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Growth of Auditory Reflexes with Stimulus Level

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GROWTH OF AUDITORY REFLEXES WITH STIMULUS LEVEL

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A thesis submitted in partial fulfillment of the requirements
for graduation with Honors in the Speech Pathology and Audiology

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Spring 2019

All requirements for graduation with Honors in the
Speech Pathology and Audiology have been completed.

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A thesis submitted in partial fulfillment of the requirements for graduation with Honors in the Department of Communication Sciences and Disorders

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Abstract:

In the human auditory system, the brainstem can modify how sound is processed in the inner ear (cochlea). The medial olivocochlear efferent reflex (MOCR) is one such inhibitory neural response originating in the brainstem. When activated, this reflex reduces amplification in the cochlea, which is believed to improve hearing in background noise. Previous research has shown that the reflex reduces amplification in the inner ear by different amounts for soft vs. loud acoustic stimuli. We hypothesized that these varying levels of reduction are equivalent to a constant reduction of stimulus input level. To measure these level changes, we used otoacoustic emissions, which are soft sounds emitted from the cochlea that can be measured with a small microphone placed in the ear canal. Otoacoustic emission amplitudes obtained with MOCR activated included a constant reduction of stimulus input; however, they also showed an additional shift. The findings suggested that previous research should be revisited using the new measurements.

Introduction:

The inner ear (cochlea) is the gateway between sound entering the outer ear and sound reaching the brain. A normally-functioning cochlea amplifies incoming sounds to improve detectability. The brainstem, however, can reduce the amplification in the cochlea via inhibitory efferent neural pathways (Guinan, 2006). One important inhibitory response is known as the medial olivocochlear reflex (MOCR). The MOCR may provide some protection from ongoing, intense acoustic stimuli. More recently, researchers have found some evidence that the MOCR system may facilitate detection of target stimuli in background noise (Kumar & Vanaja, 2004; Smith & Keil, 2015).

The basilar membrane (BM) is the structure in the cochlea that vibrates in response to sound. Hair cells on the BM amplify the vibrations, especially at low to mid stimulus levels. The BM vibrations can approach their maximum amplitude and become compressed and distorted in the presence of background noise. This makes it difficult to separate signals from a noisy background. The MOCR reduces cochlear amplification, restoring the ability to encode sounds accurately, as shown in Figure 1.

A. **B.**

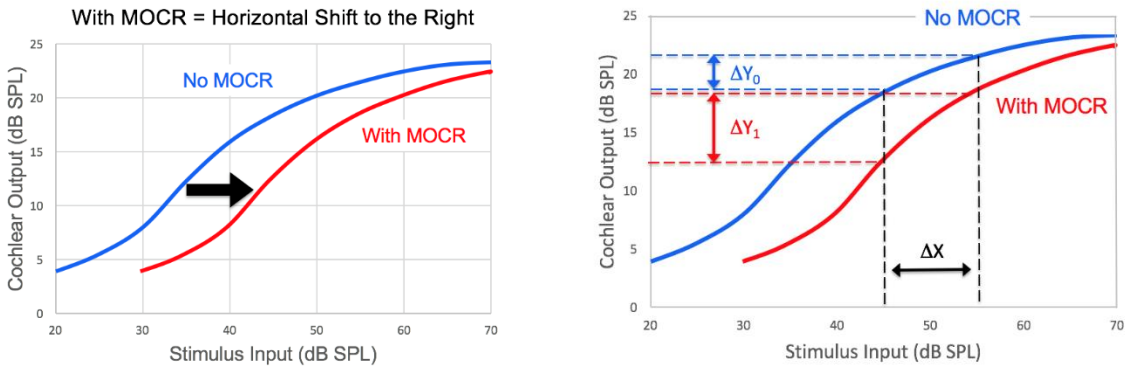

Figure 1: Changes in cochlear output (e.g. BM vibration) when MOCR is activated. A. The effective input sound level is reduced (seen as a horizontal shift to the right). B. This results in more linear, less compressed and distorted, output. For a given change in the input (Δ_X), the corresponding change in cochlear output will be greater when MOCR is activated ($\Delta Y_1 > \Delta Y_0$). Larger changes in cochlear output will be easier for the auditory system to encode and interpret.

The MOCR is typically measured by presenting soft clicks to one ear and broadband noise to the opposite ear. The clicks are used to elicit otoacoustic emissions (OAEs), which are soft sounds emitted by the inner ear in response to incoming sound (in this case, the click stimulus). OAEs are a byproduct of the cochlear amplification process. In order to quantify MOCR, OAEs are typically measured with and without noise present in the opposite ear. When the noise is present, the MOCR is activated, and the OAEs show reduced amplitudes. The amount of reduction in OAE amplitudes indicate the strength of the MOCR.

Evidence suggests that for a given noise level, MOCR strength may vary depending on the click stimulus level (Aguilar et al., 2015; Hood et al., 1996). This finding has implications for our understanding of cochlear mechanics and the perceptual consequences of the reflex. However, previous studies have important limitations. Chiefly, previous studies have presented click trains in which the clicks are closely spaced in time (Hood et al., 1996; Veuillet et al., 1991). The energy present in clicks spaced closely in time may be integrated by the auditory

system, causing unintentional activation of the MOCR by the probe itself. Ideally, the probe (the clicks) do not activate the MOCR at all, and only the noise causes the MOCR to activate. Additionally, previous studies have looked for reflex effects over a long time after the presentation of each click. A long-time window is likely to include energy obtained from places in the cochlea unrelated to active amplification, and therefore MOCR activation. In the present study, we used a restricted time window to more accurately isolate the MOCR. A table comparing previous studies to our current research paradigm can be seen in Appendix B.

The purpose of this study was to better understand the functioning of the olivocochlear reflex by characterizing how stimulus level influences the measured reflex strength. We improved on previous studies by spacing our clicks further apart in time (200 ms instead of 50 ms), preventing out probe clicks from inadvertently activating the MOCR. We also analyzed the OAEs using a short temporal window that included only the active amplification region.

Methods:

A. Subjects

Thirty-eight normal-hearing adults participated (24 females, 18-30 years; mean = 22.1 years, SD = 3.2 years). All subjects had normal otoscopic findings, normal middle ears via 226-Hz tympanograms, pure-tone air conduction thresholds ≤15 dB HL at octave frequencies from 0.25 to 8 kHz, bilaterally, and signal-to-noise ratios ≥ 8 dB on an OAE screening test. The inclusion criteria were set at 15 dB HL; however, subjects were first screened at 10 dB HL, and only 3% of tested frequencies required increasing the presentation level to 15 dB HL instead of 10 dB HL. No subjects reported trouble communicating in quiet or noisy environments, inner or middle ear surgeries (excluding ear tubes as a child), vertigo, tinnitus, regular exposure to loud noises without earplugs, or ototoxic medications. All subjects had corrected-to-normal vision. A full list of inclusion and exclusion criteria are included in Appendix A. The research protocol was approved by the University of Iowa Institutional Review Board and written informed consent was obtained from all subjects.

B. Screening

Subjects who passed the inclusion criteria underwent a standard, clinical hearing screening. First, subject's ears were visually examined with an otoscope to check for excessive earwax. For eligibility in the study, the subject's otoscopic examination had to be unremarkable with no sign of disorders in the ear or excessive wax. The subject's eardrum mobility was checked with tympanometry, in which a soft ear-tip was placed in the ear and pressure was introduced into the ear canal. To qualify for the study, the results had to show normal middle ear function according to standard clinical norms. Subjects sat quietly during these procedures. Next, pure-tone hearing thresholds were measured by presenting soft beeps through earphones while

the subject clicked a button if he/she heard the sound. This testing took place in a sound booth in the lab while the subject sat in a recliner. The above screening procedures took approximately 10 minutes.

If the subject also passed the hearing screening, they underwent otoacoustic emissions (OAEs) testing. Subjects sat quietly in a recliner in a sound booth during testing. A soft ear-tip was placed in their ears. The subject heard a series of clicks. The clicks were presented at safe, comfortable listening levels. In order to be eligible, the subject had to have OAEs present at criterion levels. This screening procedure took approximately 8 minutes.

C. Testing

For eligible subjects who wished to continue, the remainder of study procedures were conducted as follows: After completing the screening protocol, subjects proceeded to MOCR testing. The subject sat quietly in a recliner inside the sound-attenuating booth. A soft ear-tip was placed in both of the subject's ears. In one ear, the subject heard clicks at various levels spaced 200 ms apart. In both ears, subjects heard an intermittent white noise. All sounds were presented at safe, comfortable listening levels. During testing, subjects were instructed to remain as still as possible and refrain from making excessive noise (excessive coughing, swallowing, talking, chewing, head movements, etc.).

The click and white noise stimuli were presented in 36 approximately 1.5-minute segments, totaling approximately 54 minutes. After each segment, the subject was required to click a button on a computer screen in order to continue. This simple task was designed to ensure the subject remained awake and alert during testing. The subject was also instructed to swallow at each break between 1.5-minute segments to equalize middle ear pressure during testing. Total

study time for consent, screening procedures, and olivocochlear reflex testing was about 1.5-2 hours.

D. Analysis

Cochlear amplification is limited to a localized place for each frequency (Figure 2). Higher stimulus levels spread the vibration pattern more broadly towards the base (entrance) of the cochlea. Only OAEs generated from the localized amplification regions were analyzed. OAEs from these regions are reduced by MOCR activation. This analysis technique was used, as stated earlier, to reduce the time window as to better view the shift caused by MOCR activation.

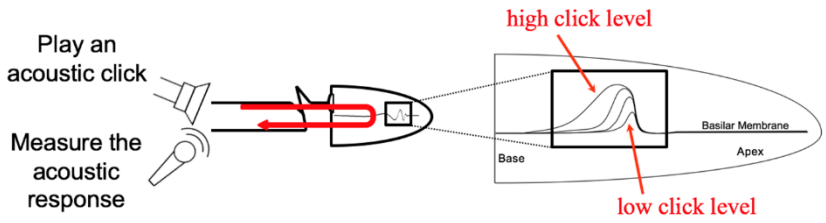

Figure 2. Measurement of OAEs. Left side schematic view of the OAE probe (loudspeaker and microphone), ear canal, and cochlea (unrolled). Right side expanded view of BM showing spread of excitation pattern as stimulus level increases.

Figure 3 shows the OAE data obtained from one individual subject. The top panels show the recorded acoustic time-waveforms for lowest and highest click levels (left and right, respectively). Note that the two waveforms are scaled differently on the y-axis, and therefore have different raw amplitudes. The bottom panels show the time-frequency spectra of the low- and high-level clicks, respectively. The time-frequency spectra were created by passing the waveforms through a series of bandpass gammatone filters. Warmer colors show larger OAE amplitudes. The area between the white lines shows the localized amplification regions. At each click level, the OAE energy within the localized region was integrated to give a measure of

overall OAE level, with and without MOCR activation. For the lowest click level, the largest OAE amplitudes (warmer colors) had a later cochlear delay, averaging between 10-15 ms. For the highest click levels, the highest OAE amplitudes were much earlier in time, averaging from 0-15 ms. The OAE amplitudes for the higher click levels not only occurred earlier in time, had a wider vibration pattern, and were associated with passive vibrations. The area between the white lines is the area where the cochlear amplification is most active, which is why it was used as the time window to be analyzed across all click levels.

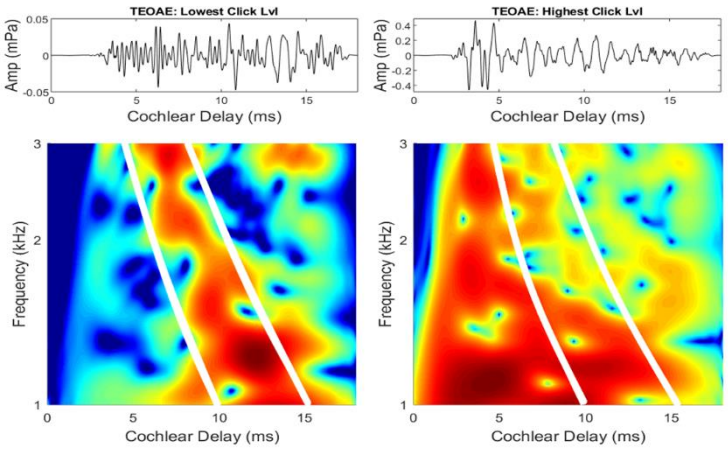

Figure 3. Time-waveforms (top row) and corresponding time-frequency spectra (bottom row) for lowest and highest click levels from one subject. Waveforms were decomposed using a gammatone filter bank. In the resulting time-frequency spectra, largest magnitudes are shown in warm colors. Low magnitudes are shown in cool colors. White, sloping lines indicate the area of active cochlear amplification. For each level, overall OAE energy was computed as the integration of energy within the white lines. Note the spread of excitation for the high level click (large amount of red can be seen to the left of the white lines). This was shown in cartoon format on the right side of Figure 2.

Results

A. Individual Results:

Of the 38 subjects, all showed a compressive growth functions with and without MOCR activation. When the MOCR was activated with noise, a shift resulted in the OAE input/output function. The OAE magnitudes obtained without MOCR were initially fit with a compressive mathematical function (a two-term power function) of the form ($y_1 = ax^b + c$). The resulting curves were then shifted in order to fit the OAE magnitudes obtained with MOCR. This was done using the equation $y_2 = a(x+k)^b + c$, with the terms *a*,*x*, and *b* fixed and the terms *k* and *c* varying. The two terms were allowed to vary, because initial efforts allowing only *k* to vary (matching our initial hypothesis of a simple x-axis shift) produced poor fits. Allowing the second term, *c*, to vary, resulted in very good fits. In this model, changes in the variable *k* represent changes along the x-axis, and changes in the variable *c* represent changes along the y-axis.

A fairly large variability was shown in the size of MOCR-induced shifts, of up to -7.25 dB in the x-axis and -3.7 dB in the y-axis. Figure 4 shows examples from 4 subjects, demonstrating this range of variability.

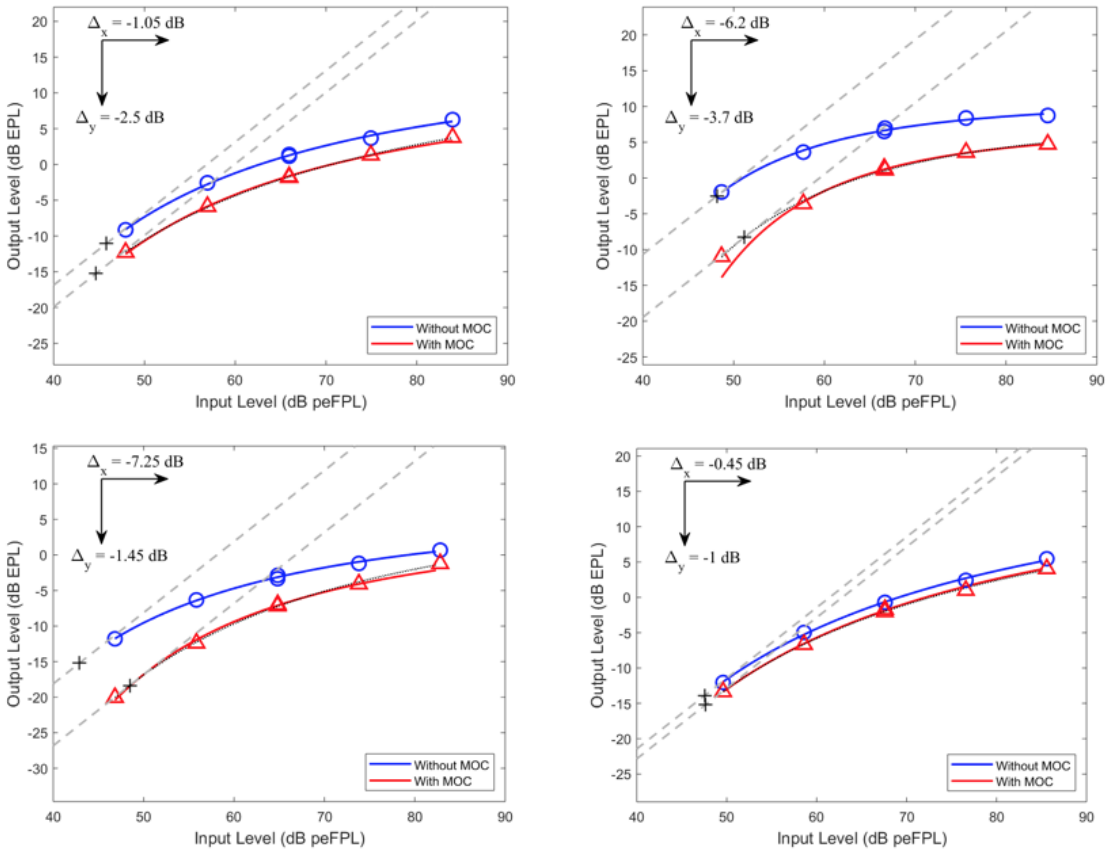

Figure 4. OAE level as a function of click level for 4 subjects. Red and blue colors show OAEs obtained with and without MOCR. Blue lines show fit of a power function to the data points (blue circles). Red lines result from shifting blue lines on the x- and y-axes by the amounts indicated in the upper left of each panel (Δ_X and Δ_Y, respectively). Dashed gray lines show linear growth. Black + symbols show the location where the slope of the fits was linear.

B. Group Results:

Group results were compiled to examine the variability amongst the subjects. Figure 5 explores several different relationships in an effort to understand the variability and y-axis shifts. OAE magnitude was not correlated with the x- axis shifts and only weakly correlated with the y-axis shifts. No correlation was found between x- and y-axis shifts (Figure 5D), and x-axis shifts were an average of 3 times larger than y-axis shifts with higher variability (Figure 5C). These relationships are explored further in the Discussion section.

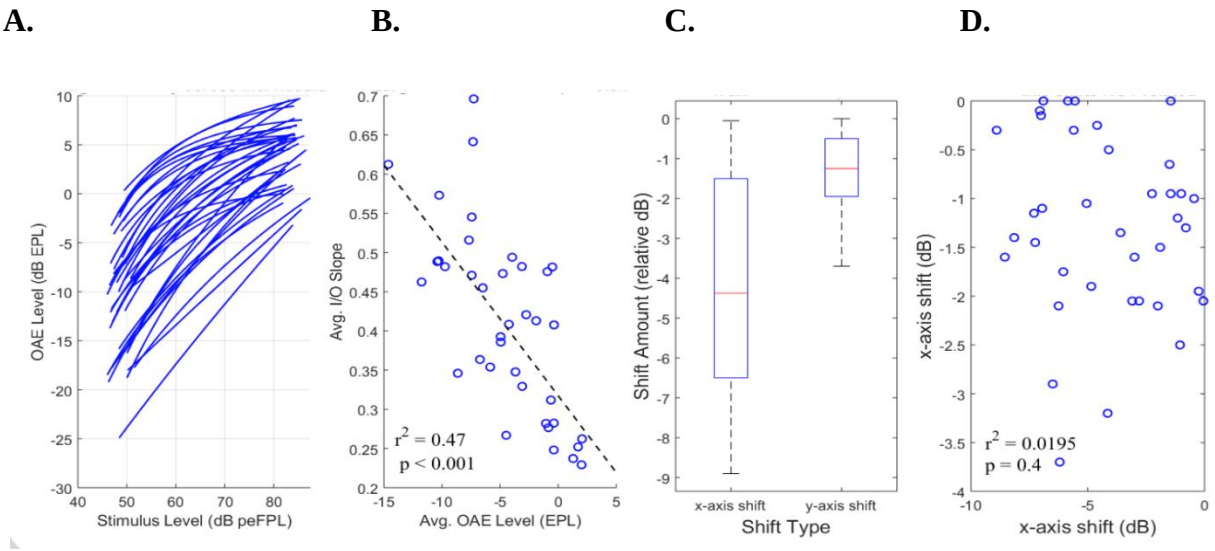

Figure 5: Group results. A. High variability in OAE input/output functions seen across 38 subjects, both in overall level and growth rate. B. Higher OAE levels tended to have more compressive growth. C. Shifts along the x-axis were larger and more variable than shifts along the y-axis. D. Shifts along the x- and y- axes were uncorrelated.

Discussion

Since all of the subjects had very good hearing, it is surprising that there was such a wide variability in MOCR strength. Furthermore, since OAE magnitude is thought to be related to the size of the cochlear amplifier and also of hearing sensitivity, it would appear that the strength of the MOCR shift was unrelated to the strength of the amplifier. However, because we used a hearing screening rather than determining actual thresholds, we were unable to see whether the size of the MOCR shift was related to actual hearing thresholds. Even though all of our subjects had hearing thresholds of 15 dB or better, some may have had thresholds as good as -10 dB HL. This large range was not accounted for in our study, and future studies should consider actual hearing thresholds for subjects to determine if a correlation could be made.

In a linear system, the equivalent x- and y-axis shifts are equal. However, the cochlea is a compressively nonlinear system rather than a linear system. Data showed that the x- and y- axis shifts were uncorrelated, so changes in one did not and could not predict changes in the other. Previous studies only focused on the y-axis shifts and reported shifts in the output level. This study showed that x-axis shifts were larger than and uncorrelated to y-axis shifts. The x-axis shift represents a piece of orthogonal information about the MOCR, and it might provide additional important information.

Based on physiological data, we expected to find that x-axis shifts fully accounted for MOCR input/output changes. However, we found that without including the y-axis shifts, the fits were poor in most cases. In most subjects, both an x- and y-axis shift were required in order to fit the observed MOCR shift.

The source of the x-axis shift is accounted for physiologically. Specifically, when MOCR is activated, acetylcholine causes ion channels to open at the base of cochlear outer hair cells

which effectively shunts the ion current, resulting in a smaller voltage across the wall of the hair cells. The cochlear amplifier sees the small voltage and produces less force. In effect, activation of MOCR is equivalent to reducing input level. A reduced input level would shift the input/output level on the x-axis.

The origin of the y-axis shifts should be explored further. A likely explanation is that the ions flowing into the outer hair cells have to pass first through a stereocilia compressive nonlinearity which subsequently drives the cochlear amplifier (which is nonlinear and compressive). The serial combination of two compressive, nonlinearities can cause both x- and y-axis shifts. Future studies should look at MOCR strength in background noise using both x- and y-axis shifts. Inclusion of x-axis shifts will add information that was not previously accounted for.

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References

Aguilar, E., Johannesen, P. T., & Lopez-Poveda, E. A. (2015). Contralateral efferent suppression of human hearing sensitivity. Frontiers in systems neuroscience, 8, 251.

Guinan JJ Jr. (2006) Olivocochlear efferents: anatomy, physiology, function and the measurements of efferent effects in humans. Ear Hear 27:589-607.

Guinan JJ Jr. (1996) The physiology of olivocochlear efferents. In: Dallos PJ, Popper AN, Fay RR (eds) The cochlea. Springer, New York, pp 435-502.

Hood, L. J., Berlin, C. I., Hurley, A., Cecola, R. P., & Bell, B. (1996). Contralateral suppression of transient-evoked otoacoustic emissions in humans: intensity effects. Hearing research, 101(1-2), 113-118.

Kumar UA, Vanaja CS (2004) Functioning of olivocochlear bundle and speech perception in noise. Ear Hear 25:142-146.

Mertes, I. (2014). *PhD Thesis*, 1-51.

Smith, D. W., & Keil, A. (2015). The biological role of the medial olivocochlear efferents in hearing: separating evolved function from exaptation. Frontiers in systems neuroscience, 9, 12.

Veuillet, E., Collet, L., & Duclaux, R. (1991). Effect of contralateral acoustic stimulation on active cochlear micromechanical properties in human subjects: dependence on stimulus variables. Journal of neurophysiology, 65(3), 724-735.

Appendix

A. Inclusion and exclusion criteria

Inclusion Criteria

- Age 18-30
- No known or suspected hearing loss
- Normal hearing at all audiometric test frequencies (i.e. hearing thresholds 15 dB HL or better at all audiometric test frequencies 250 Hz-8 kHz, measured using standard clinical audiology practice)
- Presence of otoacoustic emissions at criterion levels using a screening protocol
- No history of ear surgery (not counting ear tubes as a child)
- No participant-reported history of otologic disease/disorder
- No tinnitus (ringing, buzzing, hissing noises in the ear) that is constant and/or disruptive to daily life
- No acute or chronic dizziness
- No medications that may affect hearing (e.g., chemotherapy agents, loop diuretics, Quinine-related drugs, aminoglycosides, salicylates)
- Normal or corrected vision
- Normal outer and middle ear exam
- Must be able to sit quietly for 70 minutes at a time
- Must be willing to remove any earrings for duration of test session

Exclusion Criteria

- Younger than 18 or older than 30
- Known or suspected hearing loss

- Failure of administered hearing screening (i.e. hearing threshold greater than 15 dB HL at any audiometric test frequency 250 Hz- 8 kHz)
- Otoacoustic emissions absent at criterion levels, assessed using screening protocol
- History of ear surgery (not counting ear tubes as a child)
- Participant-reported history of otologic disease/disorder
- Tinnitus (ringing, buzzing, hissing noises in the ear) that is constant and/or disruptive to daily life
- Regular exposure to loud sounds without the use of earplugs or muffs
- Acute or chronic dizziness
- Medications that may affect hearing (e.g., chemotherapy agents, loop diuretics, Quinine-related drugs, aminoglycosides, salicylates)
- Vision impairment not corrected with glasses or contacts
- Abnormal outer and/or middle ear exam
- Cannot sit quietly for 70 minutes at a time
- Unwilling to remove earrings for the duration of the test session

B. Comparison of previous studies to current study

Previous Studies	**Current Study**
Shorter click levels 50ms: Can get partial activation if you give clicks every 50ms and reduces the amount of change you see	Longer level clicks-200ms: We were able to get high clicks with the series, but we had to space them far apart to not activate Middle Ear Reflex partially
Calibration done in SPL	Calibration in FPL (forward pressure level) Our study accounted for differences in ear canal size and middle ear reflectance
Analysis across full time shows smaller MOCR shift because the amplifier isn't there	Analysis focuses on amplifier reduction
Single stimulus level and looked at y-axis shift	Used series input/output and look at multiple levels of x-axis shift