevant treatment to prevent and treat noise-induced tinnitus.

15. SUBJECT TERMS

Tinnitus, Deafness, Neurotrophins, NT-3, Synaptopathy, Noise, Small Arms Fire, Cochlea, Auditory, Hidden Hearing Loss

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1. **INTRODUCTION:**
Studies test an underlying mechanism and potential mechanism-based treatment for noise-induced tinnitus in the rat model. We hypothesize that noise-induced loss of synaptic connection between Inner Hair Cells (IHC) and the auditory nerve (AN) contributes to the induction of tinnitus and repairing this loss will decrease the incidence of tinnitus. Treatment with the neurotrophic factor NT-3 was previously shown by our consultant Dr. Corfas to induce significant IHC-AN synapse reconnection after a different type of noise in his mouse model (Suzuki et al., 2016). In our first phase of studies we reported we can duplicate these results using a more military relevant small arms fire (SAF)-like noise in the rat model, showing a large and significant re-connection when this treatment is applied 1 day after the noise. During Years Two and Three we tested NT-3 treatment beginning after a delay of 1 week to determine if it remains effective in inducing re-connection of IHC-AN synapses. We find a more variable, less consistent, re-connection, effective in some treated rats and not others, and also see variability across different regions of the cochlear spiral. This has relevance to those in the field that might not be able to get immediate treatment. Year Two and Three studies tested if the NT-3 in poloxamer treatment given one day after noise (when re-connection is more consistent) reduces the incidence of tinnitus. These studies are still underway (see section on Unanticipated Problems for reasons behind delay). Reconnection could reduce the incidence of tinnitus but could also be effective in treating "Hidden Hearing Loss" that can impair speech understanding (Liberman et al., 2016, 2017). Either or both would provide benefit to Veterans and those in general population exposed to noise.

2. **KEYWORDS:**
Tinnitus, Deafness, Neurotrophins, NT-3, Synaptopathy, Noise, Small Arms Fire, Cochlea, Auditory, Hidden Hearing Loss

3A. MAJOR GOALS - from Statement of Work (SOW):

YEAR THREE:

Timeline & Milestones: Aim 1 studies continued (staggered start)

Aim 1: ***Test the hypothesis that rapid reconnection of Inner Hair Cell –Auditory Nerve (IHC-AN) synapses that are lost as a consequence of a Small Arms Fire (SAF)-like impulse noise, will prevent chronic tinnitus from appearing.***

TASK 1: Determine if NT-3 elevation treatment beginning 1 day after a SAF-like noise induces effective reconnection of lost IHC-AN synapses and if this will subsequently prevent Tinnitus from appearing (compared to noise-exposed rats without NT-3 elevation treatment).

- ***Subtask 1***: Determine the influence of NT-3 elevation treatment given 1 day after SAF-like noise on the appearance of tinnitus based on Gap Detection & and behavioral (operant conditioning) metrics compared to noise-exposed rats without NT-3 elevation treatment
- ***Subtask 2***: Determine the influence of NT-3 elevation treatment given 1 day after SAF-noise on noise-induced changes to IHC-AN synapses, loss of inner and outer hair cells and loss of spiral ganglion neurons

Task 1 Milestones: 1. Determine efficacy in inducing re-connection.
2. Determine treatment effects on tinnitus

Aim 2: ***Test the hypothesis that a later reconnection of the IHC-AN synapses that are lost as a consequence of noise will be less effective in preventing tinnitus. Determine the effectiveness of NT-3 treatment given at 1-2 (Aim 2A) or 6 (Aim 2B) weeks following SAF-like noise in inducing repair of IHC-AN synaptic connections and in reducing the incidence of Tinnitus***.

Task 2A: Determine if NT-3 elevation treatment beginning 1-2 weeks after a SAF-like noise induces effective reconnection of lost IHC-AN synapses and if this will subsequently prevent Tinnitus from appearing (compared to noise-exposed rats without NT-3 elevation treatment).

- ***Subtask 1***: Determine the influence of NT-3 elevation given 1-2 weeks after SAF-like noise to prevent the appearance of tinnitus based on Gap Detection and behavioral (operant conditioning) metrics. Compare the efficacy to treatment 1 day after noise (results from Aim 1B – Subtask 1)
- ***Subtask 2***: Determine the influence of NT-3 elevation given 1-2 weeks after SAF-like noise on Noise-Induced changes to Inner Hair Cell –Auditory Nerve (IHC-AN) synaptic connections. Determine the efficacy in inducing IHC-AN synaptic 're-connection" compared to when the treatment is given 1 day after noise (results from Aim 1B – Subtask 2)

Task 2B: Determine if NT-3 elevation treatment beginning 6 weeks after a SAF-like noise induces effective reconnection of lost IHC-AN synapses and if this will subsequently prevent Tinnitus from appearing (compared to noise-exposed rats without NT-3 elevation treatment).

- ***Subtask 1***: Determine the influence of NT-3 elevation 6 weeks after SAF-like noise to prevent appearance of tinnitus based on Gap Detection and behavioral (operant conditioning) metrics. Compare the efficacy in reducing incidence of tinnitus to treatment beginning 1 day or 1-2 weeks after noise.
- ***Subtask 2***: Determine the influence of NT-3 elevation beginning 6 weeks after SAF-like noise on Noise-Induced changes to Inner Hair Cell –Auditory Nerve synaptic connections, loss of Inner and Outer Hair Cells and loss of Spiral Ganglion Neurons. Compare the efficacy of 're-connection" to treatment 1 day or 1-2 weeks after noise

Task 2 Milestones: 1. Determine efficacy in re-connection (Year 2 and 3)
2. Determine treatment effects on tinnitus (Years 3 and 4)

3Ca. ACCOMPLISHMENTS:

Major Activities Task 1:

Aim 1	Group 5 –	Sham Noise – no NT-3
Aim 1	Group 6 –	SAF-like Noise – no NT-3
Aim 1	Group 7 –	Sham Noise – NT-3 elevation treatment given 1 day after noise
Aim 1	Group 8 –	SAF-like Noise – NT-3 elevation treatment given 1 day after noise

Major Activities Task 2:

Aim 2	Group 5 –	Sham Noise – no NT-3
Aim 2	Group 6 –	SAF-like Noise – no NT-3
Aim 2	Group 9 –	Sham Noise – NT-3 post-treatment 1-2 weeks after noise
Aim 2	Group 10 –	SAF-like Noise – NT-3 post-treatment 1-2 weeks after noise

Rats received base-line measures of auditory brain stem response (ABR) and Gap Detection (GD). Rats then received either operant conditioning or Gap Detection as metrics for later tinnitus testing. Animals were then randomly divided into groups receiving either Sham noise or SAF-like noise in one ear (left ear only). Animals in each group were then again randomly divided and received either Poloxamer containing NT-3 or Poloxamer only (no NT-3), delivered with a trans-tympanic approach into the left middle ear by the round window, done one day after the noise or sham (Groups 7 & 8) or one to two weeks after the noise or sham (Groups 9 & 10). All animals then receive testing with either the GD and Operant Conditioning as metrics for the presence of tinnitus. After two months of assessments all rats are tested for ABR and then euthanized. Cochleae are processed to determine hair cell loss and loss of IHC-AN synaptic connections.

Unanticipated Problems: These were discussed in our request for a no-cost extension, as given below:
First, as mentioned in previous Progress Reports, there were delays in manufacturers (e.g. Kinder) providing all the critical components of behavioral tinnitus testing stations resulting in delays of our getting the systems and stations functional. Because of these delays we needed to postpone the start of the study tasks involving testing for tinnitus by over 6 months. These tasks (given below) were the sub-tasks that involved testing if reconnection

of inner hair cell – auditory nerve connections lost following noise would influence the subsequent appearance of tinnitus:

- ***Aim 1 - Subtask 1***: Determine the influence of NT-3 elevation treatment given 1 day after Small Arms Fire (SAF)-like impulse noise on the appearance of tinnitus based on Gap Detection & and behavioral (operant conditioning) metrics compared to noise-exposed rats without NT-3 elevation treatment
- ***Aim 2 - Subtask 1***: Determine the influence of NT-3 elevation given 1 week after SAF-like noise to prevent the appearance of tinnitus based on Gap Detection and behavioral (operant conditioning) metrics. Compare the efficacy to treatment 1 day after noise (results from Aim 1 – Subtask 1).

Second, there was a "ramping down" of research activities at the University of Michigan starting in February 2020, because of the COVID-19 pandemic. We were able to continue testing animals already in study, but at a reduced level due to staffing constraints. We were not able to order new animals or do any new procedures. We were able to begin a "ramp up" at the University of Michigan in mid-summer 20202 and were able to order new animals, do surgeries and begin new studies, but constraints on the number of staff that can be in at one time are still in place so we cannot operate at full capacity. This influenced the subtasks listed above as well as Subtask 2 of Aim 2 (listed below):

- ***Aim 2 -Subtask 2***: Determine the influence of NT-3 elevation beginning 6 weeks after SAF-like noise on Noise-Induced changes to Inner Hair Cell –Auditory Nerve synaptic connections, loss of Inner and Outer Hair Cells and loss of Spiral Ganglion Neurons. Compare the efficacy of 're-connection" to treatment 1 day or 1-2 weeks after noise

Because of these delays we will were allowed another 12 months to carry out studies as proposed. We were able to reduce spending commensurate with the reduced activities and carry over sufficient dollars to fund these studies for the additional 12 months necessary.

Major Activities 2: Because of the delay (mentioned above) in being able to use the needed metrics to test rats for tinnitus, the studies first focused on the assessing synaptic connections, since this does not require tinnitus testing stations to be utilized to generate initial results. Studies first examined NT-3 treatment given one day after the SAF-like noise for repair of lost IHC-AN synapses (Groups 5 – 8) and compared this to the efficacy we found using anti-excitotoxicity treatments given before the noise (for preventing loss). The analysis examining anti-excitotoxicity treatment given before the SAF-like noise was completed in Year One and results were published in 2019 (Altschuler et al, 2019). Studies examining efficacy of trans-tympanic NT-3 in poloxamer applied at the round window 1 day following the SAF-like noise in inducing reconnection of lost IHC-AN synapses in Groups 5-8 were completed in Year One with assessment completed in Year Two. We are currently in the process of examining NT-3 elevation treatment given 1 weeks after the noise (Task 2 - Groups 9 and 10). Once this assessment in completed we will compare to results from treatment 1 day results after the noise (Groups 7 and 8) and submit this for publication.

RESULTS:

Studies examining pre-treatment with anti-excitoxicity agents were published (Altschuler et al., 2019). Studies comparing pre-treatment to NT-3 post treatment 1 day after noise were completed during Year One, assessed in Year Two and are summarized below:

Sprague Dawley rats were tested for ABR and only rats with normal responses were placed in study. The SAF-like impulse noise groups received 50 biphasic impulses over 2.5 minutes at 154 dB SPL given unilaterally (with a speculum) to the left ear. They received a second ABR within one hour following the noise and were then randomly divided into a group receiving NT-3 in poloxamer 1 day after the noise or a group receiving poloxamer only 1 day after the noise. Eight µl of Poloxamer with or without NT-3 was placed in the middle ear by the round window of the left cochlea with a trans-tympanic approach 1 day after the noise. Animals received a third ABR assessment 7 days later and were then euthanized. Cochleae received intrascalar fixation with 4% paraformaldehyde fixative and were then processed for assessment of hair cell loss and loss of IHC-AN synaptic connections, using CTBP2 ribbon immunolabeling as a marker for IHC synapses.

SAF-like noise exposed rats showed a significant temporary threshold shift in the left ear of ~25 dB at 8 kHz and no shift at 16 and 32 kHz when assessed an hour following the noise. There was complete recovery of ABR thresholds and DPOAE (at the frequencies tested) 10 days after the noise exposure in both NT-3 treated and non-treated SAF-like noise exposed rats. There was no loss (over normal baselines) of inner or outer hair cells at 10-11 days following the SAF-like noise in either NT-3 treated or untreated rats. CTBP2 synaptic labeling (number of synapses per IHC) was assessed in regions of the cochlear spiral 5.0 mm and 6.5 mm from the apex. These regions were chosen for examination based on finding an SAF-like noise induced loss of synapses that was prevented by anti-excitotoxicity pre-treatment in Altschuler et al. (2019). Results showed SAF-like noise produced a large loss of IHC-AN synaptic connections compared to shams and our normative data base. In the region of the cochlea 5 mm from the apex, the "normal" number of synapses per inner hair cell is 21.7 +/- 2.8. The SAF-like noise exposure significantly ($P<0.05$) reduced this to 11.1 +/- 9.7 synapses per inner hair cell. The NT-3 treatment restored this to 22.8 +/- 0.6 comparable to normal (**Figure 1**) and significantly greater ($P<0.05$) than without treatment. This suggests almost complete reconnection of lost IHC-AN synapses. The numbers were also highly comparable to what was seen with anti-excitotoxicity pre-treatment to prevent loss (**Altschuler et al., 2019).**

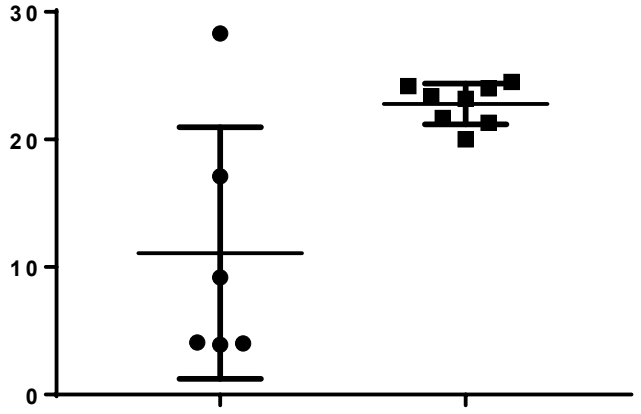

Figure 1A – A scatter plot comparison of the number of CTBP2 puncta (a marker for Inner Hair Cell – Auditory Nerve (IHC-AN) synaptic connections) per Inner Hair Cell - 5.0 mm from the apex with SAF noise exposed rats and no NT-3 treatment on the left and noise exposed rats receiving NT-3 one day after SAF noise on the right. The mean for rats receiving noise exposure and no treatment is 11.1 +/- 9.7. The mean for rats receiving noise exposure and NT-3 treatment is 22.8 +/- 0.6. This is significantly greater ($P<0.05$) than the mean for noise and no treatment. The "normal" number from rats with sham noise and no treatment is 21.7 +/- 2.8

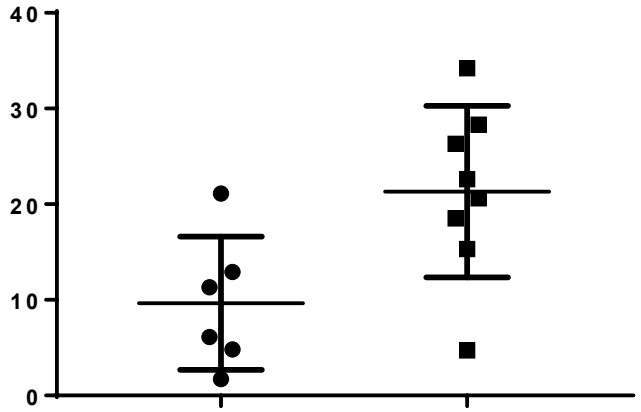

Figure 1B – A scatter plot comparison of the number of CTBP2 puncta (a marker for Inner Hair Cell – Auditory Nerve (IHC-AN) synaptic connections) per Inner Hair Cell - 6.5 mm from the apex, with SAF noise exposed rats and no NT-3 treatment on the left and noise exposed rats receiving NT-3 one day after SAF noise on the right. The mean for rats receiving noise exposure and no treatment is 9.7 +/- 2.9. The mean for rats receiving noise exposure and NT-3 treatment is 21.3 +/- 2.3. This is significantly greater ($P<0.05$) than the mean for noise and no treatment. The "normal" number from rats with sham noise and no treatment is 21.2 +/- 3.2. treatment is 11.1 +/- 9.7.

Conclusions: Our results show that a clinically relevant trans-tympanic application of NT-3 in poloxamer on the round window can induce a significant re-connection of IHC-AN synaptic connections that are lost following an SAF-like noise exposure, even when treatment is one day following the noise. This treatment paradigm would be more applicable to those in the service than pre-treatment and could provide recovery from Hidden Hearing Loss following noise exposure.

SubTask Two studies are examining re-connection when NT-3 treatment is delayed and given 1-2 weeks after the noise. Initial results show less consistent reconnect, with some treated rats showing substantial reconnection but others none. These studies are largely completed, with results showing a more variable, less consistent, re-connection, effective in some treated rats and not others. We also see variability across different regions of the cochlear spiral. This suggests that re-connection with treatment 1 week after noise exposure is possible, but earlier treatment would be recommended when possible. There are only a few more subjects to be assessed and then this can be finalized and submitted for publication.

SubTask One studies are still ongoing and testing whether the rapid (and more consistent) reconnection will reduce the incidence of noise-induced tinnitus. Studies will then be added investigating the influence of later reconnection (and correlating efficacy in reducing tinnitus with the efficacy in inducing re-connection and requiring a larger 'n" for this purpose). Some results for the 1 day NT3 treatment influence on tinnitus have been obtained but many animals are still in study and blinded.

What opportunities for training and professional development has the project provided?

Nothing to Report

How were the results disseminated to communities of interest?

- One publication has appeared in 2019:

Altschuler RA, Halsey K, Kanicki A, Martin C, Prieskorn D, DeRemer S, Dolan DF.(2019) Small Arms Fire-like noise: Effects on Hearing Loss, Gap Detection and the Influence of Preventive Treatment. Neuroscience - [Epub ahead of print] PMID:30053484

- One Invited Platform Presentation by Dr. Altschuler:

Altschuler RA: "Noise Induced Hearing Otopathology and Tinnitus: Mechanisms and Strategies for Prevention and Repair" at the International Hearing Loss Conference at the Niagara on the Lake, Ontario, Canada, May 5-9, 2019.

Plans for next reporting period

Year Four of the no-cost extension will continue the Aim 1 (Task 1) and Aim 2 (Task 2) with rats in all the groups entering and completing an "in-life phase" of noise exposure (or sham) and NT-3 treatment 1 day (Task 1) or 1-2 weeks (Task 2) after the noise exposure (or no treatment) followed by testing for indication of tinnitus:

TASK 1 (Aim 1)

1. Base-line Auditory Brain Stem Response (ABR), Gap Detection (GD and Pre-Pulse Inhibition (PPI) of the Acoustic Startle Reflex (ASR) and Distortion Production OtoAcoustic Emission (ODPOAE)and training in operant conditioning
2. Noise exposure (or sham noise)
3. NT-3 treatment (or poloxamer only without NT-3) one day after the noise
4. Testing for tinnitus (using GD and Operant Conditioning) for two months
5. Final ABR and DPOAE

TASK 2 (Aim 2)

1. Base-line Auditory Brain Stem Response (ABR), Gap Detection (GD and Pre-Pulse Inhibition (PPI) of the Acoustic Startle Reflex (ASR) and Distortion Production OtoAcoustic Emission (ODPOAE)and training in operant conditioning

2. Noise exposure (or sham noise)
3. NT-3 treatment (or poloxamer only without NT-3) one to two weeks after the noise
4. Testing for tinnitus (using GD and Operant Conditioning) for two months
5. Final ABR and DPOAE

After the in-life phase animals are then euthanized and assessed for hair cell loss and loss of Inner Hair Cell – Auditory Nerve synaptic connections.

4. **IMPACT:**

There were three important results that impact hearing research and rehabilitation:

- Our studies show that a military relevant small arms fire (SAF) – like impulse noise that does not cause a permanent hearing loss or loss of sensory cells in the cochlea will still produce a large loss of synaptic connections between the sensory cells and the auditory nerve in the rat model. Other studies have shown such loss can influence hearing processing and speech understanding in a noisy environment
- We published results showing that pre-treatment with anti-excitotoxicity agents can prevent the small arms fire-like noise from causing this loss of connections.
- Our more recent results show that a treatment with NT-3 even one day following the SAF-like impulse noise will induce re-connection and repair of the lost connections, comparable to what was found with prevention prior to noise. Treatment following noise will be more applicable and the trans-tympanic middle ear approach to applying NT-3 is feasible for clinical application. Our new Year 3 results show that treatment at a later time (1 week) following noise can still be very effective in some subjects, but results are less consistent and approximately 1/3 of subjects do not have significant re-connection. This would support treatment as soon as possible after noise, but with some potential for effectiveness even 1 week after the noise

There is also more general impact for study results:

- demonstrated NT-3 can induce re-connection of lost synapses
- effective anti-excitotoxicity treatments

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

Nothing to Report

REFERENCES

Altschuler RA, Halsey K, Kanicki A, Martin C, Prieskorn D, DeRemer S, Dolan DF (2019) Small arms fire-like noise: Effects on hearing loss, gap detection and the influence of preventive treatment, Neuroscience 2019 May 21;407:32-40. PMID: 30053484

Liberman MC, Epstein MJ, Cleveland SS, Wang H, Maison SF. (2016) Toward a Differential Diagnosis of Hidden Hearing Loss in Humans. PLoS One. 11(9):e0162726. PMID:27618300

Liberman MC, Kujawa SG. (2017) Cochlear synaptopathy in acquired sensorineural hearing loss: Manifestations and mechanisms. Hear Res.;349:138-147. PMID:28087419

Suzuki J, Corfas G, Liberman MC. (2016) Round-window delivery of neurotrophin 3 regenerates cochlear synapses after acoustic overexposure. Sci Rep. 6:24907. PMID:2710859

5. CHANGES / PROBLEMS:
There was delay in being able to apply metrics for the presence of tinnitus significantly delaying tinnitus assessments so that completion of Tasks will be delayed and a no-cost extension into a Year Four was provided to allow completion of tasks

6. PRODUCTS:

Other publications, conference papers, and presentations.
Nothing additional over what was reported above

Website(s) or other Internet site(s)
Nothing to report

Technologies or techniques
Nothing to report

Inventions, patent applications, and/or licenses
Nothing to report

Other Products
Nothing to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS:

Name:	Richard Altschuler
Project Role:	Principal Investigator
Researcher Identifier (e.g. ORCID ID):	richardaltschuler
Nearest person month worked:	3
Contribution to Project:	Responsibility for the supervision of the histopathology, quantitative assessments of hair cells and the connection between hair cells and auditory nerve. He will interpret results, trouble shoot methods and make decisions on directions.
Funding Support:	Changes Since Last Report New Awards: R01 DC018003 (King) 04/01/20 – 03/31/24 1.2 calendar months NIH Source of Support: USA Noise-Induced Synaptic Loss and Vestibular Dysfunction The proposed experiments will provide evidence for how excessive noise damages the vestibular system and affects vestibular-dependent behavior. This knowledge could provide insights to help therapists alleviate or reduce the most egregious effects of noise on vestibular function and balance. Role: Co-Investigator

Name:	David Dolan
Project Role:	Co-Investigator
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	1
Contribution to Project:	Responsible for directing the auditory brain stem response (ABR) measures including thresholds and input-output function, and overseeing the assessment of gap detection and pre-pulse inhibition of the acoustic startle reflex as well as the assessment and interpretation of these results. He will also oversee the noise exposures.
Funding Support:	No Changes

Name:	Bryan Pfingst
Project Role:	Co-Investigator
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	0
Contribution to Project:	Dr. Pfingst is an expert in behavioral psychophysical evaluation of hearing. He provide guidance on the operant conditioning test for tinnitus.
Funding Support:	No Changes

Name:	Susan Shore
Project Role:	Co-Investigator
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	0
Contribution to Project:	Provide advice and assist in interpretation of data
Funding Support:	Changes Since Last Report New Awards: R01 DC018284 (Roberts) 06/10/20 – 05/31/25 0.48 calendar months Circuit Mechanisms for Auditory Processing in the Inferior Colliculus The overall objective of this project is to determine the functional roles and circuit connectivity of VIP and NPY neurons, two classes of inferior colliculus stellate neurons that we recently identified. The results will establish how an excitatory and an inhibitory class of stellate neurons integrate ascending and descending auditory input, influence long-range postsynaptic targets, and respond to simple and complex sounds. Role: Co-Investigator

Name:	Sue Deremer
Project Role:	Research Lab Specialist Inter
Nearest person month worked:	1
Contribution to Project:	Ms. Deremer is responsible for the Auditory Brain Stem Response (ABR) measures, DPOAE and the noise exposures at KHRI. She assists Diane Prieskorn with the animal surgeries and drug delivery (by poloxamer on the round window niche) at KHRI. She also is responsible for animal terminations and fixation of cochleae.
Funding Support:	N/A

Name:	Diane Prieskorn
Project Role:	Research Lab Specialist Senior
Nearest person month worked:	1
Contribution to Project:	Ms. Prieskorn is responsible for all animal surgeries and drug delivery (by poloxamer on the round window niche) at KHRI and training the Partnering PI staff at WSU in this method. She also assists in ABR measures and assessment.
Funding Support:	N/A

Name:	Lisa Kabara
Project Role:	Research Technician Associate
Nearest person month worked:	12
Contribution to Project:	Ms. Kabara will be responsible for carrying out the Gap Detection an operant conditioning metrics to test for tinnitus.
Funding Support:	N/A

Name:	Courtney Stewart
Project Role:	Research Fellow
Nearest person month worked:	2
Contribution to Project:	Dr. Stewart will further develop the assessment of IHC-AN synapses and assessments of changes from NT-3 enrichments and provide analysis and correlation with tinnitus metrics.
Funding Support:	N/A

Name:	Hannah Beck
Project Role:	Research Lab Technician Intermediate
Nearest person month worked:	10
Contribution to Project:	Ms. Beck (100% effort) is responsible for animal surgeries and drug delivery (by poloxamer on the round window niche) at KHRI, ABR measures and assessment as well as carrying out the Gap Detection an operant conditioning metrics to test for tinnitus.
Funding Support:	N/A

What other organizations were involved as partners?

Wayne State University, Detroit Michigan, is a Partnering Institution to this project. They will be sending in their collaborative Progress Report separately.

8. SPECIAL REPORTING REQUIREMENTS

Nothing to Report

9. APPENDICES:

Nothing to Report