Generalizability of clinically measured acoustic reflexes to brief sounds

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Middle ear muscle contractions (MEMC) can be elicited in response to high-level sounds, and have been used clinically as acoustic reflexes (ARs) during evaluations of auditory system integrity. The results of clinical AR evaluations do not necessarily generalize to different signal types or durations. The purpose of this study was to evaluate the likelihood of observing MEMC in response to brief sound stimuli (tones, recorded gunshots, noise) in adult participants ($N = 190$) exhibiting clinical ARs and excellent hearing sensitivity. Results revealed that the presence of clinical ARs was not a sufficient indication that listeners will also exhibit MEMC for brief sounds. Detection rates varied across stimulus types between approximately 20% and 80%. Probabilities of observing MEMC also differed by clinical AR magnitude and latency, and declined over the period of minutes during the course of the MEMC measurement series. These results provide no support for the inclusion of MEMC as a protective factor in damage-risk criteria for impulsive noises, and the limited predictability of whether a given individual will exhibit MEMC in response to a brief sound indicates a need to measure and control for MEMC in studies evaluating pharmaceutical interventions for hearing loss. © *2019 Acoustical Society of America*. https://doi.org/10.1121/1.5132705

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I. INTRODUCTION

Middle ear muscle contractions (MEMC) have been considered potential sources of protection from impulsive noises for over 50 years (Ward, 1968) due to their expected attenuation of signals through the middle ear. It is fundamental to the hypothesis of protection that the MEMC will occur at known times and with known acoustic effects. There is scant research examining MEMC in response to brief sounds, such as gunshots, using a population known to have an intact system activating the MEMC. If, in this population, reflexive MEMC in response to acoustic elicitors are known to occur and follow a dependable response pattern, the inclusion of MEMC in damage-risk criteria (DRC) for impulsive noise might be justified. However, uncertainty with respect to the occurrence or strength of the MEMC would not recommend them for inclusion in DRC. Furthermore, differential likelihoods of eliciting MEMC across stimuli, listeners, and occasions could complicate the interpretation of studies evaluating interventions for hearing impairment, including pharmaceutical interventions.

A. Middle-ear muscle contractions and the acoustic reflex (AR)

MEMC are a broad phenomenon involving the stapedius and/or tensor tympani muscles activated via acoustic and/or non-acoustic stimuli. The two muscles contract to pull in anatomically opposite directions, resulting in increased impedance and decreased sound transmission through the auditory pathway (Gelfand, 1984). Acoustic and non-acoustic activation of the MEMC can be elicited via loud acoustic signals (Moller, 2012), pneumotactile stimulation of various facial regions (Klockhoff and Anderson, 1959, 1960), as part of the startle response (Borg *et al.*, 1984), swallowing (Wersall, 1958), eye movement (Gruters *et al.*, 2018), and head movements (Salomon and Starr, 1963). The mechanisms of activation for MEMC are not well understood, likely include direct and indirect pathways (Moller, 1984), and might vary depending on the mode of stimulation.

The AR is a small subset of MEMC involving the bilateral contraction of the stapedius muscles in response to moderate to loud acoustic stimulation (Borg, 1972). The AR has been used clinically to examine the integrity of the auditory system, from the middle ear to the brainstem, with test parameters selected to maximize the probability of detection (Jerger *et al.*, 1975; Olsen *et al.*, 1975; Silverman and Silman, 1995). Despite the use of optimal test parameters, ARs elicited via diagnostic criteria are not pervasive (Flamme *et al.*, 2017; McGregor *et al.*, 2018), and AR magnitude is quite variable across individuals (Barry and Resnick, 1976; Dallos, 1964; Freeman and Sohmer, 1990). Nolle *et al.* (2004) found complete loss of the AR in nearly half of a group of individuals following blunt trauma of the head, despite normal hearing levels. This variability complicates estimates of these effects for any one person or ear.

Despite the broad historical use of ARs in clinical settings, there is very limited information on the prevalence of

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MEMC elicited by short duration acoustic stimuli, which may be more generalizable to impulsive noise. Rossi and Solero (1983, 1984) examined the parameters of MEMC as a function of varied stimulus durations, and concluded that stimulus duration has a large influence on the MEMC. The authors determined there was a "critical time" below approximately 100 ms stimulus durations where amplitude, duration, onset time, and overall "efficiency" (defined as a function of duration and amplitude) reacted nonlinearly and less predictably. The onset latency of the MEMC varied from 90 to 114 ms for stimulus durations ranging from 3 to 1000 ms, with shorter duration signals producing longer onset latencies (Rossi and Solero, 1983). Additionally, the magnitude of the MEMC decreases with decreasing acoustic stimulus duration (Gelfand *et al.*, 1981; Rossi and Solero, 1982, 1983), even when a constant energy level is maintained (Rossi and Solero, 1984). A limitation of these studies is that results were based on small sample sizes of individuals known to exhibit MEMC to brief sounds. There is a dearth of studies of AR for brief sounds that employ large samples of listeners, which complicates inferences beyond simple central tendencies of the response.

B. Current roles of MEMC in DRC

MEMC have been included as a protective mechanism in some DRC used to estimate the hazards of impulsive noises in military populations (Price, 2007a,b; Price and Kalb, 1991; Ward, 1968). DRC describe the level and probability of damage for a variety of exposures with the goal of predicting and preventing injury in the intended population. Although it would be ideal to protect 100% of exposed persons, practical constraints have led to the convention that the DRC for impulsive noise should aim to protect 95% of the exposed population (Ahroon *et al.*, 2011; Carr and Fisher, 1971; Chan *et al.*, 2001; Johnson, 1997; Patterson *et al.*, 1985; Price, 2007b; Ward, 1968). Assessments of whether this goal has been met should establish the desired level of protection with high (e.g., 95%) certainty. Together, these requirements imply an expectation that any protective phenomenon (e.g., MEMC) included in DRC policy applied to the entire exposed population should protect at least 95% of exposed persons with at least 95% confidence. Protective phenomena meeting these criteria shall be described as *pervasive* for the purpose of the current study.

For impulsive noise exposures, the current military standard permits the use of two methods to calculate permissible amounts of allowable impulsive noise. One method, LIAeq100ms, relies on the integrated energy in the acoustic waveform (MIL-STD-1474E, 2015). The second method, the Auditory Hazard Assessment Algorithm for Humans (AHAAH), is an electro-acoustic model of sound transmission through the ear. The AHAAH returns auditory risk units [ARU, previously also labeled auditory hazard units (AHU) and auditory damage units (ADU)] for warned and unwarned exposures. The ARU values are subsequently transformed into exposure limits. The AHAAH model assumes (1) MEMC are present and identical for all exposed persons and do not account for individual variability, (2) warning or awareness of an impending impulse advances the onset of the MEMC to the extent that it is expected to be fully contracted prior to the arrival of the impulse, and (3) for unwarned conditions, "significant stimulation" (i.e., an initial impulse noise) will elicit the onset of the MEMC at 9 ms (default value) and rise to a maximum contraction that is sustained through any remaining impulses, regardless of the interstimulus interval or number of impulses (Price and Kalb, 2018). This last point is particularly relevant to the present study since it assumes that, even though the latency of the reflexive MEMC may be too long to engage in time for an initial unwarned impulse, the AHAAH model assumes that the MEMC will not relax, and will therefore provide some protection from subsequent impulses. There is limited evidence to support these claims about the human middle ear, as the AHAAH model utilizes data from the cat ear and considerable interpolation based on speculation by the developers (Price and Kalb, 2018). The current study was designed to describe the likelihood of responses of reflexive MEMC to brief sound stimuli within a group of highly screened participants with the goal of elucidating what, if any, role MEMC should play in DRC for impulsive noises.

Despite the current implementation of DRC to prevent and reduce hearing loss, analyses of military hearing conservation audiometric results have shown protection levels are significantly poorer than the desired 95% level. A review of 1983–2003 data in the Defense Occupational Environmental Health Readiness System–Hearing Conservation (DOEHRS–HC) database found that each year 10%–18% of military personnel in the database showed significant threshold shifts or other hearing degradation (Humes *et al.*, 2005). Ahroon *et al.* (2011) also determined that, for United States (U.S.) Army soldiers, less than 95% of soldiers exhibit normal hearing levels {normal is defined as hearing levels suitable for unrestricted duty, categorized as having an H-1 profile [average threshold at 0.5, 1, and 2 kHz not more than 25 dB hearing level (HL), with no individual level greater than 30 dB HL at these frequencies, and threshold at 4 kHz not more than 45 dB HL]; AR 40-501, 2008}. When compared across military occupational specialties (MOS), the MOS most likely to involve frequent exposure to impulsive noises (infantryman and indirect fire infantryman) exhibited the lowest proportion of soldiers with normal hearing (84%–87%; Ahroon *et al.*, 2011). The definition of normal hearing using the H-1 profile is considerably broader than clinical standards of normal hearing (Clark, 1981), which likely leads to an underestimate of clinically defined hearing loss. From a rehabilitative standpoint, the U.S. Department of Veterans Affairs reports that hearing problems, including tinnitus, are by far the most prevalent service-connected disability among American veterans, with more than 2.9×10^6 veterans receiving hearing loss and/or tinnitus related disability compensation as of the end of fiscal year 2017 (Veterans Benefits Administration, 2018). Current DRC for protecting against hearing loss, especially for impulsive noise exposures, require improvement.

The goal of DRC to provide appropriate recommendations for preventing hearing loss from impulsive noise exposures not only protects warfighters, but keeping their hearing intact also improves performance. Hearing conservation is vital to the warfighter, contributing to mission effectiveness,

survivability, lethality, and overall quality of life (Garinther and Peters, 1990; Keller *et al.*, 2017; Sheffield *et al.*, 2017). Excellent hearing is an asset in offensive and defensive operations to locate adversaries, determine the whereabouts of friendly and enemy fire and vehicles, determine the type of explosive device, and detect enemy positions, radio transmissions, and verbal messages (Army Hearing Program, 2015). Impulsive noise is a major source of excessive noise in the military, and exposure limits are informed by DRC. Efforts to clarify the likelihood of MEMC for impulsive noise and determine whether certain clinical measures can be used to predict who exhibits MEMC to brief sound stimulus will lead to increased protection and preservation of hearing.

C. Impact of unknown variability on pharmaceutical interventions for hearing loss (PIHL)

The current study was designed to provide details on the prevalence of MEMC elicited by short duration stimuli. Specifically, this study examined the likelihood that people who exhibit clinical ARs also exhibit MEMC to brief sounds. This study also examined the associations between MEMC to brief sounds and demographic and clinical descriptors. This information will further expand knowledge of the characteristics of MEMC in response to brief sound, thus providing evidence-based (or medically based) guidance to inform of the role of MEMC within DRC and the controlling of middle ear effects in PIHL studies. The consequent improvements in the accuracy of DRC will benefit warfighters and other personnel exposed to impulsive noises.

II. METHODS

The current study was designed to examine MEMC under laboratory conditions. During the initial visit, participants completed hearing and noise related questionnaires, clinical audiometric procedures, including video otoscopy, air and bone conduction hearing testing, immittance measures, a screening of cranial nerves V and VII, and a pupillary conditioning task. Participants meeting the study inclusion and exclusion criteria (Table I) during the initial visit were invited to complete the experiment visit. During the experiment visit, participants completed a brief hearing questionnaire, air conduction hearing testing, clinical immittance measures, a series of acoustic and non-acoustic reflexive tasks, and a randomly selected conditioning task of MEMC with simultaneous electromyographic measurements occurring during the reflexive and conditioning tasks. All experiment protocols and procedures were directed by custom MATLAB (The MathWorks, Inc., Natick, MA) execution scripts.

A. Participants

Participants were 190 (71% female) non-institutionalized adults between the ages of 18 and 55 years old at their initial visit. Participants were drawn from the general population in and around Kalamazoo, MI, between the years of 2015 and 2017, and were invited to participate in the initial visit without regard to hearing ability or middle ear status. Human research subject protection oversight was provided via institutional review boards at Western Michigan University and the U.S. Army Medical Research and Materiel Command. Participants were reimbursed for their time at the end of each visit.

B. Instrumentation

A Welch-Allyn Digital Macroview® video otoscope (Welch-Allyn, Skaneateles, NY) was used at both visits to examine the external ear and tympanic membrane, and provide a record of the visual inspection. Middle ear assessments, including conventional 0.226 kHz tympanometry, wideband immittance and tympanometry, ARs, and AR decay, were obtained using an Interacoustics Titan® middle ear analyzer (Interacoustics, Eden Prairie, MN).

Audiometric stimuli were delivered using the Nelson Acoustics Audiometric Research Tool (ART; Nelson Aocustics, Elgin, TX) automatic audiometry software utilizing National Instruments (NI) Hybrid PXI/PXIe-4461 modules (National Instruments, Austin, TX). This system-controlled signal output to Sennheiser HDA-200 circumaural earphones (air conduction; Sennheiser, Wedemark, Germany) and a RadioEar B-71 bone oscillator (bone conduction; RadioEar, Middlefart, Denmark), and tracked participant responses via a custom response switch box. Pure tone testing was conducted in a double-walled sound booth with ambient noise levels permitting testing below −10 dB HL at all stimulus frequencies.

TABLE I. Experimental visit inclusion and exclusion criteria.

Inclusion criteria
Ages 18+ years
Willingness to participant in study for 2–4+ hours over two visits
No current ear pain or history (hx) of Bell's Palsy, concussion, traumatic brain injury (TBI), unexplained dizziness
Those involved in mock firing will be regular occupational/recreational shooters
Exclusion criteria
Features/physical disabilities that interfere with a probe fit of MEMC (e.g., birth defect, surgery, earrings)
Ear canal size/shape inappropriate for use with ear canal probe tips
Excessive cerumen, irritation, infection of ear (dismissal or postponement)
Pure tone air conduction hearing thresholds poorer than 10 dB at octave-band center frequencies from 0.125 kHz to 1 kHz, poorer than 20 dB HL from 2 to 8 kHz
Thresholds differing by more than 20 dB across ears at any frequency
Abnormal middle ear function based on clinical wideband reflectance (WBR), wideband tympanometry (WBT)
Absence of clinical contralateral AR (regarding 0.02 mmho immittance change and growth) for the monitored ear at all elicitor frequencies
Abnormal cranial nerve (CN) V (trigeminal) or CN VII (facial) nerve function

The instrumentation used during the experiment visit was controlled using a Windows-based (Microsoft, Redmond, WA) personal computer (PC) workstation (Dell model 7910, Dell, Austin, TX) connected to a NI PXIe-1082 chassis. NI PXI/PXIe (hybrid) 4461 dynamic signal analyzer and PIXIe-4499 modules were used to produce probe click and acoustic elicitor stimuli and simultaneously sample all input channels during recording. An Etymotic Research ER-10X® otoacoustic emissions probe (Etymotic Research, Elk Grove Village, IL) was used to present probe click stimuli in the monitored ear and transduce the signal in the ear canal. An Etymotic Research ER-4PT® high-output commercial insert earphone was used to deliver acoustic elicitor stimuli of the reflexive MEMC. A Delsys Bagnoli® eight-channel electromyography (EMG) system (Delsys, Natick, MA) equipped with dry double-differential surface electrodes was used to monitor the activity of selected muscle groups.

Instrumentation used for daily calibration procedures included the G.R.A.S. Type 43AA ear simulator and a G.R.A.S. RA0045 occluded ear simulator (G.R.A.S., Twinsburg, OH). A Quest QC-20 acoustic calibrator (Quest, Oconomowoc, WI) was used for daily calibration, and the accuracy of this calibrator was regularly validated using a G.R.A.S. Type 42AP Intelligent Pistonphone. Microphone signals were preamplified (G.R.A.S. Type 26AC) and routed through a power supply (G.R.A.S. Type 12AA) prior to digitization using a NI hybrid PXI/PXIe-4461 dynamic signal analyzer module mounted within a NI PXIe-1082 chassis.

C. Stimuli

Pure tone air conduction thresholds were obtained bilaterally at octave frequencies from 0.125 to 8 kHz plus the interoctave frequencies of 3 and 6 kHz. Bone conduction thresholds were obtained at 0.5, 1, 2, and 4 kHz with forehead transducer placement. The threshold was defined as the lowest presentation level producing a 50% or greater likelihood of response on at least three ascending trials, using a 5-dB step via the modified Hughson-Westlake procedure (Carhart and Jerger, 1959). In addition to thresholds, the ART software retains the detailed history of stimulus presentations and responses leading to each threshold.

Ipsilateral and contralateral clinical AR traces were obtained in each ear using pure tone elicitors at 0.5, 1, 2, and 4 kHz and a conventional 0.226 kHz probe tone. The elicitor signal duration was between 700 and 800 ms. Elicitors were presented in 5 dB increments beginning at 80 dB HL and ceasing when a repeatable immittance change of 0.05 mmho was measured, or at 100 dB HL, whichever occurred first (Fig. 1). Presentation levels never exceeded 100 dB HL. A relatively high criterion immittance change of 0.05 mmho (0.02 mmho is a common clinical immittance change threshold, and was the level used to indicate the presence of an AR in the current study) was used to allow the examiners to view and track growth of the MEMC with increasing presentation level. Wideband absorbance and tympanometry were completed using a band-limited click stimulus. Tympanometry and wideband tympanometry were completed using a single pressure sweep from +200 to −300 daPa.

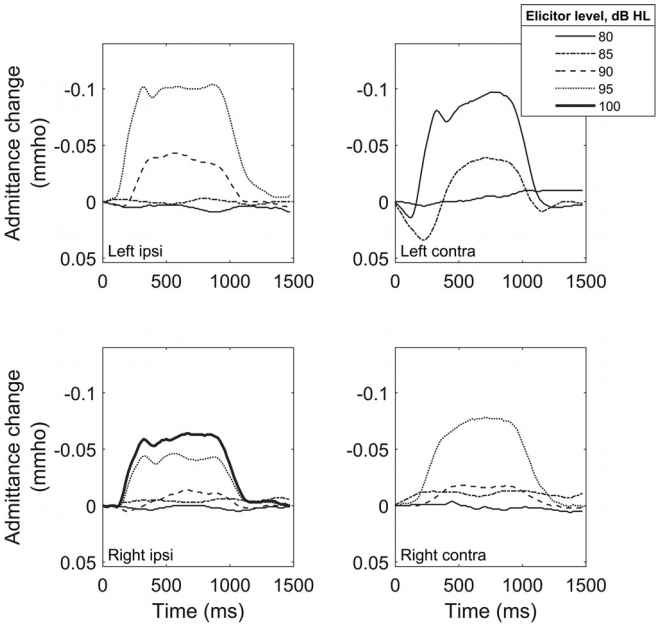

FIG. 1. Example of left and right ear traces at each laterality (ipsilateral and contralateral) for one participant, elicited via conventional clinical acoustic reflex (AR) stimuli. The horizontal axis on each plot represents time, and the vertical axis represents change in admittance. An upward deflection of admittance change from the baseline indicates a decrease in admittance in this figure. Results demonstrate growth with increasing presentation level, ceasing when a repeatable impedance change of at least 0.05 mmho was identified.

During the experiment visit, a total of nine brief acoustic elicitors were presented via the Etymotic Research ER-4PT® earphone to the ear contralateral to the ear monitored for responses of MEMC. Three of these were recordings of a single 0.22 caliber rifle shot, a single 5.56 × 45 mm Armalite Rifle (AR-15) (Armalite, Phoenix, AZ) rifle shot, and a single 0.50 caliber [0.50 Browning Machine Gun (BMG), Browning, Morgan, UT] rifle shot, each within a 50 ms window. Five elicitor stimuli were 100 ms duration pure tone signals of 0.5, 1, 2, 4, and 8 kHz. A 100 ms sample of white noise served as the ninth elicitor stimulus. A 100 ms duration was adopted for all signals capable of sustained presentation based on findings by Rossi and Solero (1983, 1984), showing unpredictable responses for signals less than 100 ms in duration. All signals were gated using a 20 ms Hanning window. The original gunshot recordings were made at a shooter's ear at a sampling rate of 200 kHz and subsequently downsampled to the 44.1 kHz sample rate used for all signals in this study. All brief sound stimuli were presented at 100 dBA field-equivalent sound exposure level (SEL_A). The sound exposure level (SEL) metric is an integrated level normalized to a duration of 1 s. An example of the 0.50 caliber (BMG) rifle elicitor stimulus presented to participants during the experiment visit is represented in Fig. 2. Peak levels were higher than the integrated energy level (Table II). LIAeq100ms (MIL-STD-1474E, 2015) integrated energy levels for the recorded gunshots were 110 dB sound pressure level (SPL). One-third octave band spectra for recorded gunshots and white noise stimuli, normalized to identical total levels to facilitate comparison, are shown in Fig. 3. The recorded 0.22 caliber rifle signal and white noise

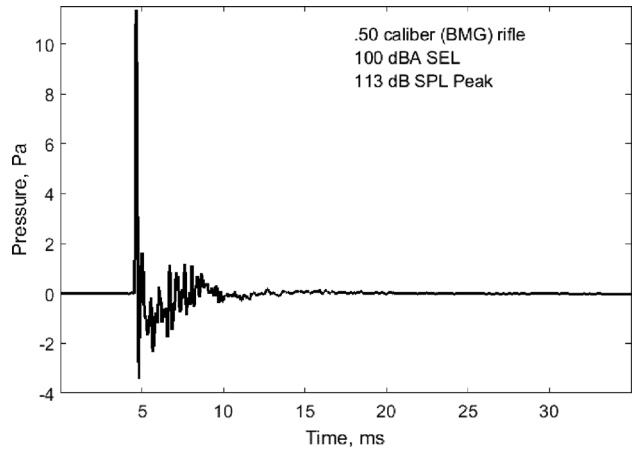

FIG. 2. Rifle (0.50 caliber BMG) waveform presented to participants via the Etymotic Research ER-4PT® earphone during the experiment visit, as measured in an occluded ear simulator.

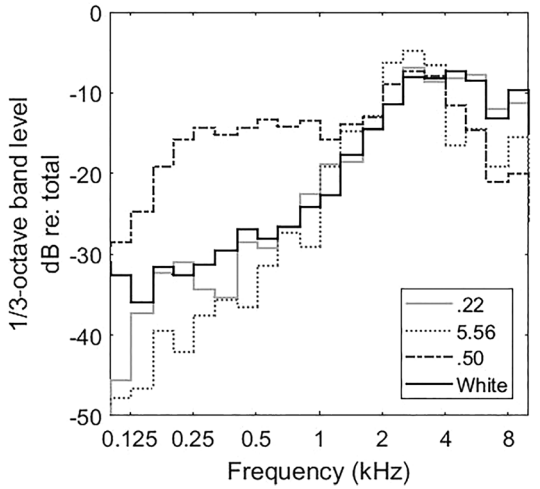

FIG. 3. One-third octave band spectra for recorded gunshots and white noise stimuli. The horizontal axis represents frequency in kHz, and the vertical axis represents the one-third octave band levels relative to the total level in the IEC 60318-4 occluded ear simulator. Individual curves represent the spectra of the individual elicitors. Spectra were normalized to identical total levels to facilitate comparison. The recorded 0.22 caliber rifle signal and the white noise had a similar spectral shape. The 5.56 × 45 mm rifle spectrum was concentrated in the 1–4 kHz region. The recorded 0.50 caliber (BMG) spectrum is more broadly distributed and had more low-frequency energy than the other signals.

had a similar spectral shape. The 5.56 × 45 mm rifle spectrum was concentrated in the 1–4 kHz region. The recorded 0.50 caliber (BMG) spectrum is more broadly distributed and had more low-frequency energy than the other signals. Elicitors were presented in the ear contralateral to the probe assembly in random order with 12 presentations of each stimulus type, using a 5 s inter-stimulus interval.

The method used to measure impedance change was modified from Keefe *et al*. (2010). The probe stimulus was a train of clicks presented at a 20 Hz repetition rate. Probe click stimuli were the impulse response of a digital filter with a passband from 0.2 to 8 kHz. These probe clicks were presented at 93 dB peak SPL in an IEC-60318-4 occluded ear simulator. The advantage of using a band-limited click over other probe stimuli (e.g., a 0.226 kHz probe) is that it allows for assessment of the responses of MEMC across a wider range of frequencies. All signals were presented and acquired using the Etymotic Research ER-10X® and digitized at a 44.1 kHz sample rate using NI PXIe-4499 dynamic signal analyzer modules. Elicitor stimulus timing was synchronized with probe stimulus presentation such that probe stimuli occurred at the same time relative to elicitor onset across all repetitions.

TABLE II. Peak sound pressure levels (SPLs) of brief sound stimuli as measured in an IEC-60318-4 occluded ear simulator. Despite the varying peak levels, all sound stimuli were presented at equal integrated energy levels (100 dB field-equivalent SEL_A).

	Stimulus	Peak level, dB SPL
Gunshot recordings	0.22 caliber rifle	114
	0.50 caliber BMG rifle	113
	5.56 × 45 mm rifle	115
Tones	0.5 kHz	115
	1 kHz	115
	2 kHz	121
	4 kHz	121
	8 kHz	118
White noise	White noise	117

D. Study procedure

Potential participants were provided with basic study details via presentations, paper handouts, and electronic mail. Those interested in participating responded by telephone or email, and a brief summary of study procedures, risks, and exclusion criteria (Table I) was provided. Those with continued interest were then scheduled for an initial visit, including a detailed description of the study, obtaining informed consent to participate, and determining candidacy to participate in the experiment visit.

After informed consent to participate was provided, participants completed a questionnaire regarding their history of ear and facial/trigeminal nerve related health issues (e.g., history of ear infections, Bell's palsy, tinnitus, recent dental work, etc.) and noise exposure history. An otoscopic examination was completed and recorded for future viewing and analyses. Pure tone air and bone conduction thresholds were obtained. The cranial nerve screening involved asking participants to perform a number of facial gestures (e.g., raise eyebrows, smile, open or close mouth) to ensure the subject had typical facial and trigeminal nerve motor function. Additionally, the investigator presented tactile stimulation to various areas on the face while the participant's eyes were closed to assess trigeminal nerve function. Immittance measures were obtained bilaterally. Results were reviewed at the completion of the visit, and eligible participants interested in continuing were scheduled for the experiment visit.

The experiment visit began and concluded with a repeat of the otoscopic examination, pure tone air conduction thresholds, conventional tympanometry, wideband reflectance, and wideband tympanometry. This protocol was conducted to assess for changes in the middle ear status or hearing levels, and monitor for changes in the unlikely event

of a temporary threshold shift. The acoustic measurement procedure of the reflexive MEMC involved both acoustic and EMG transducers controlled via custom MATLAB execution scripts operating on the computer workstation (The MathWorks, Inc., Natick, MA). The Etymotic ER-10X® system was used for both probe signal presentation and ear canal response recordings, and the Etymotic ER-4PT® was used for contralateral delivery of the brief elicitor stimulus. Elicitor stimuli were presented in the ear contralateral to the volunteer's self-reported trigger hand (i.e., the hand that would most likely be used to pull a trigger on a firearm).

Surface EMG recordings of multiple muscles were included in the protocol of the reflexive MEMC to help identify artifacts in the ear canal recordings associated with movement, and differentiate between contractions that are limited to the middle ear versus coordinated contractions across multiple muscles (e.g., a startle response). The muscles monitored included the orbicularis oculi (OO), masseter (MAS), the suprahyoid complex (SH), the biceps brachii (BIC), and the flexor digitorum superficialis (FDS; Fig. 4). The OO, MAS, and SH muscles share common neural supplies to the middle ear muscles. With the exception of the FDS muscle, the EMG electrodes were placed contralateral to the ear containing the ER-4PT® (stimulus presentation). The FDS electrode was placed on the ipsilateral side to correlate the output of the electrode with additional instrumentation in non-reflexive tasks, the results from which are beyond the scope of the current study.

E. Data processing and analysis

Custom MATLAB (The MathWorks, Inc., Natick, MA) scripts were used to review and verify all manually input data and procedure results. Atypical observations were flagged for further review, and judgments regarding MEMC were made using plots with the modified and original datasets superimposed. Otoscopic recordings were reviewed and characterized based on a number of possible descriptors (e.g., presence of cerumen, tympanic membrane visibility, redness, scarring, perforations, or other abnormal landmarks). ART threshold and ascending/descending trial patterns were reviewed and analyzed for the purpose of quality assurance and evaluation of threshold reliability. Raw clinical AR measurements obtained from the Interacoustics Titan® were uploaded into MATLAB and Stata (StataCorp LLC, College Station, TX) software for analyses.

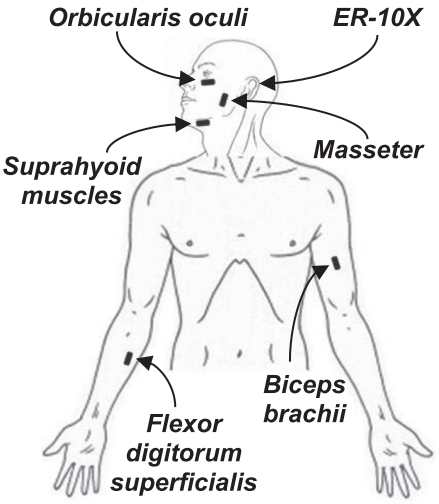

FIG. 4. EMG electrode locations and associated muscles monitored during the experiment visit. The muscles monitored included the OO, MAS, the SH, the BIC, and the FDS. Laterality is relative to acoustic probe (ER-10X®) placement.

1. Detection of MEMC to brief sounds

MEMC to brief sounds were measured and analyzed using a method modified from Keefe *et al.* (2010). Ear canal recordings of probe clicks were divided into baseline intervals and elicitor intervals based on temporal proximity to elicitor stimuli (e.g., tones, gunshots, or white noise). The response of the MEMC was detected by assessing the root-mean-square (RMS) differences between the click waveform developed in the ear canal during the elicitor interval and the average waveform developed during baseline intervals. The impedance change caused by MEMC presented as a consistent change in the RMS response differences associated with the elicitor stimulus presentation.

The RMS click differences were plotted as a function of time (regarding elicitor onset) for each repetition of the elicitor presentation (Fig. 5). The dark stair plot in Fig. 5 shows the 25th percentile averaged RMS responses for 1 participant across all 12 presentations of 1 acoustic reflexive task stimulus. Three independent raters (authors G.A.F., S.M.T., and K.K.D.) examined the traces for evidence of stimulus-linked changes in the RMS plot, and provided a binary judgment of the presence or absence of MEMC regardless of response amplitude. Traces were presented in random order, and

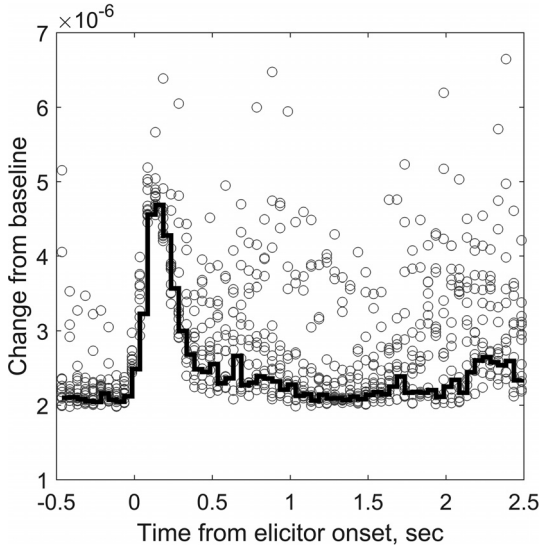

FIG. 5. Example of measured MEMC in response to a noise burst. The horizontal axis represents time from the onset of the noise burst stimulus. The vertical axis represents the change in RMS amplitude of the signal developed in the ear canal, relative to baseline observations obtained prior to the onset of each elicitor. Circles represent changes in RMS amplitude, observed in 50 ms intervals. The noise burst stimulus was presented 12 times, yielding 12 symbols in each time interval. MEMC are indicated by the systematic change in baseline between 0 and approximately 0.35 s. The line represents the 25th percentile of mean integrated deviations across trials of elicitor stimuli of the MEMC.

raters were unaware of participant identification and elicitor type. Figure 6 demonstrates the variability in response patterns for one participant in response to the 0.5 kHz, 0.50 caliber rifle, and 8 kHz stimuli. In this example, all three raters judged the 0.5 kHz and 0.50 caliber traces as present responses of MEMC and the trace at 8 kHz as an absent response of MEMC.

2. Classifying clinical AR results

The raw AR traces obtained with the Interacoustics Titan® middle-ear analyzer were retained for analysis and to calculate descriptive variables for each combination of ear, laterality, presentation level, and stimulus frequency. The area under the curve of each AR trace was calculated by taking the sum of the immittance changes between stimulus onsets and stimulus offsets. Mean of area was calculated within the Titan® software as the average amplitude of the immittance change. Peak AR amplitude was calculated as the maximum immittance change value between stimulus onset and stimulus offset.

Latency was defined as the period between the onset of the stimulus and the change in immittance. In traces including an initial decrease in immittance (i.e., dip) prior to the rise, the period between stimulus onset and onset of the dip was also recorded. Duration was defined as the length of time the immittance change remained above two standard deviations from the mean of each trace's baseline period. Additionally, change in onset latency with increasing level was assessed as change in time per dB change in elicitor level.

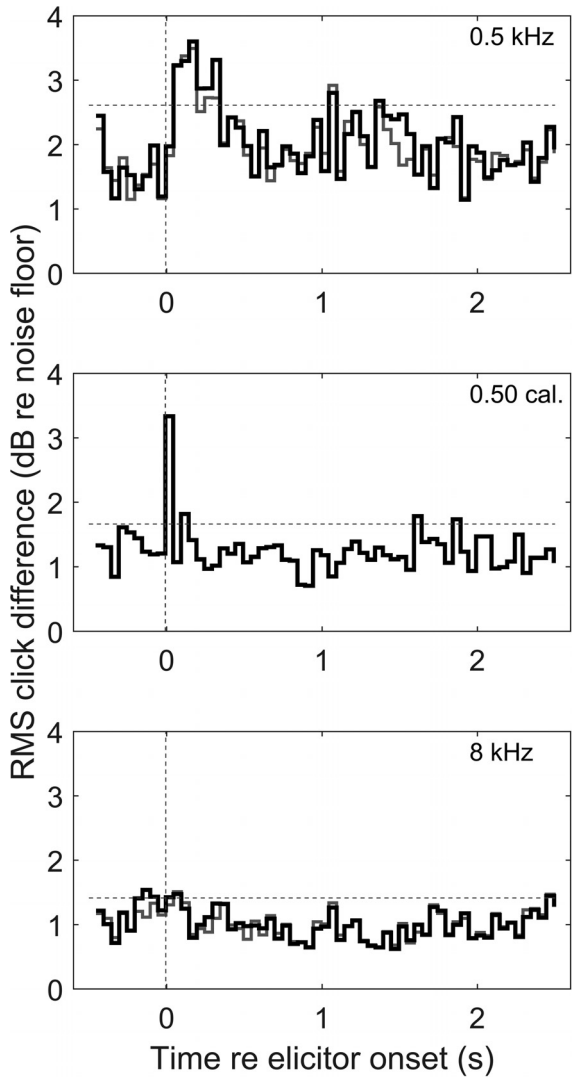

FIG. 6. An example of the 25th percentile averaged RMS responses for one participant across three brief sound stimuli. Time is represented on the horizontal axis, while RMS click differences are represented vertically. The vertical dashed line at time = 0 represents the onset of the brief sound stimulus, and the horizontal dashed line represents the 95th percentile boundary of responses. Each step in the stair plot represents one 50 ms period. The dark stair plot represents the RMS averaged responses with the exclusion of atypical observations, and the grey stair plot represents the original dataset. Responses for the 0.5 kHz and 0.50 caliber stimuli were unanimously judged as present by all three raters, while the 8 kHz response was judged as absent by all three raters.

3. Inferential analyses

Stata software (StataCorp LLC) was used to perform univariable and multivariable analyses, examining the relationship between demographic, hearing, immittance, and other variables related to the rating results of the MEMC using logistic regression or cross-tabulation. Multivariable models were developed using conventional procedures (Hosmer *et al.*, 2013), wherein univariable results were used to discard variables unlikely to retain significance in the multivariable model ($p > 0.2$), and a final multivariable model was developed by sequentially discarding variables that failed to retain significance in the multivariable context.

III. RESULTS

A. Prevalence of reflexive MEMC

All participants ($N = 190$) included in the experiment portion of the study exhibited AR responses to typical clinical AR stimulus, along with evidence of response growth with increasing presentation level, in each ear and each laterality. The proportions of participants in which all three raters identified reflexive MEMC (strict), and where two of the three raters (loose) identified reflexive MEMC, are presented for each of the brief acoustic elicitor stimuli (Fig. 7). While white noise [proportion = 0.71, confidence interval (CI) 0.66–0.76] and 1 kHz brief tonal stimuli (proportion = 0.63, CI 0.57–0.69) elicited the highest proportions of responses, there were no acoustic stimuli that approached 95% response rates. When examining the stimuli presented in this study, the stimuli most generalizable to warfighter exposures, the 0.22 caliber, 5.56 × 45 mm, and the 0.50 caliber gunshot recordings, elicited responses of MEMC in fewer than 50% of participants.

Logistic regression was used to examine univariable relationships between the strict ratings of the reflexive MEMC and demographic and clinical factors (Table III). Except where otherwise defined, results were presented in laterality relative to the ear presented with the elicitor stimulus, which was typically the same side as the participant's dominant hand. For example, ipsilateral results indicate those results on the side presented with brief sound stimulus, and contralateral results indicate results on the probe side. There were a large number of hearing, immittance, and

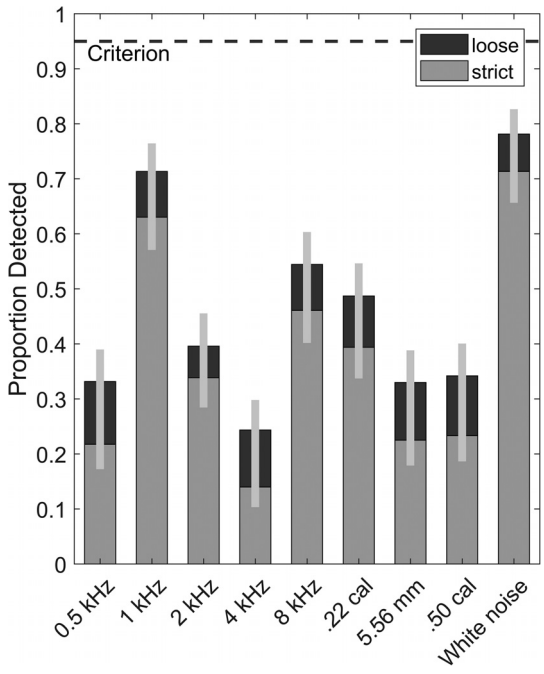

FIG. 7. Observed proportion of MEMC for brief acoustic stimuli. Lightly shaded results represent agreement among all three raters (strict criterion), and darkly shaded results represent 2/3 rater agreement (loose criterion). Error bars span the lower 95% confidence interval (CI) of the strict criterion to the upper 95% CI of the loose criterion results. There were no brief acoustic stimuli that reached pervasiveness (e.g., the lower bounds of the strict 95% CI rests at or above the 95% horizontal dashed criterion line).

clinical AR descriptive variables significant in the independent univariable analyses.

Multilevel mixed-effects logistic regression was used to examine the relationships between all variables significant in the univariable models. A number of frequency-specific clinical AR descriptives were examined one at a time within the model to minimize estimation difficulties. The final model (Table IV) included only those variables significant at the $p \leq 0.05$ level using robust standard errors. Continuous variables were grouped into quintiles and further examined for monotonicity and linearity. Post-estimation likelihood ratio tests were used to verify that each of the variables in the final model improved the model fit significantly, and results of Wald tests of multiple equation maximum likelihood were significant for each variable in the final model. Margins and pairwise comparisons using Bonferroni correction were used in *post hoc* analyses.

B. Correlates of reflexive MEMC

The strongest predictor of MEMC to brief sounds was the type of brief sound stimulus presented (Fig. 8). The white noise and 1 kHz stimuli were most likely to elicit reflexive MEMC, while the 5.56 mm and 0.50 caliber rifles, 0.5 kHz tone, and 4 kHz tone were the least likely to elicit this response. The correlations between observations of MEMC across stimuli were weak (Table V), indicating that the presence of MEMC to one brief sound stimulus is not a good indicator of exhibiting MEMC to a different brief sound stimulus. Although the mean correlation across stimuli was

TABLE III. Odds ratios (OR), 95% CIs, and significance observed during univariable analyses. Univariable relationships were examined using strict (consensus) ratings across judges. Audiometric and immittance results from the initial visit were used. Dominant hand, and more specifically, the hand used when triggering a firearm, was used to determine probe and elicitor side during testing of the reflexive MEMC. Results are presented as ipsilateral (i.e., right side for a right-handed shooter) or contralateral (i.e., elicitor presented to right side, and MEMC measured in the left ear for a right-handed shooter). Y, yes; N, no.

Univariable model	OR	95% CI	*p*	Retained?
Demographics				
Age	1.34	(1.14–1.57)	0.0003	Y
Gender	1.18	(0.95–1.46)	0.1299	Y
Hearing				
Pure tone air conduction (AC) threshold, contralateral				
0.5 kHz	0.99	(0.97–1.01)	0.4883	N
1 kHz	1.00	(0.98–1.02)	0.8261	N
2 kHz	1.03	(1.01–1.05)	0.0004	Y
4 kHz	0.99	(0.97–1.00)	0.1235	Y
8 kHz	1.01	(0.99–1.02)	0.2005	N
Pure tone AC threshold, ipsilateral				
0.5 kHz	1.04	(1.01–1.05)	0.0007	Y
1 kHz	1.03	(10.1–1.05)	0.0056	Y
2 kHz	1.02	(1.01–1.04)	0.0077	Y
4 kHz	1.01	(0.99–1.02)	0.4376	N
8 kHz	1.02	(1.01–1.04)	0.0006	Y
Air-bone gap (0.5–2k average)	1.03	(1.00–1.05)	0.0305	Y
Immittance				
Tympanometry				
Volume	0.40	(0.28–0.57)	0.012	Y
Immittance	1.08	(0.94–1.25)	0.2818	N
Pressure	1.01	(1.00–1.01)	0.0031	Y
Gradient	1.00	(0.99–1.00)	0.7042	N
WBR resonance frequency	0.99	(0.99–1.00)	0.6907	N
WBT pressure	1.01	(0.99–1.02)	0.0712	Y
Clinical AR				
Number of AR present, contralateral	1.24	(1.08–1.41)	0.0011	Y
Number of AR present, ipsilateral	1.03	(0.85–1.25)	0.7581	N
Magnitude quintiles, contralateral				
0.5 kHz	1.13	(1.05–1.22)	0.0008	Y
1 kHz	1.14	(1.07–1.23)	0.0001	Y
2 kHz	1.13	(1.06–1.22)	0.0005	Y
4 kHz	1.13	(1.05–1.21)	0.0008	Y
Onset (dip or rise), contralateral				
0.5 kHz	0.99	(0.99–1.00)	0.0219	Y
1 kHz	0.99	(0.99–1.00)	0.0005	Y
2 kHz	1.00	(0.99–1.00)	0.9042	N
4 kHz	0.99	(0.99–1.00)	0.4336	N
Duration, contralateral				
0.5 kHz	1.00	(0.99–1.00)	0.0598	Y
1 kHz	1.00	(0.99–1.00)	0.1558	Y
2 kHz	1.00	(0.99–1.00)	0.8912	N
4 kHz	1.00	(0.99–1.00)	0.4643	N
Area under curve, contralateral				
0.5 kHz	1.18	(1.05–1.31)	0.0025	Y
1 kHz	1.11	(1.01–1.21)	0.0158	Y
2 kHz	1.20	(1.10–1.31)	0.0001	Y
4 kHz	1.19	(1.08–1.31)	0.0003	Y

TABLE III. (*Continued*)

Univariable model	OR	95% CI	*p*	Retained?
Max AR level tested, contralateral				
0.5 kHz	0.97	(0.95–0.99)	0.0234	Y
1 kHz	0.96	(0.93–0.98)	0.0008	Y
2 kHz	0.96	(0.94–0.99)	0.0013	Y
4 kHz	0.95	(0.94–0.97)	0.0000	Y
Brief MEMC				
Brief sound stimulus type	1.06	(1.04–1.08)	0.0000	Y
Self-report history				
Tinnitus	0.81	(0.65–1.00)	0.0463	Y
Hx of middle ear disorder	1.05	(0.87–1.26)	0.6313	N
Hx of occupational noise exposure	0.83	(0.66–1.04)	0.1052	Y
Hx of non-occupational noise exposure	0.89	(0.73–1.08)	0.2364	N
Hx of firearm use	0.94	(0.77–1.14)	0.5451	N

0.22, the strongest correlations were among some of the recorded gunshot stimuli, which were as great as 0.54.

These findings suggest there is large variability and a decreased likelihood of detectable MEMC for various short duration stimuli in participants known to have clinical ARs. The white noise appears most likely to elicit MEMC among those included in the current study. Brief sound stimuli responses should not be used to generalize to other types of brief sounds, even when presented at the same *A*-weighted energy level, and results do not imply that, all other things equal, white noise is less harmful than other signals due to an increased likelihood of MEMC. The present results do not suggest that reflexive MEMC are a prevalent form of protection from any brief sound.

Participants with larger ear canal volumes were less likely to exhibit MEMC to brief sounds. The pattern generally followed a downward sloping trend with increasing ear canal volume, with significant differences in results beginning in quintile 3 (1.159–1.288 ml), compared to participants in quintile 1 (0.646–0.981 ml). Significant differences occurred despite values in both quintiles residing within the normative range (Margolis and Heller, 1987). An examination of reflectance measurements on cadaver ears revealed that although measurement location and ear canal cross-sectional volume play a very

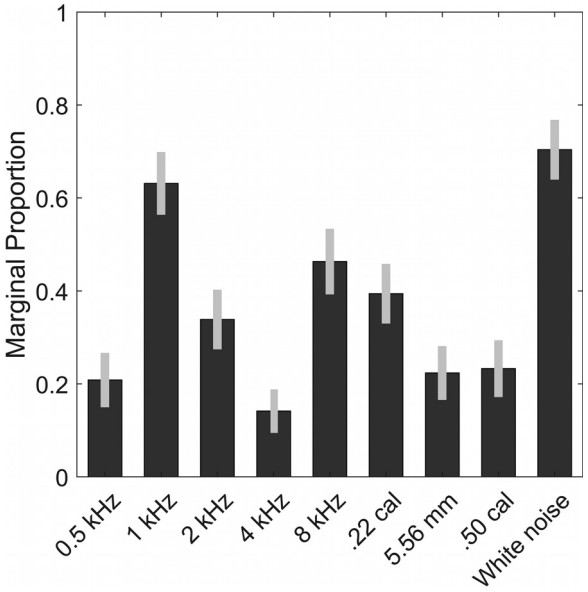

FIG. 8. Marginal proportions and 95% CIs of observed MEMC for each brief sound stimulus type. White noise and the 1 kHz tone elicitor stimuli exhibited the greatest likelihood of eliciting reflexive MEMC.

TABLE IV. Odds ratios, 95% CI, and statistical significance of strict reflexive task (RT) rating results by factors included in the final model. Ref, reference value.

Multivariable model—Strict RT ratings	Odds ratio	95% CI	*p*
Brief sound stimulus			
0.22 caliber rifle recording	Ref	—	—
0.50 caliber BMG rifle recording	0.36	(0.22–0.59)	<0.001
5.56 × 45 mm rifle recording	0.34	(0.22–0.51)	<0.001
0.5 kHz	0.30	(0.18–0.51)	<0.001
1 kHz	3.76	(2.26–6.26)	<0.001
2 kHz	0.72	(0.45–1.17)	0.188
4 kHz	0.17	(0.09–0.28)	<0.001
8 kHz	1.47	(0.89–2.44)	0.135
White noise	5.84	(3.63–9.40)	<0.001
Tympanometric volume quintiles (ascending order), contralateral			
1	Ref	—	—
2	0.60	(0.29–1.24)	0.167
3	0.28	(0.14–0.57)	<0.001
4	0.39	(0.19–0.79)	0.009
5	0.24	(0.11–0.51)	<0.001
Clinical AR magnitude at 2 kHz quintiles (ascending order), contralateral			
1	Ref	—	—
2	1.19	(0.49–2.85)	0.701
3	2.07	(0.93–4.63)	0.076
4	2.56	(1.12–5.85)	0.026
5	2.75	(1.22–6.20)	0.015
Clinical AR onset at 1 kHz quintiles (descending order), contralateral			
1	Ref	—	—
2	1.17	(0.57–2.43)	0.669
3	0.73	(0.37–1.44)	0.366
4	0.88	(0.45–1.71)	0.700
5	0.34	(0.17–0.68)	0.002
Brief sound stimulus test order			
First three stimuli presented	Ref	—	—
Middle three stimuli presented	1.05	(0.77–1.42)	0.757
Last three stimuli presented	0.67	(0.49–0.92)	0.012

TABLE V. Correlation matrix examining the relationships between proportions of MEMC by stimulus type. Correlations were generally low between stimulus types (mean correlation was 0.22), with the highest correlation between the 0.22 caliber rifle shot and the 5.56 × 45 mm AR-15 shot (0.54).

	0.5 kHz	1 kHz	2 kHz	4 kHz	8 kHz	0.22 caliber	5.56 mm	0.55 caliber
1 kHz	0.23							
2 kHz	0.18	0.26						
4 kHz	0.33	0.13	0.35					
8 kHz	0.02	0.02	0.06	0.14				
0.22 caliber	0.22	0.14	0.28	0.32	0.16			
5.56 mm	0.20	0.26	0.33	0.29	0.09	0.54		
0.50 caliber	0.24	0.25	0.15	0.20	0.01	0.33	0.50	
White	0.17	0.22	0.31	0.19	0.20	0.33	0.21	0.17

small role in reflectance measures, variations in middle ear cavity volume may produce large changes in reflectance results and explain intersubject variability (Voss *et al.*, 2008). The effect of middle ear cavity volume would likely also be present in living participants. Regardless of the cause of this finding, an examination of marginal predictions for only the participants with the smallest ear canals shows simply a 7%–12% increase in marginal rates of MEMC when compared to the entire participant population.

A number of clinical AR patterns were examined to determine the relationships between clinical ARs and MEMC elicited by brief sound stimuli (Table III). There were only two variables that showed significance in the final model (Table IV). Clinical contralateral AR magnitude at 2 kHz was positively correlated to the likelihood of exhibiting a response of reflexive MEMC to brief sounds. Additionally, participants with shorter AR latencies at 1 kHz, contralaterally, were more likely to exhibit MEMC to brief sounds.

The nine brief acoustic stimuli of the reflexive MEMC were presented in randomized order for each participant. Results showed that the final three stimuli presented, regardless of stimulus type, were significantly less likely to elicit a stimulus-linked change in impedance when compared to the initial six brief sound stimuli. There were no significant differences between the initial six stimuli presented. This finding suggests that the elicited response might extinguish over a period of minutes and/or lose magnitude as the exposure sequence becomes more familiar to the listener. This is concerning for any potential application of the MEMC in military DRC assessments for situations when multiple gunshots are presented over a period of minutes or hours.

IV. DISCUSSION

This study was conducted to ascertain the degree to which reflexive MEMC to brief sounds could be expected in a large sample of individuals exhibiting clinical AR and having excellent hearing sensitivity. The results indicated that reflexive MEMC elicited by brief sounds are not pervasive in this population and were observed in only 70%–80% of participants for the most effective elicitors (1 kHz and white noise). Rates of reflexive MEMC for the 5.56 mm and 0.50 caliber rifle recordings did not exceed 50% (Fig. 7). White noise and the 0.22 caliber rifle signal had similar spectra (Fig. 3) and same field-equivalent SEL_A, but had vastly different likelihoods of eliciting MEMC (Fig. 7). The 0.50 caliber would be expected to produce the broadest excitation, but this increased spectral breadth did not appear to increase the likelihood of MEMC. Inferential analyses indicated that the likelihood of observing reflexive MEMC is related to the elicitor stimulus, ear canal volume, clinical AR magnitude and latency, and the amount of time elapsed since the start of measurement (Table IV). Taken together, these results indicate that although reflexive MEMC might be elicited occasionally for some listeners with some stimuli, one cannot expect that the observation of reflexive MEMC for one stimulus is a reliable indication that reflexive MEMC can be expected with another stimulus.

A. Generalizability of clinical AR

The rates of MEMC observed in the current study likely overestimate rates of MEMC that would be seen in a warfighter population presenting with H-1 hearing threshold levels, which are considerably less stringent than the current study inclusion criteria, or the general unscreened population. Rates of response of MEMC to clinical AR stimulus decrease with worsening hearing levels, even within the range of hearing levels required for unrestricted military duty (H-1 profile; McGregor *et al.*, 2018). Additionally, the suggestion of decreased prevalence of MEMC with increasing numbers of presentations in a single session, regardless of the mechanism causing this phenomenon, may lead to even less protection of MEMC over exposure events lasting more than a few minutes. It is unclear whether this reduction in rate of MEMC would hold for more sporadic repetitions throughout a day, as may be more common in operational settings.

Clinical AR results are not good indicators of MEMC for brief sounds and should not be generalized to other stimulus types. This finding is an important distinction for any DRC implementing MEMC as a protective factor. Clinical ARs can be useful in assessing the integrity of some parts of the auditory system in the context of a comprehensive audiological evaluation, provided that other potential non-acoustic elicitors of MEMC (e.g., facial muscle activity, general startle) are controlled. However, the observation of a clinical AR in a clinical setting does not inform expectations of whether a listener can also be expected to exhibit MEMC for non-clinical elicitors in non-clinical environments. The operational environment differs greatly from the clinic, and there is little evidence that clinical or laboratory measurements of ARs will generalize to the field.

Diagnostic AR stimuli have significantly longer durations than impulse noises from firearms. Current diagnostic AR signal durations range from 500 ms (Stach, 1987) to 1500 ms (GSI Tympstar Pro user manual, Grason-Stadler, Eden Prairie, MN) and longer, while the impulse envelope durations from firearm discharge rarely exceeds 15 ms in non-reverberant environments. Stimulus duration impacts the response likelihood of MEMC (Jones *et al.*, 2019). The highest presentation levels for the 700–800 ms duration clinical AR stimuli used in this study were between 101 and 105 dB LeqA. The brief sound stimuli at these frequencies were presented at 110 dB LeqA for 100 ms, and the response rates to these stimuli declined even though they were presented at a higher level, which suggests that stimulus durations at or below 100 ms might be too brief to elicit MEMC dependably. The results of this study are consistent with prior studies (Rossi and Solero, 1983, 1984; Rossi *et al.*, 1985a,b), showing nonlinear and less-predictable responses to stimulus durations less than about 100 ms.

Although much is still unknown about MEMC (Moller, 1984; Mukerji *et al.*, 2010), recent studies hypothesize connections between cochlear synaptopathy (i.e., the loss of auditory-nerve connections with cochlear inner hair cells) and decreased acoustic MEMC, despite normal audiometric hearing levels (Valero *et al.*, 2017; Valero *et al.*, 2018;

Wojtczak *et al.*, 2017). Low spontaneous-firing rate fibers (low-SR fibers) are responsive to high SPLs and might be instrumental to triggering the MEMC (Valero *et al.*, 2018; Wojtczak *et al.*, 2017). Further, it is important to recognize that the spontaneous spike rate of low-SR fibers is less than one spike per second, with higher levels of temporal jitter than high SR fibers (Bourien *et al.*, 2014; Heil and Peterson, 2015; Liberman, 1978). Absent or unreliable MEMC in response to brief sounds might be consistent with the triggering mechanism of the MEMC, which is dependent on low-SR fibers.

There are also stimulus level considerations to examine when comparing clinical AR elicitors and brief sound signals, or impulsive signals, which are common exposures to the warfighter. Typical clinical AR stimulus levels range from 80 dB HL to 100 dB HL, whereas peak firearm levels often exceed 140 dB SPL (Flamme *et al.*, 2009; Meinke *et al.*, 2014; Nakashima and Farinaccio, 2015). Although one may assume that MEMC increase with increasing level, responses of MEMC have not been tested with signals at levels typical of peak firearm levels due to technical limitations. At extremely high levels, the level of the impulsive noise reaches the microphone used to measure changes in impedance within the ear canal and contaminates the recording. The peak levels presented in this study reached 121 dB SPL, and although these levels are lower than typical peak firearm levels presented to an unprotected ear, this is a realistic signal level when single or double hearing protection is worn (Fackler *et al.*, 2017; Murphy *et al.*, 2015) and can be used to inform of the likelihood of MEMC for impulsive signals that are slightly below the 140 dB peak protection level (MIL-STD-1474E, 2015).

Estimates of the likelihood of MEMC presented in this study were based on the presence or absence of a stimulus-linked change in impedance, although the pattern of results varied significantly between participants and within participants for varying stimuli. Clinical AR magnitude and latency were the only significant predictive characteristics of those examined. Other clinical AR characteristics were not correlated to the likelihood of MEMC to brief sounds. The variations in clinical AR results did not correlate strongly with variations in MEMC to brief sounds, which suggests that clinical AR measures cannot be used to predict responses of MEMC to brief sounds.

Many MEMC identified had low magnitudes and would not likely provide a protective effect against subsequent gunshots or other noise exposure relevant to warfighters. In the realm of impulsive noises, decreased amplitudes of MEMC may result in trivial protection. In addition, 13% of the clinical AR traces presented with a dip, or decrease in impedance, prior to the rise in impedance typical of an AR. The method used in the present study to identify MEMC in response to brief sounds was sensitive to absolute changes in the impedance of the system, and was therefore not responsive to the direction of the change. However, if an initial reduction in impedance is present in response to brief sounds, the MEMC could increase rather than decrease a listener's exposure. According to Freeman and Sohmer (1990), the dip typically increases with increased acoustic stimulation level, effectively increasing the level of exposure reaching the cochlea for more hazardous stimuli. Additionally, the MEMC provide attenuation predominantly in the low frequencies (<1 kHz; Schairer *et al.*, 2007), which limits their utility as a protective factor for exposures containing substantial mid- and high-frequency energy.

B. Implications for DRC policy

The hearing criteria for unrestricted duty (H-1 profile) for warfighters is based on pure tone hearing thresholds (AR 40-501, 2008), and these criteria permit hearing thresholds consistent with a lower likelihood of clinical ARs (Flamme *et al.*, 2017). Additionally, it is not reasonable to assume that people with excellent hearing sensitivity will exhibit clinical ARs (Flamme *et al.*, 2017; McGregor *et al.*, 2018) because good sensitivity to low-level sounds does not necessarily imply a fully normal auditory system (Kujawa and Liberman, 2009). Low-SR fibers are unresponsive at low stimulus levels (Schmiedt *et al.*, 1996; Valero *et al.*, 2016), and if the hypotheses regarding the triggering of MEMC by low-SR fibers are correct, it should not be assumed that normal hearing sensitivity guarantees dependable MEMC. It is especially important to avoid such assumptions for individuals who have been exposed to excessive noise and might have been affected by synaptopathy (Kujawa and Liberman, 2009).

The examination of the results of brief stimuli MEMC and the relationship to hearing levels and a number of additional clinical and demographic factors demonstrate no reliable predictive indicators or demographic characteristics that ensure a warfighter will achieve significant hearing protection resulting from MEMC. The strongest predictor of MEMC to brief sounds was stimulus type, suggesting that the likelihood of the response of MEMC is stimulus dependent. In a military environment, there is little control over the types of impulsive noise exposures experienced by an individual.

In the current study, 9% ($n = 25$) of the participants who completed the initial visit of the study did not exhibit clinically accepted AR responses at any elicitor frequency in at least one ear (left or right) or one laterality (ipsilateral or contralateral). Among those individuals with no measurable clinical AR, 88% exhibited hearing levels that would qualify them for unrestricted military duty. It is unknown whether these participants exhibit MEMC to brief sound stimuli because they were dismissed from this study (Table I). However, the lack of AR responses using clinical test procedures might indicate that these individuals would also be less likely than the participants in the current study to exhibit a response to brief sound stimuli. Additionally, more men than women enter military service, and previous studies have shown that males are less likely to exhibit an AR (Flamme *et al.*, 2017; Hall, 1982); the gender distribution in the current study was biased toward females (29% male), suggesting that the current results might overestimate the rate of MEMC in the military population.

Some developers of DRC have assumed protective MEMC for a number of years based on an assumption that all ears react identically and robustly to the presence or expectation of impulsive noise. The current study

demonstrates that MEMC in response to brief sound stimuli are not pervasive, may not always be protective, and are not sufficiently predictable based on clinical or demographic information. The results of this study provide strong evidence against the use of MEMC within DRC for impulsive noise.

The AHAAH model assumes the initial impulse in a series of impulses fully activates protective MEMC for all remaining impulses with a vague role for the interstimulus interval between impulses. Results of the current study indicate the initial presentation of a brief sound will not elicit MEMC for 20%–80% of individuals. Protective MEMC cannot be expected for exposure to any impulse in a series of unwarned impulses, regardless of the interstimulus interval. The current results suggest that users of MIL-STD-1474E require updated instructions given the inclusion of AHAAH in that standard.

C. Implications for PIHL studies

Military populations would benefit from advancements of pharmaceutical interventions to prevent hearing loss due to impulsive noise exposure. The current DRC recommendations have not prevented hearing loss to the degree desired, and hearing related disabilities remain widespread and affect more than the most susceptible 5% of military personnel (Ahroon *et al.*, 2011).

Studies on PIHL, especially when examining the effects of impulsive noise stimuli on the cochlea and other areas medial to the outer and middle ear structures, should account for individual differences in outer and middle ear structures and, more specifically, the functionality of MEMC. The function of MEMC cannot be assumed to be pervasive, even in individuals with excellent hearing (Flamme *et al.*, 2017; McGregor *et al.*, 2018). The current study demonstrates that MEMC are not pervasive and not characteristically equal within a fairly homogenous group exhibiting excellent hearing. MEMC should be controlled for in PIHL studies to ensure that results are not confounded by individual differences. The preferred approach for exerting such control would depend on the study design, but could include monitoring of the MEMC during the exposure phase of the study.

D. Study limitations

The results of the current study apply to stimulus levels that are considerably lower than the impulsive sounds addressed by DRC for impulsive noise. Peak levels presented here ranged from 113 to 121 dB SPL in the ear canal, and these are significantly lower than typical peak levels addressed in DRC, which often exceed 140 dB SPL. Higher levels were not presented in the current study in order to prevent temporary or permanent hearing loss in participants (Hunter *et al.*, 1999; Schairer *et al.*, 2007). Schairer *et al.* (2007) also point out that many elicitor levels of MEMC, even those considered safe, may be uncomfortable to individuals. Higher levels are also more likely to produce startle responses involving facial muscle activity (Ludewig *et al.*, 2003), which could also elicit MEMC, but should not be relied upon in DRC because startle responses can extinguish rapidly as the stimulus loses novelty and be influenced by cognitive factors. In addition, although stimuli used here are significantly shorter in duration than typical clinical AR stimuli, impulsive noises addressed in DRC are typically shorter yet, which could lead to even lower levels of responses of MEMC and less predictability based on clinical responses (Rossi and Solero, 1983, 1984). It is difficult to examine MEMC with human participants using firearms due to the impulse passing through the hearing protector and contaminating the probe signal.

The nature of RMS calculations does not take into account the direction of immittance change during calculations of the MEMC. There may be cases where impedance decreased during the period of elicitor presentation, thus providing increased sound transmission into the cochlea. A normal feature of some MEMC includes a dip, or period of decreased impedance, prior to the increase in impedance caused by the contraction of middle ear muscles. Some investigators have suggested that this phenomenon is a consequence of a slight improvement in the coupling between middle ear ossicles (Freeman and Sohmer, 1990) or a temporary partial decoupling of the ossicular chain during the initial stages of stapedial contraction (Feldman and Zwislocki, 1965). In addition, it has been shown (in a small number of individuals) that admittance (Feeney and Keefe, 1999) and middle-ear motion (Jones *et al.*, 2017) can actually increase for frequencies between 2 and 4 kHz (Feeney and Keefe, 1999; Jones *et al.*, 2017) during a response of MEMC. The analyses of MEMC to brief sounds were based on stimulus-linked changes of any type, and drew no distinction between an increase or decrease in impedance.

Prevalence estimates reported in the current study were based on visual review of results by three separate raters. There is a possibility of rater error and/or bias in these judgments. Observed proportions using the loose criterion (i.e., requiring only two of three raters) did not change the overall findings or increase prevalence to a level of pervasiveness required for inclusion in DRC (Fig. 7). Additionally, raters were instructed to provide a binary judgment to any stimulus-linked impedance change, and there were often cases where the change in impedance was sufficiently small as to provide no substantial protection against high level noise. Initial attempts of automated detection of MEMC showed significantly lower prevalence than the results presented here.

V. CONCLUSIONS

In this study, MEMC were measured in response to brief sound stimuli for a group of highly screened participants in a laboratory setting. MEMC elicited by brief sounds were not pervasive in a highly screened group of participants, all of whom exhibited responses of MEMC to clinical AR stimuli. Inferential results presented here were based on any evidence of a response of MEMC to brief sound stimulus, regardless of the characteristics of the MEMC, and would indicate that not all MEMC detected here are protective.

Clinical AR measures are not indicative of responses of MEMC for brief sounds and should not be generalized to other stimulus types. These results present a challenge to

developers of impulsive noise DRC about the use of MEMC as a protective factor. However, the likelihood of MEMC for brief sounds is not sufficiently low that they can be disregarded as a potential effect modifier in PIHL studies. Failing to control this factor could artificially reduce effect sizes and lead to premature rejection of potentially beneficial therapies.

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