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I, Lamiaa Abdelrehim, hereby submit this original work as part of the requirements for the degree of Doctor of Philosophy in Communication Sciences and Disorders.

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Expanding Audiologic Evaluations with Narrowband Noise Acoustic Reflex Growth Functions

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Expanding Audiologic Evaluations with Narrowband Noise Acoustic Reflex Growth Functions

A dissertation submitted to the

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Abstract

The acoustic reflex (AR), characterized by an involuntary contraction of the middle ear muscles in response to auditory stimuli, has been a component in routine audiological evaluations for several decades. This reflex is a complex interaction of ear mechanics and the underlying neural and physiological processes (Jerger et al., 1974). The acoustic reflex growth function (ARGF) delineates the relationship between the AR response's amplitude and the intensity level of the eliciting acoustic stimulus (Dallas, 1964). Such measurements gain particular significance in pathologies affecting the auditory nerve pathway. Valero et al. (2016) suggested that the ARGF may provide a valuable approach for objectively assessing peripheral auditory nerve fibers and the auditory brainstem.

This study's foremost objective is to characterize ARGFs for narrowband noise stimuli which may have utility in assessing the peripheral auditory nerve and the associated centers of the auditory brainstem in humans. Furthermore, the investigation aims to elucidate the relationship between ARGF patterns and speech-in-noise test outcomes among individuals with normal hearing. The study compared ARGFs and acoustic reflex thresholds (ARTs) for narrowband noise stimuli to tonal stimuli in 34 adult participants with normal pure-tone hearing thresholds and normal speech-in-noise performance. As such, this research provides data describing a normative range for ARGFs using novel stimuli which may be helpful in the identification of peripheral auditory nerve degeneration, which is refractory to detection through conventional audiograms and some electrophysiological tests.

The results indicated that participants were at minimal history of noise exposure oise-induced hearing loss and displayed normal hearing thresholds across audiometric frequencies

ranging from 250 to 8000 Hz. All participants also exhibited detectable distortion product otoacoustic emission (DPOAE) responses, confirming normal cochlear outer hair cell function.

The study found that acoustic reflex thresholds (ARTs) for narrowband noise (NBN) activators were significantly lower than those for tonal activators, particularly at 1, 2, 3, and 4 kHz frequencies. Notably, the ARGF metrics, specifically the admittance change, were higher for NBN stimuli than tonal stimuli, especially at 1, 2, and 4 kHz frequencies. This suggests a broader dynamic range for NBN ARGFs than for tonal ARGFs. The ARGF slope measurements indicated that the highest ARGF was for 2 kHz NBN activators. This result was consistent across two commonly used clinical immittance measurement devices.

The study also explored intersubject variability in the ARGF slope, employing the coefficient of variation (CV) as a metric. High frequencies, specifically the 2- and 3-kHz NBN activators, demonstrated more consistent responses among subjects, indicated by lower CV values. This finding highlights the potential of these frequencies in yielding more reliable ARGF measurements. The study did not find significant correlations between ARGFs and speech-in-noise test scores. This lack of correlation was expected, however, given that all participants had speech-in-noise test scores clustered tightly around the normal range.

This study suggests that NBN activators may be more effective for assessing the ARGF, particularly at mid-to-high frequencies. The response to NBN activators may have more clinical potential than tonal ARGF assessments given the reduced variability and greater dynamic range. NBN ARGFs may specifically be added to the clinical tools for diagnosis of auditory neuropathology.

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Finally, my heartfelt thanks to my mother, to whom I owe everything I have achieved. Her endless support, help, and love have been my constant source of strength and inspiration throughout my life.

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List of Abbreviation

1. AR - Acoustic Reflex
2. ARGF - Acoustic Reflex Growth Function
3. ART - Acoustic Reflex Threshold
4. MEMR - Middle Ear Muscle Reflex
5. AN - Auditory Nerve
6. SNR - Signal-to-Noise Ratio
7. NIHL - Noise-Induced Hearing Loss
8. DIIP - Desensitization, Interference Reduction, and Injury Protection
9. HTL - Hearing Threshold Level
10. dB HL - Decibels Hearing Level
11. dB SL - Decibels Sensation Level
12. SRT - Speech Reception Threshold
13. WRS - Word Recognition Scores
14. DPOAE - Distortion Product Otoacoustic Emissions
15. dB SPL - Decibels Sound Pressure Level
16. TPP - Tympanogram Peak Pressure
17. LBN - Low-Band Noise
18. HBN - High-Band Noise
19. BBN - Broadband Noise
20. dB - Decibels
21. ANFs - Auditory Nerve Fibers
22. SR - Spontaneous Rate
23. OHCs - Outer Hair Cells
24. CS - Cochlear Synaptopathy
25. HHL - Hidden Hearing Loss
26. ABR - Auditory Brainstem Response
27. EFR - Electrically Evoked Response
28. IV-AGs - Intravenous Aminoglycosides
29. GSI - Grason-Stadler Incorporated
30. dB HL - Decibels Hearing Level
31. mmho - Millimhos
32. CV - Coefficient of Variance
33. SD - Standard Deviation
34. SE - Standard Error
35. SL - Sensation Level
36. NBN - Narrowband Noise
37. ΔY - Change in Admittance

Chapter 1

Introduction

The acoustic reflex (AR), also known as the middle ear muscle reflex (MEMR), is characterized as an involuntary bilateral contraction of the stapedial muscle in the middle ear triggered by sound stimuli of moderate to high intensity (Borg, 1973; Mangham et al., 1980). The recording of the acoustic reflex threshold (ART), defined as the lowest intensity level at which the reflex is detected, has been a longstanding component of comprehensive audiological evaluations (Hung & Dallos, 1972; Silman & Gelfand, 1981a; Silman et al., 1978; Wilson, 1981). In combination with tympanometry assessment of the mechanical function of the middle ear, the AR procedure provides diagnostic insights into the integrity of the auditory nerve and lower brainstem structures (Hung & Dallas, 1972; Silman & Gelfand, 1981a; Silman et al., 1978; Wilson, 1981). When sound enters the ear canal, the tympanic membrane converts it into mechanical energy, which is then delivered to the inner ear through the ossicular chain. With high-intensity sound, the middle ear muscles contract and stiffen the ossicular chain. This reflexive contraction is mediated via a neural pathway that includes the auditory nerve, lower brainstem centers, and the facial nerve. The contraction reduces the transmission of sound energy, potentially protecting the inner ear from intense sounds (Liden et al., 1964). Originally introduced for middle ear lesion diagnosis, the AR is most useful for differential diagnosis of inner ear lesions and retro-cochlear pathologies like auditory neuropathy and acoustic neuroma (Moller, 1988).

The AR's efficacy in protecting against intense sounds has been debated, given the rarity of such intense impulse sounds in nature (Katz et al., 2002). Borg (1984) suggested that the AR's role is multifaceted and includes desensitization, interference reduction, and injury protection. The desensitization aspect of AR, evidenced in studies involving bats (Henson, 1965) and humans (Salomon & Starr, 1963; Borg & Zakrisson, 1975), might facilitate environmental awareness during self-generated noises like chewing or speaking. The AR acts as a high-pass filter, improving hearing and signal-to-noise ratio (SNR) by dampening low-frequency sounds below 1 kHz (Simmons, 1964). The low-frequency sound attenuation supports the idea that AR helps reduce interference from one's vocalizations, thereby enhancing the clarity of external sounds (Borg, 1984). Moreover, the reflex's potential in preventing noise-induced hearing damage is indicated by studies where animals with disabled stapedial muscles exhibited greater noise-induced hearing loss (NIHL) than those with intact stapedial muscles (Lawrence, 1960; Sokolovski, 1973; Borg, 1977, 1982).

In addition to measuring the absolute threshold of the AR, the change in AR magnitude can also be tracked as a function intensity of the reflex-activating stimulus. As described in this study, the acoustic reflex growth function (ARGF) describes the variation in AR magnitude (i.e., change in admittance measured at the plane of the tympanic membrane) across the range from the ART to nearly the maximum stimulation intensity of the AR-activating stimulus (e.g., 100 dB HL). In this way, ARGFs offer an assessment of a portion of the dynamic range of the auditory neurons that respond to moderate to intense stimuli (Dallos, 1964; Beedie & Harford, 1973; Silman et al., 1978; Block & Wiley, 1979; Thompson et al., 1980; Peterson & Liden, 1972; Hall, 1982; Silman & Gelfand, 1981; Wilson, 1981).

Recent studies highlight the ART and ARGF's potential in detecting auditory neuron pathologies, especially among the high-threshold, low-spontaneous rate auditory nerve fibers, including cochlear synaptopathy related to aging and noise exposure (Furman et al., 2013; Sergeyenko et al., 2013; Kujawa & Liberman, 2015; Valero et al., 2016; 2018; Shaheen et al., 2015; Flamme et al., 2017; McGregor et al., 2018; Wojtczak et al., 2017). The ARGF procedure is time-efficient and could serve as a screening tool to detect possible hidden hearing loss and cochlear synaptopathy for which additional diagnostics (e.g., (e.g., speech-in-noise measures and auditory evoked potentials, respectively) would be required to specify the extent and severity.

Commented [BE1]: Not all of these studies assessed the ART/ARGF, correct?

Recent research, notably by Trevino et al. (2023), has highlighted that the intensity and frequency spectrum of the activator stimulus plays a significant role in influencing Acoustic Reflex Growth Functions (ARGFs). Different studies have explored the impact of various factors on Acoustic Reflex Growth Functions (ARGFs), notably including sensorineural hearing loss (Silman & Gelfand, 1981; Sprague et al., 1981), the effect of advanced age (Silman & Gelfand, 1981; Thompson et al., 1980), and the static acoustic immittance at the tympanic membrane in the absence of the acoustic reflex (Wilson, 1979, 1981; Silman et al., 1978). These factors contribute to the variability observed in ARGF measurements. Additionally, variability in testing parameters across studies have been noted, particularly concerning stimulus type, frequency, intensity, temporal aspects of the stimulus, probe tone type, and step size used in measuring acoustic reflexes. This variability in methodology leads to differing results even for similar degrees and types of auditory disorders (Tripathy et al., 2018). Such procedural discrepancies highlight the need for a more standardized approach in clinical settings to reduce the test-related variability of ARGFs.

This study aims to compare and contrast Acoustic Reflex Growth Functions (ARGFs) for traditional tonal and broadband noise stimuli with those for less commonly used narrowband noise (NBN) stimuli. The incorporation of NBN stimuli into the acoustic reflex test battery is hypothesized to be useful as a measure of peripheral auditory nerve pathology.

Establishing a normative range for NBN ARGFs in individuals with normal hearing and normal speech-in-noise abilities could lay the groundwork for their potential use in the early detection of changes in the auditory nervous system, as suggested by Saxena et al. (2015), Sprague et al. (1981), and Lutolf et al. (2003) who studied tone-evoked ARGFs. The NBN-evoked ARGF approach described in this study is hypothesized to be sensitive to dysfunction/abnormalities within the auditory nervous system.

Significance

While the traditional ART has been extensively studied, recent attention has shifted towards the ARGF, which provides an extended assessment of auditory nerve function by measuring changes in acoustic reflex magnitude as a function of increasing stimulus intensity (Dallos, 1964; Beedie & Harford, 1973; Silman et al., 1978; Block & Wiley, 1979; Thompson et al., 1980; Peterson & Liden, 1972; Hall, 1982; Silman & Gelfand, 1981; Wilson, 1981). The ARGF's diagnostic value is thought to lie in its ability to identify pathologies across specific auditory neuron types and lower brainstem centers (Sexena et al.,2015; Valero et al.,2018). Recent animal studies emphasize its role in detecting subtle changes in auditory nerve fibers, particularly high-threshold, low-spontaneous rate fibers, providing potential detection of cochlear synaptopathy (Valero et al., 2016; 2018; Wojtczak et al., 2017).

The significance of this study is focused on exploring the utility of narrow-band noise (NBN) in measuring acoustic reflex growth functions (ARGFs), comparing them with those measured using traditional pure tone and broadband noise stimuli. Previous studies (Jerger et al., 1986; Silman, 1979; Wilson & McBride, 1978; Korabic & Cudahy, 1984; Sprague et al., 1985; Bharadwaj et al., 2019; Feeney & Keefe, 2001; Feeney et al., 2017; Schairer et al., 2007) predominantly focused on broadband noise (BBN) and pure tones in measuring the acoustic reflex (AR), suggesting a lower threshold for BBN-evoked ARs. These findings suggest that NBN-evoked ARs may also have a lower threshold than tonal stimuli and thus provide a broader range of intensities across which to measure ARGFs.

By focusing on NBN ARGFs, this study aims to fill a gap in research, offering a new perspective on the understanding and application of AR measurements. The potential implications of using NBN stimuli for ARGF measurement are manifold. NBN, with its more focused frequency range compared to broadband noise, might provide more frequency-specific insights into the AR mechanism, refining the diagnostic information provided by ARGF measurements.

This research holds substantial potential to impact clinical audiology practice. If NBN proves effective in eliciting an AR at lower thresholds and ARGFs with broader intensity ranges, it could expand current diagnostic approaches, especially in identifying and assessing auditory nervous system disorders.

Specific Aims & Hypotheses

Specific Aim 1: Establish normative ranges for acoustic reflex growth functions (ARGFs) using narrowband noise stimuli in adult listeners with normal audiograms with minimal history of noise exposure**.** The normative range for ARGF will be characterized by the following metrics: admittance change and ARGF slope.

Specific Aim 2: Examine the relationship between ARGFs and speech-in-noise intelligibility in adult listeners with normal audiograms.

Specific aim 3: Investigate the reliability of ARGFs across different equipment.

Chapter 2

Background and Literature Review

Acoustic immittance measurements

Acoustic immittance measurements, comprising tympanometry and acoustic reflex (AR) testing, play an essential role in diagnostic audiology. These measurements offer information for diagnosing various ear conditions.

Tympanometry: Procedure and Significance

Both tympanometry and AR testing involve the use of a specialized probe inserted into the ear canal. This probe, fitted with a rubber tip to ensure an airtight seal, connects to several key components, including a loudspeaker for probe tone generation, an ipsilateral pressure pump, a manometer for measuring ear canal pressure, and a monitor microphone. Common probe tones used in these tests include frequencies of 226, 678, and 1000 Hz. The loudspeaker emits the probe tone into the ear canal, while the monitor microphone detects changes in sound pressure level, allowing for the inference of acoustic admittance/compliance. Tympanometry involves varying air pressure in the ear canal from positive to negative relative to atmospheric pressure, with compliance inferred by the probe microphone measurements. The resulting tympanogram graphically represents the middle ear's compliance, ear canal volume, and middle ear pressure. Tympanograms are categorized into three types: Type A (normal middle ear function), Type B (flat line indicating potential middle ear pathology), and Type C (negative middle ear pressure).

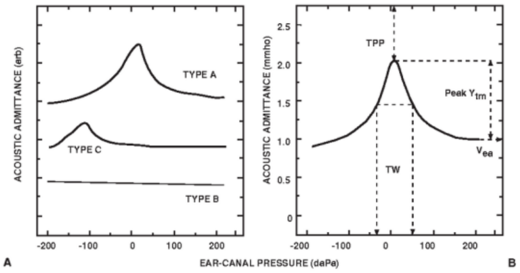


Figure 1. The diagram presents two approaches for characterizing 226 Hz tympanograms: a qualitative method (A) categorizes the shape of the tympanogram into Type A, B, or C, following Jerger's classification from 1970, and a quantitative method (B) evaluates the tympanogram based on several metrics, including the equivalent volume of the ear canal (Vea in cm^3), the peak static acoustic admittance (peak Ytm in mmho/ml), the tympanogram peak pressure (TPP in daPa), and the width of the tympanogram (TW in daPa), as outlined by Shanks & Shohet in 2008.) (Shanks & Shohet, 2008).

Acoustic Impedance and Admittance: Fundamental Concepts

Acoustic immittance encompasses acoustic admittance, impedance, and their related components, from which sound energy transmission through the middle ear can be inferred. Acoustic impedance (Z) represents the resistance to acoustic energy flow and is determined by the highest achievable sound pressure (P) for a given volume velocity (U). High impedance signifies greater resistance and impedance of sound transmission through the middle ear. This impedance is evaluated by examining the phase angle, including the algebraic phase and the P-U difference. Conversely, acoustic admittance (Y) assesses the passage of acoustic energy through the middle ear structures. Admittance, particularly relevant in multi-frequency and 226-Hz tympanometry, quantifies the volume velocity associated with a given unit of sound pressure. Admittance and impedance are mathematically related, where Z = 1/Y. Thus, a middle ear with low impedance exhibits high admittance and vice versa.

Complex Admittance: Magnitude, Phase Angle, and Components

Complex admittance includes both real and imaginary components, represented by conductance (G) for the imaginary part and susceptance (B) for the real part. The equation Y = G + B illustrates this relationship. Conductance relates to the absorption of sound waves, while susceptance can be split into compliance susceptance, associated with the stiffness of the middle ear, and mass susceptance associated with the mass of the middle ear. Compliance susceptance, inversely related to stiffness, is out of phase with mass susceptance at specific frequencies. The relationship between frequency and compliance susceptance is inverse. Research by Wiley et al. (1998) indicates that acoustic susceptance directly correlates with frequency in the middle ear. When mass susceptance and compliance susceptance are balanced, the system reaches its point of resonance.

Acoustic Reflex (AR)

Overview of the Acoustic Reflex (AR)

The AR is a feedback mechanism involving the middle ear, neural, and brainstem structures. The understanding of the AR neural pathway has been significantly advanced through animal research involving various species, including rabbits (Borg, 1973, 1977), rats (Rouiller, 1989), and cats (Lyon, 1978; Lyon & Malmgren, 1982). Initial studies, particularly those in rabbits, primarily focused on evaluating the reliability of the AR and its response to lesions in the auditory pathway. These investigations have demonstrated that the neuronal architecture of the reflex pathway is similar across different species, greatly enhancing our understanding of the AR pathway (Mukerji, 2010).

Neural Pathway of the Acoustic Reflex

The neural pathway of the AR is a complex path that begins with the presentation of sound to the ear. The sound is transduced by the mechanical movement of the middle ear ossicles that articulate with the cochlea's oval window. These ossicles function to transmit vibrational energy into the fluid-filled cochlea, leading to the displacement of sensory cells, known as hair cells (Mukerji, 2010). (Mukerji, 2010). The displacement of the basilar membrane within the cochlea and the associated hair cell stimulation results in the propagation of action potentials via the auditory nerve. The excitation of afferent auditory neurons leads to stimulation of the cochlear nucleus in the brainstem, which is considered part of the central auditory pathway (Trevino et al.,2023). The neural signal ascends to the ventral cochlear nucleus and then travels through the brainstem. The efferent auditory pathway is a descending neural tract that begins near the superior olivary complex (SOC) (White & Warr, 1983; Wilson & McBride,1978). This system encompasses the medial and lateral olivocochlear pathways, consisting of both crossed and uncrossed neurons that project to the organ of Corti. These neurons predominantly make synaptic connections with the outer hair cells (OHCs) or with the ganglion cells of the spiral neuron located beneath the inner ear cells. Although some neurons positioned outside the SOC contribute to the acoustic reflex arc, influencing the muscles of the middle ear, the majority of motoneurons that regulate the contraction of the stapedius and tensor tympani muscles are situated close to the nuclei of the facial or trigeminal nerves (Lee et al.,2006). Consequently, a facial nerve branch activates the stapedius muscle, leading to its bilateral contraction. This action hardens the ossicular chain in the middle ear, reducing sound transmission.

In summary, the acoustic reflex is mediated by a complex neural pathway involving the cochlea, the auditory periphery, the central auditory nervous system, and the middle ear muscles. It plays a crucial role in attenuating intense sound energy and protecting the inner ear (Venet et al.,2011). This activation of both ipsilateral and contralateral pathways leads to the bilateral contraction of the stapedius muscle, resulting in a 'stiffening' of the tympanic membrane, which predominantly reduces low-frequency sounds (Borg & Zakrisson, 1974; Moller, 1974a; Mukerji, 2010). Disruptions along this pathway can alter or eliminate the reflex response. The AR threshold and AR magnitude depend on the intensity, frequency, and spectral bandwidth of the AR activator stimuli (Olsen, 1975; Stach, 1987; Margolis, 1993).

Diagnostic Value of Acoustic Reflexes in Auditory Assessments

The AR represents an objective tool in the diagnosis of hearing loss and other auditory pathology. The reduction or absence of the acoustic reflex is a key indicator of conditions such as retrocochlear pathology, where lesions in the brainstem may impede reflex transmission (Olsen et al., 1975; Rouiller et al., 1989). The reflex's bilateral nature means that brainstem pathologies can disrupt the contralateral activation of the reflex by interfering with the neural transmission in the reflex arc's descending pathways (Rouiller et al., 1989).

The AR has been effectively utilized in evaluating cochlear hearing loss. The degree and particular configuration of hearing loss have a significant impact on the AR response (Jerger et al., 1972). In cases of mild sensorineural hearing loss (SNHL), where hearing threshold levels (HTL) are 25–40 dB HL, the ART is typically detected at stimulus levels ranging from 70- 90 dB HL. However, when HTL exceeds 40 dB HL, there is a corresponding increase in ART (Margolis, 1993). People with moderate hearing loss (HTL 40–55 dB HL), for example, often have ARTs in the 95 dB HL range (Katz et al., 2002). In severe to profound sensorineural hearing loss (HTL > 70 dBHL), the ART response may either be absent or only present at the highest stimulus levels (e.g., 105-110 dB HL).

Additionally, age-related changes in the AR response have been observed. Studies have shown that across the course of a person's lifetime, the AR response tends to have lower ART as one approaches adulthood suggesting neural maturation. With increasing age, Katz et al. (2002) describe increases in ART and a decrease in AR magnitude that may be used as markers of cochlear aging.

The Impact of Stimulus Characteristics and Probe Parameters on AR Responses

AR testing starts by inserting a specialized probe that seals within the ear canal and measures changes in eardrum compliance in response to auditory stimuli. The ARGF is typically measured using a probe tone and an elicitor tone. The probe tone is a constant low-level tone that is used to monitor the acoustic impedance of the ear, while the elicitor tone is a louder tone that triggers the acoustic reflex.

In clinical practice, the use of single-frequency pure-tone stimuli at 500, 1000, 2000, and 4000 Hz for AR recordings is the standard protocol. However, some individuals with normal hearing may display either elevated or absent AR reactions to 4000 kHz tones. Jerger et al.'s 1986 study attributed this distinct response at 4000 Hz to quicker onset times and faster adaptation rates for higher-frequency stimuli, supporting Wilson and colleagues' earlier findings from 1978. The characteristics and frequency spectrum of AR-eliciting stimuli significantly influence the resultant response. Research indicates that the duration of these stimuli notably impacts the AR response, in line with temporal integration effects identified in psychoacoustic studies. For example, a decrease in the duration of the elicitor corresponds with an increase in the ART. This phenomenon is more pronounced in adults with sensorineural hearing loss, suggesting the potential diagnostic value of elicitor duration in discerning auditory differences among individuals. A 2019 study by Deiters and colleagues explored the influence of varying auditory stimulus durations on AR in people with normal hearing. This study revealed that brief 100 ms tones at 4 kHz generated the lowest ART, in contrast to same-length tones at 1 kHz, which elicited the highest ART.

Besides pure tones, both broadband noise (BBN) and narrowband filtered noise (NBN) have been tested as stimuli. Noise stimuli, such as BBN, generally result in lower ART thresholds than pure tones in adults, as noise activates a broader range of cochlear frequencies. This conclusion is supported by Silman's 1979 research and subsequent studies through the 1980s and 1990s. Wilson and McBirde’s 1976 research noted that the ART for BBN is over 20 dB lower than for pure tones, indicating a more expansive dynamic range (DR) for AR assessment. The dynamic range of the acoustic reflex, reflecting the intensity span over which the compliance increases from ART level to saturation, varies depending on the stimulus. For pure tones, this range spans approximately 15-20 dB, as documented in research (Jerger et al., 1972; Beedie & Harford, 1973; Margolis & Popelka, 1975; Kaplan et al., 1977). For broadband noise, a wider 20-30 dB range has been observed, aligning with an average acoustic reflex threshold of 79.5 dBHL.

Although little research has been done on narrowband noise (NBN) stimuli, Peterson and Linden's study from 1972 is notable because it used narrowband noise (NBN) stimuli centered around 1, 2, and 4 kHz to look into ARTs for non-tonal stimuli. This study showed that responses to NBN and white noise stimuli were approximately 15 dB lower than to single-frequency pure tones. This finding indicates that the acoustic reflex triggered by NBN possesses a broader dynamic range than that elicited by single-frequency pure tones. This suggests that NBN stimuli may be more effective in activating the acoustic reflex and capturing a wider range of auditory responses. Further research is needed to explore NBN stimuli's potential benefits and applications in various clinical settings. This could lead to improved diagnosis and treatment of hearing disorders.

Key Measurable Characteristics of Acoustic Reflex

The acoustic reflex (AR) possesses various measurable characteristics, including the acoustic reflex threshold (ART), acoustic reflex magnitude, reflex decay, and reflex latencies. These characteristics are utilized in assessing neural integrity (Anderson et al., 1970; Mangham et al., 1980; Wilson & Margolis, 1999). The ARGF, which describes the relationship between AR magnitude and activator level above the AR threshold, may be particularly useful for diagnosis of pathology across different types of auditory neurons (e.g., moderate-threshold fibers versus high-threshold fibers).

Acoustic Reflex Threshold

The acoustic reflex threshold (ART) denotes the minimum level of acoustic stimulation required for detectable stapedius muscle contraction. It is not possible to directly record the change in admittance caused by this contraction. Instead, tympanometers measure changes in sound pressure level within the ear canal during tympanometry and acoustic reflex procedures from which acoustic admittance can be inferred. In adults with normal hearing, the ART is reported at 70–100 dB HL using single-frequency pure tone activators (Wilson & McBride, 1978; Silman & Gelfand, 1981b). Activator stimulus type and frequency spectrum affect the ART values (French-Saint-George & Stephens, 1977; Wilson, 1979). Broadband noise activators demonstrate 12–20 dB lower ART compared to pure tone activators. The lower ART is thought to be related to the critical bandwidth of the activator. Flottorp et al. (1971) and Djupesland & Zwislocki (1973) studies suggested that increasing the stimulus bandwidth does not change the ART until it goes over the critical bandwidth, which lowers the acoustic reflex threshold. Consequently, the critical band for the acoustic reflex operates similarly to those in behavioural evaluations of loudness, albeit with a wider span (Djupesland & Zwislocki, 1973; Flottorp et al., 1971).

The Acoustic Reflex Growth Function (ARGF)

Overview

The acoustic reflex growth function illustrates the relationship between stimulus intensity and the alteration in tympanic membrane admittance (Y) during contraction of the stapedius muscle (Silman et al., 1978). The growth function investigates how the magnitude of the inducing sound causes this reflexive response to increase or grow. This growth function generally depicts a positive relationship between stimulus level and admittance change magnitude. For pure tones with a single frequency, the growth function is linear. This is very different from the curvilinear pattern seen for broadband noise at lower levels of intensity, which is then followed by a mostly linear function (Silman et al., 1978). Recent advancements in measuring the ARGF have enabled more sensitive detection of auditory nerve fiber (ANF) damage. Studies in both animals and humans have demonstrated the potential of ARGF to detect early cochlear damage more sensitively than routine ART measurements (Valero et al., 2016, 2018; Wojtczak et al., 2017; Guest et al., 2019a; Bharadwaj et al., 2019; Bramhall et al., 2022).

ARGF metrics

Recent investigations have shed light on various aspects of the ARGF, with a particular focus on dynamic range, compliance/admittance change, and slope. The dynamic range of ARGF is defined as the range of activator levels required to elicit a notable change in acoustic reflex (AR) admittance. Studies by Dallos (1964), Djupesland et al. (1967), Hunter et al. (1999), Levine et al. (1993), and Peterson & Liden (1972) consistently report this range falling between 15 to 28 dB above the acoustic reflex threshold (ART). This range signifies the span of sound levels capable of triggering a reflex growth in response to an activator, such as a tone or noise. The ARGF dynamic range is quantified as the dB difference between the lowest intensity sound inducing a reflex (ART) to the upper intensity level chosen for the measurement (e.g., 95-100 dB HL). Notably, Sprague et al. (1981) observed an increase in the dynamic range with the expansion of activator bandwidth beyond one octave.

Change in admittance: In the context of measuring the ARGF, admittance change is assessed by subtracting the acoustic reflex magnitude at the acoustic reflex threshold from the magnitude at each activator level. Acoustic compliance change and admittance change (ΔY) are distinct yet related concepts in auditory measurements. Acoustic compliance change specifically quantifies alterations in the ease with which the middle ear structures can deform or move in response to changes in air pressure, focusing on the compliance component of admittance (Danaher & Pickett, 1974; Green & Margolis, 1984; Hall, 1982; Kunov, 1977; Newall et al., 1978; Niswander & Ruth, 1976). It measures the difference in compliance between the static state (measured without the reflex) and the dynamic state (measured during reflex activation), often expressed in millilitres per decibel (ml/dB). On the other hand, admittance change is a broader term encompassing the overall responsiveness of the middle ear to sound, considering not only compliance but also mass and resistance (Silman et al., 1978; Wilson, 1981). Admittance is typically measured in millimhos (mmho), and its change reflects modifications in the combined effects of compliance, mass, and resistance during reflex activation. In summary, while acoustic compliance change corresponds to a specific aspect of admittance related to compliance, admittance change provides a more comprehensive view of the middle ear's responsiveness by considering multiple factors.

ARGF slope: The slope of the ARGF is graphically represented by plotting the difference in sound stimulus intensity in decibels (dB) against change in the acoustic reflex response magnitude in milliliters (ml), often measured as compliance change. This slope delineates the rate at which the reflex response changes in magnitude with increasing sound intensity (Wilson and McBride (1978). Typically sigmoidal, the ARGF slope begins with a gradual increase (low slope) at the reflex threshold, steepens in mid-intensities, and levels off as the response nears its maximum. The calculation of slope ratios, derived from the dynamic range of admittance change to intensity change, may be a metric that is sensitive to auditory nerve pathology (Cannavo et al., 2008).

Variables affecting the ARGF.

Variability in the ARGF can be attributed to several factors such as age, sensorineural hearing loss, and the static immittance of the acoustic system (Silman & Gelfand, 1981a; Thompson et al., 1980; Wilson, 1981; Sprague et al., 1981). A recurring focus in various research is the influence of aging on the acoustic reflex growth function (ARGF). A study by Thompson and colleagues (1980) highlighted a progressive decline in the growth rate in amplitude as individuals age, indicating that although the acoustic reflex thresholds are comparably stable across different ages, the growth in amplitude tends to decrease as one age.

Further research by Silman and Gelfand (1981a) on subjects aged 61 to 84 years underscored age-associated alterations in the ARGF, notably a diminished overall growth function magnitude and a tendency for the growth functions to reach saturation at lower levels of stimulation in older individuals. Wilson's (1981) research corroborated these observations, demonstrating that individuals older than 50 show reduced magnitudes in their acoustic reflexes and a more frequent saturation in their ARGFs. The collective results from these studies underscore age-related alterations in the stapedius muscle and its impact on ARGF, emphasizing elevated acoustic reflex thresholds, decreased growth function magnitudes, and heightened susceptibility to saturation, particularly in individuals older than 50. When sensorineural hearing loss is present, both pure tones and broadband noise show linear ARGFs. However, these functions change depending on the level of hearing loss (Silman et al., 1978). The static acoustic admittance value refers to the admittance at the tympanic membrane just before the application of a stimulus. Silman and Gelfand's (1981) and Wilson's (1979) studies demonstrated a positive correlation between a higher static acoustic admittance value and a larger acoustic reflex (AR) magnitude. To account for the considerable inter-subject variability in static admittance, normalization techniques were employed in studies by Silman et al. (1978), Silman and Gelfand (1981b), Thompson et al. (1980), and Wilson (1981). These normalization techniques involved using the magnitude change in sensation level relative to the acoustic reflex threshold (ART).

Factors Influencing Acoustic Reflex Growth Functions (ARGF): Activator Frequency, Probe Tone, and Stimulus Type

Previous research has suggested several stimulus factors that significantly affect the measurement and interpretation of ARGFs, including probe tone intensity, stimulus spectrum, and activator frequency. A noteworthy observation by Silman and Gelfand (1981) revealed a linear increase in ARGF with higher activator levels when utilizing a 1000 Hz tonal activator. However, this linear pattern shifted when broadband noise (BBN) activators were employed, showcasing a linear increase in AR magnitude only up to 10 dB above the threshold, beyond which the ARGF plateaued. Moreover, studies by Beedle & Harford (1973), Møller (1961), and Wilson (1979) demonstrated that the steepness of ARGF rises with the frequency of tonal activators, underscoring the impactful role of activator frequency. Møller's (1961) investigation specifically noted a steeper ARGF slope with the 1500 Hz activator than the 500 Hz activator in individuals with normal hearing aged 19 to 30.

In Cunningham's (1976) study, an analysis of acoustic reflex (AR) magnitude and impedance using stimuli at 750, 1000, and 2000 Hz in individuals with normal hearing showed that the most significant AR magnitude was observed with the 1000 Hz stimulus. The acoustic reflex growth function (ARGF) slopes were notably steeper at 1000 and 2000 Hz than at 750 Hz. On the other hand, Dickens and Womersley (1985) found a steeper ARGF slope with the 1000 Hz stimulus than the 2000 Hz stimulus. Peterson and Liden (1972) noted a decrease in the ARGF slope for a 4000 Hz stimulus when contrasted with 250, 1000, and 2000 Hz stimuli in normal-hearing subjects. Kaplan and colleagues (1977) observed the steepest ARGF slope with a 2000 Hz stimulus, whereas the 4000 Hz stimulus was associated with the least steep slope. Wilson and McBride (1978) reported an increase in AR magnitude with increasing stimulus levels across all frequencies tested, except at 4000 Hz, where the most significant AR was seen with the 1000 Hz stimulus. Wilson (1981) further identified that the ARGF slopes for 500, 1000, and 2000 Hz stimuli were significantly steeper than those for 250, 4000, and 6000 Hz tonal stimuli.

While various studies have explored differences in ARGF slopes across activators, few statistical analyses have been completed for comparing ARGF slopes among different stimuli. Møller (1962a) and Silman (1984) suggested no significant variations in ARGF slopes for activators at 500, 1000, and 2000 Hz. However, a study by Sprague et al. (1981), which statistically analyzed impedance data from individuals with normal hearing, found that ARGF slopes for 4000 Hz activators were less steep than those for 500 and 1000 Hz, though these differences were not statistically significant. Supporting these findings, Saxena et al. (2015) indicated no significant differences in ARGF slopes for 500, 1000, and 2000 Hz activators.

Results from earlier research show that the type of activator utilized can significantly affect the ARGF slopes; the 4000 Hz tone activator produced the least steep slope. Compared to tonal activators, BBN activators typically result in less steep ARGF slopes. Wilson and McBride's (1978) study on the effect of probe tone frequency on ARGF revealed that 660 Hz probing tones result in far steeper slopes in admittance than those at 220 Hz, with AR magnitudes at 660 Hz being nearly five times larger than at 220 Hz. When comparing the impedance of the 220 Hz and 660 Hz probing tones, Sprague and colleagues (1981) observed that the differences in impedance caused the steeper slopes at 660 Hz and lower peak AR magnitudes. While the sharpest slope in compliance susceptance change was observed with a 1000 Hz probe tone, Lutolf and colleagues (2003) found that the most dramatic ARGF slope in conductance change was observed with a 678 Hz probing tone.

Clinical Diagnostic Potential of Acoustic Reflex Growth Functions (ARGFs)

Research has increasingly focused on the factors that affect ARGF measurements. ARGFs can be significantly affected by various factors, including retro-cochlear lesions, brainstem issues, the effects of certain medications, and auditory processing disorders. These factors lead to diverse ARGF slope characteristics. Comprehending these influences may be beneficial for clinical diagnostics.

Retrocochlear Lesions: ARGF patterns are frequently distinct in those with retro cochlear lesions, particularly those affecting the brainstem and eighth cranial nerve. Following experimental treatments, such as the implantation of a balloon device in a monkey's internal auditory canal, which may cause statoacoustic nerve compression, significant alterations in ARGF slopes have been seen (Mangham & Miller, 1979). According to Mangham et al. (1980) and Harrison et al. (1989), individuals with cerebellar lesions had shallower ARGFs, and patients with acoustic malignancies had decreased slopes in their ARGFs. The decrease in the ARGF slope is probably caused by tumors compressing the auditory nerves, leading to reduced nerve activity. Moreover, Borg (1977) noted that in rabbits with surgically induced brainstem lesions, ARGF patterns were abnormal, exhibiting smaller ARs and shallower slopes.

Auditory Processing Disorders: The influence of auditory processing impairments on ARGFs has been supported by research conducted by Saxena et al. (2015). The study revealed that children with auditory processing difficulties exhibited ARGF slopes that were comparatively shallower compared to their typically developing peers and adults with hearing impairments. Significantly, the observed difference was particularly evident in ARGF experiments incorporating asymmetrical activation. Borg and Moller (1968) showed that administering specific drugs that affect the central nervous system is linked to a reduction in the ARGF slope.

Ototoxicity: Blankenship et al. (2021) study offers intriguing insights into the ARGF in individuals with cystic fibrosis (CF) and exposure to intravenous aminoglycosides (IV-AGs).

The study reveals distinctive patterns in extended high-frequency thresholds and ARGF responses among different exposure groups. Notably, the findings challenge the conventional expectation of a shallow ARGF in ototoxicity cases reported by Wojtczak et al. (2017), as individuals with IV-AG exposure demonstrated an enhanced ARGF compared to both control and no IV-AG exposure CF groups. The observed shifts in mean cumulative absorbed power for the acoustic reflex further emphasize the uniqueness of the ARGF response in the context of aminoglycoside exposure. The discussion suggests a potential link between IV-AG exposure and central auditory dysfunction, proposing mechanisms of central gain in response to peripheral damage. However, the exact interplay remains to be elucidated. The study underscores the need for further research to explore functional consequences, such as speech perception, tinnitus, and hyperacusis, and highlights the importance of considering confounding variables in future investigations.

Exploring the Efficacy of Acoustic Reflex Growth Functions Test (ARGF) in Diagnosing Cochlear Synaptopathy

The paradox of adults with normal hearing thresholds but difficulties in challenging auditory environments has led to the exploration of cochlear synaptopathy (CS). In this condition, neural connections between spiral ganglion neurons and inner hair cells deteriorate. This 'Hidden Hearing Loss' eludes standard audiometric profiles (Gatehouse & Noble, 2004; Kumar et al., 2007; Hind et al., 2011; Kujawa & Liberman, 2009; Schuette & McAlpine, 2011). Studies highlight the role of HHL in speech perception in noisy environments, a significant concern due to its prevalence and underdiagnosis (Stamper & Johnson, 2015; Viana et al., 2015; Konrad-Martin et al., 2012). The challenge lies in the absence of in vivo diagnostic tools for CS, making detection difficult (Bharadwaj et al., 2019; Bramhall et al., 2019).

Physiological Characteristics and Vulnerabilities of ANFs

In the mammalian auditory system, there are two main types of afferent neurons, classified as types I and II, found within the spiral ganglia. These neurons play a crucial role in transmitting auditory information from the cochlea to the cerebral cortex. Type I afferent fibers predominantly innervate inner hair cells (IHC) and are considered the primary conduit for transmitting auditory signals. In contrast, Type II neurons have a less clear role in auditory information transmission, and their specific functions remain unclear.

Auditory nerve fibers (ANFs) are further categorized based on their spontaneous firing rate (SR) into three groups: low-SR (spontaneous rate < 20 spikes/sec), high-SR (spontaneous rate > 20 spikes/sec), and middle-SR fibers. Low-SR fibers constitute 40% of ANFs, while high-SR and middle-SR fibers collectively represent 60%. Studies have shown that all three types of ANFs can innervate the same inner hair cell (IHC), but they exhibit distinct anatomical variations corresponding to their respective SRs.

High-SR fibers, characterized by thicker morphology and larger terminals, engage with the pillar side of IHCs, while low-SR fibers, with slimmer axons and smaller terminals, contact the modiolar side of IHCs. The anatomical differences include longer ribbons at synapses on the modiolar side. Low-SR fibers are particularly noteworthy due to their vulnerability to glutamatergic excitotoxicity, attributed to an abundance of voltage-gated calcium channels. Research, such as that by Furman et al. (2013), has demonstrated that low-SR and medium-SR ANFs are more susceptible to noise-induced damage compared to high-SR fibers.

The distinctive characteristics of low-SR fibers, including their extended dynamic range and crucial role in speech perception amidst background noise, underscore their importance in auditory function. However, the contribution of high-SR fibers to the neural response following the loss of low-SR fibers remains unclear. Recent studies, including those by Schaette and McAlpine (2011) and Suthakar & Liberman (2021), explore the intricate relationship between low and high-SR fibers, providing insights into the complexities of noise-induced auditory system pathologies and the need for further investigation into the specific physiological activities impacted by ANF degeneration.

A Review of Key Studies

The ARGF has emerged as a significant diagnostic tool in the investigation of cochlear synaptopathy, specifically for its potential in detecting auditory nerve fiber (ANF) trauma. In a study by Valero et al. (2016), the investigation focused on acoustic reflex threshold (ART) and amplitude in mouse models with noise-induced cochlear synaptopathy. The results indicated an elevated ART and reduced AR amplitude in the noise-exposed group compared to controls, demonstrating ARGF's sensitivity in detecting primary neural degeneration after noise exposure. This study laid the groundwork for further exploration into the diagnostic potential of ARGF.

Building on these findings, Mepani et al. (2020) extended the investigation to normal-hearing individuals. They employed three distinct methods, including ART measurement with a 226 Hz probe tone, wideband tympanometry, and a custom wideband technique. The study revealed that individuals exhibiting reduced speech-in-noise scores also demonstrated diminished AR amplitude and elevated ART, suggesting a potential link between these measures and cochlear synaptopathy, particularly impacting intensity coding and speech-in-noise perception.

Further adding to the body of research, Wojtczak et al. (2017) examined AR in normal-hearing individuals with tinnitus. Their study identified attenuated AR in this group, suggesting a possible relationship between cochlear synaptopathy and tinnitus. This connection highlighted ARGF's potential utility in diagnosing more complex auditory conditions.

In a more recent study by Kampel et al. (2021), a comparison between noise-exposed veterans and non-veterans was conducted, assessing variables such as ABR Wave I amplitude, EFR response, and AR magnitude. The study found diminished ABR Wave I amplitude, EFR response, and AR magnitude in subjects with a history of high noise exposure. Notably, while there were correlations between ABR and EFR, ARGF metrics did not correlate with these measurements, indicating the potential involvement of distinct neural populations.

The comparative analysis of these studies reveals a consistent theme. ARGF's potential in detecting ANF damage and cochlear synaptopathy, particularly in subjects with normal auditory thresholds but reduced speech-in-noise perception. However, differences in focus and findings, such as the unique aspects explored by Wojtczak et al. and Kampel et al., point to ARGF's diverse diagnostic capabilities. These studies collectively suggest the potential clinical utility of ARGFs for diagnosis of auditory neuropathologies.

Chapter 3

Methods

Participants

A total of 34 adults aged between 18 and 45 years were recruited for the study. The sample size was determined using GPower statistical software, with an effect size of 0.4, significance level (α) of 0.05, and desired statistical power of 80%. The effect size choice of 0.4 aimed to bolster the study's strength due to limited comparable data (Cunningham & McCrum-Gardner, 2007). Inclusion criteria included adults with bilaterally normal hearing (thresholds ≤ 25 dB HL for 250-8000 Hz) and ≤ 10 dB audiometric air-bone gaps (0.25-4.0 kHz). Participants had no history of ear surgeries, were native English speakers, and showed no cognitive/neurological issues. All participants signed informed consent prior to participation. The University of Cincinnati Institutional Review Board approved the study. Data collection occurred at the University of Cincinnati Speech and Hearing Clinic.

Methodology

Noise Exposure Questionnaires

Participants completed a brief noise exposure history questionnaire before commencing the hearing evaluation procedures. This questionnaire, comprising three concise questions, was specifically designed to capture information related to participants' historical exposure to elevated noise levels, encompassing both occupational and non-occupational contexts (Chertoff et al., 2017). A numerical scoring system was implemented, where participants scoring 5 or higher on the questionnaire were identified as individuals potentially at an increased risk of developing noise-induced hearing loss, in line with the criteria established by Chertoff and colleagues (2017). This assessment mechanism facilitated the identification and categorization of participants based on their noise exposure history.

Otoscopic Examination

A comprehensive otoscopic examination of the external ear, ear canal, and tympanic membrane was conducted. This examination aimed to exclude any outer ear abnormalities that could impact hearing or influence acoustic reflex measurements.

Audiometric Hearing Evaluation

Participants were situated comfortably within a double-walled sound isolation booth. Audiometric thresholds were acquired utilizing Grason-Stadler Incorporated (GSI) audiometry, focusing on determining pure-tone air conduction thresholds. This assessment, completed with TDH39 supra-aural headphones, encompassed the following frequencies: 250, 500, 1000, 2000, 3000, 4000, 6000, and 8000 Hz.

Speech Reception Threshold (SRT) and Word Recognition Scores (WRS)

The SRT was determined for each participant to determine the lowest intensity level at which speech stimuli could be reliably perceived. Word recognition scores were used to gauge the participant's ability to understand speech-in-quiet at a comfortable volume level. A sample of the participants' speech-in-quiet comprehension abilities is provided by this assessment when combined with the SRT analysis (Guthrie & Mackersie, 2009).

Speech-in-Noise Testing

1.AzBio test

The Arizona Biomedical Institute (AzBio) speech test was utilized to assess speech performance in noisy environments (Spahr & Dorman, 2004; Spahr et al., 2012). This test includes 15 sets of sentences, each comprising around 20 sentences. These sentences are typically five to ten words in length, averaging about 142 words per set. To determine AzBio scores, the number of accurately repeated words is divided by the total word count. Previous research (Spahr et al., 2012) confirmed the consistency of these sentences across various sets. The AzBio sentences were presented ipsilaterally through TDH39 supra-aural headphones, set at a constant 60 dB HL throughout all test conditions. The AzBio multi-talker babble noise was introduced as background noise, and the signal-to-noise ratio (SNR) was adjusted for quiet, +10 dB SNR, +5 dB SNR, and 0 dB SNR settings.

2. NU-6 test

The Northwestern University Auditory Test No. 6 corpus (NU-6), sourced from Auditec, Inc., was administered to further assess speech-in-noise performance. The order of the tested ears was randomly selected. For each ear, four distinct NU-6 word lists were administered, with each list containing 50 phonemically-balanced words. Participants were tested in four conditions: first, in quiet, and subsequently, under conditions with decreasing signal-to-noise ratios (SNRs), including +10 dB to + 5 dB, and 0 dB SNR. Across various conditions, these target word lists were presented at a level of 55 dB HL (55 dB HL is generally equivalent to speech at normal conversational levels). The determination of the overall score involved calculating the percentage of the number of accurately repeated words in each condition.

Distortion Product Otoacoustic Emissions (DPOAE)

Distortion product otoacoustic emissions (DPOAEs) provide an objective assessment of cochlear amplifier function. The Interacoustics Titan v.3.4.0 was used for measurements. Primary tone stimuli (f2) were generated at 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, and 10 kHz, with an f2/f1 ratio of 1.22 and L1/L2 intensities of 65 and 55 dB SPL. The recorded distortion product analyzed was 2f1-f2. The DPOAE at 2f1–f2 was obtained from ear canal sound pressure via time-domain and spectral averaging. The sequence of DPOAE testing was randomized, resulting in the first ear tested being either the right or left ear, depending on the participant.

Acoustic Immittance testing

a. Tympanometry

Tympanometry was conducted using the Titan Suite from Interacoustics. A probe-tone frequency of 226 Hz was utilized, with ear-canal pressure changes ranging from -600 daPa to + 300 daPa in each ear. Ear canal volume, tympanic membrane compliance, and middle-ear pressure were assessed according to the normal limits defined by Margolis and Heller (1987).

b. Acoustic Reflexes Measurements

b.1. Acoustic Reflex Threshold (ART)

The ART was assessed using the Titan Suite from Interacoustics. The procedure involves measuring changes in acoustic admittance as inferred from the sound pressure level of an ipsilateral probe tone at 226 Hz, with the reflex evoked by an ipsilateral elicitor at 0.5, 1, 2, or 4 kHz. The elicitor was presented at increasing sound levels beginning at 65 dB HL and increasing in 5 dB increments until the ART was detected. The threshold at each elicitor frequency was defined as the lowest dB level producing an admittance change ≥ 0.02 ml, followed by an increase in magnitude (i.e., an increase in admittance change).

b.2. Acoustic Reflex Growth Function (ARGF) Measurement

The acoustic reflexes (AR) and tympanometry were assessed using a GSI Tympstar (Version 2) and an Interacoustics Titan unit. The probing tone used in both studies was a 226 Hz tone. During the experimental procedure, the participants were instructed to abstain from verbal communication, mastication, or the execution of orofacial gestures. The tympanometry tests encompassed applying pressure levels ranging from -600 to +300 daPa, with a pace of 200 daPa per second. Determining the peak pressure in data for the 226-Hz tympanometry tests was conducted automatically.

The GSI Tympstar was utilized to conduct ipsilateral atrioventricular (AR) testing at 226 Hz. These tests were performed using the tympanometry peak pressure (TPP) obtained from the tympanometry tests conducted at the same probe frequency. Seven activators were used in these AR tests: three noise stimuli (low-band noise [LBN] with energy between 250-1600 Hz and high-band noise [HBN] with energy between 1600-4000 Hz), four tones (500, 1000, 2000, and 4000 Hz), and broadband noise (BBN) were used. The pressure was swept at 200 daPa/s for the GSI Tympstar, from 200 daPa to -400 daPa. To maintain the maximal activator level within the comfort range, activators were offered in 5 dB increments from 50 dB HL to 95 dB HL. The AR thresholds were established as the minimum activator level in dB HL, which resulted in a change in admittance of at least 0.02 ml, followed by two repeated or confirmed responses. The change in admission, denoted as Y ARGF, was measured at every activator level. If a probe fit was leaky, the probe was reinserted, and the test was conducted three times at each level, with the average answer considered.

For the Titan Interacoustics device, AR measurements were conducted using a 226 Hz probe tone with pure tonal stimuli (500, 1000, 2000, 3000, and 4000 Hz) and narrow-band noise stimuli (NBN) at 1, 2, 3, and 4 kHz. The measurements were ipsilateral and adhered to the Interacoustics standard for both consistency and accuracy. This included Automatic Gain Control (AGC) to protect against loud probe tone stimuli in small ear canals. The probe tone level was set at 85 dB SPL (approximately 69 dB HL), with automatic air pressure and a compliance range of 0.1 to 8.0 ml at the 226 Hz probe tone (ear volume: 0.1 to 8.0 ml) and 0.1 to 15 mmho at probe tones of 678, 800, and 1000 Hz.

Additionally, AR responses were elicited using band-pass filtered noise stimuli that adhered to specific spectral properties. This included Low Pass noise (LPN) targeting reflexes within the 500 Hz to 1600 Hz range, and High Pass noise (HPN) covering the 1600 Hz to 4000 Hz range. The Y ARGF curves were constructed by plotting the change in acoustic compliance from 50 to 95 dB SPL HL in 5 dB increments.

Potential order effects were eliminated by randomly assigning the AR activator stimuli to each participant in a different order. Each experimental session comprised one tympanometry test and 15 ARGF tests. These tests consisted of eight ARGF tests conducted with the GSI Tympstar, utilizing the 226 Hz probe tone at the tympanometric peak pressure obtained from 226-Hz tympanometry. Furthermore, nine ARGF tests were conducted with the Titan tympanometry, employing the 226 Hz probe tone at the tympanometric peak pressure.

Data Processing

The Y ARGF was analyzed at the ART, with the activator level systematically raised from 50 to 95 dB HL. To minimize the variability of AR threshold values across participants, the ARGF data were transformed from activator intensity in dB HL to dB Sensation Level, as originally proposed by Sprague et al., (1981). The dB SL values were calculated using the individual's ART as a reference point, denoting ART as 0 dB SL. This transformation was applied to each ARGF test condition. The change in admittance caused by the acoustic reflex possesses two distinct characteristics: amplitude and direction. AR amplitude represents the absolute value of the admittance change, regardless of whether the change is negative (indicating increased middle-ear stiffness) or positive (indicating decreased middle-ear stiffness)."Direction" signifies whether the admittance increased or decreased compared to the baseline value. The ARGFs essentially represent the plots of the change in the admittance as a function of activator stimulus intensity (see Fig. 7). The ARGF was evaluated using 226 Hz probe tones, measuring two parameters: ARGF admittance change (ΔY ARGF) and ARGF slope across multiple tonal and noise activator stimuli. The average ΔY ARGF and ARGF slopes were computed across ears for each frequency and each type of activator.

The primary focus of the analysis was on two key parameters. The first parameter investigated was the AR admittance change, determined by the difference between the maximum and minimum admittance values across various activator levels. This difference, ΔY ARGF, was measured in milliliters (ml) to quantify the change in admittance. The second parameter of interest was the slope of the Y ARGF curve, which applied to both tonal and noise activators. To calculate the ARGF slope, measured in ml/dB, the change in admittance magnitude was divided by the corresponding change in activator intensity levels, employing a linear fit approach. The Y ARGF and ARGF slope were calculated across all ears for each frequency and type of activator used in the study for a comprehensive analysis.

The criteria for excluding AR data were as follows:

- A dataset was eliminated if less than three data points were gathered for a particular activator.
- The complete dataset for a given individual was eliminated if Y ARGF data was found for fewer than three distinct activators within that individual.

Statistical Analysis

The data were analyzed, and plots were generated using SigmaPlot software (version 15). Descriptive statistics, encompassing metrics such as the mean, standard deviation (SD), coefficient of variance (CV), minimum, maximum, skewness, and standard error of the mean (SE), were computed. When the normality test did not meet the necessary assumptions, the

Kruskal-Wallis H test, which is a nonparametric alternative to the one-way ANOVA, was employed to assess variations in Acoustic Reflex Growth Function (ARGF) measures between tonal and narrow-band noise (NBN) activators. This nonparametric test, relying on mean ranks, investigated differences across stimuli. In the first assessment, the dependent variable was the change in ΔY ARGF, with the activator level as the independent variable. In the second evaluation, the dependent variable was the slope of ARGFs, while the independent variable consisted of different activators. The significance level (α) was set at 0.05.

Chapter 4

Results

Noise Exposure Assessment

The noise exposure questionnaire (Chertoff et al., 2017), revealed a low risk of noise-induced hearing loss among the study participants. This questionnaire consisted of three targeted questions, administered before the hearing evaluation procedures, to collect information on the participants' historical exposure to high noise levels, encompassing both occupational and non-occupational environments.

Hearing Thresholds

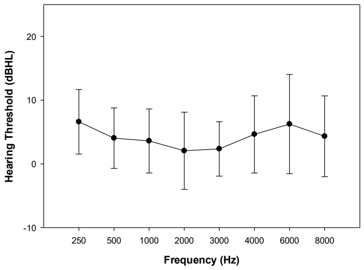
The 34 participants all presented with hearing threshold levels (HTL) within the normal hearing range defined by the American Speech-Language-Hearing Association (ASHA, 2005), as listed in Table 1 along with participants’ demographics and as illustrated in Figure 1. Statistical analysis did not identify any notable differences in HTL between the participants' right and left ears. Consequently, the data were merged across ears and analyzed as a group of 68 ears tested at each audiometric frequency. All ears exhibited HTL values < 20 dB HL across the entire range of tested frequencies, spanning from 250 to 8000 Hz.

Table 1. Participant Demographic Details.

Participants in total	34 (68 ears)
Age in years **Mean** **Range**	 25.47 (19.3-44)
Gender **Female:** **Male**	 30 4
Mean 3-freq* HTL in dB HL (SD)	2.89 (5.28)
Mean 226-Hz static acoustic admittance in millimhos (SD)	0.69 (0.27)
Mean SRT in dB HL (SD)	5 (3.89)

HTL = Hearing Threshold Level, computed by averaging the hearing thresholds at 0.5, 1.0, and 2.0 kHz. SRT = Speech Reception Threshold. SD = Standard Deviation.

Figure 1. Hearing Threshold Levels (HTL)

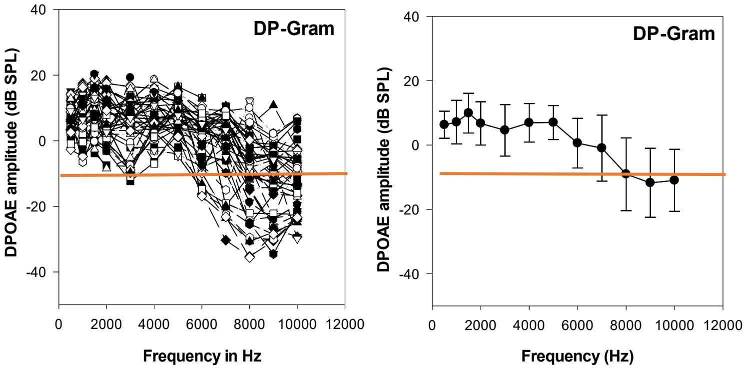


HTL in decibels Hearing Level (dB HL) for audiometric frequencies ranging from 0.25 to 8 kHz (mean ± 1 SD) were within the normal hearing range for all 68 ears.

DPOAE Results

DPOAE measurements were utilized as an initial screening tool to identify possible dysfunction in the cochlear outer hair cells, which might not be detectable through conventional pure-tone audiometry. Notably, all 68 ears displayed detectable DPOAE responses with amplitudes exceeding -10 dB SPL at three or more tested frequencies, as illustrated in Figure 2. Participants with absent DPOAE were excluded from full participation in the normative arm of the study.

Figure 2. Distortion Product Otoacoustic Emission (DPOAE) Amplitudes



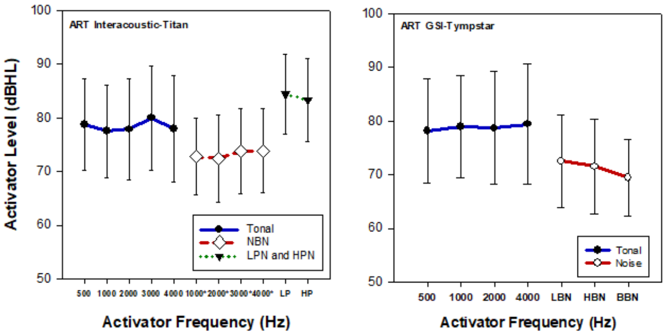
DPOAE amplitudes are displayed for all ears across f2 frequencies. The left panel displays raw DPOAE amplitudes in dB SPL for all ears at frequencies ranging from 0.5 to 10 kHz. The right panel illustrates the overall mean DPOAE amplitude values (±1 SD). DPOAE amplitudes are typically higher at lower frequencies and decrease at higher frequencies, with increased variability at the higher frequency range. Notably, above 4000 Hz, a decline in DPOAE amplitude and a rise in variance are observed among ears. The red lines represent the lower limit for normal DPOAE amplitude (-10 dB SPL), as established in a normative study by Ramos et al. (2013).

Tympanograms

All 68 ears in the study cohort displayed Type A tympanograms (Jerger & Jerger ,1971; Jerger et al.,1972), indicating normal middle-ear function according to adult normative values (middle-ear compliance 0.3–1.5 cm³, middle-ear pressure –100 to +50 daPa, and ear canal volume between 0.6 and 1.5 cm³).

Acoustic Reflex Threshold (ART)

Figure 3. Acoustic Reflex Threshold (ART)



This figure represents the mean values (± 1 SD) of the ART in dB HL for all 68 ears. The data compares ART across different stimulus types, including tonal and noise bands, using the two pieces of equipment: Interacoustics Titan and GSI Tympstar. A slight increase in the variance of the ART is noted at higher-frequency tonal stimuli compared to lower frequencies.

1. ART Using Interacoustics Titan

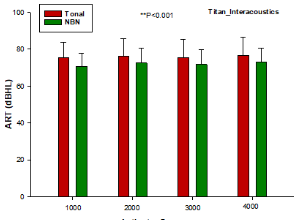
Table 2. Ipsilateral ART Using Different Activator Stimuli Using Interacoustic Titan Equipment.

AR Activator Stimulus											
	Single Frequency Tone (SF)					*NBN*				*Pass Noise*	
	500	*1000*	*2000*	*3000*	*4000*	*1000*	*2000*	*3000*	*4000*	*LP*	*HP*
Mean	79.44	79.29	76.17	78.51	80.67	72.8	71.5	73.76	72.86	86.41	87.38
SD	8.45	8.63	9.46	9.66	9.91	7.15	8.12	7.9	7.83	7.5	7.74
Median	85	85	80	85	80	75	75	80	75	90	85
Max	90	90	95	95	95	90	90	90	90	95	95
Min	55	55	55	50*	50*	55	55	50*	50*	70	65
SEM	0.67	0.63	0.73	0.79	0.82	0.76	0.85	0.70	0.97	1.13	1.23
Skewness	-0.47	-0.62	-0.24	-0.53	-0.34	-0.61	-0.44	-0.65	-0.87	-0.60	0.36

Ipsilateral ART were recorded from the same ear using a 226 Hz probe, measured with the Interacoustics Titan tympanometry equipment. ART values are provided for different activator stimuli. *A minimum ART value of 50 dB HL was observed in 5 ears. The ART values with NBN activators significantly lower (mean difference = 3.930, SD = 0.378, SEM = 0.189, $p < 0.001$) compared to those obtained with tonal activators at corresponding frequencies (1, 2, 3, and 4 kHz). Additionally, the results show that ART values are generally higher for LPN and HPN activators than for other activator types. These differences were found to be statistically significant ($p < 0.05$). T-tests demonstrated significant differences in mean ART values between NBN activators and both low-pass and high-pass activators ($p < 0.05$). Pairwise comparisons were conducted between activator stimuli at specific frequencies and their corresponding narrowband noise (NBN) versions (Figure 4). These comparisons revealed a consistent pattern of significantly lower ART values ($p < 0.001$) for 1000 Hz tone compared to 1000 NBN, 2000 Hz tone compared to 2000 NBN, 3000 Hz tone compared to 3000 NBN, and 4000 Hz tone compared to 4000 NBN.

Furthermore, multiple pairwise comparisons were conducted using ANOVA to assess differences between various activator stimulus combinations. These comparisons demonstrated significant variations ($p < 0.05$) in ART values between low pass activators (LPN) and NBN at 1000, 2000, 3000, and 4000 Hz, as well as between LPN and 4000 Hz tonal activator. Similarly, significant differences were found in the comparisons between HPN and NBN activators at 1000, 2000, 3000, and 4000 Hz, as well as between HPN and 4000 Hz tonal activators. On the other hand, no significant differences were detected in the comparisons between LPN and 3000 Hz tone, LPN and 1000 Hz tonal, LPN and HPN, HPN and 2000 Hz tonal, HPN and 3000 Hz tonal, or HPN and 1000 Hz tonal activator.

Figure 4. Comparison of ART Mean Values with Tonal vs. NBN Stimuli



This figure displays the mean ART values in dB HL, illustrated with ±1 standard deviation (SD), using tonal (represented in green) and narrowband noise (NBN, represented in red) stimuli. The NBN stimuli elicited lower ARTs than the tonal stimuli across all frequencies (frequencies not visible on the x-axis in the figure). A statistically significant difference was observed ($p < 0.001$) for all four activators in the comparison.

2. ART using GSI-Tympstar

Table 3. Ipsilateral ART with Different Activator Stimuli Using GSI Tympstar Equipment

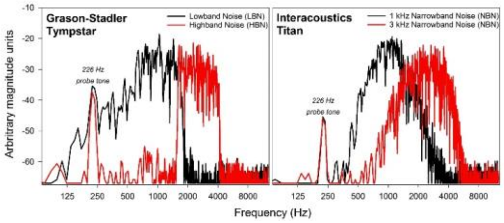
AR Activator Stimulus							
Activator	Single Frequency Tone (SF)				Noise		
	500Hz	1000 Hz	2000 Hz	4000 Hz	LBN	HBN	BBN
Mean	78.147	79.000	78.662	79.426	72.574	71.397	69.412
SD	9.696	9.463	10.363	11.180	8.660	7.010	7.151
Median	85	85	80	85	75	75	70
Max	90	90	90	95	90	90	80
Min	55	55	55	55	50	50	50
SE	1.176	1.148	1.257	1.356	1.050	0.850	0.867
Skewness	-0.372	-0.476	-0.389	-0.413	-0.221	-0.0433	-0.513

This table presents ipsilateral Acoustic Reflex Thresholds (ARTs) in dB HL for various activator stimuli, measured using GSI Tympstar equipment (n = 68 ears). Broadband noise (BBN) stimuli were observed to trigger lower ARTs compared to other types of stimuli.

3. ART across-equipment comparison

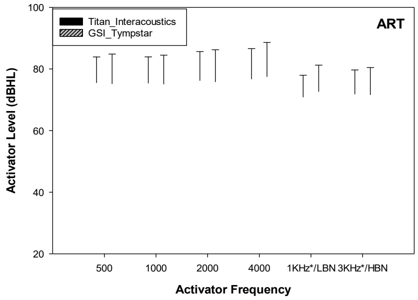
One-Way Repeated Measures ANOVA, comparisons were made between the activator with comparable bandwidth between two equipment, 1 kHz NBN, 3 kHz NBN on Titan versus LBN and HBN using the GSI Tympstar, respectively (Figure 5). The analysis found no statistically significant differences between these groups' acoustic reflex thresholds (ART). The F-statistic for both comparisons was 0.339 with ps of 0.797. Mean ART values for 1 kHz NBN and HBN were 70.809 dB HL (SD 7.156) and 71.544 dB HL (SD 8.905), respectively. For 3 kHz NBN and HBN, mean ART values were 71.765 dB HL (SD 7.906) and 71.544 dB HL (SD 8.905), respectively (Figure 6).

Figure 5. Comparison of Acoustic Spectra Between LBN/HBN Noise and Narrowband Noise Stimuli.



The left panel of this figure illustrates the acoustic spectra of low-band noise (LBN) and high-band noise (HBN) as generated by the GSI Tympstar. The right panel displays the spectra for 1 kHz and 3 kHz narrowband noise stimuli produced by the Interacoustics Titan. The bandwidths of LBN and HBN noise on the GSI Tympstar are comparable to those of the narrowband noise stimuli on the Interacoustics Titan.Similarly, comparing 500, 1000, 2000, and 4000 Hz tone between Titan and GSI revealed no statistically significant difference ($p > 0.05$; Figure 6).

Figure 6. Comparison of ARTs Between Interacoustics Titan and GSI Tympstar Devices.



This figure illustrates the comparison of Acoustic Reflex Thresholds (ARTs) measured using the Interacoustics Titan and GSI Tympstar immittance devices with equivalent stimuli. The results indicate no significant differences in ARTs between the two devices for the same stimulus types.

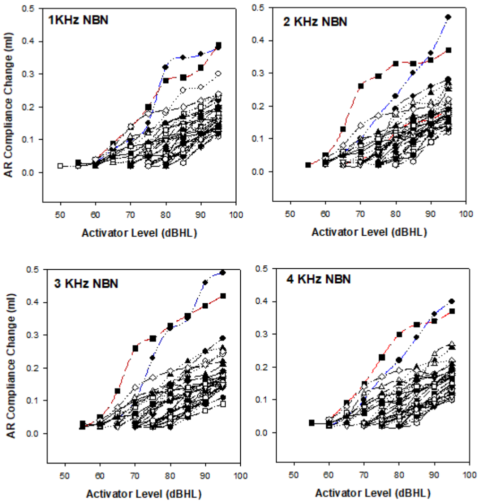
ARGF

1. Y ARGF.

1.a. Y ARGF using Interacoustics Titan

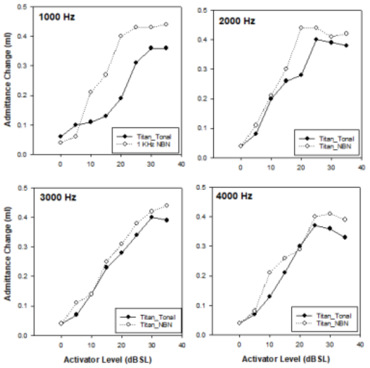
The term "Y ARGF" refers to the alteration in admittance (Y) that occurs at the tympanic membrane, which is determined by the magnitude of the activator stimulus. The assessment of Y ARGF, encompassing both the magnitude and slope of AR, was performed by employing a 226 Hz probing tone across various tonal and noise activator levels for every participant. The first measurement used the change in admission in milliliters (ml) to calculate the AR magnitude for different activator levels. By computing the difference between the admittance at the ART level and the admittance at the maximal stimulation level (95 dB HL), the change in AR magnitude (ΔY) was ascertained. Figure 7 depicts the relationship between the activator stimulus intensity (dB HL) and each participant's absolute value of the AR magnitude in milliliters. The study revealed a positive correlation between the levels of the activator stimulus and the progressive increase in the Y ARGF. The study observed a statistically significant relationship between the activator level and Y ARGF across all activators ($p < 0.001$, as established by a one-way ANOVA on ranks).

Figure 7. Y ARGF Relative to Activator Intensity.



This figure depicts the Y Acoustic Reflex Growth Function (ARGF) across activator intensities from 50 to 95 dB HL for ipsilateral Acoustic Reflexes (ARs) using 1, 2, 3, and 4 kHz narrowband noise (NBN) activators for 34 subjects (68 ears), recorded with the Interacoustics Titan equipment (n = 68 ears). Most data points cluster around a trend that shows increasing ARGF with higher activator levels. However, the red and blue dashed curves distinctly deviate from the main cluster, representing the average responses from two participants with notably higher and steeper Y ARGF curves. These outliers suggest a greater than typical growth in reflex amplitude as a function of stimulus intensity, which is significantly different from most participants.

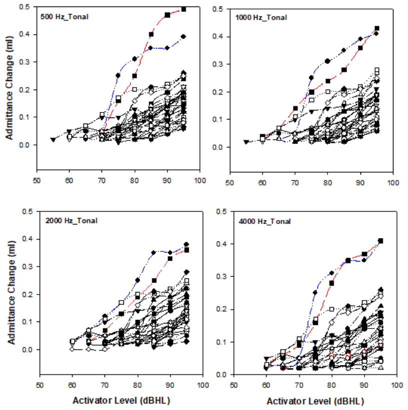
Figure 8. Admittance Change of The ARGF Using Interacoustic Titan Equipment.



This figure presents the mean values for the ARGF admittance change as a function of activator intensity in decibels sensation level (dB SL) for ipsilateral Acoustic Reflexes (ARs) in response to tonal and narrowband noise (NBN) activators at 1, 2, 3, and 4 kHz frequencies. The data was collected using Interacoustics Titan equipment with a sample size of 68 ears. It was observed that Y AR magnitudes for NBN stimuli were greater than those for tonal stimuli at the four activator frequencies. The Y ARGF values at 1000, 2000, 3000, and 4000 Hz increased progressively with the activator level up to 25 dB SL. Beyond this intensity, a plateau effect occurred, consistent with the saturation of neural fibers as described by Silman and Gelfand (1981). The influence of activator level on Y ARGF was found to be statistically significant across all activators ($p < 0.001$, as determined by a one-way ANOVA on ranks).

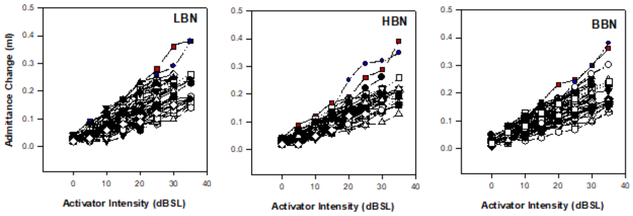
1.b Y ARGF using GSI Tympstar

Figure 9. Admittance Change of The ARGF for Tonal Activator Using GSI-TympStar Equipment.



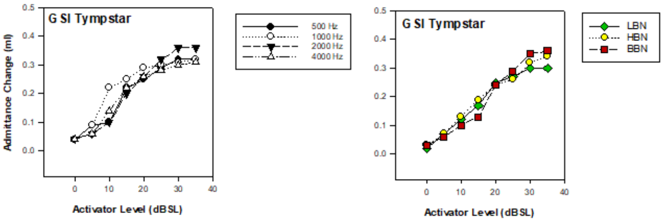
This figure demonstrates the admittance change of the ARGF as a function of activator intensity level, which ranges from 50 to 95 dB HL, for ipsilateral acoustic reflexes to tonal stimuli at frequencies of 500, 1000, 2000, and 4000 Hz. The measurements were conducted using GSI Tympstar equipment, with a sample size of 68 ears. The red and blue curves within the graph represent the average responses from two participants whose Y ARGF measurements were notably higher, and steeper compared to those from the other 32 participants, indicating a significant deviation from the average response patterns.

Figure 10. Individual Ears Admittance Change of The ARGF for Tonal Activator Using GSI-TympStar Equipment.



This figure illustrates the admittance change of the ARGF in response to increasing activator intensity levels from 50 to 95 dB HL for individual ears. The activators used include LBN, HBN, and BBN, with measurements taken using GSI Tympstar equipment. The sample encompassed 68 ears. The graph is expected to show the progressive increase in AR amplitude with rising intensities of the different noise activators. The red and blue curves within the graph represent the average responses from two participants whose Y ARGF measurements were notably higher, and steeper compared to those from the other 32 participants, indicating a significant deviation from the average response patterns.

Figure 11. Mean Values of Admittance Change of the ARGF for Tonal Activator Using GSI-TympStar Equipment.



The figure portrays the mean values of the admittance change as a function of activator intensity in decibels sensation level (dB SL). The responses were elicited using tonal stimuli at frequencies of 0.5, 1, 2, and 4 kHz, as well as LBN, HBN, and BBN stimuli, with the GSI Tympstar unit on a sample of 68 ears. The graph is designed to show how the mean Y ARGF values vary with different types of auditory stimuli at specified intensities.

In a One-Way RM ANOVA focused on examining the changes in admittance between tonal and noise activators, it was found that the Y ARGF was higher in noise than in tonal activators, with significant differences identified between these two ($p = 0.046$). The analysis successfully passed both the normality test ($p = 0.473$) and the equal variance test ($p = 0.115$), ensuring the corresponding assumptions/criteria were met. A notable finding from the pairwise comparison, conducted using the Bonferroni t-test, was the significant difference observed between the 2000 Hz frequency and lowband noise (LBN). This difference was quantified with a mean difference of 0.0400 ml that was significant ($p = 0.038$). Contrarily, other pairwise comparisons involving 2000 Hz with HBN, and BBN did not demonstrate significant differences.

ARGF Slope

1. ARGF Slope using Titan Interacoustic

The *ARGF slope in (ml/dB)* is calculated as the rate of change in the acoustic reflex response magnitude (measured in milliliters of compliance change) with respect to the sound stimulus intensity (measured in decibels) from the ART to the maximum level.Y represent the acoustic reflex response magnitude and X represent the sound stimulus intensity, then the ARGF slope can be mathematically expressed as:

ARGF slope $=\Delta Y/\Delta X$

Where:

- ΔY is the change in acoustic reflex response magnitude,
- ΔX is the change in sound stimulus intensity.

In practice, to calculate the ARGF slope, you would typically take two points on the curve of the graph plotting Y against X and use the formula for slope between two points. In the current study, we calculate the ARGF slope considering point one at the ART and point two at the maximum stimulus level of 95 dB HL. This approach to slope calculation provides a quantifiable measure of the ARGF's responsiveness across the specified dynamic range in our sample population.

$$\text{ARGF slope} = \frac{Y_{95dB} - Y_{ART}}{95 - X_{ART}}$$

Where:

Y_{95dB} is the AR magnitude at the maximum level of stimulation (95 dB HL)

Y_{ART} is the acoustic reflex response magnitude at the Acoustic Reflex Threshold (ART)

X_{95dB} is the sound stimulus intensity at the maximum level of stimulation (95 dBHL)

X_{ART} is the sound stimulus intensity in dB HL at the ART

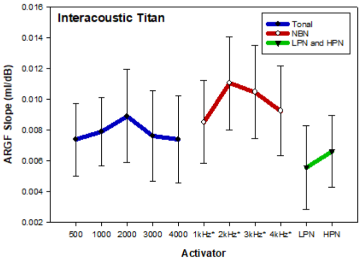
Table 4. ARGF Slope Measured Using Titan Interacoustics Equipment.

Activator Stimulus											
	Tonal Stimuli					*NBN*				*Bandpass Noise*	
	500	*1000*	*2000*	*3000*	*4000*	*1000*	*2000*	*3000*	*4000*	*LP*	*HP*
Mean	0.007	0.008	0.010	0.007	0.008	0.008	0.011	0.010	0.009	0.005	0.006
SD	0.004	0.003	0.004	0.002	0.003	0.002	0.002	0.002	0.003	0.003	0.002
Max	0.028	0.018	0.029	0.019	0.018	0.015	0.014	0.0112	0.015	0.0160	0.0120

Min	0.001	0.0005	0.002	0.002	0.001	0.002	0.003	0.003	0.002	0.001	0.0008
SE	0.0005	0.0004	0.0005	0.0003	0.0004	0.0003	0.006	0.0002	0.0003	0.0004	0.0003
CV(%)	62.08	52.75	45.31	37.54	45.48	33.94	33.62	29.09	37.27	58.11	50.20
Skewness	2.224	0.728	1.009	*0.205*	2.376	0.074	0.56	0.591	0.735	1.502	1.041

This table presents the ARGF slope values for different activator stimulus types, including tonal stimuli at frequencies of 500, 1000, 2000, 3000, 4000 Hz, narrowband noise (NBN) at 1000, 2000, 3000, 4000 Hz, and low-pass noise (LPN), and high-pass noise (HPN), measured using the Titan Interacoustics unit. The sample size comprised 68 ears.

Figure 12. Ipsilateral ARGF Slope Comparison Across Activator with Interacoustic-Titan Equipment.



The figure displays the ARGF slopes, along with ± 1 SD, for ipsilateral ARs elicited by tonal, NBN, LPN, and HPN activators using the Titan unit. The ARGF slopes are observed to be higher for the noise activators (NBN, LPN, HPN) compared to the corresponding tonal activators. Notably, the ARGF slope at 2000 Hz was significantly higher than those for other tonal activators, as determined through a one-way ANOVA on ranks ($p < 0.05$).

Tonal vs. NBN Stimuli Frequencies

In the first comparison, we looked at four pairs of frequencies: 1000 Hz tonal vs. 1 kHz NBN, 2000 Hz tonal vs. 2 kHz NBN, 3000 Hz tonal vs. 3 kHz NBN, and 4000 Hz tonal vs. 4 kHz NBN. A t-test revealed a significant difference in the 3000 Hz tonal versus 3 kHz NBN pair ($p = 0.02$). There was also a trend towards significance in the 1000 Hz tonal versus 1 kHz NBN pair ($p = 0.080$), and a similar trend in the 2000 Hz tonal versus 2 kHz NBN pair ($p = 0.05$). However, no significant differences were found in the other frequency pairs.

ARGF slope at 2 kHz and 3 kHz Frequencies

The ARGF slope for the 2 kHz and 3 kHz narrowband noise (NBN) frequencies was compared with those for low-pass noise (LPN) and high-pass noise (HPN) activators. Results indicate that the NBN activators at the 2 kHz and 3 kHzfrequency demonstrate a higher ARGF slope than LPN and HPN. It was found that the ARGF slope for the 3 kHz NBN frequency differed significantly in mean values when compared to both LPN and HPN activators, with a p-value of 0.028, indicating a higher ARGF slope. Similarly, at the 2 kHz frequency, a significant difference in mean values was observed between the LPN and HPN activators ($p = 0.003$).

Comparison of LPN and NBN Frequencies

The study investigated the differences between LPN and various NBN activator frequencies. Significant differences were observed between the mean values of LPN and all four NBN frequencies: 1 kHz ($p = 0.036$), 2 kHz ($p = 0.003$), 3 kHz ($p = 0.025$), and 4 kHz ($p = 0.027$). Additionally, the mean values of HPN (High-Pass Noise) showed significant differences at 1 kHz ($p = 0.041$) and 2 kHz ($p = 0.005$). However, the differences between HPN and the 3 kHz ($p = 0.092$) and 4 kHz ($p = 0.065$) frequencies were insignificant.

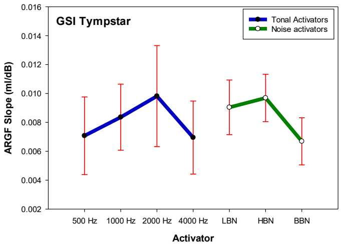
ARGF Slope using GSI TympStar device

Table 5. ARGF Slope Measured Using GSI TympStar Equipment.

Activator stimulus							
	Tonal stimuli				Noise		
	500 Hz	1000 Hz	2000 Hz	4000 Hz	LBN	HBN	BBN
*Mean	0.007	0.008	0.009	0.007	0.006	0.005	0.005
SD	0.00268	0.00229	0.00349	0.00251	0.00189	0.00164	0.00163
Max	0.0180	0.0127	0.0200	0.0140	0.0106	0.01000	0.0105
Min	0.00240	0.00267	0.00200	0.000948	0.00200	0.00240	0.00267
SE	0.000326	0.000277	0.000424	0.000305	0.000229	0.000199	0.000198
Skewness	1.814	0.621	1.778	0.907	0.211	0.601	0.731

This table presents the ARGF slope in ml/dB values for different activator stimulus types, including tonal stimuli at frequencies of 500, 1000, 2000, 4000 Hz, LBN, HBN, and BBN, measured using the GSI-TympStar unit. The sample size comprised 68 ears. The ARGF slopes for tonal stimuli at 500, 1000, 2000, and 4000 Hz were similar in range to those for LBN, HBN, & BBN (see Fig. 13).

Figure 13. Comparison of ARGF Slopes for Tonal vs Noise Activator Using GSI-TympStar.



This figure illustrates the ipsilateral ARGF slopes, represented as mean values with ±1 SD, for LBN, HBN, and BBN activators using the GSI Tympstar unit. The ARGF slopes for these noise activators are generally like those obtained for tonal activator stimuli, indicating comparable reflex responsiveness across different types of auditory stimuli.

The average ARGFs were plotted in dB SL up to levels of 35 dB SL. Activator levels beyond 35 dB were not included due to the limited instances of ARs recorded at high sensation levels relative to the ART. The 5 ears in which ARTs were observed at 50 dB HL had ARGFs that extended up to 45 dB SL. However, the corresponding ARGFs were truncated at 35 dB SL to align them with the data from the majority of the other ears. To investigate the influence of the right versus left ears on ARGFs, a General Linear Model (GLM) analysis was conducted, which showed no significant ear-related differences; thus, data from both ears were merged for analysis. Subsequently, a one-way ANOVA was employed to assess the mean ARGF activator levels ranging from 0 to 35 dBSL relative to the ART.

The mean ARGF slope is highest for the 2000 Hz tonal stimulus, followed closely by the 1000 Hz tonal stimulus. The noise stimuli (LBN, HBN, BBN) have mean ARGF slopes that are generally lower than the highest tonal stimuli (2000 Hz and 1000 Hz) but comparable to or slightly higher than the 500 Hz and 4000 Hz tonal stimuli. The standard deviation values are consistently lower for the noise stimuli (LBN, HBN, BBN) than the tonal stimuli. This indicates less variability in the ARGF slope response to noise stimuli. Among the tonal stimuli, the 2000 Hz frequency shows the highest variability (SD), while the 500 Hz and 1000 Hz frequencies show comparable variability.

Inter-subjects' variability in ARGF Slope and Admittance Changes

In this study, the Coefficient of Variation (CV) was utilized to assess the intersubject variability of the ARGF slope and changes in admittance across various activators. The CV is a statistical measure used to evaluate the relative dispersion or variability of data points around the mean across different subjects. It is calculated as the ratio of the standard deviation (SD) to the mean of the measurements, and is often expressed as a percentage:

$$\mathrm{CV} = \left(\frac{\mathrm{SD}}{\mathrm{Mean}}\right) \times 100\%$$

where:

- SEM is the Standard Error of Measurement,
- Mean is the average of the measurements.

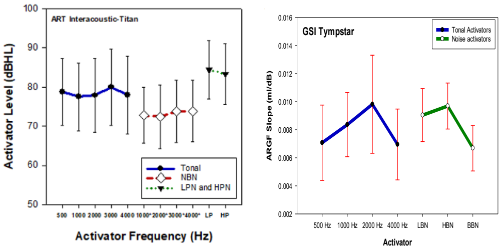
The CV measurement allows for a standardized assessment of measurement variability across subjects, with a higher CV indicating greater variability among subjects' responses, and a lower CV suggesting more consistent responses across the study population.

The CV was employed to evaluate the intersubject variability of ARGF slope and admittance changes across different auditory activators, as detailed in Tables 4 and 5. For the ARGF slope, the highest intersubject variability was observed at the 500 Hz frequency with a CV of 62.08%, indicating notable differences in responses among subjects at this frequency. This variability decreased at the 1000 Hz and 2000 Hz frequencies, with CVs of 52.75% and 45.31%, respectively. The 3000 Hz frequency showed more uniformity among subjects, as reflected by a lower CV of 37.54%. The narrowband noise (NBN) activators generally exhibited lower intersubject variability, particularly at 3 kHz, with the lowest CV of 29.09%, suggesting more uniform auditory responses among different subjects.

Similarly, the analysis of changes in ARGF demonstrated varying degrees of intersubject variability. The 500 Hz frequency showed high variability with a CV of 54.26%, while the 1000 Hz and 2000 Hz frequencies exhibited moderate variability, with CVs of 44.35% and 41.62%, respectively. The 3000 Hz and 4000 Hz frequencies displayed moderate variability, with CVs of 41.74% and 47.34%. Notably, the NBN activators at 1 kHz, 2 kHz, and 3 kHz frequencies presented relatively lower intersubject variability, indicating more consistent responses among subjects, with the 2 kHz NBN frequency showing a particularly low CV of 31.11%.

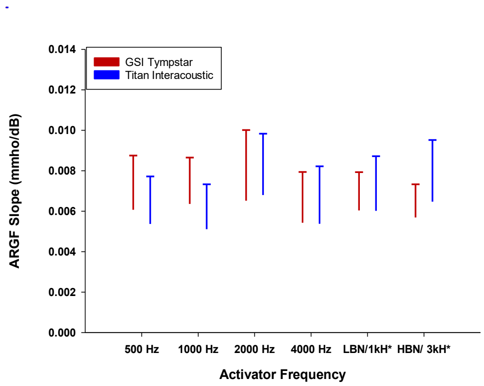
AFGF Slope Across Equipment Comparison

Figure 14. Comparison of ARGF Slopes Across Equipment.



This figure displays the mean values ±1 SD of ARGF slopes, across two different equipment: Titan (left panel) and GSI Tympstar (right panel), for both tonal and noise activators. To aid in comparison, stimuli with similar characteristics were consistently color-coded across the different devices. Notably, the ARGF slope at 2000 Hz is significantly higher than that of the other tonal activators in both devices, as indicated by the statistical significance ($p < 0.05$, determined by a one-way ANOVA on ranks).

Figure 15. Across-Equipment Comparison of ARGF Slope for Various Activators.

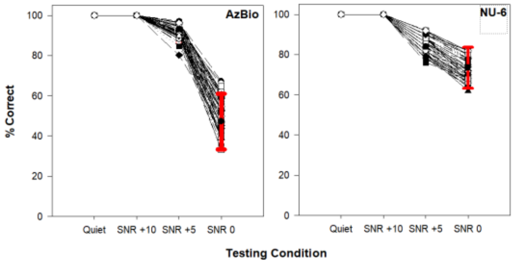


This figure presents a comparison of the mean values (±1 SD) of the ARGF slopes at a 226 Hz probe tone, using similar activators across two types of equipment: the Titan and GSI devices. The ARGF slope was evaluated using both devices for single-frequency pure tone activators at 500, 1000, 2000, and 4000 Hz. Activators with similar frequency spectra in both devices, such as LBN on the GSI device compared to 1 kHz NBN and HBN on the GSI compared to 3 kHz NBN, were analyzed. The results from the T-test revealed no statistically significant differences in the ARGF slopes for similar activators when assessed with these two devices ($P > 0.05$, paired t-test).

A one-way ANOVA was conducted to examine the effects of frequency and equipment on the Acoustic Reflex Growth Function (ARGF) slope. The analysis revealed a significant effect of frequency on the ARGF slope ($F(3, 7) = 6.00$, $p < 0.001$), suggesting that different frequencies influenced the ARGF slope considerably. Contrary to initial findings, there was no significant effect of equipment type on the ARGF slope (F(1, 7) = 4.59, p = 4.53e-06). Moreover, the interaction between frequency and equipment was also found to be non-significant (F(3, 7) = 4.59, p = 4.53e-06), indicating that the effect of frequency on ARGF slope was consistent across the two equipment types. These findings suggest that while frequency plays a crucial role in determining ARGF slope, the type of equipment used does not significantly affect this outcome.

Speech in Noise Test (SIN)

Figure 16. AzBio and NU-6 Tests Under Various Listening Conditions**.**



The figure presents the mean word correct percentages for two speech recognition tests – the AzBio test and the NU-6 – under various testing conditions: Quiet, Signal-to-Noise Ratios (SNR) of +10, +5, and 0. This analysis included a total of 68 ears and revealed no significant difference in performance between the right and left ears. In quiet conditions and at an SNR of +10, the AzBio test showed a consistent performance with 100% accuracy. However, performance distinctions emerged at SNRs of +5 and 0, indicating an increased susceptibility to background noise. Paired t-tests revealed statistically significant differences in mean word correct percentages between the AzBio and NU-6 tests at both +5 and 0 SNR (P < 0.001). The confidence intervals for these differences in means, at +5 SNR (4.873 to 7.165) and at 0 SNR (-

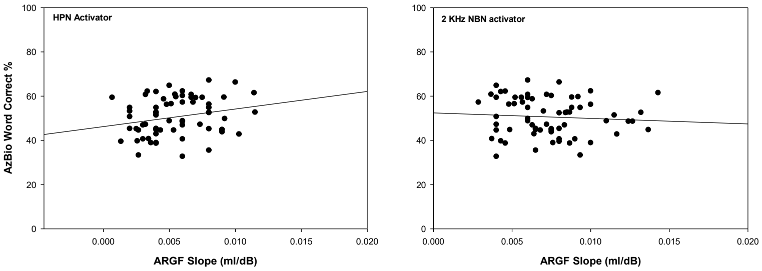
23.506 to -19.982), underscore the tests' divergent sensitivity to noise. Notably, the more pronounced disparity observed at 0 SNR reflects the AzBio test's design to simulate realistic, noisy listening environments, contrasting with the quieter conditions typically used in other assessments.

Predictive Value of the ARGF Slope Models for AzBio and NU-6

Multiple linear regression analyses were performed to evaluate the capability of ARGF slope values at various frequencies to predict speech recognition outcomes measured by AzBio at 0 SNR and NU-6 scores at 0 SNR, utilizing Titan Interacoustic equipment with tonal and noise activators. The predictive model for AzBio at 0 SNR yielded an R-squared of 0.313, indicating that approximately 31.3% of the variability in AzBio scores at 0 SNR could be explained by the model, and an adjusted R-squared of 0.178, which accounts for the number of predictors in the model. The residuals of this model were found to be normally distributed. Notably, the ARGF slope at 2 kHz NBN was identified as a significant negative predictor (P = 0.021), while the slope at HPN had a significant positive effect (P = 0.018), as illustrated in Figure 17. Other frequencies did not present significant predictive value for AzBio scores.

In contrast, the model accurately predicted NU-6 scores at 0 SNR had a lower explanatory power, with an R-squared of 0.214, suggesting that only 21.4% of the variance in the NU-6 scores at 0 SNR is accounted for by the model. The adjusted R-squared further reduced to 0.0601, reflecting the diminishing predictive strength after adjustment. The residuals for this model were not normally distributed, which can indicate potential issues with the model assumptions. In this case, none of the ARGF slopes emerged as significant predictors of the NU-6 scores, with all p-values exceeding the threshold of 0.05.

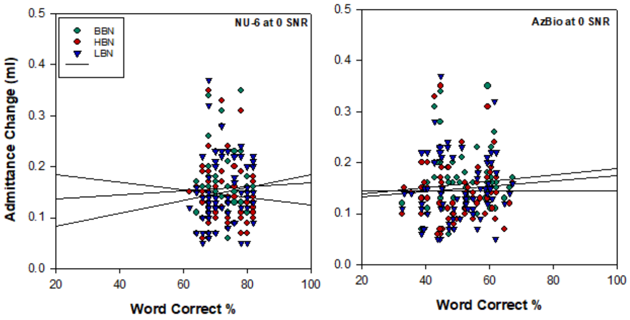
Figure 17. Correlation between ARGF Slope and AzBio Speech in Noise Test Score at 0 SNR.



This figure illustrates the relationship between the Acoustic Reflex Growth Function (ARGF) slope, measured in milliliters per decibel (ml/dB), and the AzBio speech in noise test scores at a 0 signal-to-noise ratio (SNR). The measurements were taken using Titan Interacoustic equipment. The graph is expected to depict how changes in the ARGF slope correlate with the performance on the AzBio speech in noise test under challenging listening conditions.

Relationship between AR admittance Changes and NU-6 and AzBio at SNR 0

Figure 18. Correlation Between Speech-in-Noise Test Scores and Admittance Change of ARGF



This scatter plot depicts the relationship between the word correct scores (%) from the AzBio and NU-6 speech recognition tests and the change in Y Acoustic Reflex Growth Function (Δ Y ARGF), particularly with low-band noise (LBN), high-band noise (HBN), and broadband noise (BBN) activators. The plot is designed to illustrate how the Δ Y ARGF values correlate with the performance on these speech recognition tests under different noise conditions, providing insights into auditory processing capabilities.

A multiple linear regression analysis was conducted to determine the predictive power of changes in admittance (ΔY ARGF) at different noise bandwidths (LBN, HBN, BBN) for speech recognition performance, as measured by the NU-6 50-word list at a 0 SNR. The model achieved marginal significance ($F(6,61) = 1.299$, $p = 0.271$), indicating a weak relationship between the independent variables and the NU-6 scores. The model's explanatory power was limited, with an R-squared value of 0.113, suggesting it accounted for only 11.3% of the variance in the speech recognition scores. Furthermore, the model's residuals did not follow a normal distribution ($p = 0.009$), which undermines the reliability of the model's predictions. Despite these limitations, the change in ARGF at HBN was identified as a statistically significant predictor for NU-6 scores at 0 SNR ($p < 0.05$), implying it may have some predictive value. The statistical power of the test was adequate (0.806).

For the AzBio test at 0 SNR, the multiple linear regression model using changes in acoustic reflex admittance at LBN, HBN, and BBN as predictors was not statistically significant ($p = 0.464$), with an R-squared of 0.0857, indicating a very small proportion of the variance in AzBio scores was explained by these variables.

Chapter 5

Discussion and Conclusions

This research analyzes the AR data from 34 individuals (68 ears) with normal hearing, normal speech-in-noise perception, and minimal noise exposure history. The aim was to establish normative values for ARGF measurements in adults with normal hearing and normal functional hearing in noise, focusing on changes in ARGF admittance and ARGF slope. An additional aim of the study was to compare ARGFs for the same participants across two immittance measurement units that are commonly used in clinical audiology assessments.

The study investigated the use of various AR activator stimuli: pure tones, broadband noise (BBN), and various filtered noises (NBN, LBN, HBN, LPN, HPN). Previous research suggested that the type and frequency spectra of activator stimuli significantly influence the AR response (Silman, 1979; Thompson et al., 1980; Margolis, 1993). The noise elicitors generally produce lower ARTs than pure tones in adults as they are hypothesized to activate a wider frequency range of the cochlea (Peterson & Liden, 1972; Wilson & McBride, 1978).

Acoustic Reflex Threshold (ART)

Although the use of NBN in AR testing has yet to be extensively explored in the literature, a previous study by Peterson and Liden (1972) indicated its potential in assessing the AR and the ARGF. This study compared ARTs elicited by traditional tonal stimuli and less-common NBN stimuli. On average, the ARTs for NBN were 5-10 dB lower than for the tonal stimuli at corresponding frequencies (1, 2, 3, and 4 kHz), as detailed in Table 2 (showing results from the Interacoustics Titan). This aligns with the findings of Peterson and Lidén's (1972) study, which used NBN stimuli centered around 1, 2, and 4 kHz to investigate ARTs. They found that ARTs to NBN were about 15 dB lower than to pure tones. Furthermore, this study found the ARTs for NBN activators were 15 dB lower than filtered noise stimuli (i.e., LPN and HPN). Additionally, ARTs elicited by LBN and HBN (see Table 3 showing results from the GSI Tympstar) were 5-10 dB lower than those elicited by tonal stimuli. These findings align with the study of Devi and Murugesan (2022), which reported ARTs for LP and HP noise that were 5–10 dB lower than tonal stimuli.

As have previous studies, this study found that BBN stimuli induced lower ARTs than pure tone stimuli by 10 dB on average. Gelfand and Piper (1984), for instance, observed a 20 dB improvement in ART when elicited with BBN stimuli as compared to tonal stimuli. Similarly, Margolis & Popelka (1975) found that ARTs elicited by pure tones were about 15 dB higher compared to those elicited by BBN. These results align with the findings of several researchers, including Silman (1979), Wilson and McBride, Sprague et al. (1985), and Feeney and Keefe (2001). Furthermore, a study by Valero et al. (2018), which examined ART using both NBN and BBN activators reported similar results. Their study focused on measuring the AR at higher frequencies (3-6 kHz) to explore its effectiveness in detecting early cochlear synaptopathy in an animal model. It hypothesized that the afferent portion of the acoustic reflex arc predominantly involves medium- and low-spontaneous rate (SR) fibers, as suggested by Kujawa & Liberman (2009). Valero et al. (2018) observed a robust correlation (r = 0.89) at higher NBN frequencies, in contrast to a weaker and non-significant association between cochlear synapse loss and ARTs at lower frequencies (r = 0.17). This finding suggests that using NBN activators in AR measurements could provide diagnostic information about the health of the auditory nerve. The research highlighted the advantage of targeting specific frequency ranges (3-6 kHz) in acoustic reflex measurement for more accurate detection of pathologies. The study notably indicated that the sensitivity to auditory nerve pathologies was significantly greater when using an NBN elicitor compared to a broadband elicitor. Our results emphasize the importance of expanding the routinely used acoustic reflex testing parameters to include NBN activators.

The lower ART with NBN activators could be related to the influence of the bandwidth and center frequency of acoustic reflex elicitors on the recruitment of auditory nerve fibers (ANFs). While broadband noise elicitors effectively engage ANFs along a large portion of the cochlea, NBN excites a restricted range of ANFs (Sprague et al., 1985). This specificity is hypothesized to synchronously excite large numbers and specific functional subgroups of ANFs, such as low versus high spontaneous rate (SR) fibers with high versus low firing thresholds. Taberner & Liberman (2006) demonstrated that broadband and octave-band elicitors, shaped to account for variations in ANF thresholds along the cochlear spiral, can effectively modulate the AR response. The study observed that the activator's frequency bandwidth significantly affected the AR thresholds and AR magnitudes, particularly in regions with synaptic degeneration or ANF loss (Valero et al., 2018). This was evident in the elevation of ARTs and reduction in maximum magnitude when the elicitor's passband included or spanned the synaptopathy region, with the most pronounced effects seen with broadband elicitors. Our research findings, which showed lower ART and higher ARGF slope recorded by NBN activators, align with these studies, supporting the hypothesis that the spectral characteristics of the elicitor in acoustic reflex measurements influence the recruitment and response of different ANF subgroups.

The use of NBN and BBN stimuli presents significant advantages, particularly in extending the dynamic range of AR testing (Peterson and Liden, 1972). It is especially beneficial in detecting ARs in a wider range of patients, such as those with sensorineural hearing loss or hyperacusis. One of the primary benefits, as emphasized by Schairer et al. (2013), is the reduced need to expose individuals to intense sounds that could be potentially harmful. BBN activators effectively elicit responses at lower levels, hence broadening the dynamic range before reaching the activator's maximum level, a point highlighted by Feeney & Keefe (1999). This approach not only minimizes the potential risk of AR assessment with high stimulus intensities but also improves its utility in a clinical setting.

ARGF Measurements

1. ARGF Admittance Change (Y ARGF)

The ARGF measurements focused on two metrics: 1) the change in admittance (ΔY ARGF) and 2) the ARGF slope in ml\dB, assessed using a 226 Hz probe tone with various tonal and noise activators. A significant finding was the effect of activator intensity level across different activators. We observed that the ARGF curve steepened as the activator stimulus intensity increased up to 15-20 dB SL (re. ART), followed by a plateau, indicative of neural fiber saturation (Borg,1973; Silman & Gelfand, 1981). These results align with Lutolf et al. (2003) and Wilson & McBride (1978), who also noted a direct correlation between the slope and change in admittance to the activator stimulus level, albeit without statistical analysis in their studies.

Our study also utilized ipsilateral tonal activators and NBN activators centered at 1, 2, 3, and 4 kHz. The results indicated that ARGF admittance changes for NBN stimuli were higher than for tonal stimuli, particularly at 1,2 and 4 kHz frequencies, with statistically significant differences ($p<0.05$). This significance was maintained across all activators ($p < 0.001$, one-way ANOVA on ranks). The results agree with previous research; Silman and Gelfand (1981) analyzed ARGF in 8 normal-hearing adults and 9 adults with sensorineural hearing loss due to cochlear disorders. Consistent with earlier findings by Silman et al. (1978), they noted that ΔY ARGF in normal-hearing subjects was higher than in those with hearing loss at comparable activator levels, with ARGF saturation occurring at high activator levels for 1000 Hz, 2000 Hz, and BBN activators in normal-hearing subjects, but absent in those with sensorineural hearing loss.

Furthermore, in this study, the ARGF measurements with NBN activators displayed a wider dynamic range compared to tonal stimuli. The results suggest that NBN AR measurements could be more effective for ARGF assessment in hearing loss cases, notably at 2-4 kHz frequencies, where a significant difference in dynamic range between noise and tonal activators was observed. This finding is in accordance with prior research suggesting a broader range in wideband ARGF due to lower ART thresholds compared to tonal ARTs (Feeney & Keefe, 2001; Feeney et al., 2003b; Schairer et., 2007; Jiang, 2014).

2. ARGF Slope

2.a. Interacoustics Titan

Our data indicated no significant differences in the ARGF slope across tonal stimuli, except for the 2000 Hz tonal stimulus, which was significantly higher than other tonal activators. The results agree with Womersley & Dickens's (1985) research that reported a steeper ARGF slope for 1000 Hz and 2000 Hz pure tone activator frequencies. The ARGF slope measured by NBN activators was higher than that of tonal activators at corresponding frequencies. The ARGF slope of the 2 kHz and 3 kHz NBN showed a higher ARGF slope than that of other filtered noise activators (LPN and HPN). The differences were statistically significant. Our results agree with Causon et al. (2020) who reported significantly greater ARGF for 2 kHz and 0.5 kHz elicitors relative to a BBN (p = .007 and p = .013, respectively). The high ARGF slope at 2 kHz might be linked to the selective sound filtering that is specific to certain frequencies. This phenomenon is closely associated with the anatomical characteristics of the ear canal. The structural design of the ear canal, resembling a long, curved, and narrow tunnel, not only provides a protective shield for the middle ear structures from external elements but also contributes to the ear canal's prominent resonance as described by the selective amplification of sound (Geisler, 1998). Sound transforms as it passes through the pinna and into the ear canal, where it encounters the resonances of both the concha and the ear canal. During this process, certain sound frequencies are selectively amplified while others are dampened, leading to a unique spectral shaping of the incoming sound by the outer ear. This selective amplification function, inherent to the external ear cavities, serves to accentuate sounds that are pivotal for human behavior and speech communication. The peak resonance of the outer ear predominantly occurs between 2,000 and 3,000 Hz, with an amplification range of approximately 15 to 20 decibels (dB) (Shaw, 1974). This heightened sensitivity of the ARGF slope to 2 kHz NBN activators could be attributed to the broader frequency spectrum these activators cover and the associated resonance characteristics, potentially engaging a wider range and number of auditory neurons.

2.b. GSI TympStar

In this study, distinct patterns were noted when comparing LBN and HBN activators with tonal activators. For LBN activators at lower frequencies (1000 and 2000 Hz), there was no significant difference in the ARGF slope (p = 0.3 and p = 0.36, respectively). However, a notable difference emerged at 4000 Hz ($p < 0.05$), indicating a significant frequency-dependent impact. In contrast, HBN activators showed significant differences in ARGF slopes compared to tonal activators at lower frequencies ($p < 0.05$), but not at higher frequencies (3000 and 4000 Hz) ($p = 0.3$). The BBN stimuli also followed a similar pattern, with no significant differences at 1000 and 2000 Hz ($p > 0.3$) but distinct variations at 3000 and 4000 Hz ($p < 0.05$). Wilson and McBride (1978) measured ARGF using a range of tonal frequencies (250, 500, 1000, 2000, and 4000 Hz) and BBN activators. The study reported that tonal activators typically had steeper slopes compared to BBN activators, though the study did not report any statistical analyses. On the other hand, Sprague et al. (1981) found no notable differences in ARGF slopes across various tonal activators (500, 1000, 4000 Hz) and a BBN activator stimuli. Their finding contrasts with this study, where significant differences were observed, particularly at higher frequencies. The discrepancies between our study and that of Sprague et al. (1981) might be attributed to different methodologies, such as the choice of activators, testing frequencies, and the criteria used for determining the presence of an acoustic reflex.

Intersubject Variability

This study employed the coefficient of variation (CV) (table 5,6) as a key metric to assess the intersubject variability of the ARGF slope. Notably, high frequencies, including the 2 and 3 kHz NBN activators, demonstrated more consistent responses, as indicated by lower CV values. This trend aligns with previous research suggesting that NBN activators could provide more uniform AR assessments, especially at high frequencies.

The variability observed at different frequencies suggests a differential sensitivity of ARGF slope to auditory stimuli. The lower variability at higher frequencies, especially with

NBN activators, points to their potential in yielding more reliable ARGF measurements. This finding is particularly significant for the 2 kHz NBN frequency, which exhibited the lowest intersubject variability. The reliability of the responses at this frequency makes it a promising candidate for future research and clinical applications, especially in the context of auditory nerve damage assessment.

In contrast, tonal activators, especially at lower frequencies, displayed higher variability which potentially limits their utility in tonal ARGF evaluations. This variability might stem from the narrower frequency spectrum of tonal stimuli compared to NBN activators. The lower variability observed with NBN activators at 2 kHz suggests their utility in detecting subtle changes in auditory nerve function.

Interestingly, our study's findings aling with previous research, emphasizing the importance of activator stimulus frequency in ARGF assessments. The 2 kHz and 3 kHz NBN stimuli, in particular, emerged as a potential candidate as ideal stimuli for screening and/or focused ARGF measurements given their low variability and their representation of a key frequency range for human hearing.

The findings from this study make a significant contribution towards establishing normative ranges for ARGFs with NBN stimuli in adult listeners with normal audiograms, normal speech-in-noise performance, and minimal reported history of noise exposure (Specific Aim 1). The lower variability observed with NBN activators, as opposed to tonal stimuli, underscores the potential of these activators in providing more accurate and reliable ARGF measurements.

Furthermore, the establishment of a normative range characterized with specific CV values across different frequencies provides an estimate of the expected variability in ARGF responses in normal hearing adults. These normative data provide a reference for future analyses, particularly in populations with auditory nerve disorders or those with significant history of noise exposure.

Central Gain and Its Impact on Acoustic Reflex Gradient Function (ARGF)

The higher AR admittance change and steeper ARGF response observed in two participants could be related to central gain. In this phenomenon, the auditory system exhibits heightened central activity in response to minor peripheral impairments. Such a mechanism could contribute to the development of other conditions like central tinnitus and hyperacusis, potentially arising from an inappropriate adaptation to diminished sensory input, as suggested by Noreña (2011). This increase in central gain may reflect the auditory system's compensatory response to maintain stable auditory perception in the face of reduced sensory input. The study by Brotherton et al. (2017) showed that a temporary reduction in auditory stimulation using earplugging can lead to a significant reduction in ART, indicating an increase in central gain. This adaptation in the central auditory system was evidenced by changes in the acoustic reflex threshold (ART), aligning with our observations of steeper ARGF admittance changes. Furthermore, studies by Formby et al. (2003, 2007) using earplugging to simulate temporary hearing loss in humans revealed changes in loudness perception and acoustic reflex. These studies found that acoustic attenuation led to a decrease in ART, a sign of increased central gain. The research by Maslin et al. (2013) and Munro and Blount (2009) also add to this body of evidence. They found that auditory attenuation through earplugging results in reduced ART in humans, which is consistent with an increase in central gain.

A recent study by Wojtczak et al. (2017) on normal-hearing individuals, both with and without tinnitus, provides insights into the potential link between a diminished AR magnitude and ARGF and cochlear nerve degeneration. Participants with tinnitus exhibited significantly weaker ARGF compared to those without tinnitus. This aligns with the growing hypothesis that auditory nerve fiber loss plays a crucial role in enhancing “central gain,” which in turn contributes to the onset and maintenance of tinnitus, as suggested by Hesse et al. (2016). Collectively, these studies underscore the adaptability of the central auditory system and its significant impact on the acoustic reflex.

Across-Equipment Comparison of ART and ARGF

1.Acoustic Reflex Thresholds (ART)

Our analysis comparing ARTs and ARGFs across different equipment, namely the GSI Tympstar and the Interacoustics Titan, revealed no significant differences. We specifically compared the ARTs for 1 kHz and 3 kHz narrowband noise (NBN) on the Titan against low-band noise (LBN) and high-band noise (HBN) using the GSI Tympstar. The results, as demonstrated in Figure 5, showed no statistically significant differences in ARTs between these groups (F-statistic = 0.339; p = 0.797). The mean ART values for 1 kHz NBN and HBN were 70.809 dB HL and 71.544 dB HL, respectively, while for 3 kHz NBN and HBN, they were 71.765 dB HL and 71.544 dB HL, respectively (Figure 6).

Moreover, when comparing tonal activators (500, 1000, 2000, and 4000 Hz) between the Titan and GSI devices, no significant differences were observed ($p > 0.05$; Figure 6). These findings underscore a high level of consistency in ART measurements across different types of immittance devices that are commonly used in clinical audiology settings.

2.Acoustic Reflex Growth Function (ARGF) Slope

Further examination of the ARGF slopes across these two devices was conducted (Figure 14). This analysis included both tonal and noise activators, with the focus on stimuli having similar characteristics for an accurate comparison. Notably, the ARGF slope at 2000 Hz was significantly higher than that of the other tonal activators in both devices, indicating a frequency-specific effect ($p < 0.05$).

An additional comparison of the mean Y ARGF slopes at a 226 Hz probe tone was carried out using similar activators across the two devices (Figure 15). The ARGF slope was evaluated for tonal activators (500, 1000, 2000, and 4000 Hz) and noise activators. The t-test analysis revealed no significant differences in ARGF slopes for comparable activators when assessed with the Titan and GSI devices ($p > 0.05$).

A one-way ANOVA was conducted to further investigate the effects of frequency and equipment on the ARGF slope. The analysis highlighted a significant effect of frequency on the ARGF slope ($F(3, 7) = 6.00$, $p < 0.001$), confirming that different frequencies have a considerable impact on the ARGF slope. However, the type of equipment used did not show a significant effect on the ARGF slope ($F(1, 7) = 4.59$, $p = 0.4$). Additionally, the interaction between frequency and equipment type was found to be non-significant ($F(3, 7) = 4.59$, $p = 0.1$), indicating that the frequency's influence on ARGF slope is consistent across different equipment types.

The consistency of both ART and ARGF slope measurements across different immittance devices, as evidenced in this study, emphasizes the reliability of these measures across two commonly-used clinical units. While activator stimulus frequency and spectrum appears to influence the ARGF slope, the results are similar across two common clinical tools/units.

ARGF and Speech-in-Noise Performance

The antimasking function of the AR is hypothesized to improve speech-in-noise understanding. The AR acts as a high-pass filter with a cutoff of around 1000 Hz (Borg,1973). This filtering mechanism is thought to reduce the masking effect of low-frequency noise on moderate-to-high-frequency signals such as speech (Liberman & Guinan,1998). Without the AR, low-frequency noise has been observed to significantly suppress the responses of high-frequency auditory nerve fibers responsible for transmitting important speech information (Delgutte 1990). The study by Anastasio & Momensohn-Santos (2005) found that individuals who did not exhibit a measurable AR showed poorer performance on sentence identification tests than those with a normal, functioning reflex, even when matched for audiometric profiles. This finding is paralleled by research on stapedectomy patients who lack a functional AR. According to Weisz et al. (2006), these patients demonstrated lower speech test scores in low-pass noise conditions in their affected ear compared to the healthy ear.

This study also focused on exploring the correlation between ARGFs and speech-in-noise (SIN) test scores across different signal-to-noise ratios (SNR). The analyses did not reveal any significant correlations although no significant correlations were expected given the fact that the SIN data for all ears fell within the normal ranges for the two tests studied. Of the 18 comparisons made, only two indicated potential correlations at 2 kHz NBN and HPN with speech-in-noise performance at 0 dB SNR. These correlations, however, were insignificant after adjusting for multiple comparisons. In a more detailed analysis using multiple linear regression models, the relationship between ΔY ARGF across various noise bandwidths (LBN, HBN, BBN) and speech recognition scores was assessed. For the NU-6 test at 0 SNR, the analysis suggested a marginal predictive relationship, as indicated by a low r-squared value of 0.113. While the ARGF change at HBN was significantly associated with NU-6 scores, the regression model for the AzBio test did not achieve statistical significance. The r-squared value of 0.0857 for the relationship between ? and the AzBio test indicated it accounted for only a minor portion of the variance in speech recognition scores.

Additionally, nonlinear regression analysis did not reveal any significant findings in predicting speech recognition scores using ΔY ARGF, regardless of the type of stimuli used. Our results align with those of Guest et al. (2019), who also reported no significant correlation between ARGF and SIN test scores in their study despite using a sample with similar reliability and variability.

Conversely, research by Mepani et al. (2019) identified a significant link between ART and performance on isolated word recognition tasks. However, this correlation was not observed in the adapted version of the QuickSIN test. The study proposed that diminished listening abilities in individuals with elevated ART thresholds might result from one or more of the following: A direct consequence of losing the antimasking effects of the AR, possibly due to brainstem circuitry dysfunction responsible for the reflex, cochlear dysfunction, which in turn reduces the reflex's efficacy or a combination of both factors. This suggests the potential role of cochlear synaptopathy as an underlying cause affecting these relationships. However, the study did not consider noise exposure, leaving it unclear if noise-induced cochlear synaptopathy could be responsible for these observations.

In a related study, Shehorn et al. (2020) found that a reduced AR magnitude correlated with decreased speech recognition. This study also linked lower AR magnitude to higher levels of lifetime noise exposure. The data for this research were gathered from a group of individuals, some of whom sought assistance with listening difficulties and others who did not. This provides an insight into the potential impact of noise exposure on AR and its subsequent effect on speech recognition capabilities.

This discrepancy across studies could stem from various factors, including differences in the speech-in-noise test they used (which involved binaural listening with spatially separated two-talker babble and a 16-alternative forced-choice format), a smaller participant sample size, and their use of the parameter of testing AR.

Limitations of the study

The limitations of our study were the sample size and its composition. With a total of 34 participants, predominantly females (30 out of 34), our study faces challenges in generalizing the findings. The skewed gender representation limits the ability to extrapolate our results across different genders.

Future Research

In the planned future research, an expansion of the current study's results will be conducted by increasing the sample size and diversifying the participant pool. This will ensure a balanced gender representation and include individuals from a broad spectrum of age groups and demographic backgrounds. Additionally, determining whether ARGF can serve as a predictor for impaired speech-in-noise performance will be an important aspect to explore. Subjects with a history of noise exposure and those who have reported difficulties in understanding speech in noisy environments will be included to thoroughly explore the relationship between ARGF and noise-induced auditory nerve pathologies.

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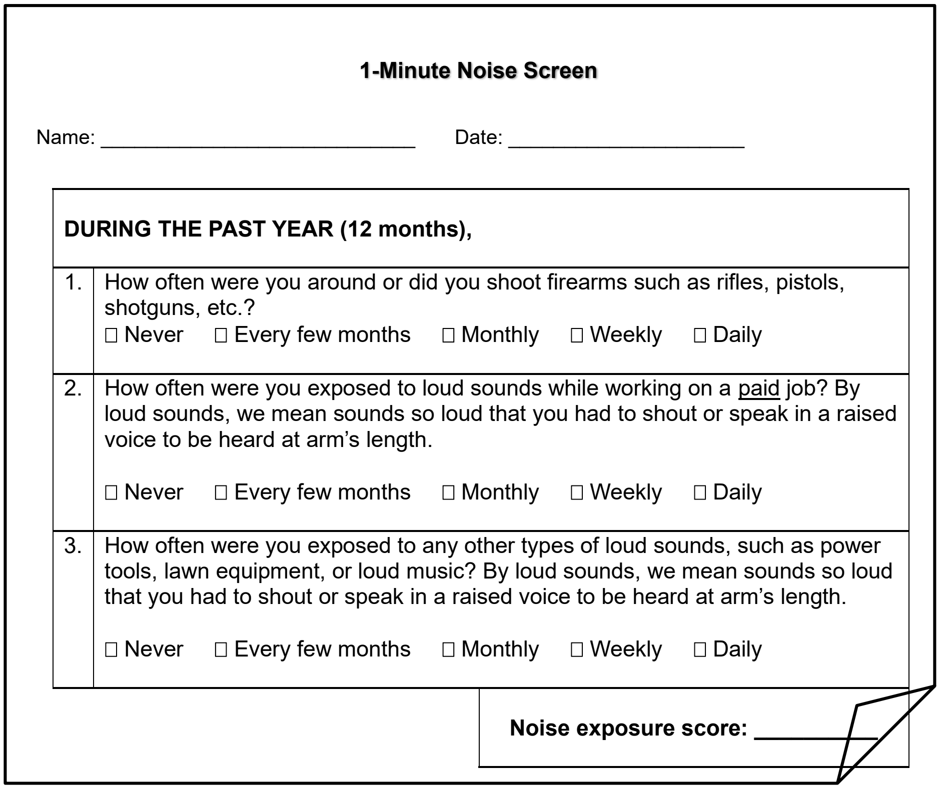
Appendix A



1-Minute Noise Screen

Name: ____________________________ Date: _____________________

DURING THE PAST YEAR (12 months),	
1.	How often were you around or did you shoot firearms such as rifles, pistols, shotguns, etc.? ☐ Never ☐ Every few months ☐ Monthly ☐ Weekly ☐ Daily
2.	How often were you exposed to loud sounds while working on a <u>paid</u> job? By loud sounds, we mean sounds so loud that you had to shout or speak in a raised voice to be heard at arm's length. ☐ Never ☐ Every few months ☐ Monthly ☐ Weekly ☐ Daily
3.	How often were you exposed to any other types of loud sounds, such as power tools, lawn equipment, or loud music? By loud sounds, we mean sounds so loud that you had to shout or speak in a raised voice to be heard at arm's length. ☐ Never ☐ Every few months ☐ Monthly ☐ Weekly ☐ Daily

Noise exposure score: __________

1-Minute Noise Screen/University of Kansas Medical Center/Hearing & Speech Department/© 2016

How to Score Your
1-Minute Noise Screen

First, give yourself the following number of points for your answer to each question:

	Never	Every Few Months	Monthly	Weekly	Daily
Question 1.	0	1	2	3	4
Question 2.	0	1	2	3	4
Question 3.	0	1	2	3	4

Then, add your three individual scores together to get your total Noise Exposure Score. Enter this total number of points in the box in the lower right corner of your card.

See the reverse side of this sheet for an explanation of your Noise Exposure Score and suggestions for how to manage your risk of developing noise-induced hearing loss.

Example:

1-Minute Noise Screen

Name: ***Example*** Date: ***07/01/2015***

DURING THE PAST YEAR (12 months),

1. How often were you around or did you shoot firearms such as rifles, pistols, shotguns, etc.?
☐ Never ☐ Every few months ☑ Monthly ☐ Weekly ☐ Daily
Score: *0* *1* *2* *3* *4*

2. How often were you exposed to loud sounds while working on a paid job? By loud sounds, we mean sounds so loud that you had to shout or speak in a raised voice to be heard at arm's length.
☐ Never ☐ Every few months ☐ Monthly ☑ Weekly ☐ Daily
Score: *0* *1* *2* *3* *4*

3. How often were you exposed to any other types of loud sounds, such as power tools, lawn equipment, or loud music? By loud sounds, we mean sounds so loud that you had to shout or speak in a raised voice to be heard at arm's length.
☐ Never ☑ Every few months ☐ Monthly ☐ Weekly ☐ Daily
Score: *0* *1* *2* *3* *4*

Noise exposure score:
6

1-Minute Noise Screen/University of Kansas Medical Center/Hearing & Speech Department/© 2016

1-Minute Noise Screen: Recommendations

If your Noise Score is in this range:	Then your Noise Risk is:	Explanation
0 to 4	Lower Risk	Based on your noise experiences during the past year, your risk of developing noise-induced hearing loss is relatively low if you continue to experience similar levels of noise in the future. However, if your noise exposures increase, your risk of developing hearing loss will increase as well. Everyone is different in their tolerance to noise, and it is difficult to predict your individual susceptibility. Still, it is important to remember that risk increases: the louder the sounds, the longer you spend around them, and the more often you are exposed. See the following tips for how you can manage your risk of developing noise-induced hearing loss. **Special note for firearm users**: If you use firearms, you are at high risk of hearing loss, even if you only use firearms every few months and have a low risk score on the 1-Minute Noise Screen. See the following tips for things you can do to manage your risk.
5 and above	Higher Risk	Based on your noise experiences during the past year, you are at risk of developing noise-induced hearing loss if you continue to experience similar or higher levels of noise in the future. Everyone is different in their tolerance to noise, and it is difficult to predict your individual susceptibility. Still, it is important to remember that risk increases: the louder the sounds, the longer you spend around them, and the more often you are exposed. See the following tips for how you can manage your risk of developing noise-induced hearing loss.

What You Can Do To Manage Your Risk:

- **Avoid loud noise when you can:** This may go without saying, but avoiding loud noise is a first step toward conserving your hearing for a lifetime. Remember, when you feel the need to shout to be heard by someone just a few feet away, the background noise levels are probably in a hazardous range. Look for quieter products when you buy noisy appliances or tools such as leaf blowers and lawn mowers. And turn down the volume when using electronic devices such as cell phones and music players.
- **Wear hearing protection whenever you are around loud noise**: When you can't avoid loud noise, be sure to wear well-fitted earplugs or earmuffs, even if your noise experiences are only occasional. Hearing protectors can be purchased at many pharmacies, and convenience, hardware, and sporting goods stores. Be sure you have proper training in the use and care of your hearing protectors, and replace them as needed. Proper and consistent use of hearing protection can lower your risk. This is especially true if you shoot firearms, where even one exposure to gunfire can damage your hearing if you are not wearing hearing protection.
- **Get regular hearing tests:** Keep an eye on your ears! Get a routine hearing test, once a year if you are in the higher risk category listed above or if you experience any increase in your exposure to noise. Keep

track of your hearing test results and ask your audiologist to compare annual tests to your earliest test to look for any significant changes that may signal a concern.

- **Take care of your ears:** See your doctor if you notice problems such as sudden changes in hearing, or pain, “fullness,” or ringing in your ears.